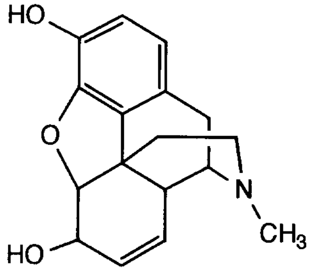
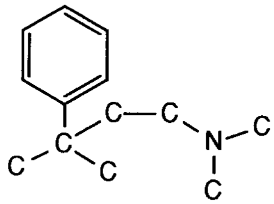
CHAPTER 12: Infrared Spectroscopy and Mass Spectrometry

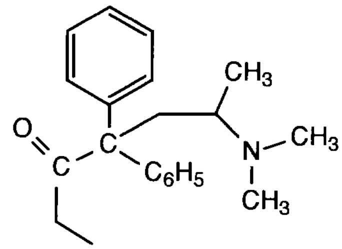
"Real World" Example:
Biologically Active Compounds: heroin, morphine, codiene, demerol, methadone
These compoubs have useful analgesic properties and harmful side affects (addiction).



Morphine



Framework necessary for biological activity: Morphine Rule



Methadone

Drug Design: Maintain positive properties, eliminate negative properties

A + **B** ⟶ **C (?)** A Puzzle

The puzzle pieces:

% composition: gives % of each element, leads to empirical formula

MS: gives molecular mass, leads to molecular formula/unsaturation # (also gives other structure clues)

IR: gives functional groups

NMR: gives carbon/hydrogen framework

Infrared Spectroscopy:

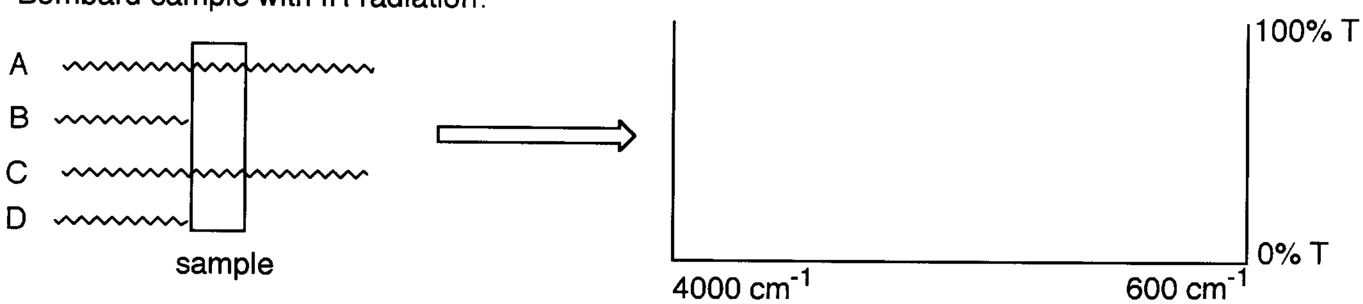
Sample is bombarded with radiation in the IR region of the electromagnetic spectrum. (Fig. 12-1, p. 502)
This is enough energy to affect molecular vibrations.

Important Terms and Relationships:

frequency: complete wave cycles that pass a fixed point in 1 second; directly proportional to energy
wavelength: distance between peaks or troughs of the wave; inversely proportional to frequency and energy
wavenumber:# of cycles of the wave in 1 cm; it is the reciprocal of the wavelength; it is directly proportional to frequency and energy (measured in reciprocal centimeters, cm^{-1})

Example: Longer the wavelength, Lower the frequency, Lower the energy
Shorter the wavenumber, Lower the frequency, Lower the energy

Bombard sample with IR radiation:

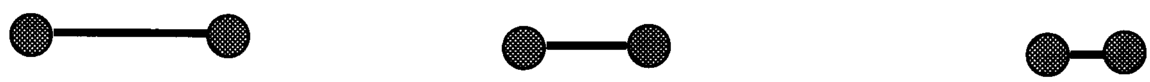


IMPORTANT QUESTION: What determines which frequencies are absorbed and which are transmitted?

Answer: IR uses only enough energy to affect molecular vibrations. When vibrations caused by IR radiation match the natural vibrations of the molecule, energy is absorbed.

Natural Vibrations of Molecules:

I. Bond Stretching (stretching vibration)



Frequency of the natural stretching vibration depends on two factors:

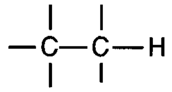
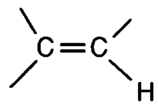
1. size of atom - heavy atoms vibrate more slowly than light atoms

2. strength (stiffness) of the bond - stronger bonds require more force to stretch and compress

Bond Stretching Frequencies:

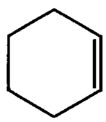
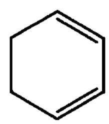
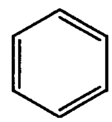
Bond	Bond Energy (kcal)	Strectching Freq. (cm^{-1})
C—H	100	3000
C—D	100	2100
C—C	83	1200
C—C	83	1200
C═C	146	1660
C≡C	200	2200
C—N	73	1200
C═N	147	1650
C≡N	213	2200
C—O	86	1100
C═O	178	1700

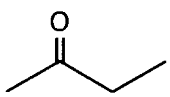
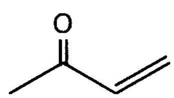
Examples: Consider the stretching frequencies of the following bonds:

a.   —C≡C—H

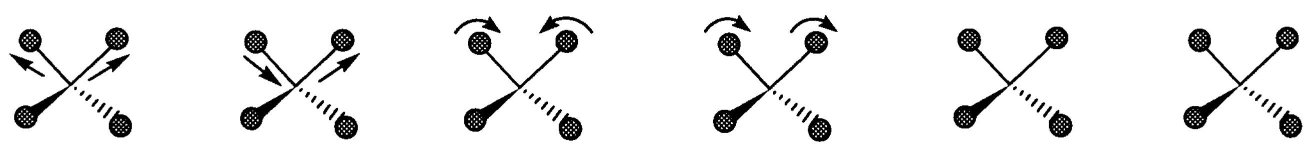
b. $H_3C—F$ $H_3C—Cl$ $H_3C—Br$

Conjugation lowers frequency

c.   

d.  

II. Molecular Stretching/Bending Vibrations

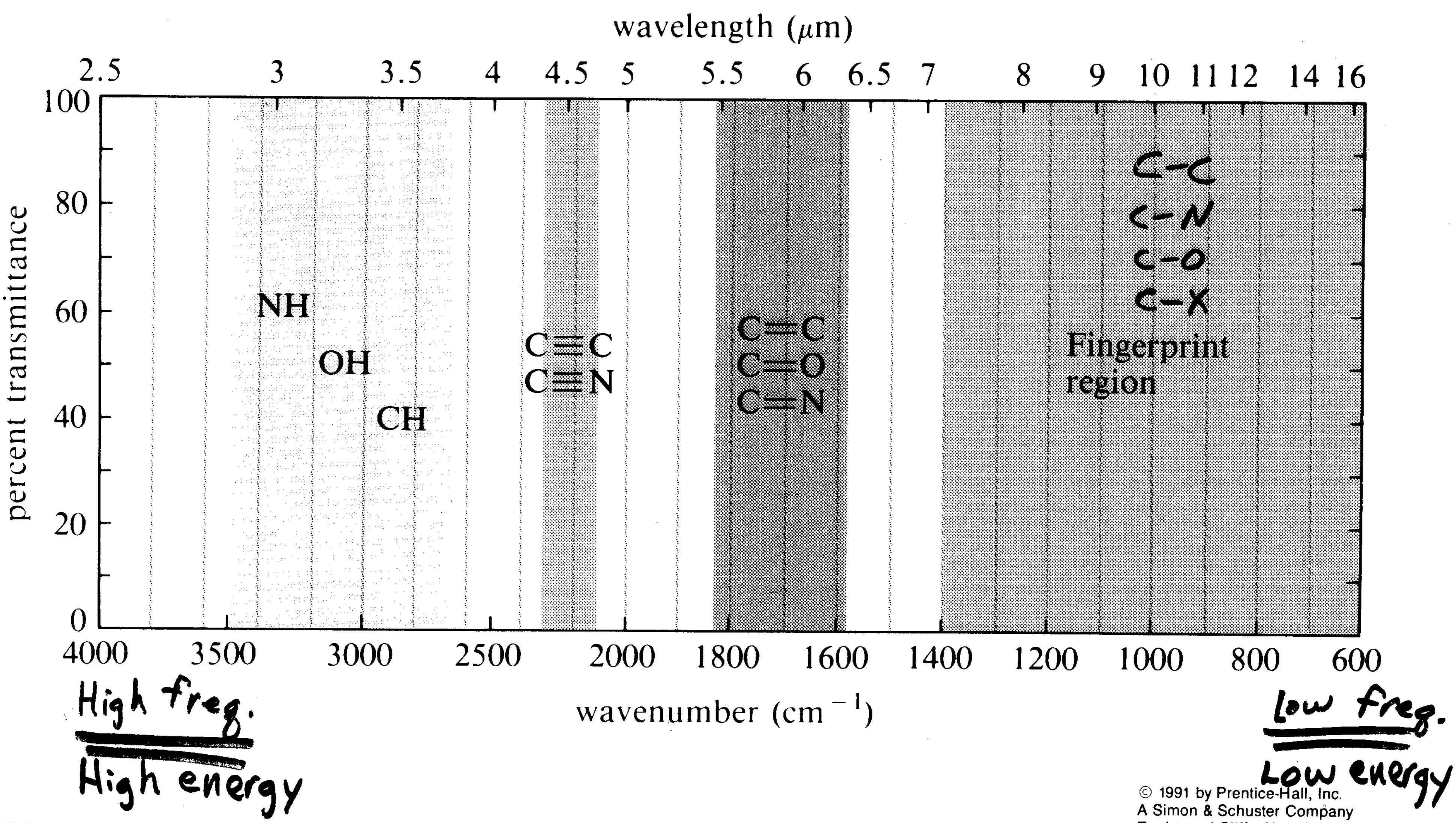


III. IR Active vs IR Inactive Vibrations:

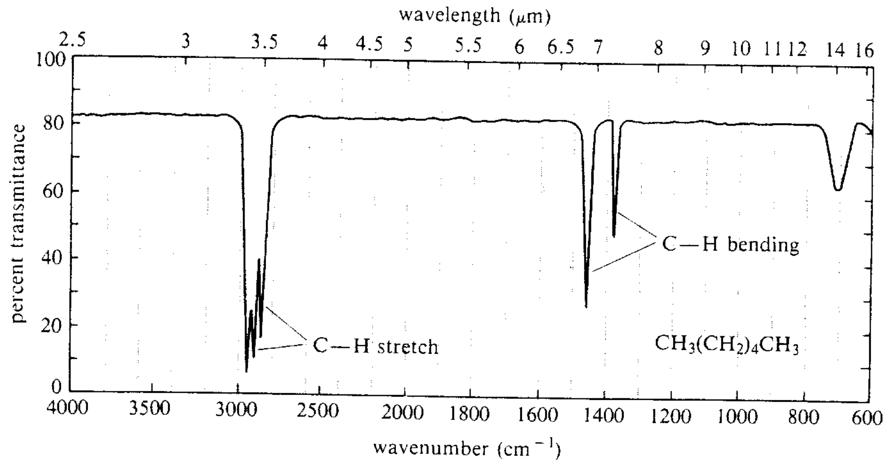
Bonds with a dipole moment (polar bonds) are IR active:
An electromagnetic wave has a component that consists of a rapidly reversing electric field. This electric field can cause bond and molecular vibrations by alternately stretching and compressing **polar bonds**.
If the vibration caused by the IR radiation matches the frequency of a natural vibration of the compound, the radiation is absorbed. (Peak observed)

Bonds with no dipole moment (nonpolar bonds) are IR inactive: Electric field component cannot stretch and compress a nonpolar bond.(No peak observed)

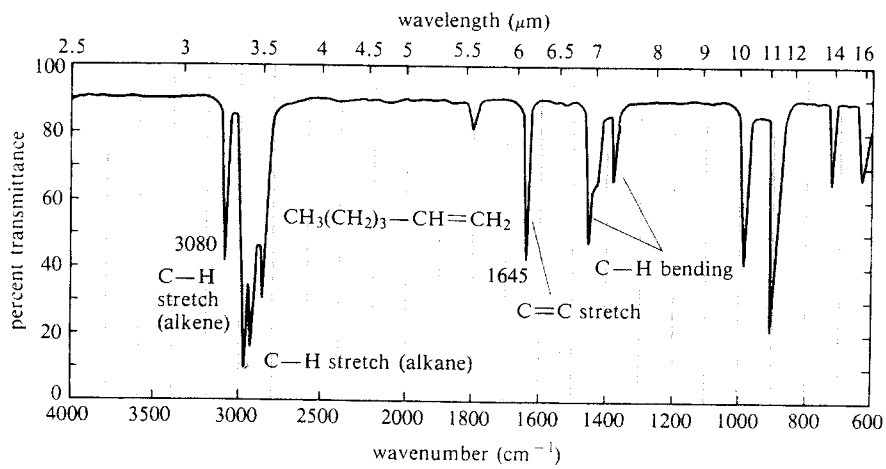
INFRARED SPECTRAL REGIONS



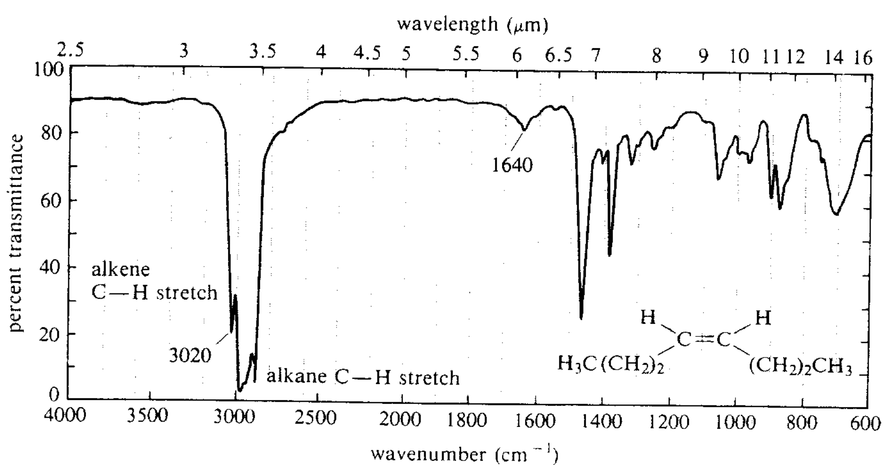
IR SPECTRUM of *n*-HEXANE



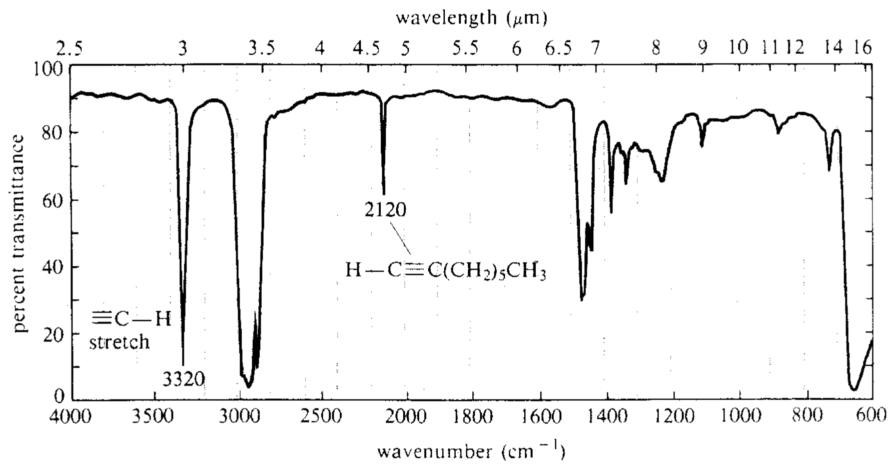
IR SPECTRUM of 1-HEXENE



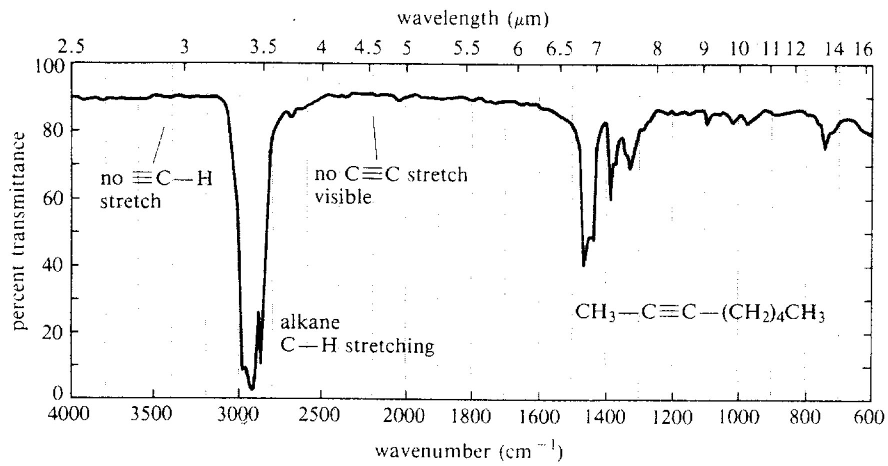
IR SPECTRUM of *cis*-4-OCTENE



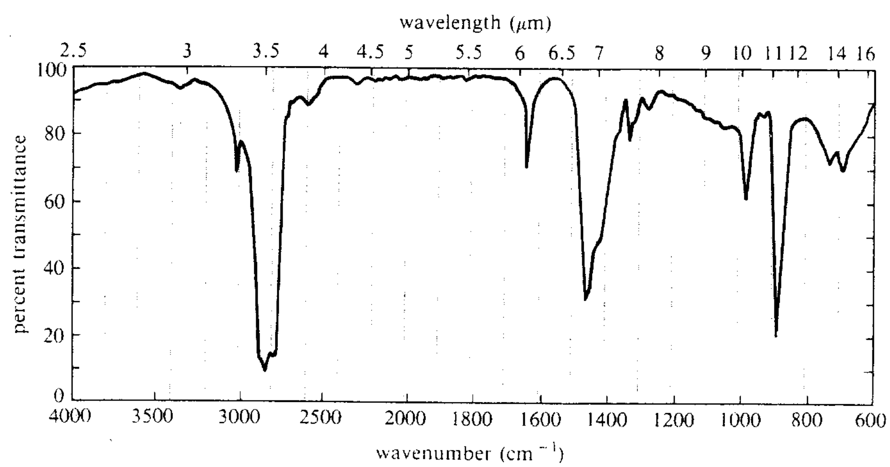
IR SPECTRUM of 1-OCTYNE

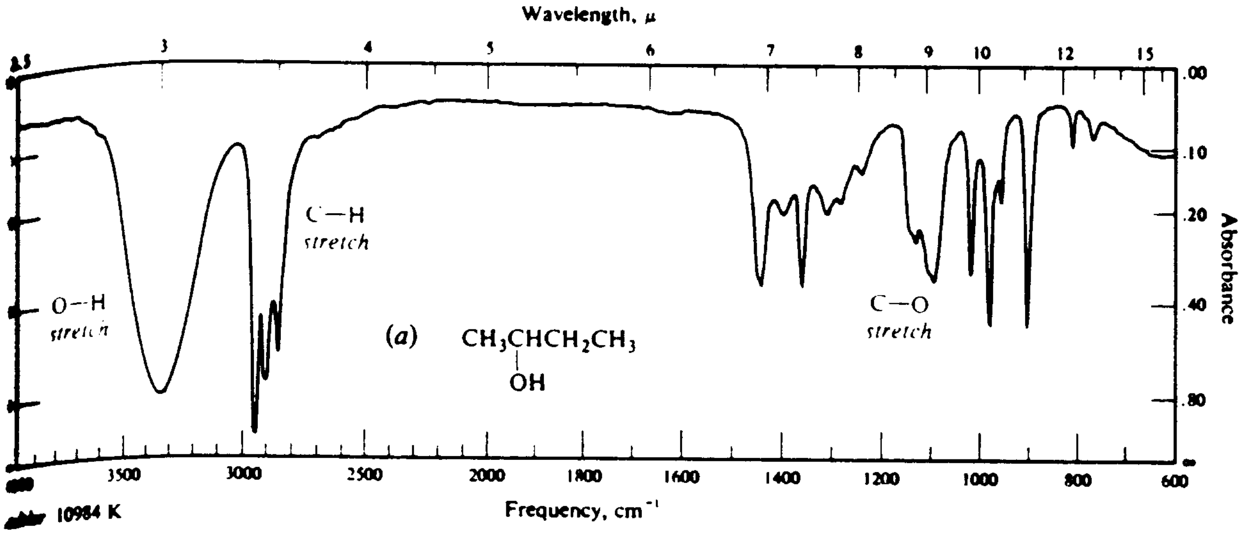


IR SPECTRUM of 2-OCTYNE

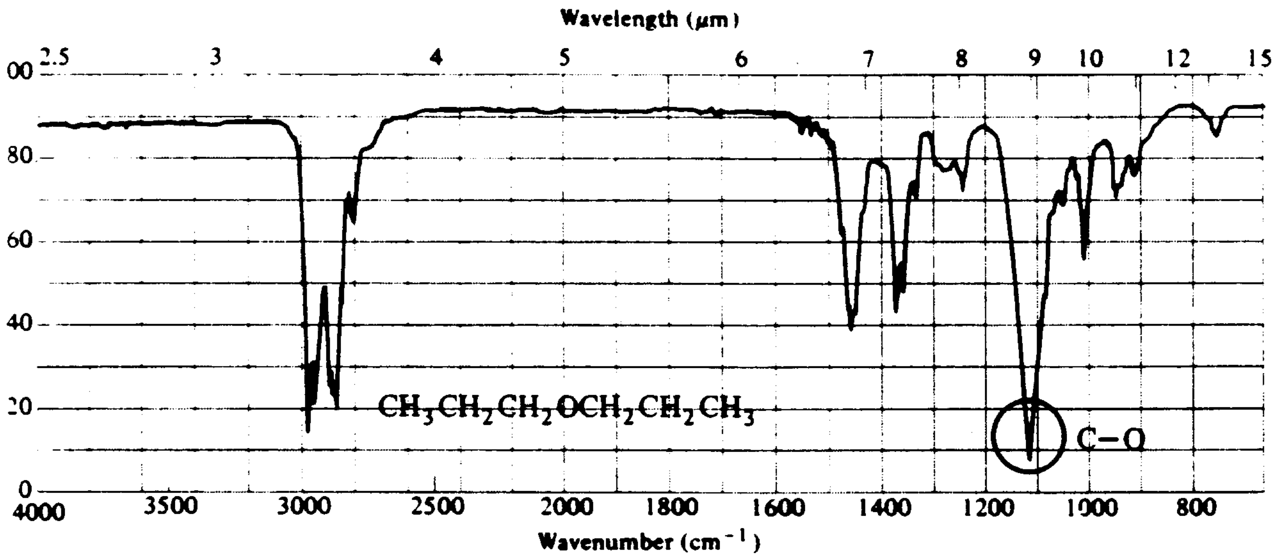


IR SPECTRUM of 1-OCTENE

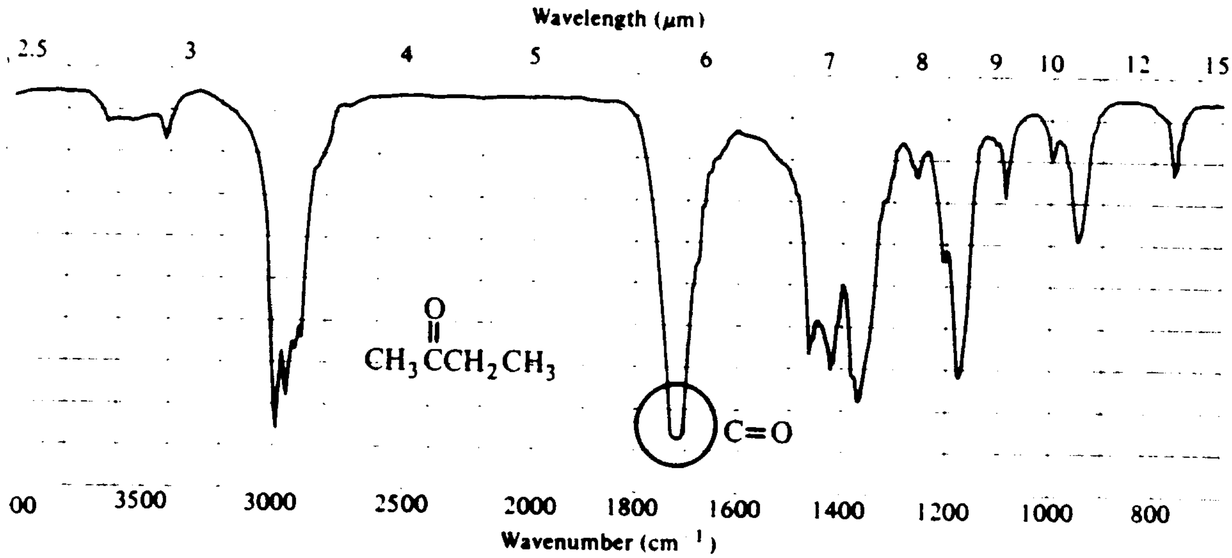



Wavelength, μ
Absorbance
O—H stretch
C—H stretch
(a) CH₃CHCH₂CH₃ OH
C—O stretch
Frequency, cm⁻¹
10984 K

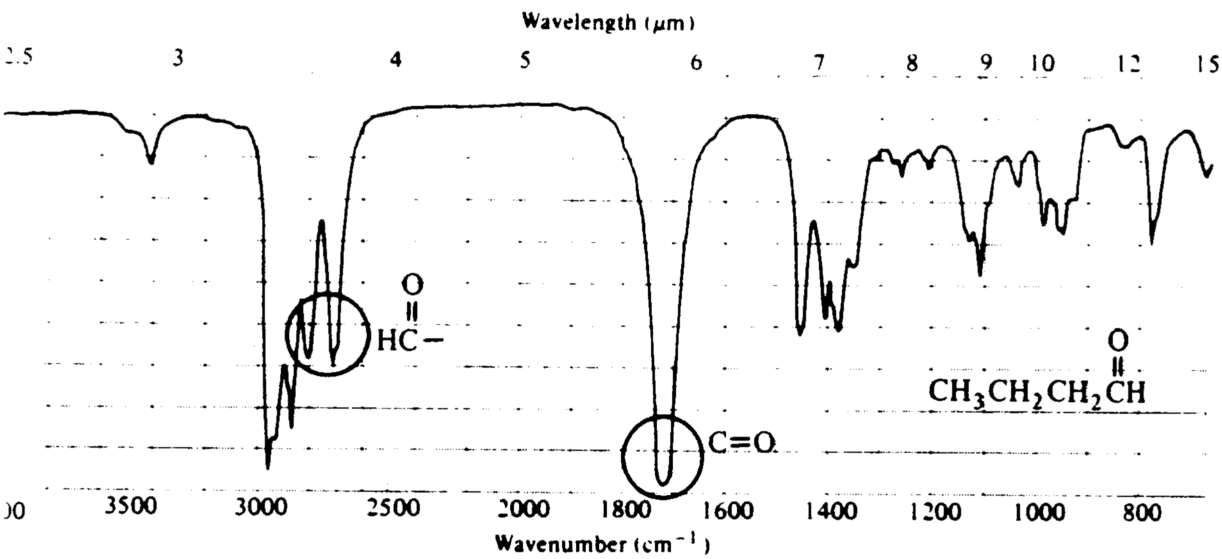
1


Wavelength (μm)
CH₃CH₂CH₂OCH₂CH₂CH₃
C—O
Wavenumber (cm⁻¹)

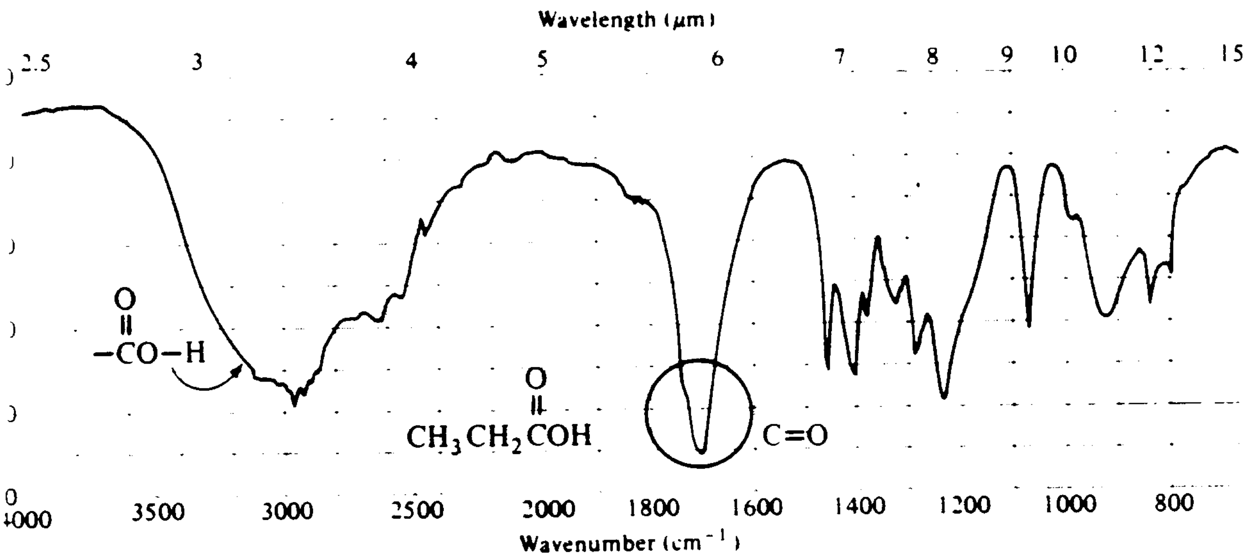
2


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
CH3CCH2CH3
O
C=O
00 3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm⁻¹)

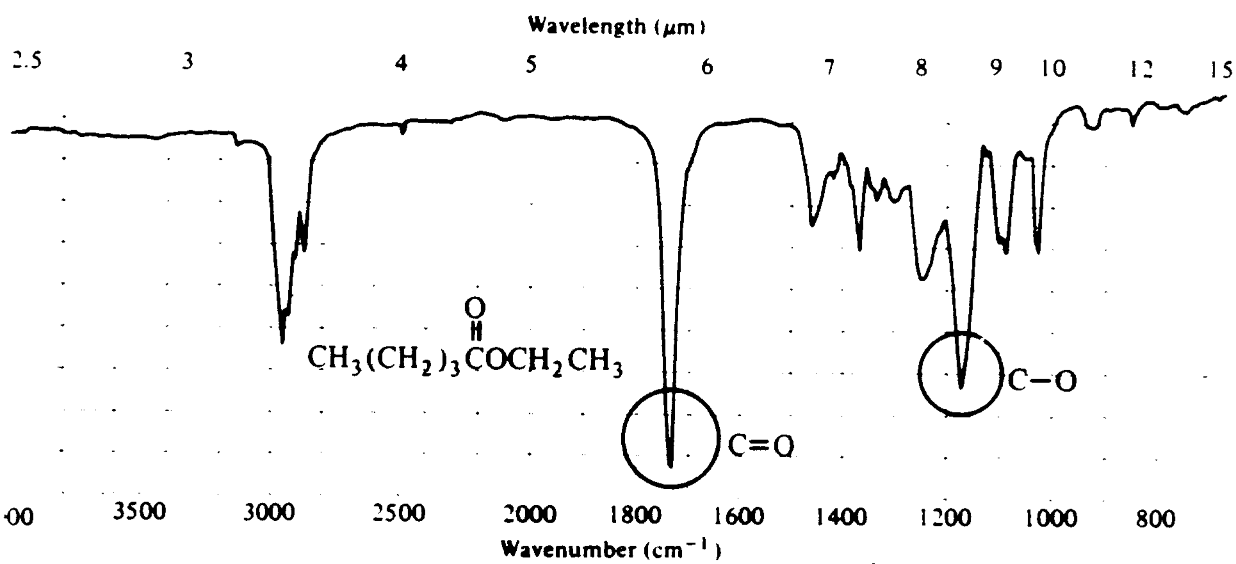
3


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
O
HC−
C=O
CH3CH2CH2CH
O
00 3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm⁻¹)

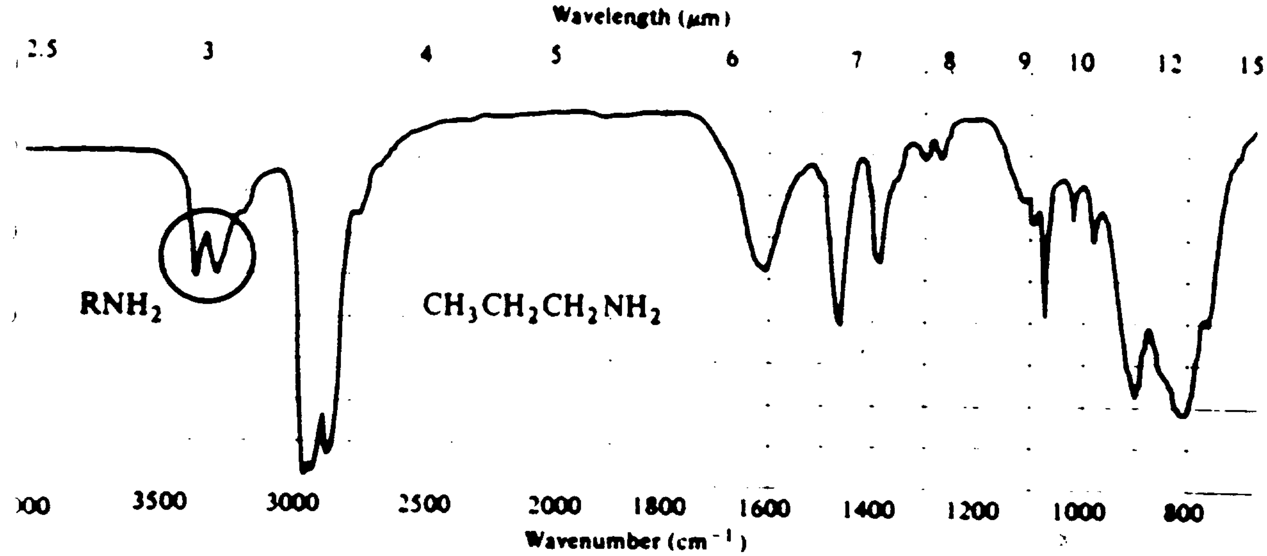
4


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
O
‖
–CO–H
O
‖
CH3CH2COH
C=O
4000 3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm⁻¹)

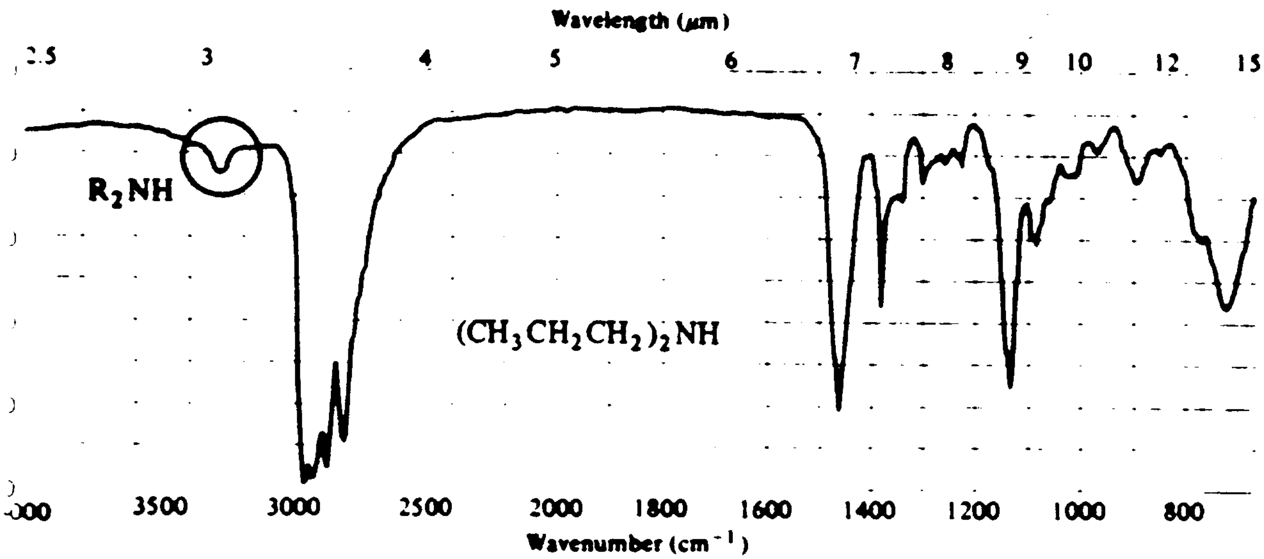
5


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
O
‖
CH3(CH2)3COCH2CH3
C–O
C=O
3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm⁻¹)

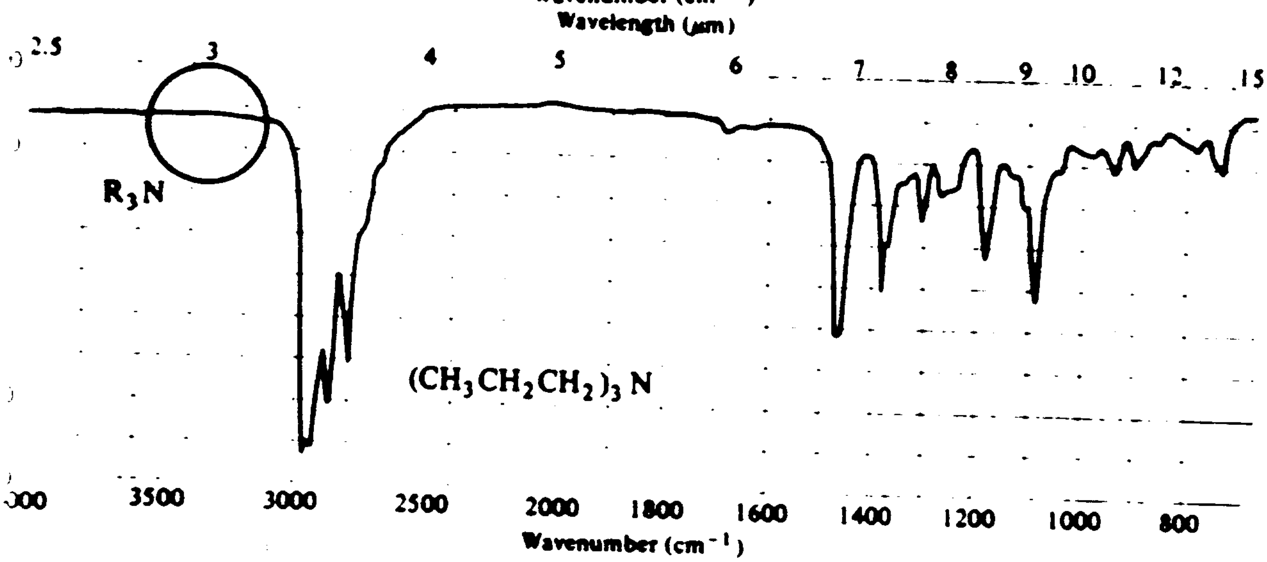
6


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
RNH_2
$CH_3CH_2CH_2NH_2$
3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm^{-1})

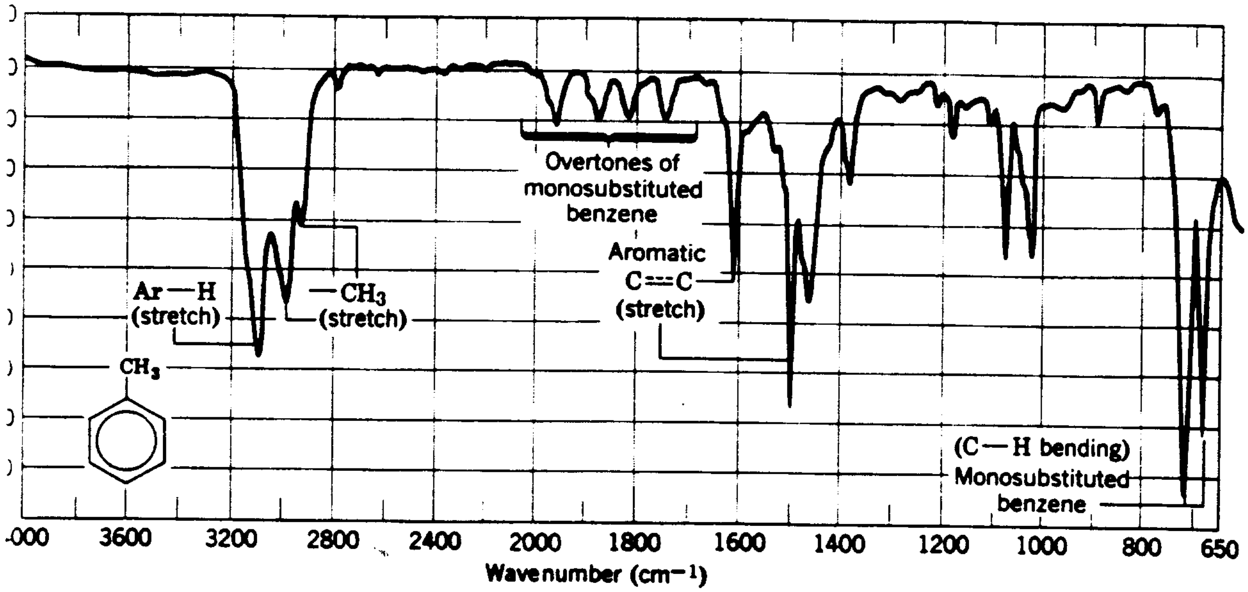
7


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
R_2NH
$(CH_3CH_2CH_2)_2NH$
3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm^{-1})

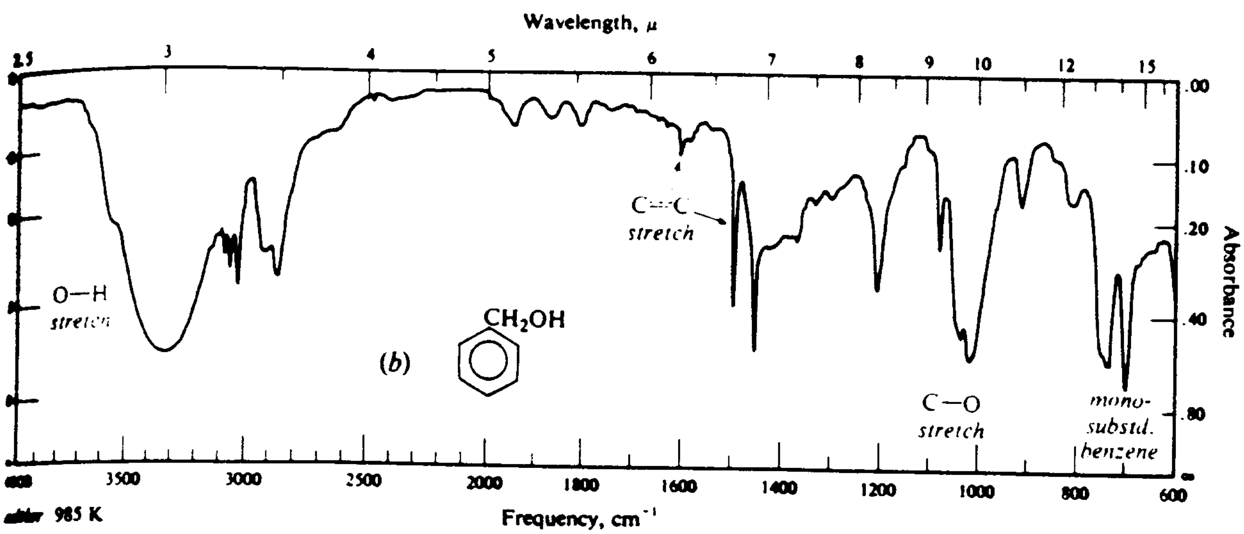
8


Wavelength (μm)
2.5 3 4 5 6 7 8 9 10 12 15
R_3N
$(CH_3CH_2CH_2)_3N$
3500 3000 2500 2000 1800 1600 1400 1200 1000 800
Wavenumber (cm^{-1})

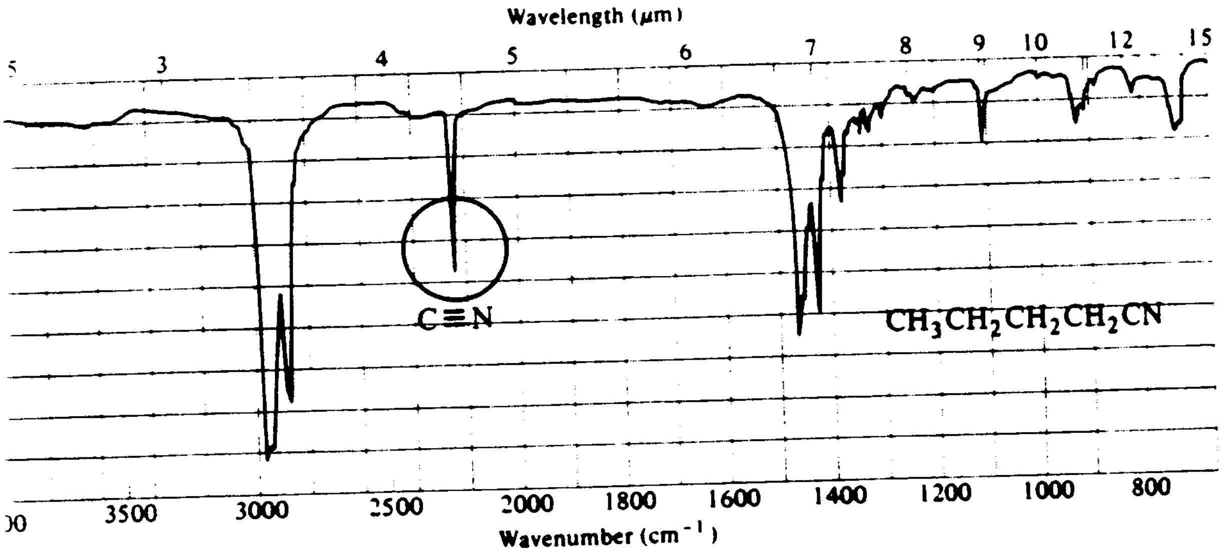
9


Overtones of
monosubstituted
benzene
Aromatic
C═C
(stretch)
Ar—H
(stretch)
—CH3
(stretch)
CH3
(C—H bending)
Monosubstituted
benzene
4000 3600 3200 2800 2400 2000 1800 1600 1400 1200 1000 800 650
Wavenumber (cm−1)

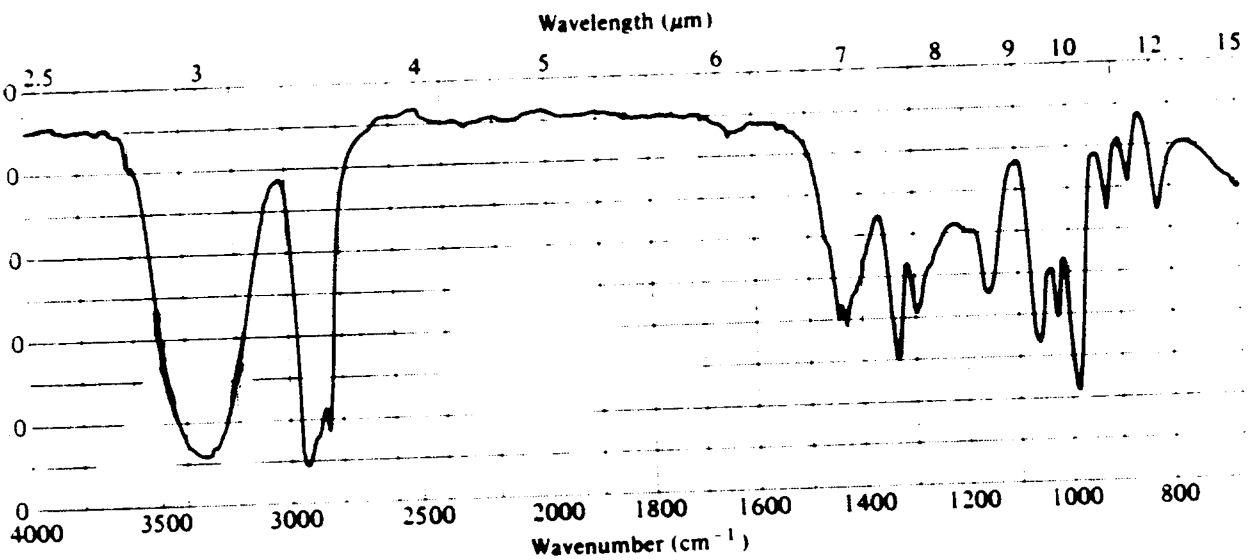
10


Wavelength, μ
2.5 3 4 5 6 7 8 9 10 12 15
.00 .10 .20 .40 .80
Absorbance
O—H
stretch
(b)
CH2OH
C═C
stretch
C—O
stretch
mono-
substd.
benzene
3500 3000 2500 2000 1800 1600 1400 1200 1000 800 600
Frequency, cm−1
985 K

11


Wavelength (μm)
3
4
5
6
7
8
9
10
12
15
C≡N
$CH_3CH_2CH_2CH_2CN$
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
Wavenumber (cm^{-1})

12


Wavelength (μm)
2.5
3
4
5
6
7
8
9
10
12
15
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
Wavenumber (cm^{-1})

13

Mass Spectrometry: Another piece of the puzzle

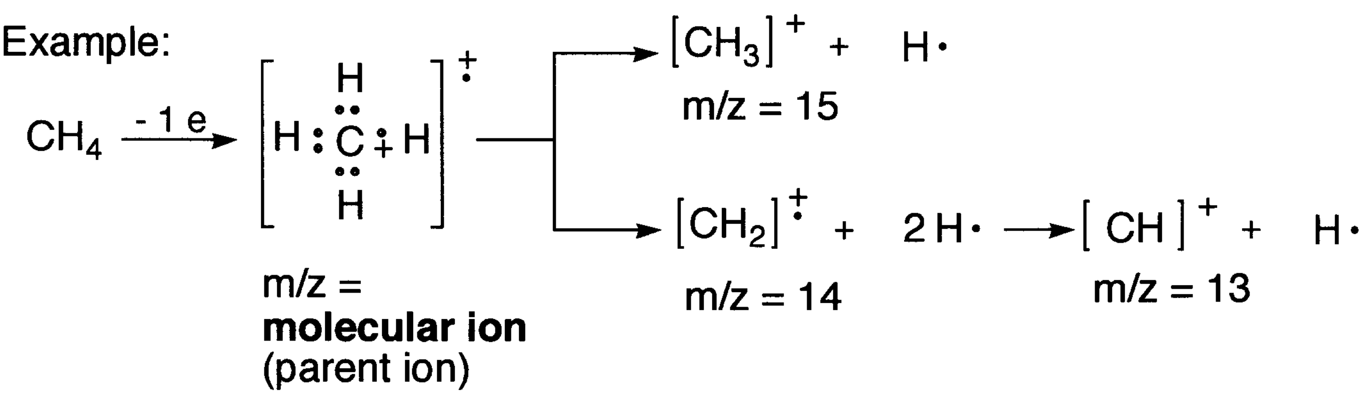
- mass of the compound ⇩ formula (especially from high resoultion MS)
- mass of fragments ⇩ structural features

Destructive technique:

high E electrons → organic molecule —(- 1 electron)→ [radical cation]$^{+\bullet}$ ↓ high energy causes molecule to break apart → + fragments + neutral fragments (radicals or small neutral molecules)

Summary:
1. In the mass spectrometer ⊕ fragments are deflected by a magnetic field to a detector.
2. Neutral fragments are not deflected and crash into walls, so not detected.
3. Magnetic field strength is varied so only fragments of a particular mass to charge ratio (m/z) enter the dector. Charge = +1, so m/z = mass.

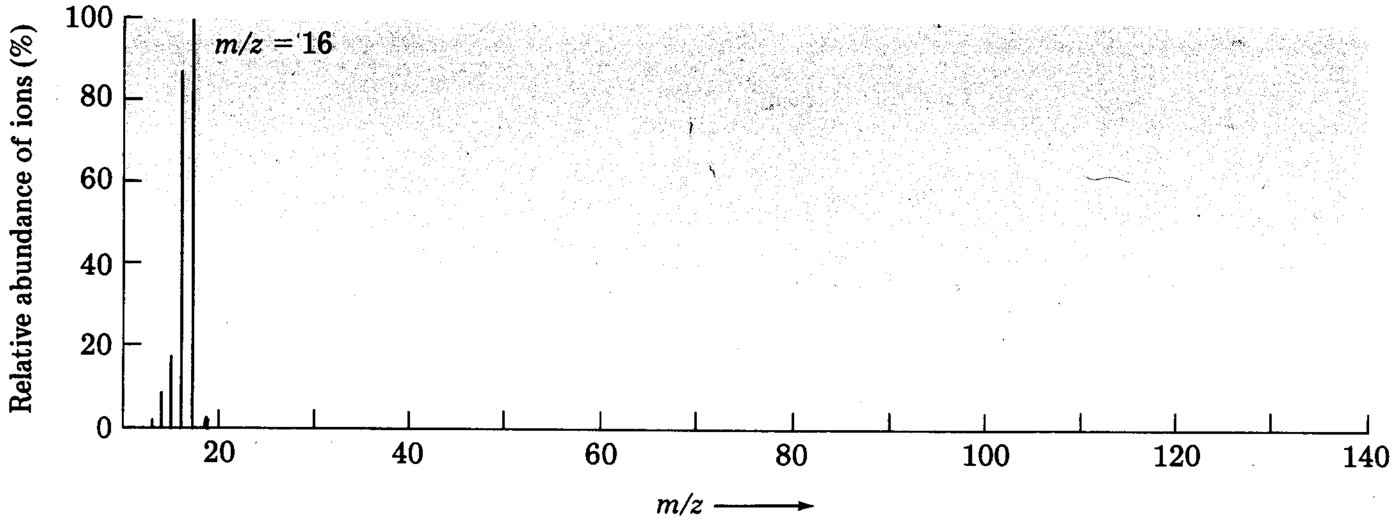
Example:



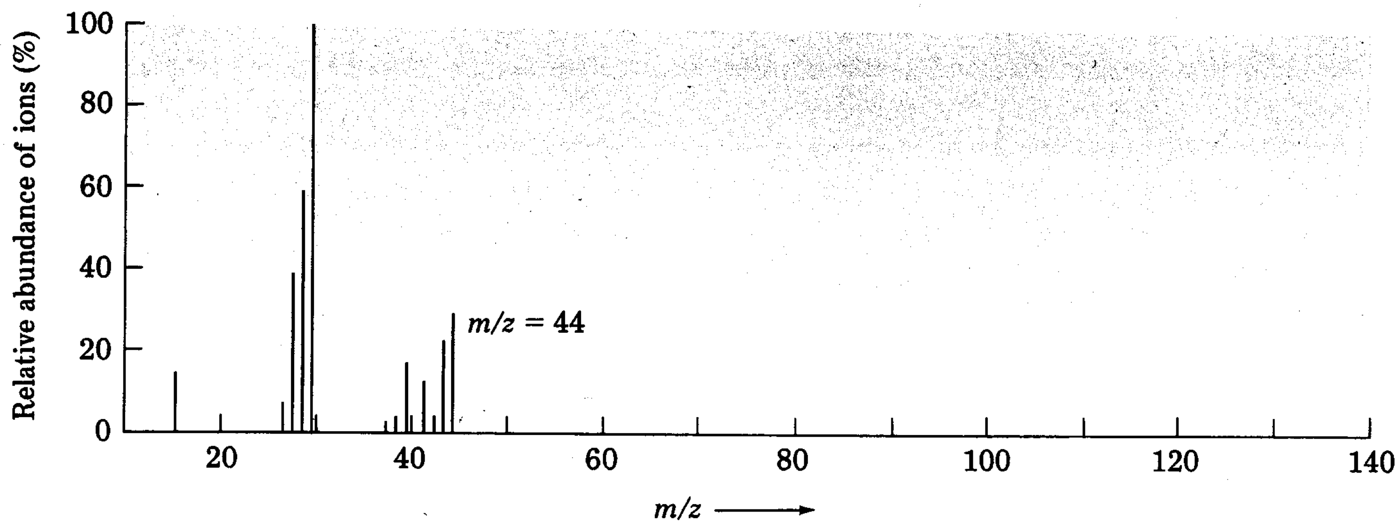
base peak: the strongest peak in the mass spec.; represents the most abundant ion; assigned an intensity of 100%; other peak intensities are proportional to the base peak; not necessarily the molecular ion peak; often represents the most stable fragment

Transparency 43 *Figure* 12.7 *Page* 418

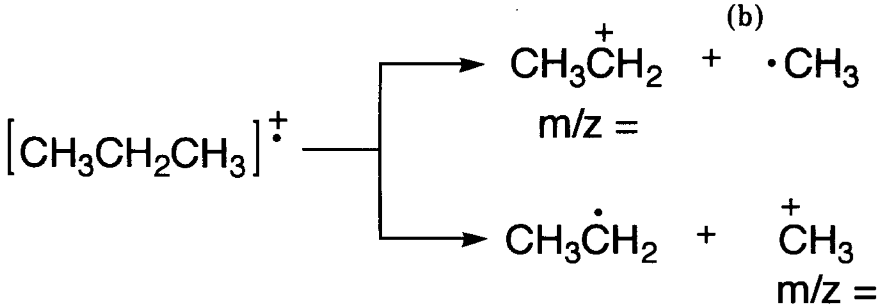
Mass spectra of (a) methane and (b) propane



(a)



(b)



High Resolution Mass Spec. (HRMS)

While mass spec. rounds masses to the nearest whole number, HRMS determines an **exact mass** or a mass to several significant figures. The exact mass allows fairly acurate determination of the molecular formula.

Example: data for an unknown compound

Molecular ion peak from mass spec: 44

possible formulas:	C_3H_8	C_2H_4O	CO_2	CN_2H_4
calculated exact mass:	44.06260	44.02620	43.98983	44.03740

Molecular ion peak from HRMS: 44.063

The unknown compound is:

Tables of calculated exact masses and formulas are available.

Isotope Peaks: observed for any peak large enough (ion is abundant enough)
- small peaks at M (mass) + 1 and sometimes M + 2

Example: see methane mass spec.

Because a small % (1.11%) of methane molecules will have a ^{13}C atom and a very small % will have a ^{2}H atom (very few would have both), we observe a small peak at m/z = 17. This peak is called the M + 1 isotope peak.

Some elements are readily identified by their isotope peaks.

Br ⟹ 2 isotopes: ^{79}Br(50.5%) and ^{81}Br(49.5%) ⟹ M and M + 2 almost equal size

Cl ⟹ 2 isotopes: ^{35}Cl(75.5%) and ^{37}Cl(24.5%) ⟹ M + 2 is 1/3 the size of M

S ⟹ 3 isotopes: ^{32}S(95.0%), ^{33}S(0.8%), ^{34}S(4.2%) ⟹ M + 2 is small, but larger than usual

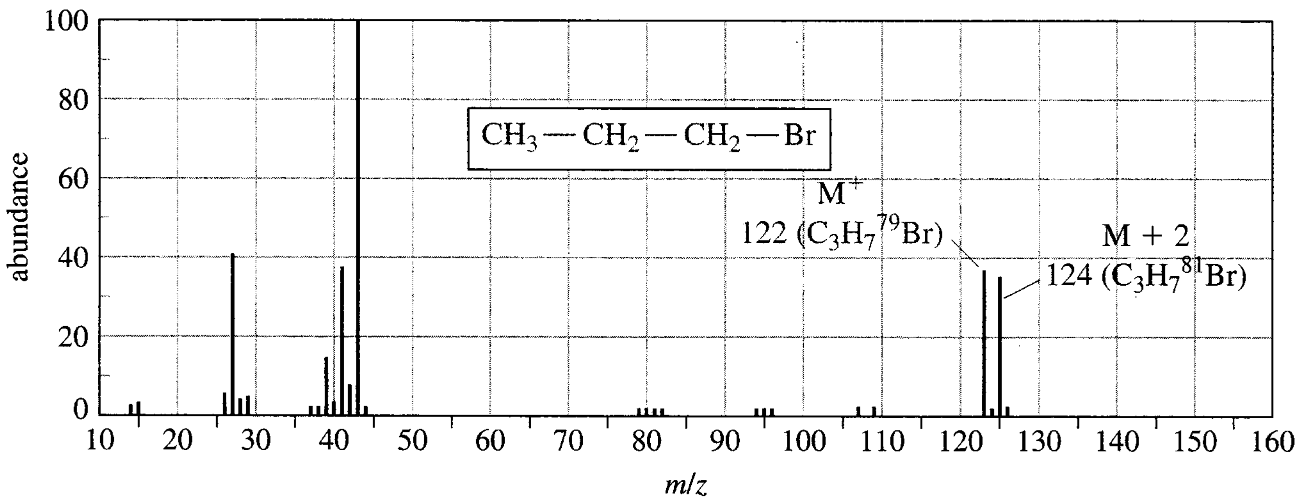
I ⟹ ^{127}I(100 %), observe I^+ at m/z=127, and a 127 unit gap

Table 12-4

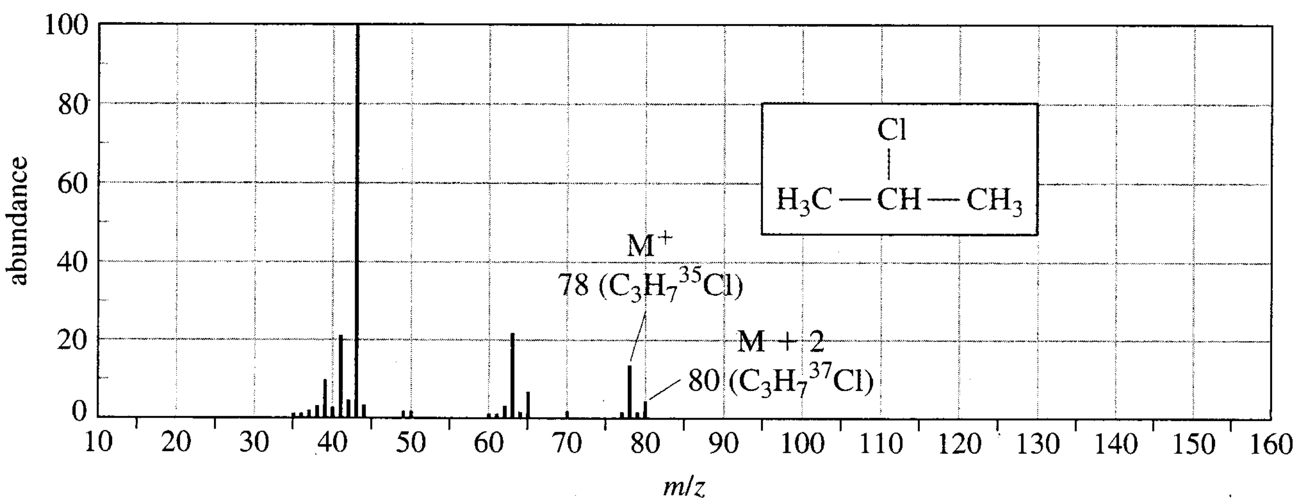
TABLE 12-4 Isotopic Composition of Some Common Elements

Element	M⁺		M+1		M+2	
hydrogen	^{1}H	100.0%				
carbon	^{12}C	98.9%	^{13}C	1.1%		
nitrogen	^{14}N	99.6%	^{15}N	0.4%		
oxygen	^{16}O	99.8%			^{18}O	0.2%
sulfur	^{32}S	95.0%	^{33}S	0.8%	^{34}S	4.2%
chlorine	^{35}Cl	75.5%			^{37}Cl	24.5%
bromine	^{79}Br	50.5%			^{81}Br	49.5%
iodine	^{127}I	100.0%				

Page 524 Mass Spectrum of 1-bromopropane

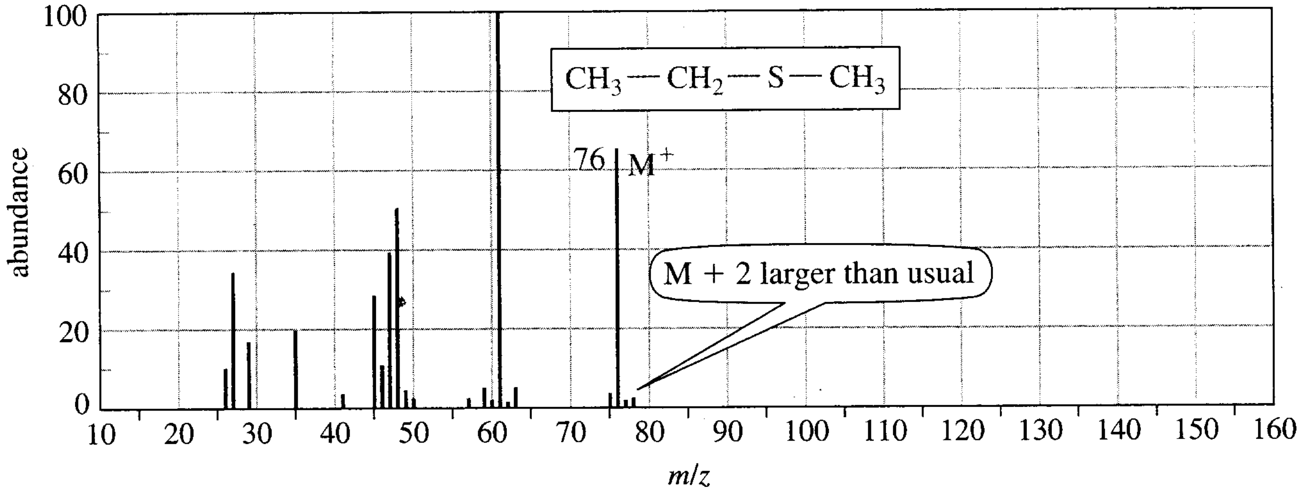


Page 524 Mass Spectrum of 2-chloropropane

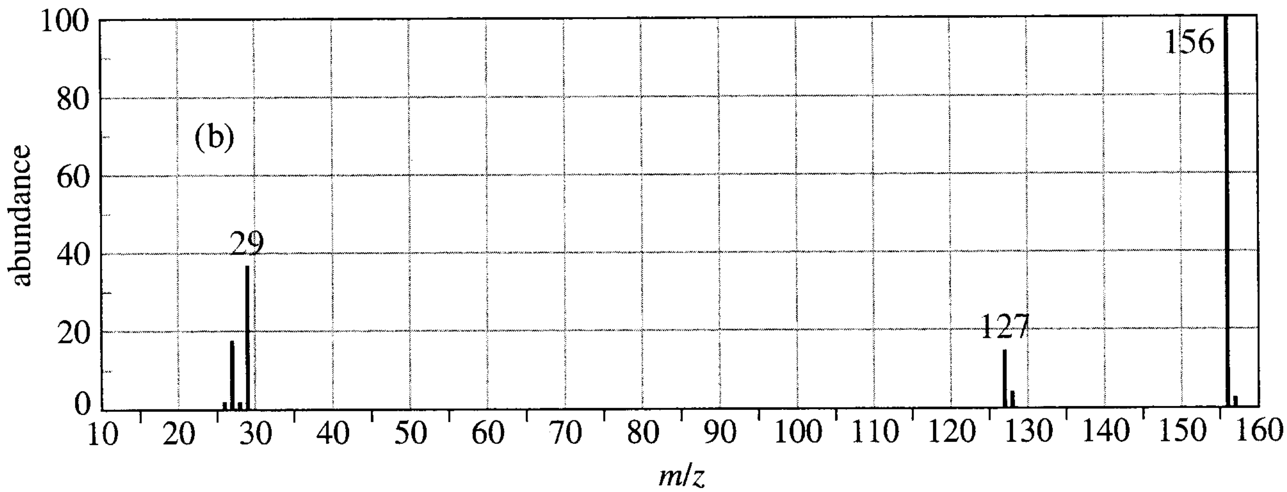


T-99

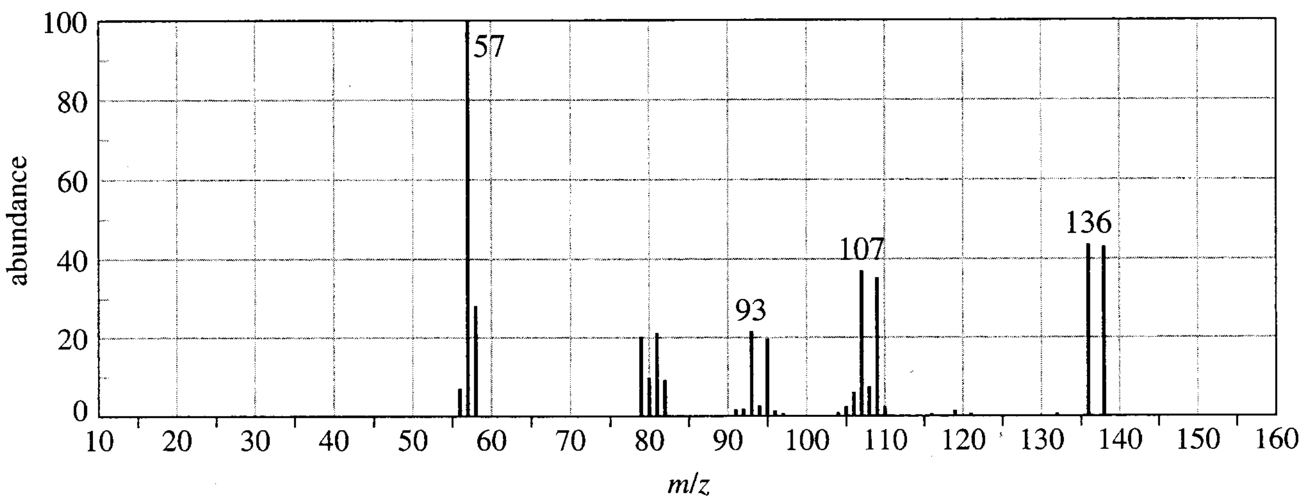
Page 524 Mass Spectrum of ethyl methyl sulfide



Prob 12-7b Mass Spectrum of iodoethane



Prob 12-20 Mass Spectrum of 1-bromobutane



Organic Chemistry, 5/e
by L.G. Wade, Jr.