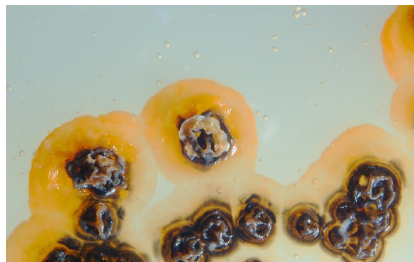


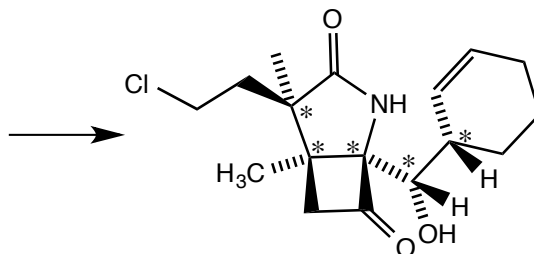
Chapter 15 and 16: Spectroscopy. Determining Molecular Structure

[Sections: 15.1-15.11, 15.16, 16.1-16.3, 16.5-16.12]

Why Should I Care About Molecular Structure?



Solinospora, a bacterium found in deep oceanic waters off the coast of the Bahamas and the Red Sea



Salinosporamide A: isolated by William Fenical's group at Scripps Institute and found to inhibit cancer-cell growth

Determining Organic Molecular Structure

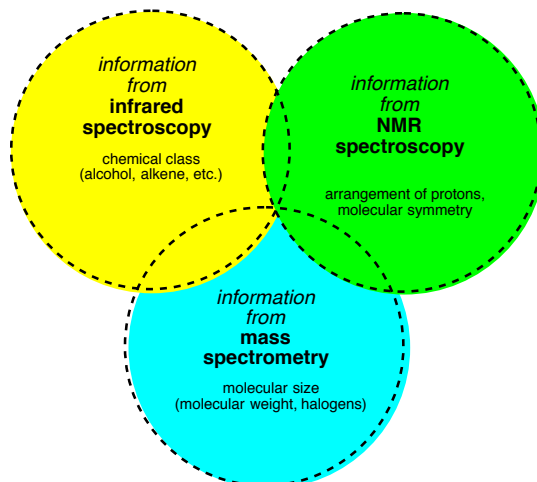
Employ a Combination of Commonly-Used Spectroscopic Methods

Infrared Spectroscopy (IR): *information on functional groups*

Mass Spectrometry (MS): *information on molecular weight*

Nuclear Magnetic Resonance Spectroscopy (NMR): *information on protons and carbons as well as molecular symmetry*

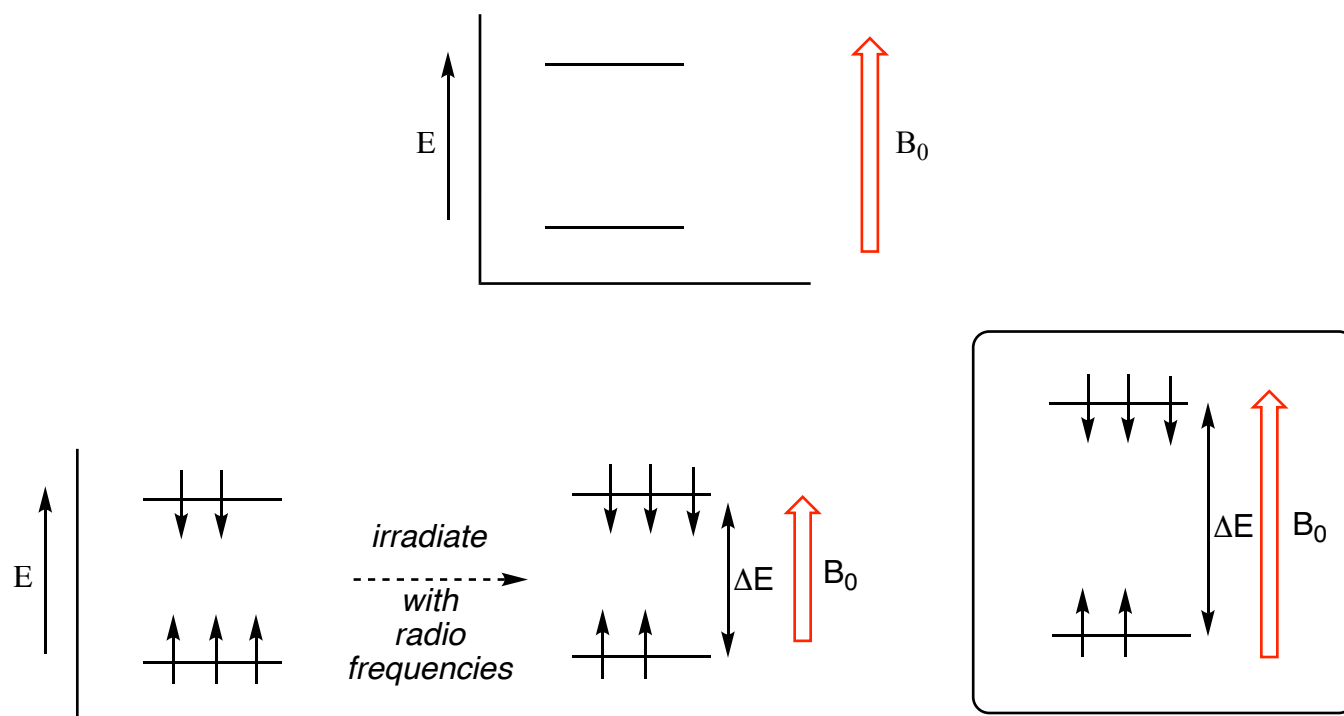
- in many cases, the combination of all three of these types of spectra provide sufficient information to assign a unique molecular structure to an unknown compound*



^1H Nuclear Magnetic Resonance Spectroscopy (Proton NMR Spectroscopy)

- Moving charges give rise to magnetic fields.
- Positively charged protons (^1H) have spin similar to that of electrons.
- The spin gives rise to a tiny magnetic field. So protons act as tiny magnets.
- Normally, the tiny magnetic fields generated by protons are randomly oriented.

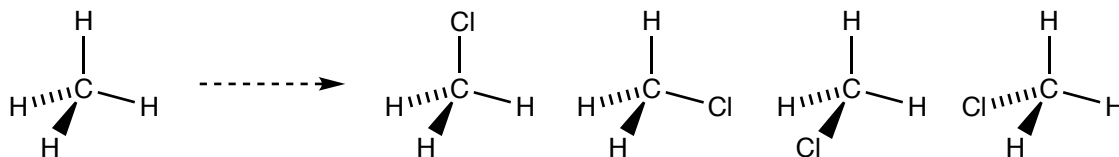
• In the presence of a strong (external) magnetic field (B_0), the magnetic fields of the individual protons align themselves in the same orientation as the external field, although they may be in the same direction (parallel) or opposite direction (anti-parallel). The parallel spin is of slightly lower energy than the anti-parallel, although both are populated.



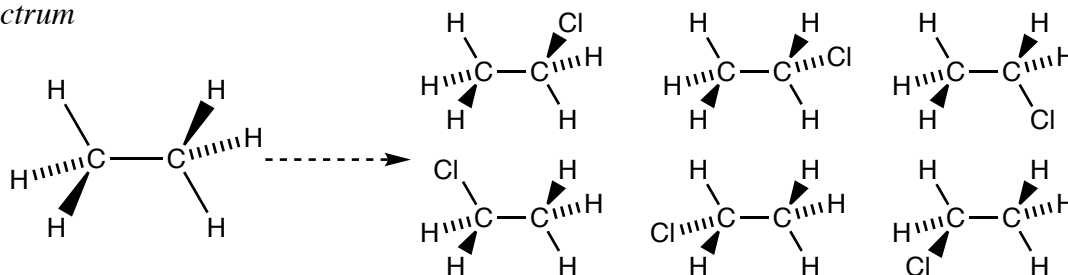
- When the protons are irradiated with the proper amount of energy, the proton can flip from one direction (parallel, for example) to the opposite direction (anti-parallel). This is the point of nuclear magnetic resonance!
- The energy at which this occurs can be measured and plotted. This gives rise to the ^1H NMR spectrum
- If ALL of the protons in a molecule "flipped" (or, are at resonance) at exactly the same energy, different types of protons could not be differentiated
- Fortunately, however, the energy at which the resonance occurs is dependent upon the "chemical environment" of those particular protons
- The stronger the magnetic field B_0 , the greater the difference in energies between the parallel and anti-parallel energy states. Therefore, stronger magnetic fields lead to better defined NMR spectra

¹H Nuclear Magnetic Resonance Spectroscopy (NMR Spectroscopy)

Chemical Environments



- methane has four hydrogens but all are considered to be in the same chemical environment (chemically equivalent) since replacing any one of the four hydrogens leads to the same compound
- therefore, methane has ONE chemical environment and will give rise to ONE signal in the ¹H NMR spectrum

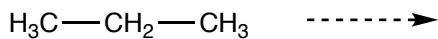


- ethane has six hydrogens but all are considered to be in the same chemical environment (chemically equivalent) since replacing any one of the four hydrogens leads to the same compound
 - therefore, ethane has ONE chemical environment and will give rise to ONE signal in the ¹H NMR spectrum
- NOTE: the three hydrogen atoms of a methyl group will always be chemically equivalent

Analyze



Analyze

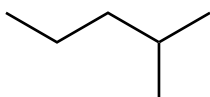
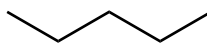
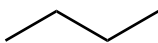


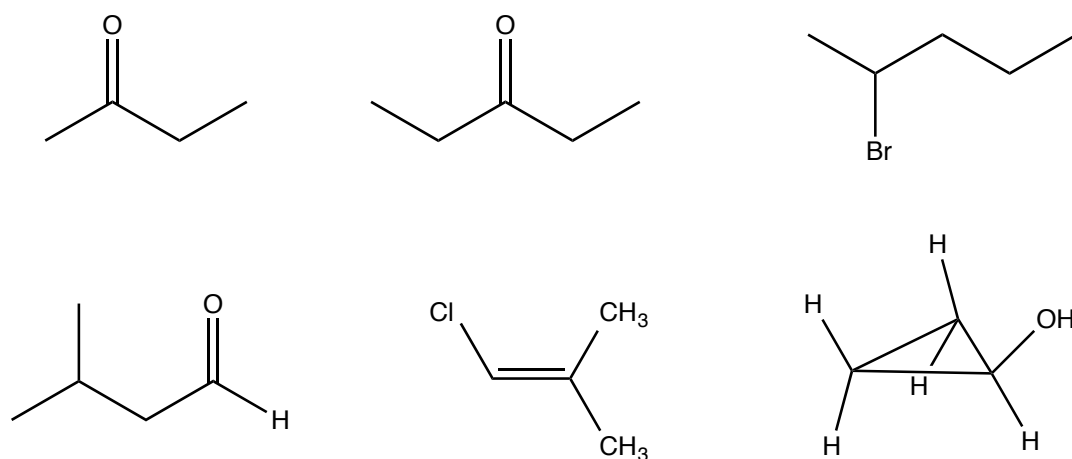
Number of chemical environments?

Number of signals in the ¹H NMR spectrum expected?

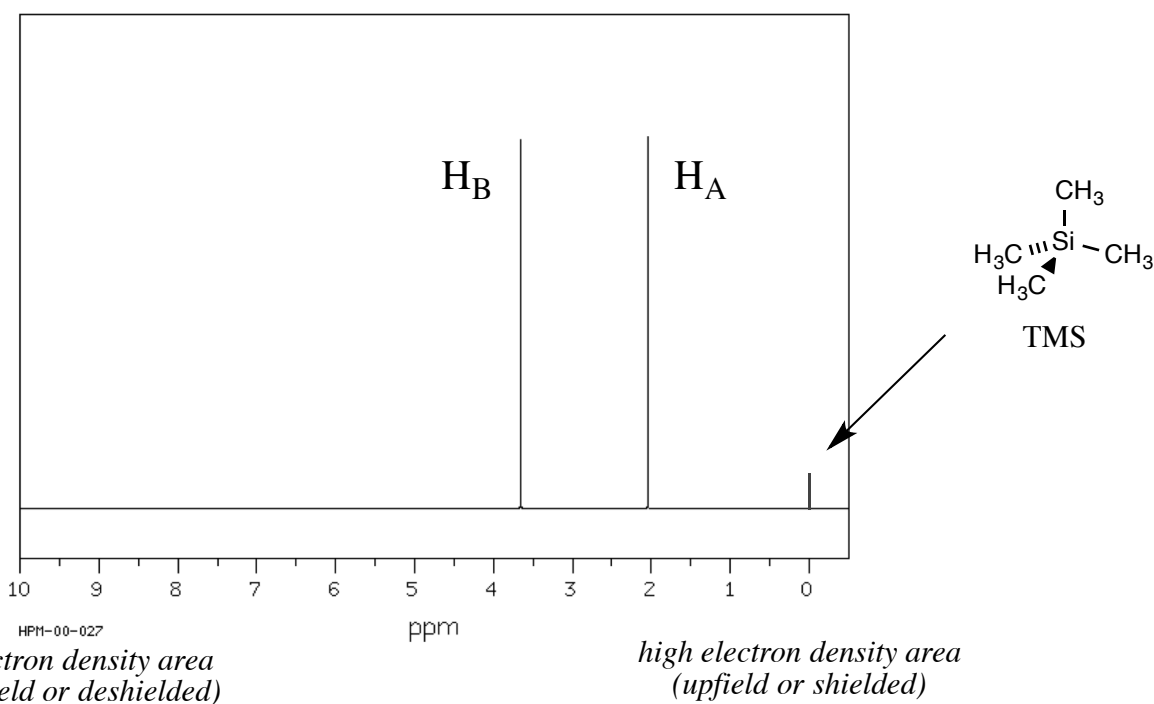
NOTE: the two hydrogen atoms of a methylene (CH₂) group will USUALLY be chemically equivalent

Predict the number of chemical environments and expected signals in the ¹H NMR spectrum:





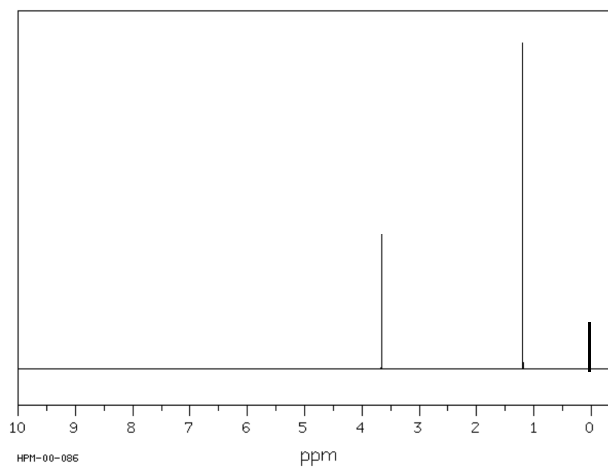
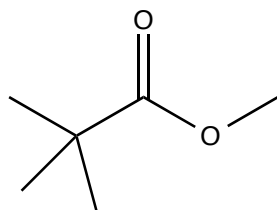
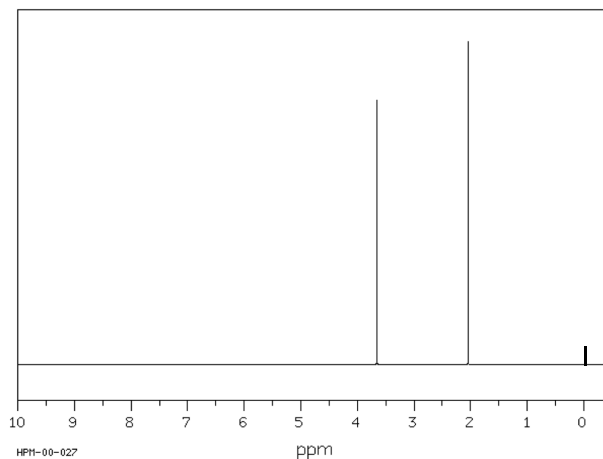
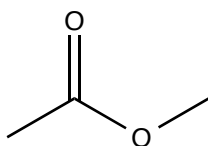
Basic Analysis of a ^1H NMR spectrum



- NMR scale = ppm = parts per million
- always set relative to a standard; usually tetramethylsilane (TMS) at 0 ppm
- protons in environments of "high" electron density are found closer to 0 ppm (said to be "upfield" or "shielded")
- protons in environments of "low" electron density are found closer to 10 ppm (said to be "downfield" or "deshielded")
- in the example above, H_A must be in a chemical environment in which it experiences higher electron density than does H_B
- the power of ^1H NMR is that certain types of protons consistently appear in the same area of the NMR spectrum, according to their chemical "environment"

Predicting Chemical Shifts: Where do the Different Chemical Environments Appear on the Spectrum?

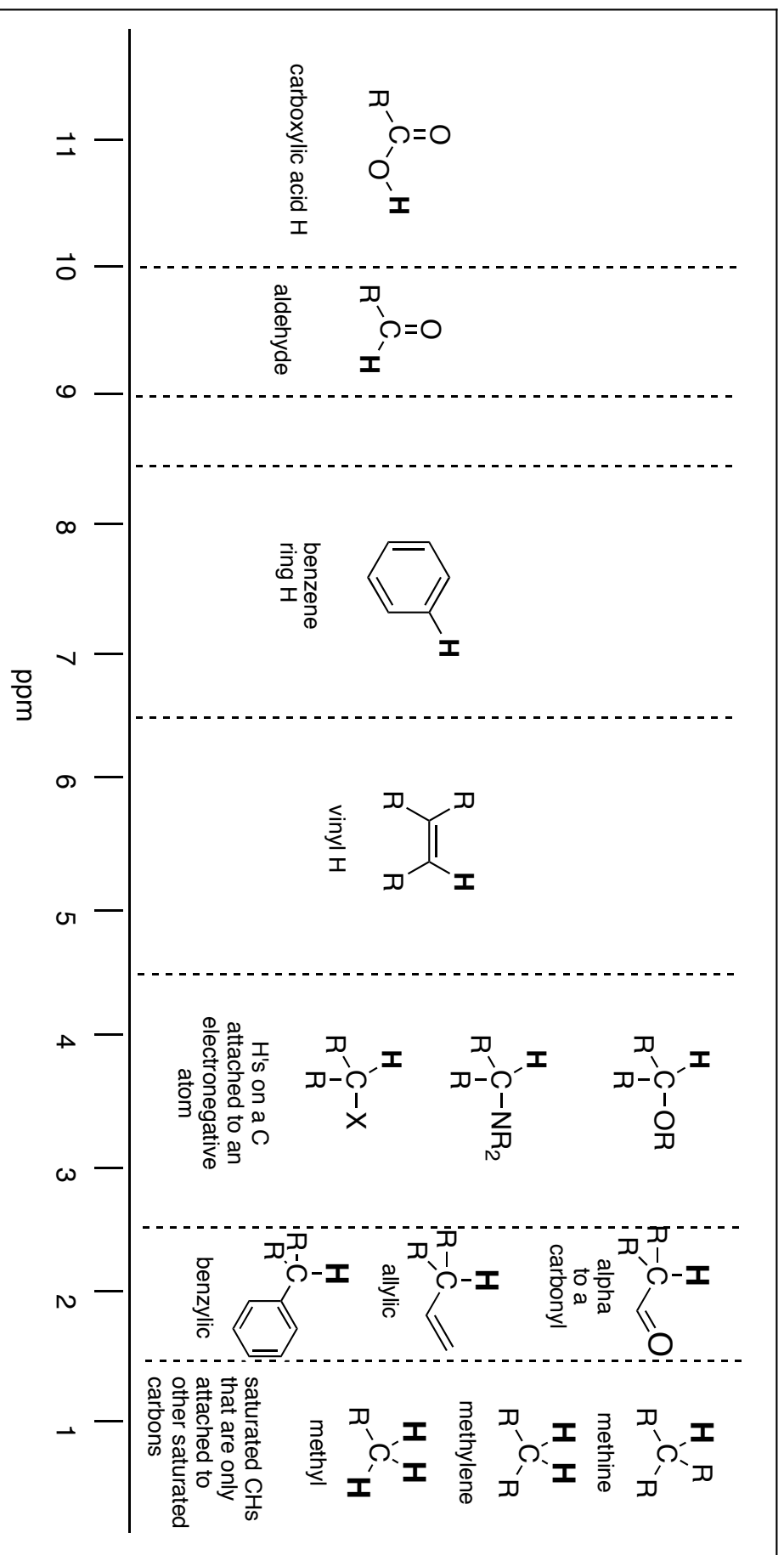
- use the "Typical Shifts" chart and webpage to predict the approximate range for the type of proton of interest



Three Rules of ¹H NMR Spectroscopy

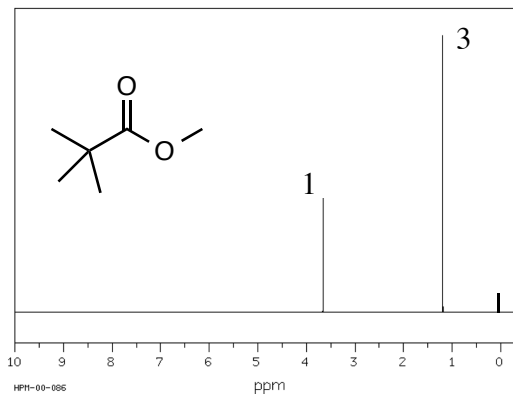
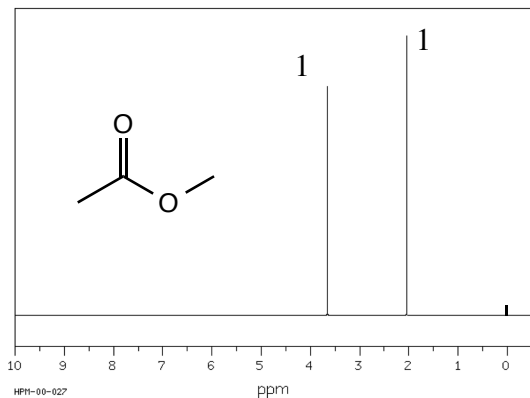
- chemically **equivalent** protons absorb at the **same** chemical shift
- chemically **inequivalent** protons absorb at **different** chemical shifts
- chemically **similar** protons absorb at **similar** chemical shift

TYPICAL CHEMICAL SHIFTS IN ^1H NMR SPECTROSCOPY



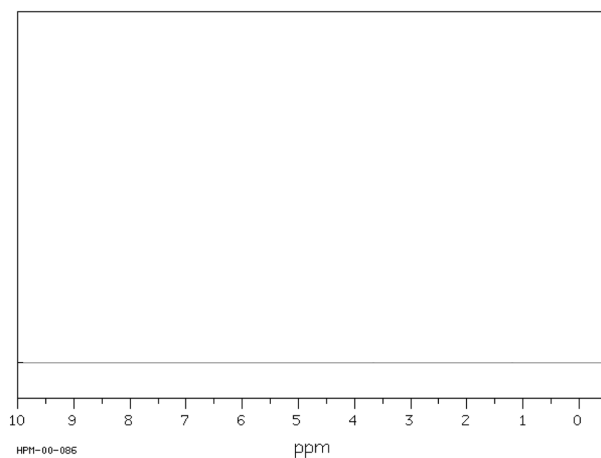
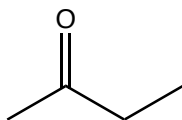
Integration

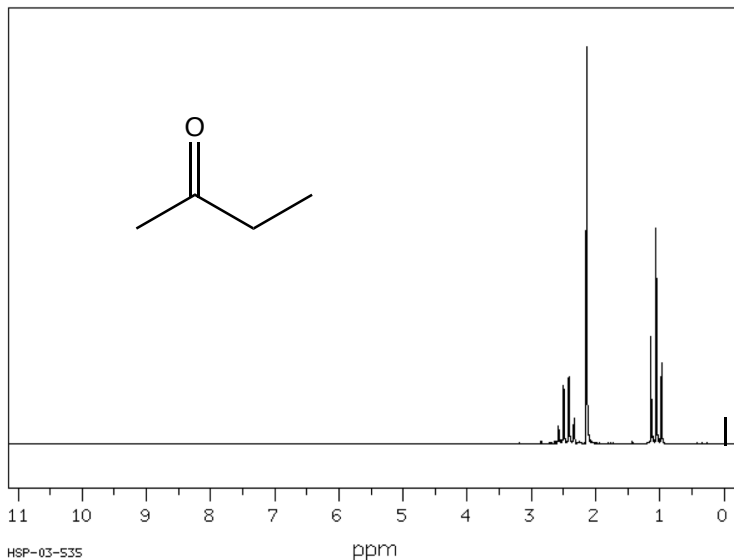
- from integration the area under each curve, a value is assigned to each signal that provides information on the relative number of protons in each chemical environment. NOTE: these may NOT be the same as the actual number of protons in that environment!



- ^1H NMR spectroscopy provides information on the chemical environment of the protons in the molecule AND the relative numbers of protons in those environments

Predict the number of signals and expected chemical shifts in the ^1H NMR spectrum of 2-butanone:

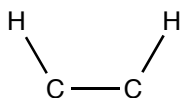




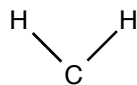
expected integration?

- protons, like electrons, generate small magnetic fields
- these magnetic fields impact the H_{eff} of neighboring protons
- the result is that simple "singlet" signals are split into more complicated "multiplets"
- the size of the multiplet can be predicted by counting the number of neighboring **chemically inequivalent** protons
- the multiplet will be equivalent to $n+1$ where n = number of neighboring chemically inequivalent protons

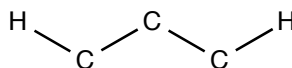
Multiplets: when does splitting occur? what will the multiplet look like?



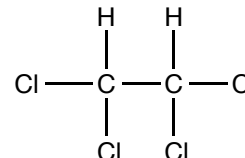
vicinal protons that are chemically inequivalent



geminal protons that are chemically inequivalent

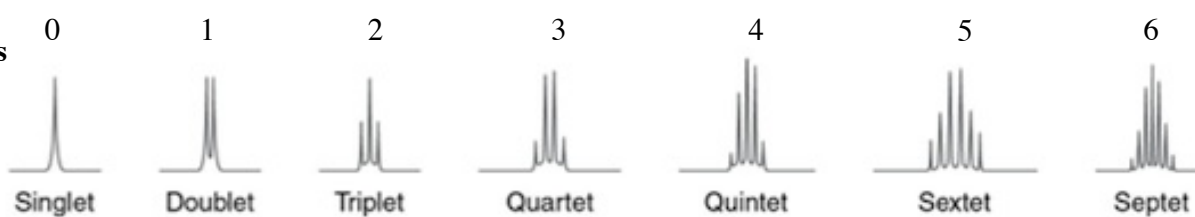


NO: too far away from each other



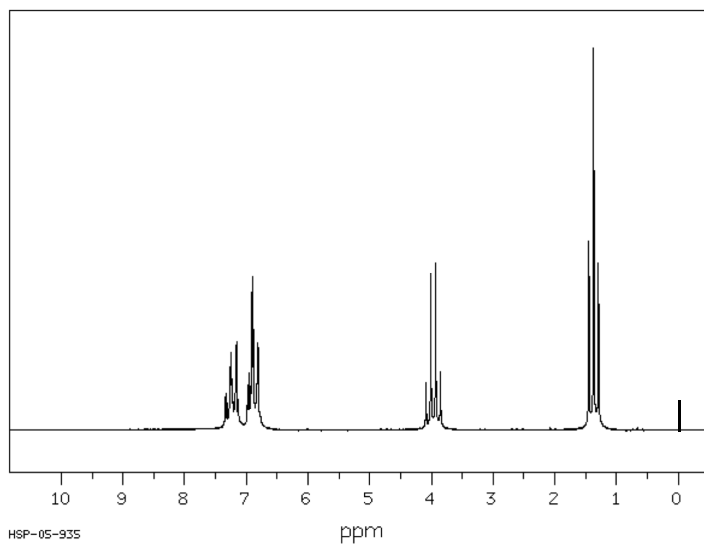
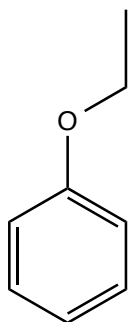
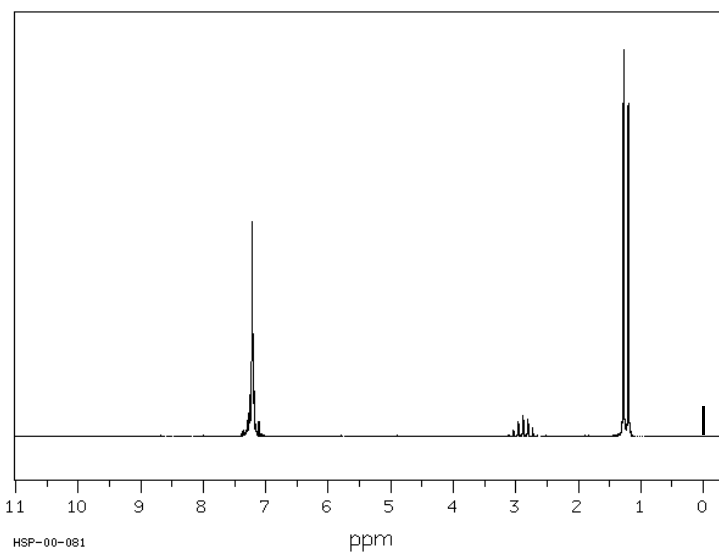
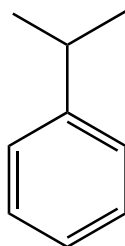
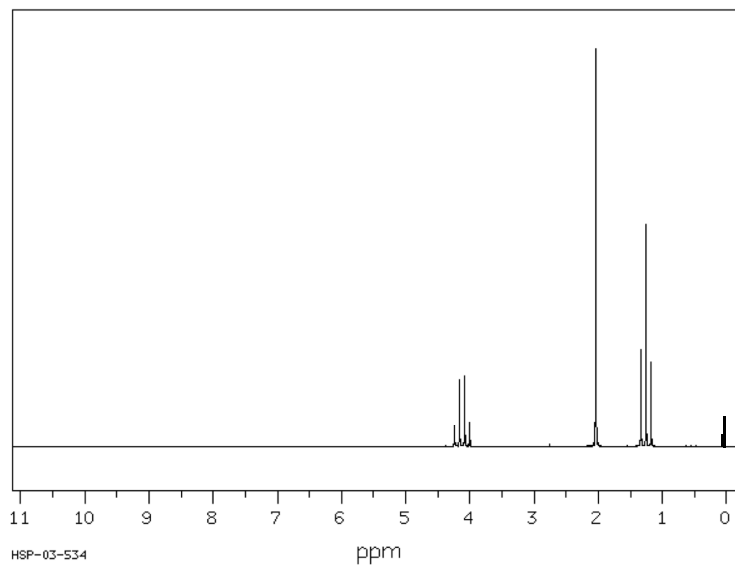
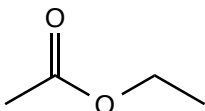
NO: chemically equivalent

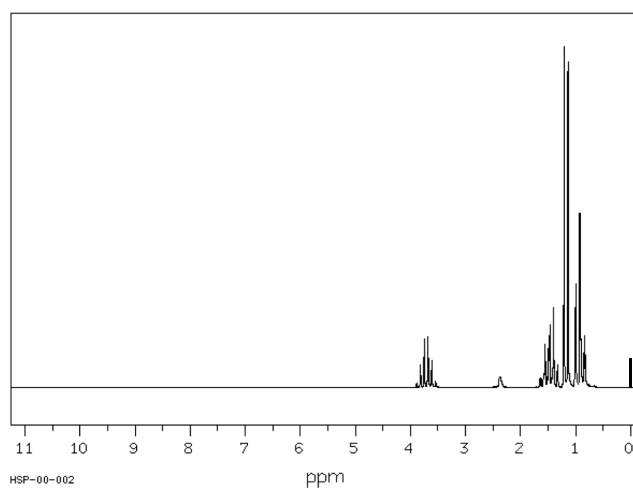
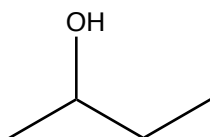
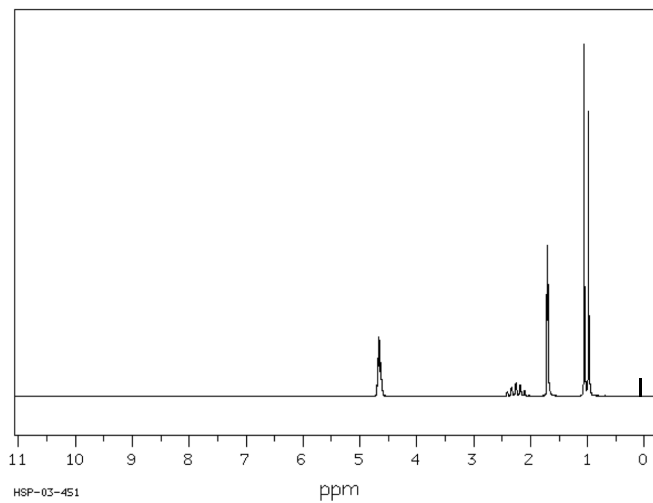
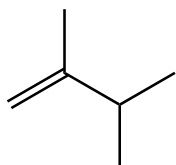
neighbors



$n+1$?

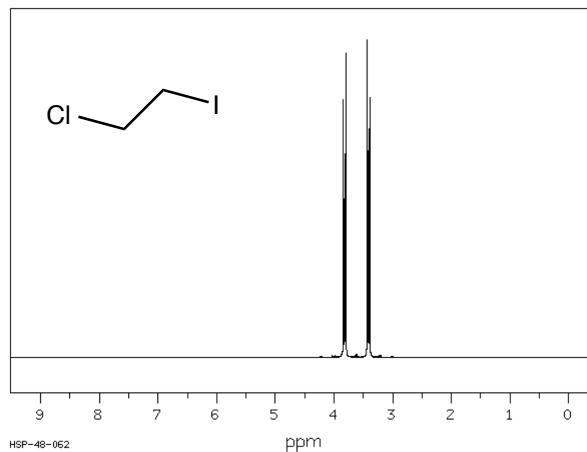
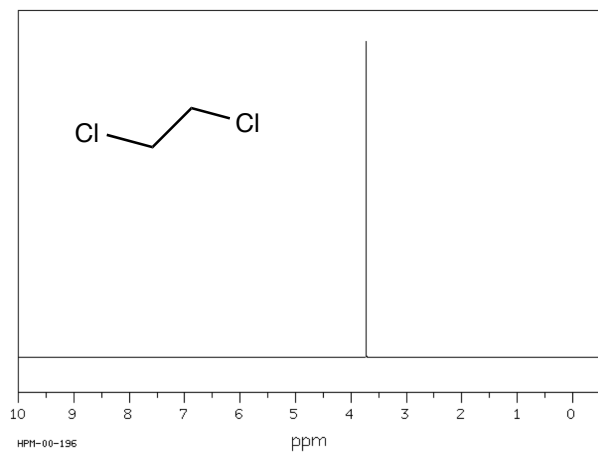
Predict the number of signals and expected **chemical shifts, multiplicities, and integrations** in the ^1H NMR spectrum for each of the following. **Properly label the NMR spectra.**



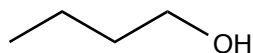


• *OH protons have variable chemical shift, dependent upon the concentration of the sample that is made up. Generally, they appear as broad singlets between 2-6 ppm*

a reminder about splitting patterns!



more on chemical shifts!

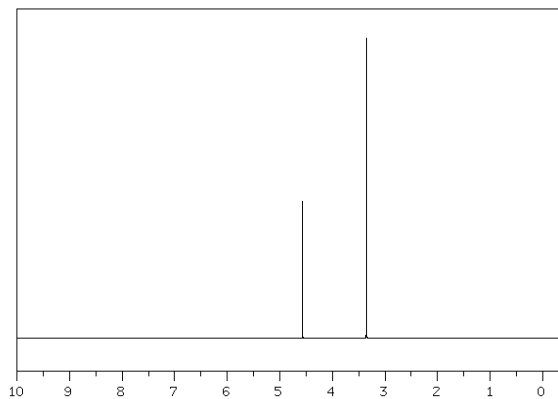
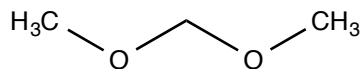
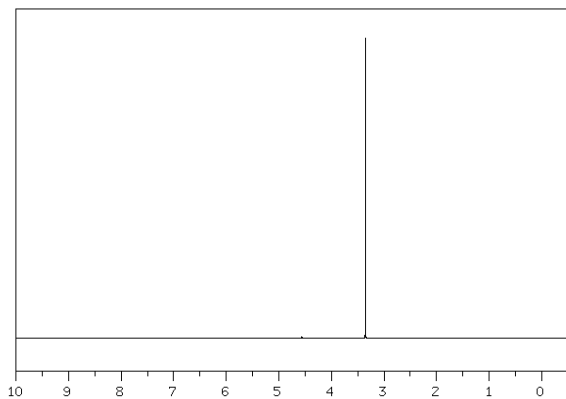
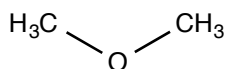


A B C D

predict:

actual:

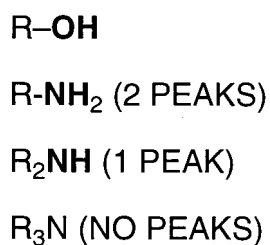
- even though not directly attached, a substituent can affect the chemical shifts of other chemical environments
- the effect drops off very rapidly as the distance to the substituent increases (greatest impact is with neighboring protons)



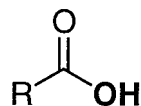
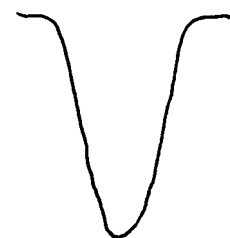
- additional substituents will exert nearly additive effects on chemical shifts

IMPORTANT INFRARED STRETCHES SUMMARY

~3500 cm⁻¹
—OH / —NH

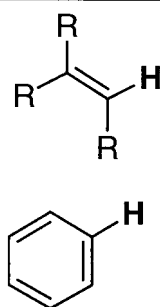


~ 3500 cm⁻¹ strong for —OH,
medium or weak for N—H



2500–3000 cm⁻¹ strong and very broad

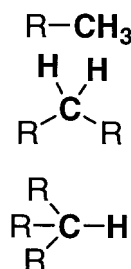
~3010 cm⁻¹
unsaturated C—H



just above 3000 cm⁻¹ f
or unsaturated C—H, usually weak



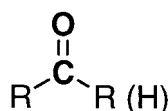
~2950 cm⁻¹
saturated C—H



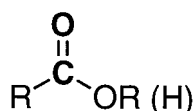
just below 3000 cm⁻¹ (2900–3000)
for saturated C—H, usually strong



~1700 cm⁻¹
carbonyl group



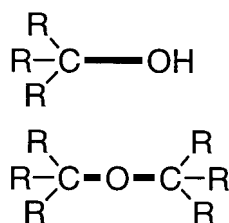
1740–1730 cm⁻¹, very strong



1735–1650 cm⁻¹, very strong



~1250–1000 cm⁻¹
C—O single bond

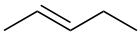
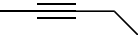
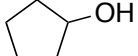

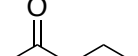
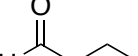
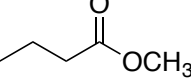
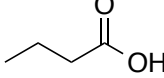
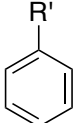
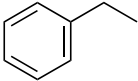


1250–1000 cm⁻¹ for C—O bond
stretching, medium to strong

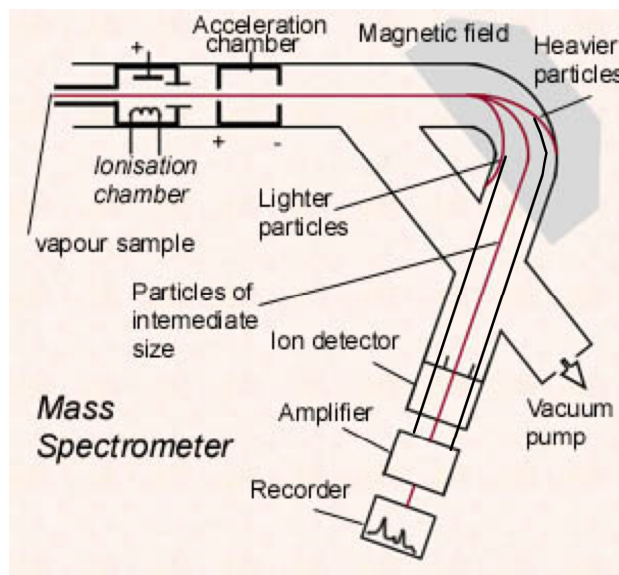


**DETERMINING THE PRESENCE OF MAJOR INFRARED STRETCHES BY
COMPOUND CLASS**

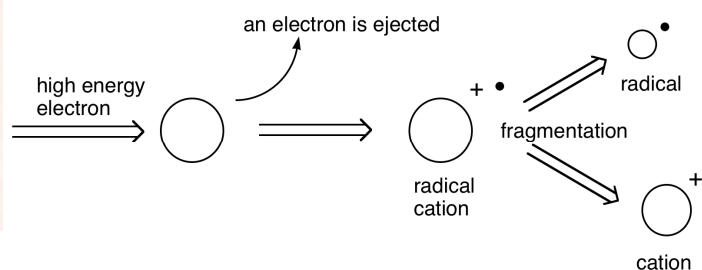
COMPOUND CLASS	THE FOLLOWING INFRARED STRETCHES ARE PRESENT:				
	-OH (~3500 cm ⁻¹)	UNSAT C-H (~3010 cm ⁻¹)	SAT C-H (~2950 cm ⁻¹)	C=O (~1700 cm ⁻¹)	C-O (~1000-1250 cm ⁻¹)
ALKANE			✓		
ALKENE		✓	✓		
ALCOHOL	✓		✓		✓
ESTER			✓	✓	✓
ETHER			✓		✓
KETONE			✓	✓	
ALKYL AROMATIC		✓	✓		
CARBOXYLIC ACID	✓		✓	✓	✓

general structure	class	example
$\begin{array}{c} R & & R \\ & \diagdown & / \\ & C=C & \\ & / & \diagdown \\ R & & R \end{array}$	alkene	
$R-C\equiv C-R$	alkyne	
$R-OH$	alcohol	
$R-O-R'$	ether	
$\begin{array}{c} O \\ \\ R-C-R' \end{array}$	ketone	
$\begin{array}{c} O \\ \\ R-C-H \end{array}$	aldehyde	
$\begin{array}{c} O \\ \\ R'-C-O-R \end{array}$	ester	
$\begin{array}{c} O \\ \\ R'-C-O-H \end{array}$	carboxylic acid	
	alkyl benzene (aromatic)	

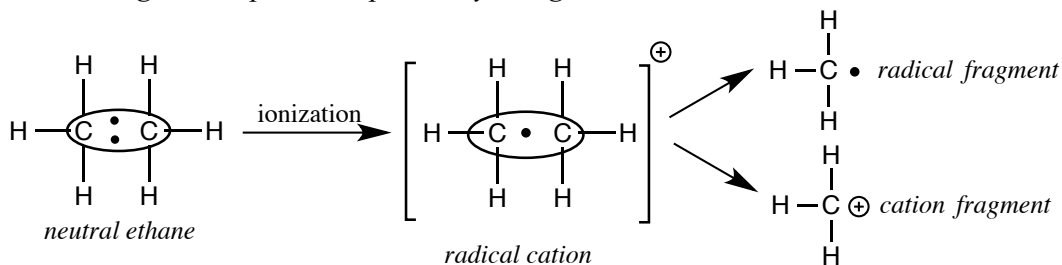
Mass Spectrometry



- mass spectrometers are kept under very high vacuum in order to keep out any types of molecules other than those to be analyzed
- the compound of interest is introduced into the ionization chamber
- molecules are "ionized" by impact with a stream of high-energy electrons which ejects an electron
- the result is a molecule with one unpaired electron (a radical) and it has a positive charge (hence a radical cation is formed)

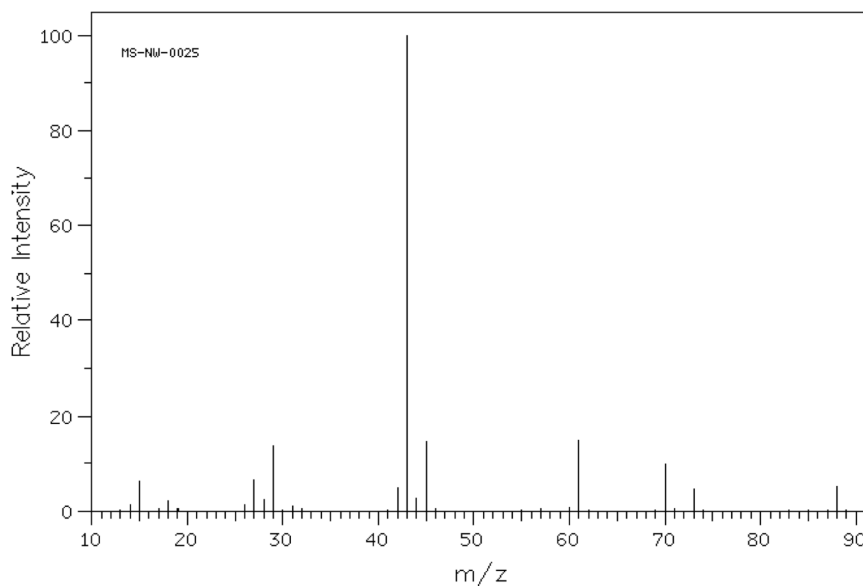


- many of the resulting ions, because of the large excess of energy from the electron bombardment, undergo "fragmentation" to give two pieces: a positively charged carbocation and a neutral radical

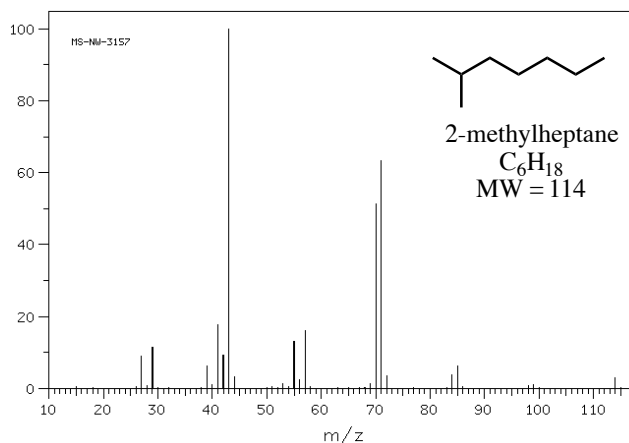
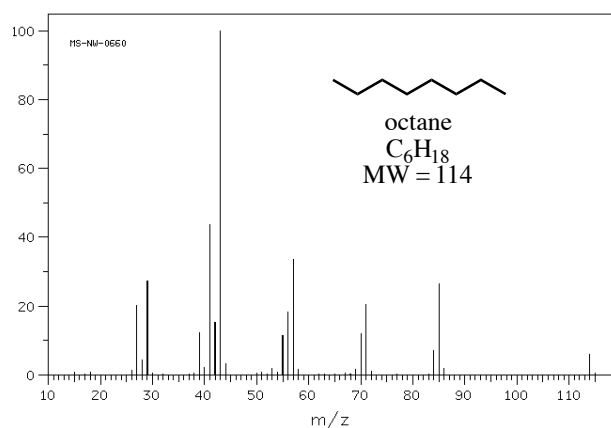


- the cation fragments travel down the chamber past a strong magnetic field. The cations are deflected according to their mass
- the mass of the carbocation fragments, and their frequency of formation, are recorded
- the radical fragments are not deflected and are not detected. Only charged species can be detected

Ethyl Acetate (MW = 88)



- if the initial ion holds together without fragmentation, it gives a peak that has the same mass as the molecular weight of the original compound. This particular ion is called the Molecular Ion peak (M^+)
 - a. if present, the M^+ peak will be at highest mass since all other fragments must be of lower mass
 - b. the M^+ peak is not ALWAYS present (for our purposes, however, it will be)
 - c. the M^+ peak may or may not be the biggest peak (the biggest peak is called the "base peak")
- under a given set of conditions, compounds fragment in a particular and reproducible manner to give a mass spectrum that is a "fingerprint" for that compound



- mass spectrometers are very sensitive to mass and can differentiate even one atomic mass unit. This allows for differentiation of "isotopes". Isotopes are atoms that contain different numbers of neutrons.

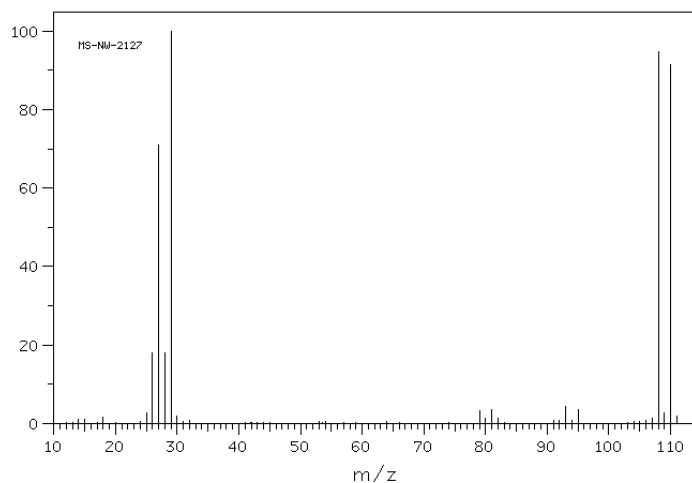
¹H is the most common isotope of hydrogen (99.9%). It contains 1 protons and 0 neutrons

²H (deuterium) is a less common isotope of hydrogen (0.1%). It contains 1 proton and 1 neutron

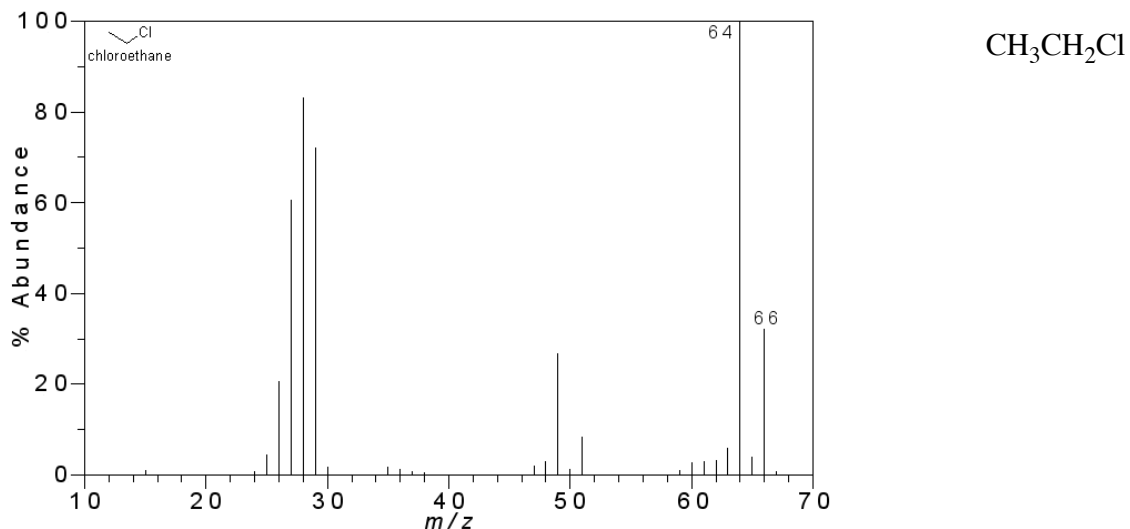
¹²C is the most common isotope of carbon (98%). It contains 6 protons and 6 neutrons

¹³C is a less common isotope of carbon (1%). It contains 6 protons and 7 neutrons

- all of the common "heavy atoms" (C, N, O) and hydrogen have a single major isotope however, two of the halogens have two major isotopes
- ⁷⁹Br and ⁸¹Br exist in a ~ 1:1 ratio. Thus half of the molecules that contain Br will have the ⁷⁹Br isotope, and the other half the ⁸¹Br isotope
- thus, molecules containing Br can be spotted quickly in the MS because there will be a pair of peaks at highest mass in a 1:1 ratio, separated by two mass units



- ^{35}Cl and ^{37}Cl exist in a $\sim 3:1$ ratio. Thus three quarters of the molecules that contain Cl will have the ^{35}Cl isotope, and the other quarter the ^{37}Cl isotope
- thus, **molecules containing Cl can be spotted quickly in the MS because there will be a pair of peaks at highest mass in a 3:1 ratio, separated by two mass units**



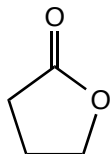
Estimating the Number of "Heavy Atoms" from a Molecular Weight

$$\frac{\text{MW} - \text{mass of halogen(s)}}{14} \cong \text{number of heavy atoms (C, O, N) in the molecule}$$

Examples

Octane = C_8H_{18} MW = 114

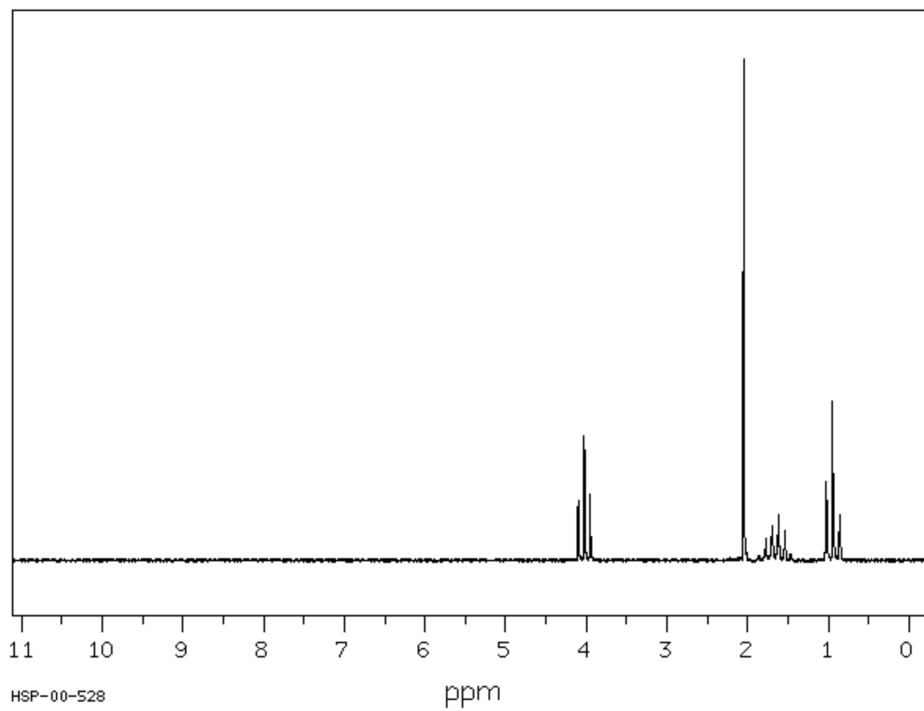
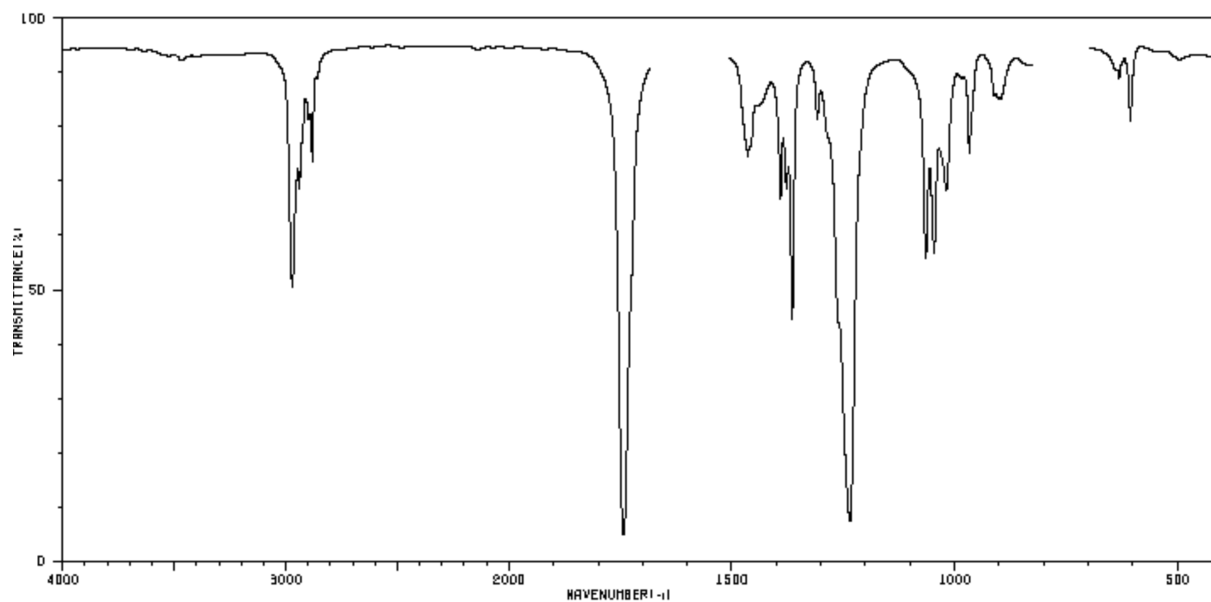
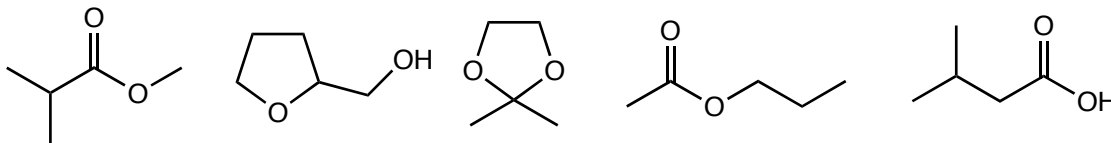
Chloroethane = $\text{C}_2\text{H}_5\text{Cl}$ MW = 64



- the MS provides information on the presence and/or absence of Br and Cl (two of the most commonly encountered halogens)
- by locating the M^+ peak, the MS also provides information on the approximate number of heavy atoms present in a molecule

Spectroscopy Problem 1

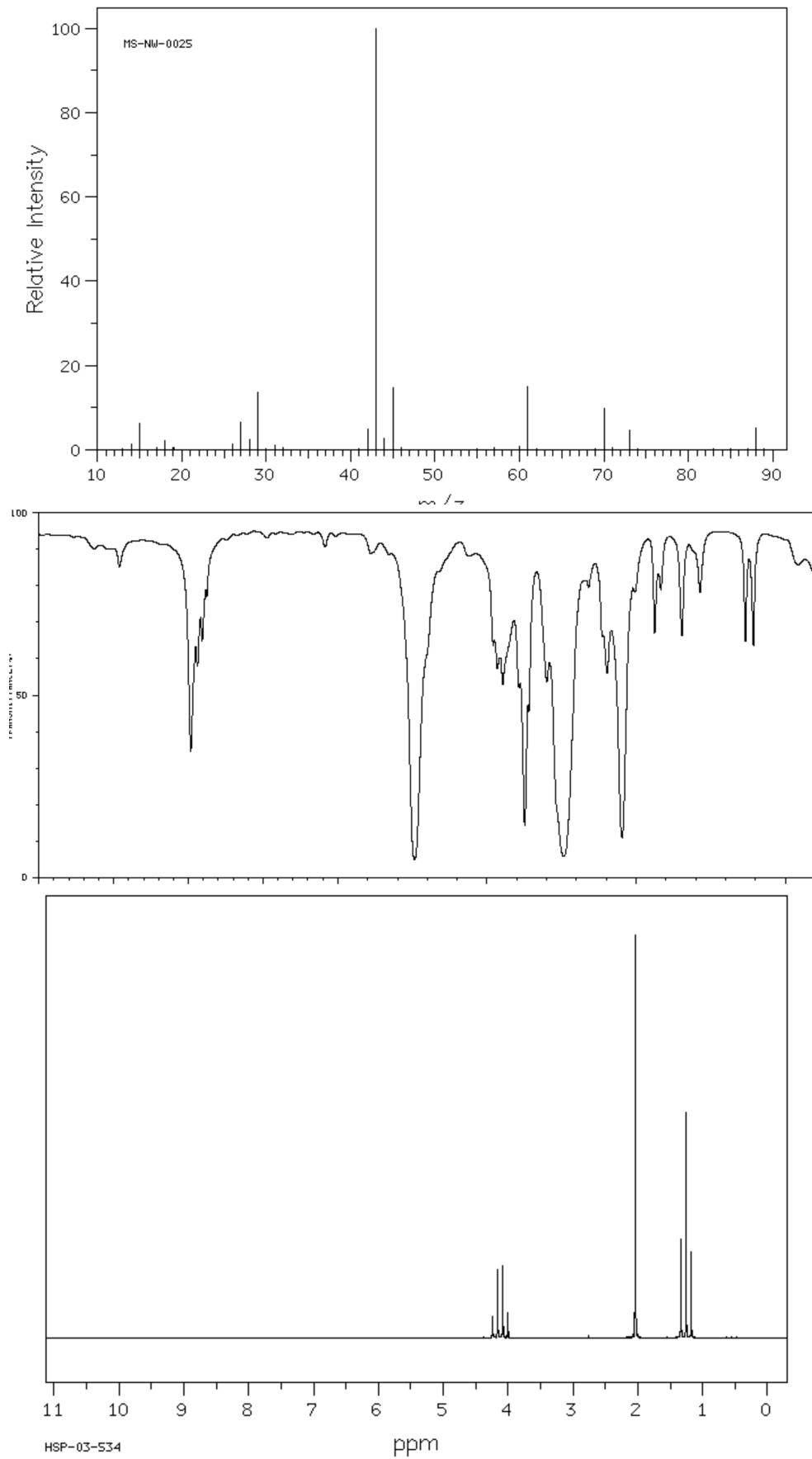
Compound with molecular formula $C_5H_{10}O_2$
Possible Structures:



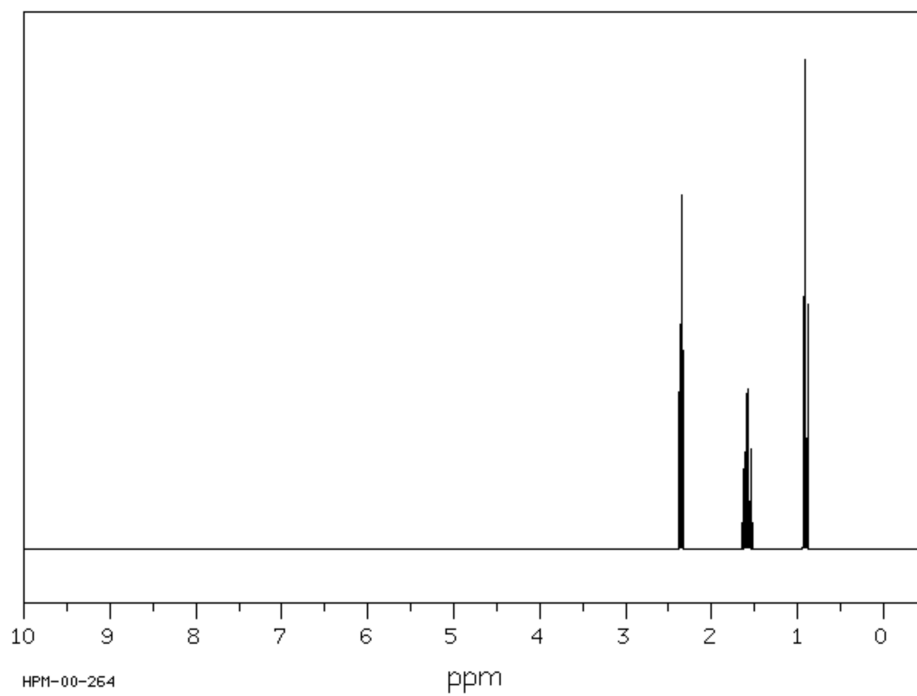
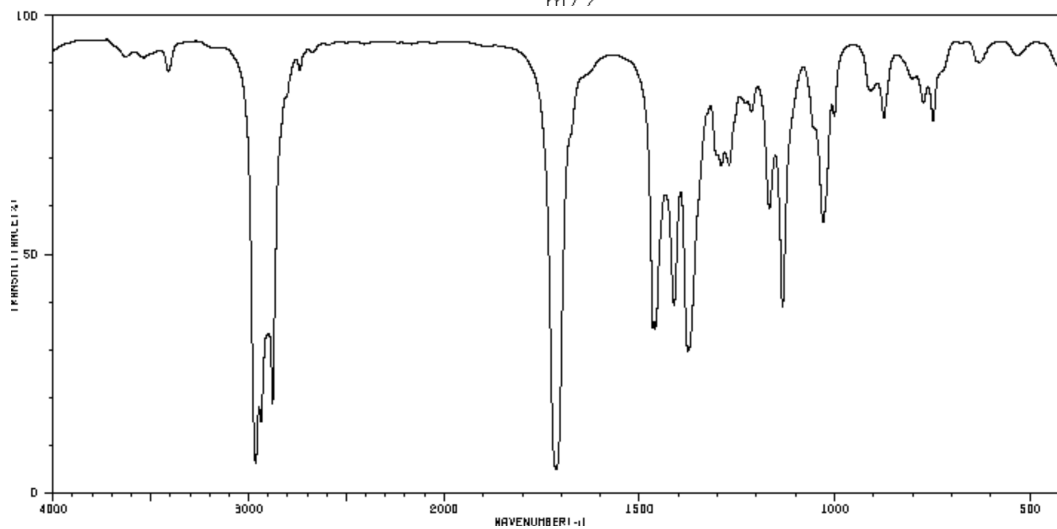
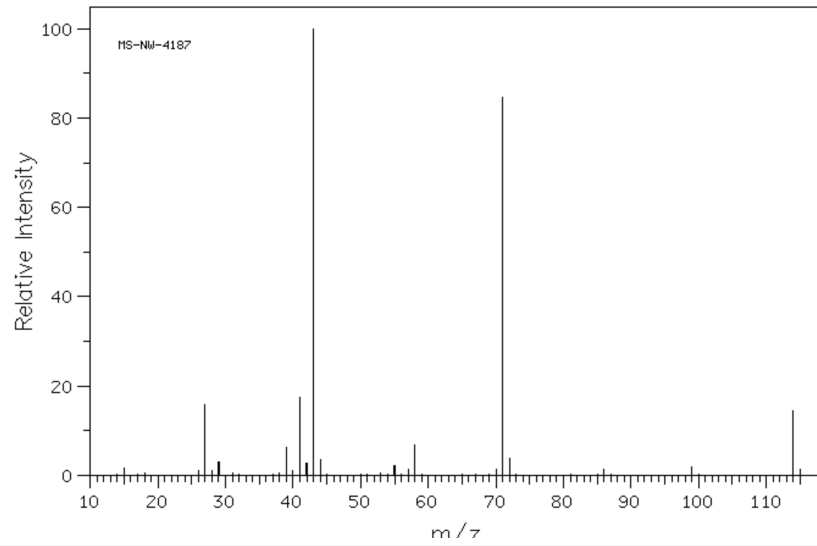
HSP-00-528

ppm

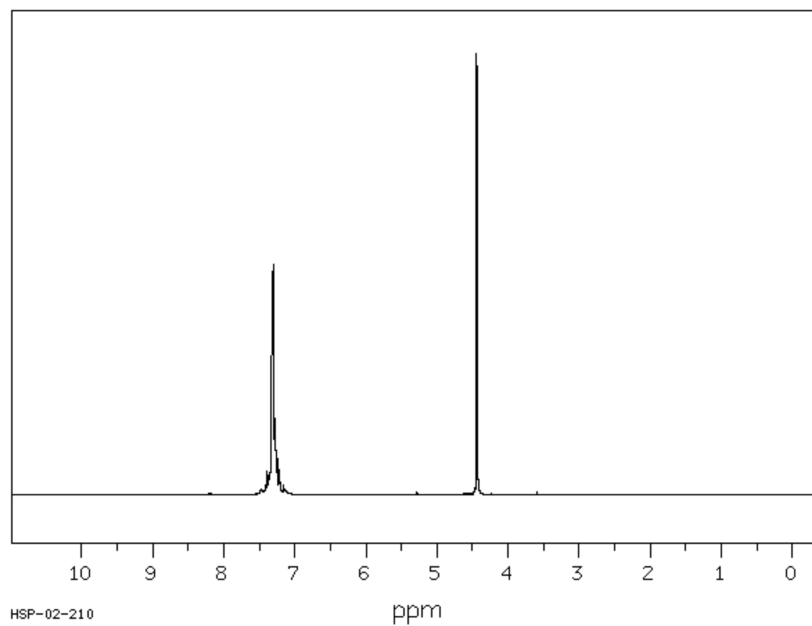
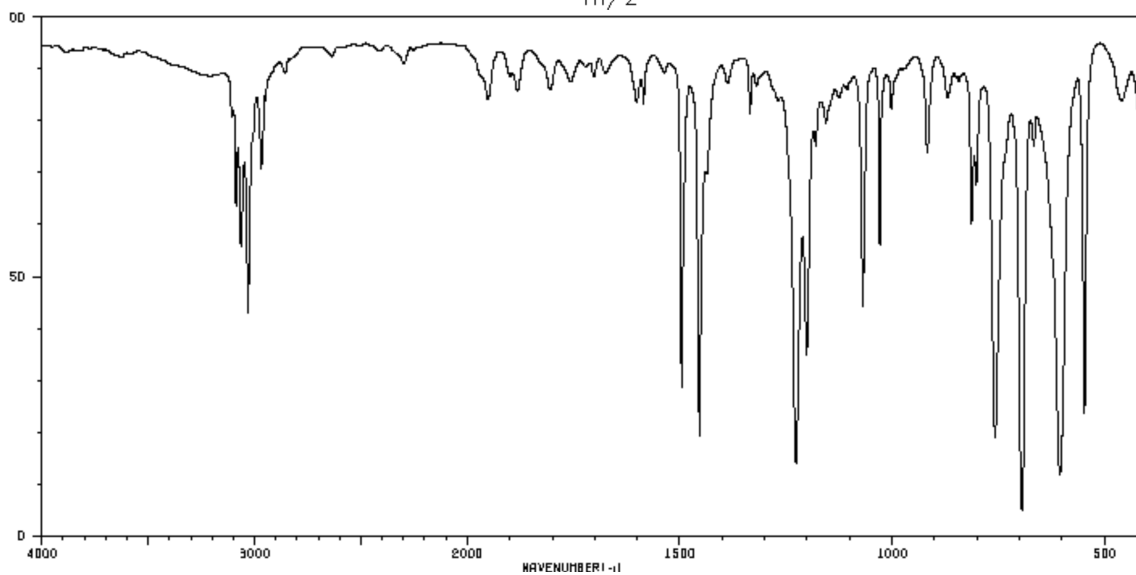
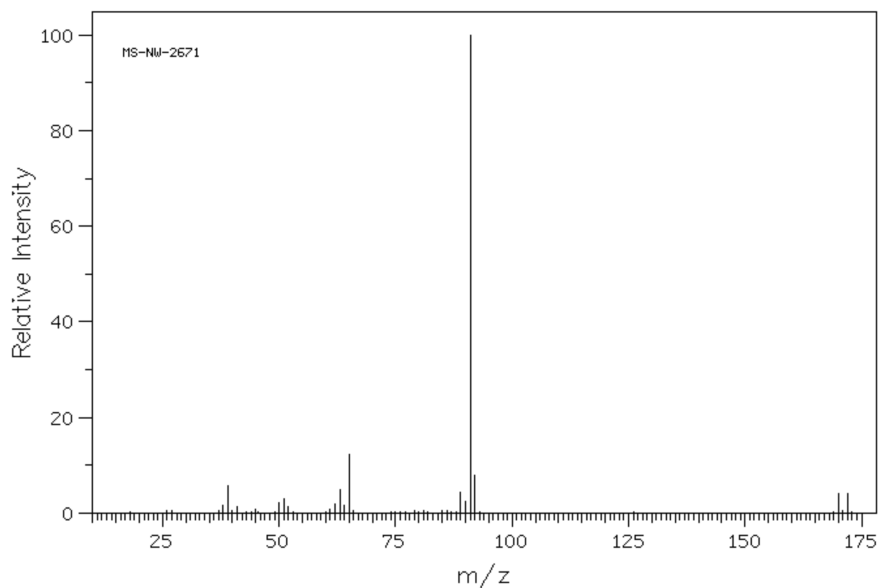
Spectroscopy Problem 2



Spectroscopy Problem 3



Spectroscopy Problem 5



Chapter 15/16 *Essential Concepts*

1. Understand the impact that external magnetic fields (B_0) have on the nuclear spins of protons, the difference between parallel and antiparallel states, and how nuclear magnetic resonance is established by irradiating with radio frequencies.
2. Be able to identify different chemical environments given a structure and assign approximate chemical shifts and multiplicities.
3. Understand what integration values mean
4. Know the 7 general regions of ^1H NMR chemical shifts!
5. Know the 5 general regions of IR spectral stretches!
6. Be able to recognize and assign the 9 common classes of organic compounds (and how to derive the class from an IR spectrum).
7. Understand how the basic processes behind collecting mass spectra. You should be able to identify the molecular ion peak (M^+), the $M+2$ peak (if present), the base peak and understand their significance.
8. Understand the importance of isotopes and be able to determine whether a Cl or Br is present in a molecule given the mass spectrum
9. Be able to properly calculate the number of heavy atoms in a molecule given the mass spectrum.
10. Be able to assimilate the information provided in NMR, IR and Mass spectra to provide a reasonable organic compound structure.