Nuclear Magnetic Resonance Spectroscopy
13C NMR Spectroscopy

Advanced Pharmaceutical Analyses

Lecture 4

13C NMR Spectroscopy:

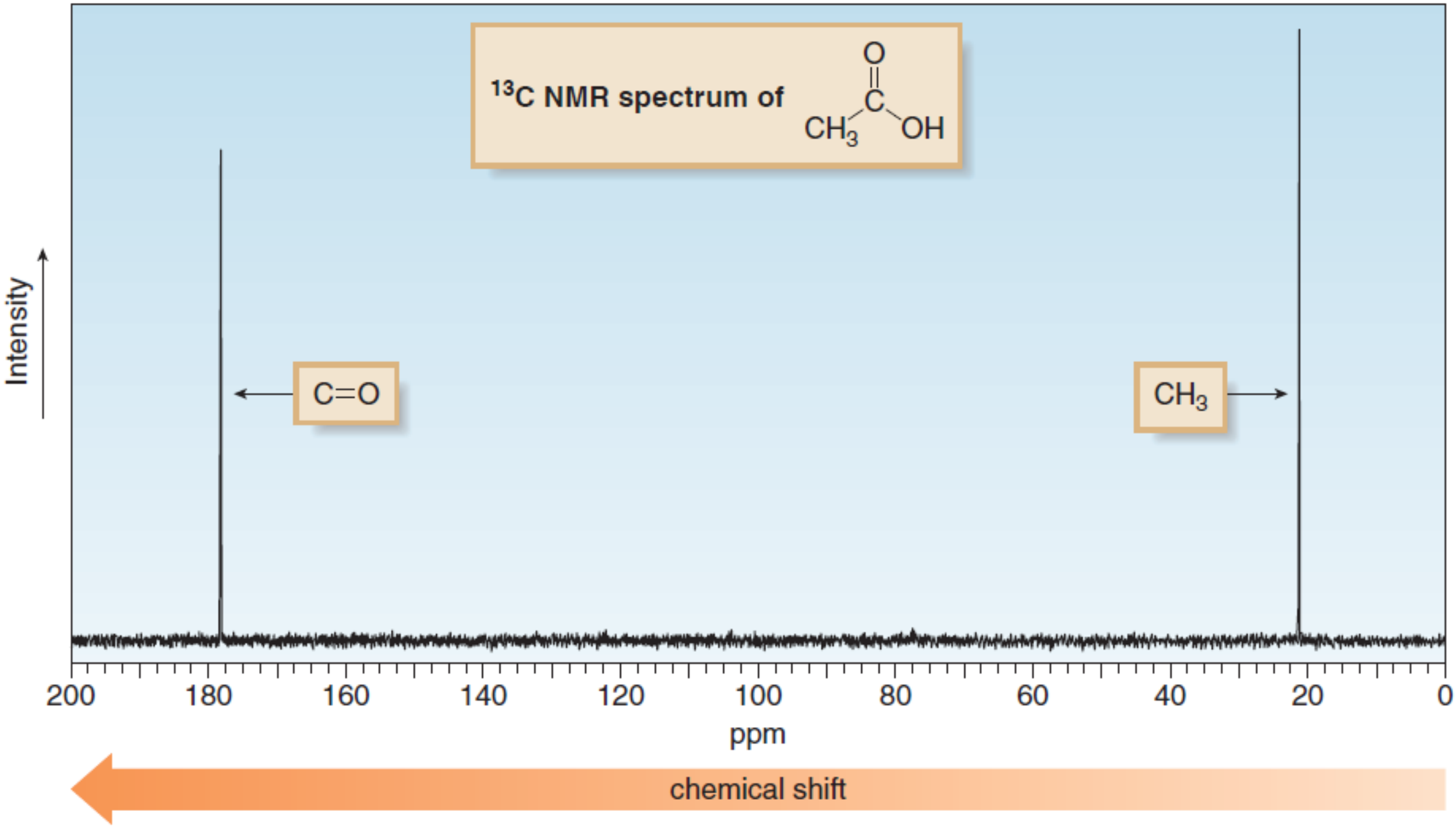
- 13C NMR spectroscopy is also an important tool for organic structure analysis.
- The physical basis for 13C NMR is the same as for 1H NMR.
- When placed in a magnetic field, B0, 13C nuclei can align themselves with or against B0.
- More nuclei are aligned with B0 because this arrangement is lower in energy, but these nuclei can be made to spin flip against the applied field by applying RF radiation of the appropriate frequency.

❖13C NMR spectra, like 1H NMR spectra, plot peak intensity versus chemical shift, using TMS as the reference signal at 0 ppm. 13C occurs in only 1.1% natural abundance,

❖ however, so 13C NMR signals are much weaker than 1H NMR signals.

❖ To overcome this limitation, modern spectrometers irradiate samples with many pulses of RF radiation and use mathematical tools to increase signal sensitivity and decrease background noise.

❖ The spectrum of acetic acid (CH3COOH) illustrates the general features of a 13C NMR spectrum.


^{13}C NMR spectrum of
O
C
CH_3
OH
Intensity
C=O
CH_3
200
180
160
140
120
100
80
60
40
20
0
ppm
chemical shift

❖13C NMR spectra are easier to analyze than 1H spectra because signals are not split. Each type of carbon atom appears as a single peak.

❖ Why aren't 13C signals split by nearby carbon atoms? Recall from Section 14.6 that splitting occurs when two NMR active nuclei—like two protons—are close to each other. Because of the low natural abundance of 13C nuclei (1.1%), the chance of two 13C nuclei being bonded to each other is very small (0.01%), and so no carbon–carbon splitting is observed.

- A 13C NMR signal can also be split by nearby protons. This 1H– 13C splitting is usually eliminated from a spectrum, however, by using an instrumental technique that decouples the proton– carbon interactions, so that every peak in a 13C NMR spectrum is a singlet.

- Two features of 13C NMR spectra provide the most structural information:

  - the number of signals observed and
  - the chemical shifts of those signals.

13C NMR: Number of Signals:

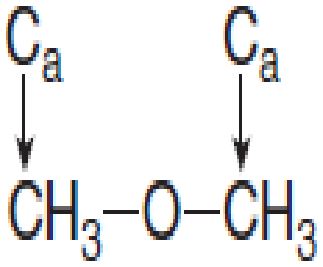
- The number of signals in a 13C spectrum gives the number of different types of carbon atoms in a molecule.

❑Carbon atoms in the same environment give the same NMR signal, whereas carbons in different environments give different NMR signals.

❑ The 13C NMR spectrum of CH3COOH has two signals because there are two different types of carbon atoms—the C of the CH3 group and the C of the carbonyl (C=O).

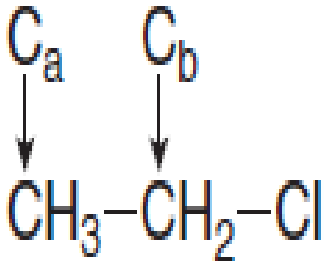
❑Because 13C NMR signals are not split, the number of signals equals the number of lines in the 13C NMR spectrum.

Thus, the ^{13}C NMR spectra of dimethyl ether, chloroethane, and methyl acetate exhibit one, two, and three lines, respectively, because these compounds contain one, two, and three different types of carbon atoms.



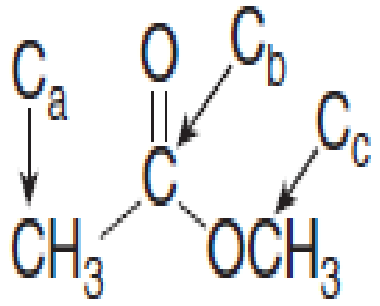
dimethyl ether

1 ^{13}C NMR signal
Both C's are equivalent.



chloroethane

2 ^{13}C NMR signals



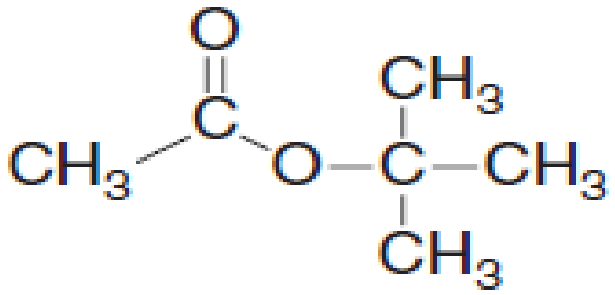
methyl acetate

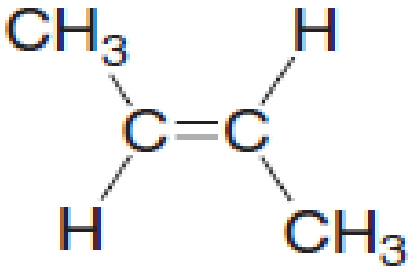
3 ^{13}C NMR signals

In contrast to what occurs in proton NMR, peak intensity is not proportional to the number of absorbing carbons, so ^{13}C NMR signals are not integrated.

How many lines are observed in the ^{13}C NMR spectrum of each compound?

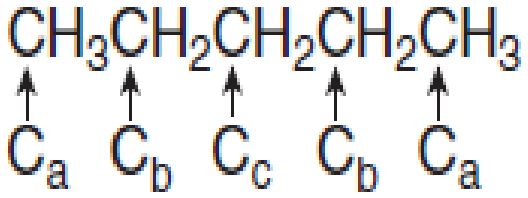
a. $CH_3CH_2CH_2CH_2CH_2CH_3$

b. 

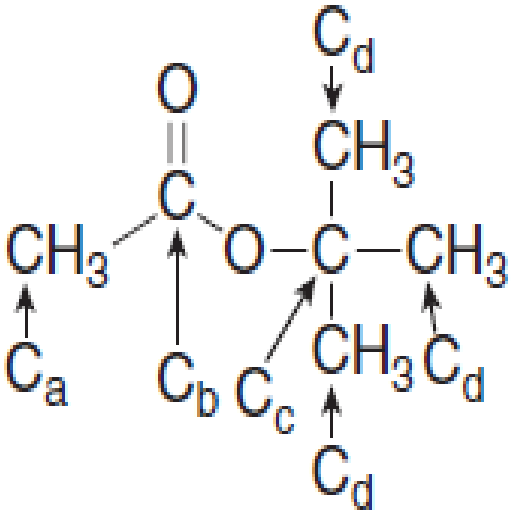
c. 

Solution

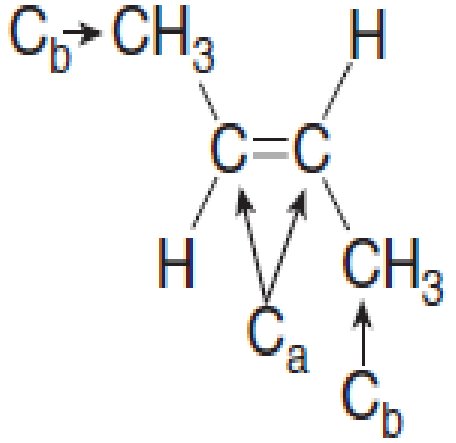
The number of different types of carbons equals the number of lines in a ^{13}C NMR spectrum.

a. 

3 types of C's
3 ^{13}C NMR signals

b. 

4 types of C's
4 ^{13}C NMR signals

c. 

2 types of C's
2 ^{13}C NMR signals

13C NMR: Position of Signals:

- In contrast to the small range of chemical shifts in 1H NMR (0–12 ppm usually), 13C NMR absorptions occur over a much broader range, 0–220 ppm.
- The chemical shifts of carbon atoms in 13C NMR depend on the same effects as the chemical shifts of protons in 1H NMR:

• The sp3 hybridized C atoms of alkyl groups are shielded and absorb upfield.

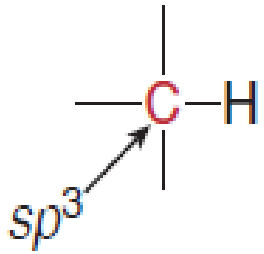
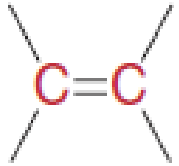
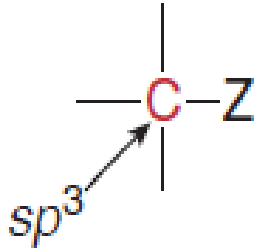
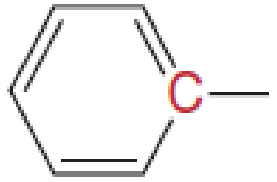
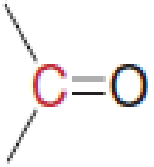
• Electronegative elements like halogen, nitrogen, and oxygen shift absorptions downfield.

• The sp2 hybridized C atoms of alkenes and benzene rings absorb downfield.

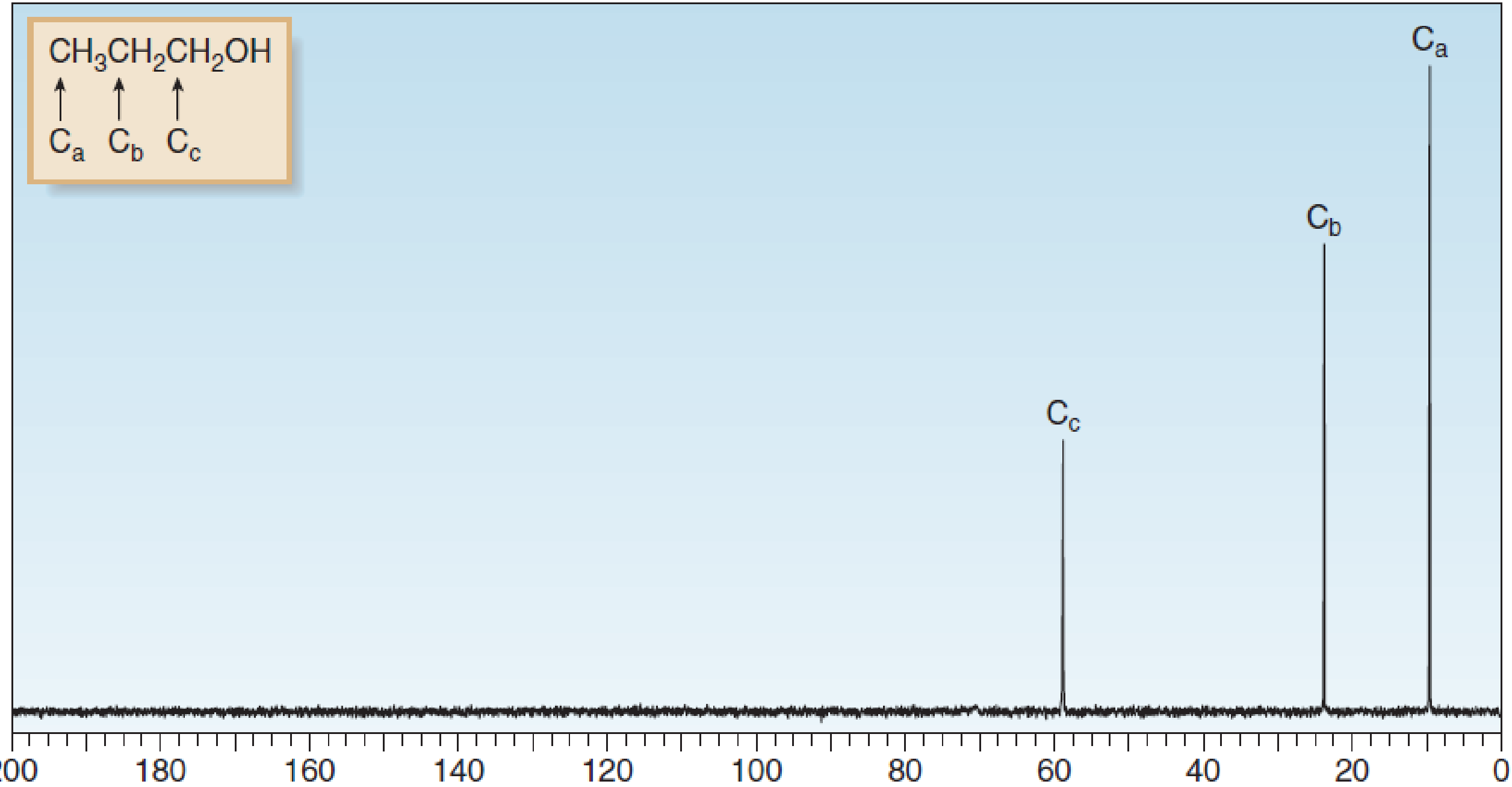
• Carbonyl carbons are highly deshielded, and absorb farther downfield than other carbon types.

Table 14.5 lists common 13C chemical shift values. The 13C NMR spectra of 1-propanol(CH3CH2CH2OH) and methyl acetate (CH3CO2CH3) in Figure 14.14 illustrate these principles.

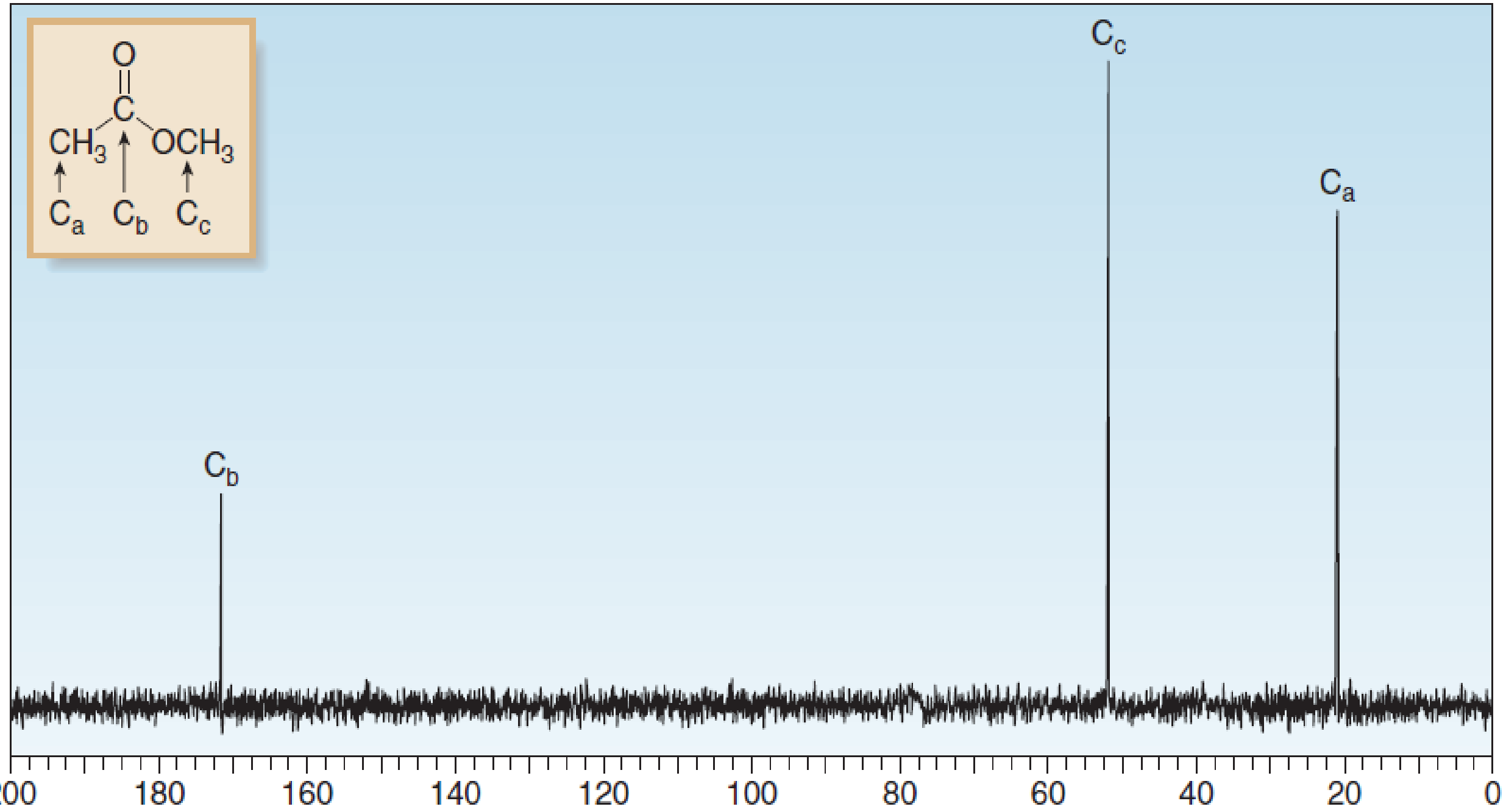
Table 14.5 Common ^{13}C Chemical Shift Values

Type of carbon	Chemical shift (ppm)	Type of carbon	Chemical shift (ppm)
	5–45		100–140
 Z = N, O, X	30–80		120–150
—C≡C—	65–100		160–210

a. 1-Propanol


$CH_3CH_2CH_2OH$
C_a C_b C_c
C_a
C_b
C_c
200
180
160
140
120
100
80
60
40
20
0

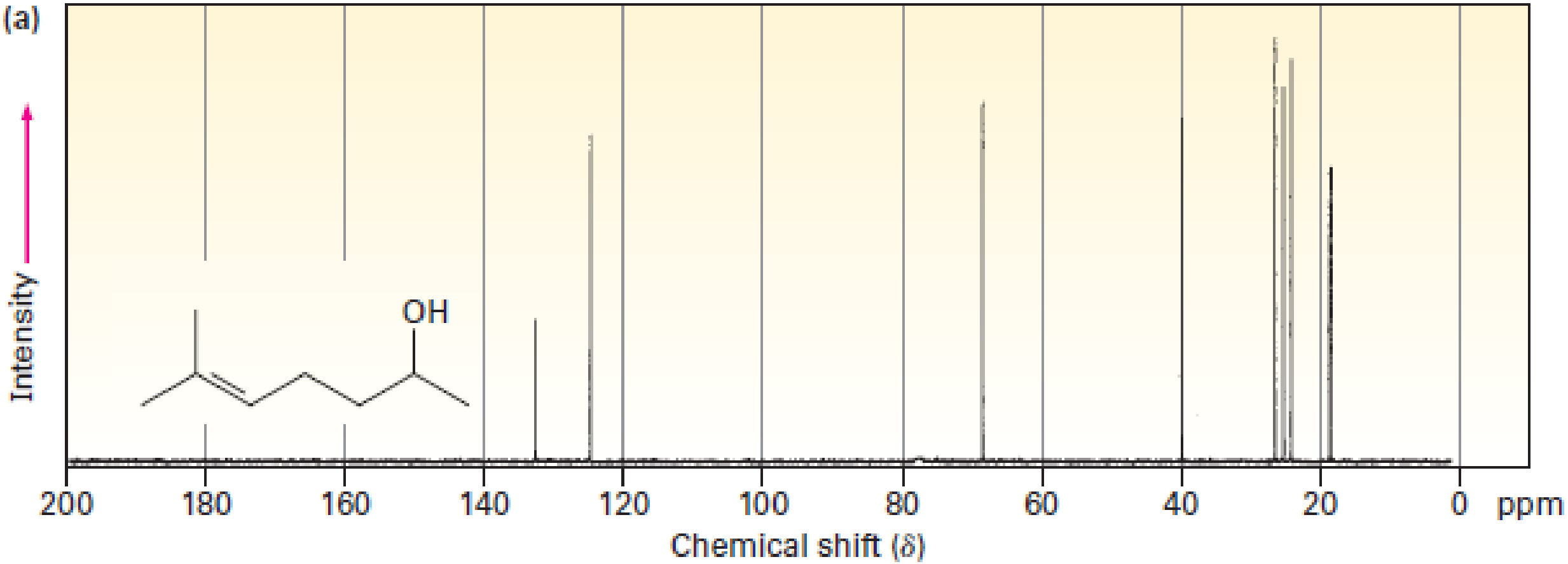
b. Methyl acetate



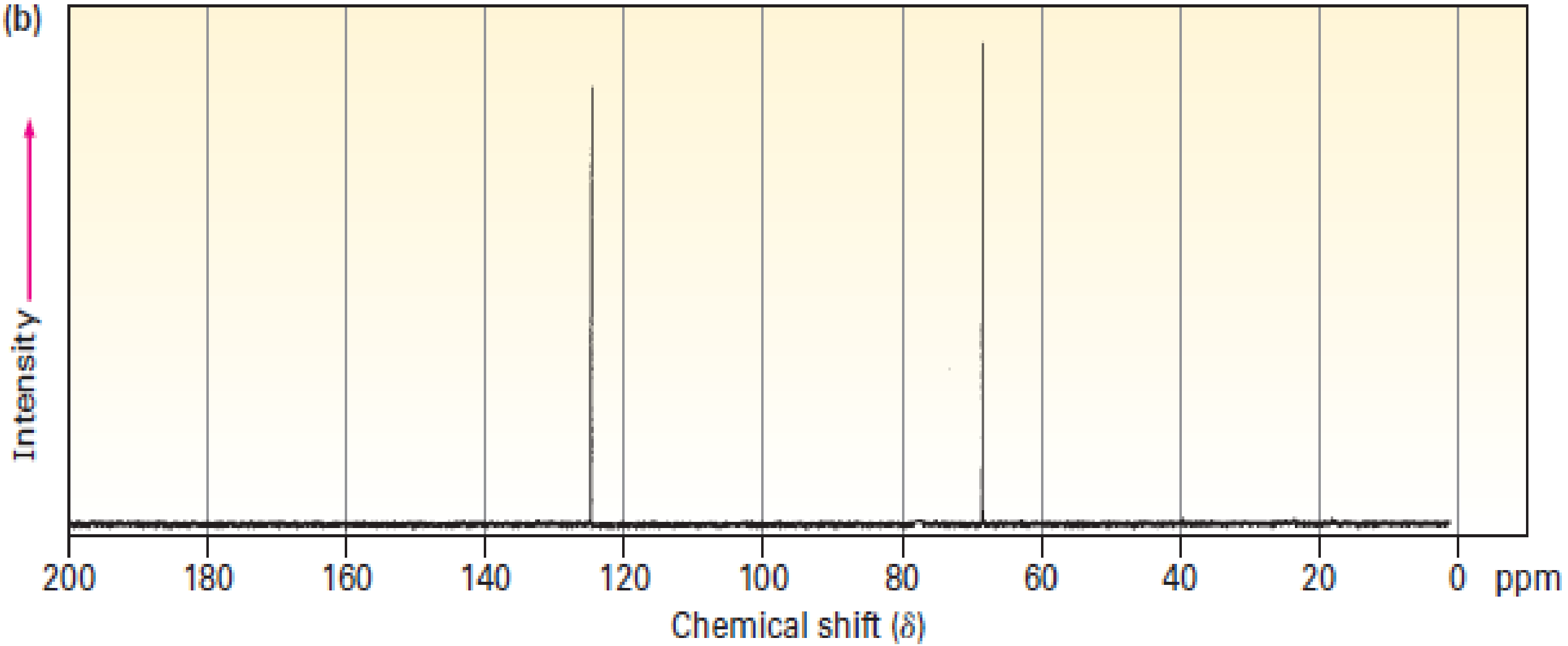
DEPT 13C NMR Spectroscopy:

Numerous techniques developed in recent years have made it possible to obtain enormous amounts of information from 13C NMR spectra. Among these techniques is one called DEPT–NMR, for distortionless enhancement by polarization transfer, which makes it possible to distinguish among signals due to CH3, CH2, CH, and quaternary carbons. That is, the number of hydrogens attached to each carbon in a molecule can be determined.

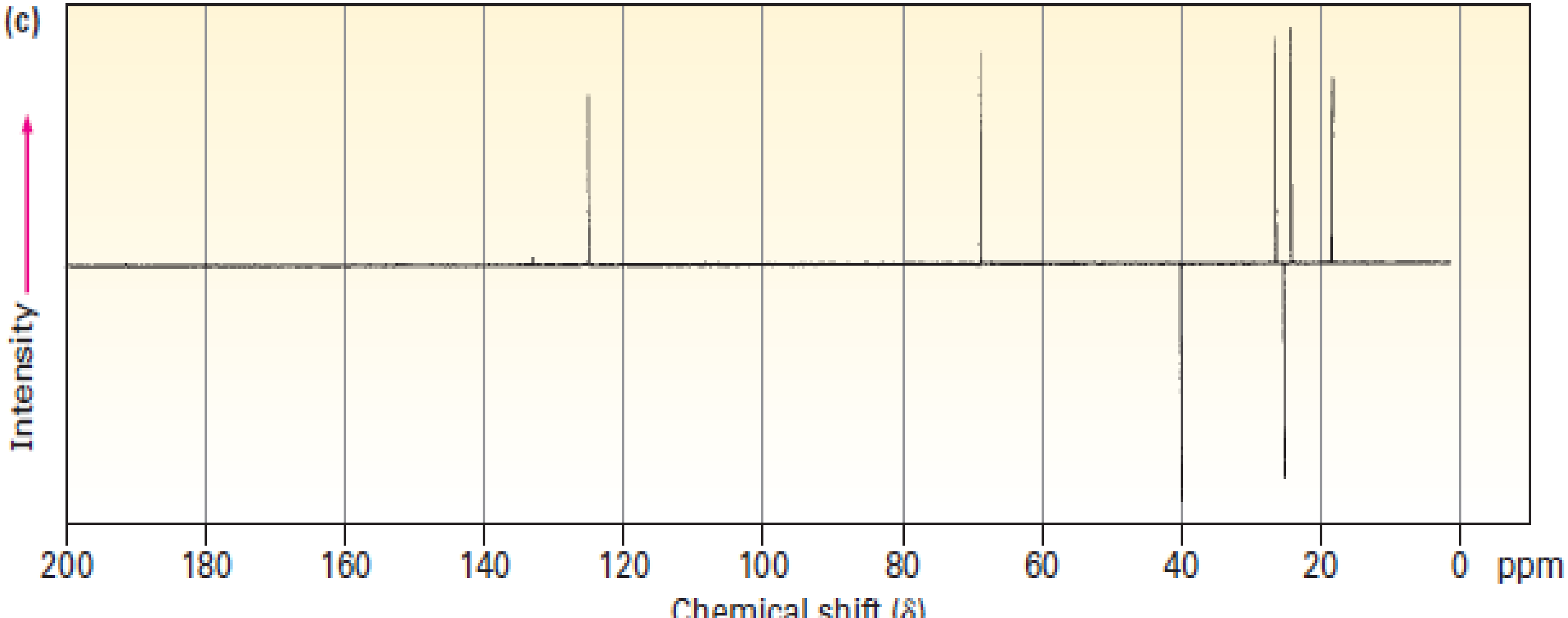
A DEPT experiment is usually done in three stages, as shown in Figure 13.10 for 6-methyl-5-hepten-2-ol. The first stage is to run an ordinary spectrum (called a broadband-decoupled spectrum) to locate the chemical shifts of all carbons.



Next, a second spectrum called a DEPT-90 is run, using special conditions under which only signals due to CH carbons appear. Signals due to CH3, CH2, and quaternary carbons are absent.



a third spectrum called a DEPT-135 is run, using conditions under which CH3 and CH resonances appear as positive signals, CH2 resonances appear as negative signals—that is, as peaks below the baseline—and quaternary carbons are again absent.



Putting together the information from all three spectra makes it possible to tell the number of hydrogens attached to each carbon. The CH carbons are identified in the DEPT-90 spectrum, the CH2 carbons are identified as the negative peaks in the DEPT-135 spectrum, the CH3 carbons are identified by subtracting the CH peaks from the positive peaks in the DEPT-135 spectrum, and quaternary carbons are identified by subtracting all peaks in the DEPT-135 spectrum from the peaks in the broadband-decoupled spectrum.

Broadband-decoupled	DEPT-90	DEPT-135
C, CH, CH_2, CH_3	CH	CH_3, CH are positive CH_2 is negative

C	Subtract DEPT-135 from broadband-decoupled spectrum
CH	DEPT-90
CH_2	Negative DEPT-135
CH_3	Subtract DEPT-90 from positive DEPT-135

Propose a structure for an alcohol, C4H10O, that has the following 13C NMR spectral data:

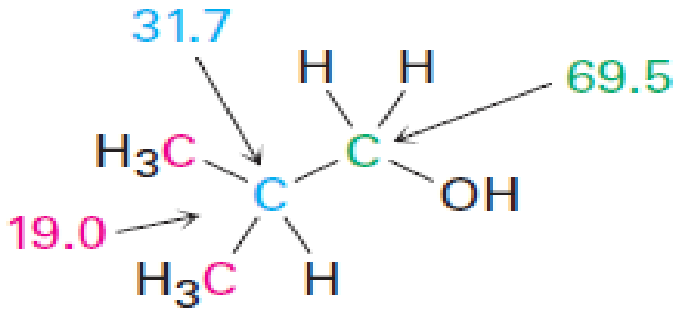
Broadband decoupled 13C NMR: 19.0, 31.7, 69.5 d;

DEPT-90: 31.7 d;

DEPT-135: positive peak at 19.0 d, negative peak at 69.5 d.

- To gain information from the 13C data, let's begin by noting that the unknown alcohol has four carbon atoms, yet has only three NMR absorptions, which implies that two of the carbons must be equivalent.
- Looking at chemical shifts, two of the absorptions are in the typical alkane region (19.0 and 31.7 d), while one is in the region of a carbon bonded to an electronegative atom (69.5 d)—oxygen in this instance.
- The DEPT-90 spectrum tells us that the alkyl carbon at 31.7 d is tertiary (CH);
- the DEPT-135 spectrum tells us that the alkyl carbon at 19.0 d is a methyl (CH3) and that the carbon bonded to oxygen (69.5 d) is secondary (CH2).
- The two equivalent carbons are probably both methyls bonded to the same tertiary carbon, (CH3)2CH] . We can now put the pieces together to propose a structure:

2-methyl-1-propanol.



2-Methyl-1-propanol

Problem 13.11

Propose a structure for an aromatic hydrocarbon, $C_{11}H_{16}$, that has the following ^{13}C NMR spectral data:

Broadband decoupled: 29.5, 31.8, 50.2, 125.5, 127.5, 130.3, 139.8 δ

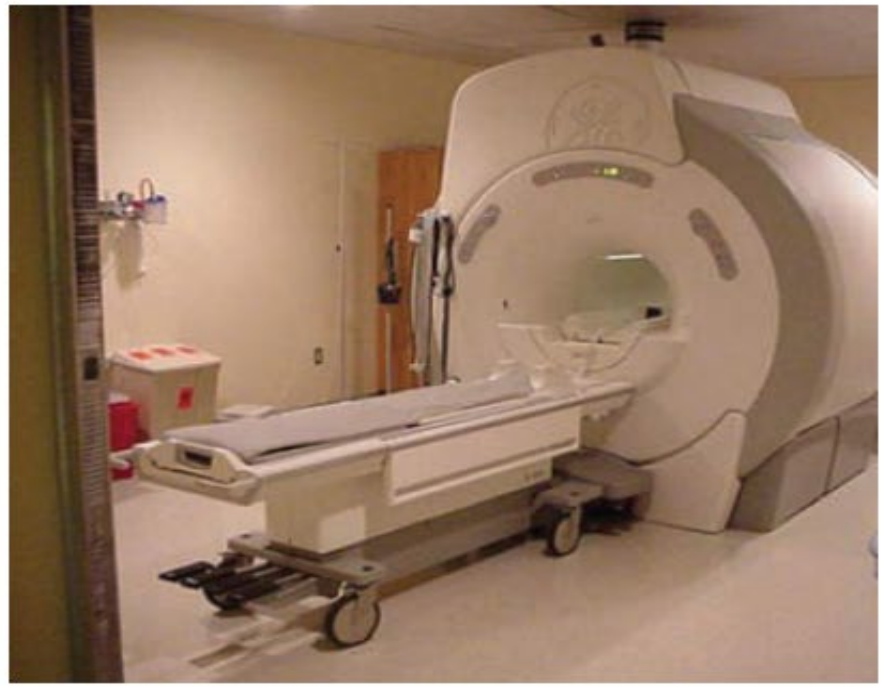
DEPT-90: 125.5, 127.5, 130.3 δ

DEPT-135: positive peaks at 29.5, 125.5, 127.5, 130.3 δ; negative peak at 50.2 δ

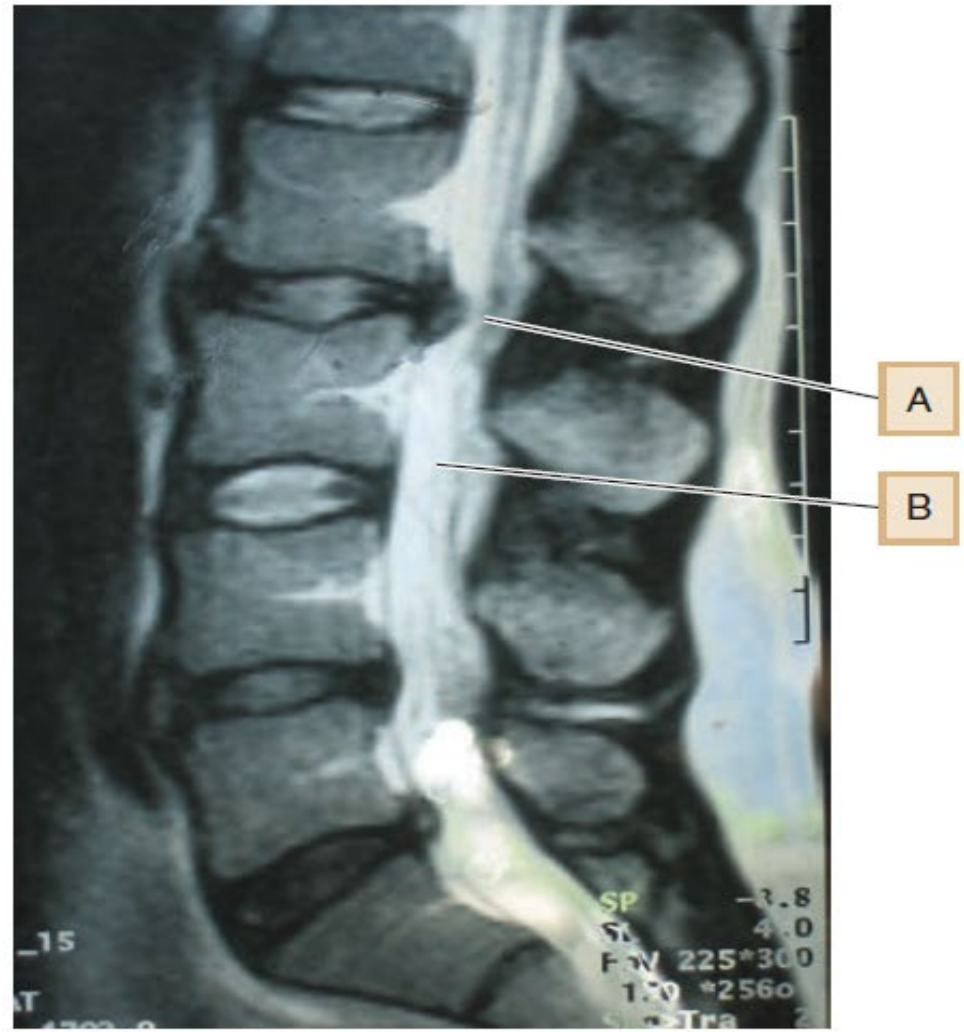
Figure 14.15

Magnetic resonance imaging

(a)



(b)



a. An MRI instrument: An MRI instrument is especially useful for visualizing soft tissue. In 2002, 60 million MRI procedures were performed. The 2003 Nobel Prize in Physiology or Medicine was awarded to chemist Paul C. Lauterbur and physicist Sir Peter Mansfield for their contributions in developing magnetic resonance imaging.

b. An MRI image of the lower back: **A** labels spinal cord compression from a herniated disc. **B** labels the spinal cord, which would not be visualized with conventional X-rays.

Magnetic Resonance Imaging (MRI):

❑Magnetic resonance imaging (MRI)—NMR spectroscopy in medicine—is a powerful diagnostic technique (Figure 14.15a). The “sample” is the patient, who is placed in a large cavity in a magnetic field, and then irradiated with RF energy. Because RF energy has very low frequency and low energy, the method is safer than X-rays or computed tomography (CT) scans that employ high- frequency, high-energy radiation that is known to damage living cells.

❑Living tissue contains protons (especially the H atoms in H_2O) in different concentrations and environments. When irradiated with RF energy, these protons are excited to a higher energy spin state, and then fall back to the lower energy spin state. These data are analyzed by a computerthat generates a plot that delineates tissues of different proton density (Figure 14.15b). MRIs can be recorded in any plane. Moreover, because the calcium present in bones is not NMR active, an MRI instrument can “see through” bones such as the skull and visualize the soft tissue underneath.