9

SEPARATION AND PURIFICATION. IDENTIFICATION OF ORGANIC COMPOUNDS BY SPECTROSCOPIC TECHNIQUES

The separation of mixtures of compounds to give the pure components is of great practical importance in chemistry. Many synthetic reactions give mixtures of products and it is necessary for you to have a reasonably clear idea of how mixtures of compounds can be separated. Almost all compounds of biochemical interest occur naturally as components of very complex mixtures from which they can be separated only with considerable difficulty.

Separations can be achieved by differences in physical properties, such as differences in boiling point, or by chemical means, wherein differences in physical properties are enhanced by chemical reactions. In this chapter we will consider some separations of compounds based on differences in physical

properties. Chemical procedures will be discussed elsewhere in connection with the appropriate classes of compounds.

Identification and structure determination are often closely allied to the problem of separation. Once a compound is separated, how do we determine whether it is identical to some previously known compound (identification) or, if that can't be done, how do we determine its chemical structure? The spectroscopic properties of molecules have proven to be extremely informative for both identification and structure determination and this chapter is mainly concerned with the application of spectroscopy for such purposes. We will give you now an overview of the spectroscopic properties of the major classes of organic compounds. In subsequent chapters, spectroscopic properties will be discussed in the context of the class of compounds under consideration.

9-1 HOW DO WE KNOW WHEN AN ORGANIC COMPOUND IS PURE?

The classical criteria for determining the purity of organic compounds are correct elemental compositions (Section 1-1A) and sharpness of melting point or constancy of boiling point. Important though these analytical and physical criteria are, they can be misleading or even useless. For instance, the analytical criterion is of no help with possible mixtures of isomers because these mixtures have the same elemental composition. The simple physical criteria are not applicable to substances that decompose when one attempts to determine the melting point or boiling point. Furthermore, boiling points are not very helpful for liquids that are mixtures of substances with nearly the same boiling point or are **azeotropes.**[1] Similar difficulties may be encountered with mixtures of solid substances that form mixed crystals or are **eutectics.**[2] Much sharper criteria for the purity of organic compounds now are provided through use of "super-separation" methods to see if any contaminants can be separated, or by spectroscopic techniques, as will be discussed later in this chapter. We begin here with a brief description of chromatographic methods of separation.

[1]An azeotrope is a mixture of two or more substances that boils at a constant temperature, either higher or lower than any of its constituents. Thus an 8.5:1 mole mixture of ethanol and water boils like a pure substance, distilling at 78.2°, which is lower than the boiling point of ethanol (78.5°) or of water (100°). In contrast, a 1.35:1 mole mixture of methanoic (formic) acid and water boils at 107.1°, which is higher than the boiling points of either methanoic acid (100.7°) or water (100°).

[2]When solid substances are mixed, the melting point of each normally is depressed. The eutectic mixture is the mixture of the solids with the lowest melting point.

9-2 CHROMATOGRAPHIC SEPARATION PROCEDURES

9-2A Gas–Liquid Chromatography

Many separation methods are based on **chromatography,** that is, separation of the components of a mixture by differences in the way they become distributed (or **partitioned**) between two different phases. To illustrate with an extreme example, suppose we have a mixture of gaseous methane and ammonia and contact this mixture with water. Ammonia, being very soluble in water (~ 90 g per 100 g of water at 1 atm pressure), will mostly go into the *water phase,* whereas the methane, being almost insoluble (~ 0.003 g per 100 g of water) will essentially remain entirely in the *gas phase.* Such a separation of methane and ammonia would be a one-stage partitioning between gas and liquid phases and, clearly, could be made much more efficient by contacting the gas layer repeatedly with fresh water. Carried through many separate operations, this partitioning procedure is, at best, a tedious process, especially if the compounds to be separated are similar in their distributions between the phases. However, partitioning can be achieved nearly automatically by using **chromatographic columns,** which permit a **stationary phase** to be contacted by a **moving phase.** To illustrate, suppose a sample of a gaseous mixture of ammonia and methane is injected into a long tube (column) filled with glass beads moistened with water (the stationary phase), and a slow stream of an inert **carrier gas,** such as nitrogen or helium, is passed in to push the other gases through. A multistage partitioning would occur as the ammonia dissolves in the water and the resulting gas stream encounters fresh water as it moves along the column. Carrier gas enriched with methane would emerge first and effluent gas containing ammonia would come out later. This is a crude description of the method of **gas–liquid chromatography** (abbreviated often as glc, GC, or called vapor-phase chromatography, vpc). This technique has become so efficient as to revolutionize the analysis and separation of almost any organic substance that has even a slight degree of volatility at some reasonably attainable temperature. The most modern glc equipment runs wholly under computer control, with preprogrammed temperatures and digital integration of the detector output. A wide variety of schemes is available for measuring the concentration of materials in the effluent carrier gas, and some of these are of such extraordinary sensitivity that only very small samples are necessary (10^{-9} g, or less).

In the usual glc procedure, a few microliters of an organic liquid to be analyzed are injected into a vaporizer and carried with a stream of gas (usually helium) into a long heated column that is packed with a porous solid (such as crushed firebrick) impregnated with a nonvolatile liquid. Gas–liquid partitioning occurs, and small differences between partitioning of the components can be magnified by the large number of repetitive partitions possible in a long column. Detection often is achieved simply by measuring changes in thermal conductivity of the effluent gases. A schematic diagram of the apparatus and a typical separation pattern are shown in Figures 9-1 and 9-2. The method is extraordinarily useful for detection of minute amounts of impurities provided

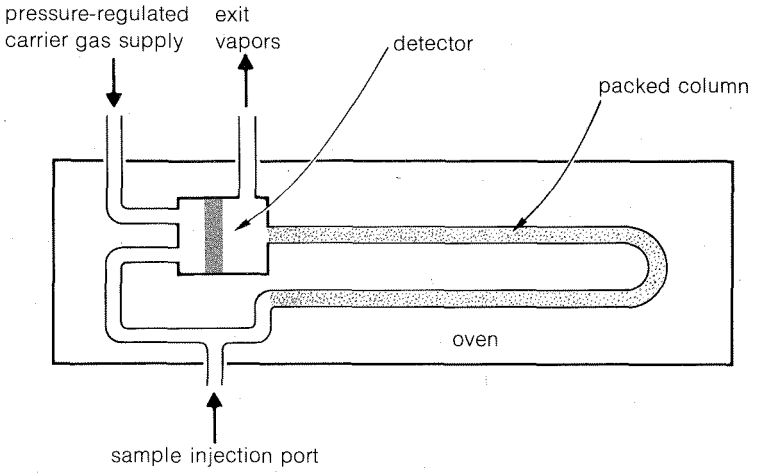


Figure 9-1 Schematic diagram of a gas–liquid chromatography apparatus. The detector is arranged to measure the difference in some property of the carrier gas alone versus the carrier gas plus effluent sample at the exit. Differences in thermal conductivity are particularly easy to measure and give reasonably high detection sensitivities.

these are separated from the main peak. Glc also can be used effectively to purify materials as well as to detect impurities. To do this, the sample size and the size of the apparatus may be increased, or an automatic system may be used wherein the products from many small-scale runs are combined.

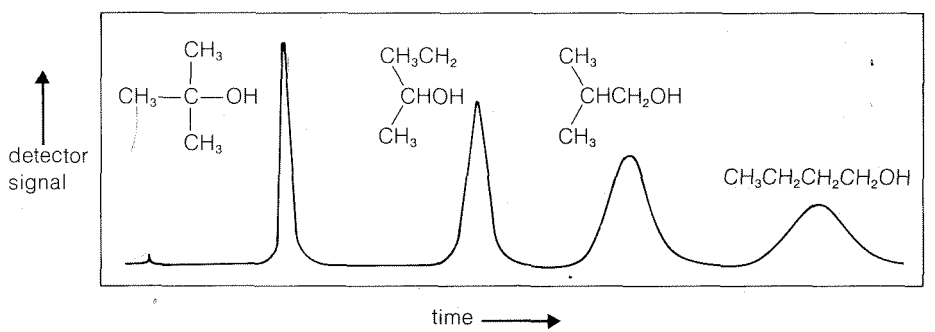


Figure 9-2 A gas–liquid chromatogram of a mixture of the isomeric butanols at constant column temperature. A tiny peak on the far left is a trace of air injected with the sample. The **retention times** of the various isomers are in the same order as the boiling points, which are, from left to right, 82°, 99.5°, 108°, and 117°. The *areas* under each peak correspond to the relative amounts of material present. Raising the column temperature at a preprogrammed rate while developing the chromatogram speeds up the removal of the slower-moving components and sharpens their peaks. Also, by diversion of the gas stream to appropriate cold traps it is possible to collect pure fractions of each component.

9-2B Liquid–Solid Chromatography

Liquid–solid chromatography originally was developed for the separation of colored substances, hence the name chromatography, which stems from the Greek word *chroma* meaning color. In a typical examination, a colored substance suspected of containing colored impurities is dissolved in a suitable solvent and the solution allowed to percolate down through a column packed with a solid adsorbent, such as alumina or silica, as shown in Figure 9-3. The "chromatogram" then is "developed" by passing through a suitable solvent that washes the **adsorbate** down through the column. What one hopes for, but may not always find, is that the components of the mixture will be adsorbed *unequally* by the solid phase so distinct bands or zones of color appear. The bands at the top of the column contain the most strongly adsorbed components and the bands at the bottom the least strongly held components. The zones may be separated mechanically, or sufficient solvent can be added to wash, or **elute,** the zones of adsorbed materials sequentially from the column for further analysis.

Liquid–solid chromatography in the form just described was developed first by the Russian biochemist M. S. Tswett, about 1906. In recent years, many variations have been developed that provide greater convenience, better separating power, and wider applicability. In **thin-layer chromatography,** which is especially useful for rapid analyses, a solid adsorbent containing a suitable binder is spread evenly on a glass plate, a drop of solution to be analyzed is placed near one edge and the plate is placed in a container with the edge of the plate below the spot, dipping into an eluting solvent. The solvent ascends the plate and the materials in the spot move upward at different rates, as on a Tswett column. Various detecting means are used—simple visual observation for colored compounds, differential fluorescence under ultraviolet light, and spraying of the plate with substances that will give colored materials with the compounds present. In favorable cases, this form of liquid–solid chromatography can be carried out with submicrogram quantities of materials.

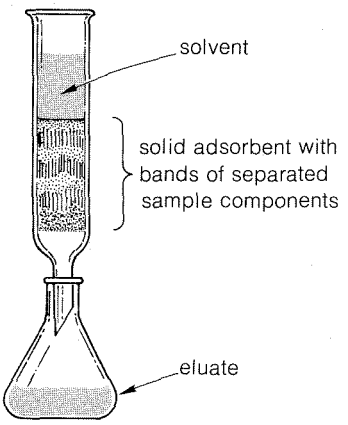


Figure 9-3 A simple chromatographic column for liquid–solid chromatography

An extremely important improvement on the Tswett procedure is **high-pressure solid–liquid chromatography.** Increasing the input pressure on the system to 20–70 atmospheres improves the speed of separations by permitting the use of much smaller solid particles (with more surface area) than would be practical for gravity-flow Tswett columns. Automatic monitoring of the column effluent by ultraviolet spectroscopy (Section 9-9) or by changes in the refractive index usually provides an effective means of determining how the separation is proceeding. With such techniques chromatograms similar to Figure 9-2 are obtained. High-pressure liquid chromatography (hplc) has great advantages for analysis and separation of high-molecular-weight heat-sensitive compounds that are unsuitable for glc.

An ingenious variation of solid–liquid chromatography is to use a solid support to which a material is attached that has a specific affinity for a particular substance to be separated. The technique is especially useful for separating enzymes, and the immobile phase can be constructed from compounds known to react with, or be complexed by, the enzyme. Some other forms of chromatography are discussed in Sections 25-4B and 25-7E.

Observation of a single peak in a given chromatographic procedure is evidence, albeit not definitive evidence, for purity. Contaminants with nearly the same properties may be very difficult to separate and, if knowing the degree of purity is highly important, one can run chromatograms with a variety of different adsorbents to see if each gives the same result. If they do, the presumption of purity improves, although it is desirable to determine whether the spectroscopic techniques to be described in the following section permit the same conclusion.

9-3 WHY CAN'T WE SEE MOLECULES? SOME GENERAL CONSIDERATIONS OF DIFFRACTION AND SPECTROSCOPIC TECHNIQUES

The most straightforward way to determine the structures of molecules would be to "see" how the nuclei are arranged and how the electrons are distributed. This is not possible with visible light, because the wavelengths of visible light are very much longer than the usual molecular dimensions. A beam of electrons can have the requisite short wavelengths, but small organic molecules are destroyed rapidly by irradiation with electrons of the proper wavelengths. Nonetheless, **electron microscopy** is a valuable technique for the study of large molecules, such as DNA, which can be stained with heavy-metal atoms before viewing, or are themselves reasonably stable to an electron beam (Figures 9-4 and 9-5).

Virtually all parts of the spectrum of electromagnetic radiation, from x rays to radio waves, have some practical application for the study of organic molecules. The use of **x-ray diffraction** for determination of the structures of

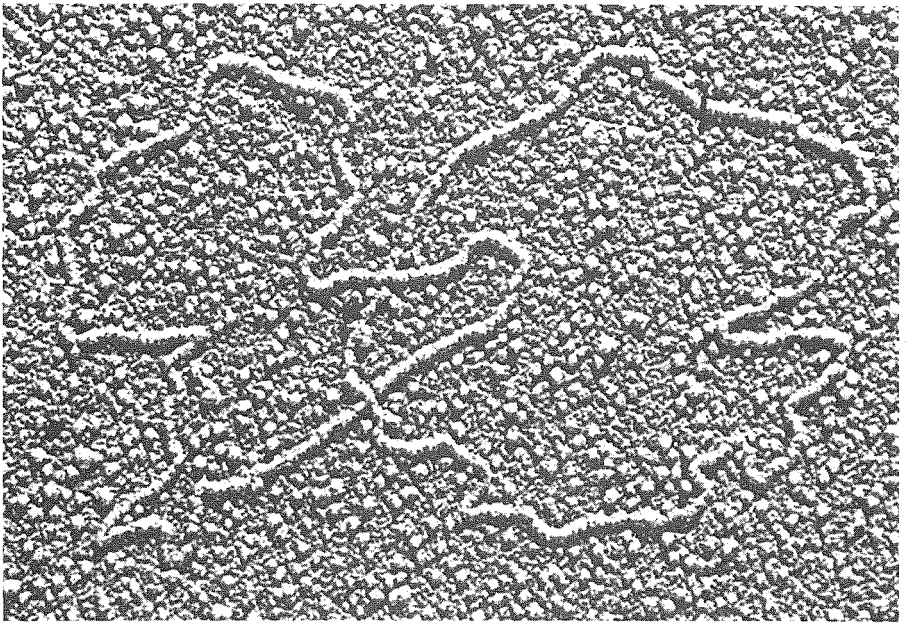
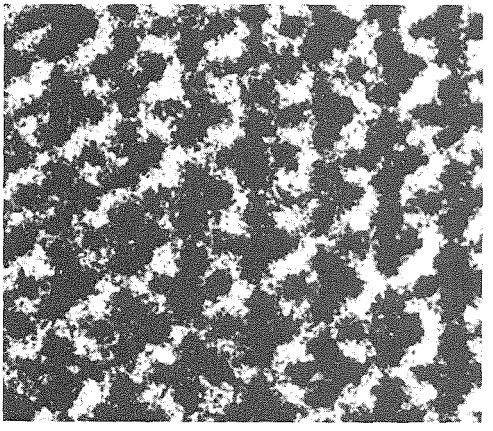


Figure 9-4 Electron micrograph (×40,000) of two linked (**catenated**) cyclic mitochondrial DNA molecules from a culture of human cells. The DNA was stained with uranyl acetate, then shadowed with platinum and palladium atoms in high vacuum to make the molecules easily visible in the electron microscope. (Photograph supplied by Dr. B. S. Hudson and the late Dr. J. Vinograd.)



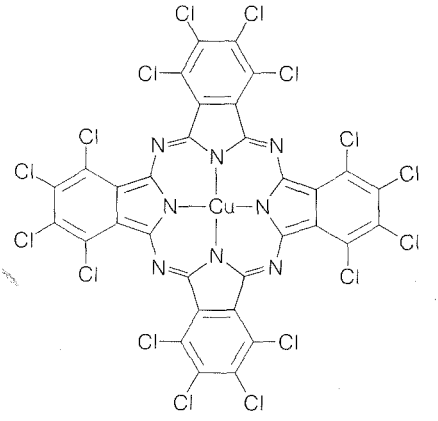


Figure 9-5 Electron micrograph (×150,000) of a thin layer of copper hexadecachlorophthalocyanine molecules. The molecules are tilted about 25° from the horizontal plane. (Courtesy JEOL, Ltd.)

molecules in crystals is of particular value, and in the past ten years this technique has become almost routine. Figure 9-6 shows the detailed arrangement of the carbons, hydrogens, and bromines in 1,8-bis(bromomethyl)naphthalene, **1**, as determined by x-ray diffraction. The apparatus and techniques used are

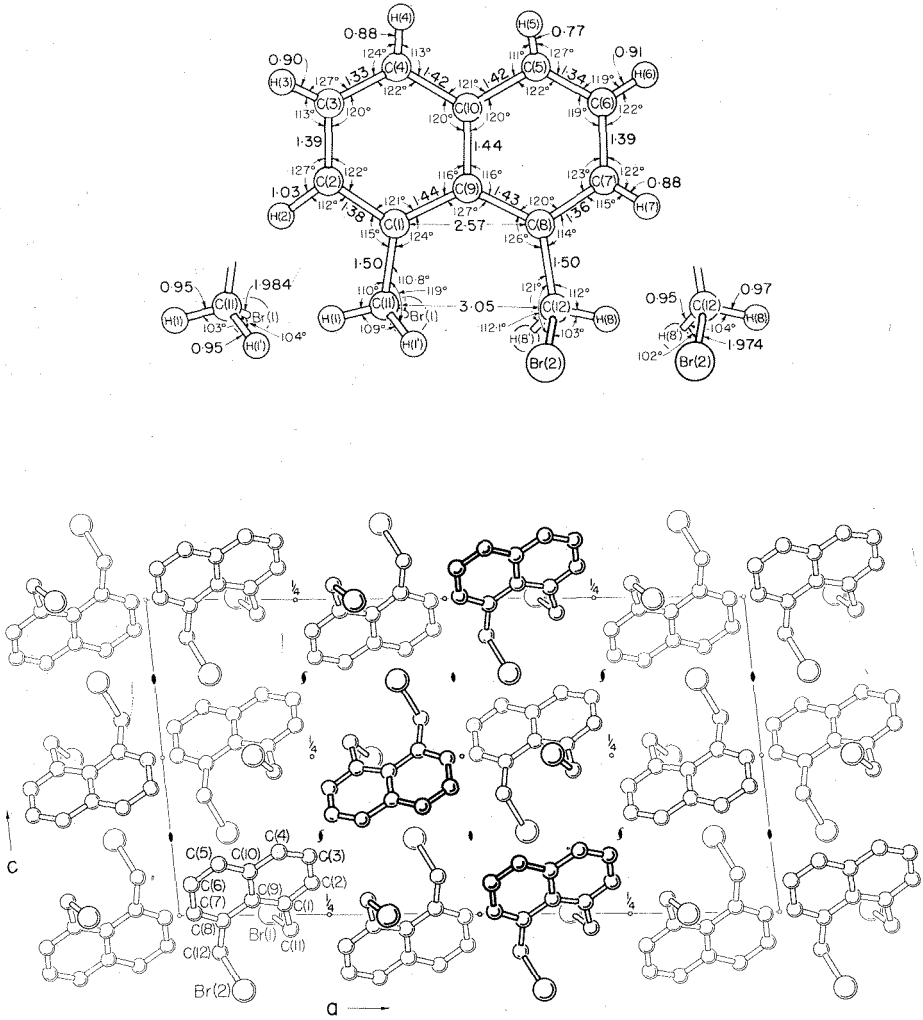
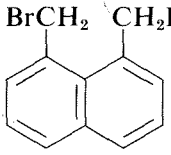


Figure 9-6 Bond lengths, angles, and arrangement of carbons and bromines in a crystal of 1,8-bis(bromomethyl)naphthalene, **1**, as determined by x-ray diffraction. Notice that the preferred conformation in the crystal has the bromines on opposite sides of the naphthalene ring.

highly complex and are not available yet to very many organic laboratories.[3]



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Other diffraction methods include **electron diffraction,** which may be used to determine the structures of gases or of volatile liquid substances that cannot be obtained as crystals suitable for x-ray diffraction, and **neutron diffraction,** which has special application for crystals in which the exact location of hydrogens is desired. Hydrogen does not have sufficient scattering power for x rays to be located precisely by x-ray diffraction.

The diffraction methods can be used to determine complete structures of organic molecules, but they are not sufficiently routine to be utilized generally in practical organic laboratory work. For this reason, in the remainder of this chapter we will emphasize those forms of spectroscopy that are generally available for routine laboratory use. As will be seen, these methods are used by organic chemists in more or less empirical ways. In general, spectroscopic methods depend on some form of excitation of molecules by absorption of electromagnetic radiation and, as we have said, virtually all parts of the electromagnetic spectrum have utility in this regard. The commonly used span of the electromagnetic spectrum is shown in Figure 9-7 along with a comparison of the various units that are employed to express energy or wavelength.

The major kinds of spectroscopy used for structural analysis of organic compounds are listed in Table 9-1. The range of frequencies of the absorbed radiation are shown, as well as the effect produced by the radiation and specific kind of information that is utilized in structural analysis. After a brief account of the principles of spectroscopy, we will describe the methods that are of greatest utility to practical laboratory work. Nonetheless, it is very important to be aware of the other, less routine, methods that can be used to solve special problems, and some of these are discussed in this and in Chapters 19 and 27.

You may have problems with the relationships among the variety of wavelength and frequency units commonly used in spectroscopy. The relationship between wavelength, frequency, and velocity should become clear to you by considering yourself standing on a pier watching ocean waves going by. Assuming the waves are uniformly spaced, there will be a uniform distance between the crests, which is λ, the wavelength. The wave crests will pass by at a certain number per minute, which is ν, the frequency. The velocity, c,

[3]A useful description of how molecular structures can be determined by "x-ray vision" is given in Chapter XI of *Organic Molecules in Action* by M. Goodman and F. Morehouse, Gordon and Breach, New York, 1973.

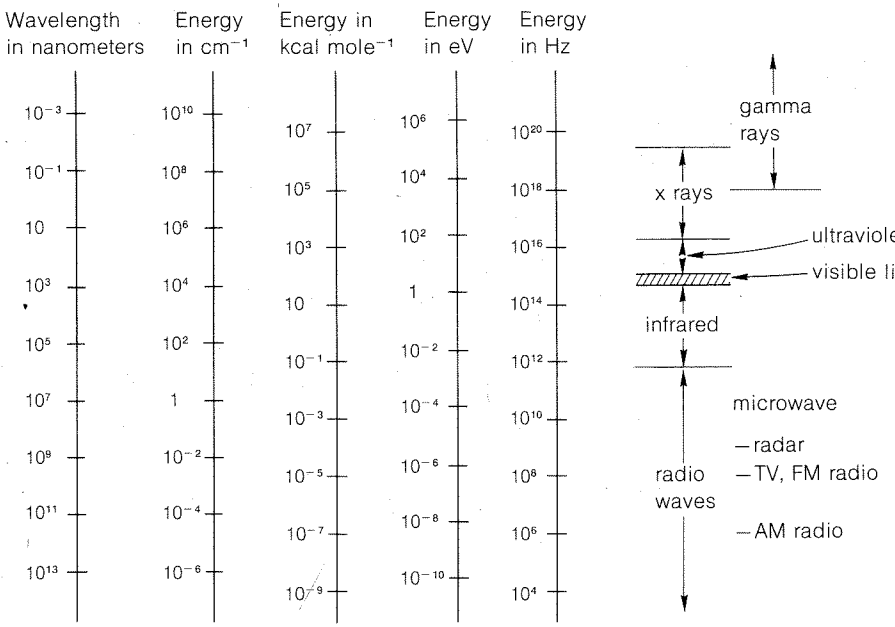


Figure 9-7 The span of the spectrum of electromagnetic radiation used in spectroscopic investigations of organic compounds along with comparison of some of the various units commonly employed for wavelength and energy of the radiation on log scales

at which the crests move by you is related to λ and ν by the relationship $c = \lambda\nu$.

This is not really very complicated and it applies equally well to water waves or electromagnetic radiation. What is almost needlessly complicated is the variety of units commonly used to express λ and ν for electromagnetic radiation. One problem is tradition, the other is the desire to avoid very large or very small numbers. Thus, as Figure 9-7 shows, we may be interested in electromagnetic wavelengths that differ by as much as a factor of 10^{16}. Because the velocity of electromagnetic radiation in a vacuum is constant at 3×10^8 meters sec^{-1}, the frequencies will differ by the same factor.

Units commonly used for *wavelength* are meters (m), centimeters (cm), nanometers (nm), and microns (μ). In the past, angstroms (A) and millimicrons (mμ) also were used rather widely.

$1\ m = 10^2\ cm = 10^9\ nm = 10^6\ \mu$

$10^{-2}\ m = 1\ cm = 10^7\ nm = 10^4\mu$

$10^{-6}\ m = 10^{-4}\ cm = 10^3\ nm = 1\mu$

$10^{-9}\ m = 10^{-7}\ cm = 1\ nm = 10^{-3}\mu = 1\ m\mu = 10\ A$

Frequency units are in cycles per second (cps) or hertz (Hz), which are equivalent (radians per second are used widely by physicists).

Table 9-1
Principal Spectroscopic Techniques Currently in Use for Analysis of Molecular Structure

Spectroscopic technique	Energy range of absorbed radiation (in wave numbers, cm^{-1})[a]	Type of excitation produced by absorbed radiation	Information obtained
Ion cyclotron resonance	10^{-6} to 10^{-5}	Excitation of ions moving in circular orbits in a magnetic field	Rates and equilibria for reactions of ions with neutral molecules in the gas phase (Section 27-8)
Nuclear magnetic resonance (nmr)	10^{-4} to 10^{-2}	Changes in nuclear spin orientations in a magnetic field	Chemical shifts and coupling constants; rapid reaction rates (Sections 9-10, 27-1, and 27-2)
Electron spin resonance (esr)	10^{-2} to 1	Excitation of unpaired electron-spin orientations in a magnetic field	Electron distribution in radicals, electron-transfer reactions (Section 27-9)
Microwave	1 to 100	Rotational excitation	Spacings of rotational energy levels; bond distances and bond angles (Section 9-6)
Infrared (ir)	100 to 10,000	Rotational-vibrational excitation	Rotational and vibrational energy levels of molecules (Section 9-7)
Raman	100 to 4,000	Rotational-vibrational excitation	Rotational and vibrational energy levels of molecules (Section 9-8)
Visible	5,000 to 25,000	Electronic excitation accompanied by vibration-rotation changes	Electronic energy levels of molecules (Section 9-9)
Ultraviolet	25,000 to 50,000	Electronic excitation accompanied by vibration-rotation changes	Electronic energy levels of molecules (Sections 9-9 and 28-1)
Photoelectron	10^5 to 10^6	Ejection of an electron from the valence or inner shell	Ionization energies of valence or inner-shell electrons of molecules (Section 27-5)
Mossbauer	10^7 to 10^9	Excitation of atomic nuclei	Electric-field gradients at the nucleus produced by differences in bond types (Section 27-6)
Mass spectrometry	Excitation produced by electrons with energies of about 10^5 cm^{-1}	Molecular ionization and fragmentation	Molecular weights; modes of fragmentation (Sections 9-11 and 27-7)

[a]These ranges are not meant to be precise, but to give you a general idea of the energy changes involved. One wave number (cm^{-1}) is equivalent to 2.86 cal $mole^{-1}$. Also see Figure 9-7 for comparison with other commonly used units of energy and wavelength.

Frequencies in the electromagnetic spectrum can be seen from Figure 9-7 generally to be large. As a result, it is common to use **wave numbers** instead of Hz or MHz (megahertz). The frequency in wave number is simply the frequency ν in Hz divided by c, the velocity of light in cm. Wave-number units are cm^{-1} and we can think of the wave number $\bar{\nu}$ as being the number of *wave crests per centimeter.*

$1\ Hz = 10^{-6}\ MHz \equiv 3.3 \times 10^{-11}\ cm^{-1}$

$10^{6}\ Hz = 1\ MHz \equiv 3.3 \times 10^{-5}\ cm^{-1}$

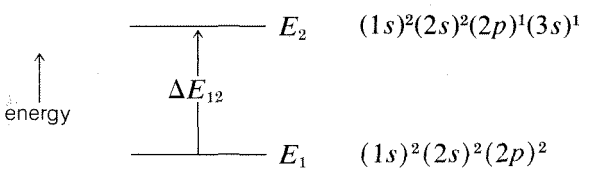
$3 \times 10^{10}\ Hz = 3 \times 10^{4}\ MHz \equiv 1\ cm^{-1}$

Exercise 9-1 Suppose you are standing on the end of a pier watching the waves and, between your position and a buoy 200 m straight out, you count 15 wave crests. Further, suppose a wave crest comes by every 15 seconds. Calculate ν in Hz, λ in m, c in m sec^{-1}, and $\bar{\nu}$ in km^{-1}.

Exercise 9-2 Blue light has $\bar{\nu} = 20{,}800\ cm^{-1}$. Calculate ν in Hz and λ in nm.

9-4 ATOMIC ENERGY STATES AND LINE SPECTRA

The energies of the hydrogenlike orbitals of various atoms were mentioned in Chapter 6 and, in particular, we showed a diagram of the most stable state $(1s)^2(2s)^2(2p)^2$ of a carbon atom (Figure 6-4). Transfer of one of the $2p$ electrons to the $3s$ orbital requires excitation of the atom to a higher energy state and this can be achieved by absorption of electromagnetic radiation of the proper wavelength. The usual way that such excitation occurs is by absorption of a single **quantum** of radiant energy, and we can say that the absorption of this amount of energy ΔE_{12}, corresponds to excitation of the atom from the **ground state** with energy E_1 to an **excited state** of configuration $(1s)^2(2s)^2(2p)^1(3s)^1$ and energy E_2:



The difference in energy, ΔE_{12}, is related directly to the frequency (ν, sec^{-1}) or wavelength (λ, nm)[4] of the absorbed quantum of radiation by the equation

$$\Delta E_{12} = h\nu = \frac{hc}{\lambda} \tag{9-1}$$

in which h is Planck's constant and c is the velocity of light. The relationship $\Delta E = h\nu$ often is called the *Bohr frequency condition.*

For chemical reactions, we usually express energy changes in kcal $mole^{-1}$. For absorption of one quantum of radiation by each atom (or each molecule) in one mole, the energy change is related to λ by

$$\Delta E_{12} = \frac{28{,}600}{\lambda(\text{nm})} \text{ kcal mole}^{-1} \tag{9-2}$$

As defined, ΔE_{12} corresponds to one **einstein** of radiation.

What we have developed here is the idea of a spectroscopic change being related to a change in energy associated with the absorption of a quantum of energy. **Spectra** are the result of searches for such absorptions over a range of wavelengths (or frequencies). If one determines and plots the degree of absorption by a monoatomic gas such as sodium vapor as a function of wavelength, a series of very sharp absorption bands or lines are observed, hence the name **line spectra.** The lines are sharp because they correspond to specific changes in electronic configuration without complication from other possible energy changes.

Exercise 9-3 Calculate the energy in kcal $mole^{-1}$ that corresponds to the absorption of 1 einstein of light of 589.3 nm (sodium D line) by sodium vapor. Explain how this absorption of light by sodium vapor may have chemical utility.

Exercise 9-4 **a.** Use Equations 9-1 and 9-2 to calculate the wavelength in nm and energy in kcal of an einstein of radiation of radio-frequency energy in the broadcast band having $\nu = 1$ MHz (1 megahertz) $= 10^6$ sec^{-1} and knowing that the velocity of light is approximately 3×10^8 meters sec^{-1}.

b. In photoelectron spectroscopy, x rays with energies of approximately 1250 electron volts are used (1 electron volt per mole = 23.05 kcal). What would λ (in nm) be for such x rays?

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[4]See Section 9-3 for discussion of the units of frequency and wavelength.

9-5 ENERGY STATES OF MOLECULES

The energy states and spectra of molecules are much more complex than those of isolated atoms. In addition to the energies associated with molecular electronic states, there is kinetic energy associated with vibrational and rotational motions. The total energy, E, of a molecule (apart from its translational[5] and nuclear energy) can be expressed as the sum of three terms:

$$E = E_{\text{electronic}} + E_{\text{vibrational}} + E_{\text{rotational}}$$

Absorption of electromagnetic radiation by molecules occurs not only by electronic excitation of the type described for atoms, but also by changes in the vibrational and rotational energies.

Both rotations and vibrations of molecules are quantized. This means that only particular values of rotational angular momentum or vibrational energy are possible. We speak of these permitted values of the energies as the vibrational and rotational energy levels.

9-6 MICROWAVE SPECTRA. ROTATIONAL SPECTRA

Rotational energy levels normally are very closely spaced so low-energy radiation, such as is produced by radio transmitters operating in the microwave region, suffices to change molecular rotational energies. Because electronic and vibrational energy levels are spaced much more widely, and because changes between them are induced only by higher-energy radiation, microwave absorptions by gaseous substances can be characterized as essentially pure "rotational spectra." It is possible to obtain rotational moments of inertia from microwave spectra, and from these moments to obtain bond angles and bond distances for simple molecules.

An example of the use of microwave spectra is provided by Figure 9-8, which shows separate rotational absorptions observed for trans and gauche conformations of propyl iodide (cf. Section 5-2).

Although microwave spectroscopy, being confined to gases, is not a routine method in the organic laboratory, it is important to us here in setting the stage for the consideration of more complex absorptions that occur with infrared radiation.

[5]Translational energy is not very important in connection with spectroscopy and will not be considered here.

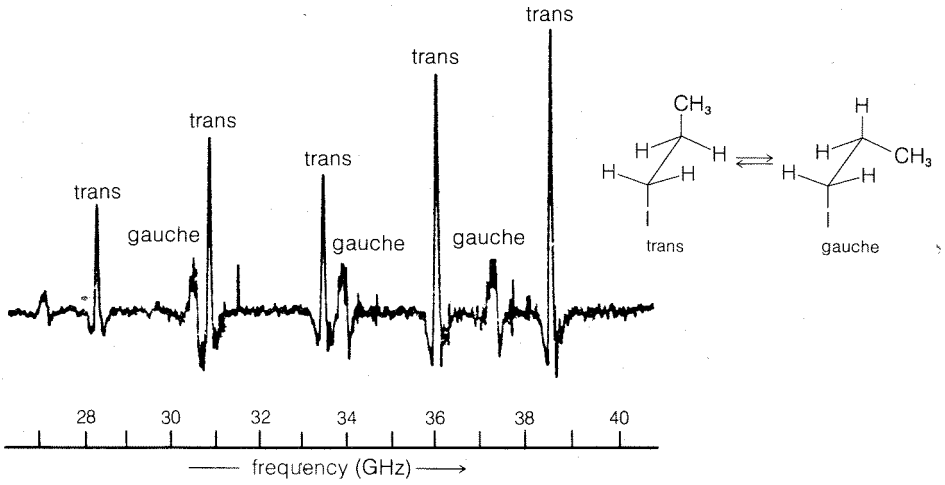


Figure 9-8 A small part of the microwave spectrum of $CH_3CH_2CH_2I$ at a pressure of 7×10^{-5} atm showing absorptions of the trans and gauche conformations. Notice the regular spacings of the lines for each conformation. That the spacings are different for the two conformations reflects their different moments of inertia. The horizontal scale is GHz (gigahertz, 10^9 Hz) and $\nu = 30$ GHz corresponds to $\lambda = 10^7$ nm, which from Equation 9-1 can be calculated to mean a rotational energy change of 0.0029 kcal $mole^{-1}$. (Spectrum courtesy of Dr. Howard Harrington, Hewlett-Packard Corp.)

Exercise 9-5 The microwave spectrum of pure *trans*-2-butenoic acid ($CH_3CH{=}CHCO_2H$) shows patterns exactly like those of Figure 9-8, which indicate the presence of two different *conformations*. What are these conformations, and why are there only two of them? (You may be helped by reviewing Section 6-5.)

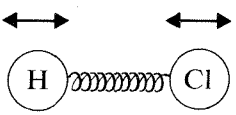
9-7 INFRARED SPECTROSCOPY. VIBRATION–ROTATION SPECTRA

At the turn of the nineteenth century Sir William Herschel discovered invisible radiation beyond the red end of the visible region of the electromagnetic spectrum. This radiation appropriately is called *infrared*, meaning "beneath the red," and it encompasses the wavelength region from 10^3 nm to 10^6 nm. You probably are familiar with the common applications of infrared to radiant heating and photography. In addition to these uses, infrared spectroscopy has become the most widely used spectroscopic technique for investigating organic structures.

Infrared spectroscopy was the province of physicists and physical chemists until about 1940. At that time, the potential of infrared spectroscopy as an analytical tool began to be recognized by organic chemists. The change was due largely to the production of small, quite rugged infrared spectrophotometers and instruments of this kind now are virtually indispensable for chemical analysis. A brief description of the principles and practice of this spectroscopic method is the topic of this section.

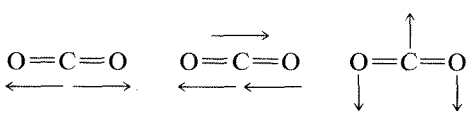
9-7A General Considerations

Absorption of infrared radiation causes transitions between *vibrational* energy states of a molecule. A simple diatomic molecule, such as H—Cl, has only one vibrational mode available to it, a stretching vibration somewhat like balls on the ends of a spring:



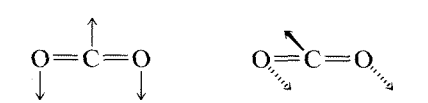
stretching vibration

Molecules with three or more atoms can vibrate by stretching and also by bending of the chemical bonds, as indicated below for carbon dioxide:



stretching vibrations bending vibration

The absorption frequencies in the infrared spectra of molecules correspond to changes in the stretching or bending vibrations or both. In general, a polyatomic molecule with n atoms will have $3n - 6$ modes of vibration of which $n - 1$ are stretching vibrations and $2n - 5$ are bending vibrations. There are circumstances, however, where fewer vibrational modes are possible. If the molecule is linear, like CO_2, then there are $3n - 5$ possible vibrations, and some of these vibrations may be equivalent (**degenerate** vibrations in the language of spectroscopists). For example, CO_2 should have $3n - 5$ or 4 vibrational modes, two of which are stretching and two of which are bending modes. However, the two bending modes are equivalent because the *direction* in which the molecule bends is immaterial; in-plane or out-of-plane bending are the same:



in-plane bending out-of-plane bending

Diatomic molecules such as HCl have one vibrational mode, but it is important to note that *symmetrical diatomic molecules,* such as O_2, N_2, Cl_2, F_2, and H_2, *do not absorb in the infrared region of the spectrum.* This is

because absorption cannot occur if the vibration is electrically symmetrical. Fortunately, then, the infrared spectra can be recorded in air because the main components of air, N_2 and O_2, do not interfere.

In practice, infrared spectra can be obtained with gaseous, liquid, or solid samples. The sample containers (cells) and the optical parts of the instrument are made of rock salt (NaCl) or similar material that transmits infrared radiation (glass is opaque).

Typical infrared spectra are shown in Figure 9-9 for 2-propanone (acetone), $CH_3—CO—CH_3$, and 2-butanone (methyl ethyl ketone), $CH_3—CO—CH_2—CH_3$. In accord with current practice, the position of absorption

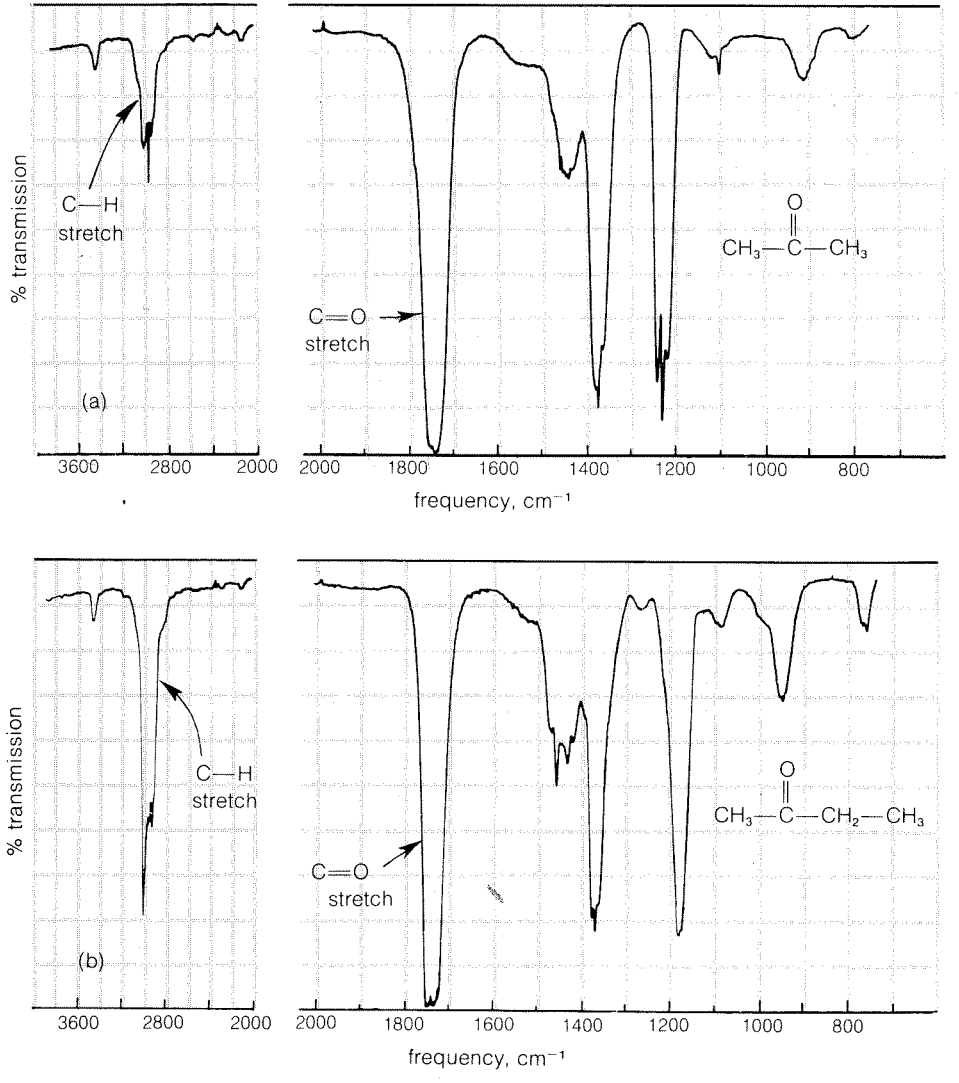


Figure 9-9 Infrared absorption spectra of (a) 2-propanone and (b) 2-butanone in the vapor phase

(horizontal scale) is recorded in units of wave numbers ($\bar{\nu}$, cm^{-1}; see Section 9-3). The vertical scale measures the intensity of radiation transmitted through the sample. Zero transmission means complete absorption of radiation by the sample as at 1740 cm^{-1} in Figure 9-9. The other absorption bands in Figure 9-9 that correspond to excitation of stretching or bending vibrations are not as intense as the absorption at 1740 cm^{-1}.

9-7B Characteristic Stretching Vibrations

What information can we derive about molecular structure from the vibrational bands of infrared spectra? Absorption of radiation in the range of 5000–1250 cm^{-1} is characteristic of the types of bonds present in the molecule, and corresponds for the most part to stretching vibrations. For example, we know that the C—H bonds of alkanes and alkyl groups have characteristic absorption bands around 2900 cm^{-1}; an unidentified compound that shows absorption in this region will very likely have alkane-type C—H bonds.

More explicitly, the band observed for 2-propanone (Figure 9-9a) at 3050 cm^{-1} arises from absorption of infrared radiation, which causes transitions between the ground vibrational state (or lowest vibrational energy level) of a C—H bond and the first excited vibrational energy level for stretching of that C—H bond. The band at 1740 cm^{-1} corresponds to the infrared absorption that causes transitions between vibrational energy levels of the C=O bond. The reason that these are transitions from the vibrational ground state is because, at room temperature, by far the largest portion of the molecules are in this state (cf. Exercise 9-9).

Stretching frequencies characteristic of the most important types of bonds found in organic molecules are given in Table 9-2. You will notice that the absorption band for each bond type is described by its position within a more or less broad frequency range and by its shape (broad, sharp) and intensity (strong, medium, weak).

A qualitative discussion of the factors that determine infrared band position and band intensities follows. To a first approximation, a chemical bond resembles a mechanical spring that vibrates with a stretching frequency $\bar{\nu}$ (cm^{-1}),

$$\bar{\nu} = \frac{1}{2\pi c}\sqrt{\frac{k}{m_1 m_2/(m_1 + m_2)}} \qquad (9\text{-}3)$$

in which k is the force constant, and m_1 and m_2 are the masses of the individual atoms at each end of the bond. The force constant k is a measure of the stiffness of the bond and usually is related to the bond strength. From Equation 9-3, we can see that the heavier the bonded atoms, the smaller will be the vibrational frequency of the bond provided k remains essentially constant.[6] Thus if we increase m_2 while holding k and m_1 constant we expect the frequency to decrease. This is just what occurs when we change the C—H bond to a C—D

[6]Remember that lower frequency means longer wavelengths and lower energy.

bond. We also see that the frequency decreases in the order C—H > C—C > C—N > C—O, which also is in the order of increasing m_2, but here matters are more complicated because k also changes.

Other things being equal, it requires more energy to stretch a bond than to bend it. Therefore the infrared bands arising from changes in the stretching vibrations are found at higher frequencies than are those arising from changes in the bending vibrations.

Another consequence of Equation 9-3 is that if m_1 and m_2 remain the same, the larger the value of k, the higher will be the vibrational frequency. Because k is expected to run more or less parallel to the bond strength, and because multiple bonds are stronger than single bonds, the absorption frequencies of multiple bonds are higher than for single bonds. Examples are the absorption of C≡C at 2100 cm^{-1}, C=C at 1650 cm^{-1}, and C—C at 1000 cm^{-1}.

Other effects besides mass and bond strength also affect infrared absorption frequencies. The structural environment of a bond is particularly important. Thus the absorption frequency of a C—H bond depends on whether it is an alkyl, alkenyl, alkynyl, or aryl C—H bond (see Table 9-2).

The intensity of an infrared absorption band arising from changes in the vibrational energy is related to the electrical symmetry of the bond. More symmetrical, less polarized bonds give weaker absorptions. In fact, if the bond is completely symmetrical, there is no infrared absorption. In contrast, unsymmetrical molecules in which the bonds are quite polarized, such as C=O bonds, show strong infrared absorptions.

Notice in Figure 9-9 that infrared spectra of organic molecules do not show very sharp absorption lines. This is because changes in rotational energies can occur together with the vibrational changes. The reason can be seen more clearly in Figure 9-10, in which each vibrational level, such as E_1 and E_2, of a molecule has associated with it closely spaced rotational levels. Transitions between E_1 and E_2 also may involve changes in rotational levels. This gives a "band" of closely spaced lines for any given vibrational change. For

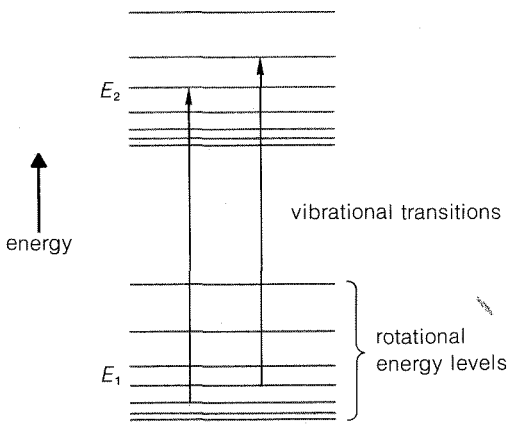


Figure 9-10 Schematic vibrational and rotational energy levels. The arrows correspond to infrared vibrational–rotational transitions of different energies.

Table 9-2
Some Characteristic Infrared Absorption Frequencies

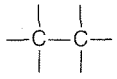
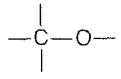
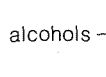
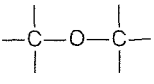
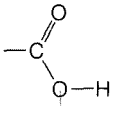
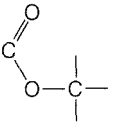
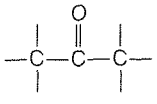
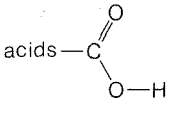
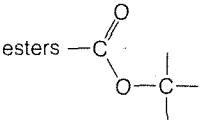
Bond	Type of compound	Frequency, cm^{-1}	Intensity
	alkanes	2800–3100	strong
	alkanes	~2200	strong
	alkenes and arenes	3000–3100	medium
≡C—H	alkynes	3200–3350	strong, sharp
	alkanes	750–1200[a]	weak to medium
	alkenes	1600–1680	variable
—C≡C—	alkynes	2050–2260	variable
—C≡N	nitriles	2200–2400	variable
	alcohols  , ethers 	980–1250	strong
	carboxylic acids 	1350–1440 1210–1320	weak to medium strong
	esters 	1035–1300	strong (two bands for unsaturated esters)
	aldehydes 	1690–1740	strong
	ketones 	1650–1730	strong
	acids  esters 	1710–1780	strong

Table 9-2 (*continued*)
Some Characteristic Infrared Absorption Frequencies

Bond	Type of compound	Frequency, cm^{-1}	Intensity
—O—H	alcohols —C—O—H, phenols =C—O—H	3400–3700	variable, sharp
—O—H[b]	hydrogen-bonded alcohols and phenols —O—H···O	3200–3400	strong, broad
—O—H	alcohols, phenols, acids (bending vibration)	1000–1450	strong
—O—H[b]	hydrogen-bonded carboxylic acids —O—H···O	2500–3300	variable, broad
$—NH_2$	amines —C—NH_2	3200–3600 (double peak)	medium
—N—H	amines —C—N—C— (H)	3100–3500 (single peak)	medium

[a]In general, C—C single-bond stretching frequencies are not very useful for identification.

[b]These bands may not appear at low concentration in solvents where intermolecular hydrogen bonding does not occur.

complex molecules, particularly in the liquid state, the "rotational fine structure" of a given vibrational band usually cannot be resolved.

Absorption of infrared radiation over the range from 600 cm^{-1} to 3600 cm^{-1} corresponds to energy-level differences, as in Figure 9-10, of 1.7 kcal $mole^{-1}$ to 10.3 kcal $mole^{-1}$.

Exercise 9-6 Use Equation 9-3 and any other pertinent data to predict which compound in each group would absorb in the infrared at the highest frequency for the changes in the stretching vibration of the specified bond. Give your reasoning.

a. R—Cl, R—Br, R—F (carbon–halogen)

b. $CH_3—NH_2$, $CH_2=NH$, $HC\equiv N$ (carbon–nitrogen)

Exercise 9-7 Which compound in each group would have the most intense infrared absorption band corresponding to stretching vibrations of the bonds indicated? Give your reasoning.

a. $(CH_3)_2C{=}O$, $(CH_3)_2C{=}CH_2$ (multiple bond)
b. $CH_3{-}CH_3$, $CH_3{-}O{-}CH_3$ (C—C *vs.* C—O)
c. $CH_3C{\equiv}CH$, $CH_3C{\equiv}CCH_3$ (multiple bond)
d. H—Cl, Cl—Cl

Exercise 9-8* How many vibrational modes are possible for (a) CS_2 (linear), (b) $BeCl_2$ (linear), and (c) SO_2 (angular)? Show your reasoning.

Exercise 9-9* Suppose an infrared absorption occurs at 3000 cm^{-1}. Calculate the corresponding frequency ν in sec^{-1}; λ in nm, angstroms, and microns, and energy change in kcal $mole^{-1}$. Using Equation 4-2 (p. 84) and neglecting ΔS, calculate the fraction of the molecules that would be in the ground state and in the first vibrational excited state (above the ground state by 3000 cm^{-1}) at 298°K.

9-7C The Fingerprint Region

Infrared absorption bands between 1250 cm^{-1} and 675 cm^{-1} generally are associated with complex vibrational and rotational energy changes of the molecule as a whole and are quite characteristic of particular molecules. This part of the spectrum is often called the "fingerprint" region and is extremely useful for determining whether samples are chemically identical. The spectra of 2-propanone and 2-butanone are seen to be very similar in the region 4000 cm^{-1} to 1250 cm^{-1} but quite different from 1250 cm^{-1} to 675 cm^{-1}. The fingerprint region of the spectrum is individual enough so that if the infrared spectra of two samples are indistinguishable in the range of frequencies from 3600 cm^{-1} to 675 cm^{-1}, it is highly probable that the two samples are of the same compound (or the same mixture of compounds).

Characteristic stretching and bending frequencies occur in the fingerprint region, but they are less useful for identifying functional groups, because they frequently overlap with other bands. This region is sufficiently complex that a complete analysis of the spectrum is seldom possible.

9-7D Alkanes and Cycloalkanes

The infrared spectra of the alkanes show clearly absorptions corresponding to the C—H stretching frequencies at 2850 cm^{-1} to 3000 cm^{-1}. The C—C stretching absorptions have variable frequencies and are usually weak. Methyl (CH_3—) and methylene (—CH_2—) groups normally have characteristic C—H bending vibrations at 1400 cm^{-1} to 1470 cm^{-1}. Methyl groups also show a

weaker band near 1380 cm^{-1}. Two sample infrared spectra that illustrate these features are given in Figure 9-11.

The infrared spectra of the cycloalkanes are similar to those of the alkanes, except that when there are no alkyl substituents the characteristic

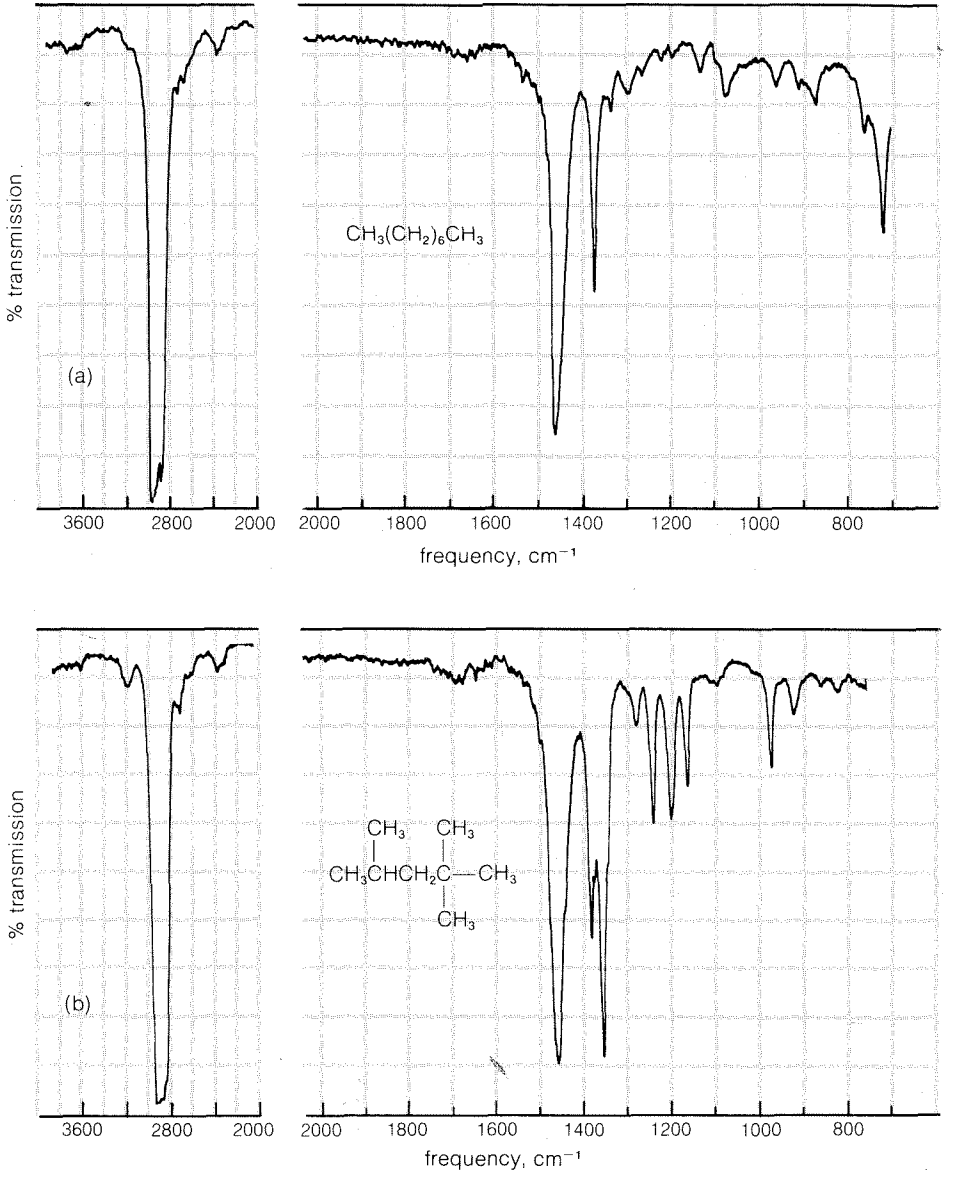


Figure 9-11 Infrared spectra of (a) octane and (b) 2,2,4-trimethylpentane as pure liquids. Notice the C—H stretching around 2900 cm^{-1} and C—H bending frequency around 1460 cm^{-1}. The bands near 1370 cm^{-1} for 2,2,4-trimethylpentane are characteristic of methyl C—H bending frequencies.

bending frequencies of methyl groups at 1380 cm^{-1} are absent. A moderately strong CH_2 "scissoring" frequency is observed between 1440 cm^{-1} and 1470 cm^{-1}, the position depending somewhat on the size of the ring. These features of the infrared spectra of cycloalkanes are illustrated in Figure 9-12 using cyclooctane and methylcyclohexane as examples.

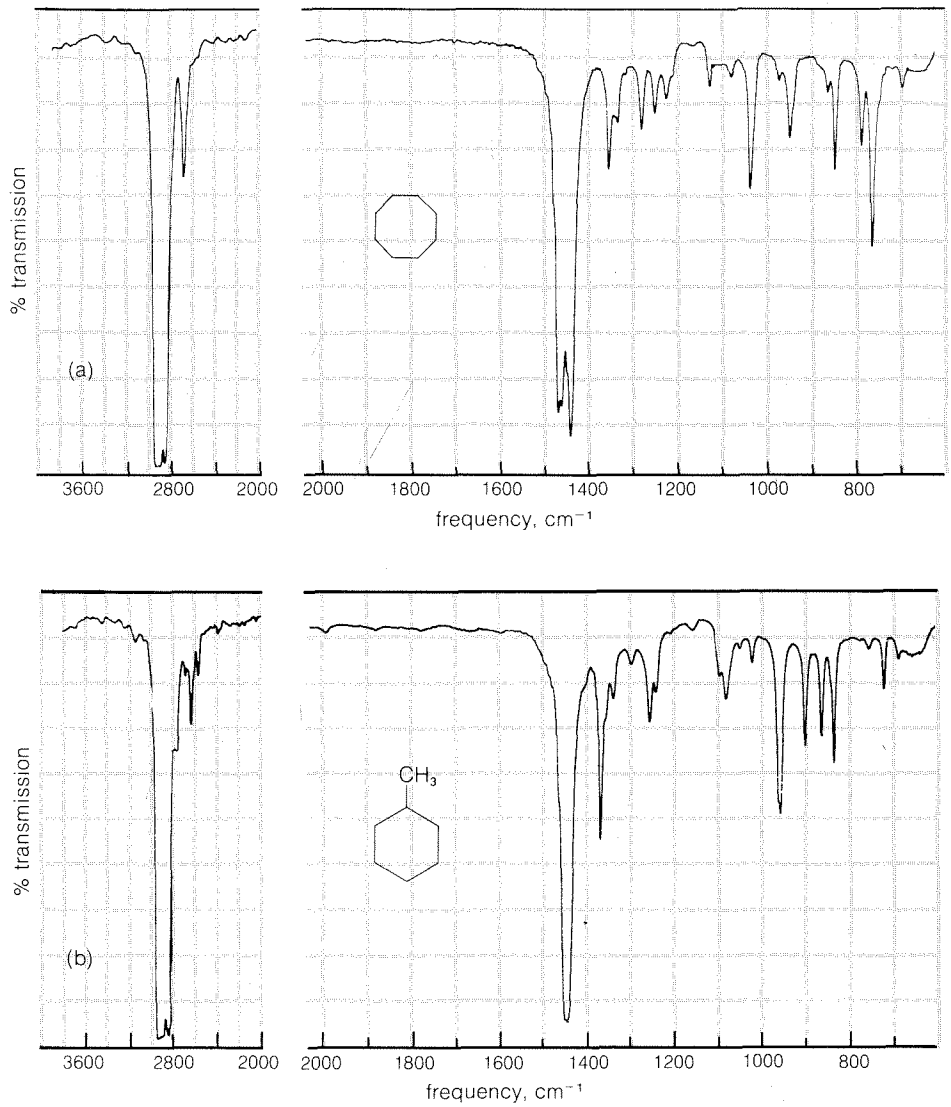


Figure 9-12 Infrared spectra of (a) cyclooctane and (b) methylcyclohexane. These spectra can be compared profitably with those in Figure 9-11.

9-7E Applications of Infrared Spectroscopy to Structure Determination

Infrared spectra are very useful both for identification of specific organic compounds, and for determining types of compounds. For example, Figure 9-13 shows the infrared spectrum of a substance, $C_4H_6O_2$, for which we wish to determine the compound type and, if possible, the specific structure. The most informative infrared absorptions for determining the compound type are between 1500 cm^{-1} and 3600 cm^{-1}. Two groups of bands in this region can be seen at about 1700 cm^{-1}(s) and 3000 cm^{-1}(s), where (s) means strong; if we used (m) it would mean medium, and (w) would mean weak. From Table 9-2 we can see that these bands are indicative of C=O (1700 cm^{-1}) and hydrogen-bonded OH of carboxylic acids (3000 cm^{-1}). The presumption is that there is a $—CO_2H$ group in the molecule, and we can derive some reassurance from the fact that the molecular formula $C_4H_6O_2$ has enough oxygens to allow for this possibility.

Table 9-2 also shows that a $—CO_2H$ group should have a C—O absorption band between 1350 cm^{-1} and 1400 cm^{-1} and O—H absorption (bending frequency) between 1000 cm^{-1} and 1410 cm^{-1}, and there is indeed a band of medium intensity at 1350 cm^{-1} and a strong band at 1240 cm^{-1}. These absorptions, being in the fingerprint region, do not *prove* that the compound is a carboxylic acid; but if there were no absorptions in the 1000 cm^{-1} to 1400 cm^{-1} range, the presence of a $—CO_2H$ group would be highly questionable.

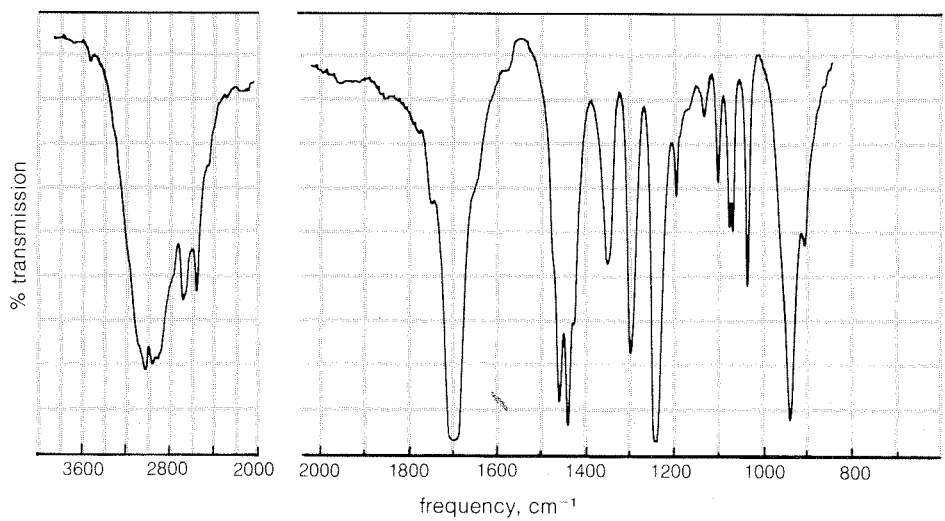
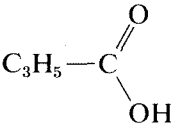
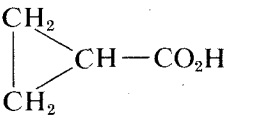


Figure 9-13 Infrared spectrum of a compound, $C_4H_6O_2$

Tentatively, then, we may write a partial structure for $C_4H_6O_2$ as



A propyl group would be C_3H_7, and C_3H_5 has two hydrogens less, which indicates the presence of a double bond or a ring. However, Table 9-2 shows that a double bond should have an absorption of variable intensity at 1600 cm^{-1} to 1680 cm^{-1} and there is no clear sign of such an absorption in Figure 9-13. The alternative to a double bond would be a ring, which for C_3H_5 has to be a cyclopropyl ring. The structure that is most compatible with the spectrum is



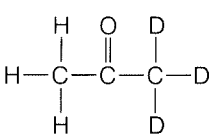
cyclopropanecarboxylic acid

Final identification may be possible by comparison with an authentic spectrum of cyclopropanecarboxylic acid, if it is available in one of the several standard compendia of infrared spectra. A total of about 150,000 infrared spectra are available for comparison purposes. You should check with the reference section of your library to see what atlases of spectral data are available to you.

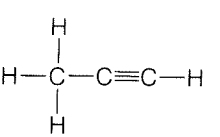
The foregoing example illustrates the way structures can be determined from infrared spectral data. For many purposes, the infrared frequencies given in Table 9-2 are both approximate and incomplete. However, you could be easily frustrated in interpreting spectral data by being burdened with a very detailed table in which the unimportant is mixed with the important. The ability to use extensive tables effectively comes with experience. You should remember that tabulated infrared frequencies indicate only the *range* in which a given vibrational transition will fall. The exact value for a particular compound usually is meaningless because it will change depending on whether the spectrum is taken of the solid, liquid, or gaseous states, the solvent used, the concentration, and the temperature. To become familiar with infrared spectra, we strongly recommend that you work Exercises 9-10 and 9-11.

Exercise 9-10 Use Table 9-2 to map the approximate positions and intensities expected for the characteristic infrared bands corresponding to the stretching vibrations of the various kinds of bonds in the following molecules:

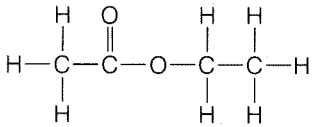
a. 1,1,1-trideuteriopropanone (trideuterioacetone)



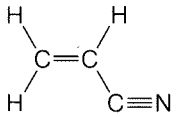
b. propyne



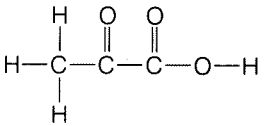
c. ethyl ethanoate (ethyl acetate)



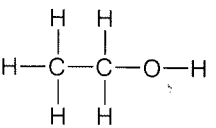
d. propenenitrile (acrylonitrile)



e. 2-oxopropanoic acid (pyruvic acid)



f. ethanol (ethyl alcohol)



(both as pure liquid and as a dilute solution in CCl_4)

Exercise 9-11 The infrared spectra shown in Figure 9-14 are for compounds of formula C_3H_6O and $C_3H_6O_2$. Use the data in Table 9-2 and the molecular formulas to deduce a structure for each of these substances from its infrared spectrum. Indicate clearly which lines in the spectra you identify with the groups in your structures.

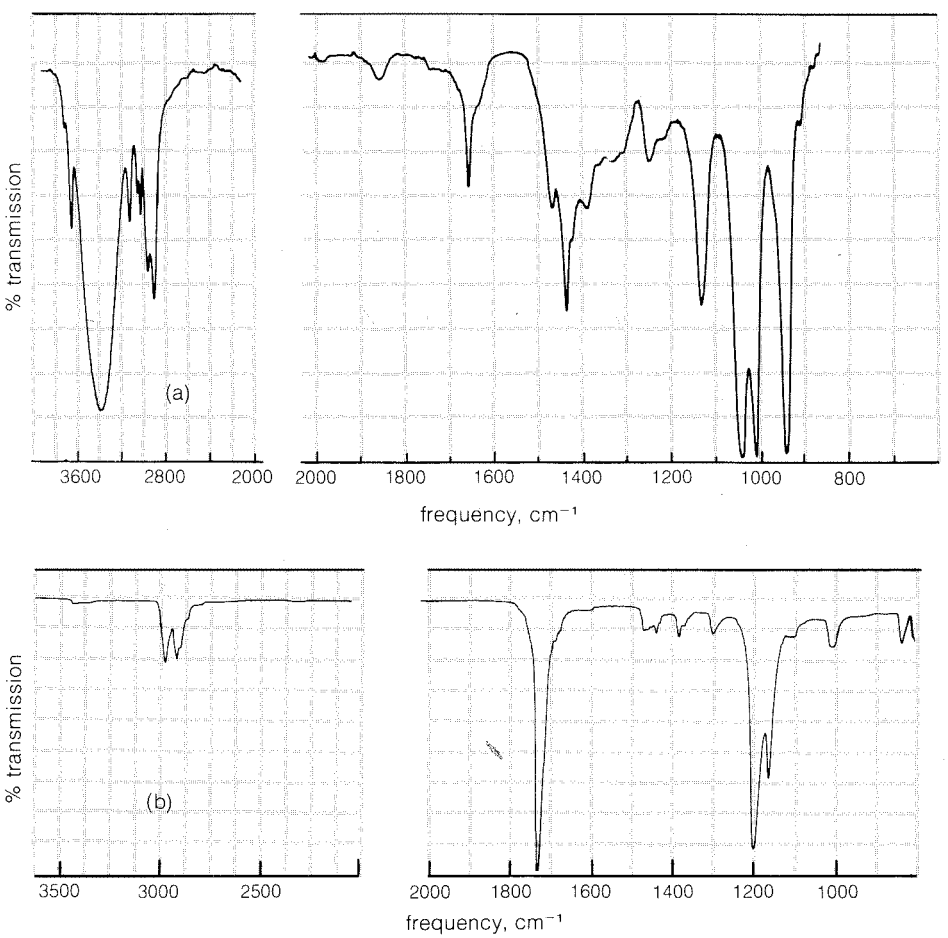


Figure 9-14 Infrared spectra for Exercise 9-11. Spectrum (a) corresponds to C_3H_6O and Spectrum (b) to $C_3H_6O_2$.

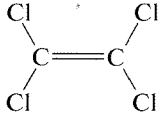
9-8 RAMAN SPECTROSCOPY

Raman spectroscopy often is a highly useful adjunct to infrared spectroscopy. The experimental arrangement for Raman spectra is quite simple in principle. Monochromatic light, such as from an argon-gas laser, is passed through a sample, and the light scattered at right angles to the incident beam is analyzed by an optical spectrometer.

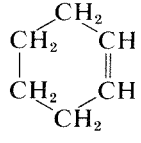
Raman spectra arise as a result of light photons being "captured" momentarily by molecules in the sample and giving up (or gaining) small increments of energy through changes in the molecular vibrational and rotational energies before being emitted as scattered light. The changes in the vibrational and rotational energies result in changes in wavelength of the incident light. These changes are detected as lines falling both above and below the wavelength of the incident light. The line positions in Raman spectra always are reported in wave numbers. Highly efficient laser Raman spectrometers are commercially available.

Although changes in wavelength in Raman scattering correspond to absorption or emission of infrared radiation, infrared and Raman spectra are not always identical. Indeed, valuable information about molecular symmetry may be obtained by comparison of infrared and Raman spectra. When a bond is *electrically symmetrical* it does not absorb infrared radiation and, for this reason, symmetrical diatomic molecules such as H_2 and O_2, which are always electrically symmetrical, do not give infrared absorption spectra. However, excitation of symmetrical vibrations does occur in Raman scattering.[7] In a molecule such as ethene, $CH_2{=}CH_2$, the double-bond stretching vibration is symmetrical, because both ends of the molecule are the same. As a result, the double-bond stretching absorption is not observable in the infrared spectrum of ethene and is weak in all nearly symmetrically substituted ethenes. Nonetheless, this vibration appears strongly in the Raman spectrum of ethene and provides evidence for a symmetrical structure for ethene.

As a general conclusion, a molecule has no important symmetry if *all* its infrared bands have counterparts in Raman scattering. To illustrate these effects, the Raman and infrared spectra of tetrachloroethene and cyclohexene are shown in Figures 9-15 and 9-16. Absorption due to the stretching vibration of the double bond in tetrachloroethene (1570 cm^{-1}) is strong in the Raman and absent in the infrared, whereas that arising from the less symmetrical double bond of cyclohexene (1658 cm^{-1}) is weak in the infrared and slightly stronger in the Raman.



tetrachloroethene



cyclohexene

[7]This is in accord with the spectroscopic "selection rules," derived from theoretical arguments, that predict which transitions between rotational and vibrational energy levels are "allowed" and which are "forbidden."

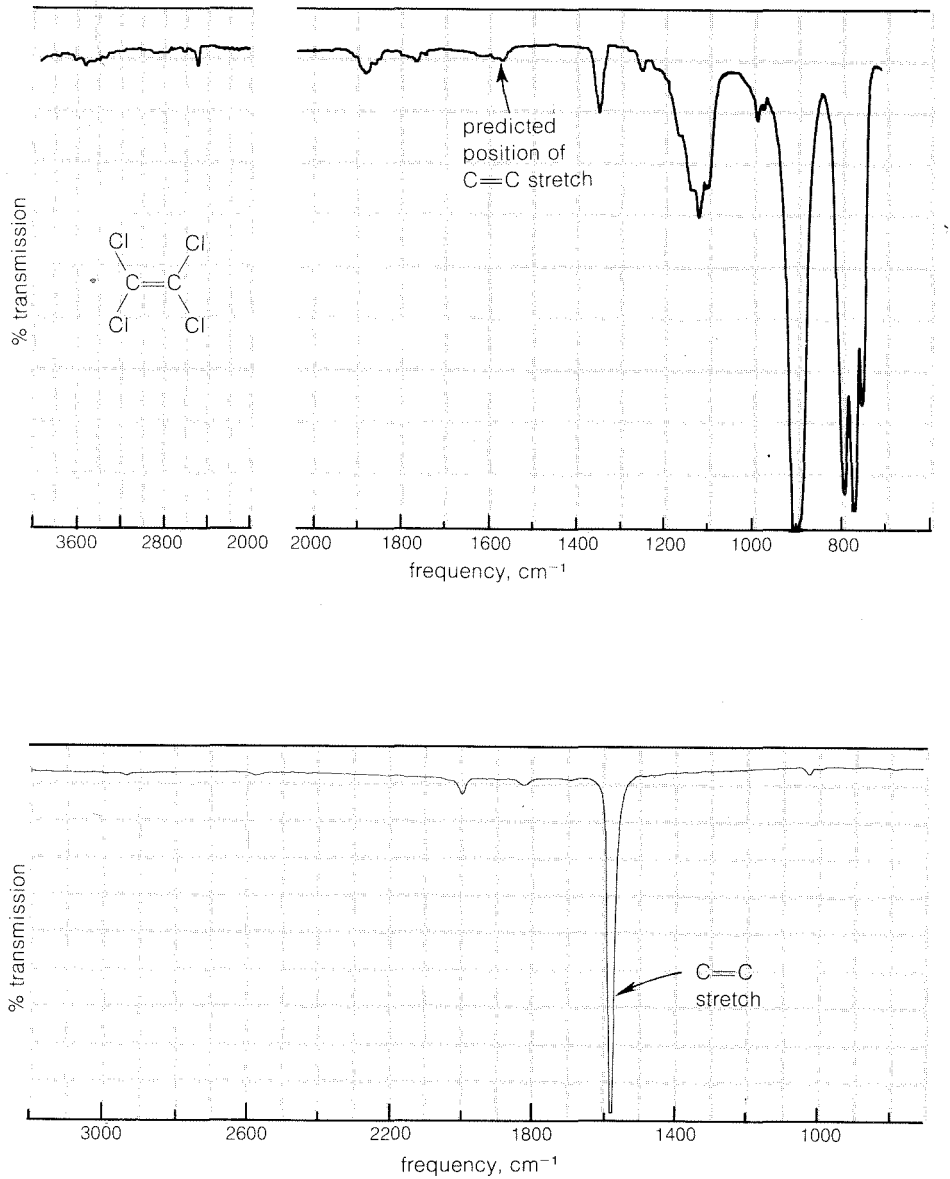


Figure 9-15 Infrared (top) and Raman spectra (bottom) of tetrachloroethene (notice that the spacings and alignment of the horizontal scales are not the same). The Raman spectrum was supplied courtesy of the Applied Physics Corporation.

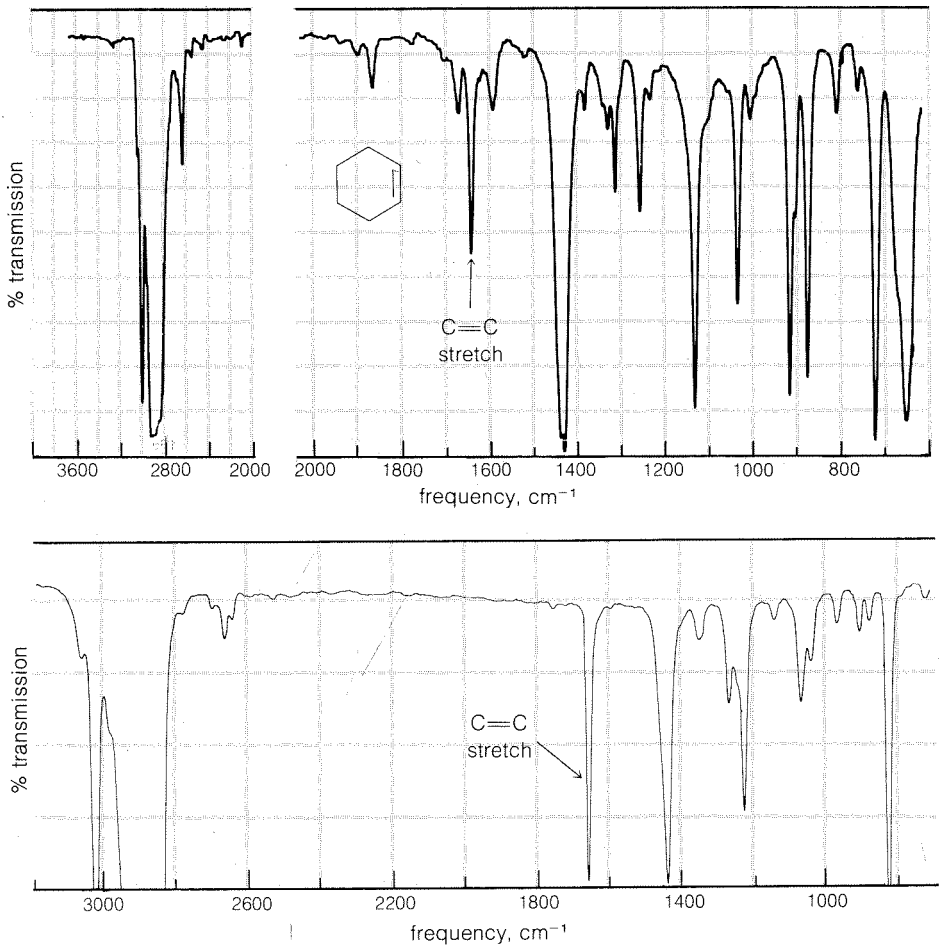


Figure 9-16 Infrared (top) and Raman spectra (bottom) of cyclohexene (notice that the spacings and alignment of the horizontal scales are not the same). The Raman spectrum was supplied courtesy of the Applied Physics Corporation.

Exercise 9-12* Classify the following molecules according to the general characteristics expected for their infrared and Raman spectra: (**a**) HC≡CH; (**b**) ICl; (**c**) CO; (**d**) $CF_2{=}CH_2$ (double-bond stretch only); (**e**) $(CH_3)_2C{=}CH_2$ and $CH_3CH{=}CHCH_3$ (double-bond stretch only).

Exercise 9-13* Carbon dioxide gives two infrared absorption bands but only one Raman line. This Raman line corresponds to a *different* vibration than the infrared absorptions. Decide which vibrational modes are infrared active (i.e., make the molecule electrically unsymmetrical during at least part of the vibration) and which is Raman active (i.e., occurs so the molecule is electrically symmetrical at all times during the vibration, see Section 9-7A).

9-9 ELECTRONIC SPECTRA OF ORGANIC MOLECULES

9-9A General Characteristics

A year after Herschel discovered infrared radiation, Johann Ritter discovered radiation beyond the violet end of the visible spectrum. This radiation came to be known as *ultraviolet* and soon was recognized as being especially effective in causing chemical reactions.

Absorption of light in the ultraviolet and visible regions produces changes in the electronic energies of molecules associated with excitation of an electron from a stable to an unstable orbital. Because the energy required to excite the valence-shell electrons of molecules is comparable to the strengths of chemical bonds, absorption may lead to chemical reactions. We discussed this briefly in Chapter 4 in connection with photochemical halogenation of alkanes; a more detailed account of photochemistry is given in Chapter 28.

The transition of an electron from the ground state, E_1, to an excited electronic state, E_2, is accompanied by vibrational and rotational changes in the molecule, as shown in Figure 9-17. It usually is not possible to resolve the resulting absorption *bands* well enough to see the fine structure due to vibration–rotation transitions. Consequently, absorptions due to electronic excitation are relatively broad.

The ultraviolet spectrum of 2-propanone (acetone) is shown in Figure 9-18. The weak absorption, which peaks (i.e., has λ_{max}) at 280 nm, is the result

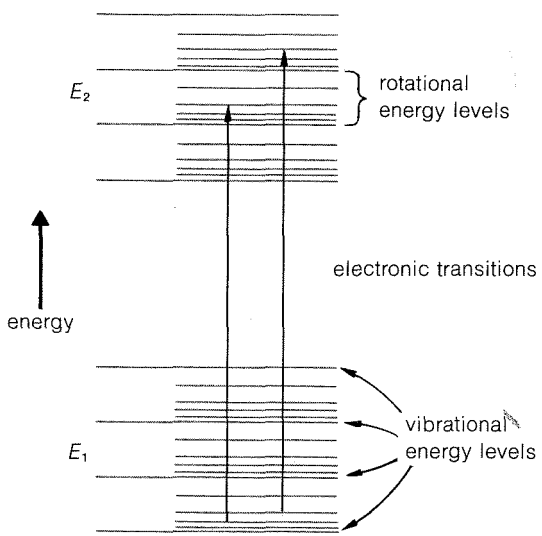


Figure 9-17 Schematic representation of electronic, vibrational, and rotational energy levels. The vertical scale is greatly distorted; rotational energy levels are normally 10^{-4}–10^{-2} kcal mole^{-1} apart, vibrational energy levels are 1–10 kcal mole^{-1} apart, while electronic transitions involve 10–1000 kcal mole^{-1}.

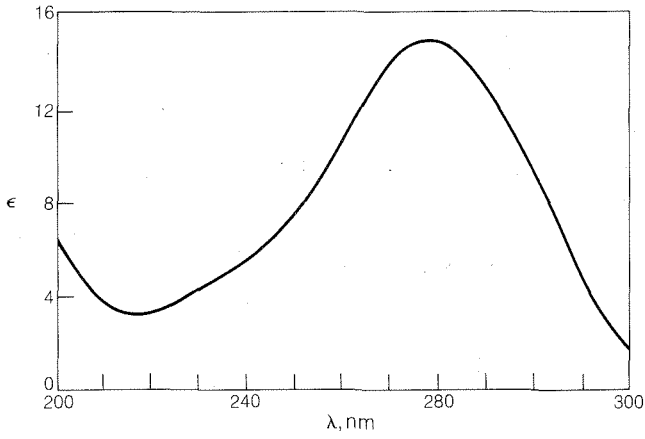


Figure 9-18 The ultraviolet spectrum of 2-propanone (acetone) in cyclohexane

of excitation of one of the unshared electrons on oxygen to a higher energy level. This is called an $n \longrightarrow \pi^*$ (often $N \longrightarrow A$) transition, in which n denotes that the excited electron is one of the unshared n electrons on oxygen and π^* (pi star) denotes that the excited electron goes to a high-energy *antibonding* orbital of the carbon-oxygen double bond (cf. Sections 6-2 and 6-4C). The same kind of $n \longrightarrow \pi^*$ transition occurs at about the same wavelength and intensity for many simple compounds of the type $R_2C{=}O$ and $RCH{=}O$, in which R is an alkyl group. In a very schematic way, we can write

$$R_2C::\underset{\cdot\cdot}{O}: \xrightarrow{n \longrightarrow \pi^*} R_2\dot{C}:\dot{\underset{\cdot\cdot}{O}}\cdot$$

There also is an absorption of 2-propanone with λ_{max} at 190 nm (the maximum is not shown in Figure 9-18), which is a different kind of excitation. This is ascribed to raising an electron in the π-bonding orbital (Section 6-4C) of the carbon–oxygen double bond to the π^* orbital. Such transitions are called $\pi \longrightarrow \pi^*$, and occur generally for substances with double bonds:

$$R_2C::\underset{\cdot\cdot}{O}: \xrightarrow{\pi \longrightarrow \pi^*} R_2\dot{C}:\dot{\underset{\cdot\cdot}{O}}:$$

Table 9-3 lists the wavelengths of maximum absorption for some typical electronic absorption bands of simple molecules. If we remember that absorptions at *longer* wavelengths correspond to *less energetic* transition, it can be deduced from the λ_{max} values that less energy is required to excite unshared (nonbonding) electrons than π electrons in double or triple bonds, which in turn require less energy than σ electrons in single bonds (Figure 9-19).

Table 9-3
Some Electronic Transitions of Simple Organic Molecules

Compound	Type	λ_{max}, nm	ϵ_{max}[a]	Solvent[b]
$(CH_3)_2C{=}O$	$n \longrightarrow \pi^*$	280.0	15	cyclohexane
	$\pi \longrightarrow \pi^*$[c]	190.0	1,100	
	$n \longrightarrow \sigma^*$[c]	156.0	strong	
$CH_2{=}CH_2$	$\pi \longrightarrow \pi^*$	175.0	10,000	vapor
$CH_2{=}CH{-}CH{=}CH_2$	$\pi \longrightarrow \pi^*$	217.0	20,900	hexane
$CH_3{-}CH{=}CH{-}CH{=}CH{-}CH_3$	$\pi \longrightarrow \pi^*$	227.0	22,500	hexane
$CH_2{=}CH{-}CH_2{-}CH_2{-}CH{=}CH_2$	$\pi \longrightarrow \pi^*$	185.0	20,000	alcohol
$CH_3{-}C{\equiv}CH$	$\pi \longrightarrow \pi^*$	186.5	450	cyclohexane
$CH_2{=}CH{-}C(=O){-}CH_3$	$n \longrightarrow \pi^*$	324.0	24	alcohol
	$\pi \longrightarrow \pi^*$	219.0	3,600	
CH_4	$\sigma \longrightarrow \sigma^*$[d]	121.9	strong	vapor
$CH_3{-}CH_3$	$\sigma \longrightarrow \sigma^*$[d]	135.0	strong	vapor
$CH_3{-}Cl$	$n \longrightarrow \sigma^*$[e]	172.5	weak	vapor
$CH_3{-}Br$	$n \longrightarrow \sigma^*$[e]	204.0	200	vapor
$CH_3{-}I$	$n \longrightarrow \sigma^*$[e]	257.5	365	pentane
$CH_3{-}O{-}H$	$n \longrightarrow \sigma^*$[e]	183.5	150	vapor
$CH_3{-}O{-}CH_3$	$n \longrightarrow \sigma^*$[e]	183.8	2,520	vapor
$(CH_3)_3N$	$n \longrightarrow \sigma^*$[e]	227.3	900	vapor

[a]The molar extinction coefficient ϵ is a measure of the absorption efficiency at the wavelength λ_{max}. Because the amount of absorption is proportional to the concentration (c moles liter^{-1}) and thickness of the sample (l cm), ϵ is obtained from the equation

$$\epsilon = \frac{1}{cl} \log_{10} \frac{I_0}{I} \quad \text{or} \quad \epsilon cl = A$$

in which I_0/I is the ratio of intensity of incident light I_0 to transmitted light I. The percent transmission of a solution is $(I/I_0) \times 100$ and the absorbance $A = \log I_0/I$. Substances for which ϵ is independent of concentration are said to obey Beer's law (or the Beer–Lambert law).

[b]It is necessary to specify the solvent because λ_{max} and ϵ_{max} vary somewhat with solvent.

[c]These assignments are not certain.

[d]Transitions $\sigma \longrightarrow \sigma^*$ correspond to excitation of a σ electron of a single bond to a higher-energy antibonding orbital of the single bond, σ^* (sigma star).

[e]Transitions $n \longrightarrow \sigma^*$ correspond to excitation of an electron of an unshared pair to an antibonding orbital (σ^*) of a σ bond.

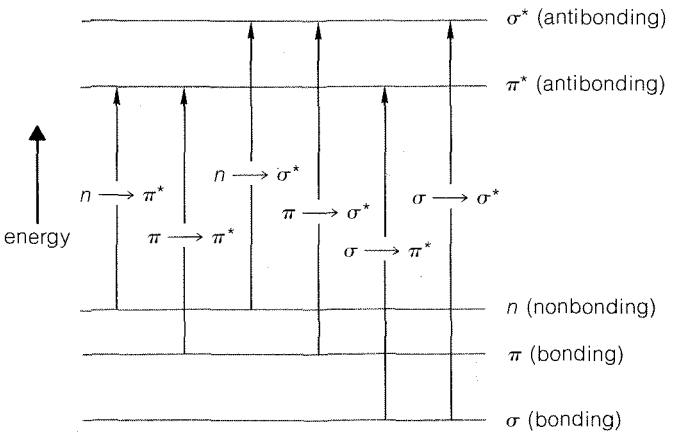


Figure 9-19 Sequence of electronic orbital energies, showing different kinds of transitions in approximate order of increasing energy, left to right. The $\sigma \longrightarrow \pi^*$ and $\pi \longrightarrow \sigma^*$ transitions usually have low transition probabilities, meaning the bands have low or zero intensities.

Exercise 9-14 List the kinds of electronic transitions that would be expected for azaethene (methyleneimine), $CH_2{=}\dot{N}H$, in order of increasing energy. Use the data in Table 9-3 to predict approximately the wavelengths at which the three lowest-energy transitions should occur.

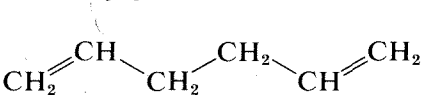
Exercise 9-15 Calculate the percentage of the incident light that would be absorbed by an 0.010*M* solution of 2-propanone (acetone) in cyclohexane contained in a quartz cell 0.1 cm long at 280 nm and at 190 nm (see footnote *a* of Table 9-3).

Exercise 9-16 Explain why the absorption band at 227.3 nm for trimethylamine, $(CH_3)_3N$, disappears in *acid* solution.

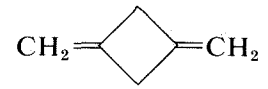
9-9B Effects of Conjugation on Electronic Spectra

The $\pi \longrightarrow \pi^*$ transition for ethene has $\lambda_{max} = 175$ nm and $\epsilon_{max} = 10{,}000$. It would be expected that an alkadiene would give an absorption spectrum similar to that of ethene but with a larger ϵ, because there are more double bonds per mole to absorb radiation. This expectation is more or less realized for compounds such as 1,5-hexadiene and 1,3-dimethylenecyclobutane, which have *isolated* double bonds, but not for 1,3-butadiene or ethenylbenzene, which

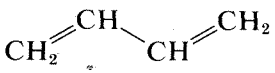
have *conjugated* double bonds (Section 3-3):



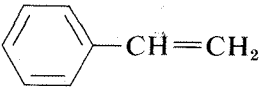
1,5-hexadiene
$\lambda_{max} = 185$ nm, $\epsilon = 20{,}000$



1,3-dimethylenecyclobutane
$\lambda_{max} < 200$ nm



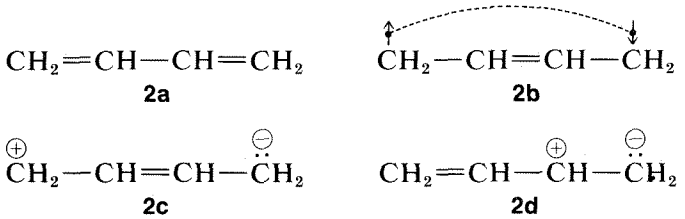
1,3-butadiene
$\lambda_{max} = 217$ nm, $\epsilon = 21{,}000$



ethenylbenzene (styrene)
$\lambda_{max} = 244$ nm, $\epsilon = 12{,}000$

In general, *conjugated systems of double bonds absorb radiation of longer wavelengths and with greater intensity than corresponding systems of isolated double bonds.* This means that the difference in energy between the normal and excited states of conjugated systems is *less* than for isolated systems of double bonds. For 1,3-butadiene and 1,5-hexadiene we can calculate from Equation 9-2 $[(28{,}600)(217 - 185)/(217 \times 185)]$ that the transition energy is about 23 kcal less for the conjugated system. The ground state of 1,3-butadiene is stabilized by perhaps 3 kcal relative to a nonconjugated system of double bonds, which means that the excited state must be much more stabilized than this if the transition energy is to be 23 kcal less than for 1,5-hexadiene.

Why is the excited state of a conjugated system of double bonds stabilized more, relative to the ground state, than for a nonconjugated system? Resonance theory provides an explanation (see Section 6-5). Of the several conventional valence-bond structures that can be written for 1,3-butadiene, four of which are shown here, **2a–2d**, only structure **2a** has a low enough energy to be dominant for the ground state of 1,3-butadiene:



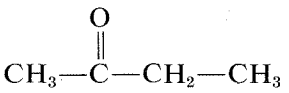
2a **2b**

2c **2d**

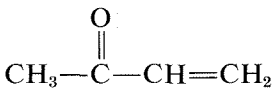
Now, when the molecule is excited to the extent of 132 kcal mole^{-1} by 217 nm ultraviolet light, its energy is so large that pairing schemes such as **2b**, **2c**, and **2d**, which are too unfavorable to contribute very much to the ground state, can be very important for the excited state. Thus the stabilization energy of the excited state, which has a multiplicity of nearly equal-energy pairing schemes, is expected to be greater than that of the ground state with one dominant pairing scheme.

The more double bonds in the conjugated system, the smaller the energy difference between the normal and excited states. The diphenylpolyenes of formula $C_6H_5{+}CH{=}CH{\rightarrow}_{\overline{n}}C_6H_5$ absorb radiation at progressively *longer* wavelengths as n is increased. This is apparent from the colors of the compounds, which range from colorless with $n = 1$, to orange with $n = 2$–7, to red with $n = 8$, as λ_{max} goes from the ultraviolet into the visible region of the electromagnetic spectrum.

Similar effects are found with conjugated C=O and C=N double bonds. For example, the electronic spectra of 2-butanone and 3-buten-2-one are shown in Figure 9-20.



2-butanone
(*methyl ethyl ketone*)



3-buten-2-one
(*methyl vinyl ketone*)

The absorption at 277 nm for 2-butanone is an $n \longrightarrow \pi^*$ transition, and with 3-buten-2-one, this absorption shifts to longer wavelengths (324 nm). There is also an intense absorption band for 3-buten-2-one at 219 nm, which is a $\pi \longrightarrow \pi^*$ transition. With 2-butanone a corresponding absorption occurs at 185 nm, which is out of the range of the spectrometer used to take the spectra of Figure 9-20.

Conjugation also can influence infrared spectra. Transitions arising from C=C and C=O stretching vibrations generally are more intense and are shifted to slightly lower frequencies (longer wavelengths) for conjugated compounds relative to nonconjugated compounds. Thus the C=C stretching of 1-butene occurs at 1650 cm^{-1}, whereas that of 1,3-butadiene is observed at 1597 cm^{-1}.

Alkanes and cycloalkanes have no low-energy electronic transitions comparable to conjugated systems or molecules with nonbonding electrons. Therefore alkanes and cycloalkanes show no absorption above 200 nm and are good solvents to use for electronic spectroscopy.

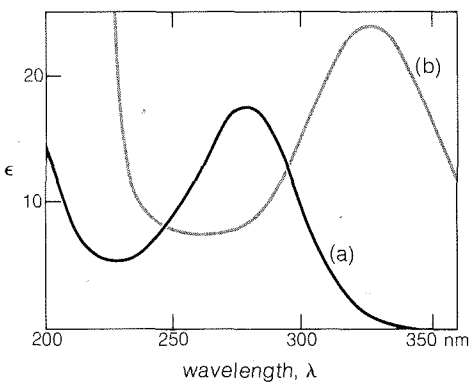


Figure 9-20 Electronic spectra of (a) 2-butanone and (b) 3-buten-2-one in cyclohexane solution

9-9C Applications of Electronic Spectroscopy

How do we use electronic spectroscopy in chemical analysis? The two principal applications are structure determinations and quantitative analysis.

The position and intensity of an electronic absorption band provides information as to chemical structure. Such absorptions normally are not as useful as infrared absorptions because they do not give as detailed information. For our purposes here, the main points to remember are:

1. A weak absorption (ϵ = 10–100) suggests an $n \longrightarrow \pi^*$ transition of an isolated carbonyl group. If this absorption is found in the region 270–350 nm an aldehyde or ketone is probable.
2. Somewhat stronger absorptions (ϵ = 100–4000) between 200 nm and 260 nm may correspond to $n \longrightarrow \sigma^*$ transitions.
3. Strong absorptions (ϵ = 10,000–20,000) usually are characteristic of $\pi \longrightarrow \pi^*$ transitions. If absorption occurs above 200 nm, a conjugated system of multiple bonds is indicated. Each additional carbon–carbon double bond shifts λ_{max} about 30 nm to longer wavelengths and enhances the intensity of absorption. Conjugation also shifts λ_{max} of $n \longrightarrow \pi^*$ transitions to longer wavelengths.

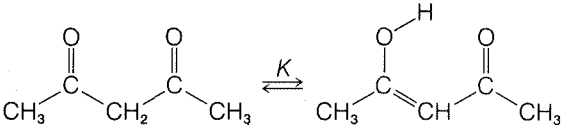
If we are dealing with compounds for which the wavelengths and the molar intensities of the absorption bands are known, then we can use the degree of absorption for quantitative analysis with the aid of the Beer–Lambert law (see Table 9-3 for definitions):

$$A = \epsilon c l$$

By measuring the absorbance A of a sample of known ϵ in a cell of known path length l, the concentration c may be determined. Because changes in absorbance reflect changes in concentration, it is possible to use absorbance measurements to follow rates of chemical reactions, to determine equilibrium constants (such as the dissociation constants of acids and bases), and to follow conformational changes in bio-organic molecules such as proteins and nucleic acids.

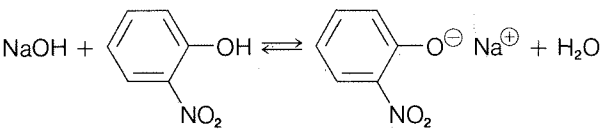
Exercise 9-17 A compound of formula C_4H_6O has two absorption bands in the ultraviolet: λ = 320 nm, ϵ = 30 and λ = 218 nm, ϵ = 18,000 in ethanol solution. Draw three possible structures that are consistent with this information.

Exercise 9-18 2,4-Pentanedione exists in equilibrium with 4-hydroxy-3-penten-2-one:

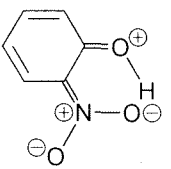


The infrared spectrum of the liquid mixture shows a broad absorption band at 3000–2700 cm^{-1} and an intense absorption band at 1613 cm^{-1}. In cyclohexane solution, the substance has λ_{max} at 272 nm with $\epsilon_{max} = 12{,}000$. (**a**) What can you conclude from this data as to the magnitude of *K*, the equilibrium constant for the interconversion of the two forms? (**b**) What can you deduce from the fact that the absorption at 272 nm is much weaker in aqueous solution (pH 7) than it is in cyclohexane?

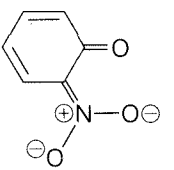
Exercise 9-19* The electronic absorption spectrum of 2-nitrobenzenol has λ_{max} in 0.1*M* HCl at 350 nm. In 0.1*M* NaOH, the benzenol is largely converted to its anion, and λ_{max} shifts to 415 nm.



The ground-state resonance forms of 2-nitrobenzenol and its anion include



2-nitrobenzenol



anion

Explain how the relative importance of these resonance forms to the ground and excited states of 2-nitrobenzenol and its anion can account for the fact that the anion absorbs at longer wavelengths than does 2-nitrobenzenol. (Review Section 6-5B)

Exercise 9-20* A solution containing the two forms of the important coenzyme nicotinamide adenine dinucleotide (abbreviated $NAD^{\oplus}$ and NADH; see Section 15-6C for structures) has an absorbance in a 1-cm cell of 0.311 at 340 nm and 1.2 at 260 nm. Both $NAD^{\oplus}$ and NADH absorb at 260 nm, but only NADH absorbs at 340 nm. The molar extinction coefficients are

Compound	260 nm	340 nm
$NAD^{\oplus}$	18,000	~ 0
NADH	15,000	6220

Calculate the proportions of $NAD^{\oplus}$ and NADH in the mixture.

9-10 NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

Nuclear magnetic resonance (nmr) spectroscopy is extremely useful for identification and analysis of organic compounds. The principle on which this form of spectroscopy is based is simple. The nuclei of many kinds of atoms act like tiny magnets and tend to become aligned in a magnetic field. In nmr spectroscopy, we measure the energy required to change the alignment of magnetic nuclei in a magnetic field. To illustrate the procedure with a simple example, consider the behavior of a proton (^1H) in a magnetic field. There are two possible alignments of this magnetic nucleus with respect to the direction of the applied field, as shown in Figure 9-21. The nuclear magnets can be aligned either with the field direction, or opposed to it. The two orientations are not equivalent, and energy is required to change the more stable alignment to the less stable alignment.

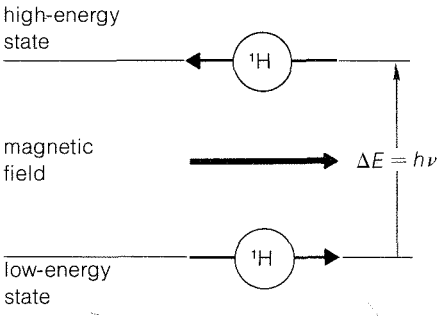


Figure 9-21 Schematic representation of the possible alignments of a magnetic nucleus (here hydrogen) in an applied magnetic field. Transitions between the two states constitute the phenomenon of nuclear magnetic resonance. The arrows through the nuclei represent the average component of their nuclear magnetic moment in the field direction.

A schematic diagram of an nmr instrument is shown in Figure 9-22. When a substance such as ethanol, $CH_3—CH_2—OH$, the hydrogens of which have nuclei (protons) that are magnetic, is placed in the transmitter coil and the magnetic field is increased gradually, at certain field strengths radio-frequency energy is absorbed by the sample and the ammeter indicates an increase in the flow of current in the coil. The overall result is a spectrum such as the one shown in Figure 9-23. This spectrum is detailed enough to serve as a useful "fingerprint" for ethanol, and also is simple enough that we will be able to account for the origin of each line. It is the purpose of this section to explain how the complexities of spectra such as that of Figure 9-23 can be interpreted in terms of chemical structure.

For what kinds of substances can we expect nuclear magnetic resonance absorption to occur? Magnetic properties always are found with nuclei of odd-numbered masses, ^1H, ^{13}C, ^{15}N, ^{17}O, ^{19}F, ^{31}P, and so on, as well as for

nuclei of even mass but odd atomic number, ^{2}H, ^{10}B, ^{14}N, and so on.[8] Nuclei such as ^{12}C, ^{16}O, and ^{32}S, which have even mass and atomic numbers, have *no* magnetic properties and do *not* give nuclear magnetic resonance signals. For various reasons, routine use of nmr spectra in organic chemistry is con-

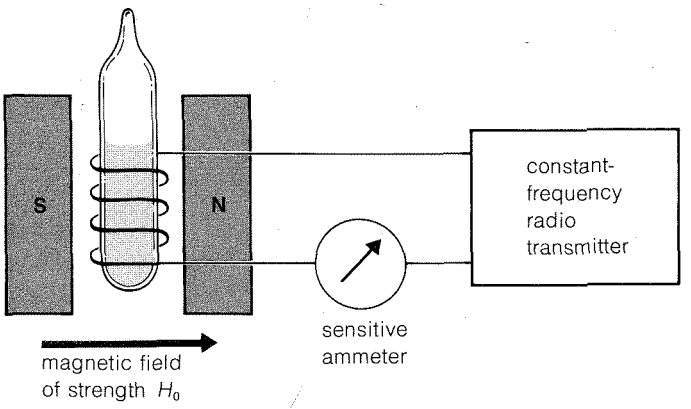


Figure 9-22 Essential features of a simple nmr spectrometer

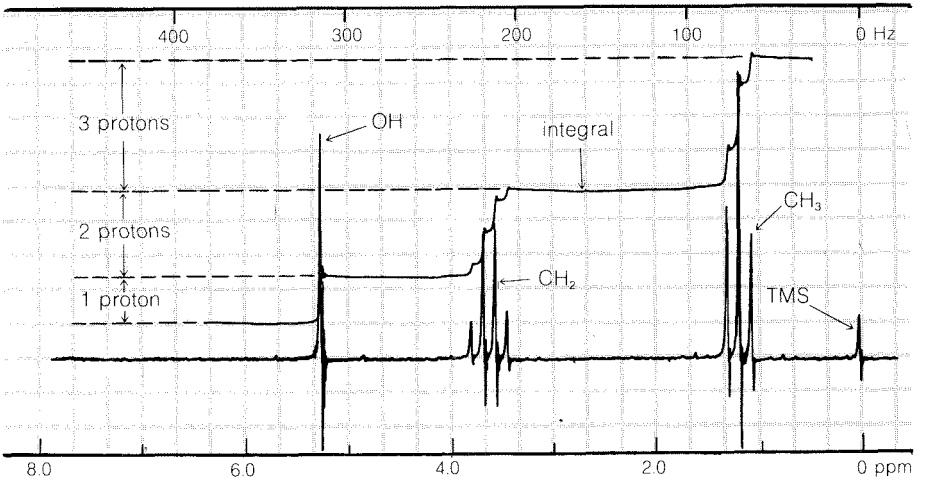


Figure 9-23 Proton nmr spectrum of ethanol (containing a trace of hydrochloric acid). Chemical shifts are relative to tetramethylsilane $(CH_3)_4Si$, that is, TMS = 0.00 ppm. The stepped line is an integral of the *areas* under each of the resonance lines.

[8]Although the principal isotopes of Cl, Br, and I have magnetic properties, because of the special character of all of these isotopes, they act in organic compounds as though they were *nonmagnetic*.

fined to ^1H, ^{19}F, ^{13}C, and ^{31}P. We shall be concerned in this chapter only with nmr spectra of hydrogen (^1H) and of carbon (^{13}C).

The kind of nmr spectroscopy we shall discuss here is limited in its applications because it can be carried out only with *liquids* or *solutions*. Fortunately, the allowable range of solvents is large, from hydrocarbons to concentrated sulfuric acid, and for most compounds it is possible to find a suitable solvent.

Nuclear magnetic resonance spectra may be so simple as to have only a single absorption peak, but they also can be much more complex than the spectrum of Figure 9-23. However, it is important to recognize that no matter how complex an nmr spectrum appears to be, it involves just *three* parameters: **chemical shifts, spin-spin splittings,** and **kinetic** (reaction-rate) **processes.** We shall have more to say about each of these later. First, let us try to establish the relationship of nmr spectroscopy to some of the other forms of spectroscopy we already have discussed in this chapter.

9-10A The Relation of NMR to Other Kinds of Spectroscopy

Nuclear magnetic resonance[9] spectroscopy involves transitions between the possible energy levels of magnetic nuclei in an applied magnetic field (see Figure 9-21). The transition energies are related to the frequency of the absorbed radiation by the familiar equation $\Delta E = h\nu$. An important difference between nmr and other forms of spectroscopy is that ΔE is influenced by the strength of the applied field. This should not be surprising, because if we are to measure the energy of changing the direction of alignment of a magnetic nucleus in a magnetic field, then the stronger the field the more energy will be involved.

Nuclear spin (symbolized as I) is a quantized property that correlates with nuclear magnetism such that when I is zero the nucleus has no spin and no magnetic properties. Examples are ^{12}C and ^{16}O. Several nuclei of particular interest to organic chemists—^1H, ^{13}C, ^{15}N, ^{19}F, and ^{31}P—have spin of $1/2$. With $I = 1/2$ there are only *two* magnetic energy states of the nucleus in a magnetic field. These states are designated with the **spin quantum numbers** $+1/2$ and $-1/2$. The difference in energy between these states, ΔE, is given by

$$\Delta E = \gamma h H = h\nu \qquad \text{or} \qquad \nu = \gamma H$$

in which h is Planck's constant, ν is in hertz, γ is a nuclear magnetic constant called the **gyromagnetic ratio,**[10] and H is the magnetic field strength at the

[9] *Resonance* in the sense used here means that the radio-frequency absorption takes place at specified "resonance" frequencies. However, you will see that almost all of the forms of spectroscopy we discuss in this book involve "resonance" absorption in the same sense.

[10] Here, γ is in Hz per gauss; physicists usually define γ in radians per sec per gauss.

nucleus. In general, H will not be exactly equal to H_0, the applied magnetic field and, as we will see, this difference leads to important chemical information. Each *kind* of nucleus (^1H, ^{13}C, ^{15}N, etc.) has its own γ value and, consequently, will undergo transitions at different frequencies at any particular value of H. This should become clearer by study of Figure 9-24.

There are several modes of operation of an nmr spectrometer. First and most common, we hold ν constant and vary (or "sweep") H_0. Close to $\nu = \gamma H$, energy is absorbed by the nuclei and the current flow from the transmitter increases until ν is exactly equal to γH. Further increase of H_0 makes $\nu < \gamma H_0$ and the current flow decreases. The form of the energy-absorption curve as a function of H_0 when H_0 is changed very slowly is shown in Figure 9-25a. The peak is centered on the point where $\nu = \gamma H$. When H_0 is changed more rapidly, transient effects are observed on the peak, which are a consequence of the fact that the nuclei do not revert instantly from the $-1/2$ to $+1/2$ state. The resulting

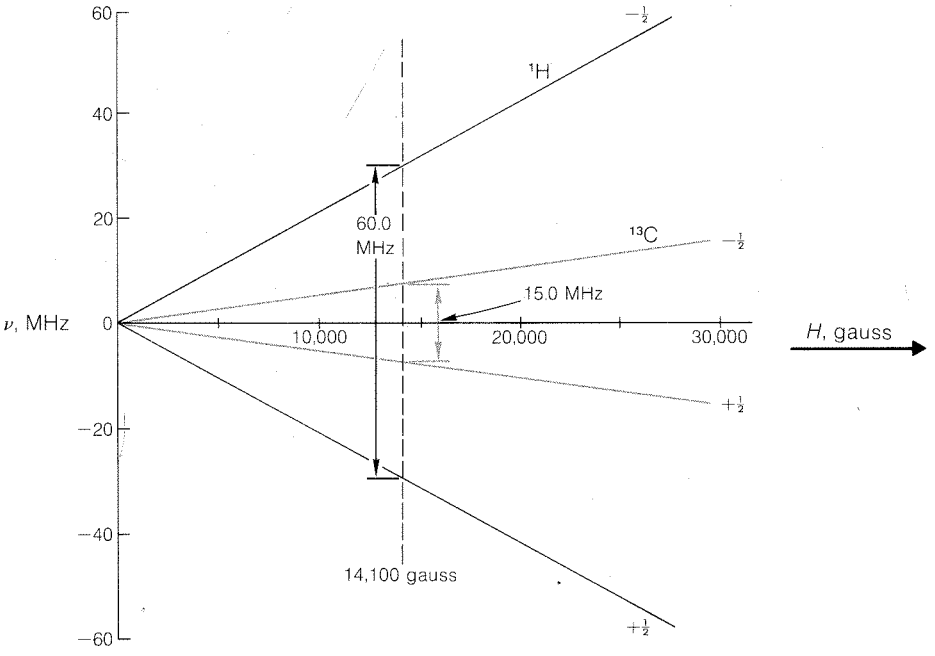


Figure 9-24 Field-frequency diagram that represents the energies (in frequency units) of the $+1/2$ and $-1/2$ magnetic states of ^1H and ^{13}C nuclei as a function of magnetic field. The vertical scale is of frequency ν in MHz (1 megahertz = 10^6 Hz = 10^6 cycles per sec) while the horizontal scale is of magnetic field in gauss. (For comparison, the Earth's magnetic field is about 0.2 gauss.) The dashed vertical line at 14,100 gauss tells us that the ^1H resonance frequency will be 60.0 MHz and the ^{13}C resonance frequency will be 15.0 MHz at this field strength.

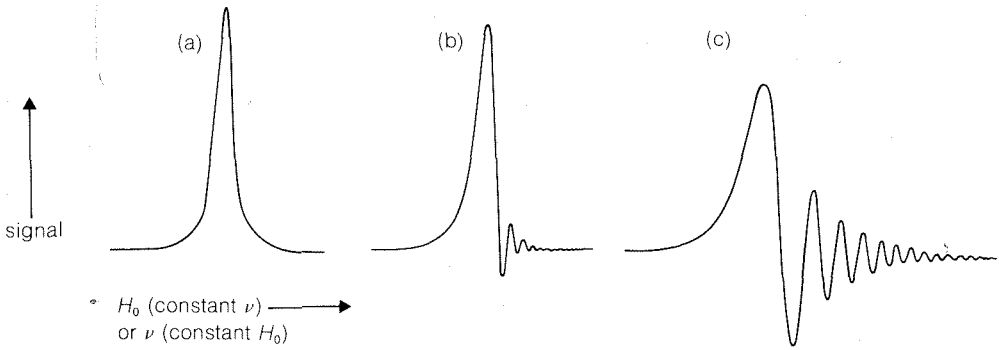


Figure 9-25 Comparison of sweep rates on nmr absorption curves: (a) 500-sec sweep, (b) 50-sec sweep, (c) 10-sec sweep. The "ringing" in the faster sweep curves is a transient effect that has a small effect on the position of the peak and none on the integral.

phenomenon is called "ringing" and is shown in Figures 9-25b and 9-25c. Evidence of ringing also will be seen on peaks of Figure 9-23.

An alternative method of running an nmr spectrometer is to hold the magnetic field constant and to sweep the transmitter frequency through the resonances. This mode of operation is more like other forms of spectroscopy and gives the same line shapes as sweeping the field (Figure 9-25).

What energy is associated with a ^1H nmr transition? The magnitude of this energy may be calculated from the relationship between energy and wavelength (frequency) of the absorbed radiation (Section 9-4). That is,

$$\Delta E = \frac{28{,}600}{\lambda} \text{ kcal mole}^{-1} \qquad \text{and} \qquad \lambda = \frac{c}{\nu}$$

The frequency ν is the operating frequency of the spectrometer, which we will take as 60 MHz or 6×10^7 Hz (cycles sec^{-1}), and the velocity of light is 3×10^8 m sec^{-1}. Hence

$$\lambda = \frac{3 \times 10^8 \times 10^9 \text{ (nm sec}^{-1})}{6 \times 10^7 \text{ (Hz)}} = 5 \times 10^9 \text{ nm}$$

and

$$\Delta E = \frac{28{,}600}{5 \times 10^9} = 5.7 \times 10^{-6} \text{ kcal mole}^{-1}$$

This is a very small energy difference, which means that only very few more of the nuclei are in the more stable $+1/2$ state than in the less stable $-1/2$ state. The equilibrium constant K for $-1/2 \rightleftharpoons +1/2$ calculated from Equation 4-2 (p. 84) for 25° (298°K) and neglecting possible entropy effects is 1.000010!

Exercise 9-21 Use Figure 9-24 to map the nmr spectrum you would expect for $^{13}CCl_3{}^1H$ in a field-sweep spectrometer in which the transmitter frequency is kept constant at 30 MHz and the magnetic field is swept from 0 to 30,000 gauss. Do the same for a frequency-sweep spectrometer when the magnetic field is kept constant at 10,000 gauss and the frequency is swept from 0 to 100 MHz. (For various reasons, practical spectrometers do not sweep over such wide ranges of field or frequency.)

Exercise 9-22* In nmr experiments, structural inferences sometimes are drawn from differences in resonance frequencies as small as 1 Hz. What difference in energy in kcal mole^{-1} does 1 Hz represent?

Exercise 9-23* The *intensity* of nmr signals normally increases markedly with decreasing temperature because more magnetic nuclei are in the $+1/2$ state. Calculate the equilibrium constant at $-90°$ for the $+1/2$ and $-1/2$ states of ^1H in a magnetic field of 42,300 gauss when the resonance frequency is 180 MHz.

9-10B The Chemical Shift

The plot of signal against magnetic field strength for ethanol in Figure 9-23 shows three principal groups of lines corresponding to the three varieties of hydrogen present: methyl (CH_3), methylene (CH_2), and hydroxyl (OH). Differences in the field strengths at which signals are obtained for nuclei of the same kind, such as protons, but located in different molecular environments, are called **chemical shifts.**

Another very important point to notice about Figure 9-23 is that the intensities of the three principal absorptions are in the ratio of 1:2:3, corresponding to the ratio of the number of each kind of proton (OH, CH_2, CH_3) producing the signal. In general, *areas under the peaks of a spectrum* such as in Figure 9-23 *are proportional to the number of nuclei in the sample that give those peaks.* The areas can be measured by electronic integration and the integral often is displayed on the chart, as it is in Figure 9-23, as a stepped line increasing from left to right. The height of each step corresponds to the relative number of nuclei of a particular kind. Unless special precautions are taken, integrals usually should not be considered accurate to better than about 5%.

Why do protons in different molecular environments absorb at different field strengths? The field strength H at a particular nucleus is *less* than the strength of the external magnetic field H_0. This is because the valence electrons around a particular nucleus and around neighboring nuclei respond to the applied magnetic field so as to **shield** the nucleus from the applied field. The way this shielding occurs is as follows.

First, when an atom is placed in a magnetic field, its electrons are forced to undergo a rotation about the field axis, as shown in Figure 9-26. Second,

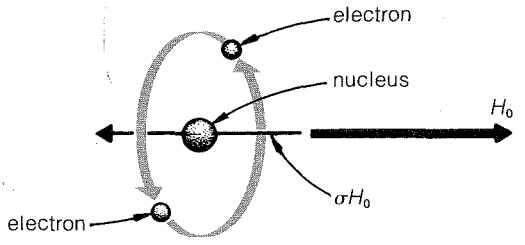


Figure 9-26 Induced magnetic field σH_0 at the nucleus as the result of rotation of electrons about the nucleus in an applied magnetic field H_0.

rotation of the electrons around the nucleus is a circulation of charge, and this creates a *small* magnetic field at the nucleus *opposite* in direction to H_0. Third, the magnitude of this *diamagnetic*[11] effect is directly proportional to H_0 and can be quantified as σH_0, in which σ is the proportionality constant. It is important to recognize that σ is not a nuclear property but depends on the *chemical* environment of the atom. Each chemically different proton will have a different value of σ and hence a different chemical shift.

The actual field H at the nucleus thus will be $H_0 - \sigma H_0$. Because σ acts to reduce the strength of the applied field at the nucleus, it is called the **magnetic shielding parameter.** The more shielding there is, the stronger the applied field must be to satisfy the resonance condition,

$$h\nu = (\gamma h)H = (\gamma h)(H_0 - \sigma H_0) = \gamma h H_0(1 - \sigma)$$

Common usage is: upfield, *more* shielding; downfield, *less* shielding; and you should remember that field-sweep spectra always are recorded with the field *increasing* from *left* to *right,*

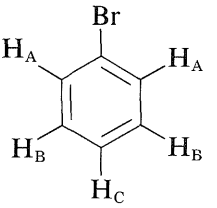
$$\underset{\text{less shielding}}{\overset{\text{low field}}{\longleftarrow}} \quad H_0 \quad \underset{\text{more shielding}}{\overset{\text{high field}}{\longrightarrow}}$$

9-10C Chemical Shift and Stereochemistry

The value of nmr spectroscopy in structure determination lies in the fact that chemically different nuclei absorb at different field strengths. In later sections we will be concerned with correlating the chemical shifts with structural features. However, before proceeding further it is extremely important that you be able to identify the number and kind of nonequivalent protons in a given structure, and therefore the number of chemical shifts to expect. This number is not always self-evident, especially when subtle factors of stereochemistry

[11] From the Greek prefix *dia* meaning through, across. The opposite of diamagnetic is **paramagnetic;** *para* meaning alongside. We shall use this term later.

intervene. For this reason, we suggest that you inspect structures **3–5** to convince yourself that the protons labeled with different letter subscripts in any one molecule are indeed chemically different.



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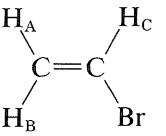

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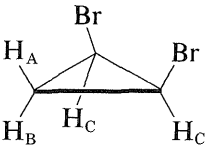
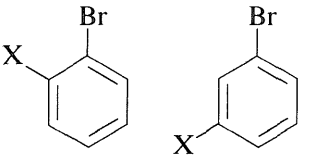
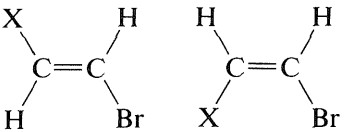


5

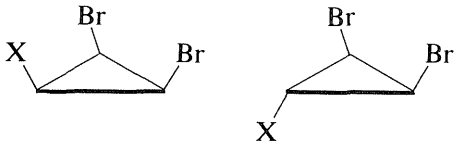
One way of checking whether two protons are in equivalent environments is to imagine that each is separately replaced with a different atom or group. If the product of replacing H_A is identical with that obtained by replacing H_B, then H_A and H_B are chemically equivalent. If the two products are nonidentical, then H_A and H_B are nonequivalent. For example, replacement of H_A or H_B in **3**, **4**, and **5** by an atom X would give different products. Therefore, H_A and H_B are nonequivalent in **3**, **4**, and **5**.



position isomers

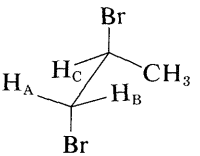


configurational isomers

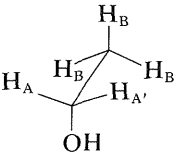


configurational isomers

Matters become more complicated with substances such as **6** and **7**:



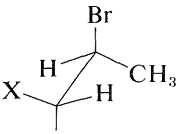
6



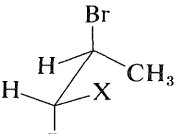
7

Notice that **6** represents a chiral molecule and if H_A and H_B each are replaced with X we get **8** and **9**, which are diastereomers (see Section 5-5). You can verify this with molecular models if necessary. Diastereomers have different

chemical and physical properties; therefore H_A and H_B in **6** are nonequivalent. They often are called **diastereotopic** hydrogens.



8



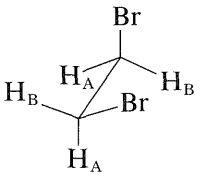
9

What of the two methylene protons in ethanol, **7**, which we have labeled as H_A $H_{A'}$? Are they identical? In a sense they are not identical because, if each were replaced by X, we would have a pair of enantiomers. Therefore, H_A and $H_{A'}$ sometimes are called **enantiotopic** hydrogens.

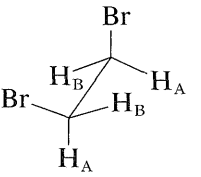
enantiomers

But, you will recall that enantiomers are chemically indistinguishable unless they are in a chiral environment. Therefore we expect shifts of enantiotopic hydrogens to be identical, unless they are in a chiral environment. To summarize, enantiotopic protons normally will have the same chemical shifts, whereas diastereotopic protons normally will have different chemical shifts.

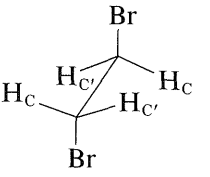
We so far have ignored the relationship of chemical shifts to conformational equilibria. Consider a specific example, 1,2-dibromoethane, for which there are three staggered conformations **10a**, **10b**, and **10c**:



10a



10b



10c

Each of these conformations is expected to have its own nmr spectrum. The two gauche forms, **10a** and **10b**, are enantiomers and their spectra should be identical. The hydrogens H_A in **10a** each are trans to the bromine on the adjacent carbon, while the H_B hydrogens are cis to the same bromines (see Section 5-5A). Consequently the H_A and H_B hydrogens are nonequivalent and would be expected to have different chemical shifts. In contrast, all of the hydrogens of the anti conformer, **10c**, are equivalent and would have the same chemical shift. Therefore we would expect to observe three chemical shifts arising from H_A, H_B, and H_C for a mixture of **10a**, **10b**, and **10c**. However,

the actual spectrum of 1,2-dibromoethane shows only *one sharp proton signal* under ordinary conditions. The reason is that the conformers are interconverted by bond rotation more rapidly than the magnetic nuclei can absorb the exciting radiation. The result is that we observe an *average* chemical shift, which reflects the relative shifts and populations of the three conformers present. If we can go to a sufficiently low temperature to make interconversion of the conformations slow (on the order of 10 times per second), then we will expect to see the three different chemical shifts H_A, H_B, and H_C with intensities corresponding to the actual populations of the conformations at the sample temperature. This is one example of the effect of rate processes on nmr spectra. Other examples and a more detailed account of how to relate the appearance of the signal to the rates of the exchange processes are given in Section 27-2.

Exercise 9-24 **a.** Identify the protons with different chemical shifts in each of the structures shown. Use letter subscripts H_A, H_B, and so on, to designate nonequivalent protons. Use models if necessary.

(i) *cis*- and *trans*-2-butene
(ii) 1,3-butadiene
(iii) 1-chloro-2,2-dimethylbutane
(iv) 2-butanol
(v) *trans*-1,2-dibromocyclopropane

b.* Why does 3-methyl-2-butanol have three methyl resonances with different chemical shifts in its proton nmr spectrum?

c.* For the compounds in Part a designate those protons (if any) that are enantiotopic or diastereotopic.

9-10D Chemical-Shift Standards and Units

Chemical shifts *always* are measured with reference to a standard. For protons or ^{13}C in organic molecules, *the customary standard is tetramethylsilane,* $(CH_3)_4Si$, which gives strong, sharp nmr signals in regions where only a very few other kinds of protons or carbon nuclei absorb. Chemical shifts often are expressed in Hz (cycles per second) relative to tetramethylsilane (TMS). These may seem odd units for magnetic field strength but because resonance occurs at $\nu = \gamma H$, either frequency units (Hz, radians sec^{-1}) or magnetic field units (gauss) are appropriate.

Ten years ago, most nmr spectrometers operated for protons with radio-frequency (rf) transmitters set at 60 MHz (6×10^7 cycles per sec) but there has been a proliferation of different proton-operating frequencies and now 30, 60, 90, 100, 220, 270, 300, and 360 MHz machines are commercially available. The cost of these machines is roughly proportional to the square of the frequency, and one well may wonder why there is such an exotic variety available and what this has to do with the chemical shift. High operating frequencies are desirable because chemical shifts increase with spectrometer frequency,

and this makes the spectra simpler to interpret. A 12-fold increase in operating frequency (as from 30 MHz to 360 MHz) means a 12-fold increase in H_0 at the point of resonance (remember $\nu = \gamma H$) and this means also a 12-fold increase in σH_0. Thus resonances that differ because they correspond to different σ values will be *twelve times farther apart* at 360 MHz than at 30 MHz. This can produce a dramatic simplification of spectra, as can be seen from Figure 9-27, which shows the effect of almost a factor of four in ν on the proton nmr spectrum of 2-methyl-2-butanol.[12]

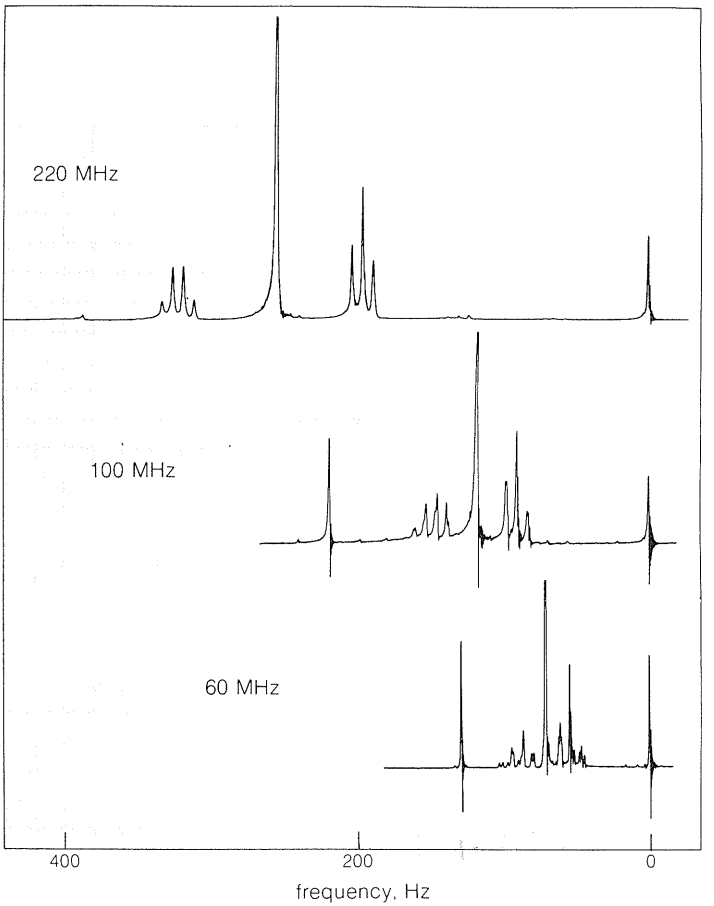


Figure 9-27 Comparison of the proton nmr spectra of 2-methyl-2-butanol at rf transmitter frequencies of 60, 100, and 220 MHz. The line at 165 Hz in the 60-MHz spectrum is due to the OH protons, and this is *off*-scale to the left in the 220-MHz spectrum. The large single line in the center of the spectra arises from the resonances of the six methyl hydrogens. The line at 0 Hz is TMS in each case.

[12]In addition to giving better separation of the lines and clearer spectra, going to higher fields also has the beneficial effect of increasing the proportions of the nuclei in the $+1/2$ state, thereby giving more intense, easier-to-detect resonances (cf. Exercise 9-23).

To reiterate, chemical shifts are strictly proportional to spectrometer frequency, thus lines 100 Hz apart at 60 MHz will be 167 Hz apart at 100 MHz. This might seem to make comparisons of nmr spectra on different spectrometers hopelessly complex but, because of the proportionality of shifts to frequency (or field), *if we divide the measured shifts in Hz* (relative to the same standard) for any spectrometer *by the transmitter frequency in MHz, we get a set of frequency-independent shifts in parts per million (ppm),* which are useful for all nmr spectrometers. Nmr shifts reported in ppm relative to TMS as zero, as shown in Figure 9-23, are called δ (delta) values:

$$\delta = \frac{(\text{chemical shift downfield in Hz relative to TMS}) \times 10^6}{\text{spectrometer frequency in Hz}}$$

Thus, if at 60 MHz a proton signal comes 100 Hz downfield relative to tetramethylsilane, it can be designated as being $(+100 \text{ Hz} \times 10^6)/60 \times 10^6 \text{ Hz} = +1.67$ ppm relative to tetramethylsilane. At 100 MHz, the line then will be $(1.67 \times 10^{-6})(100 \times 10^6) = 167$ Hz downfield from tetramethylsilane.

Typical proton chemical shifts relative to TMS are given in Table 9-4.[13] The values quoted for each type of proton may, in practice, show variations of 0.1–0.3 ppm. This is not unreasonable, because the chemical shift of a given proton is expected to depend somewhat on the nature of the particular molecule involved, and also on the solvent, temperature, and concentration.

A positive δ value means a shift to lower field (or lower frequency) with respect to TMS, whereas a negative δ signifies a shift to higher field (or higher frequency). The δ convention is accepted widely, but you often find in the literature proton shifts with reference to TMS reported as "τ values." The τ scale has the TMS reference at +10 ppm, so most proton signals fall in the range of $\tau = 0$ to $\tau = +10$. A τ value can be converted to the appropriate δ value by subtracting it from 10. Life with nmr spectra would be simpler if the τ scale would just go away.

9-10E Correlations Between Structure and Chemical Shifts

Proton chemical shifts are very valuable for the determination of structures, but to use the shifts in this way we must know something about the correlations that exist between chemical shift and structural environment of protons in organic compounds. The most important effects arise from differences in electronegativity, types of carbon bonding, hydrogen bonding, and chemical exchange.

[13]Many other proton-shift values are available in *NMR Spectra Catalog,* Volumes 1 and 2, Varian Associates, Palo Alto, Calif., 1962, 1963.

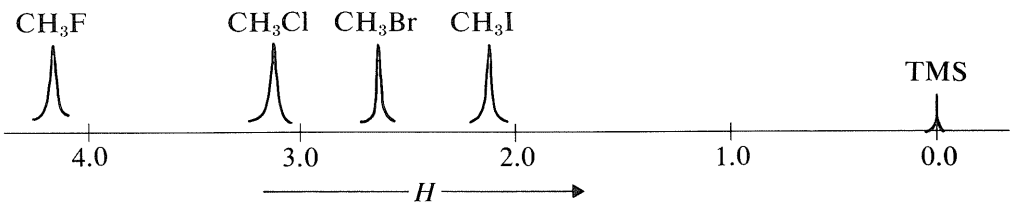
Electronegativity

Consider first the chemical shifts of protons attached to an sp^3 *carbon,* $-\overset{|}{\underset{|}{C}}-H$.

The degree of shielding of the proton by the carbon valence electrons depends on the character of the substituent atoms and groups present, and particularly on their electron-attracting power, or electronegativity. For a grouping of the type $H-\overset{|}{\underset{|}{C}}-X$, the shielding will be *less* as X is more electron withdrawing relative to hydrogen:

$X\leftarrow\overset{|}{\underset{|}{C}}-H$ if X is electron-withdrawing, the proton is deshielded

For example, the proton chemical shifts of the methyl halides (Table 9-4) show decreasing shielding, hence progressively low-field chemical shifts with increasing halogen electronegativity (F > Cl > Br > I):



The effect of electronegativity on a more remote proton as in $H-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-X$ is expected to be smaller as more bonds intervene. In fact, the CH_3 resonances of 19 quite different CH_3CH_2X derivatives fall in a range of not more than 0.6 ppm compared to 3 ppm for the CH_2 proton resonances (see Table 9-4). Figure 9-28 shows how the shift differences between the CH_3— and the —CH_2— protons in some CH_3CH_2X derivatives depend on the electronegativity of X, using the electronegativity defined by L. Pauling (see Section 10-4B). The trend is not wholly linear, but the proton chemical-shift differences become larger the more electronegative X becomes. We can predict with some confidence, therefore, that a molecule such as XCH_2CH_2Y will have lower-field chemical shifts (larger δ) for XCH_2— than for —CH_2Y if X is more electronegative than Y:

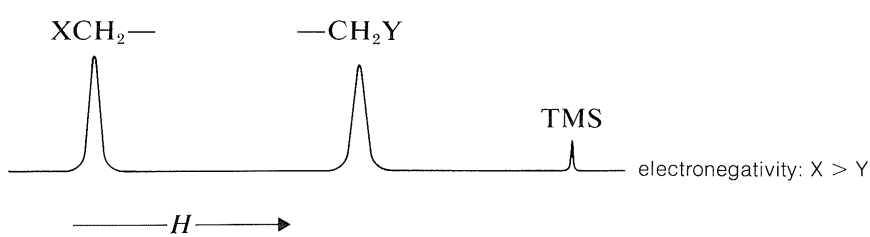


Table 9-4
Typical Proton Chemical-Shift Values (δ) in Dilute $CHCl_3$ Solutions

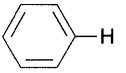
	Substituted Alkanes			
X	δ CH_3X	δ RCH_2X	δ R_2CHX	σ^a
—H	0.23	0.9	1.25	0.00
—R	0.9	1.25	1.5	0.47
—F	4.26	4.4	—	—
—Cl	3.05	3.4	4.0	2.53
—Br	2.68	3.33	4.1	2.33
—I	2.16	3.2	4.2	1.82
—OH	3.47	3.6	3.6	2.56
—OR	3.3	3.4	—	2.36
—OAr	3.7	3.9	—	3.23
—O—C(=O)—R	3.6	4.1	5.0	3.13
—O—C(=O)—Ar	3.8	4.2	5.1	—
—SH	2.44	2.7	—	—
—SR	2.1	2.5	—	1.64
—NR_2	2.2	2.6	2.9	1.57
—NHC(=O)R	2.8	—	3.2	—
—NO_2	4.28	4.4	4.7	—
—CHO	2.20	2.3	2.4	1.70
—C(=O)—R	2.1	2.4	2.5	1.70
—C(=O)—Ar	2.6	3.0	3.4	1.70
—C(=O)—OH	2.07	2.3	2.6	1.55

Table 9-4 (continued)
Typical Proton Chemical-Shift Values (δ) in Dilute $CHCl_3$ Solutions

Substituted Alkanes

X	δ CH_3X	δ RCH_2X	δ R_2CHX	σ[a]
$-\overset{\overset{O}{\|}}{C}-OR$	2.1	2.3	2.6	1.55
$-\overset{\overset{O}{\|}}{C}-NH_2$	2.02	2.2	–	1.59
$-CR{=}CR_2$	1.8	2.3	2.6	1.32
$-C_6H_5$	2.3	2.7	2.9	1.85
$-C{\equiv}CR$	2.0	–	–	1.44
$-C{\equiv}N$	2.0	2.3	2.7	1.70

Multiple-Bonded C—H

$R_2C{=}CH_2$	$R_2C{=}CHR$		$R-\overset{\overset{O}{\|}}{C}-H$	$RC{\equiv}C-H$
~5.0	~5.3	7.3	~9.7	~2.5

OH, NH, and SH Compounds

ROH	ArOH	$RC(=O)-OH$	RNH_2	$R_3\overset{\oplus}{N}H$	$RC(=O)NH_2$	RSH	ArSH
0.5–5	5–8	9–12	~1.0	~7.5	~7.8	~1.5	~3.0

[a]Effective shielding constants relative to H as zero. The use of these σ values is described in Section 9-10E.

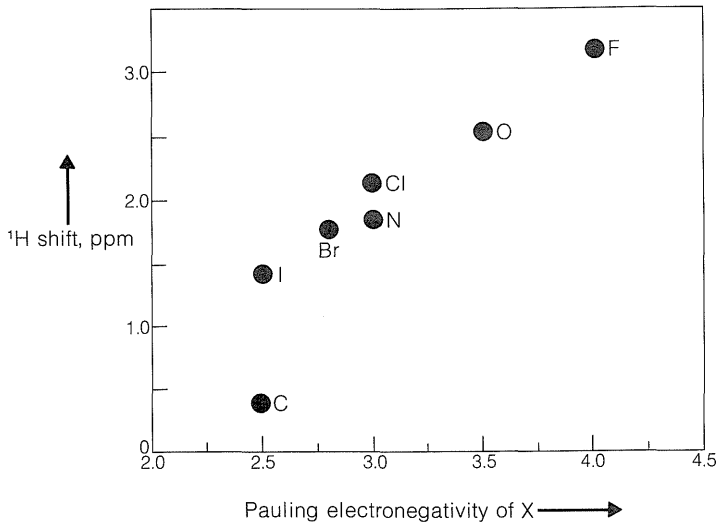


Figure 9-28 Chemical-shift differences between the CH_3 and CH_2 protons of CH_3CH_2X derivatives as a function of the Pauling electronegativity of X (see Section 10-5A)

When two electronegative groups, X and Y, are bonded to the *same* carbon, as in XCH_2Y, the protons are expected to be less shielded and come into resonance downfield of the methylenes of XCH_2CH_2Y. There is an approximate relationship (Equation 9-4) between the shifts of the XCH_2Y protons and the effective shielding constants (σ) of X and Y known as *Shoolery's rule.*

$$\delta = 0.23 + \sigma_X + \sigma_Y \qquad (9\text{-}4)$$

Appropriate values of σ for use with this equation are given in Table 9-4.

Exercise 9-25 Use Equation 9-4 to calculate the chemical shift of the $-CH_2-$ protons on (**a**) CH_2Cl_2, (**b**) $ClCH_2OCH_3$, and (**c**) $C_6H_5CH_2CO_2H$.

Effects of Carbon Bond Type

The shifts of the protons of alkanes and cycloalkanes fall in the range 0.9–1.5 ppm with C—H protons coming at the low-field end of this range and $-CH_3$ protons coming at the high-field end (see Table 9-4).

Alkenic hydrogens (vinyl hydrogens, $\diagdown\!\!\diagup C{=}CH-$) normally are observed between 4.6–6.3 ppm, which are 3.5–5 ppm toward *lower* fields than

the shifts of protons in alkanes and cycloalkanes. This means that alkenic hydrogens in an organic compound can be easily distinguished from alkane hydrogens.

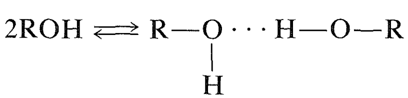
Aromatic protons, such as those in benzene, have shifts at still lower fields and commonly are observed at 7–8 ppm. In contrast, alkynic protons of the type —C≡CH give resonances that are *upfield* of alkenic or aromatic protons and come at 2–3 ppm. Another effect associated with multiple bonds is the large difference in shift between a $—CH(OCH_3)_2$ proton, which normally comes at about 5.5 ppm, and aldehyde protons, —CH=O, which are much farther *downfield* at 9–11 ppm.

Clearly, the shifts of a proton depend on whether the carbon forms single, double, or triple bonds. In a magnetic field, the circulation of electrons in the π orbitals of multiple bonds induced by the field (Figure 9-26) generates diamagnetic shielding effects in some regions of the multiple bond and paramagnetic deshielding effects in other regions. Apparently, protons attached to double-bonded carbons are in the deshielding zones and thus are downfield while protons attached to triple-bonded carbons are in the shielding zones and are observed at rather high field.

Hydrogen Bonding

When a proton is directly bonded to a strongly electronegative atom such as oxygen or nitrogen its chemical shift is critically dependent on the nature of the solvent, temperature, concentration, and whether acidic or basic impurities are present. The usual variations in chemical shift for such protons are so large (up to 5 ppm for alcohols) that no very useful correlations exist.

Hydrogen bonding is the major reason for the variable chemical shifts of OH and NH protons. In general, hydrogen bonding results in *deshielding*, which causes the resonances to move downfield. The extent of hydrogen bonding varies with concentration, temperature, and solvent, and changes in the degree of hydrogen bonding can cause substantial shift changes. This is very evident in the nmr spectrum of ethanol taken at different concentrations in CCl_4 (Figure 9-29). The hydroxyl resonance will be seen to move upfield at the lower concentrations. This is the result of decreasing association by hydrogen bonding through equilibria such as



Chemical Exchange

Many OH and NH compounds are weak acids and weak bases and can undergo autoprotolysis, which means that a proton can be transferred from one molecule to another. Suppose we have a compound such as 2-aminoethanol, $H_2NCH_2CH_2OH$. This substance normally would be expected to have an NH_2 proton resonance at about 1 ppm and an OH proton resonance at about 3 ppm. Autoprotolysis equilibria can *exchange* the protons between the

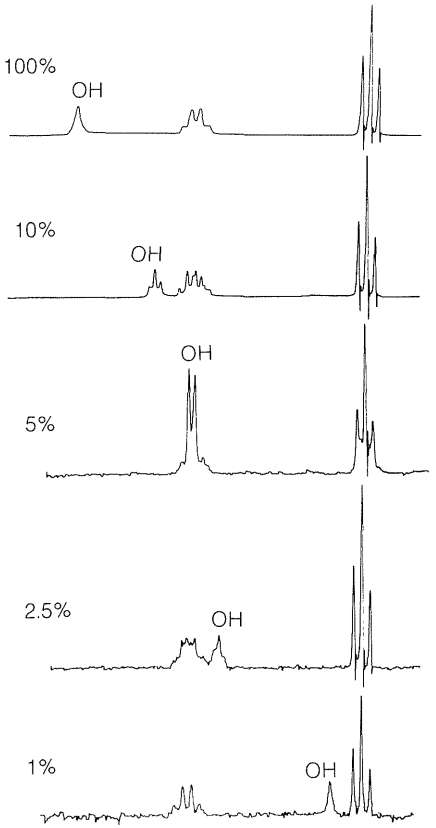


Figure 9-29 Proton spectra of ethanol at 60 MHz, showing how the OH resonance changes in position with percent concentration in CCl_4. (The background noise level increases at the lower concentrations because the receiver gain has been increased to maintain constant height of the CH_3 resonances.) The changes in appearance of the OH resonance—broad at 100% (compared to Figure 9-23), a triplet at 10%, broad at the other concentrations—is a consequence of slow exchange of the OH protons only from molecule to molecule, as will be discussed in Section 9-10I. There is no significant change in the relative shifts of the CH_2 and CH_3 lines as the concentration is changed.

molecules and also from one end to the other as shown in Equations 9-5 and 9-6, even if the equilibria are not very favorable:

$$NH_2CH_2CH_2OH \rightleftharpoons {}^{\oplus}NH_3CH_2CH_2O^{\ominus} \tag{9-5}$$

$$2NH_2CH_2CH_2OH \rightleftharpoons {}^{\oplus}NH_3CH_2CH_2OH + NH_2CH_2CH_2O^{\ominus} \tag{9-6}$$

Such equilibria can be established very rapidly, especially if traces of a strong acid or a strong base are present. In such circumstances, a *single*

average ($-NH_2$, $-OH$) proton signal is observed, because the excitation of a given proton from its lower-energy magnetic state to its higher-energy magnetic state occurs while it is partly on oxygen and partly on nitrogen. This is the same kind of chemical-shift averaging that occurs for rapidly equilibrating conformations (see Section 9-10C).

Exercise 9-26 If the $-NH_2$ protons of 2-aminoethanol, $NH_2CH_2CH_2OH$, have a shift of 1.1 ppm and the $-OH$ proton has a shift of 3.2 ppm, what will be the observed average ($-NH_2$, $-OH$) proton shift if exchange is very fast?

Exercise 9-27 In reasonably concentrated solution in water, ethanoic acid (acetic acid) acts as a weak acid (less than 1% dissociated). Ethanoic acid gives two proton nmr resonance lines at 2 and 11 ppm, relative to TMS, whereas water gives a line at 5 ppm. Nonetheless, mixtures of ethanoic acid and water are found to give only two lines. The position of one of these lines depends on the ethanoic acid concentration, whereas the other one does not. Explain how you would expect the position of the concentration-dependent line to change over the range of ethanoic acid concentrations from 0–100%.

9-10F Application of Chemical Shifts to Structure Determination

To see how nmr and infrared spectra can be used together for structure determination we shall work through a representative example.

The objective is to assign a structure to the compound $C_4H_8O_3$ whose nmr spectrum is shown in Figure 9-30 and whose infrared spectrum shows prominent bands at 2900 cm^{-1}, 1750 cm^{-1}, 1000 cm^{-1}, and 1100 cm^{-1}.

The infrared spectrum indicates $\backslash C{=}O$ / (1750 cm^{-1}), C—H (2900 cm^{-1}), and C—O (1000 cm^{-1}, 1100 cm^{-1}). The position of the carbonyl band suggests that it is probably an ester, $R-\overset{\overset{O}{\|}}{C}-O-R$. A carboxylic acid is ruled out because there is no sign of an O—H stretch.

The nmr spectrum shows three kinds of signals corresponding to three kinds of protons. The integral shows these are in the ratio of 2:3:3. From this, we can conclude that they are two different kinds of CH_3— groups and a $-CH_2-$ group.

The chemical shifts of the presumed CH_3 groups are at 3.70 ppm and 3.35 ppm. Because the compound contains only C, H, and O, the data of Table 9-4 suggest that these resonances arise from OCH_3 groups. The low-

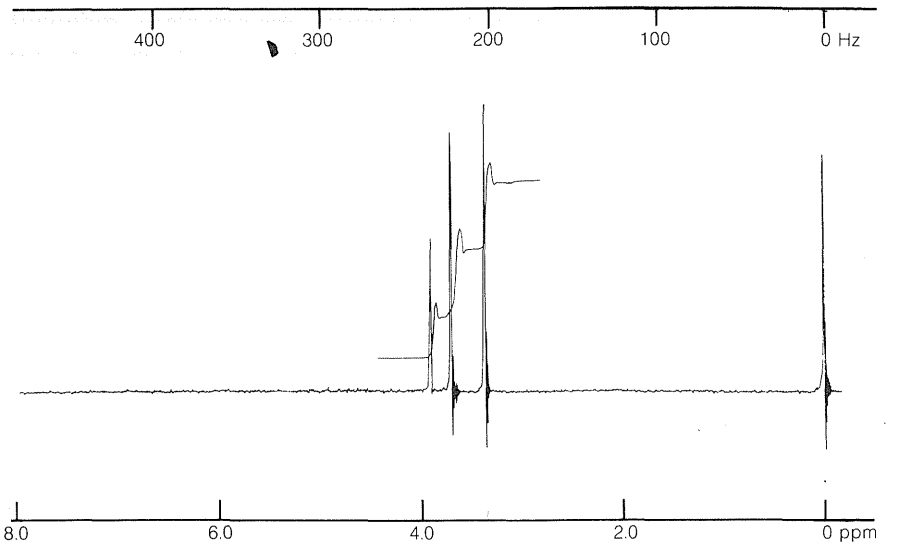


Figure 9-30 Proton nmr spectrum of a compound, $C_4H_6O_3$, at 60 MHz relative to TMS = 0.00 ppm.

field resonance is likely to be $-\overset{\overset{O}{\|}}{C}-OCH_3$ (we know from the infrared that there probably is an ester function), while the higher-field resonance is possibly an ether function, $-OCH_3$. If you put all of this information together, you find that $CH_3OCH_2CO_2CH_3$ is the only possible structure. To check whether the CH_2 resonance at 3.9 ppm is consistent with the assigned structure we can calculate a shift value from Equation 9-4:

$$\delta = 0.23 + \sigma_{OCH_3} + \sigma_{O=COCH_3}$$
$$\delta = 0.23 + 2.36 + 1.55 \quad = 4.14 \text{ ppm}$$

The agreement between the calculated and observed shifts is not perfect, but is within the usual range of variation for Equation 9-4. We can be satisfied that the assigned structure is correct.

Exercise 9-28 The proton nmr spectrum of a compound of formula $C_6H_{12}O_2$, is shown in Figure 9-31. The signals are shown relative to TMS as the standard, and the stepped line is the integral of the area under the peaks from left to right. The infrared spectrum of the same compound shows a broad band at 3300 cm^{-1} and a strong band at 1700 cm^{-1}. Deduce the structure of the compound and name it by the IUPAC system.

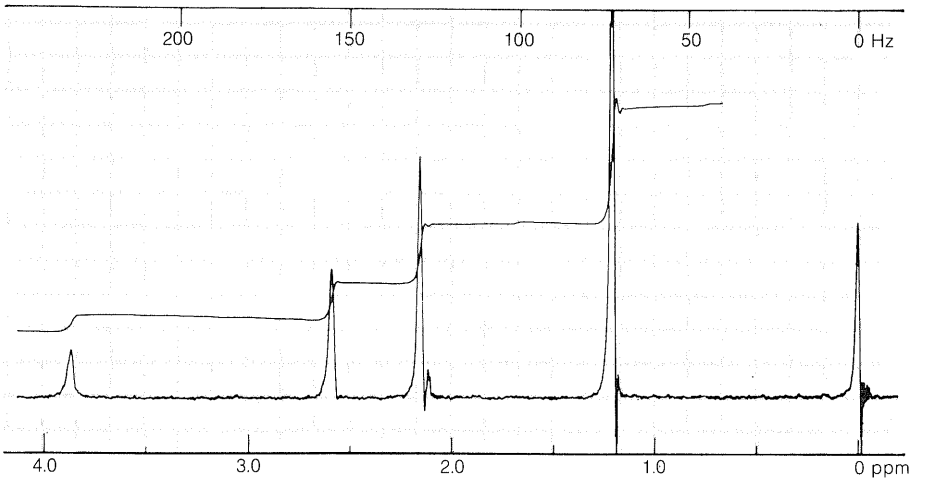


Figure 9-31 Proton nmr spectrum of a compound, $C_6H_{12}O_2$, at 60 MHz relative to TMS at 0.00 ppm. The stepped line is the integral running from left to right. See Exercise 9-28.

Exercise 9-29 Sketch the proton chemical shifts in ppm and Hz as well as the integral you would expect for each of the following substances at 60 MHz. (The spin-spin splitting of the resonance lines evident in Figures 9-23 and 9-27, but not seen in Figure 9-31, can be safely neglected with all of the compounds listed.)

a. $(CH_3)_3CCH_2OCH_3$

b. $CH_3COC(CH_3)_3$

c. $HCOC(CH_3)_2CHO$

d. 

e. $(CH_3)_2C{=}CCl_2$

f. $(CH_3)_3COC{\equiv}CH$

g. $(CH_2Cl)_3CCO_2H$

h.* *cis*-1-methyl-4-*tert*-butyl-1,2,2,3,3,4,5,5,6,6-decachlorocyclohexane (See Sections 10-2C and 10-2D.)

Exercise 9-30 Write structures for compounds with the following descriptions. (There may be more than one correct answer, but only one answer is required.)

a. C_2H_6O with *one* proton nmr shift

b. C_6H_{12} with *one* proton nmr shift

c. C_5H_{12} with *one* proton nmr shift

d. C_4H_8O with *two* different proton nmr shifts

e. $C_4H_8O_2$ with *three* different proton nmr shifts

f. C_4Cl_8 with *two* different ^{13}C nmr shifts

9-10G Spin-Spin Splitting—What We Observe

If you look at the nmr spectrum of ethanol, CH_3CH_2OH, in Figure 9-23, you will see that the CH_2 resonance is actually a group of *four* lines and the CH_3 resonance is a group of *three* lines. This three-four line pattern for the grouping CH_3CH_2X ($X \neq H$) also is evident in the 220 MHz spectrum of 2-methyl-2-butanol (Figure 9-27) and in the 60 MHz spectrum of ethyl iodide (Figure 9-32).

Why do certain proton resonances appear as groups of equally spaced lines rather than single resonances? The facts are that *nonequivalent* protons on contiguous carbons $H_B-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-H_A$, such as ethyl derivatives CH_3CH_2X, interact magnetically to "split" each other's resonances. This multiplicity of lines produced by the mutual interaction of magnetic nuclei is called **"spin-spin splitting,"** and while it complicates nmr spectra, it also provides valuable structural information, as we shall see.

An example of a complex proton spectrum is that of ethyl iodide (Figure 9-32). To a first approximation, the two main groups of lines appear as *equally spaced* sets of three and four lines, arising from what are called "first-order spin-spin interactions." Matters are further complicated by additional splitting of the "three-four" pattern of ethyl iodide, as also can be seen in Figure 9-32. This additional splitting is called "second-order" splitting.

When there are so many lines present, how do we know what we are dealing with? From where do we measure the chemical shift in a complex group of lines?

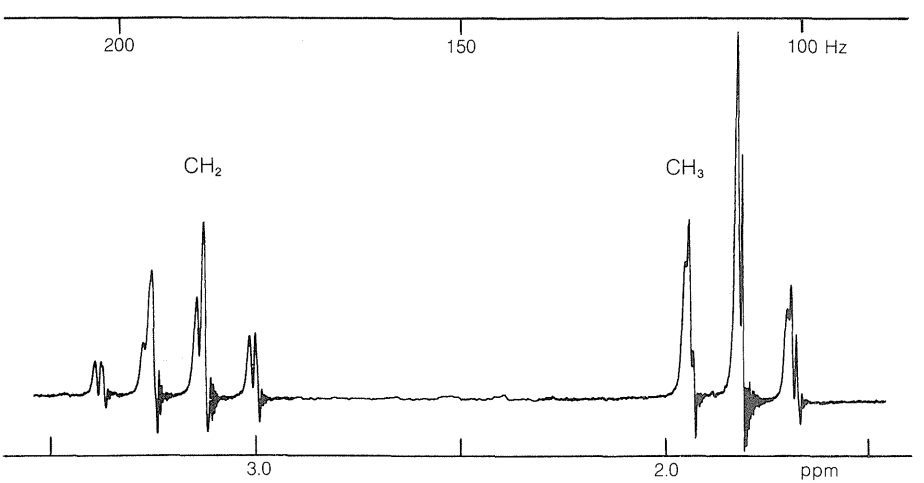
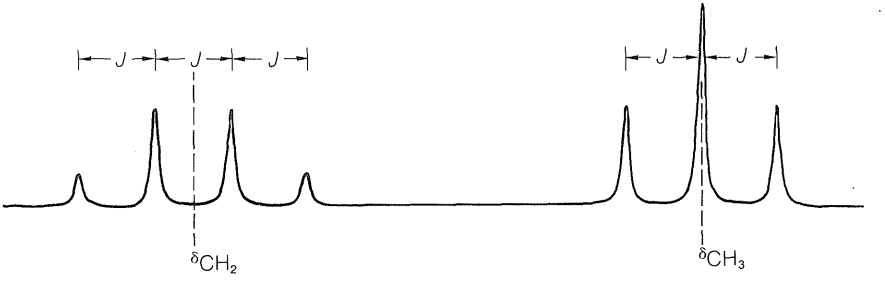


Figure 9-32 High-resolution nmr spectrum of ethyl iodide, CH_3CH_2I, at 60 MHz relative to TMS, 0.00 ppm. The first-order splitting pattern is seen in the well-separated "three-four" line pattern for the CH_3—CH_2 resonances. The second-order splitting is the additional fine structure superimposed on the three-four pattern.

First, the chemical shift normally is at the *center* of the group of lines corresponding to first-order splitting. In ethyl iodide, the chemical shift of the methyl protons is centered on the middle line of the triplet; the chemical shift of the methylene protons is in the center of the quartet:

Second, the chemical shift can be recognized by the fact that it is directly proportional to the transmitter frequency, ν. If we double ν, the chemical shifts double. In contrast, the first-order spin-spin splittings remain the same. By this we mean that the magnitude (in Hz) of the spacing between the lines of a split resonance is independent of the transmitter frequency, ν. This spacing corresponds to what is called the **spin-spin-coupling constant,** or simply the **coupling constant,** and is symbolized by J.

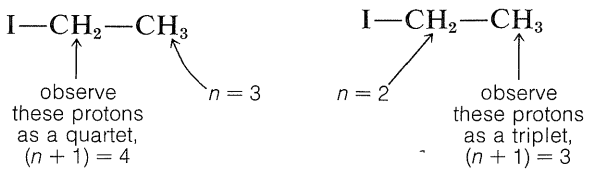


δ_{CH_2} and δ_{CH_3} *are directly proportional to the transmitter frequency of the spectrometer, but the internal spacings of the split resonances, J, are not* (see Figure 9-27).

Third, the second-order splitting tends to disappear with increasing transmitter frequency. For ethyl iodide (Figure 9-32), the second-order splitting at 60 MHz is barely discernible at 100 MHz and disappears at 200 MHz. This also can be seen to occur for the three-four splitting pattern of 2-methyl-2-butanol as a function of ν (Figure 9-27).

The next question is how can we understand and predict what spin-spin splitting patterns will be observed? And how do they give us structural information? The important point is that the *multiplicity of lines for protons of a given chemical shift often is seen to be* $(n + 1)$, *in which n is the number of protons on the contiguous carbons.* For example, the CH_2 resonance of the ethyl group of ethyl iodide is a *quartet* of lines because of the spin-spin inter-

action with the neighboring three protons ($n = 3$) of the methyl group. Likewise, the CH_3 group is a *triplet* of lines because of spin-spin interactions with the two protons ($n = 2$) of the methylene group.



The spin-spin splitting patterns observed for some different combinations of protons on contiguous carbons are given in Figure 9-33, where X and Y are groups that give no spin interactions with the protons. The value of these patterns, when observed, lies in the way that they indicate the number of equivalent protons on contiguous carbons. For instance, a two-three line pattern, where the two-part has an integrated intensity twice that of the three-part, suggests the grouping $XCH_2—CHY_2$.

The ratios of the line intensities in the spin-spin splitting patterns of Figure 9-33 usually follow simple rules. A doublet appears as two lines of

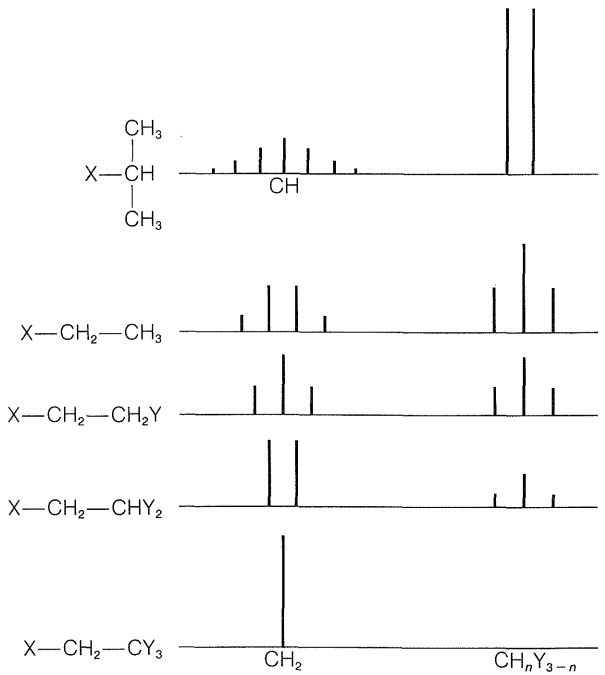
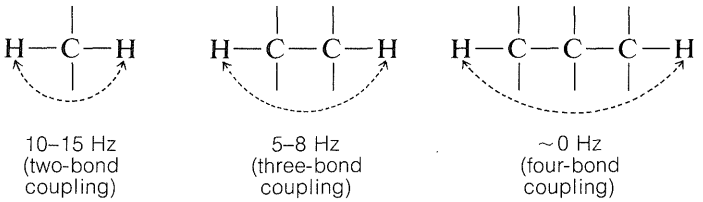


Figure 9-33 Schematic proton nmr spectra; X and Y are *nonmagnetic* nuclei. For 2-propane derivatives, as at the top, the CH_3 resonances are double because of the splitting produced by the single proton on C2. For the ethane derivatives, the right set of lines is always a triplet when observable because of the *two protons of the* $X—CH_2—$ *group*. We assume here that the chemical shifts of the CH_nY_{3-n} protons are independent of the number of Y substituents.

equal intensity; a triplet as three lines in the ratio 1:2:1; a quartet as four lines in the ratio 1:3:3:1; a quintet as 1:4:6:4:1, and so on. The intensities follow the binomial coefficients for $(x + y)^n$ where n is the number of protons in the splitting group. Thus when $n = 4$, we have $x^4 + 4x^3y + 6x^2y^2 + 4xy^3 + y^4$, or 1:4:6:4:1.

The spectrum of $(CH_3O)_2CHCH_3$ (Figure 9-34) provides an excellent example of how nmr shows the presence of contiguous protons. The symmetrical doublet and 1:3:3:1 quartet are typical of the interaction between a single proton and an adjacent group of three, that is, $\backslash CH—CH_3$. The methyl protons of the (CH_3O) groups are too far from the others to give demonstrable spin-spin splitting; thus they appear as a single six-proton resonance.

In general, the magnitude of the spin-spin splitting effect of one proton on another proton (or group of equivalent protons) depends on the *number and kind* of intervening chemical bonds and on the spatial relationships between the groups. For simple systems without double bonds and with normal bond angles, we usually find for *nonequivalent* protons (i.e., having different chemical shifts):



10–15 Hz (two-bond coupling)

5–8 Hz (three-bond coupling)

~0 Hz (four-bond coupling)

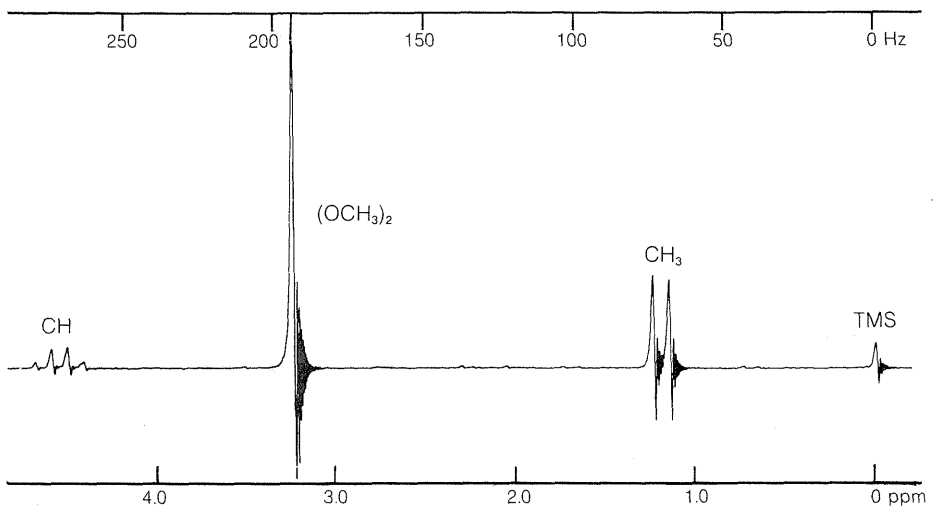
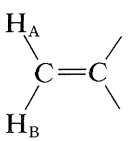
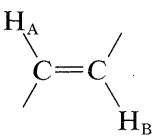


Figure 9-34 Proton nmr spectrum of 1,1-dimethoxyethane (dimethyl acetal), $(CH_3O)_2CHCH_3$, at 60 MHz relative to TMS, 0.00 ppm.

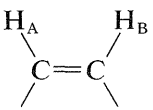
Where restricted rotation or double- and triple-bonded groups are involved, widely divergent splittings are observed. For double bonds, the **two-bond couplings** between two nonequivalent hydrogens located on one end are characteristically small, while the **three-bond couplings** in —HC=CH— are larger, especially for the trans configuration:



0–3 Hz

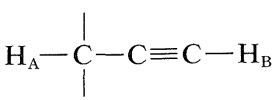


11–19 Hz

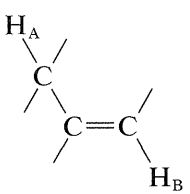


7–10 Hz

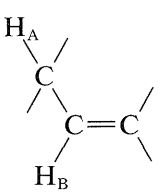
Coupling through four or more bonds is significant for compounds with double or triple bonds. Examples of these so-called **long-range couplings** and some other useful splitting values follow:



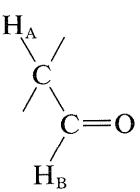
2–3 Hz



0.5–2.5 Hz



4–10 Hz



1–3 Hz

Finally, chemically equivalent protons do not split each other's resonances.

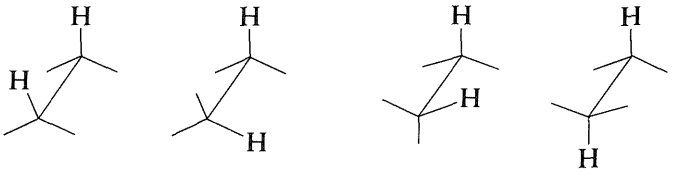
Exercise 9-31 Sketch the proton nmr spectrum and integral expected at 60 MHz, with TMS as standard, for the following substances. Show the line positions in Hz; neglect spin-spin couplings smaller than 1 to 2 Hz and all second-order effects. Remember that chlorine, bromine, and iodine (but not fluorine) act as nonmagnetic nuclei.

a. CH_3Cl
b. CH_3CH_2Cl
c. $(CH_3)_2CHCl$
d. $CH_3CCl_2CH_2Cl$
e. $(CH_3)_3CCl$
f. $CHCl_2CHBr_2$
g. $CH_3CHClCOCH_3$
h. $CH_3CH_2CO_2CH_2CH_3$
i. $ClCH_2CH_2CH_2I$
j. $(ClCH_2)_3CH$

9-10H Proton-Proton Splittings and Conformational Analyses

A very important characteristic of three-bond proton-proton couplings, H—C—C—H, is the way that they depend on the conformation at the

C—C bond. Typical values for several particular conformations are



For protons in groups such as ethyl groups, in which rotation is rapid and the favored conformations are staggered (but none of the staggered conformations is preferred over the others), average proton-proton splittings are observed. The average for CH_3CH_2— splittings is about 7 Hz, which corresponds to [2 × 4.5 (gauche) + 12 (trans)]/3.

Exercise 9-32* The proton-proton coupling in 1,1,2,2-tetrachloroethane cannot be observed directly because the chemical shift is zero. However, measurements of the splittings in $^{13}CCl_2H—^{12}CCl_2H$ show that the proton-proton coupling in $CHCl_2CHCl_2$ is 3.1 Hz. Explain how you can use this information to deduce the favored conformation of $CHCl_2CHCl_2$. Draw a sawhorse representation of the preferred conformation.

Exercise 9-33 The proton-proton coupling in *meso*-2,3-dibromobutanedioic acid (determined by the same procedure as for 1,1,2,2-tetrachloroethane, see Exercise 9-32) is 11.9 Hz. Write a sawhorse structure for the preferred conformation of this molecule.

9-10I Proton-Proton Splitting and Chemical Exchange

You may have wondered why the hydroxyl proton of ethanol produces a single resonance in the spectrum of Figure 9-23. It is quite reasonable to expect that the hydroxyl proton would be split by the neighboring methylene protons because they are only three bonds apart, —C(H)(H)—O—H. However, this coupling will not be observed if the hydroxyl protons are exchanging rapidly between the ethanol molecules (Section 9-10E). When proton exchange is rapid, the spin interactions between the $—CH_2—$ and —OH protons average to zero.

At intermediate exchange rates, the coupling manifests itself through line broadening or by actually giving multiple lines. If you look at the several spectra of ethanol in Figure 9-29, you will notice how the shape of the OH resonance varies from a broad singlet to a distinct triplet.

> Rapid chemical exchange of magnetic nuclei is not the only way that spin-coupling interactions can be averaged to zero. The same effect can be achieved by a technique known as double resonance. To understand how this is done, consider two coupled protons H_A and H_B having different chemical shifts. Suppose that H_A is selectively irradiated at its resonance frequency ν_A while at the same time we observe the resonance signal of H_B. The coupling between H_A and H_B disappears, and H_B shows a *single* resonance. Why is this so? By irradiation of H_A, the H_A nuclei are changed from the $+1/2$ state to $-1/2$ and back again sufficiently rapidly that the neighboring nucleus H_B effectively "sees" neither one state nor the other. The magnetic interaction between the states therefore averages to zero. This decoupling of magnetic nuclei by double-resonance techniques is especially important in ^{13}C nmr spectroscopy (Section 9-10L) but also is used to simplify proton spectra by selectively removing particular couplings.

9-10J Use of Nuclear Magnetic Resonance Spectroscopy in Organic Structural Analysis

The solution of a typical structural analysis problem by nmr methods utilizes at least four kinds of information obtained directly from the spectrum. They are: chemical shifts (δ), line intensities (signal areas), spin-spin splitting patterns (line multiplicities), and coupling constants (J). We already have shown how chemical shifts are used in the absence of spin-spin splitting. We now will illustrate how more complex spectra may be analyzed.

Figure 9-35 shows the proton nmr spectrum for a compound of formula C_3H_6O. There are three principal groups of lines at 9.8, 2.4, and 1.0 ppm. Look at the multiplicity of these groups before reading further.

There are several ways to approach a problem such as this, but probably the easiest is to start with the integral. The relative heights of the stepped integral for the principal groups of lines can be obtained by a pair of dividers, with a ruler, or with horizontal lines drawn as in Figure 9-23. The integral suggests that one hydrogen is responsible for the resonance at 9.8 ppm, two hydrogens at 2.4 ppm, and three at 1.0 ppm. Three hydrogens in a single group suggest a CH_3— group, and because there is a three-four splitting pattern, it is reasonable to postulate CH_3—CH_2—. Subtracting C_2H_5 from the given formula C_3H_6O leaves CHO, which, with normal valences, has to be —CH=O. The spectrum thus appears to be consistent with the structure CH_3CH_2CH=O (propanal) as judged from the molecular formula and the spin-spin splitting pattern, which indicates the CH_3CH_2— grouping. To be sure of the structure, we should check it against *all* of the available information. First, from the shifts (Table 9-4) we see that the single proton at 9.8 ppm fits almost perfectly for RCHO, the two-proton —CH_2C=O resonance at 2.4 ppm is consistent

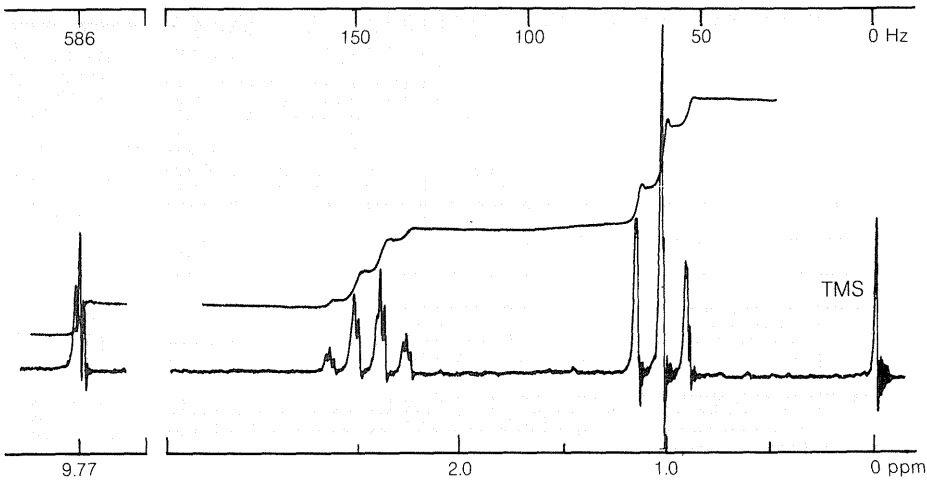


Figure 9-35 Nmr spectrum and integral for a compound of formula C_3H_6O at 60 Hz relative to TMS

with that reported for $—CH_2COR$, while the three-proton line at 1.0 ppm checks with 0.9 ppm for CH_3R.

What about the couplings? The three-four pattern has a spacing of slightly over 7 Hz, which is just right for an ethyl group (compare Figures 9-23 and 9-32). The doubling up (almost obscured by second-order splitting) of the $—CH_2—$ resonance and the splitting of the $—CH{=}O$ resonance into a 1:2:1 triplet indicate about a 2-Hz coupling for the $—CH_2—CH{=}O$ group. Three-bond couplings between —CHO and adjacent $—CH_2—$ protons appear to be generally smaller than $—CH_2—CH_3$ couplings.

We usually would not rely on nmr alone in a structure-analysis problem of this kind, but would seek clues or corroboration from the infrared, electronic, or other spectra, as well as chemical tests. In later chapters we will have many problems that will be facilitated by the use of both nmr and infrared spectra. A further worked example will illustrate the approach.

A compound has the composition C_3H_3Br and gives the infrared and nuclear magnetic resonance spectra shown in Figure 9-36. The problem is how to use this information to deduce the structure of the compound. The molecular formula tells us the number and kind of atoms *and* the number of multiple bonds or rings. The formulas of the corresponding C_3 hydrocarbon without the bromine would be C_3H_4, or *four* hydrogens less than the saturated alkane C_3H_8. This means there must be two double bonds or the equivalent—one triple bond or one ring and one double bond.[14] Because from the formula we suspect unsaturation, we should check this out with the infrared spectrum. There is a band at 2120 cm^{-1}, which is indicative of an unsymmetrically sub-

[14]If two rings were present, this also would give four hydrogens less than the alkane. However, two rings are not possible with only three carbons.

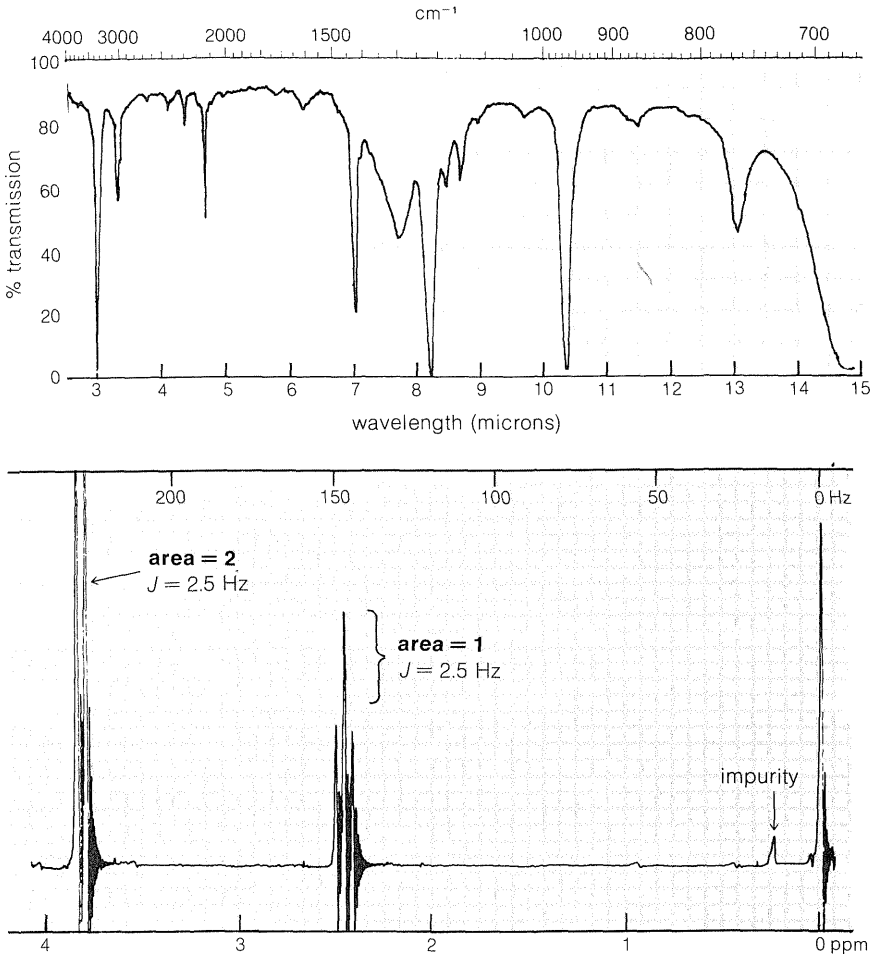


Figure 9-36 Infrared and nmr spectra for a compound of formula C_3H_3Br. The infrared spectrum here is different from others shown in this book in being linear in wavelength, λ, instead of in wave numbers, $\bar{\nu}$. The units of wavelength here are microns (10^{-6} cm).

stituted —C≡C— group (Table 9-2). The strong, sharp band at 3300 cm^{-1} further tells us that the substance is a 1-alkyne —C≡C—H.

The proton nmr spectrum shows that there are only two principal groups of lines—a two-proton doublet at 3.85 ppm and a one-proton triplet at 2.45 ppm. The two-three splitting pattern combined with the 2:1 proton ratio suggests a CH_2 group coupled with a CH group. The structure must be 3-bromopropyne, $BrCH_2C{\equiv}CH$. To confirm the assignment, the chemical shifts should be checked (Table 9-4). The ≡C—H at 2.45 ppm agrees well with the tabulated value of 2.5 ppm. There is no tabulated data for —C≡C—CH_2Br but the observed shift at 3.85 ppm is at slightly lower fields than the tabulated 3.33 ppm for —CH_2Br. This is expected because of the triple bond. The correlation of Equation 9-4 predicts a value of 4.0 ppm.

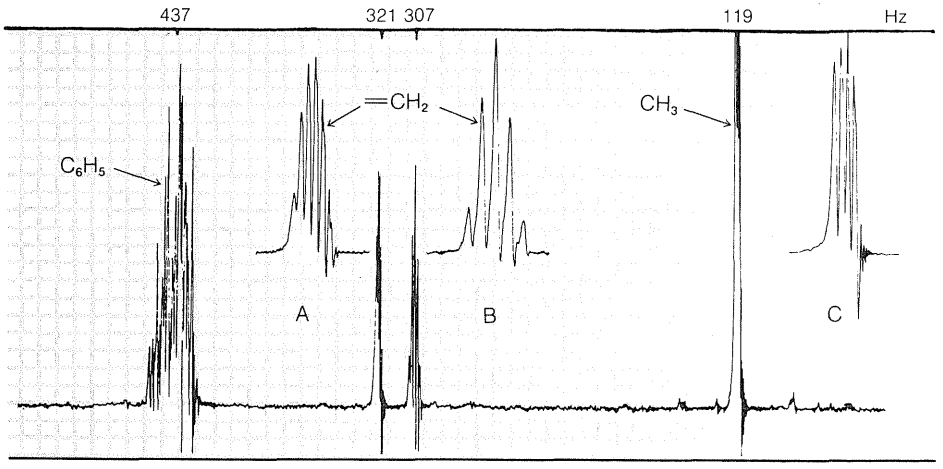


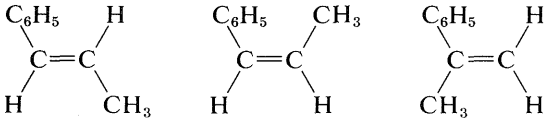
Figure 9-37 Nuclear magnetic resonance spectrum of C_9H_{10} at 60 MHz. The calibrations are relative to the protons of TMS. The insets show the peaks centered on 321, 307, and 119 Hz with an expanded scale. The spacing between the peaks is 1.5 Hz for Group B at 307 Hz, and 0.75 Hz for Groups A and C at 321 and 119 Hz. The C_6H_5 protons are coupled to each other, not to A, B, or C.

Very often, a proton will be spin-coupled to two or more *different* protons, and the couplings are not necessarily the same. When this happens, the resulting spectrum can be quite complex, as our next example shows.

A compound C_9H_{10} gives the nmr spectrum of Figure 9-37. There are clearly four kinds of protons in the molecule at $\delta = 7.28$ ppm, 5.35 ppm, 5.11 ppm, and 1.81 ppm. Although the integral is not shown, the main groups of lines have intensities from low-field to high-field in the ratio of 5:1:1:3.

The five-proton signal at 7.28 ppm is typical of a phenyl group, C_6H_5, and the one-proton signals at 5.35 and 5.11 ppm are in the region for alkenic protons, $-CH=C\begin{matrix}/\\ \backslash\end{matrix}$. The three-proton signal at 1.81 ppm is typical of a methyl group on a carbon–carbon double bond, $CH_3-\underset{|}{C}=C\begin{matrix}/\\ \backslash\end{matrix}$.

There are only three ways to put together a phenyl ring, $CH_3-\underset{|}{C}=C\begin{matrix}/\\ \backslash\end{matrix}$, and two HC= protons such that they add up to C_9H_{10}. They are



11 **12** **13**

We can distinguish between these three possible structures on the basis of the splitting patterns observed and expected from the coupling of the alkenic and methyl protons. The observed splittings are shown in expanded form inset in Figure 9-37, and the three mutually coupled groups are labeled as A, B, and C.

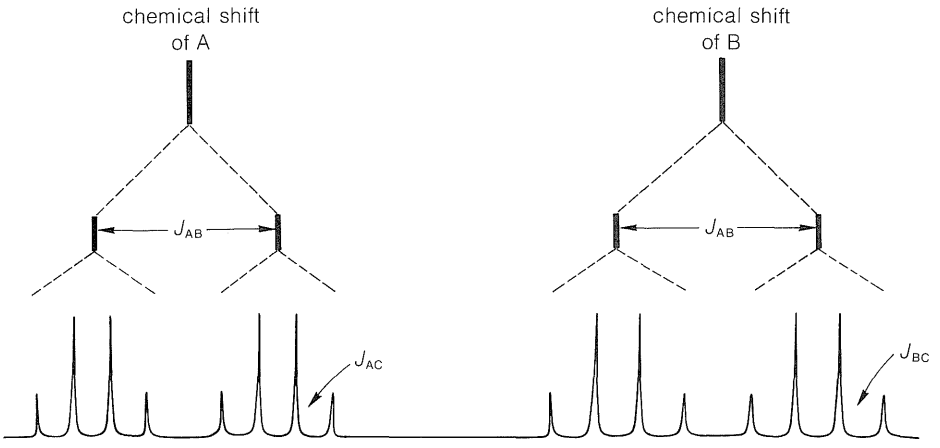
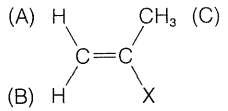


Figure 9-38 Spin-spin splitting patterns predicted for the nmr signals of the two alkenic protons (A and B) of a methyl-substituted alkene of the type:



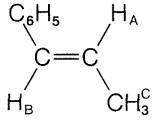
where $J_{AB} \gg J_{BC} > J_{AC}$

Coupling between A and B (designated by the constant J_{AB}) should give four lines, two for A and two for B, as shown in Figure 9-38. Because A and B also are coupled to the three hydrogens of the methyl group (C), each of the four lines corresponding to J_{AB} will be further split (into 1:3:3:1 quartets). If $J_{AC} \neq J_{BC}$, then the spacing of the lines in the two sets of quartets will not be the same.

According to the foregoing analysis, the maximum number of lines observable for the A and B resonances is sixteen (8 for A and 8 for B). In fact, only eleven are visible (6 for A and 5 for B), which means that some of the sixteen possible lines must overlap. Without examining all possibilities, we can see that the actual situation can be reproduced if $J_{AB} \cong J_{BC} \cong 2J_{AC} = 1.5$ Hz. Figure 9-39 shows that these values lead to five coincidences and eleven lines. There is no simple explanation of why $J_{AB} \cong J_{BC} \cong 2J_{AC}$. The only structure that is consistent with $J_{AB} = 1.5$ Hz is **13**, or 2-phenylpropene; the other possibilities are excluded because J_{AB} should be about 10 Hz for **12** and 16 Hz for **11**.

Exercise 9-34* **a.** Show how the assignment of $J_{AB} = J_{BC} = 2J_{AC}$ leads to the prediction of four equally spaced and equally intense lines for the methyl resonance of 2-phenylpropene.

b. What would the splittings of the alkenic and methyl protons look like for *trans*-1-phenylpropene if $J_{AB} = 16$ Hz, $J_{AC} = 4$ Hz, and $J_{BC} = 0$ Hz?



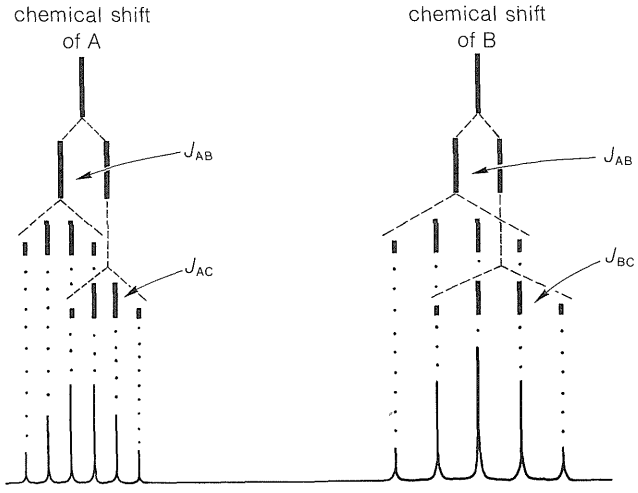
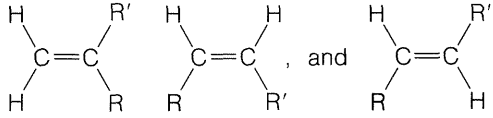


Figure 9-39 Same as Figure 9-38, except that now $J_{AB} \cong J_{BC} \cong 2J_{AC}$

Exercise 9-35 Interpret fully each of the proton nmr spectra shown in Figure 9-40 in terms of the given structures. For spin-spin splittings, explain how the patterns arise and predict the intensities expected from simple theory.

Exercise 9-36 Figure 9-41 shows proton nmr spectra and integrals at 60 MHz for three simple organic compounds. Write a structure for each substance that is in accord with both its molecular formula and nmr spectrum. Explain how you assign each of the lines in the nmr spectrum.

Exercise 9-37 Figure 9-42 shows the proton nmr spectrum of a compound, $C_5H_8O_2$. Which of the following structures fits the spectrum best? Explain. Remember that the protons of



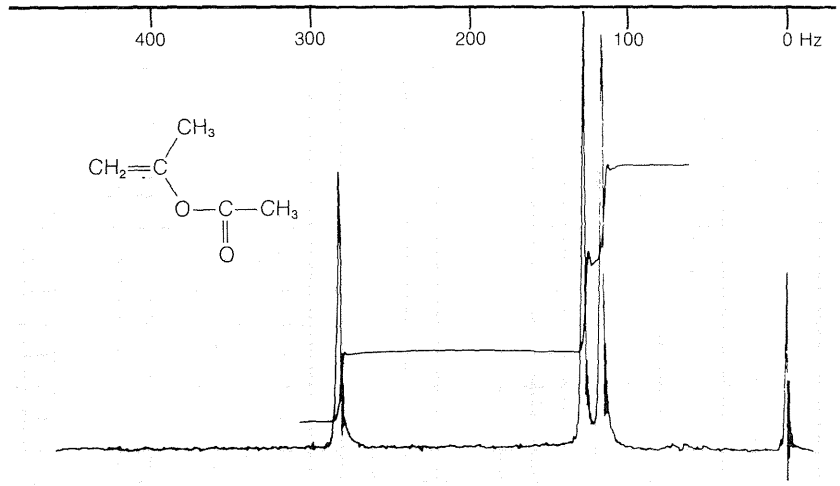
are expected to be nonequivalent; that is, they have different chemical shifts if R and R′ are different groups.

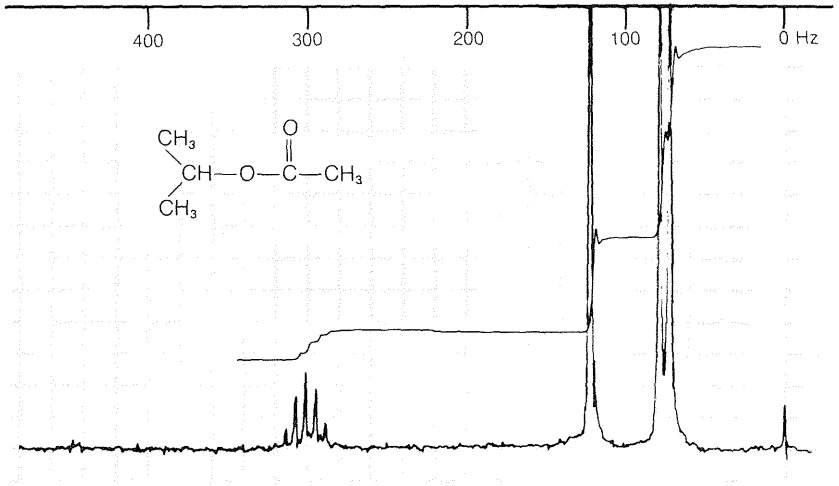
$CH_3CH{=}CHCO_2CH_3$ $(CH_2)_2CHCO_2CH_3$

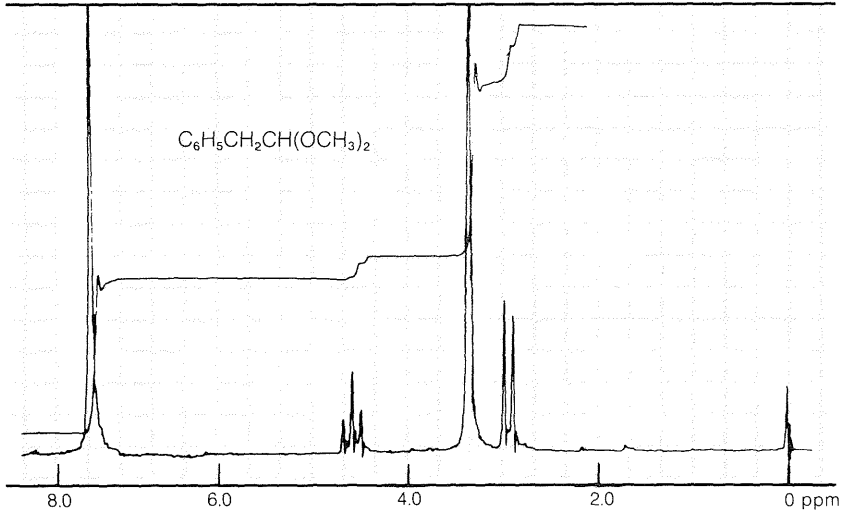
$CH_2{=}CHCO_2CH_2CH_3$ $CH_2{=}CHCH_2CO_2CH_3$

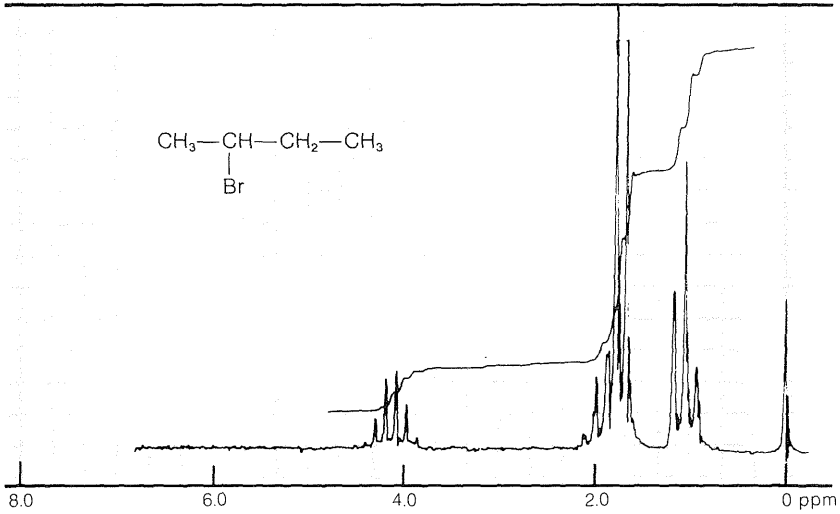
$CH_2{=}C(CH_3)CO_2CH_3$ $HCO_2CH_2CH_2CH{=}CH_2$

$CH_2{=}C(OCH_3)COCH_3$ $OCH_2CH_2CH_2CH_2C{=}O$


400
300
200
100
0 Hz
CH3
CH2=C
O—C—CH3
O


400
300
200
100
0 Hz
CH3
CH—O—C—CH3
CH3
O


C6H5CH2CH(OCH3)2
8.0
6.0
4.0
2.0
0 ppm


CH3—CH—CH2—CH3
Br
8.0
6.0
4.0
2.0
0 ppm

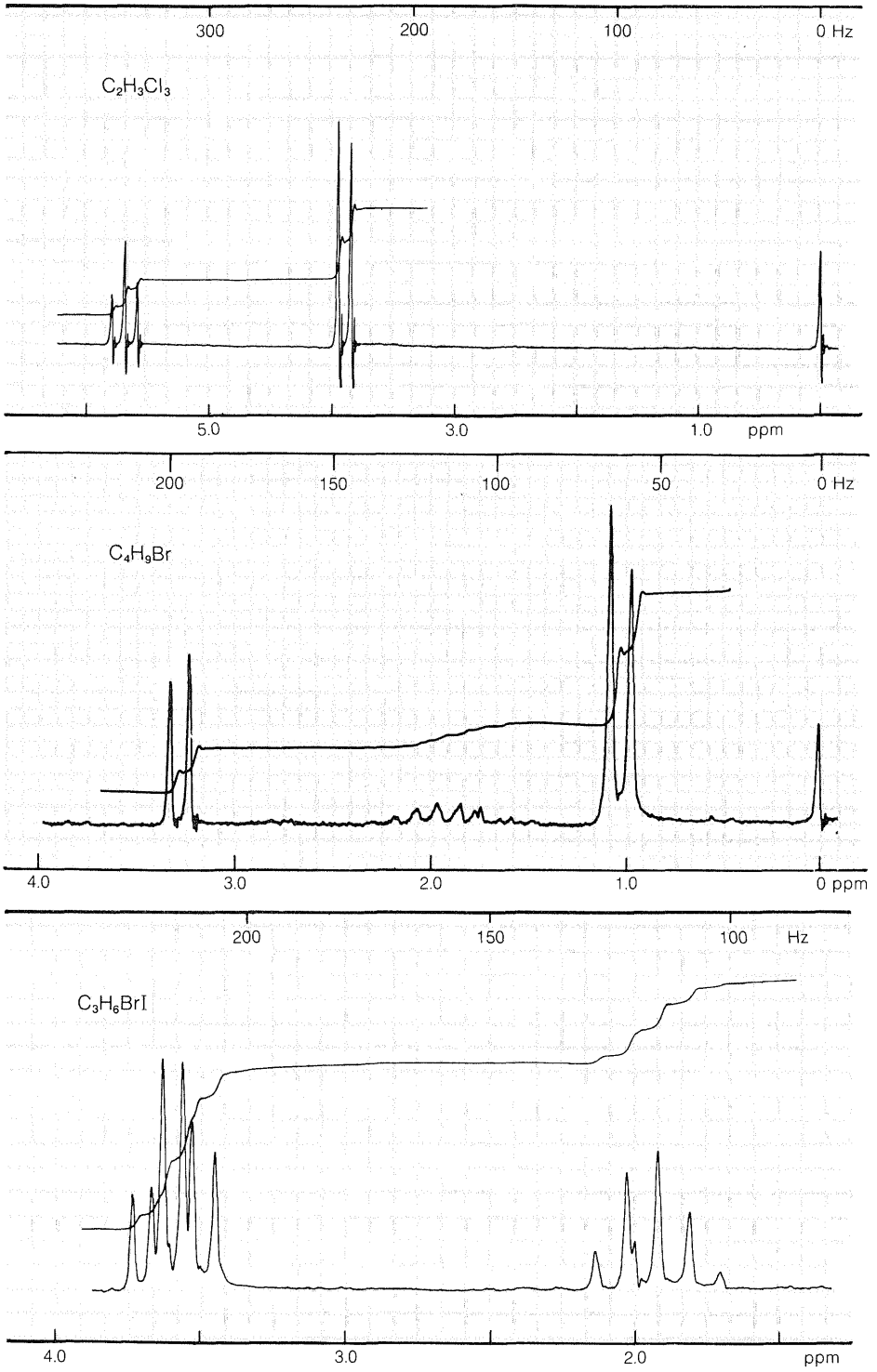


Figure 9-41 Proton nmr spectra and integrals for some simple organic compounds at 60 MHz relative to TMS, 0.00 ppm. See Exercise 9-36.

◀ **Figure 9-40** Proton nmr spectra at 60 MHz relative to TMS = 0.00 ppm. See Exercise 9-35.

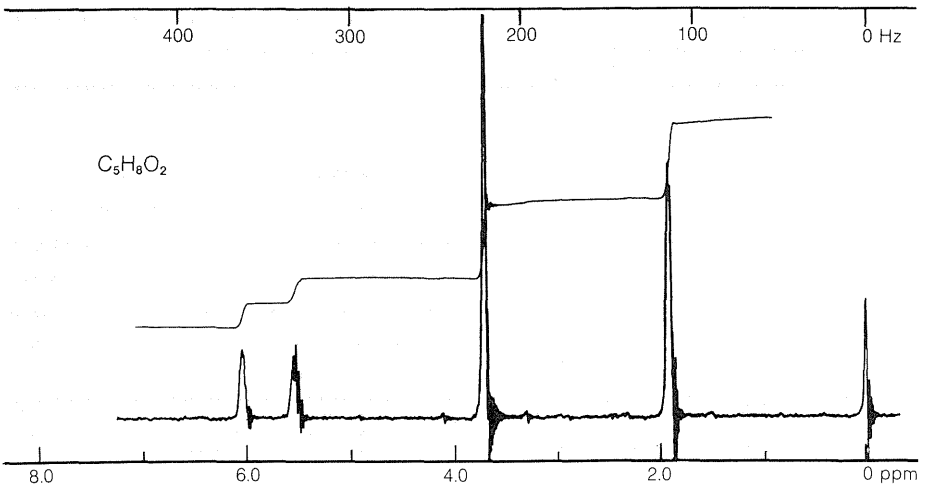
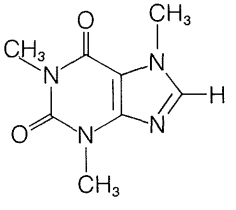
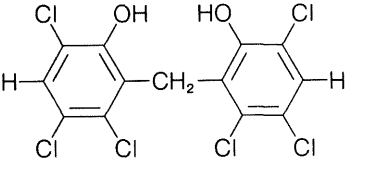


Figure 9-42 Proton spectrum of a compound, $C_5H_8O_2$, at 60 MHz relative to TMS as standard. See Exercise 9-37.

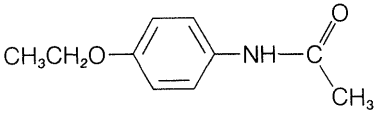
Exercise 9-38 Suppose that you had six unlabeled bottles containing caffeine, hexachlorophene, phenacetin, DDT, 1,3-dimethyluracil, and 1-phenylethanamine. The nmr spectrum of each of these compounds is shown in Figure 9-43. Match the lettered spectra with the appropriate individual structures so the bottles can be labeled properly. Give your reasoning.



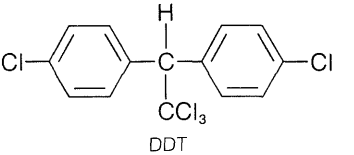
caffeine



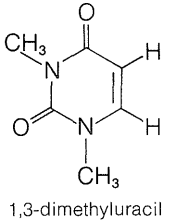
hexachlorophene



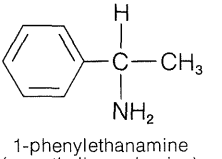
phenacetin



DDT



1,3-dimethyluracil



1-phenylethanamine
(α-methylbenzylamine)

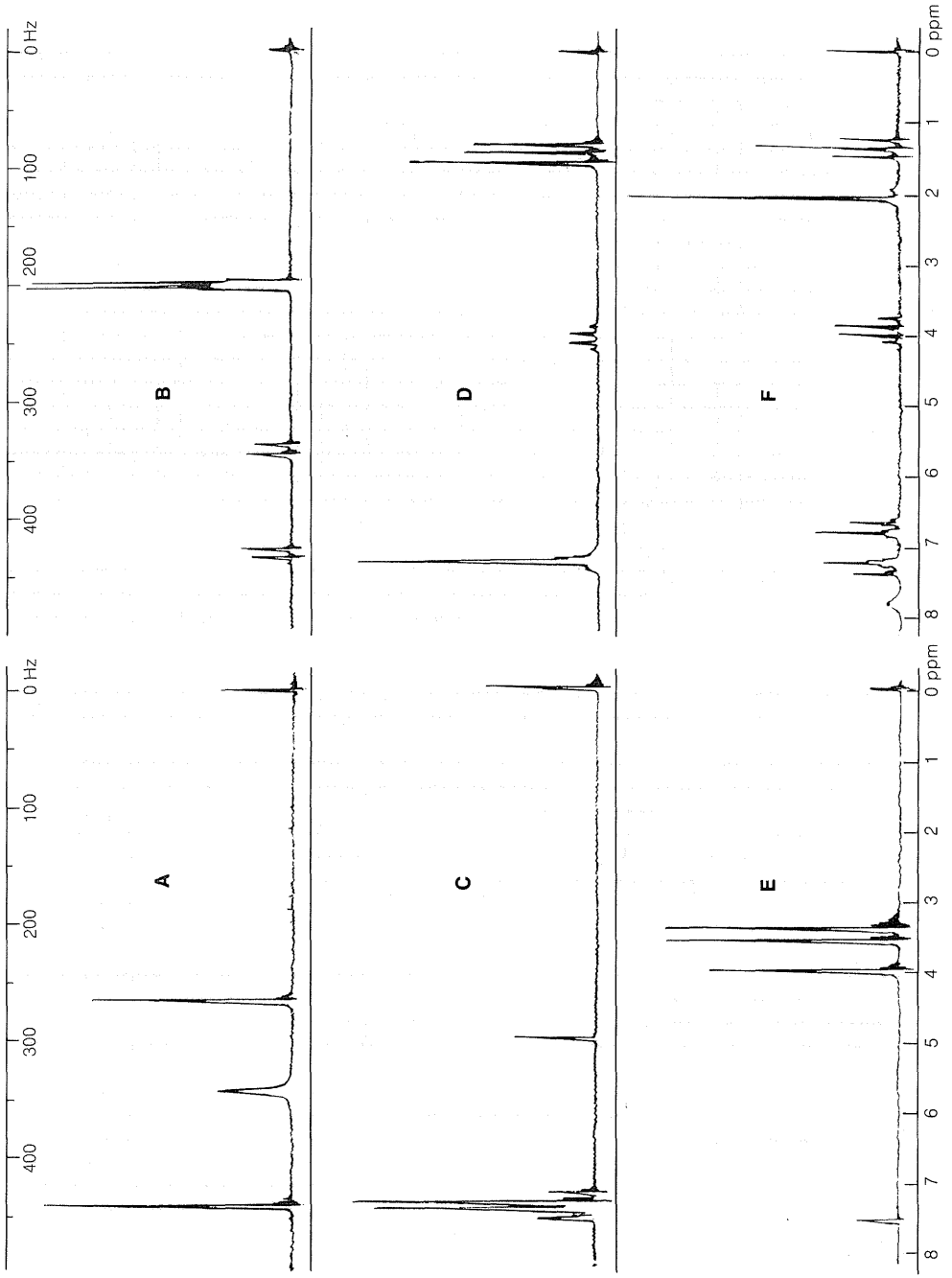


Figure 9-43 Proton nmr spectra of compounds at 60 MHz. See Exercise 9-38.

9-10K Chemical-Shift Effects on Spin-Spin Splitting

The simple n + 1 rule for predicting the multiplicity of spin-coupled proton signals often breaks down whenever the chemical-shift difference between the protons in different groups becomes comparable to coupling constants for magnetic interaction between the groups. Under these circumstances, you may expect to see more lines, or lines in different positions with different intensities, than predicted from the simple first-order treatment. One example is the effect of changing chemical shift on a two-proton spectrum with $J = 10$ Hz (Figure 9-44).

We see in Figure 9-44 that even when the shift is 7.5 times larger than the coupling, the outside lines are weaker than the inside lines. This general kind of asymmetry of line intensities also is apparent in the spectrum of ethyl iodide (Figure 9-32), in which the lines of each group are more like 0.7:2.5:3.5:1.3 and 1.2:2.0:0.8, rather than the 1:3:3:1 and 1:2:1 ratios predicted from the first-order treatment. The asymmetry is such that two groups of lines that are connected by spin-spin splitting in effect "point" to one another—the lines on the "inside" of the pattern are stronger than predicted from the first-order treatment, whereas those on the "outside" are weaker. The effect can be put to practical use, as illustrated in the following exercise.

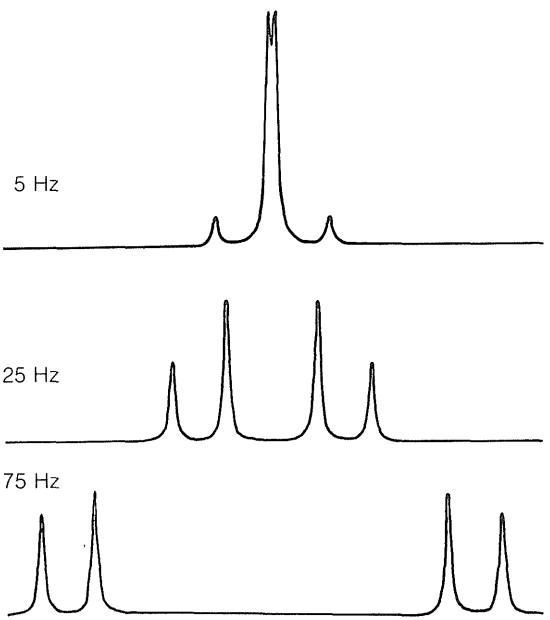


Figure 9-44 Representation of the changes in line positions and intensities for a two-proton system with a coupling constant, J, of 10 Hz and the indicated chemical-shift differences. Only a single sharp line is observed if the shift difference is zero.

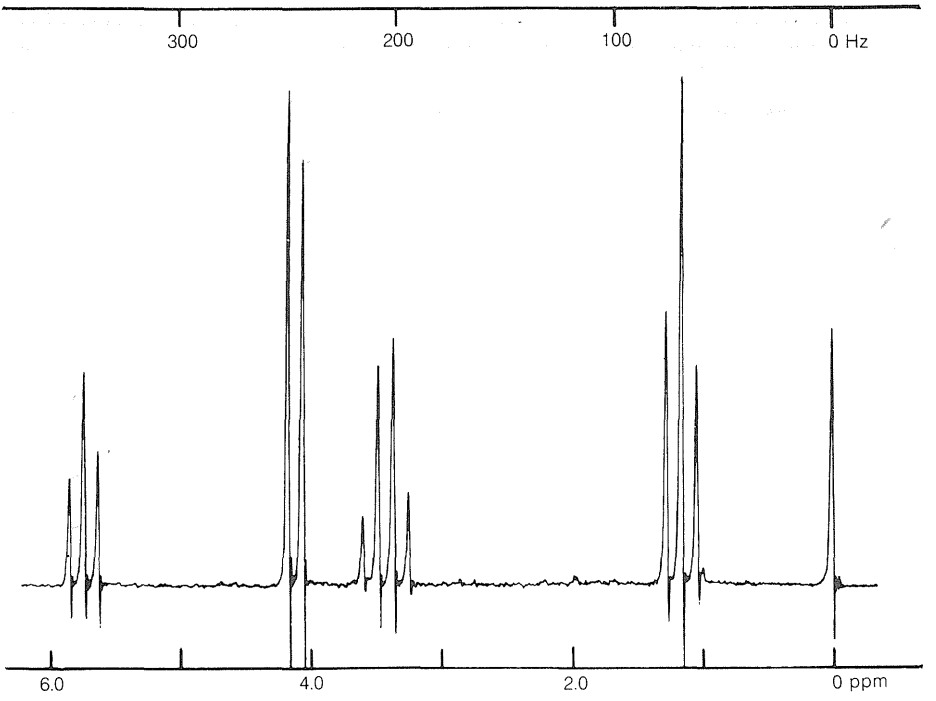


Figure 9-45 See Exercise 9-39. The spectrum corresponds to a mixture of two compounds with molecular formulas $C_4H_{10}O$ and $C_2H_3Br_3$.

Exercise 9-39 Show how one can use the asymmetry of the line intensities of the 60-MHz proton spectrum in Figure 9-45 to show which groups of lines are interconnected by spin-spin coupling. Write structural formulas for the compounds involved that fit the observed splitting patterns and chemical shifts.

To explain the effect of chemical shifts on second-order splitting is beyond the scope of this book. In fact, we haven't really explained first-order splitting, although more on this topic will be found in Section 27-3. But regardless of how many lines appear in a complex nmr spectrum, they can be rationalized in terms of the chemical shifts, coupling constants, and exchange effects. Furthermore, the overall signal intensities remain proportional to the number of protons giving rise to the signals.

When there are many hydrogens and small chemical-shift differences, as in alkanes, the proton nmr spectra may have so many closely spaced resonance lines that they merge together to give a series of smooth, more-or-less feature-

less peaks. The proton spectrum of octane (Figure 9-46a) is an excellent example of this type of spectrum. Useful information often can be obtained from such spectra as to the ratio of CH_3 : CH_2 : CH by investigation of the integrals over the range of alkane proton absorptions. Figure 9-46 illustrates how this can be done for octane and 2,2,4-trimethylpentane.

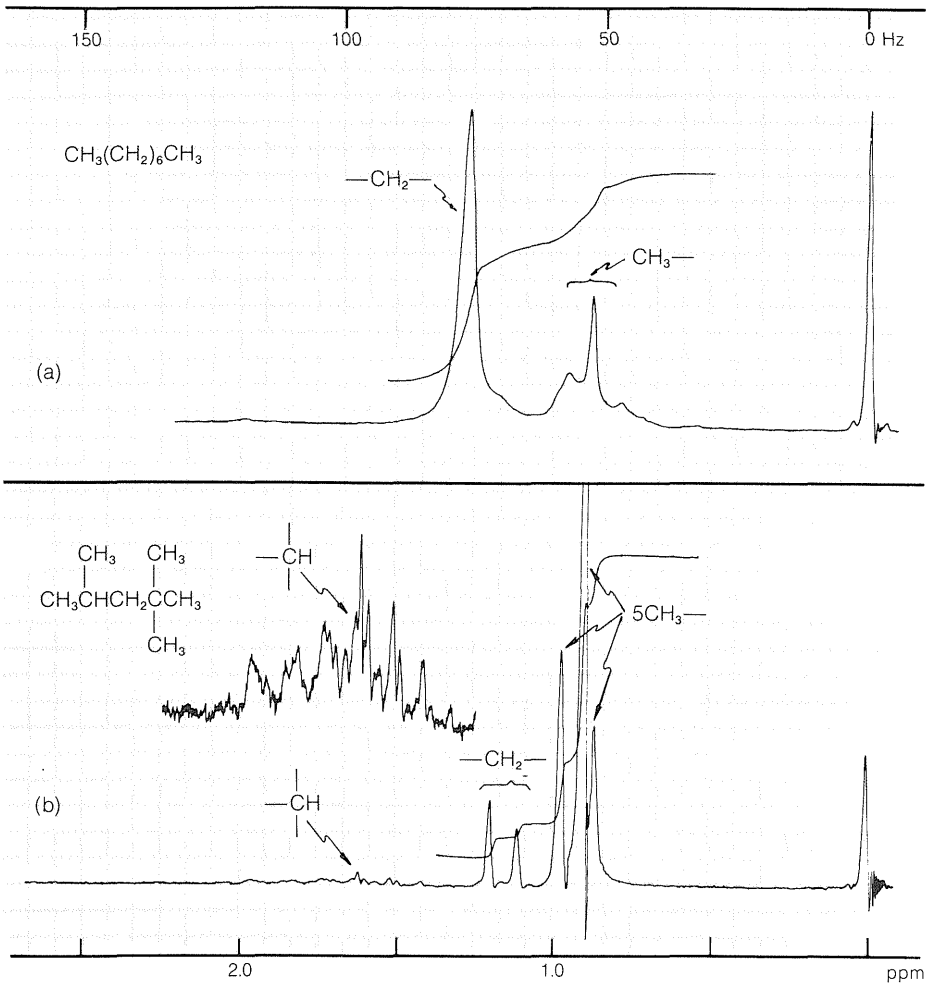


Figure 9-46 Proton nmr spectra of (a) octane and (b) 2,2,4-trimethylpentane at 60 MHz relative to TMS as standard. The upper left curve of (b) represents the spectrum from 1.25–2.25 ppm at increased sensitivity to show the details of the $-\overset{|}{\underset{|}{C}}-H$ absorption. Notice that the ratio of CH_3 to CH_2 usually can be determined from the integrals centered on 0.9 ppm and 1.25 ppm and will be 6:2 ($n - 2$) for an unbranched alkane with n carbons. For octane (a), the integral ratio is 1:2 or 6:12.

9-10L Carbon-13 Nuclear Magnetic Resonance Spectroscopy

In recent years ^{13}C nmr spectroscopy using ^{13}C of natural abundance (1.1%) has become an important tool for organic structural analysis. That this did not happen sooner is because ^{13}C has a much smaller magnetic moment than ^{1}H and the small moment combined with the small natural abundance means that ^{13}C is harder to detect in the nmr than ^{1}H by a factor of 5700. This is a large difference and can be put in the proper context in the following way. Suppose two people are talking in a noisy room and one is trying to hear the other. The common request is "talk louder." If this is not possible then the request is "say it again" or "talk more slowly." Either of the latter requests amounts to an integration of signal versus noise and takes time. Improvement in signal-to-noise for a given communication is achieved as the *square root* of the *time* of communication. On the crucial *time basis*, ^{13}C nmr signals require $(5700)^2 \cong 30{,}000{,}000 \times$ more time to get the same signal-to-noise ratio as in ^{1}H nmr for the same number of nuclei per unit volume. This is a problem.

Electronic improvements and use of communication theory, with emphasis on the "say-it-again" technique, have provided the means for obtaining routine ^{13}C spectra for even fairly dilute solutions of quite complex molecules.

Some of the same kinds of structural effects are important for ^{13}C chemical shifts as for proton chemical shifts (Section 9-10E). For example, there is a similar parallel between ^{13}C shift differences in compounds of the type CH_3—CH_2—X and electronegativity (Figure 9-47) as between the corresponding

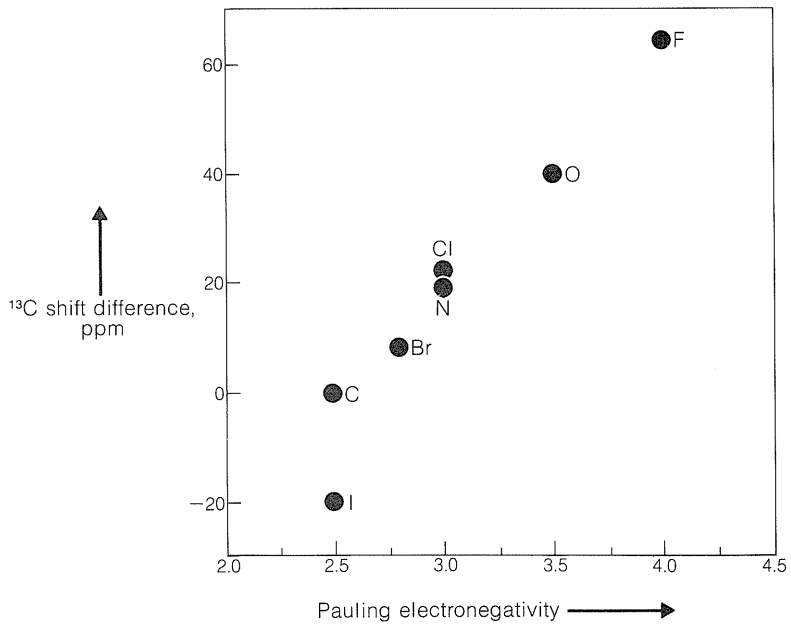
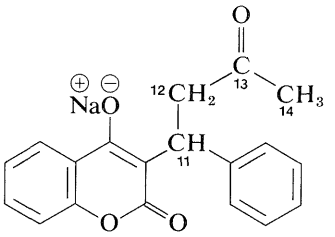


Figure 9-47 Carbon-13 chemical-shift differences for C1 and C2 of CH_3CH_2X derivatives as a function of Pauling electronegativity. The methyl carbons of CH_3CH_2X derivatives are 15–22 ppm downfield from the ^{13}C of TMS.

proton shifts and electronegativity (Figure 9-28). It is important to notice that ^{13}C shifts in ppm units are much larger than those of protons. This is because carbon uses *p* orbitals in forming bonds, whereas hydrogen uses *s* orbitals. We therefore will expect to find that the nuclei of other elements that use *p* orbitals in bonding, such as ^{15}N, ^{19}F, and ^{31}P, also will have larger shifts than for protons, as indeed they do.

A structural application of ^{13}C nmr, which shows its power in an area where ^{1}H nmr is indecisive, is shown in Figure 9-48. Here, we see the high-field ^{13}C resonances of a substance known variously as Coumadin, or the sodium salt of warfarin, **14**, which is used widely as a blood anticoagulant in the treatment of diseases such as phlebitis. It also has substantial utility as a rat poison because of its anticoagulant action.



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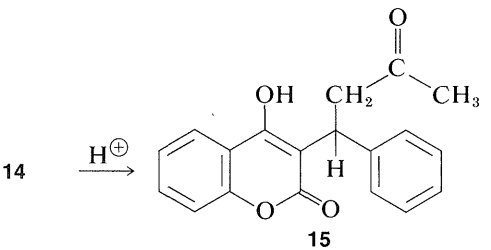
The spectra of Figure 9-48 show *no* splittings of the ^{13}C resonances by the hydrogens *directly attached* to the carbons, even though such splittings normally are quite large (125–320 Hz). The reason is that, while the ^{13}C spectra were taken, protons were simultaneously subjected to strong irradiation at their resonance frequency, which, as far as spin-spin splitting goes, causes them to act as nonmagnetic nuclei, such as Cl, Br, and I. This double-resonance technique for removing the ^{13}C–H splittings is called **proton decoupling** (see Section 9-10I).

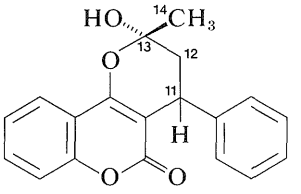
There is no indication of any abnormality in the chemical shifts of carbons 11, 12, and 14 shown in Figure 9-48a. Furthermore, there is a downfield resonance 216.5 ppm from the carbons of TMS (not shown in Figure 9-48a) which is typical of a C=O carbon corresponding to C13. When **14** is treated with acid, we expect the product (warfarin) of structure **15** to be formed, which should have a ^{13}C spectrum much like that shown in Figure 9-48a:



15

In fact, the ^{13}C nmr spectrum of the product, Figure 9-48b, is much more complex. The C11, C12, and C14 resonances of Figure 9-48a now come in unequal pairs. Furthermore, the C=O carbon resonance of **14** has disappeared and two new lines are observed at 99.6 ppm and 103.4 ppm farther upfield.

The ^{13}C data indicate clearly that warfarin is not **15** in solution but is a mixture of two diastereoisomers (**16** and **17**, called cyclic hemiketals) resulting from addition of the —OH group of **15** to the C=O bond:



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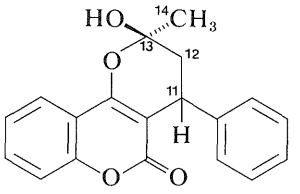

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This is one example of the power of ^{13}C nmr to solve subtle structural problems.

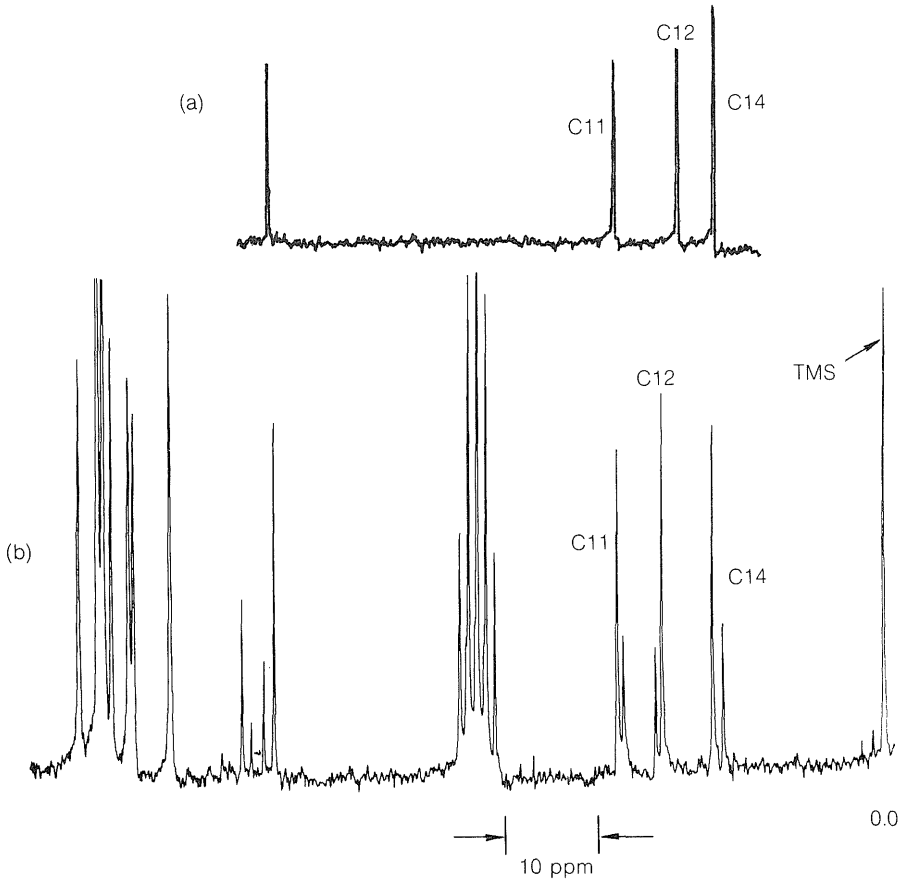


Figure 9-48 Proton-decoupled ^{13}C nmr spectrum at 15.1 MHz of the upfield region of (a) the sodium salt of warfarin (**14**) showing on the right side the resonances of C11, C12, and C14. This part of the spectrum can be compared with the more complete ^{13}C spectrum (b) of warfarin itself (**16** and **17**). The gaggle of evenly spaced sharp peaks toward the center of the spectrum arises from the solvent, $O(CD_2CD_2)_2O$.

Exercise 9-40 Explain why it is correct to characterize **16** and **17** as diastereoisomers and not enantiomers.

Exercise 9-41* When one takes the proton nmr spectrum of ordinary trichloromethane (chloroform, $CHCl_3$) under high gain, the spectrum shown in Figure 9-49 is obtained. The weak outside peaks are separated by 210 Hz and together have an integrated intensity of slightly over 1% of the main peak. Explain how these weak proton signals arise.

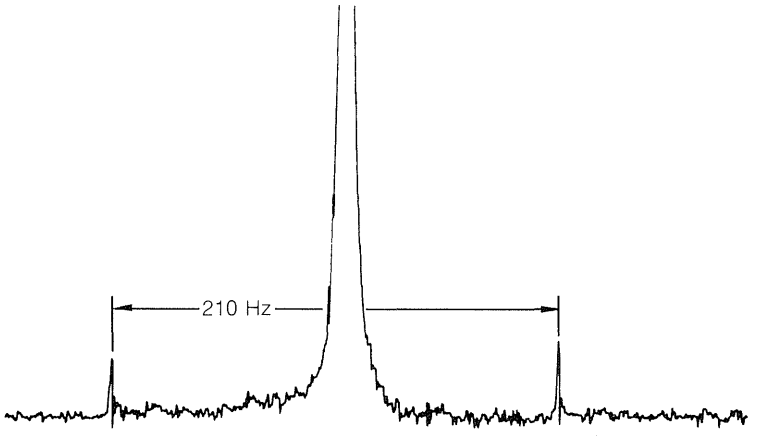
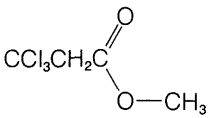


Figure 9-49 Proton nmr spectrum at 60 MHz of trichloromethane taken with high-detection sensitivity. See Exercise 9-41.

Exercise 9-42* With reference to the data summarized in Figure 9-47 and the discussion in this section, sketch qualitatively the proton-decoupled ^{13}C spectra you would expect for

(**a**) $(CH_3)_3CCH_2OH$ and

(**b**) 

Exercise 9-43* Figure 9-50 shows the ^1H and ^{13}C nmr spectra of a compound $C_6H_{10}O$. With the aid of these spectra, deduce the structure of $C_6H_{10}O$. It will be seen that the ^{13}C spectrum is quite simple, even though the proton spectrum is complex and difficult to interpret.

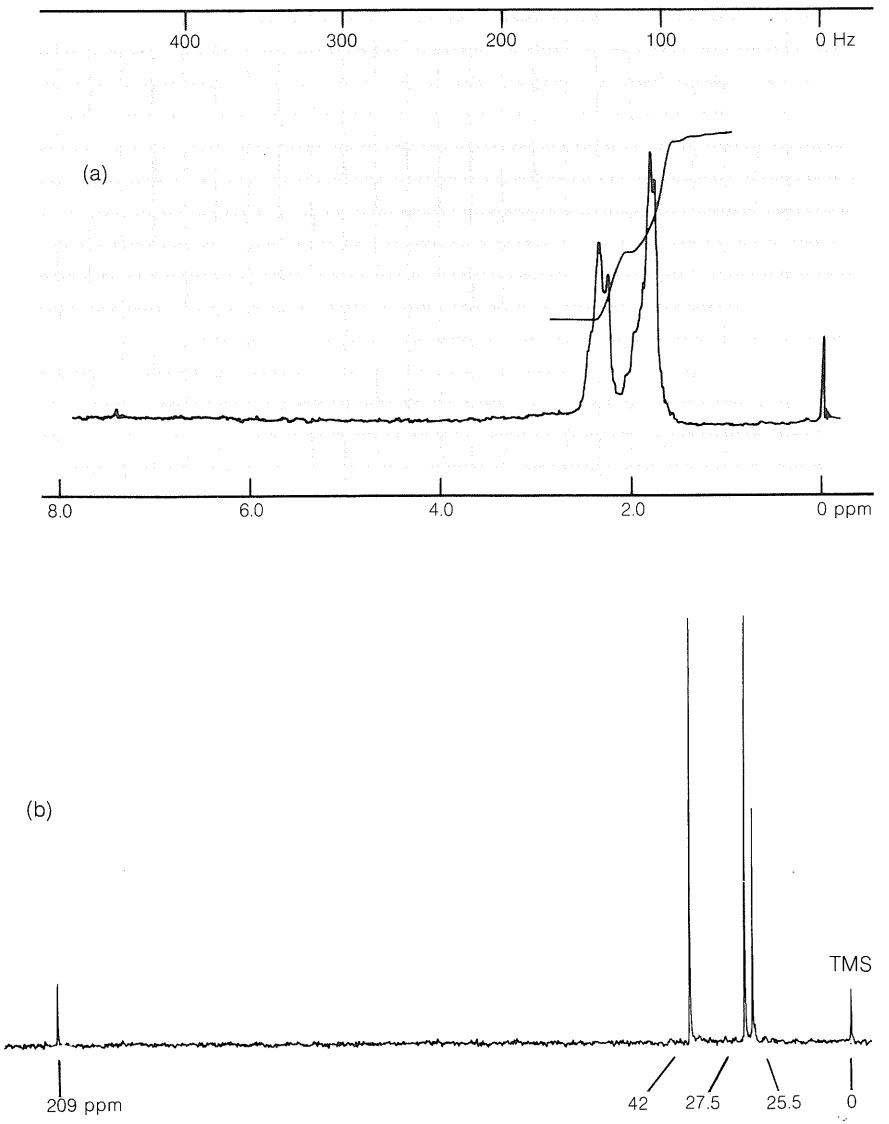


Figure 9-50 (a) Proton and (b) ^{13}C spectra of a compound $C_6H_{10}O$ taken at 60 MHz and 15.1 MHz, respectively. Because of the special way the ^{13}C spectrum was determined, the peak at 209 ppm is smaller than it should be. The intensity of this peak is, correctly, the same as the peak at 25.5 ppm. See Exercise 9-43.

9-11 MASS SPECTROSCOPY

The usual application of mass spectroscopy to organic molecules involves bombardment with a beam of medium-energy electrons (50–100 eV or 1150–2300 kcal mole^{-1}) in high vacuum, and analysis of the charged particles and fragments so produced. Most mass spectrometers are set up to analyze positively charged fragments, although negative-ion mass spectrometry also is possible. The elements of a mass spectrometer are shown in Figure 9-51. The positive ions produced by electron impact are accelerated by the negatively charged accelerating plates and sweep down to the curve of the analyzer tube where they are sorted as to their mass-to-charge (m/e) ratio by the analyzing magnet. With good resolution, only the ions of a single mass number will pass through the slit and impinge on the collector, even when the mass numbers are in the neighborhood of several thousand. The populations of the whole range of mass numbers of interest can be determined by plotting the rate of ion collection as a function of the magnetic field of the analyzing magnet.

Mass spectra of 2-propanone, 2-butanone, and propanal are shown in Figure 9-52. Each peak represents ions of particular masses formed as the result of fragmentation of the molecule produced by electron impact into $CH_3^{\oplus}$, $CH_3CH_2^{\oplus}$, $CH_3CO^{\oplus}$, and so on. The "cracking patterns" are, of course, functions of the energy of the bombarding electrons and serve as an extraordinarily individual fingerprint of the particular molecules. For instance, 2-propanone and propanal are isomers, yet their cracking patterns are strikingly different.

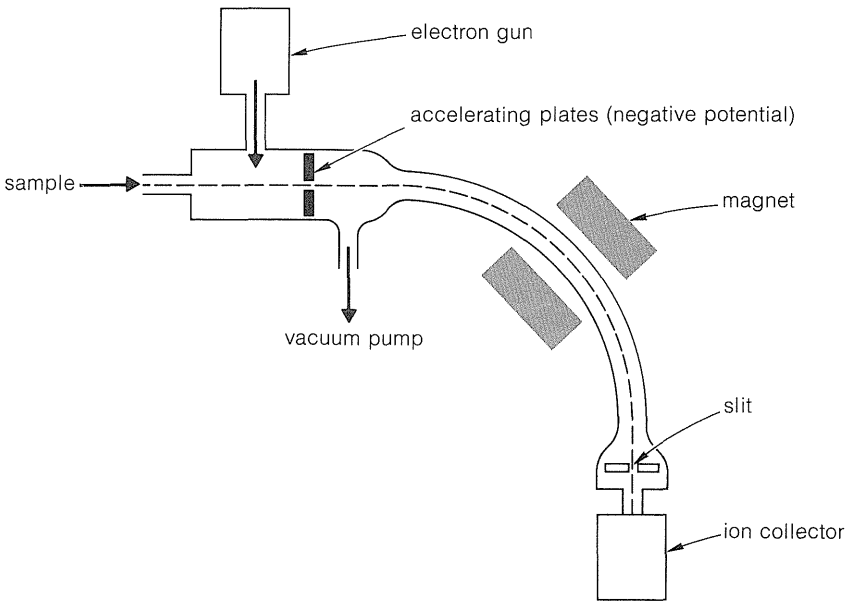


Figure 9-51 Schematic diagram of a mass spectrometer

The peak that is highest in mass number is of considerable importance because it corresponds to the parent molecule (M) minus one electron (designated as M^+) and provides a highly accurate method for measuring molecular weights. Incorrect molecular weights will be obtained if the positive ion, M^+, becomes fragmented before it reaches the collector, or if two fragments combine to give a fragment heavier than M^+. The peak of M^+ is especially weak with alcohols and branched-chain hydrocarbons, which readily undergo fragmentation by loss of water or side-chain groups. With such compounds the peak corresponding to M^+ may be 0.1% or less of the highest peak in the spectrum, which is called the **base peak** and usually is assigned an arbitrary intensity of 100.

The pressure of the sample in the ion source of a mass spectrometer is usually about 10^{-5} mm, and, under these conditions, buildup of fragments to give significant peaks with m/e greater than M^+ is rare. One exception to this is the formation of $(M + 1)^+$ peaks resulting from transfer of a hydrogen atom from M to M^+. The relative intensities of such $(M + 1)^+$ peaks are usually sensitive to the sample pressure and may be identified in this way.

With the molecular weight available from the M^+ peak with reasonable certainty, the next step is to determine the *molecular formula.* If the resolution of the instrument is sufficiently high, quite exact masses can be measured, which means that ions with m/e values differing by one part in 50,000 can be distinguished. At this resolution it is possible to determine the elemental composition of each ion from its exact m/e value (see Exercise 9-44).

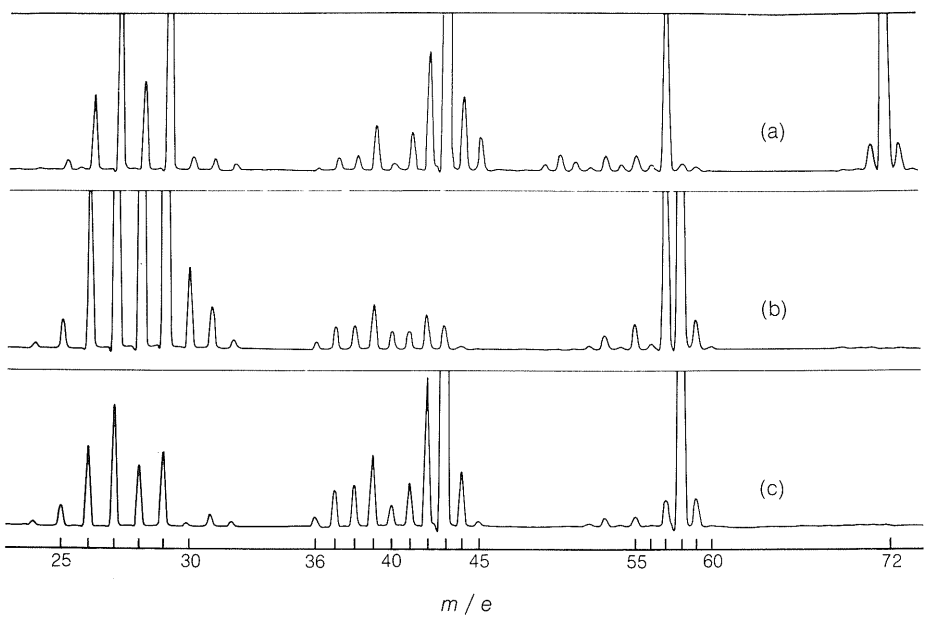


Figure 9-52 The mass spectra of (a) 2-butanone, (b) propanal, and (c) 2-propanone. These spectra were supplied through the courtesy of Dr. D. P. Stevenson of the Shell Development Company.

Exercise 9-44 Explain how a mass spectrometer, capable of distinguishing between ions with *m/e* values differing by one part in 50,000, could be used to tell whether an ion of mass 29 is $C_2H_5^{\oplus}$ or $CHO^{\oplus}$.

Many mass spectrometers in routine use are incapable of resolving ions with *m/e* values that differ by less than one mass unit. In this event, the determination of elemental composition is not always straightforward. However, elemental composition can be determined by the method of *isotope abundance*. We will illustrate this with the following simple example.

The highest peaks corresponding to M^+ in the mass spectrum of an unknown sample have *m/e* equal to 64 and 66 with relative intensities of 3:1. What is the elemental composition? The 3:1 abundance ratio is uniquely characteristic of the chlorine isotopes, ^{35}Cl:$^{37}Cl = 3:1$. The mass peaks at 64 and 66 are therefore both molecular ions; the 64 peak is of an ion containing ^{35}Cl and the 66 peak is of an ion containing ^{37}Cl. The remaining atoms in the molecule must add up to $(64 - 35) = 29$, or $(66 - 37) = 29$ mass units. There are several possible combinations of C, H, N, and O that give mass 29; they are N_2H, CHO, CH_3N, and C_2H_5.[15] Of these, the combination with Cl that makes the most chemical sense is C_2H_5, and the formula of the molecule therefore is C_2H_5Cl, chloroethane.

This example illustrates how *m/e* values of *ions that differ only in isotopic composition can be used to determine elemental compositions.* The important isotopes for this purpose in addition to those of chlorine are the stable isotopes of natural abundance, ^{13}C (1.1%), ^{15}N (0.37%), ^{17}O (0.04%), ^{18}O (0.20%). As a further example, suppose that we have isolated a hydrocarbon and have determined from its mass spectrum that $M^+ = 86$ mass units. In the absence of any combination reactions there will be an $(M + 1)^+$ ion corresponding to the same molecular ion but with *one* ^{13}C in place of ^{12}C. The intensity ratio $(M + 1)^+/M^+$ will depend on the number of carbon atoms present, because the more carbons there are the greater the probability will be that one of them is ^{13}C. The greater the probability, the larger the $(M + 1)^+/M^+$ ratio. For n carbons, we expect

$$\frac{\text{abundance of } (M + 1)^+}{\text{abundance of } M^+} = n \times \%\ ^{13}\text{C abundance}/100$$

[15] Tabulations of elemental compositions of C, H, N, and O for mass values up to 250 are listed in many texts on mass spectrometry. Consult these tables to see all possible alternatives. See also J. H. Beynon, *Mass Spectrometry and its Applications to Organic Chemistry,* Elsevier Publishing Co., Amsterdam, 1960.

If the measured $(M + 1)^+/M^+$ ratio is 6.6:100, then

$$\frac{6.6}{100} = n \times 1.1/100$$

$$n = 6$$

The only hydrocarbon formula with $M^+ = 86$ and $n = 6$ is C_6H_{14}.

Nitrogen (as ^{15}N) and oxygen (as ^{17}O) also contribute to $(M + 1)^+$, if present, while ^{18}O and *two* ^{13}C's contribute to $(M + 2)^+$. The calculated intensities of $(M + 1)^+$ and $(M + 2)^+$ relative to M^+ (as 100) are tabulated in Table 9-5 for elemental composition of ions up to C_{20}. The table applies to fragment ions as well as molecular ions, but the intensity data from fragment ions very often is complicated by overlapping peaks.

Table 9-5
Isotopic Contributions for Carbon and other Elements to Intensities of $(M + 1)^+$ and $(M + 2)^+$ relative to M^+ (100)

C_n	$(M+1)^+$	$(M+2)^+$	C_n	$(M+1)^+$	$(M+2)^+$
C_1	1.1	0.000	C_{11}	12.1	0.67
C_2	2.2	0.012	C_{12}	13.2	0.80
C_3	3.3	0.036	C_{13}	14.2	0.94
C_4	4.4	0.073	C_{14}	15.4	1.10
C_5	5.5	0.12	C_{15}	16.5	1.27
C_6	6.6	0.18	C_{16}	17.6	1.46
C_7	7.7	0.25	C_{17}	18.7	1.65
C_8	8.8	0.34	C_{18}	19.8	1.86
C_9	9.9	0.44	C_{19}	20.9	2.07
C_{10}	11.0	0.54	C_{20}	22.0	2.30

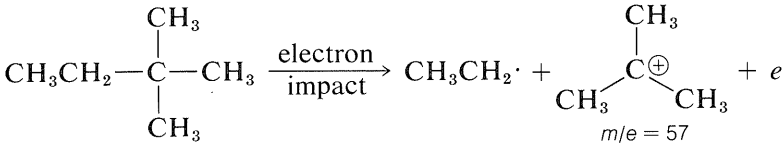
For each additional element present, add per atom
$(M + 1)^+$ ^{15}N, 0.37; ^{17}O, 0.04; ^{33}S, 0.80
$(M + 2)^+$ ^{18}O, 0.20; ^{34}S, 4.44; ^{37}Cl, 32.5; ^{81}Br, 98

Exercise 9-45 **a.** Calculate the relative intensities of the $(M + 1)^+$ and $(M + 2)^+$ ions for a molecule of elemental composition $C_3H_7NO_2$.
b. The M^+, $(M + 1)^+$, and $(M + 2)^+$ ion intensities were measured as 100, 8.84, and 0.54 respectively, and the molecular weight as 120. What is the molecular formula of the compound?

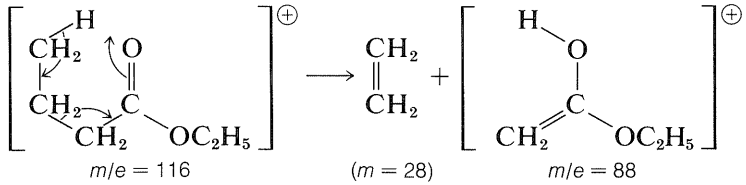
c. In our example of how natural ^{13}C can be used to determine the number of carbon atoms in a compound with $M^+ = 86$ and a $(M+1)^+/M^+$ ratio of 6.6/100, we neglected the possible contribution to the $(M+1)^+$ peak of the hydrogen isotope of mass 2 (deuterium). The natural abundance of deuterium is 0.015%. For a compound of composition C_6H_{14}, how much do you expect the deuterium to contribute to the intensity of the $(M+1)^+$ peak relative to the M^+ peak?

The next step in the analysis of a mass spectrum is to see what clues as to structure can be obtained from the fragment ions. It would be a serious error to imagine that in mass spectra nothing is observed but simple nonspecific fragmentation of organic molecules on electron impact. Actually, even though electron impact produces highly unstable molecular ions, there is a strong tendency for breakdown to occur by reasonable chemical processes, and this may involve straightforward fragmentation or rearrangement of atoms from one part of the molecule to another.

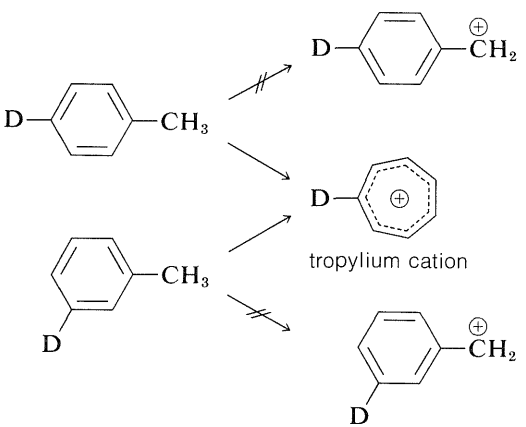
In general, fragmentation occurs at the weakest bonds, and the most abundant fragments also are the most stable ones. For instance, hydrocarbons fragment preferentially at branch points, partly because the C–C bonds are weaker here than elsewhere along the chain, and partly because the ionic fragments are more stable. As an example, consider 2,2-dimethylbutane. There is no molecular ion evident in its mass spectrum because it cleaves so readily at the quaternary carbon to give the *m/e* 57 peak corresponding to the most abundant fragment ion. This ion is presumably the *tert*-butyl cation and the alternate cleavage to the less stable ethyl cation with $m/e = 29$ is much less significant.



An excellent example of a rearrangment with fragmentation is provided by the M^+ ion of ethyl butanoate, which breaks down to give ethene and the M^+ ion of an isomer of ethyl ethanoate called its "enol form."



An interesting and complex rearrangement occurs on electron impact with methylbenzene (toluene). An intense peak is observed having m/e for $C_7H_7^{\oplus}$, but the ion involved appears to be a symmetrical $C_7H_7^{\oplus}$ ion, rather than a phenylmethyl cation. The evidence for this is that the fragmentation patterns found in the mass spectrometry of the ion itself are the same, no matter which of the monodeuteriomethylbenzenes is used as starting material. This rearrangement occurs because of the high delocalization energy of the symmetrical $C_7H_7^{\oplus}$ ion (usually called "tropylium cation") and because its charge is spread out more evenly over the carbons than would be the charge for the phenylmethyl cation (see Section 8-7B).



Exercise 9-46 Show how the molecular weights of 2-propanone, propanal, and 2-butanone can be estimated from the mass spectra in Figure 9-52. Suggest a possible origin for the strong peaks of mass 57 in the spectra of propanal and 2-butanone, which is essentially absent in 2-propanone, although 2-propanone (and 2-butanone) show strong peaks at mass 43.

Exercise 9-47 The mass spectrum of propylbenzene has a prominent peak at mass number 92. With (3,3,3-trideuteriopropyl)benzene, this peak shifts to 93. Write a likely mechanism for breakdown of propylbenzene to give a fragment of mass number 92.

Exercise 9-48 The mass spectra of alcohols usually show peaks of $(M - 18)$, which correspond to loss of water. What kind of mechanisms can explain the formation of $(M - 18)$ peaks, and no $(M - 19)$ peaks, from 1,1-dideuterioethanol and 1,1,1,3,3-pentadeuterio-2-butanol?

Exercise 9-49 Explain how the postulated rearrangement of the M^+ ion of ethyl butanoate (p. 344) is supported by the fact that the 2,2-dideuterio compound gives a

peak with $m/e = 90$; the 3,3-dideuterio isomer gives a m/e 88 peak, while the 4,4,4-trideuterio isomer gives a m/e 89 peak.

Exercise 9-50 What is the likely structure for the major fragment ion with $m/e = 45$ derived from methoxyethane (methyl ethyl ether) on electron impact?

Exercise 9-51 A certain halogen compound gave a mass spectrum with molecular ion peaks at m/e 136 and 138 in about equal intensities. The nmr spectrum of this compound gave only a single resonance around 1.2 ppm. What is the structure of the compound? Give your reasoning.

Exercise 9-52* The mass spectra of three compounds, A, B, and C, are given below in tabular form. Only the peaks of significant intensity are reported.

A		B		C	
m/e	I	m/e	I	m/e	I
27	12.8	37	3.28	27	19.69
41	13.0	38	8.57	28	5.74
42	5.91	50	13.70	29	19.19
*43	100.00	51	16.30	*31	100.00
44	2.47	*77	48.28	32	1.42
45	0.98	*112	100.00	33	0.19
*71	3.94	113	6.84	43	8.13
*86	10.0	*114	32.14	*45	43.89
87	0.56	115	2.10	*46	18.89
88	0.04	116	0.06	47	0.43

a. Compound A is $CH_3CH_2CH_2-\overset{\overset{O}{\|}}{C}-CH_3$. Show how this material can fragment to give the peaks marked with an asterisk and, where possible, how the isotope peaks help establish your assignments.

b. Determine the molecular weight and the molecular formula of Compounds B and C from the spectral data. Suggest a likely structure for each peak marked with an asterisk.

Additional Reading

Chromatography

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