An MRI may be taken in any plane, essentially independently of the patient's position, allowing optimum visualization of the anatomical feature of interest. By contrast, the plane of a computed tomography (CT) scan, which uses X-rays, is defined by the position of the patient within the machine and is usually perpendicular to the long axis of the body. CT scans in other planes may be obtained only if the patient is a skilled contortionist.

Most of the signals in an MRI scan originate from the hydrogens of water molecules because these hydrogens are far more abundant in tissues than are the hydrogens of organic compounds. The difference in the way water is bound in different tissues is what produces much of the variation in signal among organs, as well as the variation between healthy and diseased tissue (Figure 14.41). MRI scans, therefore, can sometimes provide much more information than images obtained by other means. For example, MRI can provide detailed images of blood vessels. Flowing fluids such as blood respond differently to excitation in an MRI scanner than do stationary tissues and normally do not produce a signal. However, the data may be processed to eliminate signals from motionless structures, thereby showing signals only from the fluids. This technique is sometimes used instead of more invasive methods to examine the vascular tree. It is now possible to completely suppress the signal from certain types of tissue (usually fat). It is also possible to differentiate intracellular and extracellular edema, which is important in assessing patients suspected of having suffered strokes.

The versatility of MRI has been enhanced by the use of gadolinium as a contrast reagent. Gadolinium, a paramagnetic metal, modifies the magnetic field in its immediate vicinity, altering the signal from hydrogen nuclei in close proximity. The distribution of gadolinium, which is infused into a patient's veins, may be modified by certain disease processes, such as cancer and inflammation. These abnormal distributions appear in the images obtained from appropriate scanning techniques.

NMR spectroscopy using ^{31}P is not yet in routine clinical use, but is being used widely in clinical research. It is of particular interest because ATP and ADP (Sections 17.20 and 27.2) are involved in most metabolic processes, so it will provide a way to investigate cellular metabolism.

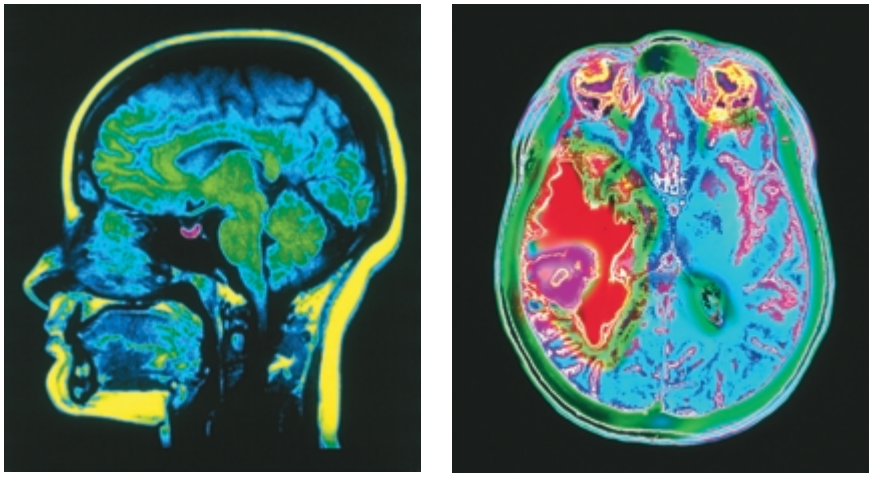


Figure 14.41 ▶
(a) MRI of a normal brain. The pituitary is highlighted (pink). (b) MRI of an axial section through the brain showing a tumor (purple) surrounded by damaged, fluid-filled tissue (red).

Summary

NMR spectroscopy is used to identify the carbon–hydrogen framework of an organic compound. When a sample is placed in a magnetic field, protons aligning with the field are in the lower-energy ***α*-spin state**; those aligning against the field are in the higher-energy ***β*-spin state**. The energy difference between the spin states depends on the strength of the **applied magnetic field**. When subjected to radiation with energy corresponding to the energy

difference between the spin states, nuclei in the α-spin state are promoted to the β-spin state. When they return to their original state, they emit signals whose frequency depends on the difference in energy between the spin states. An **NMR spectrometer** detects and displays these signals as a plot of their frequency versus their intensity—an **NMR spectrum**.

Each set of chemically equivalent protons gives rise to a signal, so the number of signals in an ^{1}H NMR spectrum indicates the number of different kinds of protons in a compound. The **chemical shift** is a measure of how far the signal is from the reference TMS signal. The chemical shift (δ) is independent of the **operating frequency** of the spectrometer.

The larger the magnetic field sensed by the proton, the higher is the frequency of the signal. The electron density of the environment in which the proton is located **shields** the proton from the applied magnetic field. Therefore, a proton in an electron-dense environment shows a signal at a lower frequency than a proton near electron-withdrawing groups. Low-frequency (upfield) signals have small δ (ppm) values; high-frequency (downfield) signals have large δ values. Thus, the position of a signal indicates the kind of proton(s) responsible for the signal and the kinds of neighboring substituents. In a similar environment, the chemical shift of methyl protons is at a lower frequency than that of methylene protons, which in turn is at a lower frequency than that of a methine proton. **Diamagnetic anisotropy** causes unusual chemical shifts for hydrogens bonded to carbons that form π bonds. **Integration** tells us the relative number of protons that give rise to each signal.

The **multiplicity** of a signal (the number of peaks in the signal) indicates the number of protons bonded to adjacent carbons. Multiplicity is described by the ***N* + 1 rule**, where N is the number of equivalent protons bonded to adjacent carbons. A **splitting diagram** can help us understand the splitting pattern obtained when a signal is split by more than one set of protons. Deuterium substitution can be a helpful technique in the analysis of complicated ^{1}H NMR spectra.

The **coupling constant** (***J***) is the distance between two adjacent peaks of a split NMR signal. Coupling constants are independent of the operating frequency of the spectrometer. Coupled protons have the same coupling constant. The coupling constant for trans protons is greater than that for cis protons. When two different sets of protons split a signal, the multiplicity of the signal is determined by using the $N + 1$ rule separately for each set of hydrogens when the coupling constants for the two sets are different. When the coupling constants are similar, the $N + 1$ rule can be applied to both sets simultaneously.

The chemical shift of a proton bonded to an O or an N depends on the degree to which the proton is hydrogen bonded. In the presence of trace amounts of acid or base, protons bonded to oxygen undergo **proton exchange**. In that case, the signal for a proton bonded to an O is not split and does not split the signal of adjacent protons.

The number of signals in a ^{13}C NMR spectrum tells how many different kinds of carbons a compound has. Carbons in electron-dense environments produce low-frequency signals; carbons close to electron-withdrawing groups produce high-frequency signals. Chemical shifts for ^{13}C NMR range over about 220 ppm, compared with about 12 ppm for ^{1}H NMR. ^{13}C NMR signals are not normally split by neighboring carbons, unless the spectrometer is run in a proton-coupled mode.

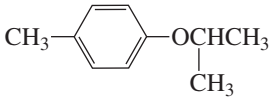
Key Terms

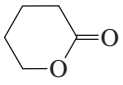
applied magnetic field (p. 527)
chemically equivalent protons (p. 531)
chemical shift (p. 533)
^{13}C NMR (p. 527)
COSY spectrum (p. 569)
coupled protons (p. 542)
coupling constant (p. 551)
DEPT ^{13}C NMR spectrum (p. 568)
diamagnetic anisotropy (p. 541)
diamagnetic shielding (p. 530)
2-D NMR (p. 569)
doublet (p. 542)
doublet of doublets (p. 547)
downfield (p. 531)
effective magnetic field (p. 530)
Fourier transform NMR (FT–NMR) spectrum (p. 530)
geminal coupling (p. 547)
gyromagnetic ratio (p. 528)
HETCOR spectrum (p. 571)
^{1}H NMR (p. 526)
integration (p. 539)
long-range coupling (p. 544)
magnetic resonance imaging (MRI) (p. 571)
methine hydrogen (p. 536)
MRI scanner (p. 571)
multiplet (p. 547)
multiplicity (p. 542)
$N + 1$ rule (p. 542)
NMR spectroscopy (p. 526)
operating frequency (p. 528)
proton-coupled ^{13}C NMR spectrum (p. 565)
proton exchange (p. 558)
quartet (p. 542)
reference compound (p. 533)
rf radiation (p. 527)
singlet (p. 541)
α-spin state (p. 527)
β-spin state (p. 527)
spin–spin coupling (p. 542)
splitting diagram (p. 554)
splitting tree (p. 554)
triplet (p. 542)
upfield (p. 531)

Problems

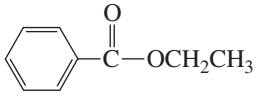
41. How many signals are produced by each of the following compounds in its

a. ^{1}H NMR spectrum? b. ^{13}C NMR spectrum?

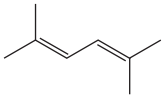
1. 

3. 

5. 

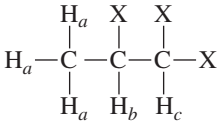
2. 

4. 

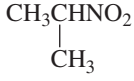
6. 

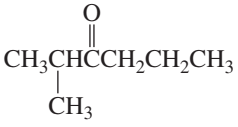
42. Draw a splitting diagram for the H_b proton and indicate its multiplicity if

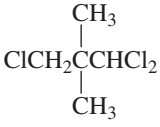
a. $J_{ba} = J_{bc}$ b. $J_{ba} = 2J_{bc}$



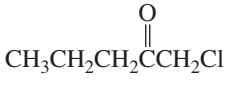
43. Label each set of chemically equivalent protons, using *a* for the set that will be at the lowest frequency (farthest upfield) in the ^{1}H NMR spectrum, *b* for the next, etc. Indicate the multiplicity of each signal.

a. 

c. 

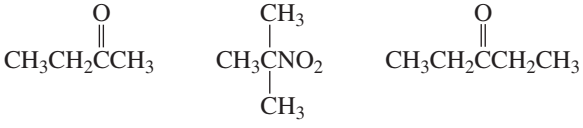
e. 

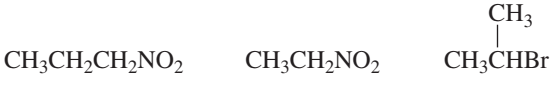
b. $CH_3CH_2CH_2OCH_3$

d. 

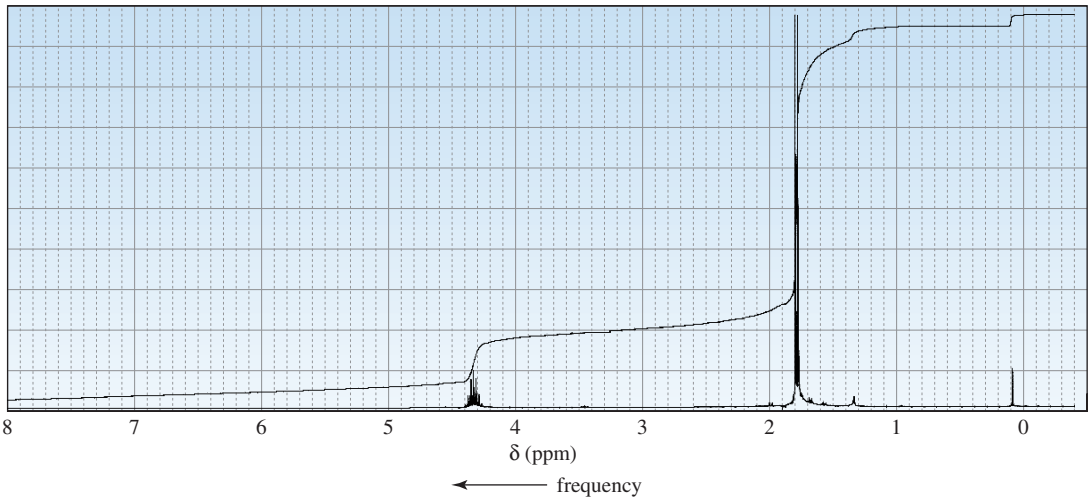
f. $ClCH_2CH_2CH_2CH_2CH_2Cl$

44. Match each of the ^{1}H NMR spectra on page 575 with one of the following compounds:

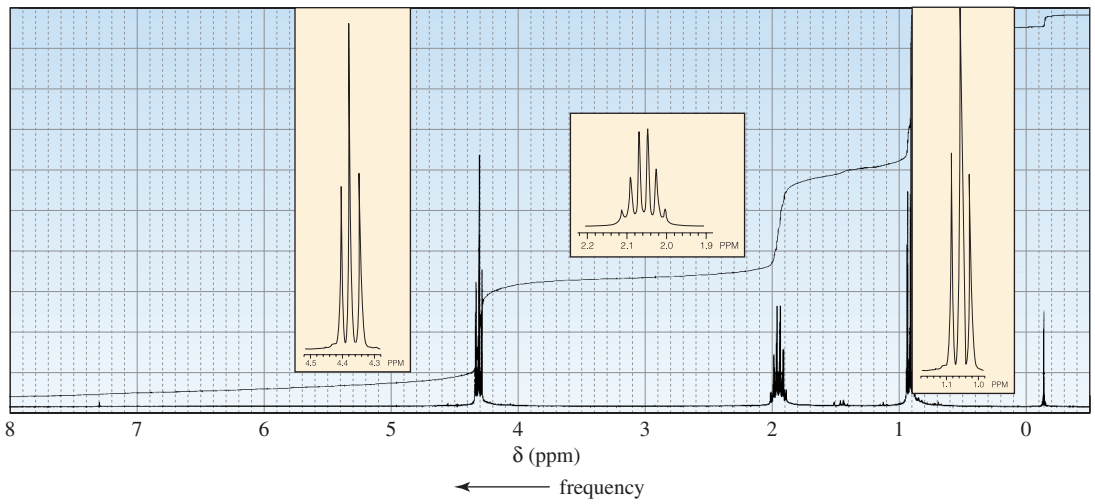




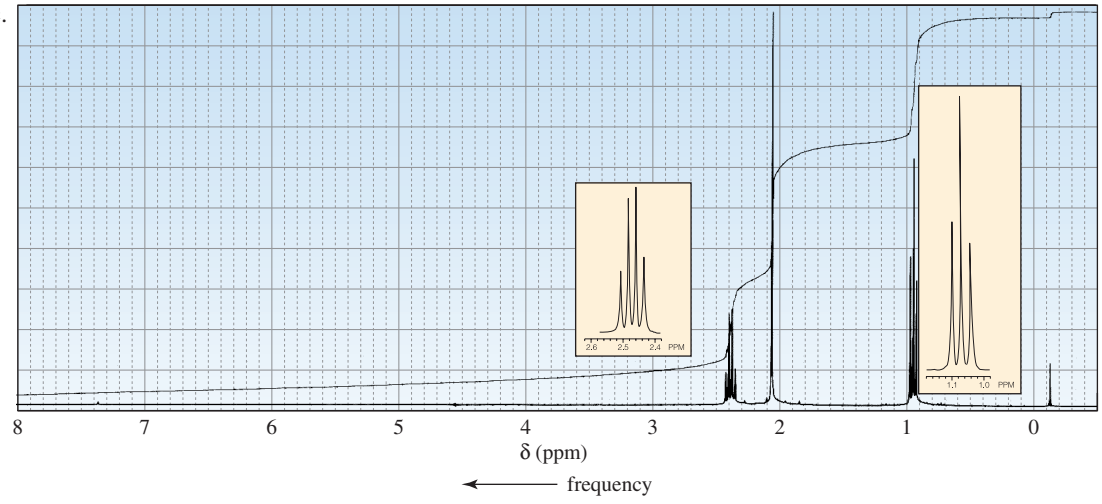
a.


8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

b.


4.5
4.4
4.3
PPM
2.2
2.1
2.0
1.9
PPM
1.1
1.0
PPM
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

c.

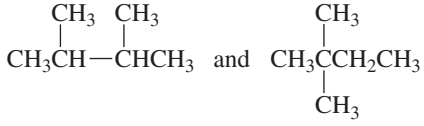

2.6
2.5
2.4
PPM
1.1
1.0
PPM
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

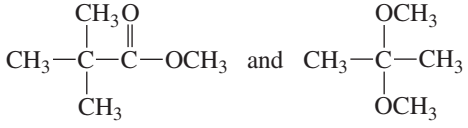
45. Determine the ratios of the chemically nonequivalent protons in a compound if the steps of the integration curves measure 40.5, 27, 13, and 118 mm, from left to right across the spectrum. Give the structure of a compound whose ^{1}H NMR spectrum would show these integrals in the observed order.

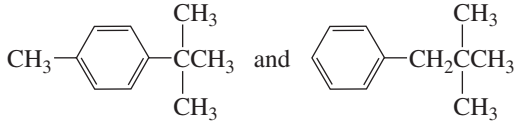
46. How could ^{1}H NMR distinguish between the compounds in each of the following pairs?

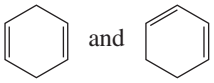
a. $CH_3CH_2CH_2OCH_3$ and $CH_3CH_2OCH_2CH_3$

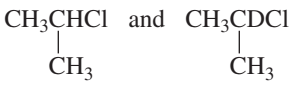
b. $BrCH_2CH_2CH_2Br$ and $BrCH_2CH_2CH_2NO_2$

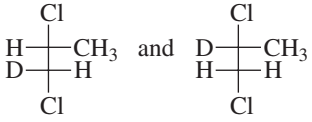
c.  and

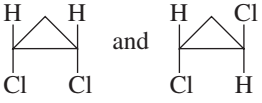
d. 

e. 

f. 

g. 

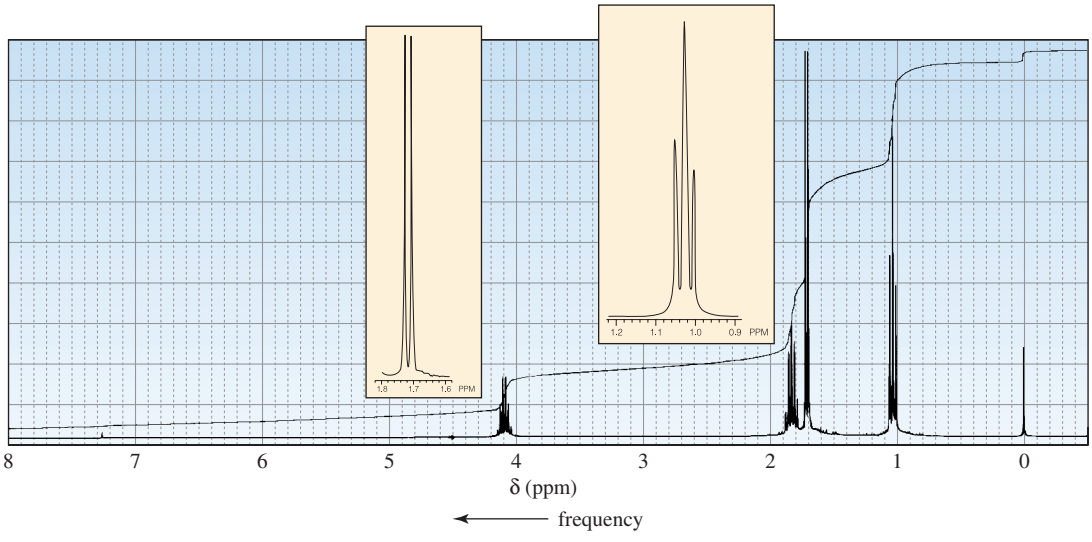
h. 

i. 

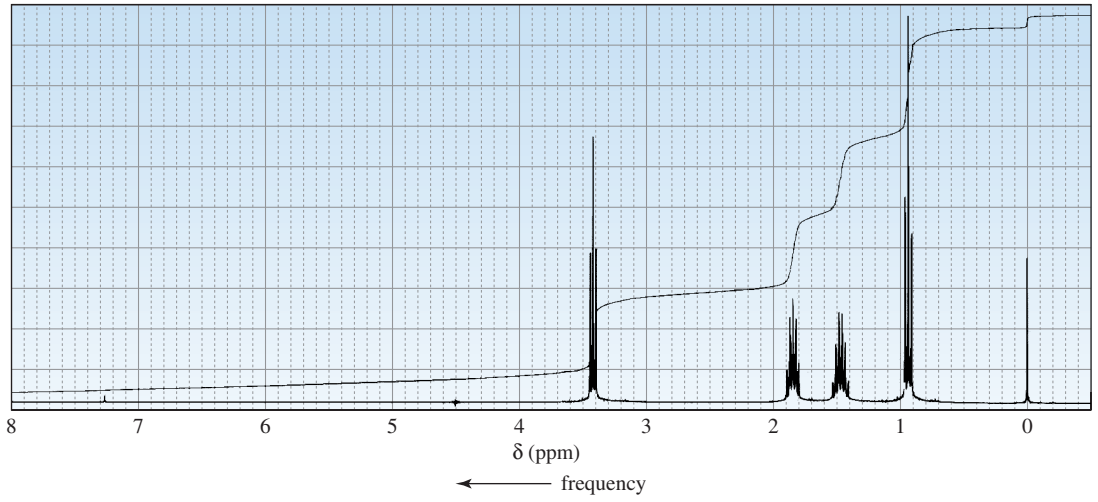
47. Answer the following questions:
   a. What is the relationship between chemical shift in ppm and operating frequency?
   b. What is the relationship between chemical shift in hertz and operating frequency?
   c. What is the relationship between coupling constant and operating frequency?
   d. How does the operating frequency in NMR spectroscopy compare with the operating frequency in IR and UV/Vis spectroscopy?

48. The ^{1}H NMR spectra of three isomers with molecular formula C_4H_9Br are shown here. Which isomer produces which spectrum?

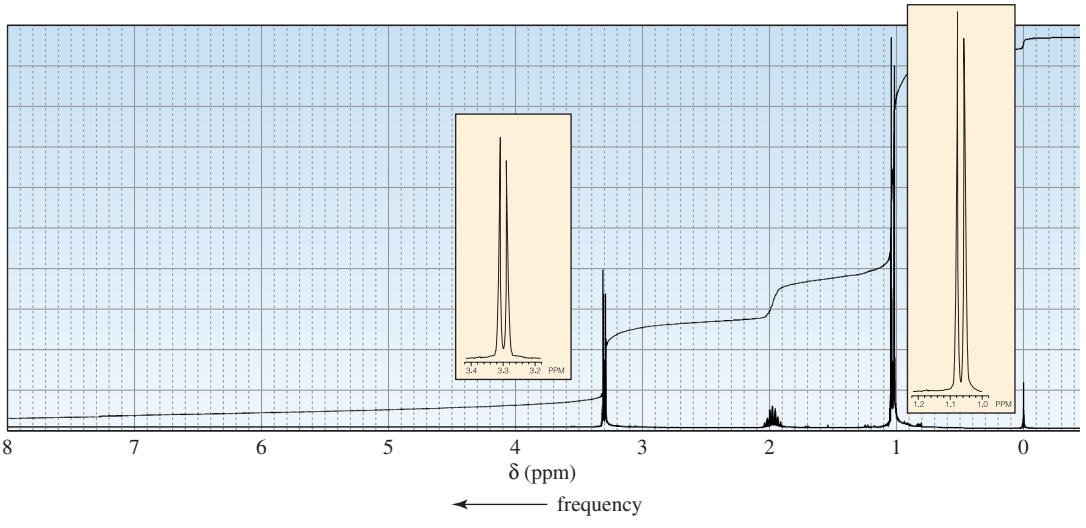
a.



b.



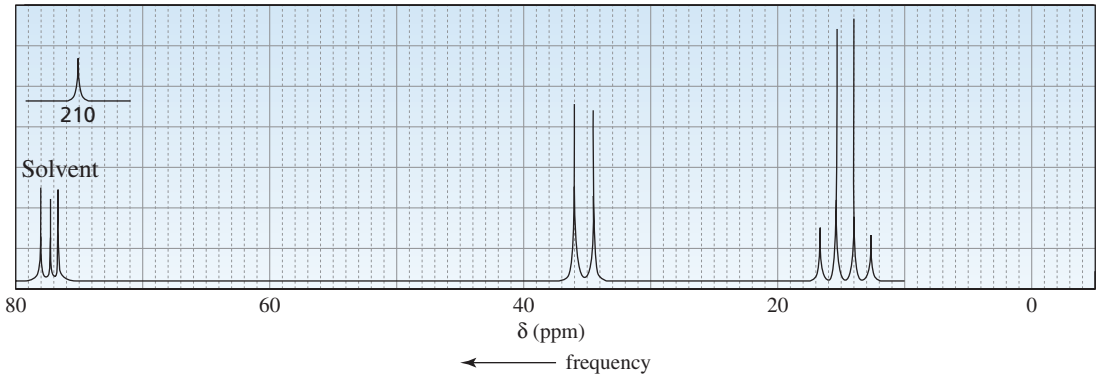
c.



49. Identify each of the following compounds from the ^{1}H NMR data and molecular formula. The number of hydrogens responsible for each signal is shown in parentheses.

a. $C_4H_8Br_2$	1.97 ppm (6) singlet 3.89 ppm (2) singlet	b. C_8H_9Br	2.01 ppm (3) doublet 5.14 ppm (1) quartet 7.35 ppm (5) broad singlet	c. $C_5H_{10}O_2$	1.15 ppm (3) triplet 1.25 ppm (3) triplet 2.33 ppm (2) quartet 4.13 ppm (2) quartet

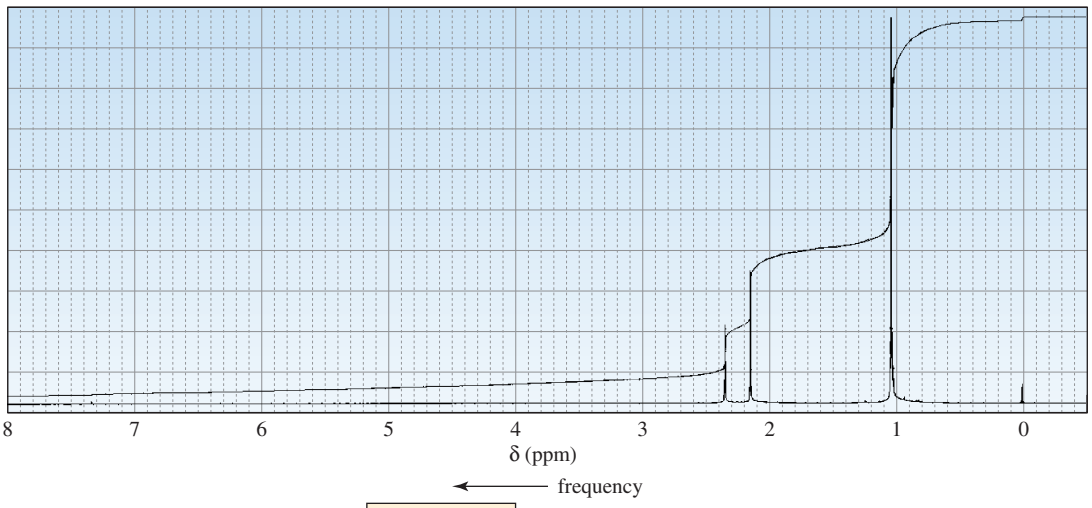
50. Identify the compound with molecular formula $C_7H_{14}O$ that gives the following proton-coupled ^{13}C NMR spectrum.



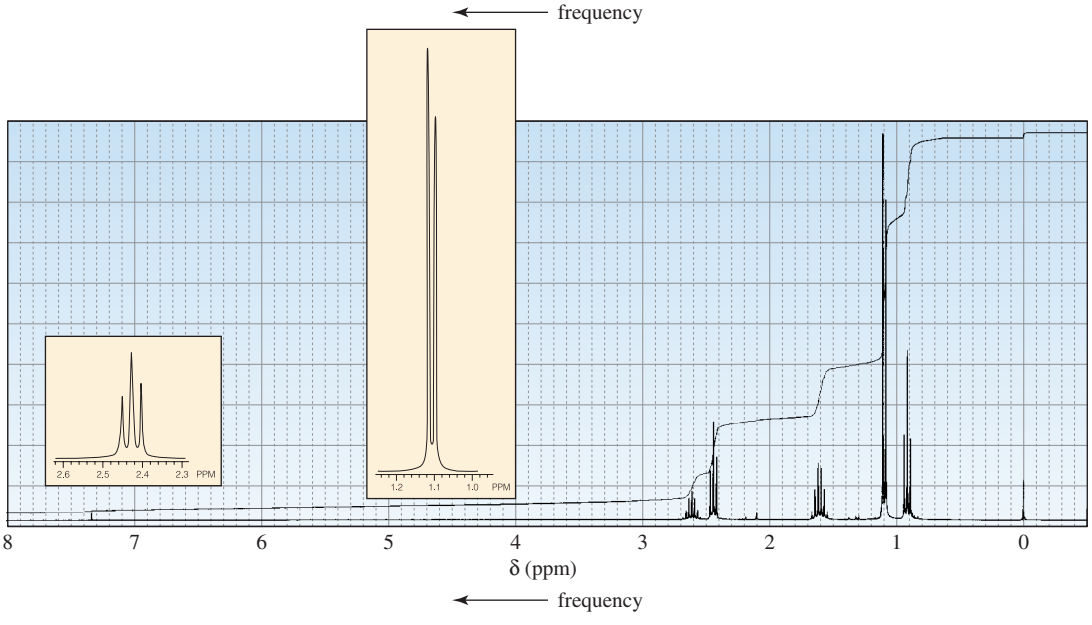
51. Compound A, with molecular formula C_4H_9Cl, shows two signals in its ^{13}C NMR spectrum. Compound B, an isomer of compound A, shows four signals, and in the proton-coupled mode, the signal farthest downfield is a doublet. Identify compounds A and B.

52. The ^1H NMR spectra of three isomers with molecular formula $C_7H_{14}O$ are shown here. Which isomer produces which spectrum?

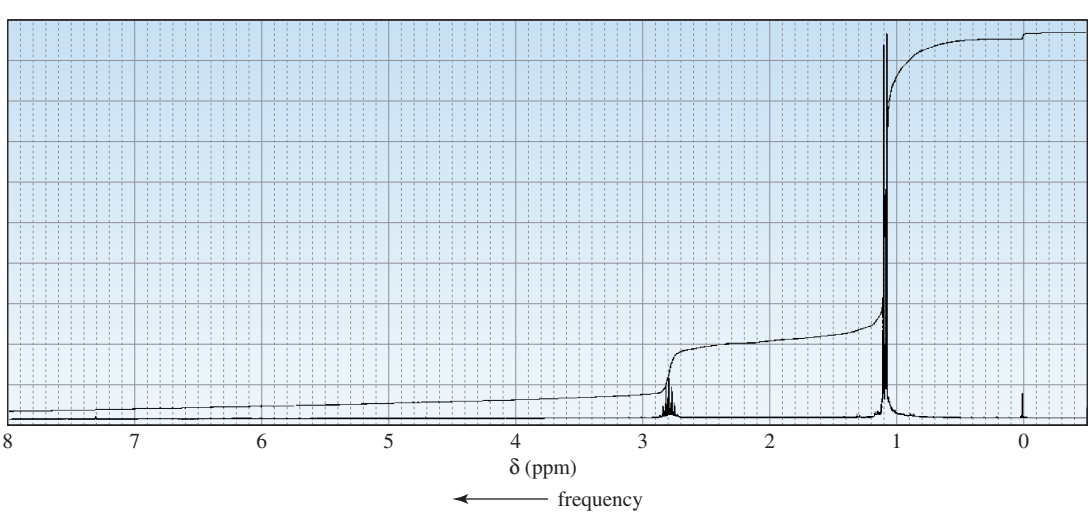
a.



b.



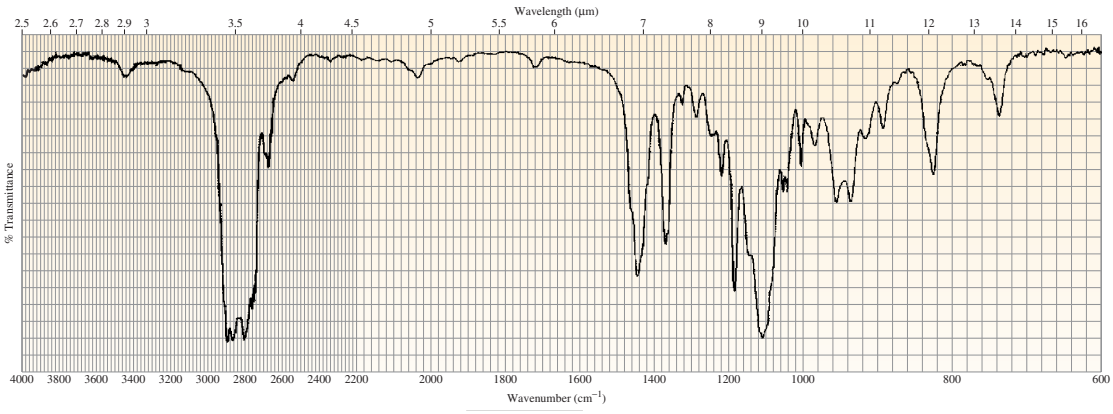
c.

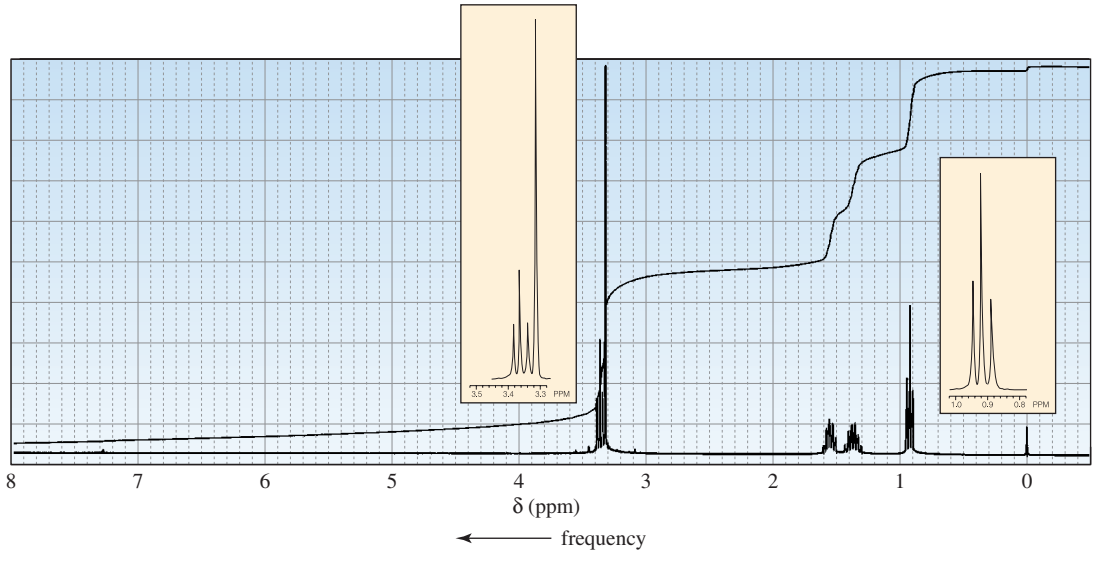


53. Would it be better to use ^{1}H NMR or ^{13}C NMR to distinguish among 1-butene, *cis*-2-butene, and 2-methylpropene? Explain your answer.

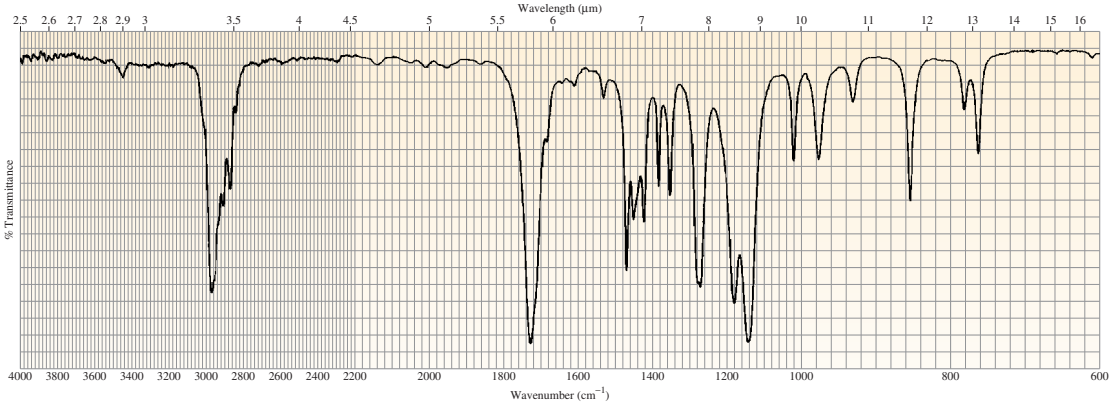
54. Determine the structure of each of the following unknown compounds based on its molecular formula and its IR and ^{1}H NMR spectra.

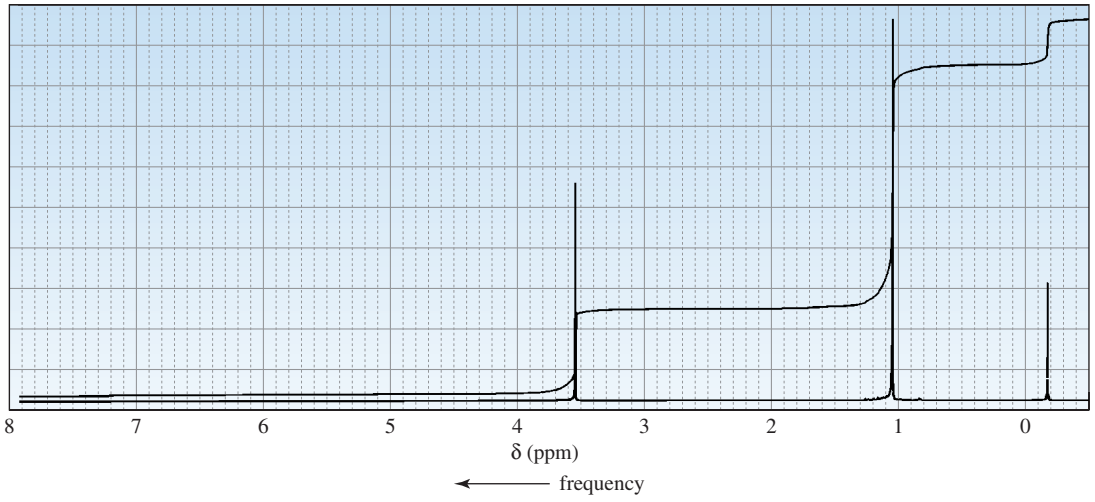
a. $C_5H_{12}O$



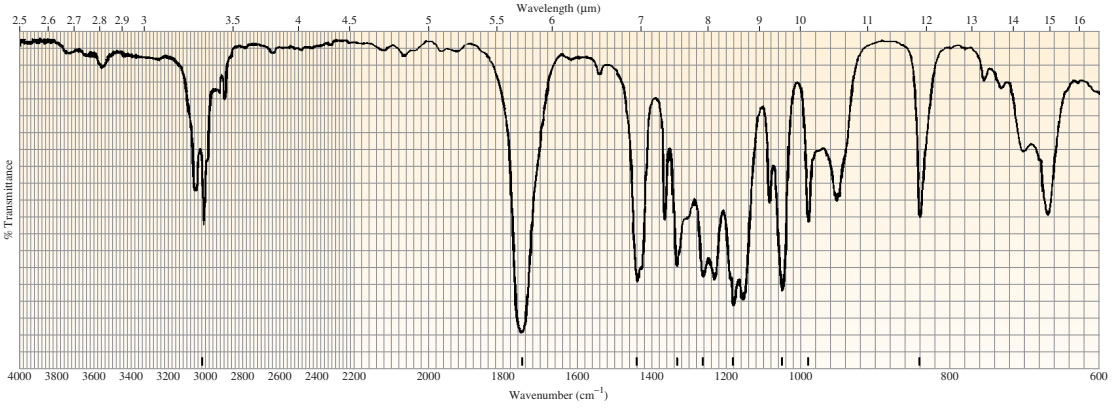


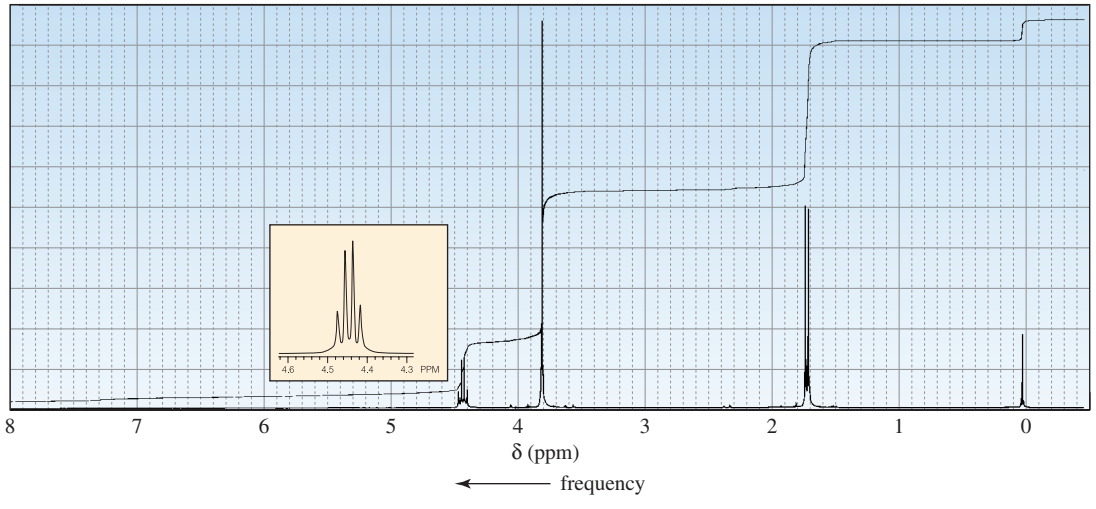
b. $C_6H_{12}O_2$



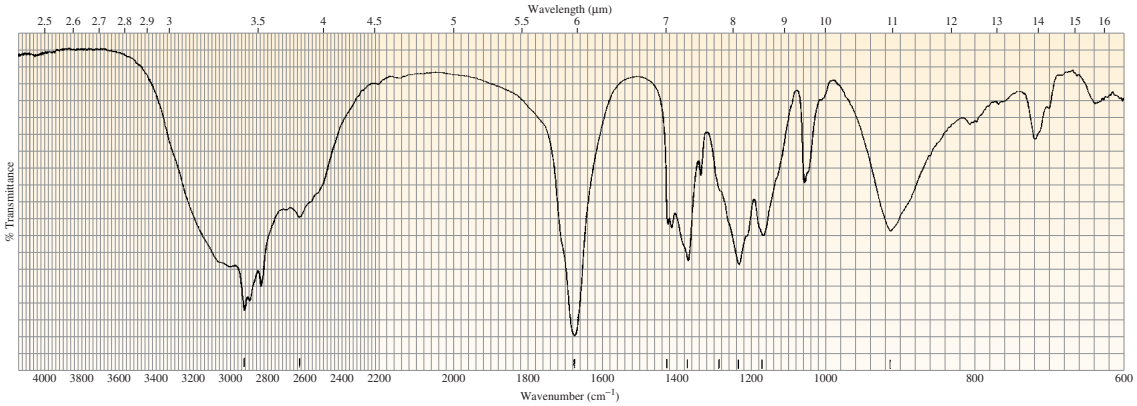

8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

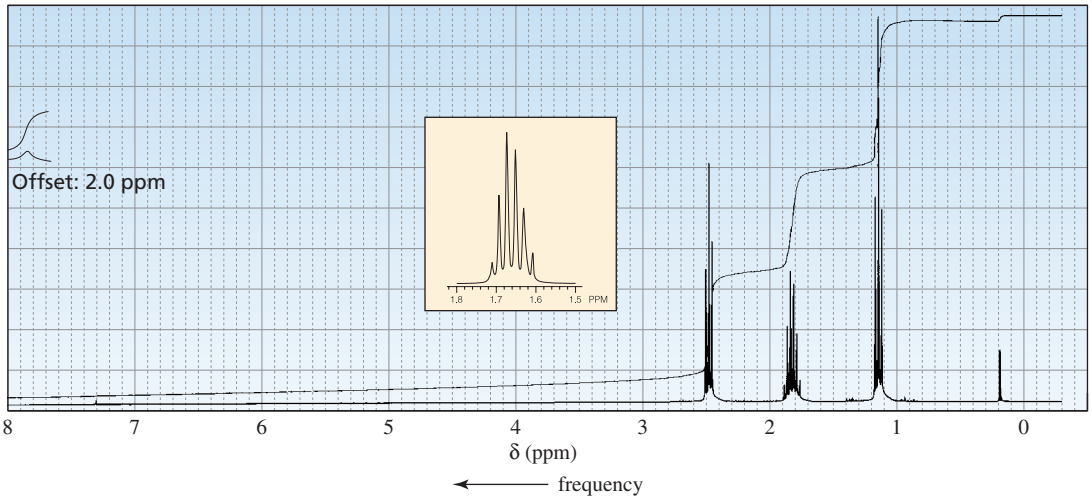
c. $C_4H_7ClO_2$


Wavelength (μm)
2.5 2.6 2.7 2.8 2.9 3 3.5 4 4.5 5 5.5 6 7 8 9 10 11 12 13 14 15 16
% Transmittance
4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600
Wavenumber (cm⁻¹)


4.6 4.5 4.4 4.3 PPM
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

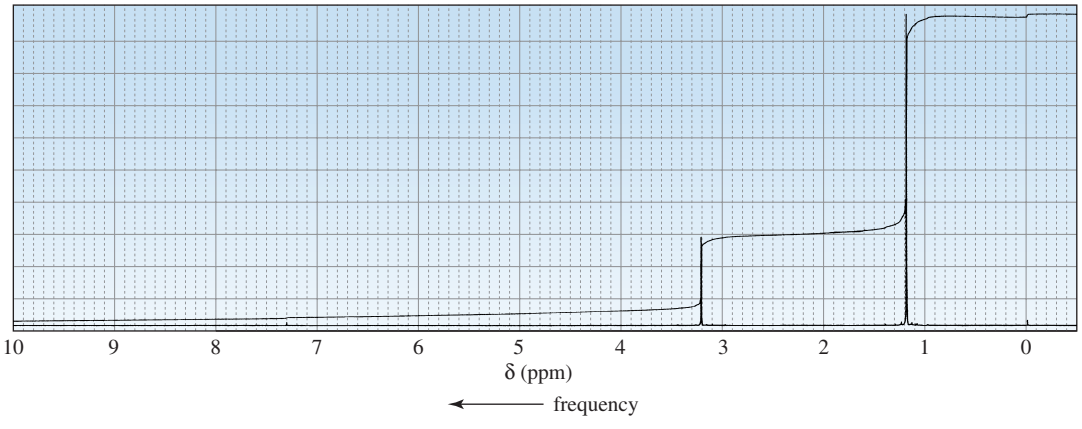
d. $C_4H_8O_2$





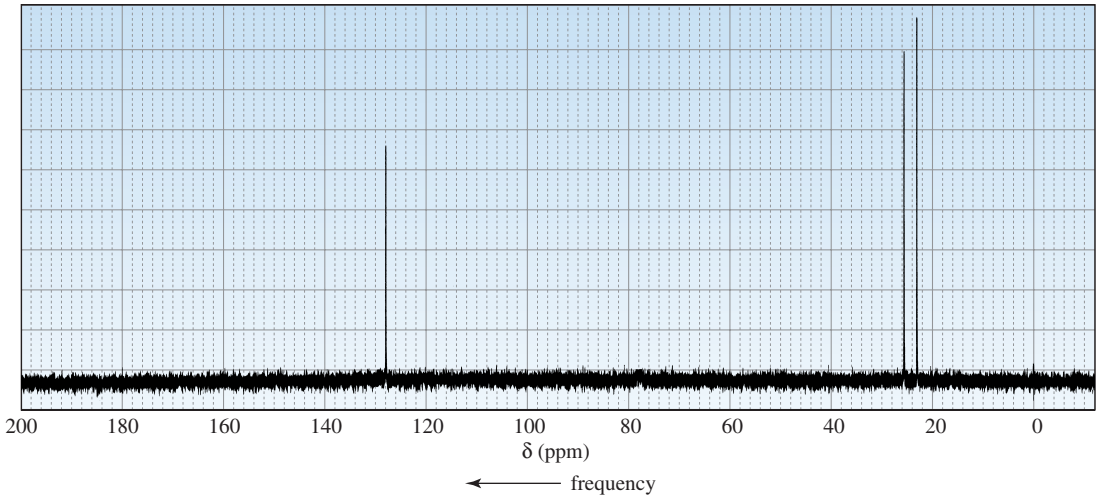
55. There are four esters with molecular formula $C_4H_8O_2$. How could they be distinguished by ^{1}H NMR?

56. An alkyl halide reacts with an alkoxide ion to form a compound whose ^{1}H NMR spectrum is shown here. Identify the alkyl halide and the alkoxide ion. (*Hint:* see Section 11.9.)

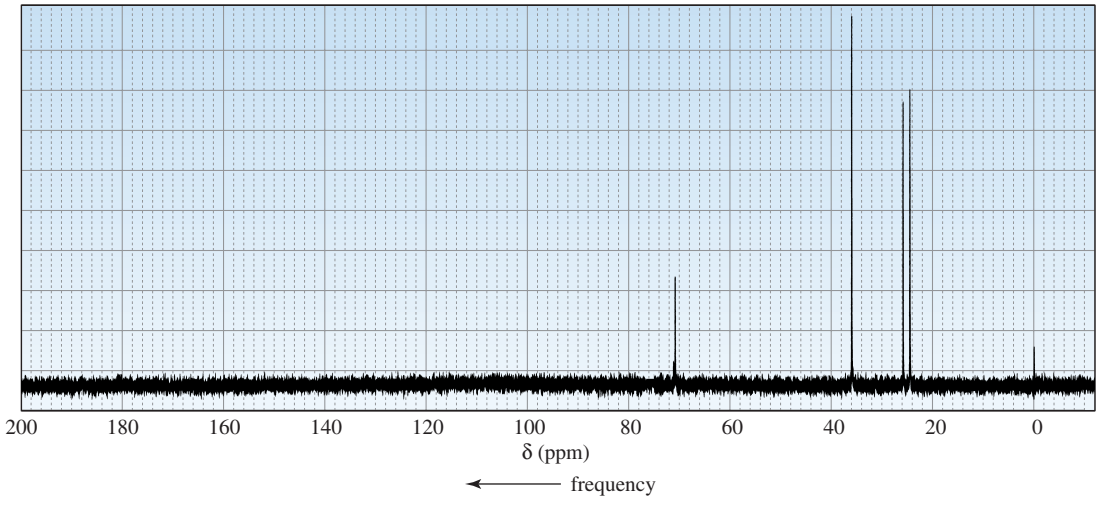


57. Determine the structure of each of the following compounds based on its molecular formula and its ^{13}C NMR spectrum.

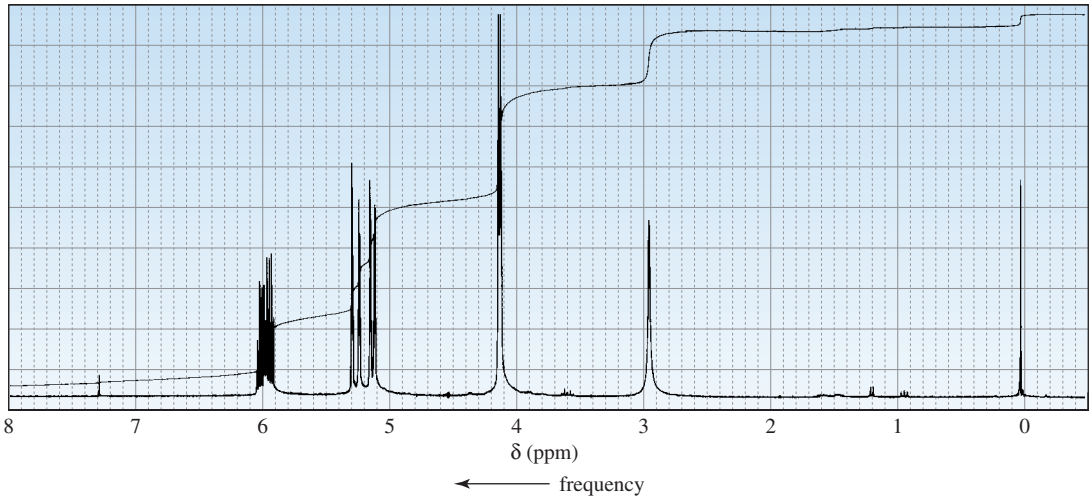
a. $C_4H_{10}O$



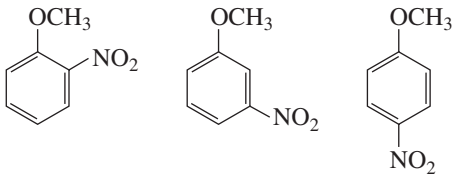
b. $C_6H_{12}O$



58. The ^1H NMR spectrum of 2-propen-1-ol is shown here. Indicate the protons in the molecule that give rise to each of the signals in the spectrum.

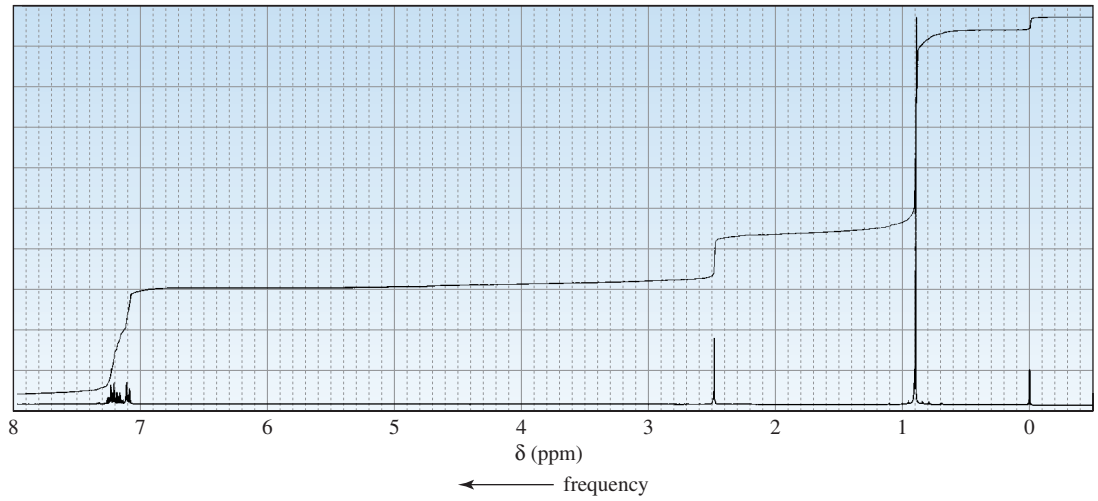


59. How could the signals in the 6.5–8.1-ppm region of their ^{1}H NMR spectra distinguish among the following compounds?

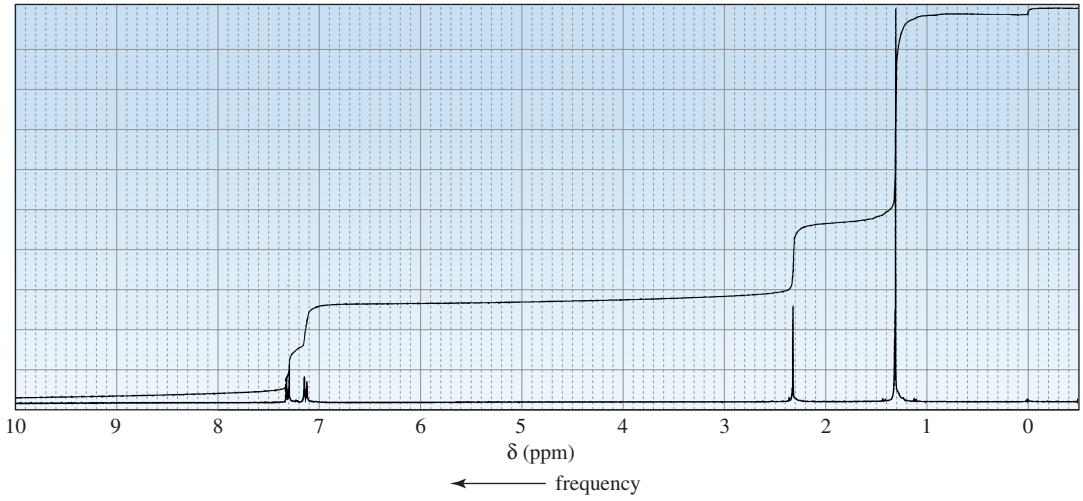


60. The ^{1}H NMR spectra of two compounds with molecular formula $C_{11}H_{16}$ are shown here. Identify the compounds.

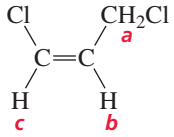
a.



b.



61. Draw a splitting diagram for the H_b proton if $J_{bc} = 10$ and $J_{ba} = 5$.

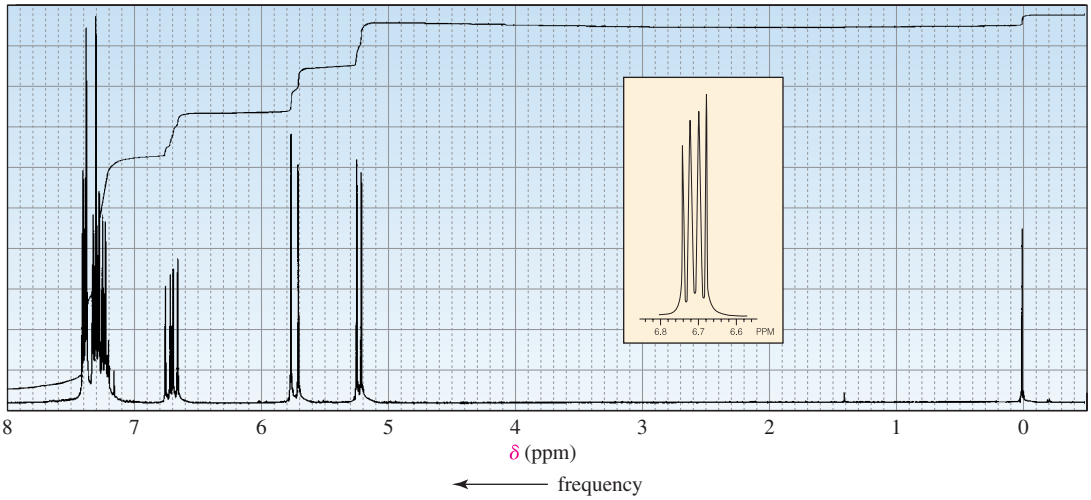


62. Sketch the following spectra that would be obtained for 2-chloroethanol:
    a. The ^{1}H NMR spectrum for a dry sample of the alcohol
    b. The ^{1}H NMR spectrum for a sample of the alcohol that contains a trace amount of acid
    c. The ^{13}C NMR spectrum
    d. The proton-coupled ^{13}C NMR spectrum
    e. The four parts of a DEPT ^{13}C NMR spectrum

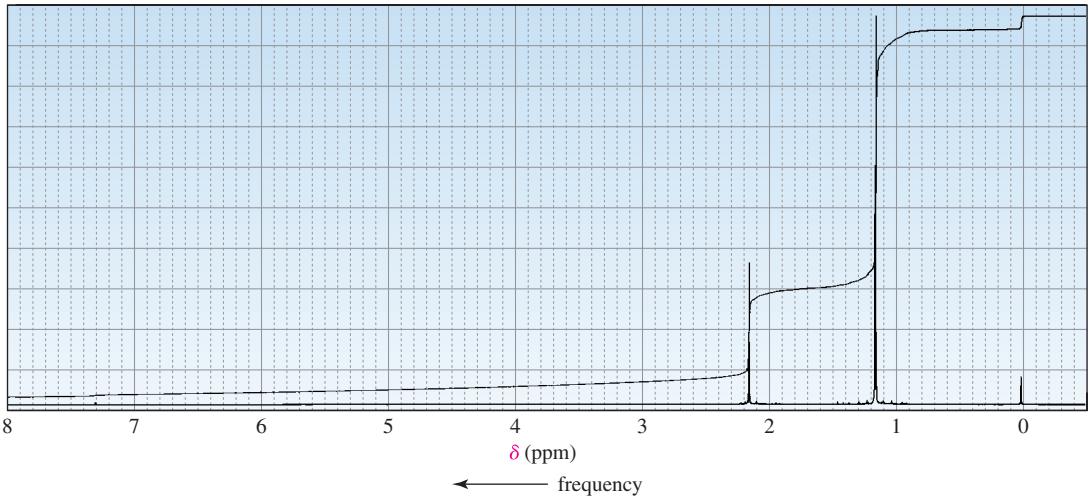
63. How could ^{1}H NMR be used to prove that the addition of HBr to propene follows the rule that says that the electrophile adds to the sp^2 carbon bonded to the greater number of hydrogens.

64. Identify each of the following compounds from its molecular formula and its ^{1}H NMR spectrum.

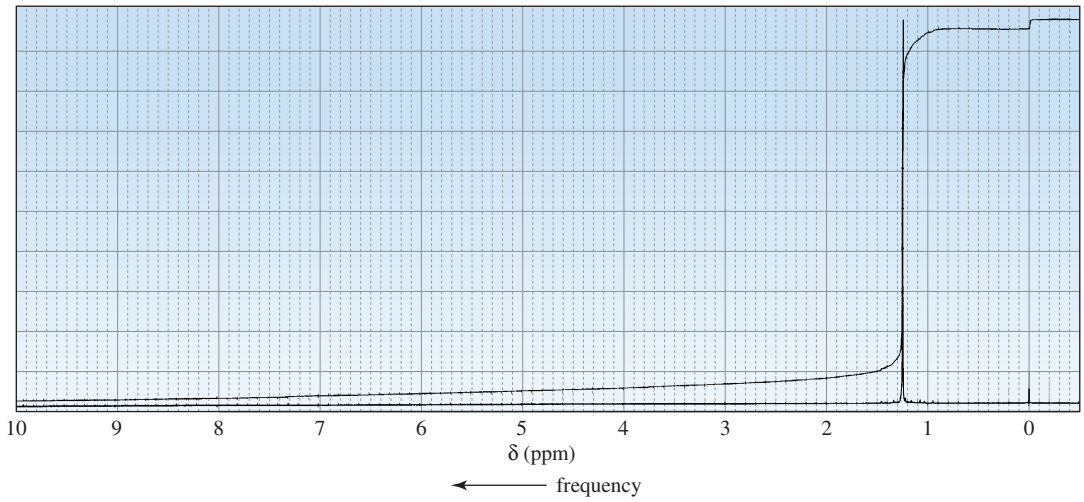
    a. C_8H_8



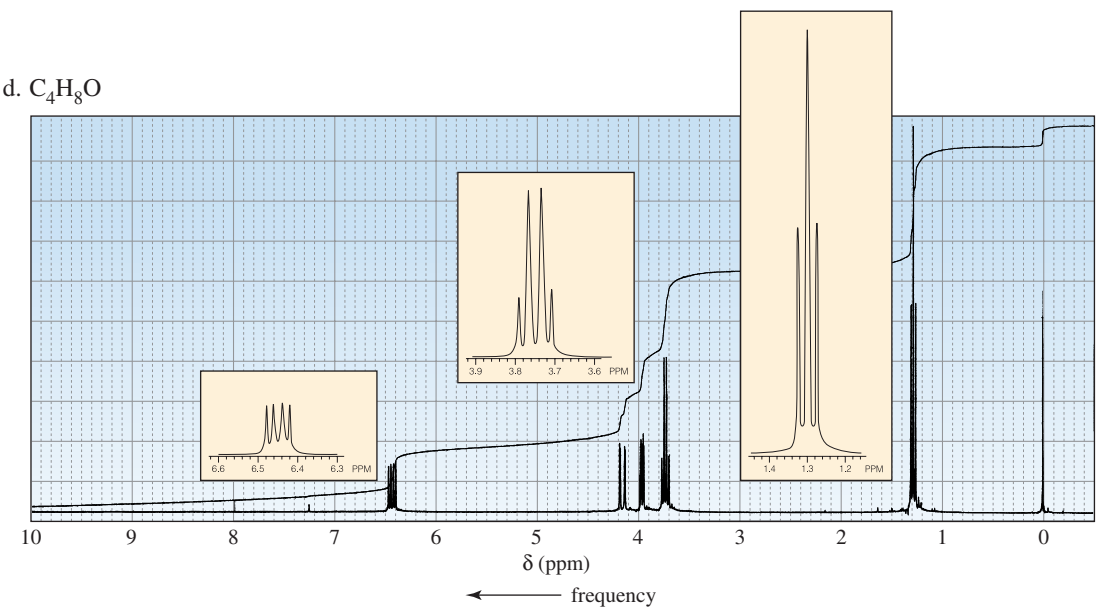
    b. $C_6H_{12}O$



c. $C_9H_{18}O$



d. C_4H_8O

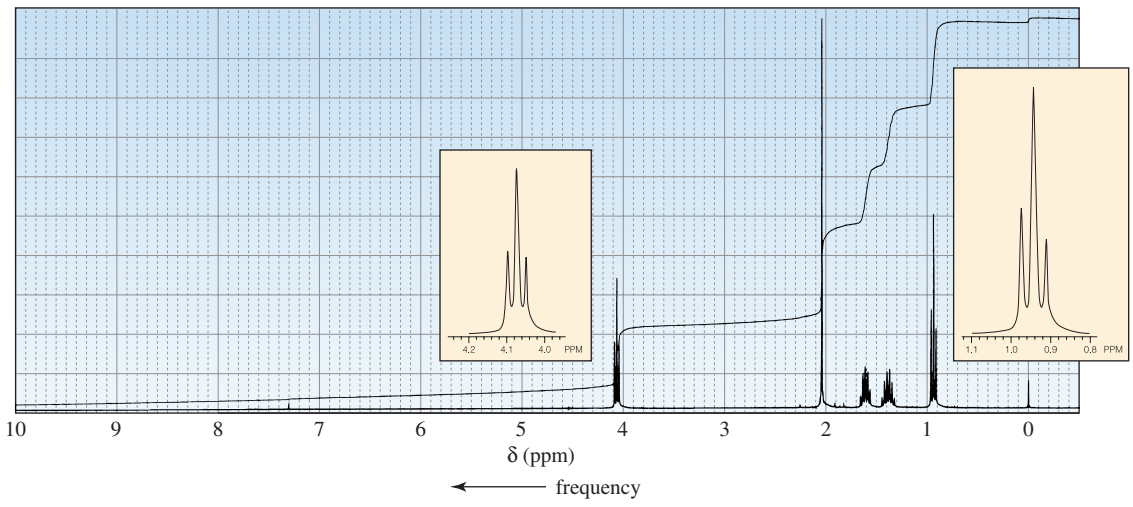


65. Dr. N. M. Arr was called in to help analyze the ^{1}H NMR spectrum of a mixture of compounds known to contain only C, H, and Br. The mixture showed two singlets—one at 1.8 ppm and the other at 2.7 ppm—with relative integrals of 1 : 6, respectively. Dr. Arr determined that the spectrum was that of a mixture of bromomethane and 2-bromo-2-methylpropane. What was the ratio of bromomethane to 2-bromo-2-methylpropane in the mixture?

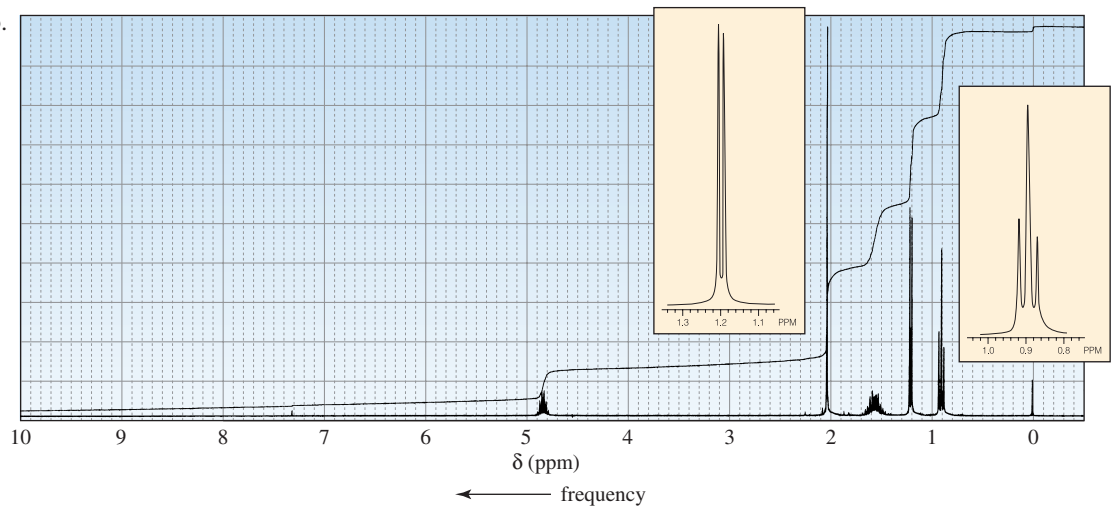
66. Calculate the amount of energy (in calories) required to flip an ^{1}H nucleus in an NMR spectrometer that operates at 60 MHz.

67. The following ^{1}H NMR spectra are for four compounds with molecular formula $C_6H_{12}O_2$. Identify the compounds.

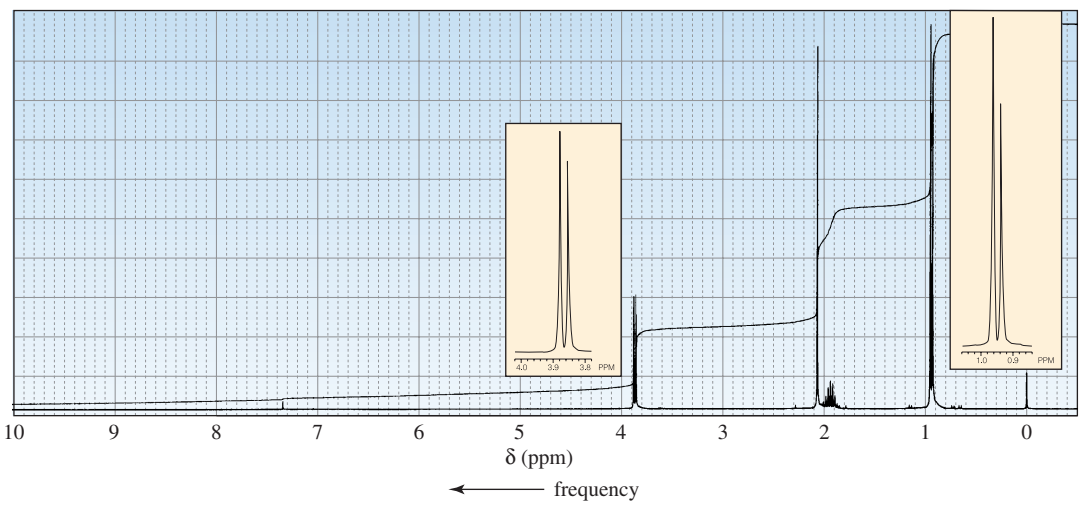
a.



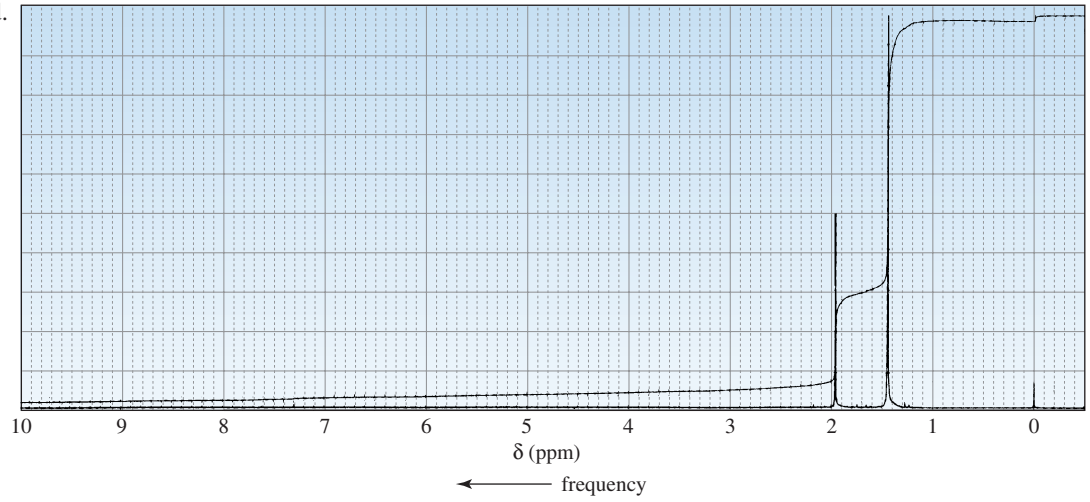
b.



c.



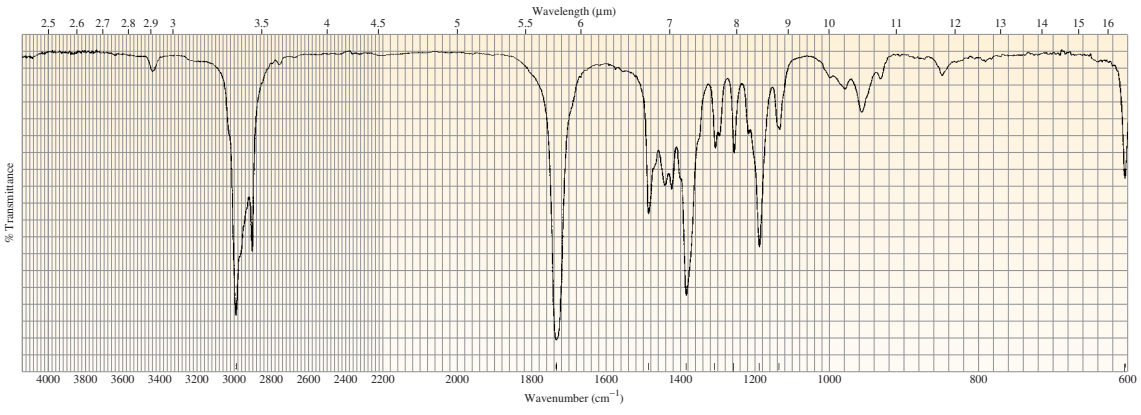
d.

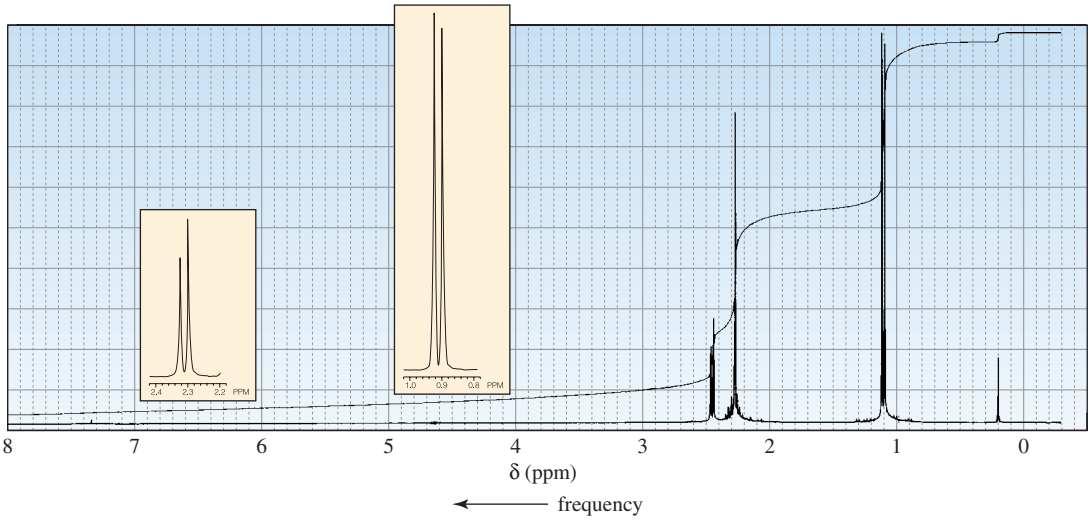


68. When compound A ($C_5H_{12}O$) is treated with HBr, it forms compound B ($C_5H_{11}Br$). The ^1H NMR spectrum of compound A has one singlet (1), two doublets (3, 6), and two multiplets (both 1). (The relative areas of the signals are indicated in parentheses.) The ^1H NMR spectrum of compound B has a singlet (6), a triplet (3), and a quartet (2). Identify compounds A and B.

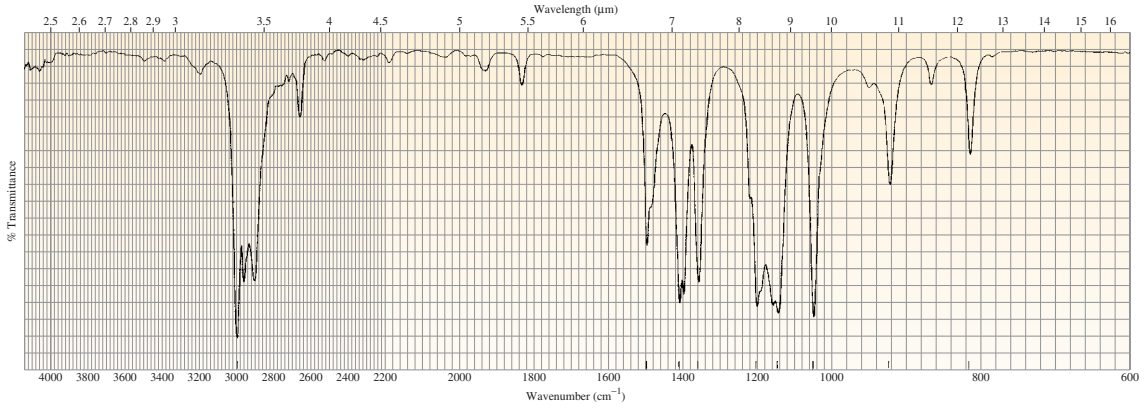
69. Determine the structure of each of the following compounds based on its molecular formula and its IR and ^1H NMR spectra.

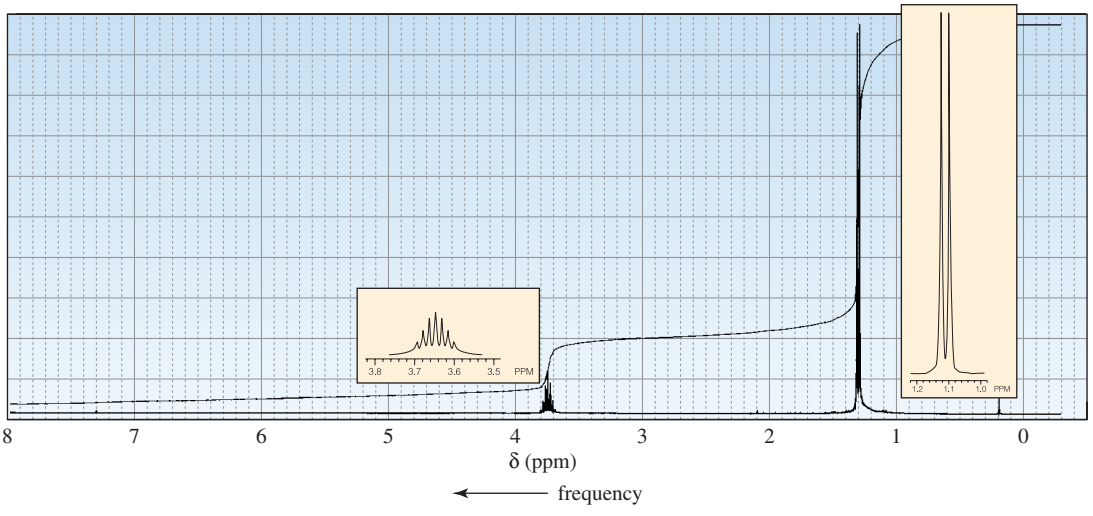
a. $C_6H_{12}O$



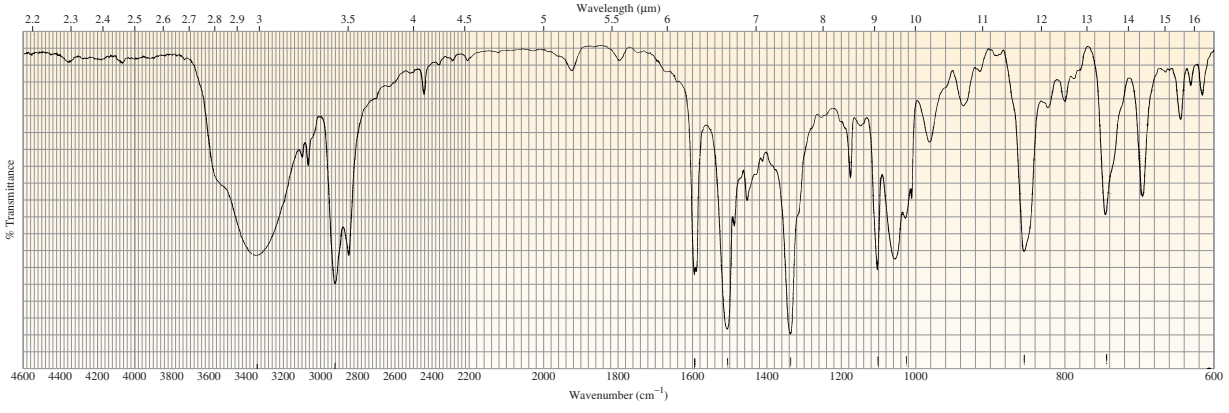


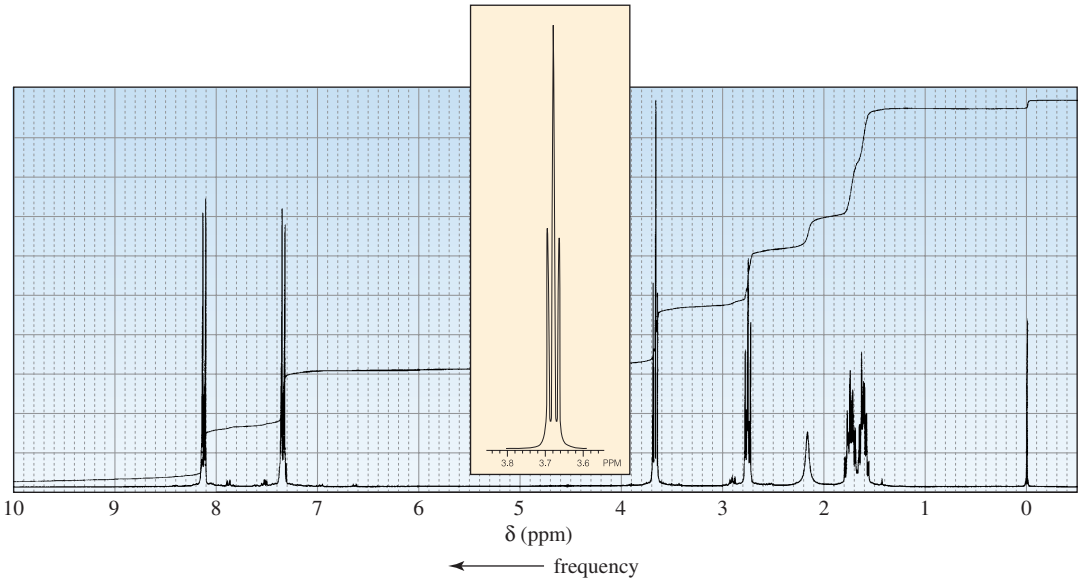
b. $C_6H_{14}O$



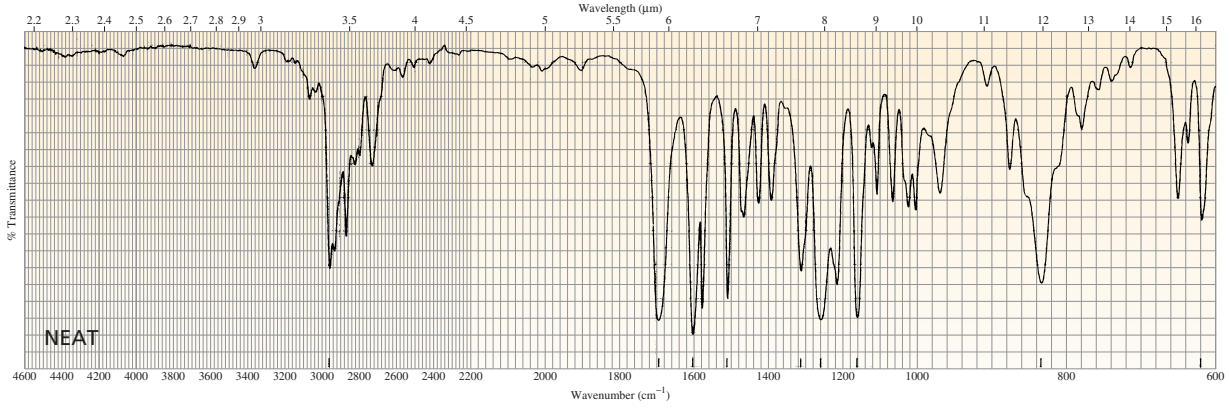


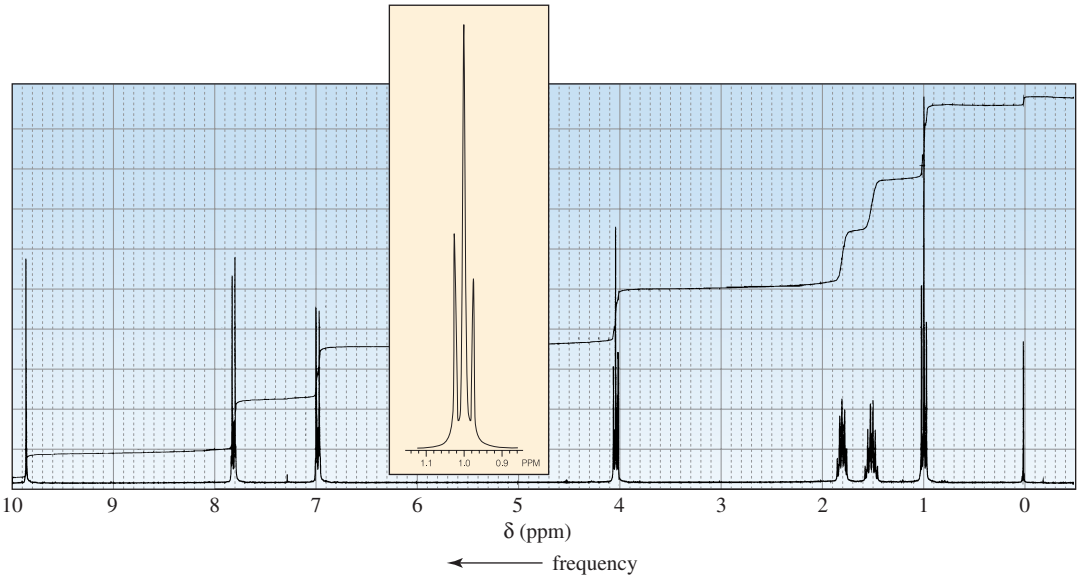
c. $C_{10}H_{13}NO_3$



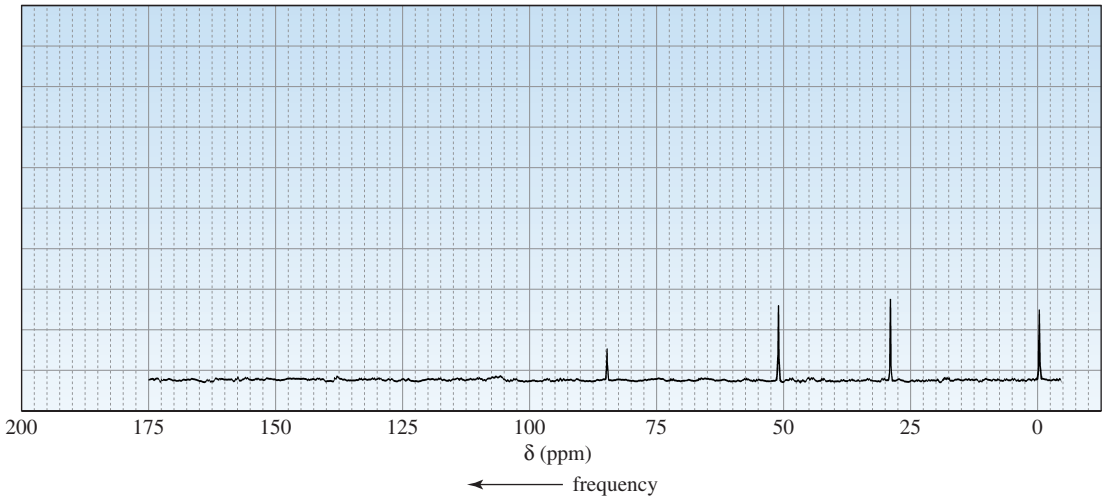

3.8
3.7
3.6
PPM
10
9
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

d. $C_{11}H_{14}O_2$


Wavelength (μm)
2.2 2.3 2.4 2.5 2.6 2.7 2.8 2.9 3 3.5 4 4.5 5 5.5 6 7 8 9 10 11 12 13 14 15 16
% Transmittance
NEAT
4600 4400 4200 4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600
Wavenumber (cm⁻¹)

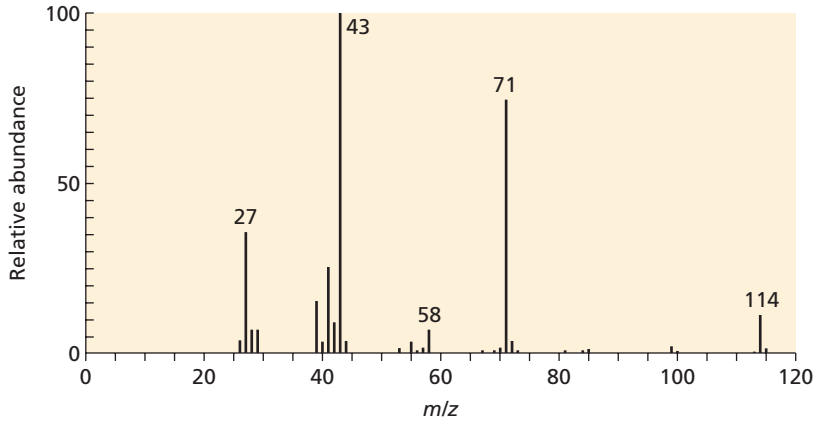

1.1
1.0
0.9
PPM
10
9
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

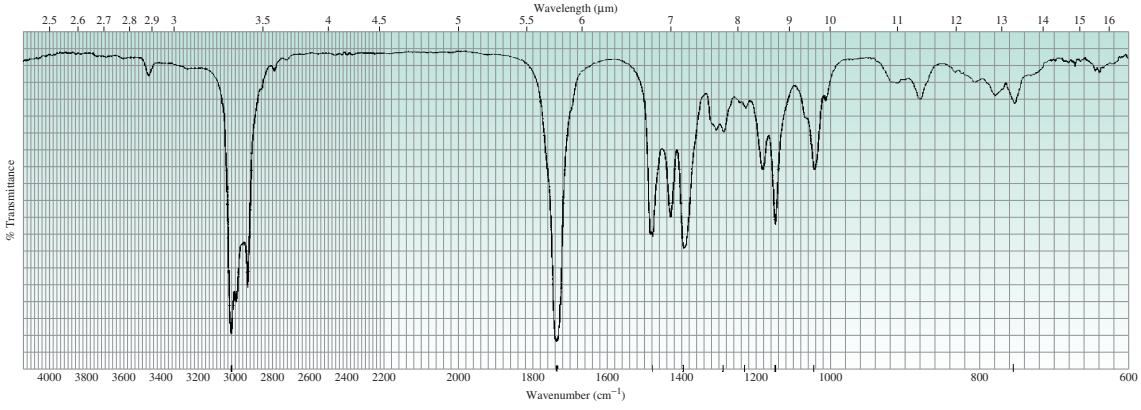
70. Identify the compound with molecular formula $C_3H_5Cl_3$ that gives the following ^{13}C NMR spectrum.

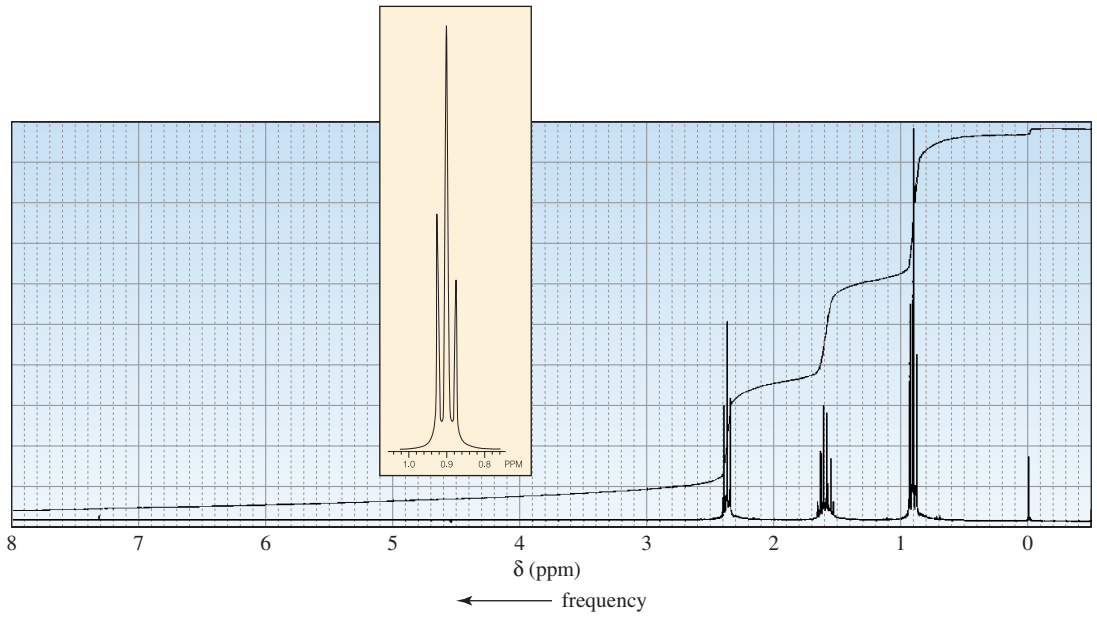


71. Determine the structure of each of the following compounds based on its mass, IR, and ^1H NMR spectra.

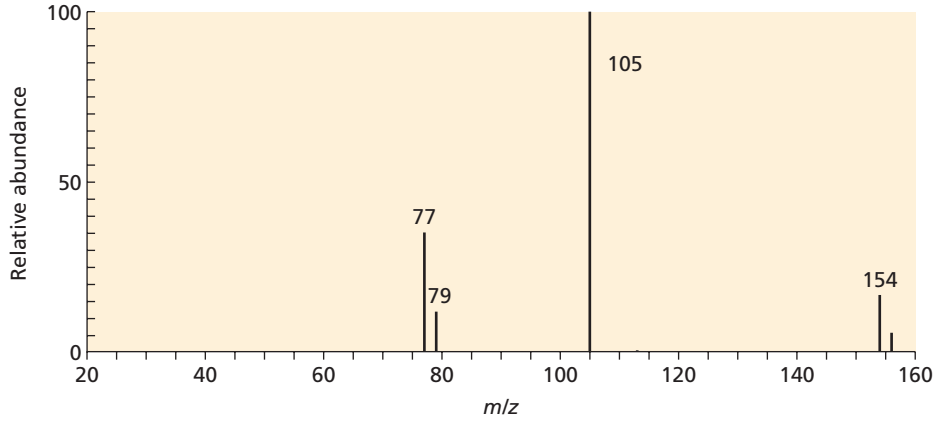
a.

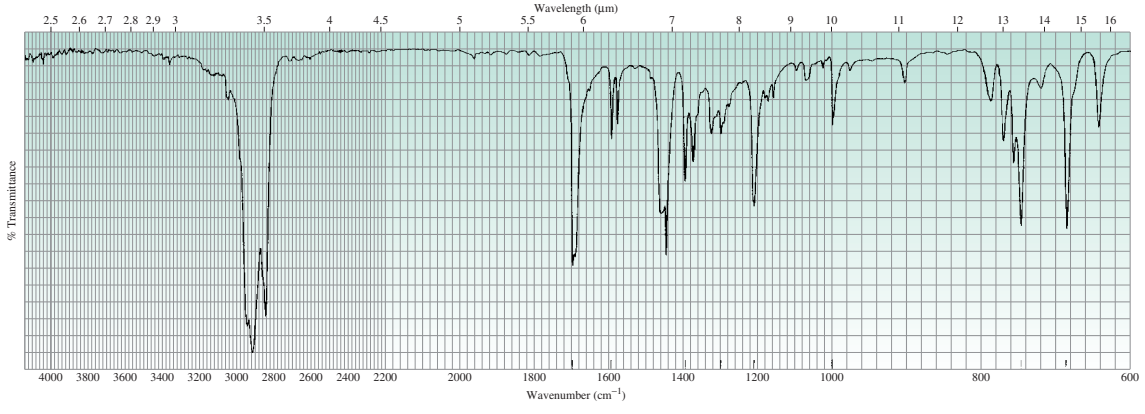


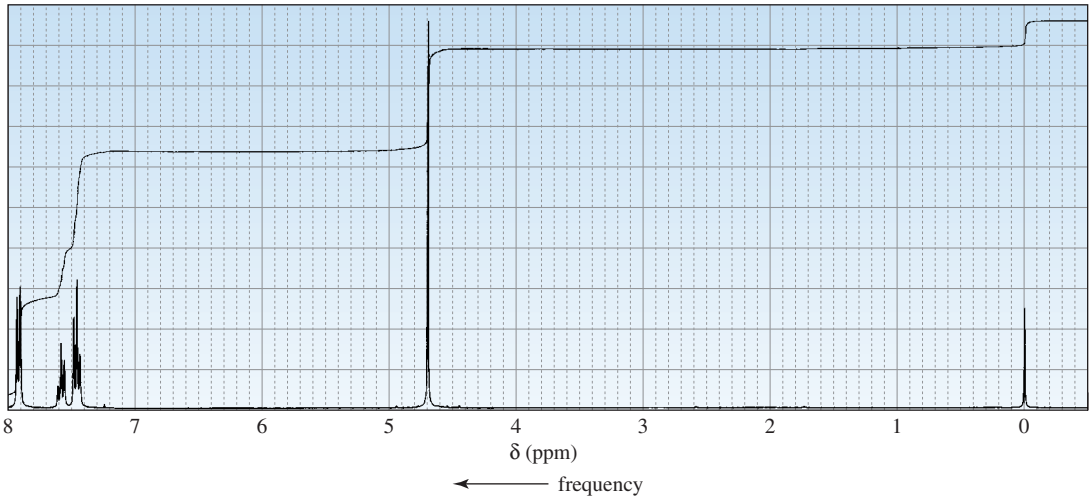



1.0
0.9
0.8
PPM
8
7
6
5
4
3
2
1
0
δ (ppm)
frequency

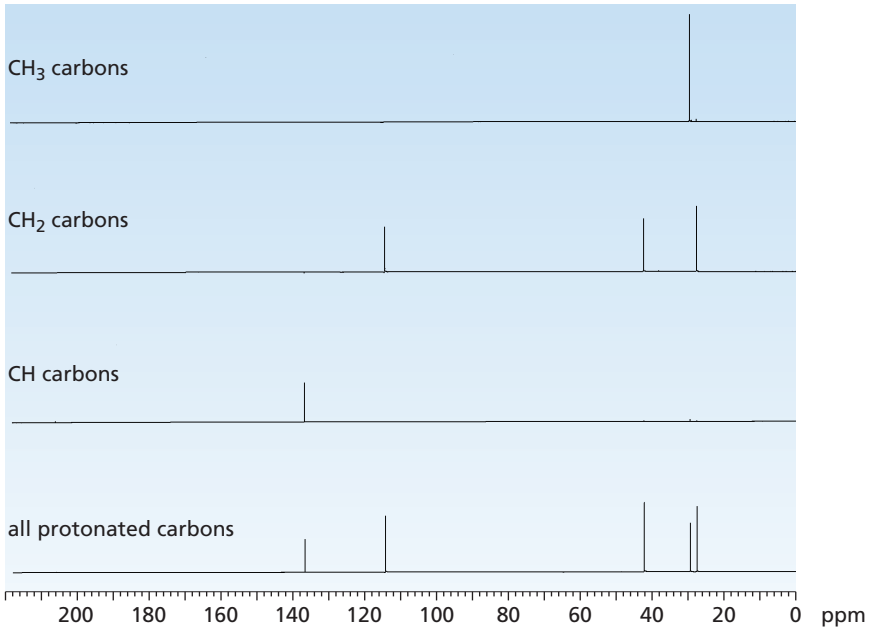
b.


100
50
0
Relative abundance
105
77
79
154
20
40
60
80
100
120
140
160
m/z


Wavelength (μm)
2.5 2.6 2.7 2.8 2.9 3 3.5 4 4.5 5 5.5 6 7 8 9 10 11 12 13 14 15 16
% Transmittance
4000 3800 3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600
Wavenumber (cm⁻¹)



72. Identify the compound with molecular formula $C_6H_{10}O$ that is responsible for the following DEPT ^{13}C NMR spectrum.



73. Identify the compound with molecular formula C_6H_{14} that is responsible for the following ^1H NMR spectrum.