

## Chapter 15 (and 2.14). Spectroscopy.

### 15.1. Introduction to Spectroscopy.

When we run a reaction in the laboratory or when we isolate a compound from nature, one of our first tasks is to identify the compound that we have obtained. There are a number of different analytical techniques that can be used to do this. We can compare its physical properties (melting point, boiling point, optical rotation, physical appearance, odor and taste) to a known compound to see if they are identical. This method is not terribly reliable. We can burn the compound, measure the amount of CO<sub>2</sub>, H<sub>2</sub>O, and other compounds that are produced, and use the proportions of the combustion products to determine an empirical formula. This method, *elemental analysis*, is the oldest method of organic structure determination. Berzelius, a Swedish chemist, invented the technique about 1808, not long after the concept of atomic weights had been invented by the Englishman John Dalton. He determined the molecular formulae of eight organic carboxylic acids and got all but one right! Elemental analysis is still used today, but it is a relatively crude method, used more to determine the purity of a compound whose structure is already known than to identify an unknown compound.

The most widely used methods of organic compound identification today are those which measure the interactions of compounds with electromagnetic radiation of different wavelengths. In order of increasing energy of the radiation, these are as follows:

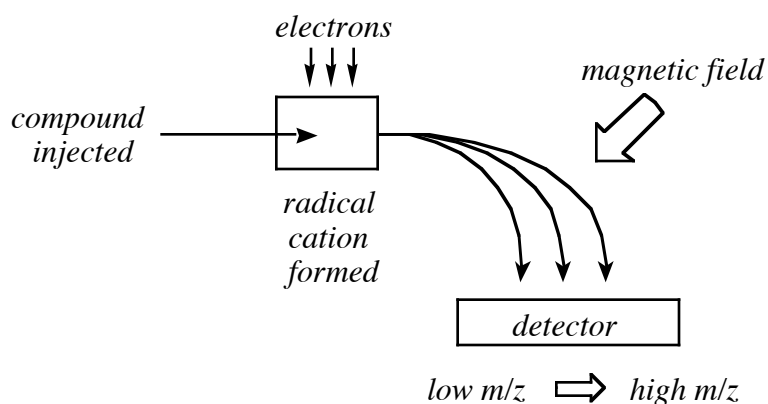
- Nuclear Magnetic Resonance (NMR) spectroscopy measures the absorption of radio waves by H or C atoms in a magnetic field. Different kinds of H or C atoms absorb energy of different wavelengths.
- Infrared (IR) spectroscopy measures the absorption of infrared radiation (heat) by organic compounds. Different functional groups (e.g., C=O, O–H) absorb energy of different wavelengths.
- Ultraviolet-Visible (UV-vis) spectroscopy measures the absorption of visible and ultraviolet light by  $\pi$  bonds in an organic compound. Bonds of different types (C=C, C=O) and with different extents of conjugation (C=C vs. C=C–C=C vs. aromatic) absorb energy of different wavelengths.

There is a fourth kind of spectroscopy, mass spectroscopy (MS), that does not involve the absorption of light. In fact, "mass spectroscopy" is a misnomer for this reason. However, it is the uni-versally used name for this technique, so we will use it too. MS provides a means of measuring the mass of a compound and certain pieces (fragments) of that compound upon blasting it with high energy electrons. This is the technique we will discuss first.

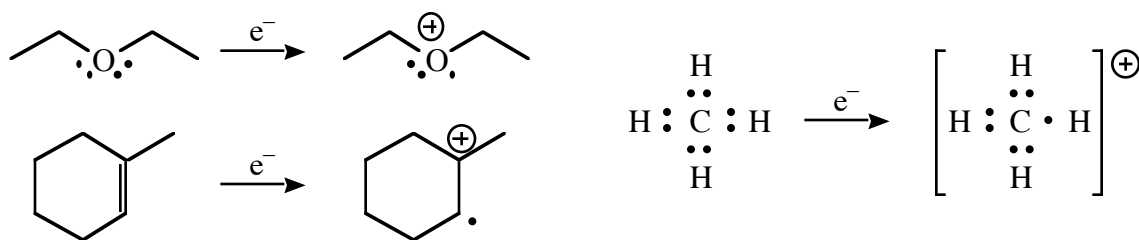
Make sure you remember how to calculate degrees of unsaturation!

## 15.2. Mass Spectroscopy.

The MS experiment works as follows. A compound is vaporized by putting it into a vacuum. It is then bombarded with high energy electrons. These electrons bounce into the compound, knocking one or more electrons out of an orbital. A *radical cation*, a compound with one unpaired electron and a positive charge, is left behind. The radical cation then passes into a magnetic field. The magnetic field causes the path of the positively charged compound to curve. The extent of curvature is determined by the *mass to charge ratio*, which is written as  $m/z$ . The detector, at the other end of the magnetic field, measures  $m/z$  by finding where the fragments emerge from the magnetic field. Usually  $z=1$ , so the method provides a measure of the mass of the particle. The quantity of fragments emerging at a particular  $m/z$  ratio, the *intensity*, is also measured.

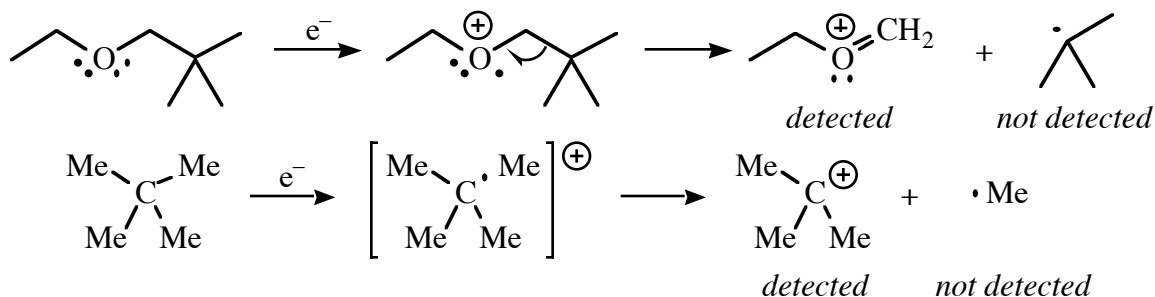


Electrons in the highest energy occupied molecular orbital (HOMO) are most likely to be ejected. They already have more energy than other electrons in the compound, so it takes less energy to eject them. The HOMO is usually a lone pair or a  $\pi$  bond, but it can be a  $\sigma$  bond if there's no other choice. (Note the order of decreasing energy.) Electrons from O, N, S and the halogens are usually ejected most readily. Note that the incoming electron does not become part of the compound. One goes in but two come out!

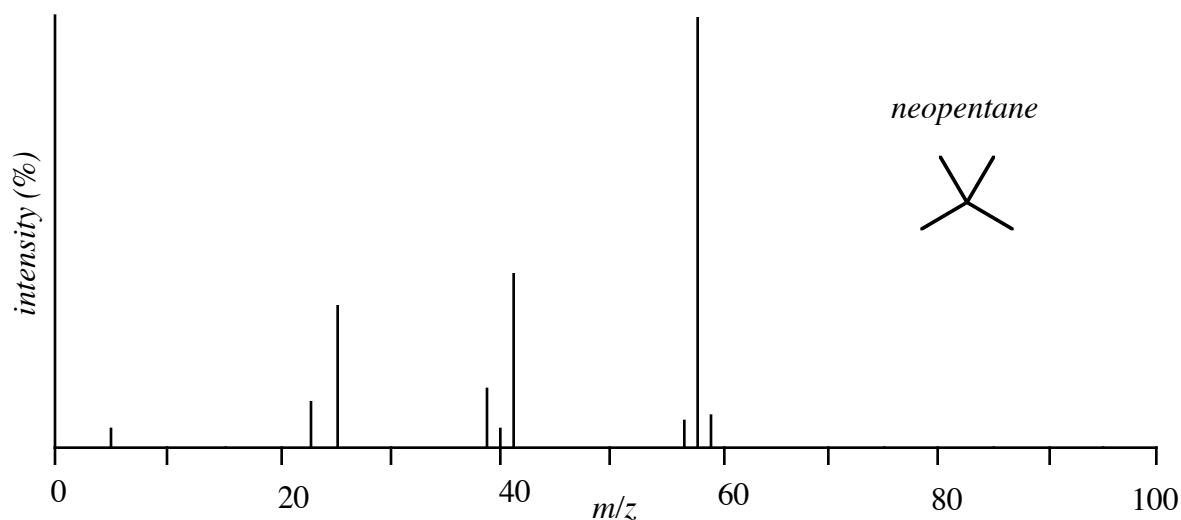


After the radical cation is formed and before it travels through the detector, it may *fragment*, that is, break up into smaller pieces. Fragmentation is a characteristic reaction of radicals. Fragmentation occurs to give a *neutral* radical and an even-electron cation, and it usually occurs to give the stabler cation. When this happens, the cation is deflected through the magnetic field and detected, and the neutral fragment is lost.

Each compound has a characteristic fragmentation pattern. These are predictable, but we're not going to worry about that.



The  $m/z$  ratios and intensities of the fragments that are detected are usually presented as a bar graph with intensity on the y-axis and the  $m/z$  ratio on the x-axis. As I said, usually only one electron is ejected from each molecule, so the x-axis is usually thought of as the mass of the fragments. The *most intense* peak is called the *base peak*. The intensities of other peaks are measured as a percentage of the base peak. The *heaviest* peak that is observed is usually the *molecular ion*,  $\text{M}^+$ , which is the unfragmented compound. If  $\text{M}^+$  is very unstable or can fragment into very stable pieces, it may not be observed at all. On the other hand, if  $\text{M}^+$  can't fragment into more stable pieces, it might be the base peak.



The simplest piece of information that the mass spectrum can give us is the molecular weight and hence formula of a compound. This can easily be distinguished to a single atomic mass unit (amu). For example,  $\text{M}^+$  for propane  $\text{Me}_2\text{CH}_2$  weighs 44 amu, while that for dimethyl ether  $\text{Me}_2\text{O}$  weighs 46 amu. If we have a sample that is one or the other of these, we can easily identify it. Similarly, if a compound has a  $\text{M}^+$  of 110 amu, its molecular formula must be either  $\text{C}_8\text{H}_{14}$ ,  $\text{C}_7\text{H}_{10}\text{O}$ ,  $\text{C}_6\text{H}_6\text{O}_2$ , or  $\text{C}_6\text{H}_{10}\text{N}_2$ . (There are tables available that tabulate the possible formulas for a given molecular ion.)

The molecular weight also gives a clue as to whether N atoms may be present. The *nitrogen rule* is the following: *A compound has an odd molecular weight if and only if there are an odd number of nitrogen atoms in its formula.* The nitrogen rule holds for compounds containing H, C, N, O, Si, P, S, or any of the halogens, i.e. for any compounds we would see in this class.

Every C-containing ion has a small peak accompanying it that weighs one mass unit more. The ratio of the intensities of the (M) and (M+1) peaks is directly proportional to the number of C atoms in the ion. The peak is due to small amounts of naturally occurring  $^{13}\text{C}$ , which has 1.1% natural abundance. The intensity of the (M+1) peak allows one to determine exactly of how many C atoms a particular ion consists. For example, a  $\text{C}_6$  ion has a 6.6% probability of having one  $^{13}\text{C}$  atom in it, so its (M+1) peak is 6.6% of the intensity of the  $\text{M}^{\ddagger}$  peak. Other isotopes that are used to identify peaks include Cl (75%  $^{35}\text{Cl}$ , 25%  $^{37}\text{Cl}$ ) and Br (50%  $^{79}\text{Br}$ , 50%  $^{81}\text{Br}$ ). Natural H, N, O, F, and I consist of almost exclusively a single isotope (deuterium and tritium have very low natural abundance), so, among elements the most commonly encountered in organic compounds, we need only to worry about isotope peaks from C, Cl, and Br.

The molecular ion, unfortunately, is not always observed. One can also gain information from the fragmentation pattern. The fragmentation pattern constitutes a kind of "fingerprint" for a compound. Different structural isomers and even stereoisomers give different fragmentation patterns, so the fragmentation pattern can be used to distinguish different compounds that have the same molecular formula. The fragmentation pattern also provides evidence for and against certain structural elements in the unidentified compound. If the major fragments can be identified, and if a reasonable mechanism for their formation from the molecular ion can be written, then this constitutes evidence that the parent ion has been correctly identified. For example, when a fragment ion of  $\text{M} = 91$  is observed, it is almost always the very stable benzyl cation  $\text{PhCH}_2^+$ , suggesting that a benzyl group is present in the parent compound. Ethyl esters,  $\text{RCO}_2\text{Et}$ , often show fragments  $\text{M} - 45$  (for the fragment  $\text{RCO}$ ) and  $\text{M} - 73$  (for the fragment  $\text{R}$ ). I don't expect you to be able to analyze fragmentation patterns.

To summarize: MS allows one to determine the *molecular weight* of an unknown compound if the  $\text{M}^{\ddagger}$  peak can be identified. An *odd molecular weight* suggests that an *odd number of N atoms* are present. The presence and size of an *M+2 peak* tells you whether *Cl or Br atoms* are present. The size of the *M+1 peak* tells you how many *C atoms* are present. The fragmentation pattern observed in MS provides clues to the *structure* of a compound. HRMS allows one to determine the *exact molecular formula* of the  $\text{M}^{\ddagger}$  peak or any other fragment.

**Problem for class.** The mass spectrum of a compound shows an  $\text{M}^{\ddagger}$  peak at 124 amu and no M+2 peaks. Determine some molecular formulas for this compound.

(1) If the molecular weight is odd, you have an odd number of N atoms. Subtract 14 from the molecular weight, and write N in your formula. In the present case, this is not necessary.

(2) It will be clear from the  $M+2$  peak how many Cl or Br atoms you have. For each Cl or Br atom, subtract 35 or 79 from the molecular weight, and write Cl or Br in your formula. In the present case, no Cl or Br atoms are present.

(3) Determine the maximum number of C atoms that can fit into the remaining molecular weight. In the present case, the answer is  $C_{10}$ , since  $10 \times 12 = 120$ . If you are given the intensity of the  $M+1$  peak, divide it by 1.1% to determine exactly how many C atoms you have.

(4) Add enough H's to make up the mass of the  $M^+$  peak. In this case,  $C_{10}H_4$ .

(5) Calculate the degrees of unsaturation in your formula. You may have too *few* (fewer than zero, i.e. a negative number) or too *many* degrees of unsaturation in your compound. (Too few degrees of unsaturation means that you have too many H atoms.)

(a) If you have *too few* number of degrees of unsaturation, you must *add* degrees of unsaturation, i.e. remove H's without changing the molecular weight. There are a few ways to do this. (1) Replace  $CH_4$  with O. This has the effect of *adding one* degree of unsaturation. (2) Replace  $C_2H_4$  with  $N_2$ . This also has the effect of *adding one* degree of unsaturation. (3) Replace  $H_{16}$  with O. This has the effect of *adding eight* degrees of unsaturation.

(b) If you have a *very large* number of degrees of unsaturation, you may want to *subtract* degrees of unsaturation. (Most of the compounds I would have you identify have 0–5 degrees of unsaturation.) Replace C with  $H_{12}$ . This has the effect of *subtracting seven* degrees of unsaturation without changing the molecular weight. In the present case, we have nine degrees of unsaturation in a  $C_{10}$  compound! It is not impossible to draw a compound with this formula —  $(HC\equiv C)_2C=C(C\equiv CH)_2$  — but it's just not a very likely formula. We can subtract seven degrees of unsaturation by converting  $C_{10}H_4$  into  $C_9H_{16}$ . Now we have just two degrees of unsaturation — much more reasonable!

(6) You now have your first reasonable formula for your compound. Once you generate a reasonable formula, you may do the following replacements to generate new formulas with the same molecular weight.

(a) Replace  $CH_4$  with O. (Adds a degree of unsaturation.)

(b) Replace  $C_2H_4$  with  $N_2$ . (Adds a degree of unsaturation.)

(c) Replace CO with  $N_2$ . (Leaves degrees of unsaturation unchanged.)

Thus:

$C_9H_{16} \rightarrow C_8H_{12}O$  (Three degrees of unsaturation.)

$C_8H_{12}O \rightarrow C_7H_{12}N_2$  (Three degrees of unsaturation.)

$C_8H_{12}O \rightarrow C_7H_8O_2$  (Four degrees of unsaturation.)

$C_8H_{12}O \rightarrow C_6H_8N_2O$  (Four degrees of unsaturation.)

$C_6H_8N_2O \rightarrow C_5H_8N_4$  (Four degrees of unsaturation.)

Etc.

(7) Draw at least one structure for each formula. It's useful to remember that a six-membered ring with three double bonds (e.g. a phenyl group,  $C_6H_5$ ; or one or more N atoms may replace CH groups in the ring) uses up four degrees of unsaturation.

**More problems to do in class:** (1) 88 amu, no M+2. (2) 119 amu, no M+2. (3) 108 amu, and there's an M+2 peak that is 1/3 the size of M.

### 15.3. Infrared Spectroscopy.

The energy of a photon of electromagnetic radiation is related to its wavelength and its frequency.

$$E = h\nu = hc / \lambda$$

where  $\nu$  is the frequency of the light (in units of  $s^{-1}$  or Hz),  $\lambda$  is the wavelength of the light (in m),  $h$  is Planck's constant ( $6.63 \times 10^{-34}$  J·s), and  $c$  is the speed of light ( $3.00 \times 10^8$  m/s). The energy of electromagnetic radiation is *directly proportional* to its frequency and *inversely proportional* to its wavelength. Infrared (IR) radiation is electromagnetic radiation with wavelengths from 750 nm to 100  $\mu\text{m}$ , although IR spectroscopy is mostly concerned with the region from 2.5  $\mu\text{m}$  to 25  $\mu\text{m}$ . IR radiation is less energetic than visible light, which has wavelengths of 400-750 nm. When IR radiation is absorbed by molecules, it causes the atoms and bonds to bend, twist, and stretch like balls on springs, deforming bond lengths and angles. This molecular motion is measured as *temperature*, so we perceive the radiation that causes it as *heat*. IR spectroscopy measures a compound's absorption of IR radiation as a function of the frequency of the radiation.

A compound absorbs IR radiation of certain wavelengths and not others because its motion is *quantized*. That is, a molecule can vibrate only at certain frequencies and not at others. The *frequencies* can be calculated using quantum mechanics equations, but we usually use empirical methods to determine which frequencies correspond to which molecular motions. The *intensity* of absorption of IR radiation of a particular wavelength is related to the *change in dipole moment* of the molecule upon undergoing the particular motion with which the wavelength is correlated. Very polar bonds show large absorptions, while nonpolar bonds show none at all.

The IR spectrum is usually presented as a graph of *transmittance* versus *wavenumber*. Wavenumber is defined as the reciprocal of the wavelength, or  $1/\lambda$ , and is measured in  $\text{cm}^{-1}$ . It is another unit of energy. The transmittance of a compound is defined as the amount of light of a particular energy which is *not* absorbed by the compound and passes through it. 100% Transmittance means that the compound does not absorb any of the light of that energy, while 0% transmittance means that it absorbs it all. When you are looking at an IR spectrum, the troughs represent low transmittance and high absorption, while the peaks represent high transmittance and low absorption. We are interested in the troughs, i.e. high absorbance regions.

The motions of all but the simplest molecules are extremely complex, so we divide the IR spectrum up into the interpretable region (4000-1500  $\text{cm}^{-1}$ ) and the *fingerprint* region (1500-800 or so  $\text{cm}^{-1}$ ). The fingerprint region is usually not interpreted, although some real IR jocks do so. Usually it's just used to identify a known compound by comparing it to a reference IR spectrum. In the interpretable region, the most important absorbances and their intensities are as follows.

O–H	about 3500 $\text{cm}^{-1}$ , strong and broad
N–H	about 3300 $\text{cm}^{-1}$ , strong
C–H	2850–3300 $\text{cm}^{-1}$ , strong to moderate
C(sp)–H	3300 $\text{cm}^{-1}$
C(sp <sup>2</sup> )–H	3000–3100 $\text{cm}^{-1}$
C(sp <sup>3</sup> )–H	2850–3000 $\text{cm}^{-1}$
C≡N	about 2250 $\text{cm}^{-1}$ , moderate
C≡C	about 2200 $\text{cm}^{-1}$ , moderate (RC≡CH) to non-existent (RC≡CR)
C=O	1650–1780 $\text{cm}^{-1}$ , <i>very</i> strong
aldehydes	1730 $\text{cm}^{-1}$
acyclic ketones	1715 $\text{cm}^{-1}$
cyclohexanone	1715 $\text{cm}^{-1}$
strained cyclic ketones	1750-1780 $\text{cm}^{-1}$
esters	1735 $\text{cm}^{-1}$
amides	1670 $\text{cm}^{-1}$
	(subtract 20–25 $\text{cm}^{-1}$ for being adjacent to a $\pi$ bond, C=C–C=O)
C=C	1500–1650 $\text{cm}^{-1}$ , intensity dependent on polarity of substituents

These absorbances, especially the carbonyl stretch, tend to stand out from the background and from each other, so they are diagnostic for these functional groups. If the absorbances are present, the functional groups are present; if they are absent, the functional groups are absent (except for C=C and C≡C). In later chapters you will learn more about the IR characteristics of particular functional groups. For now I want you to know the ranges above.

To summarize: IR spectra allow one to determine the *presence or absence of certain functional groups* in a compound. It is especially useful for identifying OH, NH, C≡X, C=C, and C=O groups.

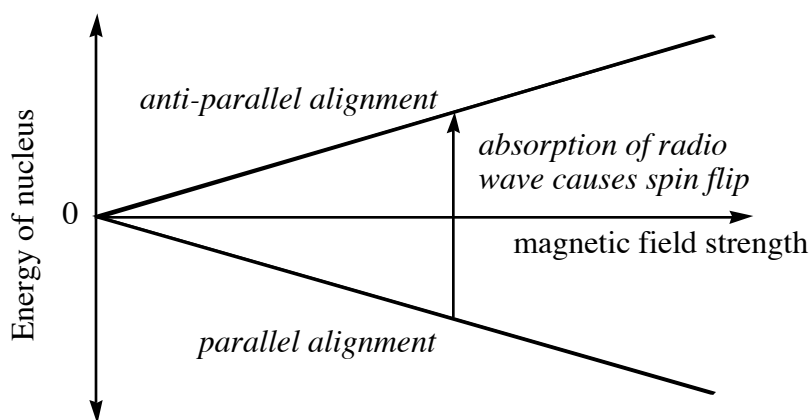
## 15.4. Physical Basis of NMR Spectroscopy.

Today the most widely used method for determining the structure of organic compounds is nuclear magnetic resonance spectroscopy, or NMR spectroscopy. NMR spectroscopy involves putting a

compound into a magnetic field and measuring the absorption of radio waves by the  $^1\text{H}$ ,  $^{13}\text{C}$ ,  $^{19}\text{F}$ ,  $^{31}\text{P}$ , or other nuclei. Each nucleus in a different environment absorbs radio waves of a different energy. For example, if one looks at the  $^1\text{H}$  NMR spectrum for a compound like  $\text{CH}_3\text{CH}_2\text{OH}$ , one sees one absorption for the O–H  $^1\text{H}$ , one for the  $\text{CH}_2$   $^1\text{H}$ 's, and one for the  $\text{CH}_3$   $^1\text{H}$ 's. The  $^{13}\text{C}$  NMR spectrum shows one absorption for each C atom in the compound. The NMR spectra thus give direct information about the nature of the chemical environment of each magnetically active nucleus in the molecule.

The physical basis of NMR spectroscopy is as follows. Many nuclear isotopes have a magnetic moment called the *nuclear spin*. This number is a multiple of  $1/2$ . The  $^1\text{H}$  has a spin of  $1/2$ , as do  $^{13}\text{C}$ ,  $^{19}\text{F}$ , and  $^{31}\text{P}$ , but  $^{12}\text{C}$  and  $^{16}\text{O}$  have spins of 0, and  $^{14}\text{N}$  and  $^2\text{H}$  have spins of 1. Only nuclei with spins of  $>0$  can be detected by NMR spectroscopy. Because the nucleus has a charge and because of its "spin", nuclei act like tiny magnets. If one applies an external magnetic field  $H_0$  to the nuclei, the tiny magnets of the nuclei align themselves with the field, some parallel and some anti-parallel. The parallel arrangement has a slightly lower energy than the anti-parallel arrangement. The difference in energy is directly proportional to the strength of the field. The proportionality constant is dependent on the nucleus.

Because the two alignments are different in energy, there is a slightly higher population of nuclei in the lower energy state than in the higher energy state. Radio waves are absorbed by the nuclei with a parallel alignment, causing them to flip to the anti-parallel alignment. Note that radio waves are *very* low energy radiation! There's not much difference in energy between the spin states, even with a very strong magnetic field.



Why should different  $^1\text{H}$  nuclei in a compound absorb radio waves of different energies? Don't they experience the same external magnetic field? They do and they don't. The external magnetic field is indeed identical for all the nuclei. However, every nucleus is surrounded by electrons. The electrons are charged, so when they experience a magnetic field, they circulate in such a way as to create an *opposing* magnetic field. This is called *shielding*. A  $^1\text{H}$  nucleus surrounded by a large number of electrons (attached to electropositive elements) will experience a much smaller magnetic field than a  $^1\text{H}$  nucleus surrounded by

a small number of electrons (attached to electronegative elements). The  $^1\text{H}$  attached to an electronegative element is said to be *deshielded*. The same is true of other nuclei.

If we keep a magnetic field constant and vary the radio wave frequency, different nuclei will *resonate* at different frequencies. We can measure this resonance and plot it as a function of radio wave frequency. In practice, though it's easier to keep the radio wave frequency constant and to vary the magnetic field. The most commonly used  $^1\text{H}$  NMR spectrometers use radio waves with frequencies of 60 MHz to 500 MHz, while the frequencies are one-fourth of this for  $^{13}\text{C}$  NMR experiments. We do the NMR experiment by dissolving the compound to be analyzed in a solvent that lacks any  $^1\text{H}$  nuclei ( $\text{CCl}_4$  or a deuterated solvent like  $\text{CDCl}_3$  or  $\text{D}_2\text{O}$ ). The solution is placed in a tube, which is placed in a magnet. The sample is irradiated with radio waves of constant frequency as the magnetic field is slowly varied. At different magnetic field strengths, different absorbances are measured.

When we vary the magnetic field, we only need to change its strength by a few millionths to observe all the different resonances of all the different atoms in the compound. This is why we measure the resonance of nuclei in *ppm*. Most  $^1\text{H}$  nuclei resonate within a range of 10 ppm of each other. Most  $^{13}\text{C}$  nuclei, on the other hand, resonate in a range of about 220 ppm of each other. The radio wave frequencies used for  $^{13}\text{C}$  NMR spectroscopy are one fourth of those used for  $^1\text{H}$  NMR spectroscopy.

We use tetramethylsilane, or TMS, which has twelve identical  $^1\text{H}$  nuclei, as a standard for  $^1\text{H}$  and  $^{13}\text{C}$  resonance. We arbitrarily define the magnetic field strength required for TMS to resonate with a given radio wave energy as 0 ppm. The resonances of other kinds of  $^1\text{H}$ 's are then measured in ppm with respect to TMS. The resonance of a particular kind of  $^1\text{H}$  is called its *chemical shift*, and it is often written as  $\delta$ . In the case of ethanol, three resonances are observed at about  $\delta$  5.5, 3.8, and 1.2 ppm *downfield* (more deshielded) of TMS. As I said, the  $^1\text{H}$ 's in most organic compounds resonate in the region 0-10 ppm, although there are exceptions to this rule.  $^{13}\text{C}$  nuclei usually resonate in the range 0-220 ppm. (TMS was chosen as a standard because most  $^1\text{H}$  and  $^{13}\text{C}$  nuclei resonate downfield of the same nuclei in TMS.) When an NMR spectrum is plotted, 0 ppm is placed on the right, with increased deshielding as we move to the left. The right of the spectrum is called *upfield*, while the left of the spectrum is called *downfield*. *The chemical shift values of the nuclei in a particular compound are independent of the radio wave frequency used to measure them.* We can use a 60 MHz or 400 MHz instrument to measure the chemical shifts of the  $^1\text{H}$ 's in ethanol, but the values are identical. The magnetic field strengths required for resonance are of course different, but the ppm change in magnetic field strength from TMS is not.

## 15.5. Interpreting NMR Spectra: Symmetry.

Let's look start to look at specific examples. The first thing to predict is how many resonances a compound will display. Just because a compound has eight  $^1\text{H}$ 's doesn't mean that eight resonances will be observed. Symmetry will often reduce the number of resonances. Let's look at methyl acetate,  $\text{CH}_3\text{OC}(=\text{O})\text{CH}_3$ . We have three C atoms, each of which is a different kind — the carbonyl C, the methyl C attached to O, and the methyl C attached to C — so we expect to see three different  $^{13}\text{C}$  resonances. We have six H atoms, but some of these have identical environments. The three H's in the methyl group attached to C have the same connections and exchange their environments constantly by rapid rotation about the C–C  $\sigma$  bond, so they experience the same deshielding, so they resonate at the same frequency. They are said to be *chemically equivalent*. Likewise for the three H's in the methyl group attached to O. But the three H's in one methyl group have a different environment from the three H's in the other methyl group (different connections). In the end we expect to see two  $^1\text{H}$  resonances for this compound. Atoms with different connectivities are in principle expected to have different resonances.

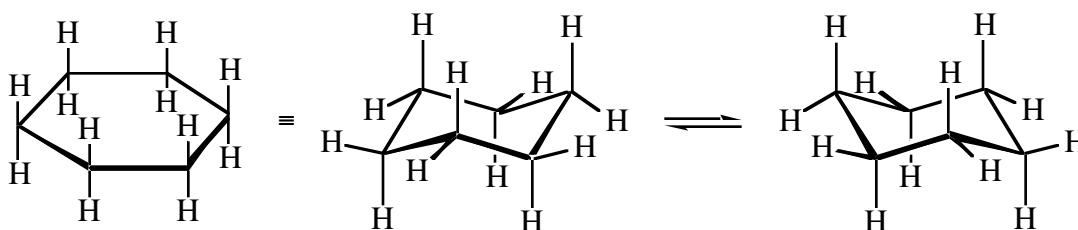
Atoms with identical connectivities may or may not be chemically equivalent. For example, in cyclopentanol, the two H atoms on C2 are not equivalent. One is *cis* to the OH, and the other is *trans* to the OH. Atoms that have the same connectivity but don't have identical resonances are said to be *chemically inequivalent*, or *diastereotopic* (from  $\tau\text{πο}\square\zeta$ , the Greek word for place, so meaning diastereomeric places).

In this class, we will label chemically equivalent atoms with identical letters, and chemically inequivalent atoms with different letters. So all three H's attached to C1 in methyl acetate will be labelled  $\text{H}_a$ , and the three attached to C3 will be labelled  $\text{H}_b$ .

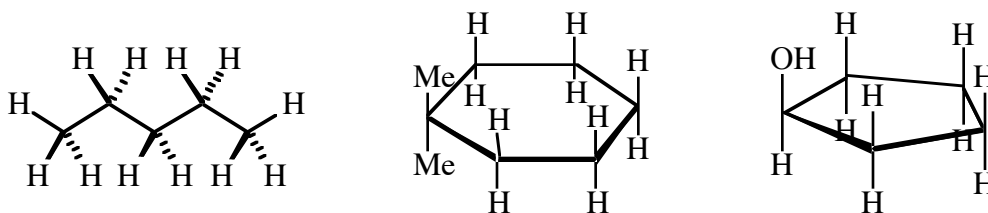
Here's a method for determining whether or not two atoms with the same connectivities are chemically equivalent. Draw the compound twice. In one of the structures, replace one of the atoms in question with a different test atom. In the other, replace the other atom in question with the test atom. If the two structures are identical or enantiomers, then the atoms in the original structure are chemically equivalent; if the two structures are diastereomers, then the atoms in the original structure are chemically inequivalent.

In any compound containing a stereocenter that has a group  $\text{XCH}_2\text{Y}$ , where X and Y are different, the H atoms in the  $\text{CH}_2$  group are always chemically inequivalent. This is because replacing one H atom in  $\text{XCH}_2\text{Y}$  with a test atom generates a new stereocenter, so replacing one or the other H atom always generates different diastereomers of the compound, our positive test for chemically inequivalent atoms. A compound doesn't have to have a stereocenter to give a positive test for chemically inequivalent atoms, though; see cyclopentanol.

Cyclohexane has axial and equatorial H's, so we might predict it would show two resonances. This would be somewhat incorrect. The amount of time required to record for a compound to interact with radio waves of 100 MHz frequency (about 10 ns) is much longer than the amount of time required for cyclohexane to flip back and forth many times. As a result, every H spends time in both the axial and equatorial positions during the time scale of the experiment, and the axial and equatorial H's can't be distinguished. At room temperature, cyclohexane shows just one resonance for all the  $^1\text{H}$ 's. However, at very low temperatures ( $-90\text{ }^\circ\text{C}$ ), where ring flipping is greatly slowed, two resonances are seen. In practice, for spectra at or around room temperature, we can look at the flat structure to determine which atoms are inequivalent, just like we did to determine whether the compound was chiral. In the case of cyclohexane, all H atoms are labelled  $\text{H}_a$  and all C atoms are  $\text{C}_a$ .



**Problems for class:** Pentane, 1,1-dimethylcyclohexane, cyclopentanol.



**Problems for home.** (1) Identify the number of  $^1\text{H}$  and  $^{13}\text{C}$  resonances each of these compounds will display. (a) *cis*-1,3-Dimethylcyclohexane. (b) Benzene. (c) Toluene (methylbenzene). (d) Diethyl ether (ethoxyethane). (e) 2-Methylpentane. (f) 3-Ethylpentane.

## 15.6. Interpreting $^1\text{H}$ NMR Spectra.

The  $^1\text{H}$  NMR spectrum gives us information about the number of chemically different H atoms, the chemical environment of each atom, the number of H atoms giving rise to each resonance, and the number of nearby magnetic nuclei (usually other H atoms). We'll talk in detail about each of these points.

*Chemically inequivalent H's resonate at different field strengths, while chemically equivalent H's resonate at the same field strength.* We have talked in detail about how you can tell whether H atoms are chemically

identical or different. For example, in 1,1-dimethylcyclohexane, we expect to see four sets of resonances: one from the Me H's, one from C2 and C6, one from C3 and C5, and one from C4.

The resonances of  $^1\text{H}$ 's tend to fall into the range 0.5-11 ppm downfield of TMS. The range can be divided into six regions.  $^1\text{H}$  nuclei in certain kinds of chemical environments resonate in certain regions, while others resonate in other regions. Saturated alkyl groups resonate from 0.5 to 1.5 ppm. H atoms on C's adjacent to C=O or C=C groups and  $\text{RC}\equiv\text{CH}$  resonate between 1.5 and 2.5 ppm. H atoms attached to C atoms bearing one heteroatom ( $\text{H}-\text{C}-\text{X}$ ; X= O, N, S, Hal) resonate between 2.5 and 4.5 ppm. Alkenyl H atoms ( $\text{R}_2\text{C}=\text{CHR}$ ) and H atoms attached to C atoms bearing two heteroatoms ( $\text{HCX}_2\text{R}$ ) resonate between 5 and 6.5 ppm. Aryl H atoms resonate between 6.5 and 8.0 ppm. Finally, H atoms in XCHO groups (X= C, N, O) resonate between 7.8 and 10.5 ppm. (These ranges are approximate; H atoms in compounds with unusual structures can resonate at unusual frequencies.) Carboxylic acid H's resonate way downfield, while alcohol and amine H's may resonate anywhere.

<u>Type of H atom</u>	<u>Chemical Shift (<math>\delta</math>)</u>
saturated alkyl	0.5-1.5
$\text{C}=\text{C}-\text{C}-\text{H}$ , $\text{O}=\text{C}-\text{C}-\text{H}$ , $\text{C}\equiv\text{C}-\text{H}$	1.5-2.5
$\text{X}-\text{C}-\text{H}$ ; X=O, N, S, Hal	2.5-4.5
$\text{C}=\text{C}-\text{H}$ , $\text{RX}_2\text{C}-\text{H}$	4.5-6.5
aryl H	6.5-8.5
$\text{O}=\text{C}-\text{H}$	7.8-10.5
alkyl O-H	varies
alkyl N-H	varies
$\text{RCO}_2\text{H}$	11.0-14.0

A H atom near *two* deshielding groups falls further downfield than if either one of the deshielding groups were present alone. For example,  $\text{MeOCH}_2\text{Me}$  has  $\delta$  about 3.4 ppm,  $\text{PhCH}_2\text{Me}$  has  $\delta$  about 2.3 ppm, but  $\text{MeOCH}_2\text{Ph}$  has  $\delta$  about 5.5. Within each region, methyl H's resonate slightly more upfield (smaller  $\delta$ ) than methylene or methine H's, and electronegative atoms or groups that are one C removed tend to shift the resonance a little more downfield (larger  $\delta$ ). The chemical shifts of H atoms attached to heteroatoms are *not constant*, even for a given compound, and vary tremendously depending on concentration, solvent, and temperature.

If one measures the areas under the resonances in a  $^1\text{H}$  NMR spectrum, one can determine the *number of H atoms contributing to each resonance*. This process is called *integration*. It used to be done by cutting the peaks out of the paper and weighing them, but today we do it by computer. Let's look at the  $^1\text{H}$  NMR spectrum of methyl formate,  $\text{HCO}_2\text{CH}_3$ . We expect to see two resonances: one at about  $\delta$  4.0 ppm for the methyl group and one at about  $\delta$  8.0 ppm for the carbonyl H. If we integrate these two peaks, the ratio of

the  $\delta$  8.0 peak to the  $\delta$  4.0 peak will be approximately 1:3, since one H atom contributed to the downfield peak while three contributed to the upfield peak. Note that we obtain only the *ratio* of H atoms contributing to the different resonances, not necessarily the total number of H atoms in that compound. For example, if we integrate the spectrum of methyl pivalate  $\text{Me}_3\text{CCO}_2\text{Me}$ , which has two resonances at  $\delta$  3.7 and 1.2 ppm, we find a 1:3 ratio of peaks, the same as in methyl formate. We can't tell *a priori* whether we have four, eight, twelve, or sixteen H atoms in the compound, just that we have two kinds of H atoms in a 3:1 ratio.

The most complex aspect of  $^1\text{H}$  NMR spectra is *spin-spin coupling*. Consider  $\text{CHBr}_2\text{CHCl}_2$ .  $\text{H}_a$  will experience a magnetic field of a particular strength, and we expect to see one resonance from it. However, there is a non-equivalent magnetic atom next door on C2,  $\text{H}_b$ .  $\text{H}_b$  has about a 50% probability of aligning *with* the external magnetic field, and about a 50% probability of aligning *against* it. When  $\text{H}_b$  aligns with the field,  $\text{H}_a$  experiences a slightly stronger magnetic field, and when  $\text{H}_b$  aligns against the field,  $\text{H}_a$  experiences a slightly weaker magnetic field. We therefore expect that the resonance due to  $\text{H}_a$  would be split into two resonances of equal height centered around the "true" resonance frequency. This expectation is true. The  $\text{H}_a$  resonance is observed to be a *doublet*. Likewise, the  $\text{H}_b$  resonance is also a doublet, due to the effect of  $\text{H}_a$  on the magnetic field experienced by  $\text{H}_b$ .

$^1\text{H}$ - $^1\text{H}$  coupling is often observed between *chemically inequivalent  $^1\text{H}$ 's* separated by *two or three bonds*. This is called *two-bond* and *three-bond coupling*. Three-bond coupling, i.e. coupling between  $^1\text{H}$  atoms on adjacent C atoms,  $\text{H}-\text{C}-\text{C}-\text{H}$ , is observed most frequently. Two-bond coupling is observed between diastereotopic H atoms. Four- and five-bond coupling is observed only occasionally in compounds with rigid geometries. *Coupling between equivalent  $^1\text{H}$ 's is not observed.*

We have seen that in  $\text{CHBr}_2\text{CHCl}_2$ ,  $\text{H}_a$  splits the resonance of  $\text{H}_b$  into two signals. The extent of splitting is called the *coupling constant* and is commonly abbreviated *J*. We have also seen that  $\text{H}_b$  splits the resonance of  $\text{H}_a$ .  $\text{H}_b$  and  $\text{H}_a$  split each other with the *same* coupling constant. *Coupling constants are usually measured in Hz*, not in ppm, because *they are independent of spectrometer frequency when expressed in Hz*. Three-bond coupling constants usually range between 0 and 12 Hz, while two-bond coupling constants may range up to 20 Hz. The  $\text{H}-\text{C}-\text{C}-\text{H}$  three-bond coupling constant is usually about 7.0 Hz when there is free rotation about the C-C bond. When there is not free rotation, as in cyclic compounds or in double bonds, the coupling constants may be very large or very small. In cyclohexanes that are conformationally locked into a chair, the coupling between adjacent axial H's is usually large, between equatorial and an adjacent axial is medium, and between adjacent equatorial H's is usually very small. The coupling between H's that are *trans* on a double bond is usually quite large (15 Hz), for *cis* it is medium sized (ca. 8 Hz), and for terminal  $=\text{CH}_2$  groups the coupling between the two H's is usually very small (ca. 1 Hz).

One can calculate coupling constants in Hz by measuring the chemical shifts of the two peaks that are split and using the formula:

$$\text{coupling constant (Hz)} = \Delta\delta \text{ (ppm)} * \text{spectrometer frequency (MHz)}$$

where  $\Delta\delta$  is the difference in the chemical shift of the two peaks.

Now consider  $\text{CHBr}_2\text{CH}_2\text{Cl}$ . There are one  $\text{H}_a$  and two  $\text{H}_b$ . Consider the environment of  $\text{H}_a$ . It experiences a magnetic field strength that is affected by the spins of its two neighbors,  $\text{H}_b$ . Before, when there was one  $\text{H}_b$ , we saw that  $\text{H}_a$  could experience two different magnetic fields, depending on whether the spin of  $\text{H}_b$  was up or down. Now,  $\text{H}_a$  might experience three different magnetic field strengths, depending on whether the  $\text{H}_b$ 's are up-up, up-down, down-up, or down-down. (Down-up is experienced the same way as up-down, since the sum of the effect on the magnetic field is 0.) The resonance for  $\text{H}_a$  will be split into three resonances, a *triplet*, with a 1:2:1 ratio.

What about  $\text{H}_b$  in  $\text{CHBr}_2\text{CH}_2\text{Cl}$ ? It has one inequivalent neighbor,  $\text{H}_a$ . Its resonance is a doublet. The distance between two lines of the triplet for  $\text{H}_a$ , the coupling constant, is the same as the distance between the two lines of the doublet for  $\text{H}_b$ . Also, the integration of the triplet due to  $\text{H}_a$  and the doublet due to  $\text{H}_b$  will give a 1:2 ratio for the two peaks. In other words, the splitting doesn't change the total area under the resonances.

Now look at  $\text{CHBr}_2\text{CH}_3$ .  $\text{H}_a$  has three neighbors  $\text{H}_b$ . These might be up-up-up, up-up-down, up-down-up, down-up-up, down-down-up, down-up-down, up-down-down, or down-down-down. As a result  $\text{H}_a$  might experience four different magnetic field strengths with a probability of 1:3:3:1. The signal for  $\text{H}_a$  is a *quartet* in the ratio 1:3:3:1. The signal for  $\text{H}_b$  remains a doublet.

The number of peaks into which a resonance is split is called its *multiplicity*. *The multiplicity of a  $^1\text{H}$  with  $n$  equivalent neighbors is  $n+1$* , with the relative intensities of the resonances given by the polynomial expansion. We call the multiplicities *singlets, doublets, triplets, quartets, quintets, sextets, etc.* Other magnetically active nuclei, such as  $^{31}\text{P}$ ,  $^2\text{H}$ , and  $^{19}\text{F}$ , can also split the resonance of a  $^1\text{H}$ .

To summarize: The  $^1\text{H}$  NMR spectrum detects a single resonance for every non-equivalent  $^1\text{H}$  in the compound. The *chemical shift* of the resonance, which is independent of spectrometer frequency when it is expressed in ppm, gives information about the chemical environment of the  $^1\text{H}$ 's. The resonances can be *integrated* to obtain the number of H atoms contributing to each resonance. The *multiplicity* of a resonance tells you how many neighbors the  $^1\text{H}$ 's contributing to that resonance have. The *coupling constant  $J$*  is independent of spectrometer frequency when expressed in Hz. The value of the coupling constant gives you information on the nature of the spatial relationship between the atoms that are coupled (two-bond or three-bond, fixed or varying orientation, etc.).

Let's look at some specific examples. Dichloroacetaldehyde,  $\text{Cl}_2\text{CHCHO}$ , has two inequivalent H atoms, H1 and H2. We expect to see two resonances, one at around  $\delta$  10.5 ppm and one around  $\delta$  5.5 ppm. (The H2 resonance is so far downfield because there are *two* Cl atoms attached to C2.) One H atom contributes to one resonance, and one H atom contributes to the other resonance, so we expect them to integrate to a 1:1 ratio. The  $^1\text{H}$  resonating at 10 ppm, H1, has one magnetically active neighbor, H2. These atoms are separated by three bonds, so we expect to see a coupling constant. The resonance at  $\delta$  10 ppm is split into two peaks of equal intensity, a *doublet*. Likewise, H2 has one magnetically active neighbor, so its resonance is split into a doublet too. The spectrum consists of two doublets. There is one H1-H2 coupling constant, so the  $J$  values for one resonance, obtained by measuring the distance between the peaks in ppm and multiplying by the spectrometer frequency, is the same as the  $J$  value for the other resonance.

Chloroacetaldehyde,  $\text{ClCH}_2\text{CHO}$ , has two kinds of inequivalent H atoms, one H1 and two H2. We expect to see two resonances, one at around  $\delta$  10.0 ppm and one around  $\delta$  4.5 ppm. One H atom contributes to the downfield resonance, and *two* H atoms contribute to the upfield resonance, so we expect them to integrate to a 1:2 ratio. This time, H1 has *two* equivalent magnetically active neighbors, so the downfield resonance is split into a *triplet* with 1:2:1 intensity. On the other hand, each H2 has one magnetically active *and inequivalent* neighbor, so the upfield resonance is split into a *doublet* of 1:1 intensity.

Acetaldehyde,  $\text{CH}_3\text{CHO}$ , has two kinds of inequivalent H atoms, one H1 and three H2. We expect to see two resonances, one at around  $\delta$  9.5 ppm and one around  $\delta$  2.2 ppm. One H atom contributes to the downfield resonance, and *three* H atoms contribute to the upfield resonance, so we expect them to integrate to a 1:3 ratio. H1 has *three* equivalent magnetically active neighbors, so the downfield resonance is split into a *quartet* with 1:3:3:1 intensity. On the other hand, each H2 has one magnetically active *and inequivalent* neighbor, so the upfield resonance is split into a *doublet* of 1:1 intensity.

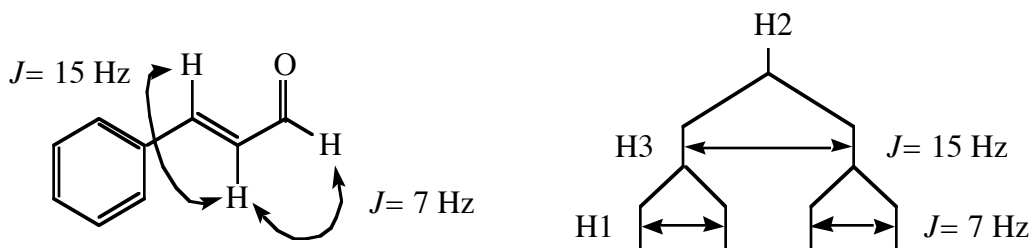
Bromoethane,  $\text{CH}_3\text{CH}_2\text{Br}$ , has two kinds of inequivalent H atoms, one H1 and two H2. We expect to see two resonances, one at around  $\delta$  3.4 ppm and one around  $\delta$  1.8 ppm. (The  $\text{CH}_3$  peak is a little more downfield of the normal saturated alkyl range because of the effect of the electronegative Br atom.) *Two* H atoms contribute to the downfield resonance, and *three* H atoms contribute to the upfield resonance, so we expect them to integrate to a 2:3 ratio. Each H1 has *three* equivalent magnetically active *and inequivalent* neighbors, so the downfield resonance is split into a *quartet* with 1:3:3:1 intensity. On the other hand, each H2 has two magnetically active *and inequivalent* neighbors, so the upfield resonance is split into a *triplet* of 1:2:1 intensity. A downfield quartet and an upfield triplet with identical coupling constants and in a 2:3 ratio is diagnostic for the presence of an ethyl group attached to an electronegative atom.

Isopropanol,  $\text{CH}_3\text{CH}(\text{OH})\text{CH}_3$ , has three kinds of inequivalent H atoms, *six* H1/H3, one H2, and one OH. We expect to see three resonances at  $\delta$  3.6, 1.2, and anywhere between 1 and 6, in 1:6:1 ratio. One tends not to see coupling between  $^1\text{H}$ 's attached to heteroatoms and C atoms, so we expect to see a doublet for

the H1/H3 resonance (one magnetically active, inequivalent neighbor), a *septet* for the H2 resonance (six neighbors, not counting the OH), and a *singlet* (possibly broad) for the OH resonance.

**Other problems to work:** 3-Chloropentane (diastereotopic H's), 1-chloropentane.

We need to discuss one more subject. Suppose we have a compound like *trans*-cinnamaldehyde,  $\text{PhCH}=\text{CHCHO}$ . H1 gives us a doublet at  $\delta$  9.67 with  $J=7$  Hz. H3 gives us a doublet at  $\delta$  7.42 with  $J=15$  Hz. (It is shifted downfield from the normal vinyl region because it is next to the aryl ring. The coupling constant for *trans* H atoms on an alkene is always particularly large.) What kind of pattern can we expect to see for H2? It has two neighbors, but they are inequivalent. The first neighbor, H3, splits the resonance for H2 into a doublet, with  $J=15$  Hz. The second neighbor, H1, splits each of the doublet peaks into another doublet, with  $J=7$  Hz. The pattern that is seen is called a *doublet of doublets*. If the H1-H2 and H2-H3 coupling constants had been the same, we would have seen an *apparent* triplet.



**Problem to work in class.** What kind of  $^1\text{H}$  NMR spectrum would you expect to see for *trans*-1-chloropropene?

Often many signals overlap each other and clean spectra aren't observed. This is especially true when you have two sets of  $^1\text{H}$ 's with *similar chemical shifts* and that are *coupled to one another*. For example, toluene. We expect to see a singlet for the  $\text{CH}_3$  group, and we do. In the aryl region we expect to see three resonances in a 1:2:2 integrated ratio for the three kinds of aryl H's, but what we see instead is either a singlet (low frequency spectrometer) or an uninterpretable mess (high frequency spectrometer) that integrates to 5 with respect to the Me resonance's 3. The reason is that the aryl H's all have similar chemical shifts, and they are all coupled to one another, so the splitting patterns are very complex (so-called *first-order coupling*). Higher frequency spectrometers tend to simplify coupling patterns, because the  $J$  values in ppm are made smaller with respect to the chemical shift differences between peaks.

**Problem for home.** (2) Predict the approximate chemical shift, integration, and multiplicity of each resonance in the  $^1\text{H}$  NMR spectrum of each of the compounds in problem (1). Assume that each set of H's resonates at a different field strength, so no overlap between signals is observed.

## 15.7. Interpreting $^{13}\text{C}$ NMR Spectra.

If you stop to think about it, the fact that we can measure  $^{13}\text{C}$  NMR spectra at all is quite remarkable. Only 11 out of 1000 C atoms is  $^{13}\text{C}$ . In contrast, almost 100% of H atoms are  $^1\text{H}$ . Thus, if we have 10 mmol of, say,  $\text{CHCl}_3$  in solution, we have 10 mmol of  $^1\text{H}$  atoms but only 100  $\mu\text{mol}$  of  $^{13}\text{C}$  atoms. When we do  $^{13}\text{C}$  NMR spectroscopy, we try to make our solutions as concentrated as possible, and we also take many spectra and add them up to increase our signal to noise ratio.

When we take a  $^{13}\text{C}$  NMR spectrum, we obtain a certain number of resonances corresponding to the number of inequivalent C atoms in the compound. The chemical shifts of each of the resonances gives us information about the nature of each of the C atoms (especially the hybridization) and the groups to which they are attached. Finally, spin-spin coupling gives us information as to the number of  $^1\text{H}$  atoms attached to each  $^{13}\text{C}$  atom.

$^{13}\text{C}$  nuclei resonate at a far wider range (220 ppm) of frequencies than do protons (ca. 10 ppm), but, like  $^1\text{H}$ 's,  $^{13}\text{C}$  nuclei with certain hybridizations tend to resonate in certain regions.  $\text{C}(\text{sp}^3)$  atoms resonate in the region between 0 and 80 ppm,  $\text{C}(\text{sp})$  between 65 and 120 ppm, aryl and alkenyl  $\text{C}(\text{sp}^2)$  between 100 and 160 ppm, and  $\text{C}=\text{O}$  between 165 and 220 ppm. There is much more overlap of ranges in  $^{13}\text{C}$  NMR than there is in  $^1\text{H}$  NMR, and it's harder to predict exactly where particular resonances will be found in each range. In the alkyl range,  $\text{C}(\text{sp}^3)\text{-O}$  tends to resonate further downfield than alkyl  $\text{C}(\text{sp}^3)$ , and alkyl  $\text{C}(\text{sp}^3)$  tends to resonate further upfield when it is  $1^\circ$  and further downfield when it is  $3^\circ$  or  $4^\circ$ . In the carbonyl region, ketones and aldehydes resonate further downfield than esters.

<u>Type of C atom</u>	<u>Chemical Shift (<math>\delta</math>)</u>
$\text{C}(\text{sp}^3)$	0-50
$\text{C}(\text{sp}^3)\text{-X}$	40-80
$\text{C}(\text{sp})$	65-120
alkenyl, aryl $\text{C}(\text{sp}^2)$	100-160
$\text{C}=\text{O}$	165-210

**Problem to work in class.** Methyl acetate shows peaks at  $\delta$  170, 50, and 20 ppm. Identify the C atom corresponding to each peak.

*Integration* of  $^{13}\text{C}$  NMR spectra is rarely done. The area under  $^{13}\text{C}$  resonances is not proportional to the number of atoms contributing to that resonance unless special experimental techniques are used. However, it is true that  $4^\circ$  C atoms tend to give signals of much weaker intensity than  $1^\circ$ ,  $2^\circ$ , and  $3^\circ$  C atoms.

One more feature of  $^{13}\text{C}$  NMR spectra needs to be discussed. If we look at a compound like chloroform  $\text{CHCl}_3$ , we notice that the C atom is attached to a magnetic atom, the  $^1\text{H}$ . This atom should affect the magnetic environment of the  $^{13}\text{C}$  nucleus, splitting it into a doublet. Actually, in normal  $^{13}\text{C}$  NMR operating mode, called *spin-decoupled mode*, we blast the  $^1\text{H}$ 's with radio waves at the same time that we measure the  $^{13}\text{C}$  resonances. (The radio waves that excite  $^1\text{H}$  nuclei are of different energy from those that excite  $^{13}\text{C}$  nuclei, so the two pulses don't interfere with one another.) The purpose of blasting the  $^1\text{H}$ 's is to cause them to flip their spins so quickly that the  $^{13}\text{C}$  nuclei can't tell whether the  $^1\text{H}$ 's are aligned with or against the magnetic field, and so no splitting is observed.

It is possible, though, to run the  $^{13}\text{C}$  spectra in *spin-coupled mode*. Under these conditions, each C atom experiences the magnetic field splitting caused by the magnetic nuclei *directly attached to it*. In practice one only needs to worry about splitting from  $^1\text{H}$ ,  $^2\text{H}$ ,  $^{19}\text{F}$ , and  $^{31}\text{P}$ . (Since  $^{13}\text{C}$  has only 1.1% natural abundance, the probability of finding a  $^{13}\text{C}$  nucleus adjacent to another  $^{13}\text{C}$  nucleus is very small, so  $^{13}\text{C}$ - $^{13}\text{C}$  splitting is not normally observed.) Just as we saw in  $^1\text{H}$  spectra, *a C atom attached to n H atoms has a multiplicity of n+1*, with intensities determined by the coefficients of the polynomial expansion. In  $^{13}\text{C}$  NMR spectra, coupling patterns are usually quite simple, because one needs only worry about  $^1\text{H}$ 's attached directly to the  $^{13}\text{C}$  atom. In other words, one-bond coupling only is seen. The resonances of  $3^\circ$  C atoms are split into doublets, those of  $2^\circ$  C atoms split into triplets, those of  $1^\circ$  C atoms split into quartets, and those of  $4^\circ$  C atoms are not split at all. C-H coupling constants in a particular compound are independent of the spectrometer frequency when they are expressed in Hz. C-H coupling constants are usually not measured or reported unless there is a particular reason to do so.

**Problem to work in class.** Predict the number of resonances, their chemical shifts, and their multiplicities in the  $^{13}\text{C}$  NMR spectrum of 4-(ethyl)isopropoxybenzene.

To summarize: The *spin-decoupled* (normal)  $^{13}\text{C}$  NMR spectrum detects a single resonance for every non-equivalent C atom in the compound. The *chemical shift* of the resonance is usually expressed in ppm, which is independent of spectrometer frequency. The chemical environment of the C atoms in a compound can be deduced by examining the chemical shifts of the resonances. In the *spin-coupled*  $^{13}\text{C}$  NMR spectrum, each resonance may be split into two to four peaks, depending on the number of H atoms attached to the C in question. The splitting distance, called the *coupling constant* or *J*, is usually expressed in Hz, which is independent of spectrometer frequency.

I want you to be able to *predict* the  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of a given compound to the extent demonstrated above. I also want you to be able to *deduce* the structure of a compound if you are given a  $^1\text{H}$  NMR spectrum and perhaps other data such as IR, MS, and  $^{13}\text{C}$  NMR spectra.

**Problem for home.** (3) Predict the approximate chemical shift and multiplicity of each resonance in the  $^{13}\text{C}$  NMR spectrum of each of the compounds in problem (1).

## 15.8. NMR Spectroscopy in Biology.

Magnetic resonance imaging, or MRI, is a new medical diagnostic technique based on the principles of NMR spectroscopy. The only reason MRI isn't called NMR is that the public is afraid of the word "nuclear". In MRI, a person is placed inside a giant magnet, and an NMR spectrum of the  $\text{H}_2\text{O}$  in his or her body is obtained. The basis of MRI is that different body tissues have different chemical environments, so the water in, say, a liver tumor has a different resonant frequency from the water in the rest of the liver. This allows the doctor to "look" into a person's body in a non-invasive manner and look for abnormal biological structures.

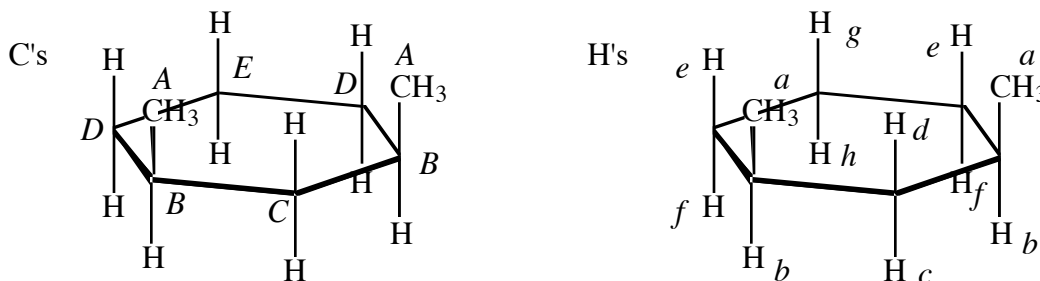
NMR spectroscopy is unique among diagnostic techniques in that it provides information about the environment of specific atoms in a molecule in solution. This is important when trying to elucidate the interactions of proteins with one another and with the small molecules to which they bind.

### Answers to problems assigned in class.

(1) Identify the number of  $^1\text{H}$  and  $^{13}\text{C}$  resonances each of these compounds will display.

(a) *cis*-1,3-Dimethylcyclohexane.

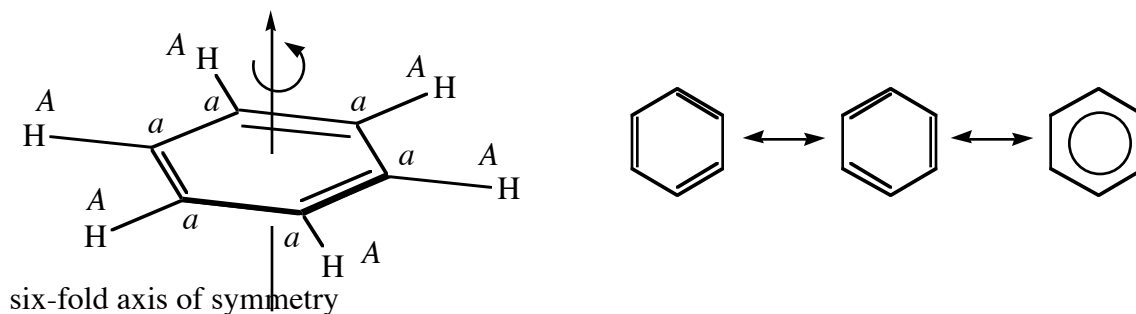
There is a plane of symmetry containing C2 and C5 that relates the two  $\text{CH}_3$ 's to one another. The plane relates C1 to C3 and C4 to C6. There is no plane that relates the H's on top of the ring to those on the bottom of the ring. Five  $^{13}\text{C}$  and eight  $^1\text{H}$  resonances will be seen.



(b) Benzene.

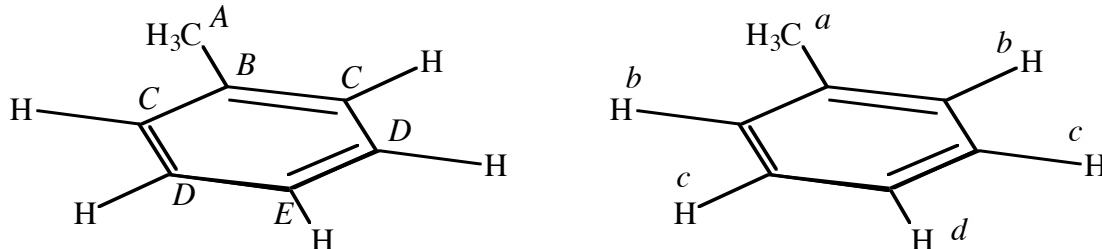
Benzene is a flat molecule. Its C atoms are  $\text{sp}^2$ -hybridized, so all the atoms in benzene are in a single plane. Benzene has a six-fold axis of symmetry through the center of the ring. Rotating benzene about

this axis maps every C and H onto the next C and H. (The double bonds don't lower the symmetry in benzene, because two equally good resonance structures for benzene can be drawn where the double bonds are drawn in different places. As a result all the C–C bonds in benzene are equivalent to one another. Often a "toilet bowl" resonance structure is drawn for benzene for this reason.) Benzene also has seven planes of symmetry. Every C is equivalent to the next C, and likewise for the H's. One  $^{13}\text{C}$  and one  $^1\text{H}$  resonance will be seen.



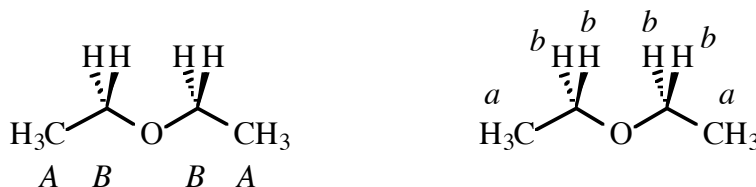
(c) Toluene (methylbenzene).

Toluene no longer has the six-fold axis of symmetry of benzene, but it has a plane of symmetry containing the Me group and two C's of the ring. Five  $^{13}\text{C}$  and four  $^1\text{H}$  resonances will be seen.



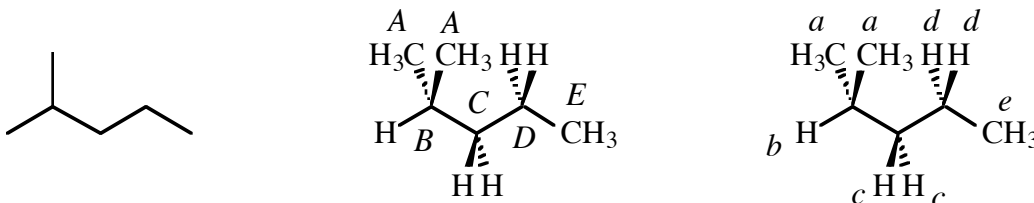
(d) Diethyl ether (ethoxyethane).

In its highest-symmetry conformation, diethyl ether has two planes of symmetry. (It also has a two-fold axis of symmetry through O in the plane of the paper.) One relates the left half of the compound to the right half; the other, containing the C's and O, relate the H's on each C to each other. Two  $^{13}\text{C}$  and two  $^1\text{H}$  resonances will be seen.



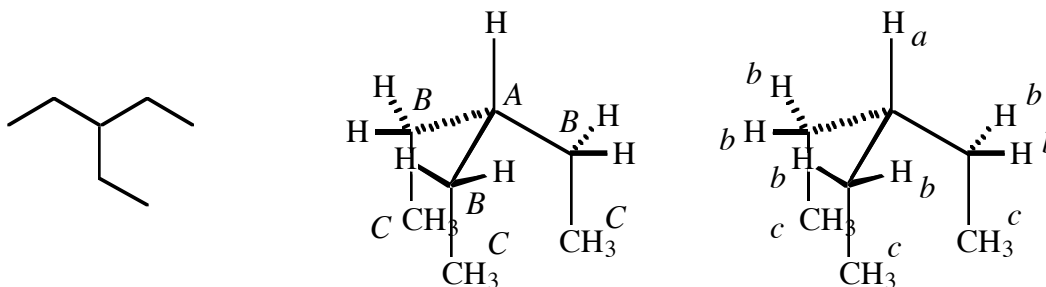
(e) 2-Methylpentane.

This compound can be drawn in a conformation in which it has one plane of symmetry, the plane of the paper. This relates the two Me groups on the one C to each other, and it relates the two H's in each CH<sub>2</sub> to one another. Five <sup>13</sup>C and five <sup>1</sup>H resonances will be seen.



(f) 3-Ethylpentane.

This compound can be thought of as three ethyl groups hanging off of one C. It has a three-fold axis of symmetry containing the central C and its H. It also has several planes of symmetry; each contains the central CH and one of the Et groups, and it relates the two H's of the contained Et group to one another and the two uncontained Et groups to one another. Three <sup>13</sup>C and three <sup>1</sup>H resonances will be seen.



(2) Predict the approximate chemical shift, integration, and multiplicity of each resonance in the <sup>1</sup>H NMR spectrum of each of the compounds in problem (1). Assume that each set of H's resonates at a different field strength, so no overlap between signals is observed.

(a) *cis*-1,3-Dimethylcyclohexane.

In reality, many of these resonances will overlap with one another and give very complex splitting patterns.

Set	$\delta$	Integration	Multiplicity
a	0.9	6	d
b	1.5	2	ddddq
c	1.2	1	dt
d	1.2	1	dt
e	1.2	2	dddd

f	1.2	2	dddd
g	1.2	1	dt
h	1.2	1	dt

(b) Benzene.

Set	$\delta$	Integration	Multiplicity
a	7.3	--	s

(c) Toluene (methylbenzene).

Set	$\delta$	Integration	Multiplicity
a	2.3	3	s
b	7.1	2	d
c	7.3	2	dd
d	7.2	1	t

(d) Diethyl ether (ethoxyethane).

Set	$\delta$	Integration	Multiplicity
a	1.3	3	t
b	3.4	2	q

(e) 2-Methylpentane.

Again, many of these resonances will overlap with one another.

Set	$\delta$	Integration	Multiplicity
a	0.9	6	d
b	1.5	1	t of septets
c	1.2	2	dt
d	1.1	2	tq
e	1.0	3	t

(f) 3-Ethylpentane.

Set	$\delta$	Integration	Multiplicity
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a	1.5	1	septet
b	1.2	6	dq
c	0.9	9	t

(3) Predict the approximate chemical shift and multiplicity of each resonance in the  $^{13}\text{C}$  NMR spectrum of each of the compounds in problem (1).

(a) *cis*-1,3-Dimethylcyclohexane.

Set	$\delta$	Multiplicity
A	10	q
B	30	d
C	25	t
D	20	t
E	23	t

(b) Benzene.

Set	$\delta$	Multiplicity
A	128	d

(c) Toluene (methylbenzene).

Set	$\delta$	Multiplicity
A	21	q
B	140	s
C	129	d
D	130	d
E	126	d

(d) Diethyl ether (ethoxyethane).

Set	$\delta$	Multiplicity
A	15	q
B	60	t

(e) 2-Methylpentane.

Set	$\delta$	Multiplicity
A	15	q
B	30	d
C	25	t
D	28	t
E	12	q

(f) 3-Ethylpentane.

Set	$\delta$	Multiplicity
A	35	d
B	25	t
C	12	q