STRUCTURE & REACTIVITY II: PURIFICATION AND SPECTROSCOPY

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1: Introduction to Spectroscopy

The structure of a compound has a big effect on its properties. But how do we know what that structure is?

The most useful methods of determining molecular structure involve the interaction of electromagnetic radiation, or light, with matter. Visible light, ultraviolet and infrared radiation, and even microwaves and radio waves interact with matter. They can each tell us different kinds of information about the materials they interact with.

How does light interact with matter?

Light has wave properties, much like the waves you could see at the ocean shore. In physics, waves can be described in a number of different ways. Waves have amplitude: there are waves that rise very tall, and others that are low. Waves also have wavelength: they may have long wavelengths, with big distances from the peak of one wave to the peak of the one coming behind it. They may have short wavelengths, with one following very closely behind another. Wavelength gives rise to a complementary property, which is frequency. When waves are close together, you can see or hear them crashing to the shore very frequently. When they are farther apart, they seem to crash to the shore with a much lower frequency.

The different colors of light that we see have different wavelengths; blue light has a shorter wavelength than red light, for example. These different wavelengths of light have different amounts of energy. This idea is described in the Planck-Einstein relation:

$$E = h\nu$$

(where E = energy, h = Planck's constant, n = frequency)

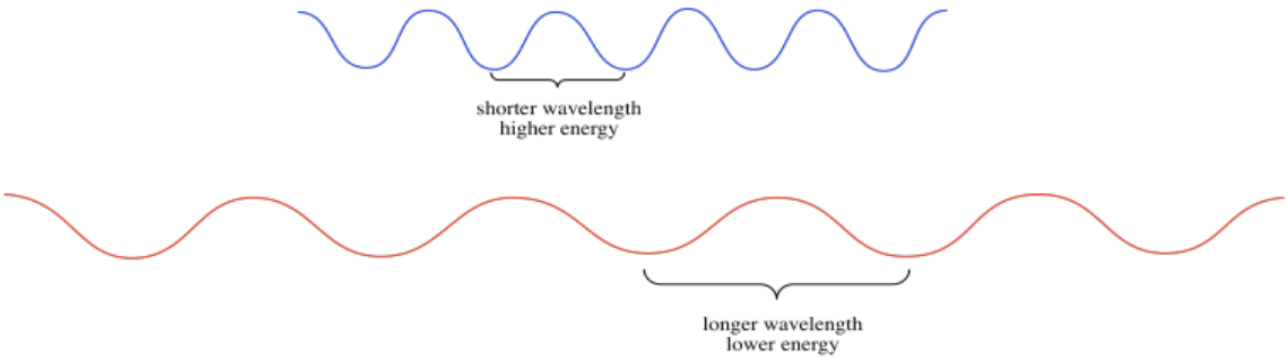
or

$$E = \frac{hc}{\lambda}$$

(where c = speed of light, λ = wavelength)

This equation means:

- Higher frequencies of light are more energetic than lower frequency ones (when the number ν gets bigger, the number E also gets bigger).
- Higher frequencies correspond to shorter wavelengths (so when the length λ gets longer, E gets smaller).



There are a couple of important and surprising points about the interaction of photons with matter:

- Light is quantized; it travels in packages, called photons, and different photons have specific amounts of energy.
- Absorption of light by matter is also quantized; only specific packages or "quanta" can be absorbed by a specific material.
- Consequently, specific compounds absorb specific frequencies of light and don't absorb others.

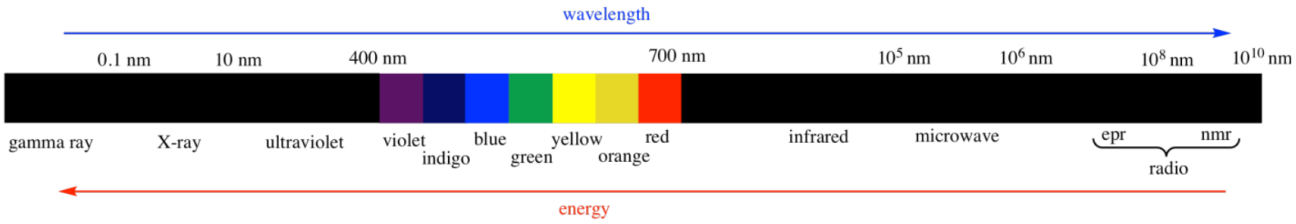
When ultraviolet and visible light are absorbed, the energy from the light is transferred to an electron. The electron is excited to a higher energy level. Only certain energy levels are available in a material, and so the material can only absorb certain photons. That means:

- A photon with **not enough** energy to reach another energy level is **not** absorbed.

- A photon with **too much** energy to reach another energy level is **not** absorbed, either; the electron **cannot** absorb some of the energy from a photon and have a little left over for later.
- The wavelength or frequency of a photon that **is** absorbed by the electron corresponds to the amount of energy needed to reach another energy level.

The same sort of event can happen "backwards": an electron can lose energy by falling to a lower energy level. The lost energy can be given up by the electron as a photon of light. The wavelength or frequency of the photon corresponds to the difference between electron energy levels. This phenomenon, in which light is absorbed by a material and then given off again, is called "fluorescence".

There are many kinds of electromagnetic radiation.



Many of these kinds of "light" can provide different kinds of information about structure. For example:

- UV-Visible spectroscopy tells us something about the electronic levels in a material. We will see more about this type of spectroscopy in another chapter. It is also discussed in a number of other places, in situations when it relates to molecular orbitals, to coordination compounds, and to photochemical reactions.
- X-rays can be used to construct an exact three-dimensional map of where the atoms lie in a crystalline material based upon how the x-rays scatter as they pass through the crystal. X-ray crystallography is a little bit too complicated for us, however.
- Radio waves interact with nuclear particles in a way that is similar to the absorption of UV light by electrons. However, this phenomenon only occurs in a strong magnetic field. The absorption of radio waves by the hydrogen nuclei in water molecules in human tissues is referred to as magnetic resonance imaging (MRI). The observation of nuclei in small molecules by a similar technique is referred to as nuclear magnetic resonance (NMR). NMR spectroscopy will be the subject of another chapter.
- Infrared light is absorbed by different bonds in a molecule. Infrared spectroscopy is the subject of another chapter.

CHAPTER OVERVIEW

2: Ultraviolet-Visible Spectroscopy

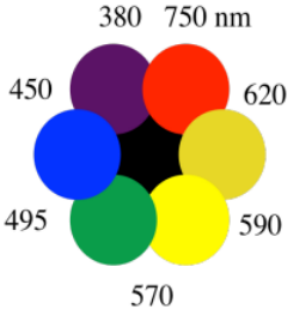
2.1: Introduction to UV Spectroscopy

To begin a story about spectroscopy, it is probably easiest to start with wavelengths of light that people can see. There are all kinds of electromagnetic radiation around us, mostly coming from the sun, and just a thin slice of the wavelengths in the middle are visible to the eye.

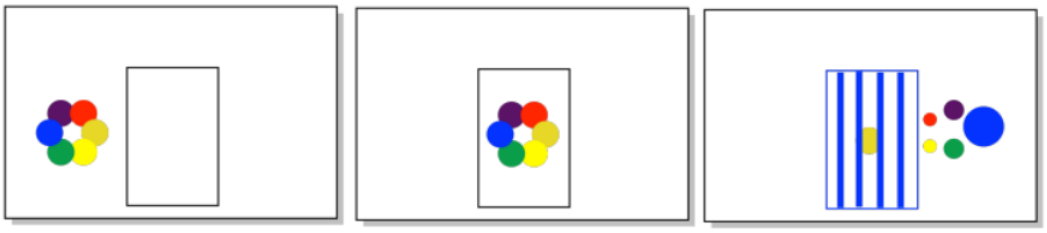
You probably already know that if you look at a white light, what you are seeing is really a composite, a blend of all different colors of light. If you shine that light through a prism (really, any glass object that varies in thickness, that has a thicker edge and a thinner edge), you can separate the white light into these different colors.

So what happens when you see a colored object? Maybe a cobalt blue pickup truck or a red barn? The object is absorbing some of those photons, those little packages of light. But the object is very selective; it will take these photons, but not those ones, and not those other ones, either.

The color that you see is made of just the leftover photons, the ones that did not get absorbed. We sometimes use the color wheel to keep track of this phenomenon. Partly because of how our eyes process light, when something absorbs a color on one side of the color wheel, we see the color on the opposite side.



When something absorbs orange photons, for instance, we see the complementary color, the one on the opposite side of the color wheel. We see blue. So the pickup truck looks blue because it absorbs the orange light. The barn looks red because it absorbs green light.



? Exercise 2.1.1

You observe a colored object. Estimate the wavelength of light that was absorbed by the object.

a) a green apple b) a yellow banana c) a red cherry d) a deep purple grape

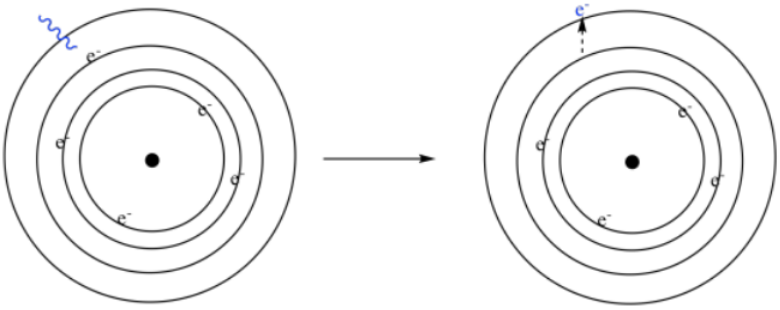
Answer

a) 700 nm (just an estimate, but maybe somewhere between 620 and 750 nm)

b) 425 nm c) 540 nm d) 580 nm

So what causes different things to absorb different colors of visible light? There are different factors with different kinds of materials. What they all have in common, however, is that they involve electronic transitions. Actually, the same is true for ultraviolet light, although we can't see that far into the spectrum. When ultraviolet or visible light are absorbed, in general the photons are interacting with electrons in the material.

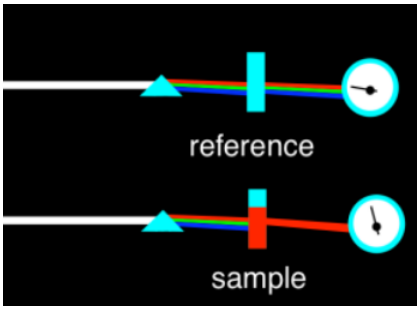
And what happens to the electrons when they interact with the light? Well, photons have energy, so when the photons interact with the electrons, they transfer their energy to the electrons. We say that the electrons *become excited*, or that they are promoted to a higher level. If we look at a simple Bohr model of the atom, from the early 20th century, we think of the electrons orbiting the nucleus in shells. Each shell is a little farther from the nucleus, and at a higher energy than the one below it. If an atom absorbs a photon, one of the electrons gets promoted to a higher level.



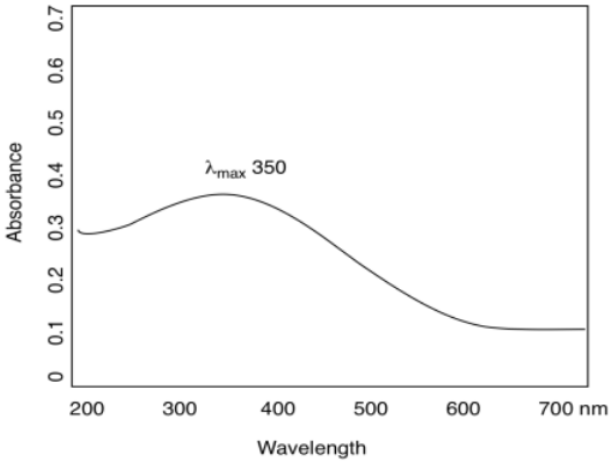
These electronic energy levels occur at very specific intervals. That's why a specific atom might absorb only specific photons. The energy of the photon has to match, more or less exactly, the amount of energy an electron would need in order to jump from one level to another.

Now, it might seem that any atom would have lots of different possible electronic energy levels giving rise to lots of possible transitions between one level and another. In that case, any atom should absorb or give off all kinds of photons, and we shouldn't see any specific color at all. However, there really are some limitations on the possible transitions in a given atom. What's more, almost all of these transitions correspond to ultraviolet energy, which we can't see anyway, and so what we do observe are the few transitions that actually involve visible light.

We can measure the wavelengths of light that are absorbed by a material using a UV spectrometer. The spectrometer produces a graph of absorbance versus wavelength. The wavelength, on the x axis, is usually measured in nanometers. The absorbance, on the y axis, is usually dimensionless; that's because it's a fraction. It's the ratio of how much light is absorbed by the sample compared to how much was absorbed by some reference, something to which we compare the sample. In most cases, the sample is dissolved in a solvent such as water of ethanol, so the reference is just plain solvent. That solution is held in a clear vessel called a cuvette, often made of quartz or a type of plastic that does not absorb much light in the wavelengths that we want to look at.

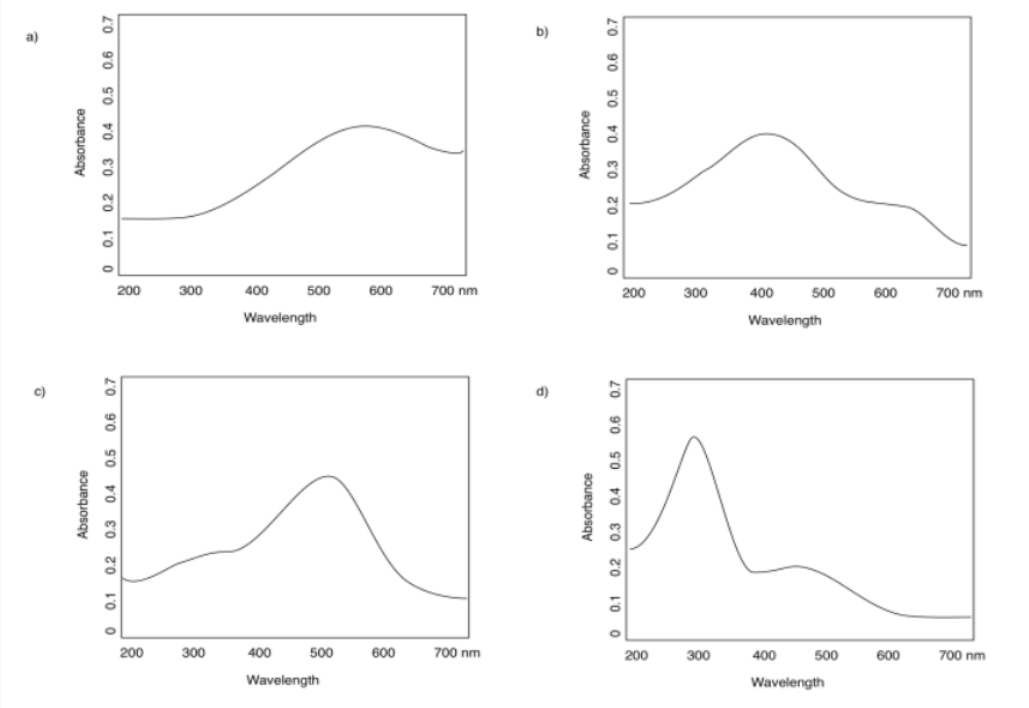


The typical graph we get looks like a wide, rounded hill, or maybe a couple of hills. It might seem like maybe there should just be one wavelength that gets absorbed, given what we have these very specific electronic transitions allowed. That may be true with gas phase atoms, but in the condensed phase -- in solids or liquids or in solutions -- things get much messier. There are lots of reasons for that, most of which seem entirely unrelated to light absorption, such as collisions and other interactions between molecules that are sloshing around in the cuvette.



At any rate, the highest point on that hill is chosen as a sort of diagnostic index, called the absorption maximum or λ_{max}. This is the wavelength at which the compound absorbs the most light. In the spectrum shown here, that point occurs around 350 nm, just outside the visible range.

Exercise 2.1.2



Answer

a) 590 nm b) 400 nm c) 500 nm d) 300 nm

Exercise 2.1.3

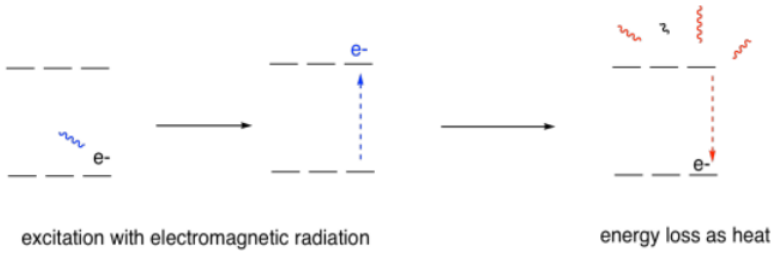
Some of the spectra in the previous question have two different absorbances: a strong one and a weak one. Estimate the absorption maxima of each.

Answer

a) 590 nm (strong); that's all b) 400 nm (strong); 600 nm (weak)

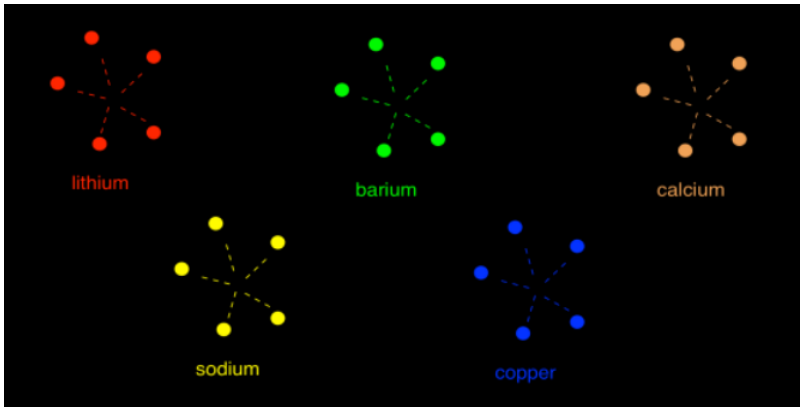
c) 500 nm (strong); 350 nm (weak) d) 300 nm (strong); 450 nm (weak)

You might wonder what happens after the electron gets excited. How does it get back down again? There are actually a few different ways for that to happen, but probably the most common way is via processes called *radiationless relaxation*, in which the energy absorbed from the photon is eventually lost to the surroundings. It often ends up in the form of heat.



On the other hand, if an excited electron were to become excited in some other way, such as by great heat, and then fall from its promoted level back down into one below, the energy it lost could be given off by a photon. This phenomenon is called emission or fluorescence, depending on the circumstances. Again, only certain photons would be given off, depending on the atom involved.

That specificity allows analysts to study the composition of certain materials, such as mineral ores, or to look for metal ions in groundwater. It also supplies some of the fun of fireworks; people have known for some time that lithium and strontium salts are good for red fireworks, copper for blue ones, calcium for orange, barium for green, sodium for yellow.



Exercise 2.1.4

Rank these fireworks from the most energetic photon emitted to the least energetic.

Answer

Remember, here we are observing the photons directly, rather than the onew complementary to the absorbed photons.

copper > barium > sodium > calcium > lithium

2.2: UV-Visible Spectroscopy - Metal Ions

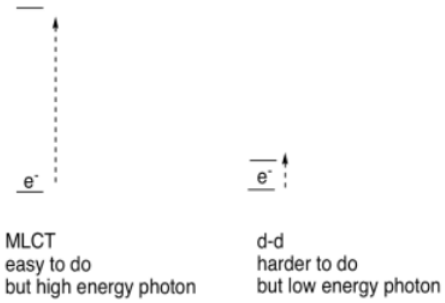
Transition metals are often associated with brightly-colored compounds. Because of their relatively low electronegativity, transition metals are frequently found as positively-charged ions, or cations. In solution, metal ions would not swim around by themselves, but would attract other molecules to them. These molecules bind to the metal ions, forming coordination complexes.

These transition metal complexes or coordination complexes have lots of electrons, and they can often interact with lots of different photons. When they do, there are a number of possible electronic transitions that can result. These transitions might involve the metal ion itself, or the *ligands* -- those molecules or ions that bind to the metal ion.

One very common transition is called a charge transfer transition. It involves the excitation of an electron from the ligand to the metal, or vice versa. Sometimes the former case is referred to as a *ligand-to-metal charge transfer*, or *LMCT*; the latter case would be a *metal-to-ligand charge transfer*, or *MLCT*. However, these two acronyms are sometimes used interchageably to suggest some sort of transition that involves both the ligand and the metal, without worrying too much about the direction.

In addition, sometimes electrons can be excited from one level to another, just on the metal ion. For transition metals, these electronic excitations are called *d-d transitions*. For transition metals, the valence electrons are in the d sub-shell, and in a d-d transition, the electron is excited from one d level to another. That sounds like it might be pretty easy -- the electron isn't going very far, after all -- but d-d transitions are actually quite inefficient. The electronic transitions involved just are not very good at capturing photons.

By comparison, it might sound like it would be difficult to move an electron from the metal all the way to the ligand, but it's actually pretty easy. These electronic transitions interact with photons very efficiently.



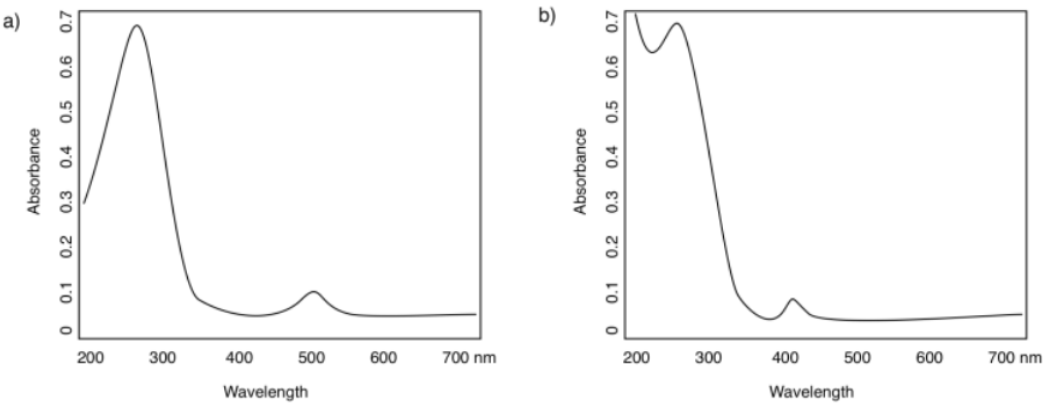
As a result, there is a kind of counterintuitive relationship in the UV-visible spectra of transition metal complexes: d-d transitions require very little energy but occur relatively infrequently, meaning they give very weak absorbances in the spectrum. MLCT transitions require much more energy but they happen frequently, leading to stronger absorbances in the spectrum.

We aren't going to worry about why different electronic transitions occur with greater or lesser efficiency; that has to do with symmetry and group theory, and some mathematics that we aren't equipped to handle right now. We just need to understand that these distinctions can influence what UV spectra look like.

? Exercise 2.2.1

Propose a formula for a simple, single-chain inosite containing only sodium counterions.

In the following spectra, assign the observed "peaks" or absorbance bands to MLCT or d-d transitions.



Answer

a) 270 nm (strong, MLCT); 500 nm (weak, d-d)

b) < 200 nm* (very strong, MLCT); 275 nm (strong, MLCT); 400 nm (weak, d-d) *can't see exactly where because the peak is so tall that we can't see the top

c) < 200 nm* (very strong, MLCT); 275 nm (strong, MLCT); 660 nm (weak, d-d)

d) < 250 nm (strong, MLCT); 300 nm (strong, MLCT); 620 nm (weak, d-d)

? Exercise 2.2.2

In the preceding spectra, predict the observed color of each of the complexes.

Answer

a) absorbs blue-green; we see orange-red

b) absorbs violet; we see yellow

c) absorbs red; we see green

d) absorbs orange; we see blue

The whole idea of UV spectroscopy is that different compounds might absorb photons of different wavelengths based on their electronic structures. We might be able to look at the UV spectrum of a compound and tell its identity or structure; that task would be especially straightforward if we had a few different options to choose from.

Now we see that the y axis also matters to some extent. A specific compound might absorb at 250 nm and at 450 nm; however, an additional characteristic of that compound might be that it absorbs *very strongly* at 250 nm and only *weakly* at 450 nm. Knowing

that information might help us distinguish the spectrum of that compound from the spectrum of another that has similar absorption wavelengths, but that shows peaks in the UV spectrum of very different sizes.

How strongly a compound absorbs photons at a particular wavelength is described by a quantity called the **extinction coefficient** (or alternatively, in different variations, the absorption coefficient or the molar absorptivity coefficient).

For example, it can be shown that aqueous potassium permanganate, $KMnO_4$, at its absorption maximum of 530 nm, has an extinction coefficient ε = 14 L g^{-1} cm^{-1}. How much light is absorbed by a sample of potassium permanganate at that wavelength depends on a couple of additional factors, however. First of all, how concentrated is the sample? The more potassium permanganate there is dissolved in the sample, the more light it can absorb. Also, the longer the light travels through the cuvette, the more permanganate it will encounter, and so the more light it will absorb.

So absorbance can be described as

$$A = \varepsilon c l \tag{2.2.1}$$

in which ε = extinction coefficient, l = path length, c = concentration.

Most cuvettes are 1 cm wide; if the extinction coefficient contains a unit of cm^{-1}, we can just use b = 1 cm and that part is taken care of. From there, the absorbance will just depend on the concentration of the permanganate.

Exercise 2.2.3

Calculate the absorbance at 530 nm for the following concentrations of potassium permanganate in a 1 cm cuvette.

a) 0.025 g /L b) 0.011 g/L

Answer

a) A = ε c l = 14 L g^{-1} cm^{-1} x 0.025 g L^{-1} x 1 cm = 0.35

a) A = ε c l = 14 L g^{-1} cm^{-1} x 0.011 g L^{-1} x 1 cm = 0.15

Exercise 2.2.4

Calculate the concentration of potassium permanganate (in g/L) given the following absorbance readings at 530 nm in a 1 cm cuvette.

a) A = 0.75 b) A = 0.21

Answer

a) A = ε c l or c = A / (ε l) = 0.75 / (14 L g^{-1} cm^{-1} x 1 cm) = 0.054 g L^{-1}

b) A = ε c l or c = A / (ε l) = 0.21 / (14 L g^{-1} cm^{-1} x 1 cm) = 0.015 g L^{-1}

Exercise 2.2.5

Although the maximum absorption is around 530 nm, the visible absorption band in potassium permanganate actually stretches from 500 to 600 nm. What colour is potassium permanganate?

Answer

Based on our colour wheel it absorbs both yellow and green; we see a mix of violet and red. ($KMnO_4$ is really a deep purple.)

Frequently, extinction coefficients have units of L mol^{-1} cm^{-1} or M^{-1} cm^{-1}. In these cases, the concentration is measured in mol L-1 rather than g L-1. The molecular weight (molar mass) of the compound, in g mol^{-1}, is the conversion factor between one unit and the other. For example, the extinction coefficient for the 530 nm peak of potassium permanganate is approximately 2 200 L mol^{-1} cm^{-1}.

Exercise 2.2.6

Confirm that the two extinction coefficients for potassium permanganate, given with different units, are actually equivalent.

Answer

$KMnO_4$ has MW = 158 g mol^{-1}

14 L g^{-1} cm^{-1} x 158 g mol^{-1} = 2212 L mol^{-1} cm^{-1}

Exercise 2.2.7

Calculate the absorbance at 530 nm for the following concentrations of potassium permanganate in a 1 cm cuvette.

a) 1.5 x 10^{-4} mol /L b) 9.0 x 10^{-5} mol/L

Answer

a) $A = \varepsilon cl = 2200 \frac{L}{mol\ cm} \times 0.00015 \frac{mol}{L} \times 1cm = 0.33$

b) $A = \varepsilon cl = 2200 \frac{L}{mol\ cm} \times 0.00009 \frac{mol}{L} \times 1cm = 0.20$

Exercise 2.2.8

Calculate the concentration of potassium permanganate (in mol/L) given the following absorbance readings at 530 nm in a 1 cm cuvette.

a) A = 0.47 b) A = 0.89

Answer

a) $A = \varepsilon cl\ or\ c = \frac{A}{\varepsilon l} = \frac{0.47}{2200 \frac{L}{mol\ cm} \times 1cm} = 2.1 \times 10^{-4} \frac{mol}{L}$

b) $A = \varepsilon cl\ or\ c \frac{A}{\varepsilon l} = \frac{0.89}{2200 \frac{L}{mol\ cm} \times 1cm} = 4.1 \times 10^{-4} \frac{mol}{L}$

See additional discussion of coordination complexes.

2.3: UV-Visible Spectroscopy of Organic Compounds

Many of the colors that we see in nature come not from simple atoms, but from molecules. Organic compounds -- carbon-based compounds, usually made by living things -- are sometimes very brightly colored. If you look out on an autumn day and see a woman in blue jeans walking beneath an orange maple, then you are observing a couple of organic compounds.

The blue color of her jeans is probably indigo, a dye known since antiquity, but often produced synthetically today. It still has the same color, but it is produced by factory workers rather than field hands.

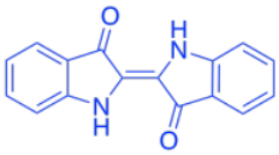


Figure 2.3.1:

The color of the leaves comes from a mix of different compounds such as carotene. Carotene is a member of a huge class of natural products called **terpenoids**.

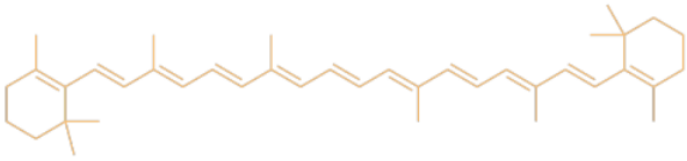


Figure 2.3.2:

? Exercise 2.3.1

What color of light is absorbed by (a) the blue jeans? (b) the leaves?

Answer a:

blue

Answer b:

orange

In most cases, the reason for the color is tied to one phenomenon in these compounds: conjugation. Conjugation is a specific pattern in the electronic arrangement of molecules. A Lewis structure of a conjugated molecule shows alternating single and double bonds between carbon atoms. In some cases, there might also be oxygen or nitrogen atoms involved in these alternating double and single bonds.

It turns out that conjugation has a very predictable effect on the energy levels of the electrons involved in those alternating bonds. It smears out the energy levels. Some of them are pushed a little higher in energy. Some drop a little lower. Many of them become spread out in between. As a result, the gaps between those energy levels becomes smaller and smaller as the amount of conjugation increases in a molecule.

Figure 2.3.3:

So, if we start to measure the UV spectra of a bunch of compounds, we start to see evidence of that conjugation phenomenon from the indigo and carotene. Each time we add a double bond to a conjugated system, the wavelength of light absorbed increases. It's a

significant increase: maybe forty or fifty nanometers for the first double bond or two that we add in conjugation, although the differences would get a little smaller if we kept adding more of them.

	λ_{max} (nm)
C=C	170
C=C-C=C	220
C=C-C=C-C=C	260

? Exercise 2.3.2

Benzoic acid has an absorption maximum at 230 nm. Where do you expect to see the absorption maximum in cinnamic acid?

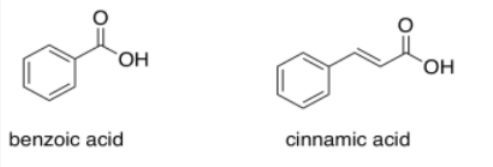


Figure 2.3.4:

Answer

Add another 30 or 40 nm and you get to 270 or 280 nm.

? Exercise 2.3.3

Polyaromatic systems have rather complicated UV spectra, but as each additional aromatic ring is added, a shift of about 30 nm occurs in the absorption maximum of the most prominent peak. If naphthalene has λ_{max} at 220 nm, where would you see λ_{max} for anthracene and tetracene?

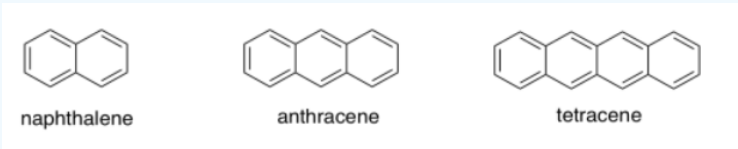


Figure 2.3.5:

Answer a:

about 250 nm

Answer b:

about 280 nm

Conjugation is responsible for much of the visible absorption by organic compounds because the energetic spacing between π and π* orbitals falls within the same energy range as visible light. As a result, electrons can be excited from a π to a π* level when that visible light is absorbed.

There are other electrons (other than the ones in the π bonds) that can be excited by absorption of visible light. If the molecule has sigma bonds, there is always a possibility of a σ to σ* transition, in which an electron in a σ bond gets excited to the antibonding level. If the molecule has lone pairs, there could be *n* to σ* transitions or *n* to π* transitions (*n* is nonbonding).

However, none of these absorb light as strongly as π to π* transitions. Just as there were differences in the strength of absorbances (extinction coefficients) in transition metal compounds (where MLCT absorbed light strongly, but d-d transitions absorbed light only weakly), we see large extinction coefficients for π to π* but only tiny coefficients for σ to σ* transitions, for example. These differences are related to the spatial relationships between the two orbitals involved in each case, rather than the energy differences.

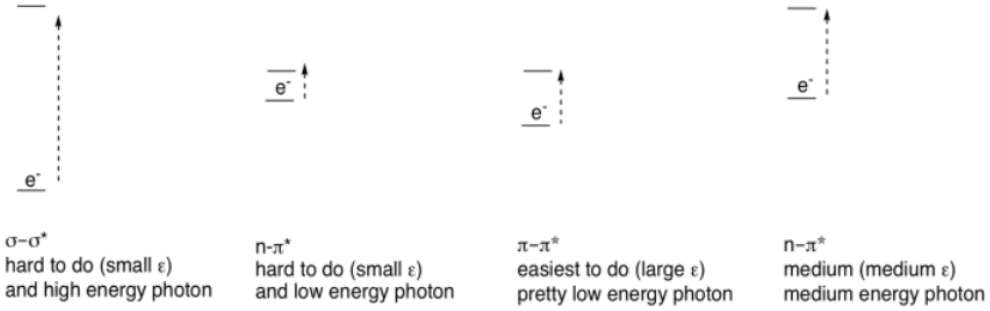


Figure 2.3.6:

Exercise 2.3.4

Organic compounds, like transition metals, can have absorptions of varying strengths. Consider the following table for quinone:

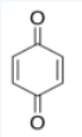
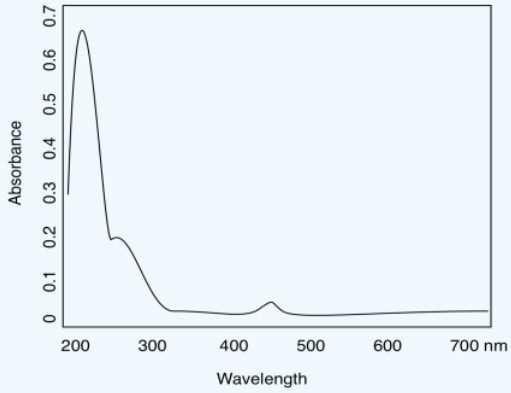


Figure 2.3.7:

λ (nm)	ε ($cm^2\ mol^{-1}$)
240	24 000
280	400
430	20

a. Use the data table for quinone to sketch a UV spectrum.
b. What color is quinone?

Answer a:

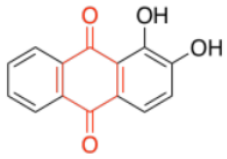


Answer b:

yellow

Structures that are very good at absorbing visible light are sometimes called *chromophores*. There are plenty of common chromophores in nature, such as that extended terpenoid structure seen in carotenes; a similar structure is found in lycopene, which gives tomatoes their red color.

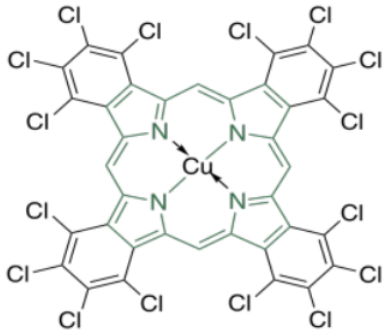
Quinones are also very commonly seen in chromophores. In humans, the most common chromophore is melanin; its brown color is derived from a quinone-based structure. A different quinone structure, alizarin, is a dye known since antiquity; it was historically derived from madder root.



alizarin contains a quinone

Figure 2.3.8:

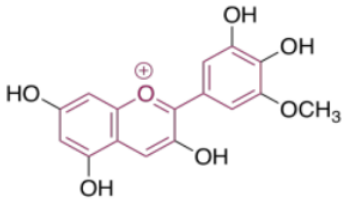
Porphyrins are also very common in humans and other organisms. They are found in compounds such as hemoglobin, known more for their oxygen-carrying ability and other indispensible properties than their color. However, they are quite brightly colored. Interestingly, the colors of porphyrins and other chromophores can be tuned quite easily through variation of side groups around the main structure. Phthalocyanin green, for example, has the same porphyrin structure as blood-red heme, but is modified by additional aromatic rings and chlorine atoms, and contains a copper rather than an iron. These color-modifying groups are called *autochromes*.



phthalocyanine green contains a porphyrin

Figure 2.3.9:

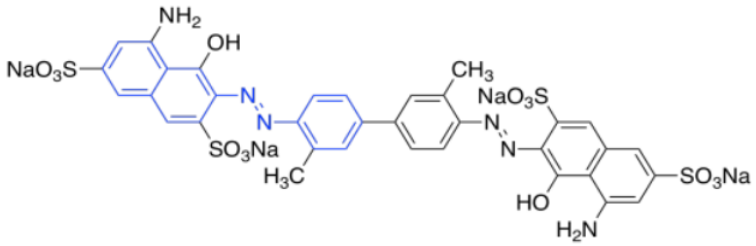
The anthocyanins are another widespread group of naturally-occurring compounds. Like porphyrins and quinones, they contain a variety of autochromes; the groups arranged around the central, three-ring structure that forms the essential chromophore of the anthocyanins. Variations among these side groups leads to a variety of colors ranging from red to blue. The one shown below gives a purple color to the flowers -- petunias -- in which it is frequently found.



purple petunidin has an anthocyanin structure

Figure 2.3.10:

One last group of common chromophores is not found in nature at all. These are the azo dyes, discovered in the 19th century and still in widespread use today.



Niagara blue is an azo dye

Figure 2.3.11:

Note that the effects of autochromes can be somewhat complicated in tuning the absorption of the main chromophore. Not only does the identity of the side group have an influence (such as the sulfonate group, SO_3^-, or an amine group, NH_2, in an azo dye), but the group's exact position is important as well. There is actually a list of rules (Woodward Rules) that can be used to predict absorption maxima of conjugated systems, but we won't go into those here.

? Exercise 2.3.5

In each of the following pigments,

i. circle the main chromophore.
ii. identify the class of chromophore.
iii. predict the observed color.

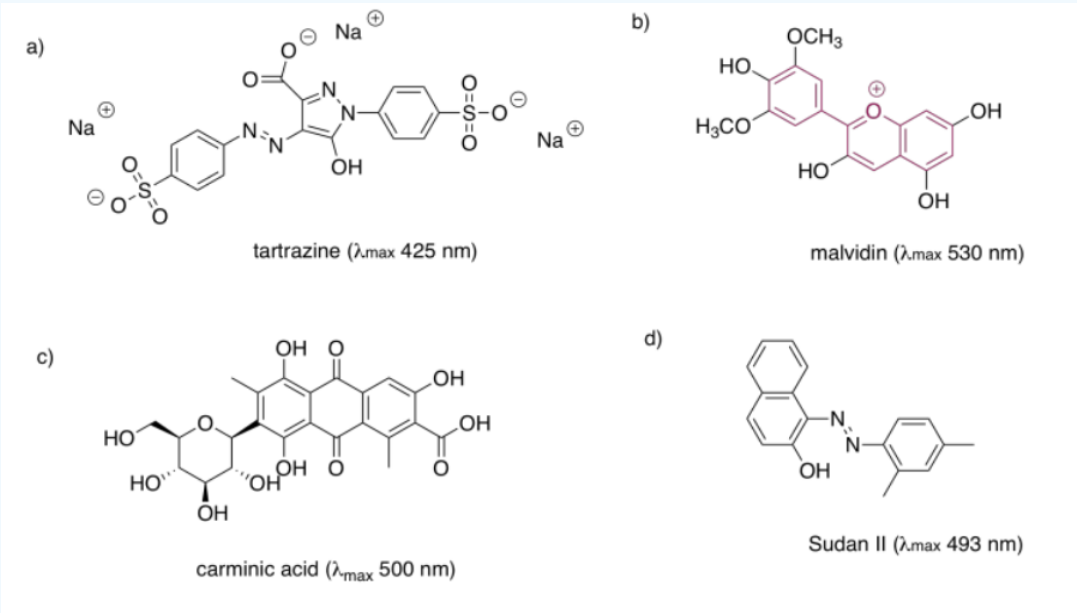


Figure 2.3.12:

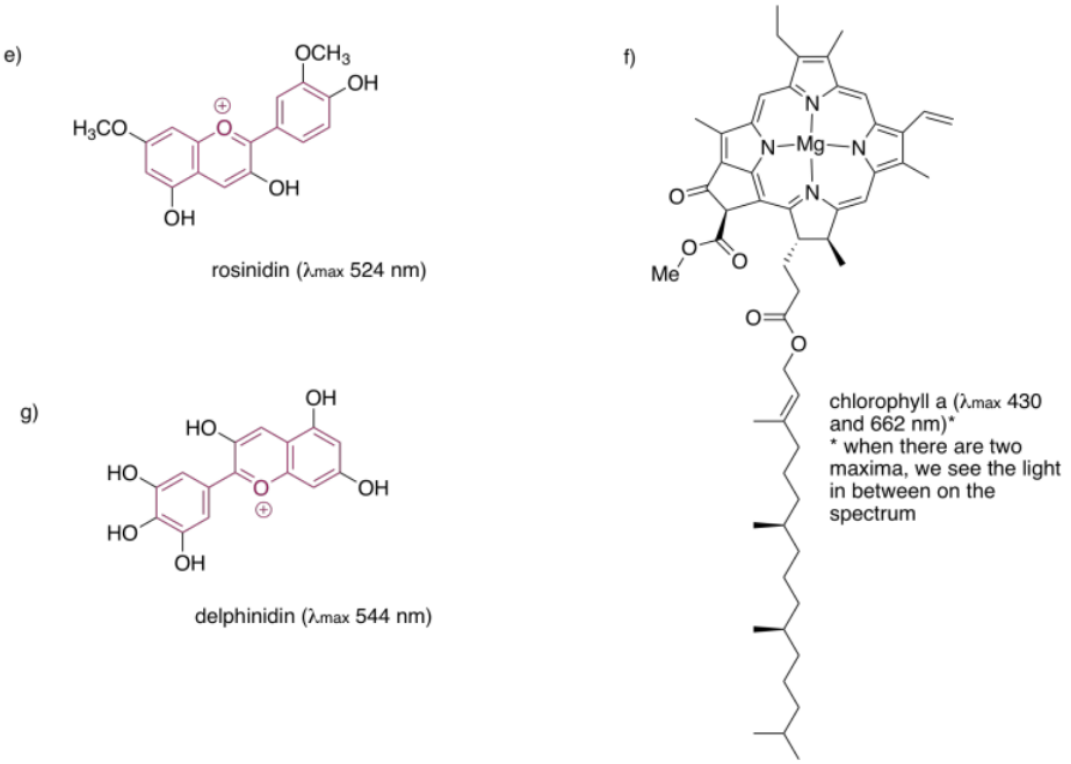
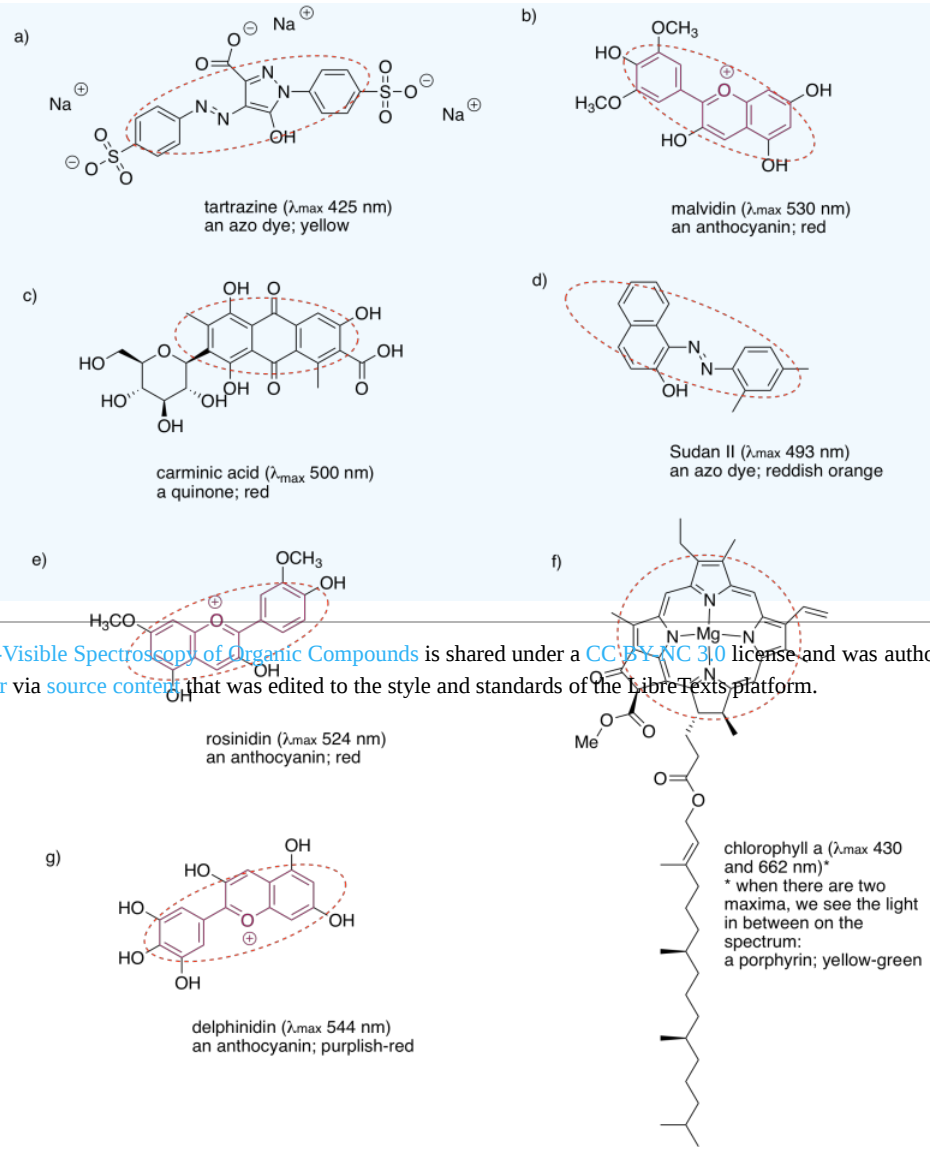


Figure 2.3.13:

Answer



2.4: UV-Visible Spectroscopy- Solutions.

Exercise 2.1.1

You observe a colored object. Estimate the wavelength of light that was absorbed by the object.

a) 700 nm (just an estimate, but maybe somewhere between 620 and 750 nm)

b) 425 nm c) 540 nm d) 580 nm

Exercise 2.1.2:

a) 590 nm b) 400 nm c) 500 nm d) 300 nm

Exercise 2.1.3

a) 590 nm (strong); that's all b) 400 nm (strong); 600 nm (weak)

c) 500 nm (strong); 350 nm (weak) d) 300 nm (strong); 450 nm (weak)

Exercise 2.1.4

Remember, here we are observing the photons directly, rather than the onew complementary to the absorbed photons.

copper > barium > sodium > calcium > lithium

Exercise 2.2.1:

a. 270 nm (strong, MLCT); 500 nm (weak, d-d)
b. < 200 nm* (very strong, MLCT); 275 nm (strong, MLCT); 400 nm (weak, d-d) *can't see exactly where because the peak is so tall that we can't see the top
c. < 200 nm* (very strong, MLCT); 275 nm (strong, MLCT); 660 nm (weak, d-d)
d. < 250 nm (strong, MLCT); 300 nm (strong, MLCT); 620 nm (weak, d-d)

Exercise 2.2.2:

a. absorbs blue-green; we see orange-red
b. absorbs violet; we see yellow
c. absorbs red; we see green
d. absorbs orange; we see blue

Exercise 2.2.3:

a) $A = \varepsilon cl = 14 L g^{-1} cm^{-1} \times 0.025 g L^{-1} \times 1 cm = 0.35$

a) $A = \varepsilon cl = 14 L g^{-1} cm^{-1} \times 0.011 g L^{-1} \times 1 cm = 0.15$

Exercise 2.2.4:

a. $A = \varepsilon cl \; or \; c = \frac{A}{\varepsilon l} = \frac{0.75}{14 L g^{-1} cm^{-1} \times 1 cm} = 0.054 g L^{-1}$
b. $A = \varepsilon cl \; or \; c = \frac{A}{\varepsilon l} = \frac{0.21}{14 L g^{-1} cm^{-1} \times 1 cm} = 0.015 g L^{-1}$

Exercise 2.2.5:

Based on our color wheel it absorbs both yellow and green; we see a mix of violet and red. ($KMnO_4$ is really a deep purple.)

Exercise 2.2.6:

$KMnO_4$ has MW = 158 g mol^{-1}

$$14 \frac{L}{g \, cm} \times 158 \frac{g}{mol} = 2212 \frac{L}{mol \, cm}$$

Exercise 2.2.7:

a) $A = \varepsilon cl = 2200 L mol^{-1} cm^{-1} \times 0.00015 mol L^{-1} \times 1 cm = 0.33$

b) $A = \varepsilon cl = 2200 L mol^{-1} cm^{-1} \times 0.00009 mol L^{-1} \times 1 cm = 0.20$

Exercise 2.2.8:

a. $A = \varepsilon cl \; or \; c = \frac{A}{\varepsilon l} = \frac{0.47}{2200 L mol^{-1} cm^{-1} \times 1 cm} = 2.1 \times 10^{-4} mol L^{-1}$

b. $A = \varepsilon cl \; or \; c = \frac{A}{\varepsilon l} = \frac{0.89}{2200 L mol^{-1} cm^{-1} \times 1 cm} = 4.1 \times 10^{-4} mol L^{-1}$

Exercise 2.3.1:

a) blue b) orange

Exercise 2.3.2:

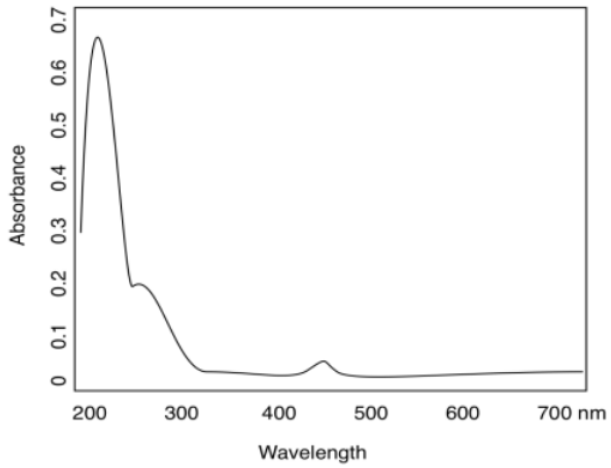
Add another 30 or 40 nm and you get to 270 or 280 nm.

Exercise 2.3.3:

a) about 250 nm b) about 280 nm

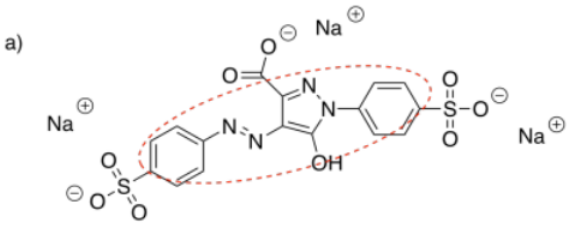
Exercise 2.3.4:

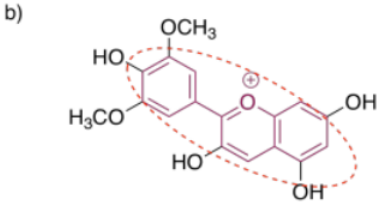
a)

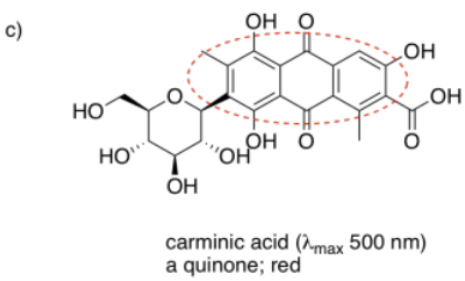


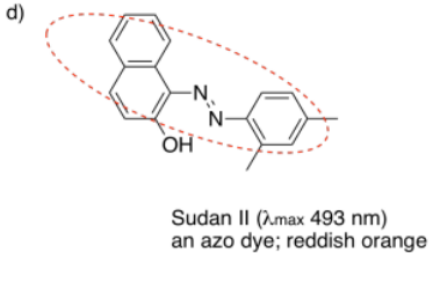
b) yellow

Exercise 2.3.5:

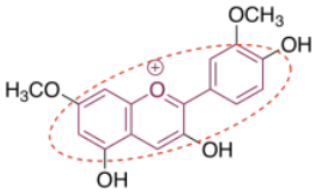






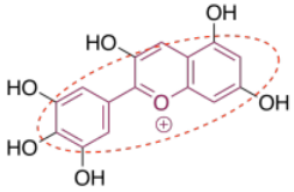


e)



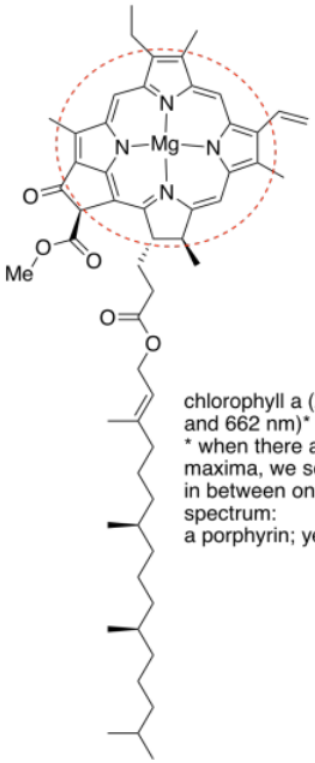
rosinidin (λ_{max} 524 nm)
an anthocyanin; red

g)



delphinidin (λ_{max} 544 nm)
an anthocyanin; purplish-red

f)



chlorophyll a (λ_{max} 430 and 662 nm)*
* when there are two maxima, we see the light in between on the spectrum:
a porphyrin; yellow-green

CHAPTER OVERVIEW

3: Infrared Spectroscopy

This chapter will focus on infrared (IR) spectroscopy. The wavelengths found in infrared radiation are a little longer than those found in visible light. IR spectroscopy is useful for finding out what kinds of bonds are present in a molecule, and knowing what kinds of bonds are present is a good start towards knowing what the structure could be.

3.1: Introduction

This chapter will focus on infrared (IR) spectroscopy. The wavelengths found in infrared radiation are a little longer than those found in visible light. IR spectroscopy is useful for finding out what kinds of bonds are present in a molecule, and knowing what kinds of bonds are present is a good start towards knowing what the structure could be.

What does an IR spectrum look like?

A spectrum is a graph in which the amount of light absorbed is plotted on the y-axis and frequency is plotted on the x-axis. An example is shown below. You can run your finger along the graph and see whether any light of a particular frequency is absorbed; if so, you will see a "peak" at that frequency. If not, you will see "the baseline" at that frequency.

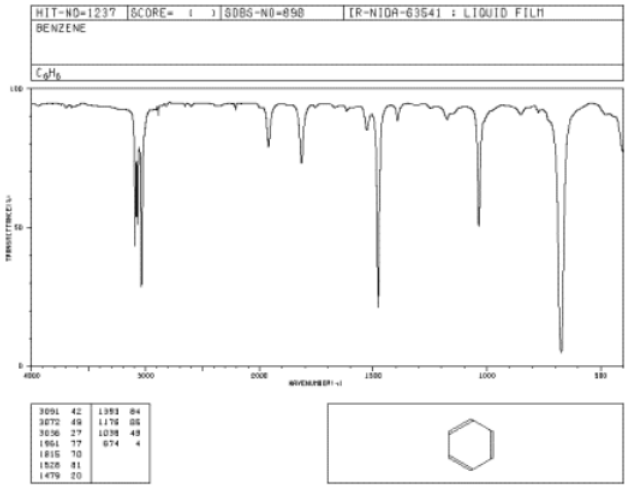


Figure 3.1.1: IR spectrum of benzene. The x-axis labels are, *from right to left*, 500, 1000, 1500, 2000, 3000 and 4000 cm^{-1}. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

In IR spectra (spectra = plural of spectrum):

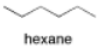
- the y axis is usually labeled "transmittance". Transmittance is the amount of light that passes through the sample.
- the unit of transmittance is percent (%).
- the x axis is labeled "wavenumbers". Wavenumbers are proportional to frequency, so the higher the frequency, the higher the wavenumber.
- the symbol for wavenumber is reciprocal centimeters (cm^{-1}).
- the x-axis is usually displayed with high wavenumber on the left and lower wavenumber on the right.

As you run your finger from left to right across an IR spectrum, you can see whether or not light is absorbed at particular frequencies. When the curve dips down, less light is transmitted. That means light is absorbed. The dip in the graph is called a peak. Different bonds absorb different frequencies of light, so the peaks tell you what kinds of bonds are present.

3.2: Hydrocarbon Spectra

All organic and biological compounds contain carbon and hydrogen, usually with various other elements as well. Hydrocarbons are compounds containing only carbon and hydrogen, but no other types of atoms. Since all organic compounds contain carbon and hydrogen, looking at hydrocarbon spectra will tell us what peaks are due to the basic C&H part of these molecules. It is sometimes useful to think of the C&H part of a molecule as the basic skeleton or scaffolding used to construct the molecule. The other atoms often form more interesting and active features, like the doors, windows and lights on a building.

The simplest hydrocarbons contain only single bonds between their carbons, and no double or triple bonds. These hydrocarbons are variously referred to as saturated hydrocarbons, paraffins or alkanes. Examples of alkanes include hexane and nonane. (You can take a look at the Glossary to see what these names tell you about the structure.)



hexane

Look at the IR spectrum of hexane. You should see:

- a set of peaks dipping down from the baseline at about 2900 cm^{-1}.
- another set of peaks dipping down from the baseline at about 1400-1500 cm^{-1}.

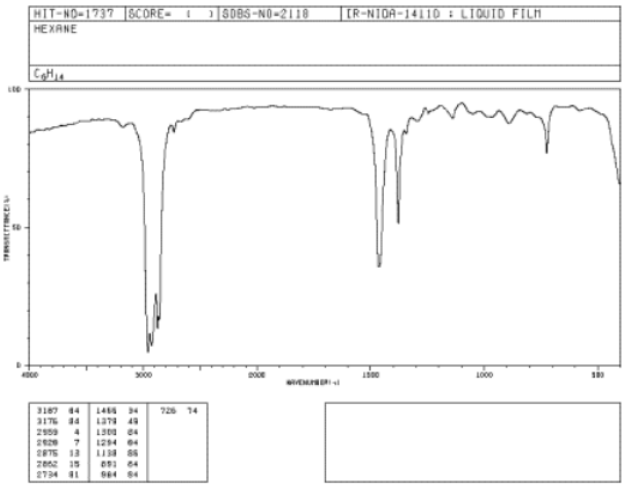


Figure 3.2.1: IR spectrum of hexane.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

If you look at an IR spectrum of any other alkane, you will also see peaks at about 2900 and 1500 cm^{-1}. The IR spectra of many organic compounds will show these peaks because the compound may contain paraffinic parts in addition to parts with other elements in them.

- These two kinds of peaks tell you that C-H bonds are present.
- Specifically, the bonds involve sp^3 or tetrahedral carbons.
- Stretching C-H bonds in alkanes absorb light at around 2900 cm^{-1}.
- Bending H-C-H angles in alkanes absorb light at around 1500 cm^{-1}.

3.3: Some Subtle Points of IR Spectroscopy

Alkanes show two sets of peaks in the IR spectrum. Alkanes contain two kinds of bonds: C-C bonds and C-H bonds. However, these two facts are not related. The reasons are explained through bond polarity and molecular vibrations.

Bond polarity can play a role in IR spectroscopy.

- nature rules that only bonds that contain dipoles can absorb infrared light.
- C-C bonds are usually nonpolar and usually do not show up as peaks in the IR spectrum.
- C-H bonds are not very polar and do not give rise to strong peaks in the IR spectrum.
- a whole lot of small C-H peaks can add up together to look like one big peak. This would happen if a molecule contained many C-H bonds (a common situation).

Molecular vibrations play a major role in IR spectroscopy.

- IR light interacts with vibrating bonds. When light is absorbed, the bond has a little more energy and vibrates at a higher frequency.
- a bond does not have an exact, fixed length; it can stretch and compress. This is called a bond stretching vibration.
- Stretching C-H bonds in alkanes absorb light at around 2900 cm^{-1}.
- bond angles can also bend; for instance, the H-C-H bond angle can compress and stretch. This is called a bending vibration.
- Bending H-C-H angles in alkanes absorb light at around 1500 cm^{-1}.

The factors that govern what bonds (and what vibrations) show up at what frequencies are easily handled by computational chemistry software. In fact, prediction of absorption frequencies in IR spectra can be done using 17th century classical mechanics, specifically Hooke's Law (devised to explain the vibrational frequencies of springs). Computation is not the focus of this chapter but it may help you keep track of what kinds of vibrations absorb at what frequencies.

Hooke's Law states:

- the vibrational frequency is proportional to the strength of the spring; the stronger the spring, the higher the frequency.
- the vibrational frequency is inversely proportional to the masses at the ends of the spring; the lighter the weights, the higher the frequency.

IR light is absorbed if it is in resonance with a vibrating bond; that means the light's frequency is the same as the frequency of the bond vibration, or else an exact multiple of it (2x, 3x, 4x...). It's a little like pushing a child on a swing: unless you are pushing at the same frequency that the swing is swinging, you will not be able to transfer your energy to the swing.

Hooke's Law in IR spectroscopy means:

- stronger bonds absorb at higher frequencies.
- weaker bonds absorb at lower frequencies.
- bonds between lighter atoms absorb at higher frequencies.
- bonds between heavier atoms absorb at lower frequencies.

Remember, there are two factors here, so you won't be able to make predictions knowing only one factor. Some strong bonds may not absorb at high frequency because they are between heavy atoms. The information is presented mostly to help you organize what bonds absorb at what general frequencies after you have learned about them.

The reasons explaining why C-H bending vibrations are at lower frequency than C-H stretching vibrations are also related to Hooke's Law. An H-C-H bending vibration involves three atoms, not just two, so the mass involved is greater than in a C-H stretch. That means lower frequency. Also, it turns out that the "stiffness" of a bond angle (analogous to the strength of a spring) is less than the "stiffness" of a bond length; the angle has a little more latitude to change than does the length. Both factors lead to a lower bending frequency.

? Exercise 3.3.1

For each of the following pairs, identify which bond would show up at a higher wavenumber in the IR spectrum:

a) C-H or C-O b) C-O or C=O c) C=N or C≡N

d) N-H or N-O e) a covalent O-H bond or a hydrogen bond in water

Answer

a) C-H shows up at higher wavenumber, because H is lighter than O

b) C=O shows up at higher wavenumber, because a double bond is stronger than a single

c) C=N shows up at higher wavenumber, because a triple bond is stronger than a double

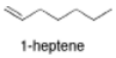
d) N-H shows up at higher wavenumber, because H is lighter than O

e) Covalent O-H shows up at higher wavenumber, because a covalent bond is stronger than a hydrogen bond

---

3.4: Carbon-Carbon Multiple Bonds

Unsaturated hydrocarbons contain only carbon and hydrogen, but also have some multiple bonds between carbons. One type of unsaturated hydrocarbon is an olefin, also known as an alkene. Alkenes contain double bonds between carbons. One example of an alkene is 1-heptene. It looks similar to hexane, except for the double bond from the first carbon to the second.



1-heptene

Look at the IR spectrum of 1-heptene. You should see:

- a set of peaks dipping down from the baseline at about 2900 cm^{-1}.
- another set of peaks dipping down from the baseline at about 1500 cm^{-1}.

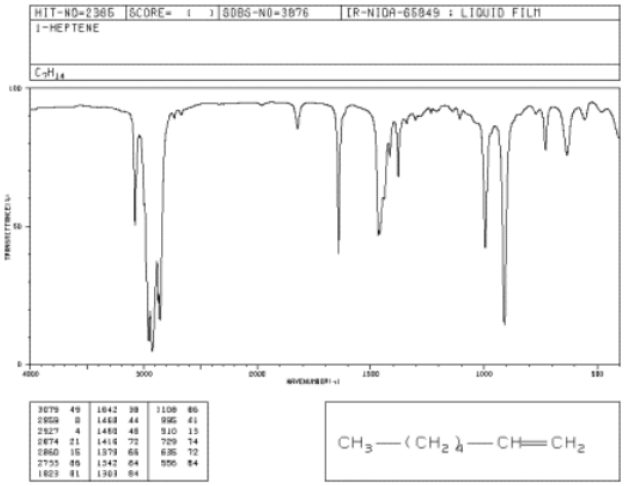


Figure 3.4.1: IR spectrum of 1-heptene.

So far, these peaks are the same as the ones seen for hexane. We can assign them as the C-H stretching and bending frequencies, respectively.

Looking further, you will also see:

- a small peak around 3100 cm^{-1}.
- a small peak near 1650 cm^{-1}.
- medium peaks near 900 and 1000 cm^{-1}.

The peak at 3100 cm^{-1} hardly seems different from the C-H stretch seen before. It is also a C-H stretch, but from a different type of carbon. This stretch involves the sp^2 or trigonal planar carbon of the double bond, whereas the peak at 2900 involves an sp^3 or tetrahedral carbon.

The peak at 1650 cm^{-1} can be identified via computational methods as arising from a carbon-carbon double bond stretch. It is a weak stretch because this bond is not very polar. Sometimes it is obscured by other, larger peaks.

The larger peaks near 800 and 1000 cm^{-1} are bending vibrations. They are due to a C=C-H bond angle that bends **o**ut **o**f the **p**lane of the double bond (remember that the carbons on either end of the double bond are trigonal planar). They are called oop bends. Oop bends are often prominent in alkenes and are easier to spot than an sp^2 C-H stretching mode or a C=C stretching mode.

? Exercise 3.4.1

Given this information about the infrared spectra of alkenes, which bond do you think is stronger, an sp^2 or an sp^3 C-H bond?

Answer

A $C_{sp}2$-H bond is stronger than a $C_{sp}3$-H bond.

Exercise 3.4.2

What do you think would happen to the peak due to carbon-carbon double bond stretching if an electronegative atom were nearby in the molecule?

Answer

The electronegative atom would polarize the nearby C=C bond. The C=C peak in the IR spectrum would become more intense; it might be a medium-sized peak instead of a weak one.

Exercise 3.4.3

Oop bends can be diagnostic of the position and geometry of double bonds.

a. Compare the oop bending modes or peaks seen in 1-heptene to those in *Z*-2-octene, aka *cis*-2-octene (in *Z*-2-octene, the double bond adopts a curled shape with alkyl substituents coming from the same side of the double bond).

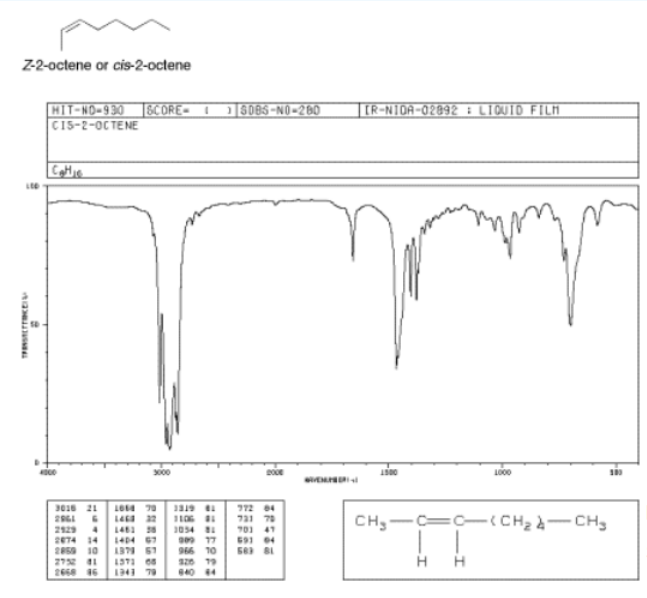


Figure 3.4.2: IR spectrum of Z-2-octene. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

b. Also compare it to *E*-2-octene, aka trans-2-octene (in which the double bond has a zig-zag shape, with alkyl substituents coming from opposite sides).

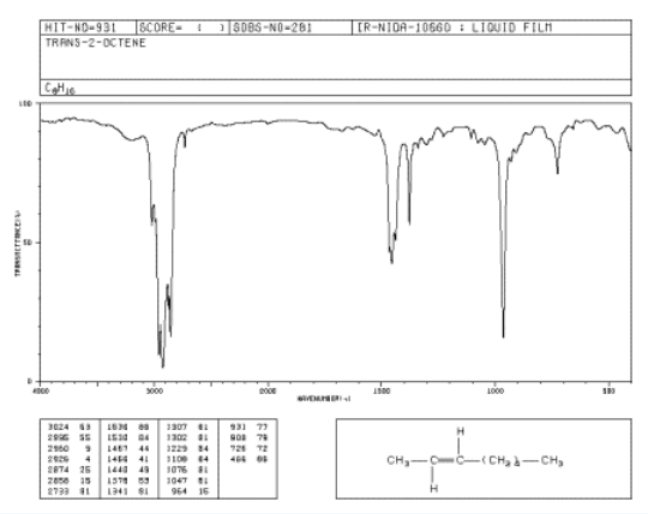
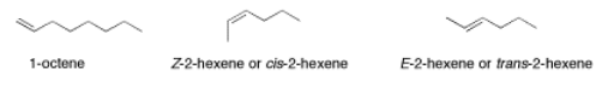


Figure 3.4.3: IR spectrum of *E*-2octene.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

c) Make predictions about the oop bending modes in 1-octene, *Z*-2-hexene and *E*-2-hexene.



Answer

a) In the terminal alkene, in which the double bond was at the end of the chain, there were two oop bends showing at 900 and 1000 cm^{-1}. In the internal, *cis*-alkene, a single oop bend shows near 700 cm^{-1}.

b) In the *cis*-alkene, a single oop bend shows near 700 cm^{-1}. In the *trans*-alkene, that single oop bend shifts closer to 1000 cm^{-1}.

c) 1-octene: two IR bands, near 900 and 1000 cm^{-1}.

cis-2-hexene: one IR bands, near 700 cm^{-1}.

trans-2-hexene: one IR band, near 1000 cm^{-1}.

? Exercise 3.4.4

Why do you think an sp^3 CH_2 bending mode occurs around 1500 cm^{-1} but a C=CH oop bending mode occurs around 800-1000 cm^{-1} ?

Answer

A CH_2 or H-C-H bending mode involves three atoms: two hydrogens and a carbon. A C=C-H oop bend also involves three atoms: two carbons and a hydrogen. The reduced mass of the atoms involved in the oop bend is greater than the reduced mass of the atoms involved in the CH_2 bend. The oop bend shows up at a lower frequency.

? Exercise 3.4.5

In the IR spectrum of 1-octyne, new peaks appear at 3300 and 2100 cm^{-1}.

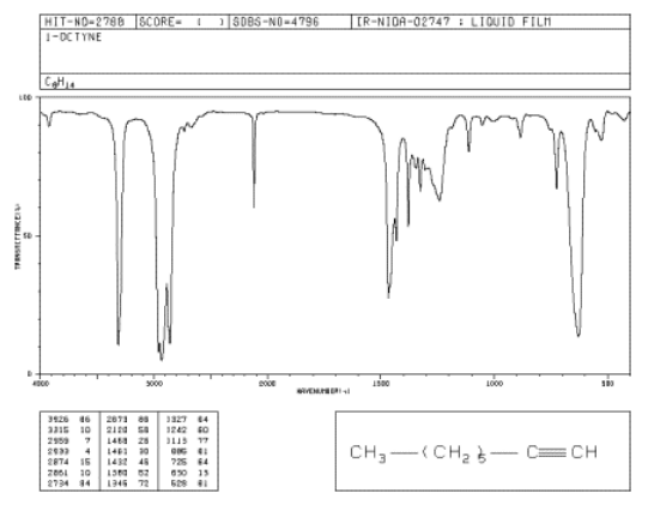


Figure 3.4.4: IR spectrum of octyne.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

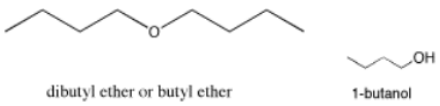
a. By comparison with the other hydrocarbons, can you identify the peak at 3300 cm^{-1} ?
b. The peak at 2100 cm^{-1} is due to a carbon-carbon bond. Which one? Compare this peak to the one seen from a carbon-carbon bond in 1-hexene and explain the differences.

3.5: Bonds to Common Heteroatoms- Oxygen

These bonds are pretty polar, so they show up strongly in IR spectroscopy. IR spectroscopy is therefore a good way to determine what heteroatom-containing functional groups are present in a molecule.

Compounds Containing C-O Single Bonds

Oxygen forms two bonds. An oxygen atom could be found in between two carbons, as in dibutyl ether, or between a carbon and a hydrogen as in 1-butanol. Dibutyl ether is an example of an ether and 1-butanol is an example of an alcohol.



dibutyl ether or butyl ether 1-butanol

If you look at an IR spectrum of dibutyl ether, you will see:

- there are the usual sp^3 C-H stretching and CH_2 bending modes at 2900 and 1500 cm^{-1}.
- there is a strong peak near 1000 cm^{-1}. This peak is due to the C-O stretching vibration.

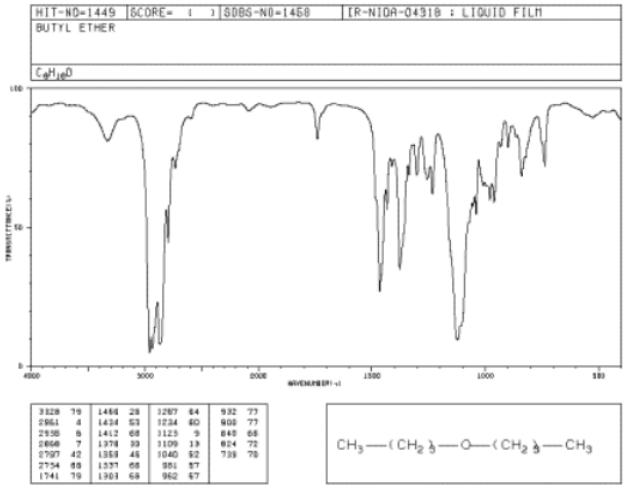


Figure 3.5.1: IR spectrum of dibutyl ether.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

If you look at an IR spectrum of 1-butanol, you will see:

- there are sp^3 C-H stretching and CH_2 bending modes at 2900 and 1500 cm^{-1}.
- there is a strong C-O stretching mode near 1000 cm^{-1}.
- there is a very large peak around 3400 cm^{-1}. O-H peaks are usually very broad like this one.

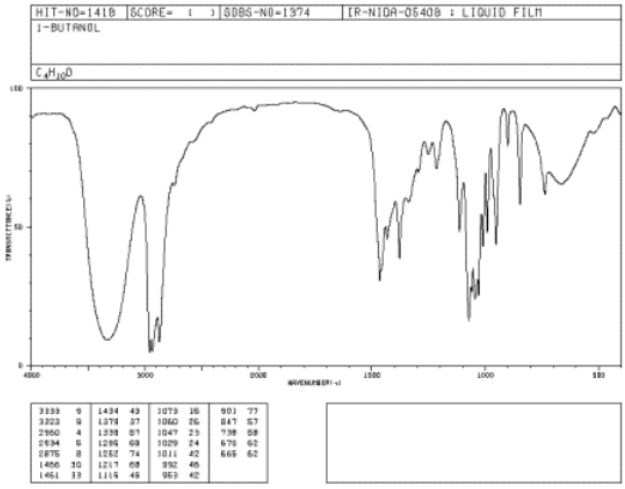


Figure 3.5.2: IR spectrum of 1-butanol.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

Peak shapes are sometimes very useful in recognizing what kind of bond is present. The rounded shape of most O-H stretching modes occurs because of hydrogen bonding between different hydroxy groups. Because protons are shared to varying extent with neighboring oxygens, the covalent O-H bonds in a sample of alcohol all vibrate at slightly different frequencies and show up at slightly different positions in the IR spectrum. Instead of seeing one sharp peak, you see a whole lot of them all smeared out into one broad blob. Since C-H bonds don't hydrogen bond very well, you don't see that phenomenon in an ether, and an O-H peak is very easy to distinguish in the IR spectrum.

? Exercise 3.5.1

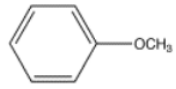
Even though there are only two C-O bonds in dibutyl ether, the C-O stretching mode is even stronger than the peak at 2900 cm^{-1} arising from 10 different C-H bonds. Explain why.

Answer

The C-O bond is much more polar than the C-H bond. More polar bonds absorb IR light much more strongly than less polar or nonpolar ones.

? Exercise 3.5.2

The IR spectrum of methyl phenyl ether (aka anisole) has strong peaks at 1050 and 1250 cm^{-1}.



methoxybenzene

a. Identify the type of bond corresponding to these two peaks.
b. Why are there two peaks for this type of bond in this molecule, and not just one?
c. Draw a second, zwitterionic resonance structure for methyl phenyl ether.
d. Use the zwitterionic resonance structure to explain why one of these bonds shows up at a higher frequency than the other one.

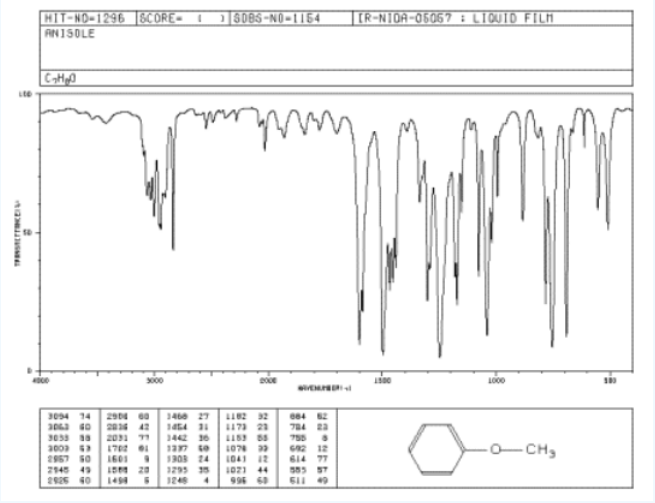


Figure 3.5.3: IR spectrum of methyl phenyl ether.

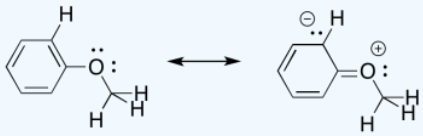
Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

Answer

a) These peaks correspond to C-O stretches.

b) There are two distinguishable C-O bonds: one is a $C_{sp}2$-O bond between the oxygen and the aromatic; the other is a $C_{sp}3$-O bond between the oxygen and the aliphatic methyl group.

c) The bond to the aromatic has some double bond character because of conjugation.



d) The partial double bond character means the $C_{sp}2$-O bond is a little stronger than the $C_{sp}3$-O bond and so the $C_{sp}2$-O bond shows up at a higher frequency.

3.6: Carbon-Oxygen Double Bonds

The largest class of oxygen-containing molecules is carbonyl compounds, which contain C=O bonds. A C=O stretch is normally easy to find in an IR spectrum, because it is very strong and shows up in a part of the spectrum that isn't cluttered with other peaks. Examples of carbonyl compounds include 2-octanone, a ketone, and butanal, an aldehyde. In an aldehyde, the carbonyl is at the end of a chain, with a hydrogen attached to the carbonyl carbon.

If you look at the IR spectrum of 2-octanone:

- there are sp^3 C-H stretching and CH_2 bending modes at 2900 and 1500 cm^{-1}.
- there is a very strong peak around 1700 cm^{-1}.

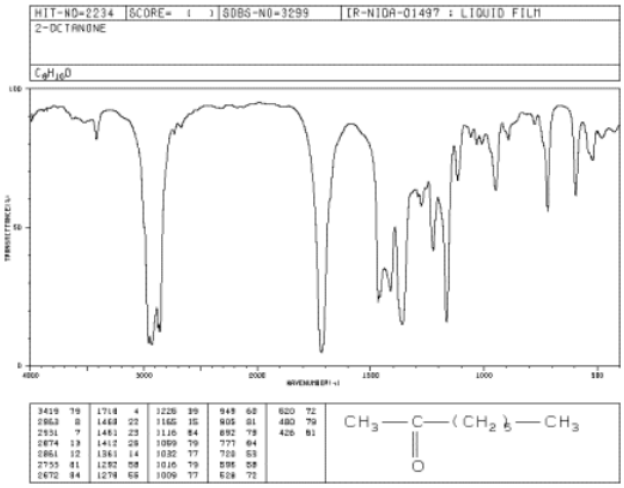


Figure 3.6.1: IR spectrum of 2-octanone.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

Even though there is just one C=O bond, the carbonyl stretch is often the strongest peak in the spectrum. That makes carbonyl compounds easy to identify by IR spectroscopy.

If you look at the IR spectrum of butanal:

- there are sp^3 C-H stretching and CH_2 bending modes at 2900 and 1500 cm^{-1}.
- there is a very strong C=O peak around 1700 cm^{-1}.
- there is a pair of medium peaks around 2700 and 2800 cm^{-1}. This is the aldehyde C-H stretching mode.

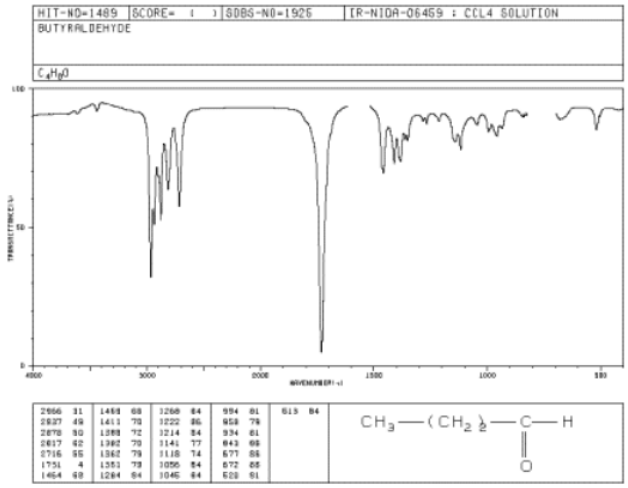


Figure 3.6.2: IR spectrum of butanal.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

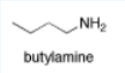
The aldehyde C-H bond absorbs at two frequencies because it can vibrate in phase with the C=O bond (a symmetric stretch) and out of phase with the C=O bond (an asymmetric stretch), and these vibrations are of different energies. The probability of the symmetric stretch and the asymmetric stretch are about equal, so the two peaks are always about the same size. This unusual C-H peak can often be used to distinguish between an aldehyde and a ketone.

3.7: Bonds to Common Heteroatoms- Nitrogen

The IR spectra of nitrogen-containing compounds can be messier than the ones you have seen so far. N-H bends and C-N stretches tend to be broader and weaker than peaks involving oxygen atoms. However, some peaks in nitrogen compounds are useful. The problems in this section will guide you through some of these features.

? Exercise 3.7.1

Amines, such as butylamine, have a very diagnostic N-H peak, although the peak is sometimes weak.



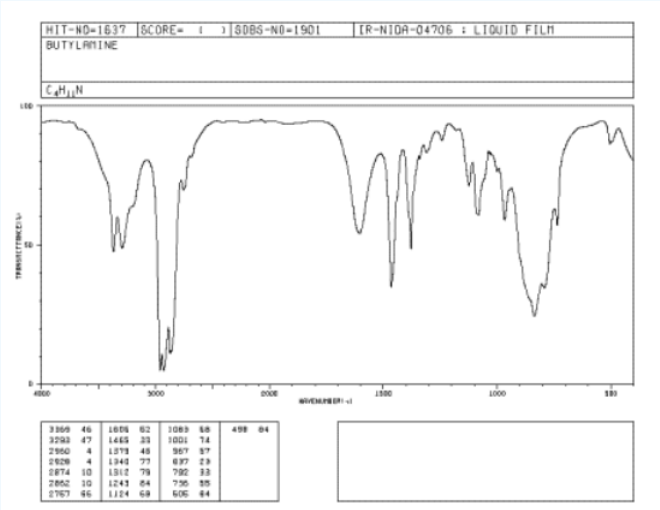


Figure 3.7.1: IR spectrum of butylamine. Source: SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

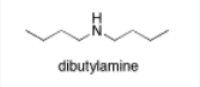
Butylamine is a primary amine, meaning the nitrogen is attached to one carbon group and two hydrogens. An N-H bond is almost as strong as an O-H bond. Can you identify the N-H peak in this spectrum?

Answer

There are actually two N-H stretching bands near 3400 and 3300 cm^{-1}. This feature is common in NH_2 groups; NH groups display only one N-H stretching band.

? Exercise 3.7.2

Dibutylamine is another example of an amine. It is a secondary amine, meaning the nitrogen is attached to one hydrogen and two other groups.



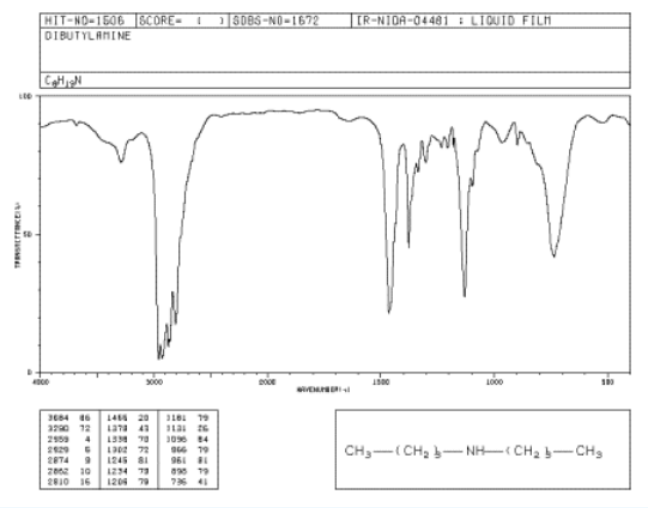


Figure 3.7.2: IR spectrum of dibutylamine. Source: SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

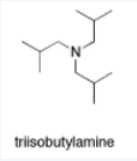
Compare its N-H peak to that of butylamine. What do you notice about the number of N-H peaks in each spectrum?

Answer

There is just one N-H stretching band near 3300 cm^{-1}.

Exercise 3.7.3

What peaks would you expect to see in the IR spectrum of triisobutylamine?



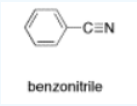
triisobutylamine

Answer

This tertiary amine has no N-H bonds. No N-H stretching frequency would appear in the IR spectrum.

Exercise 3.7.4

Benzonitrile has no N-H bonds but it does have a carbon-nitrogen triple bond that shows up in the IR spectrum. Identify the corresponding peak on the spectrum, plus two other peaks.



benzonitrile

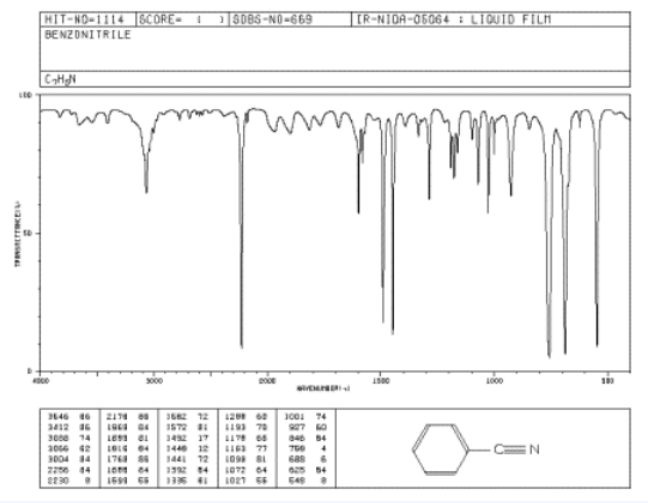


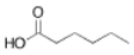
Figure 3.7.1: IR spectrum of benzonitrile. Source: SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

Answer

Figure 3.7.1: IR spectrum of benzonitrile. Source: SDBSWeb: http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

3.8: More Complicated Spectra

Sometimes more complicated heteroatomic functional groups, containing bonds to more than one heteroatom, have slightly different spectra. Carboxylic acids feature a hydroxyl group bonded to a carbonyl. Hexanoic acid, a carboxylic acid in a six-atom chain, is one example.



hexanoic acid

If you look at the IR spectrum of hexanoic acid:

- there are CH_2 bending modes at 1500 cm^{-1}.
- there is a very strong C=O peak around 1700 cm^{-1}.
- there is a medium C-O peak around 1250 cm^{-1}.
- the sp^3 C-H and O-H stretching modes are less clear.

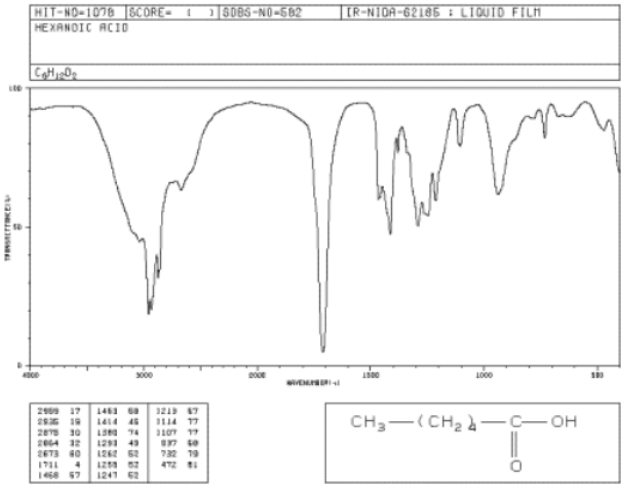
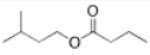


Figure 3.8.1: IR spectrum of hexanoic acid. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

At first, the O-H peak appears to be absent. The C-H stretch appears to be very broad. The wide peak between 3000 and 2600 cm^{-1} is really the usual C-H stretch with a broad O-H stretch superimposed on it. The low frequency vibration of this O-H bond is related to the partial dissociation of protons due to strong hydrogen bonding.

? Exercise 3.8.1

Isopentyl butanoate has a C-O stretch at 1200 cm^{-1}. We saw earlier that an ether had a C-O stretch around 1000 cm^{-1}. Explain the differences in these bond stretches.



isopentyl butanoate aka isopentyl butyrate

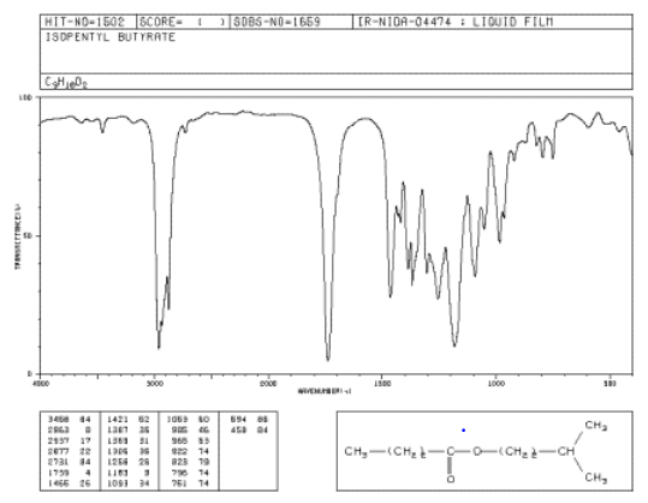
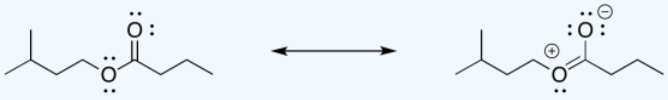


Figure 3.8.2: IR spectrum of isopentyl butanoate. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

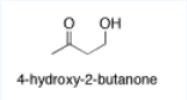
Answer

The $C_{sp}2$-O bond is conjugated, so there is some double bond character, making the bond stronger and moving the IR peak to higher frequency.



Exercise 3.8.2

Locate an O-H, a C-O and a C=O bond stretch in an IR spectrum of 4-hydroxy-2-butanone.



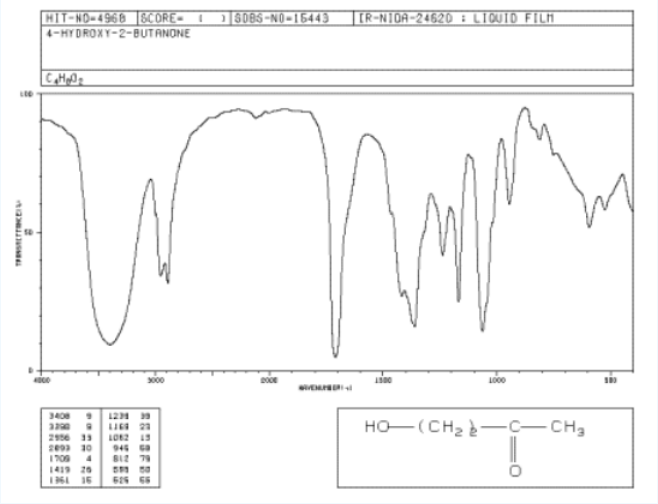


Figure 3.8.3: IR spectrum of 4-hydroxy-2-butanone. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

Answer

OH: 3400 cm^{-1} (strong, broad)

C=O: 1700 cm^{-1} (strong)

C-O: 1050 cm^{-1} (strong)

3.9: Misleading Peaks

There are some practical problems that can make IR interpretation in real life more difficult. Being aware of these problems may make you double-check your suspicions:

- water in the sample. Since water contains O-H bonds, water in a sample will make it appear as if the compound contains O-H bonds. There are experimental techniques for removing water from a sample but they must be done carefully.
- overtones in a spectrum. Overtones are absorptions occurring at different multiples of the normal frequency. Strong overtones of carbonyl peaks often occur at about twice the normal wavenumber. A large peak at 1750 cm^{-1} might be accompanied by a smaller peak at 3500 cm^{-1}, and could be confused with an O-H peak.

In addition, there are complications that you may run into based on the instrument or technique used to obtain the spectrum.

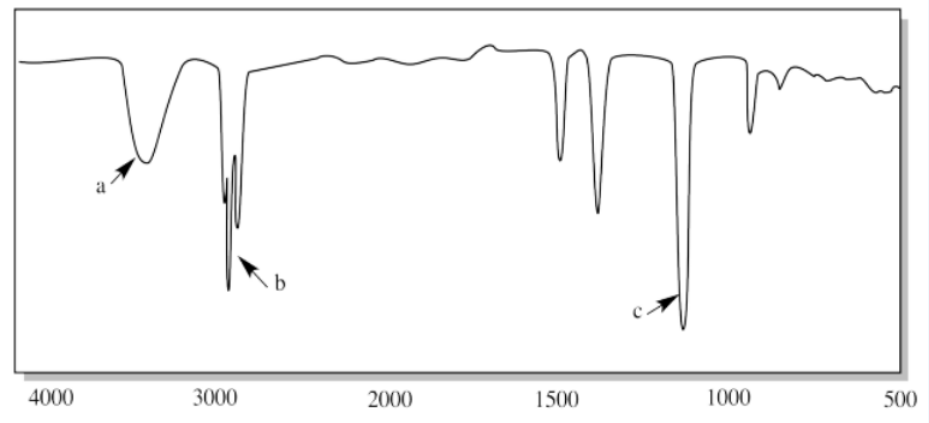
- Note that the x-axis scale on the spectrum is not uniform: the scale is indexed every 1000 cm^{-1} between 4000 and 2000 cm^{-1} and every 500 cm^{-1} below that. Spectra from different instruments may display this scale differently.
- Different techniques may lead to increased absorption at one end of the spectrum vs. the other. For example, an OH stretch is much more dominant if the sample is prepared in a KBr mull than if the spectrum is obtained via attenuated total reflectance.

3.10: Additional Problems

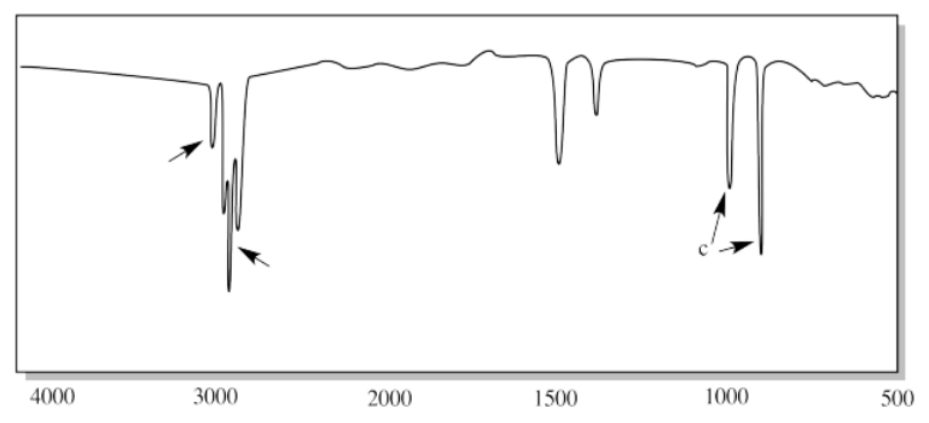
Exercise 3.10.1

For each of the following hand-drawn cartoons of IR spectra, identify the bond(s) that correspond to the indicated peaks.

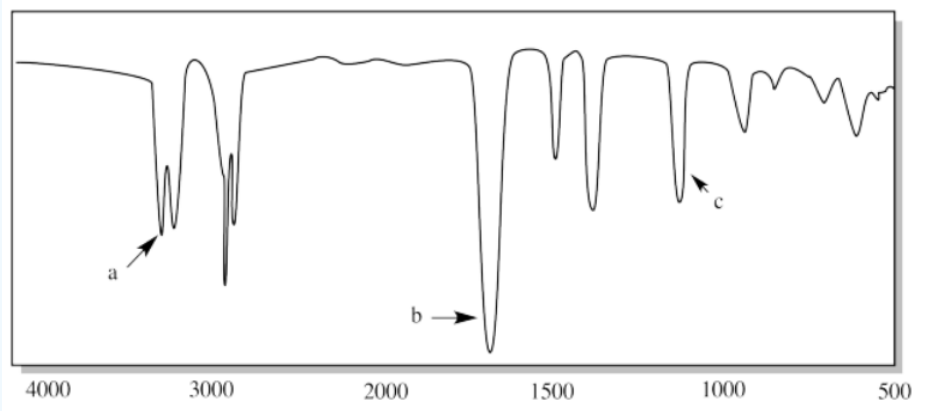
i.



ii.



iii.



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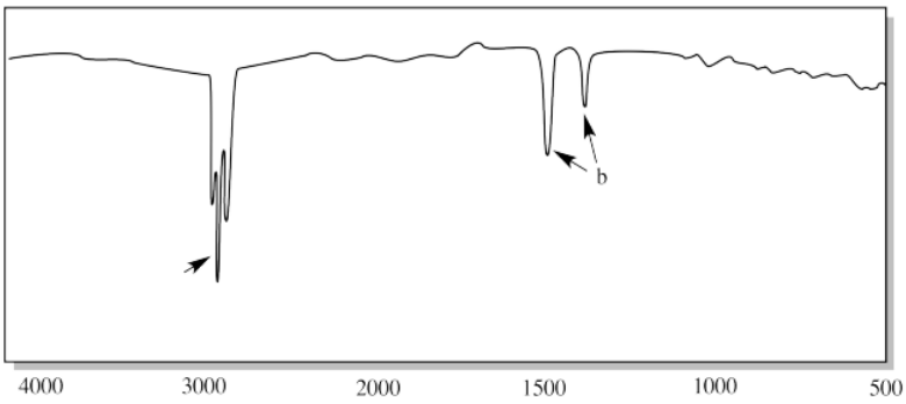
b
4000
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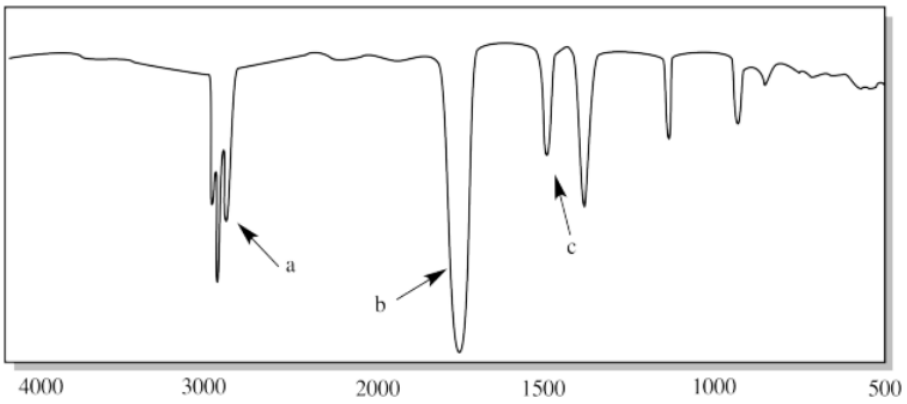
v.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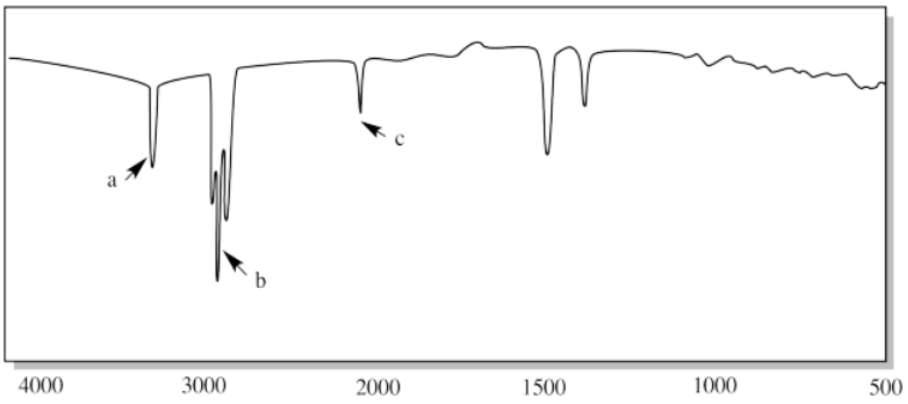
vi.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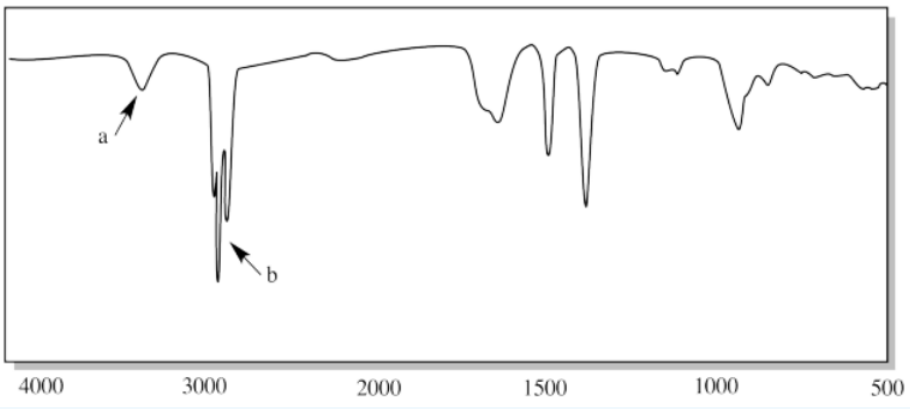
vii.


a
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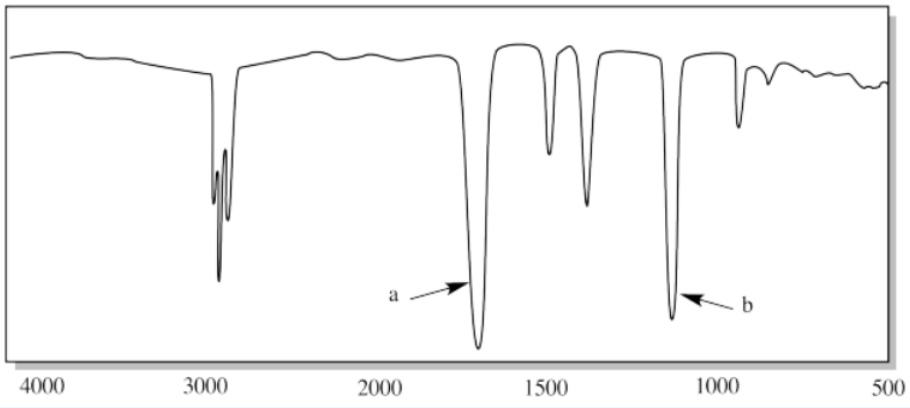
viii.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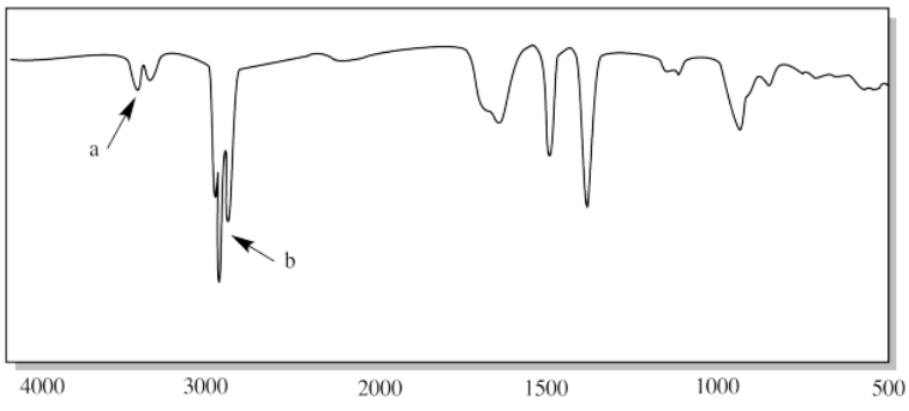
ix.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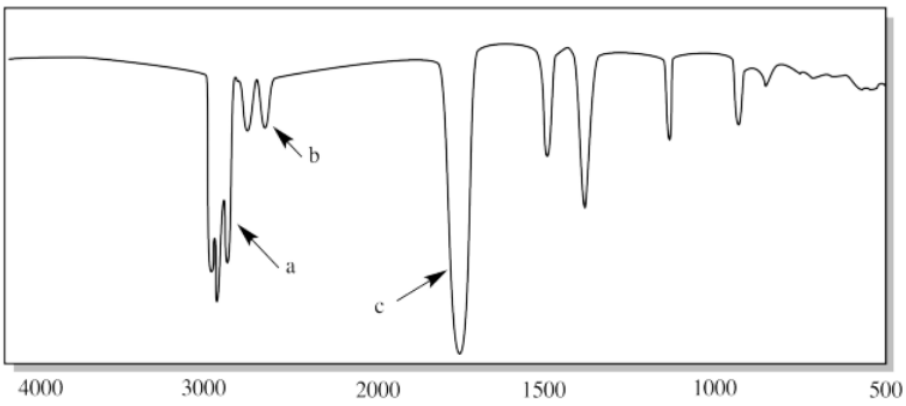
x.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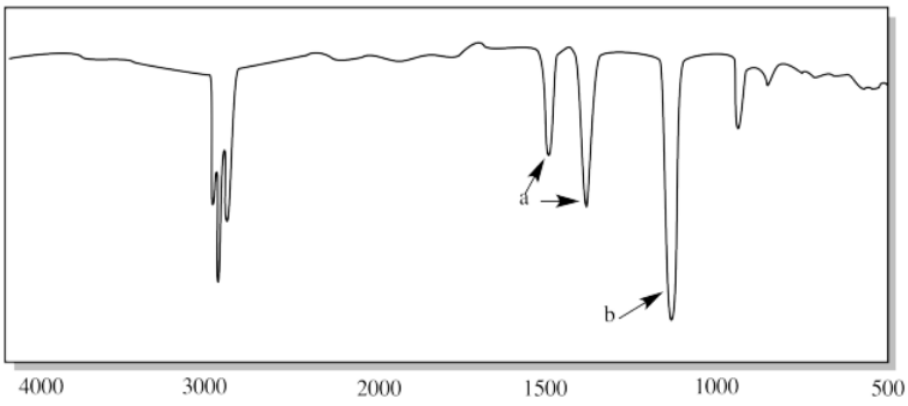
xi.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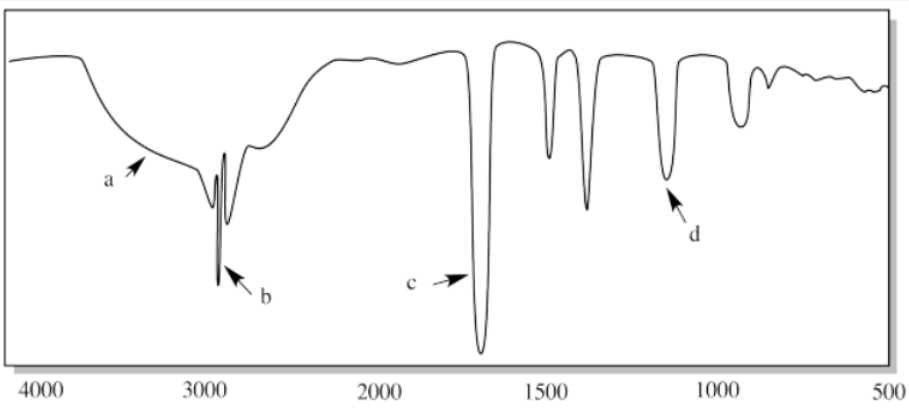
xii.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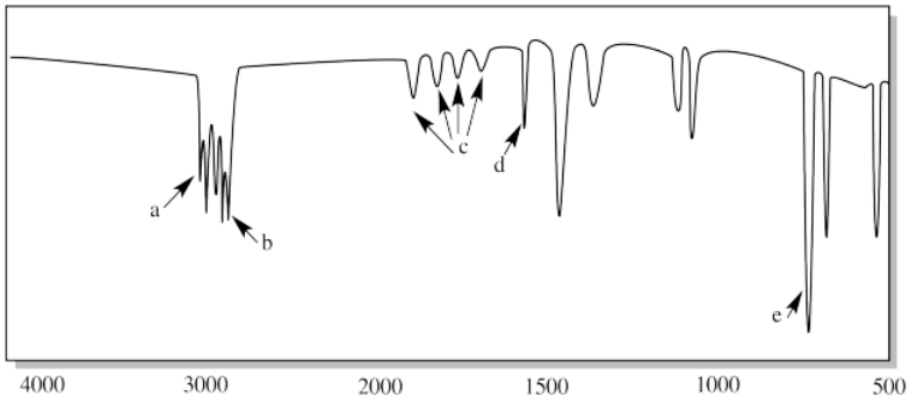
xiii.



Answer

i. a) O-H b) sp^3 C-H c) C-O

ii. a) sp^2 C-H b) sp^3 C-H c) C=C-H (oop bend)

iii. a) N-H (two of them) b) C=O c) C-N

iv. a) sp^3 C-H b) H-C-H (CH_2 bend)

v. a) sp^3 C-H b) C=O c) H-C-H (CH_2 bend)

vi. a) sp C-H b) sp^3 C-H c) C≡C

vii. a) N-H b) sp^3 C-H

viii. a) C=O b) C-O

ix. a) N-H (two of them) b) sp^3 C-H

x. a) sp^3 C-H b) aldehyde C-H c) C=O

xi. a) H-C-H (CH_2 bend) b) C-O

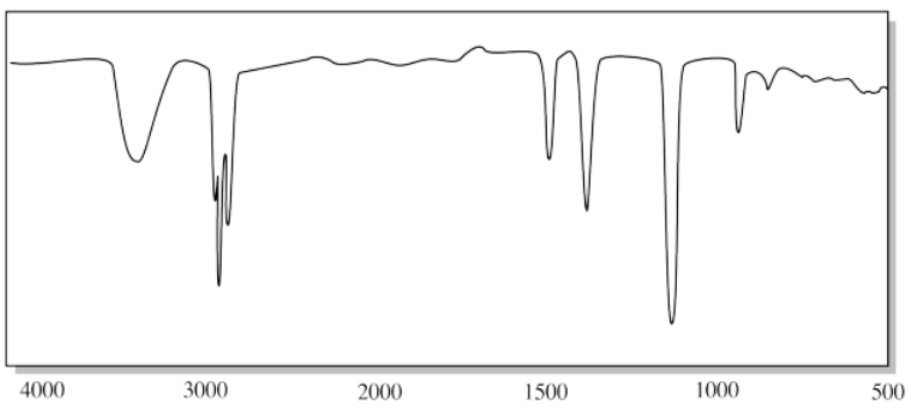
xii. a) O-H (very broad in CO_2H) b) sp^3 C-H c) C=O d) C-O

xiii. a) sp^2 C-H b) sp^3 C-H c) aromatic overtones d) C=C

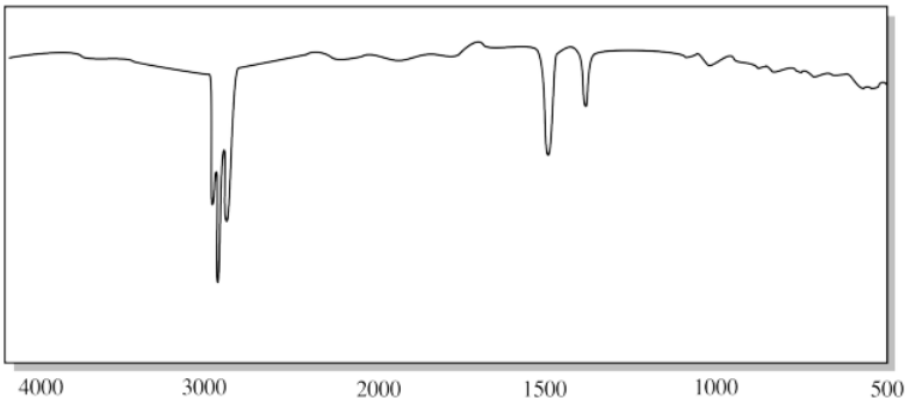
Exercise 3.10.2

For each of the following hand-drawn cartoons of IR spectra, identify the functional group suggested by the spectrum.

a)



b)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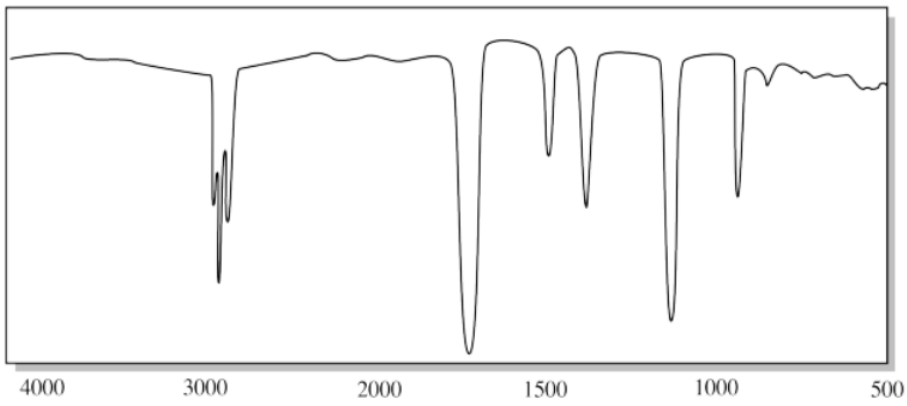
c)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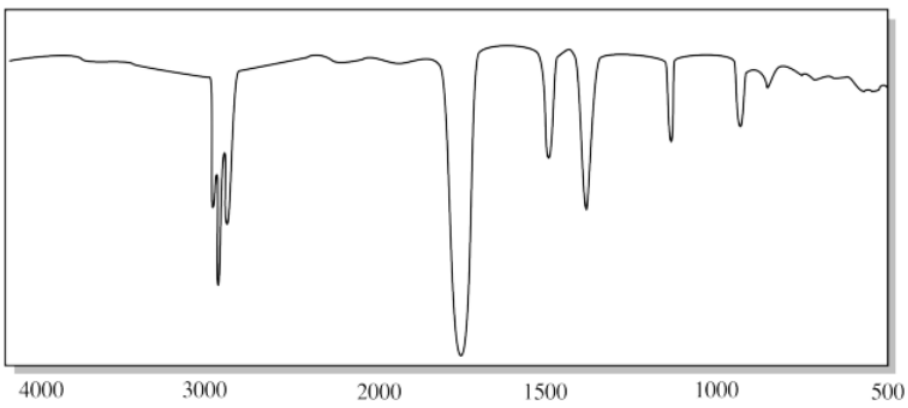
d)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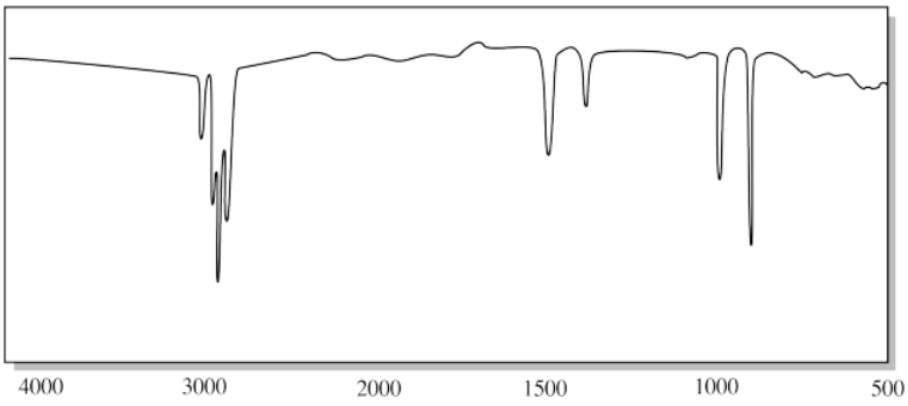
e)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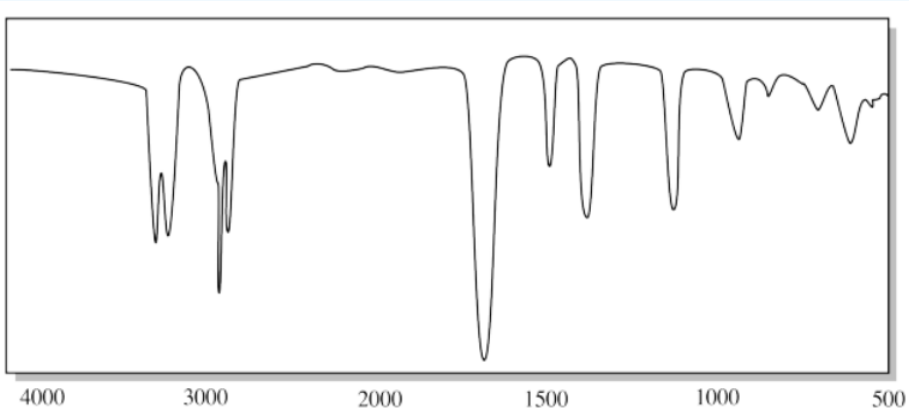
f)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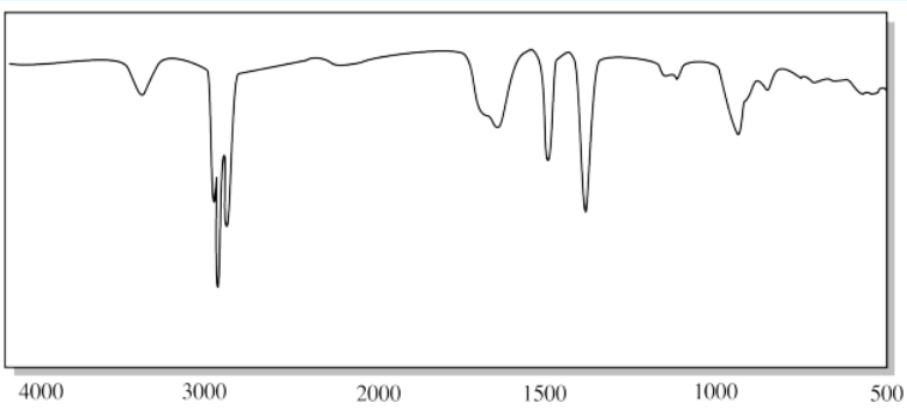
g)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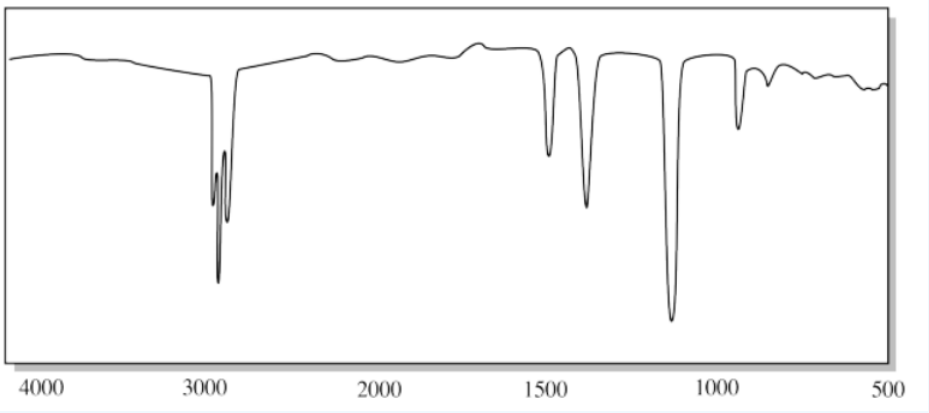
h)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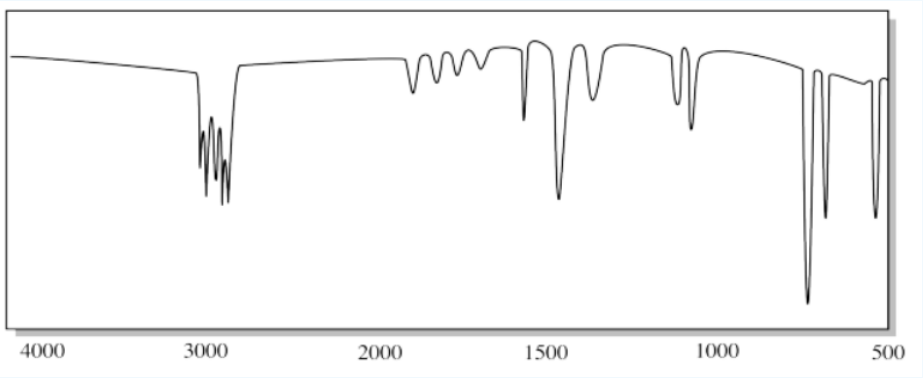
i)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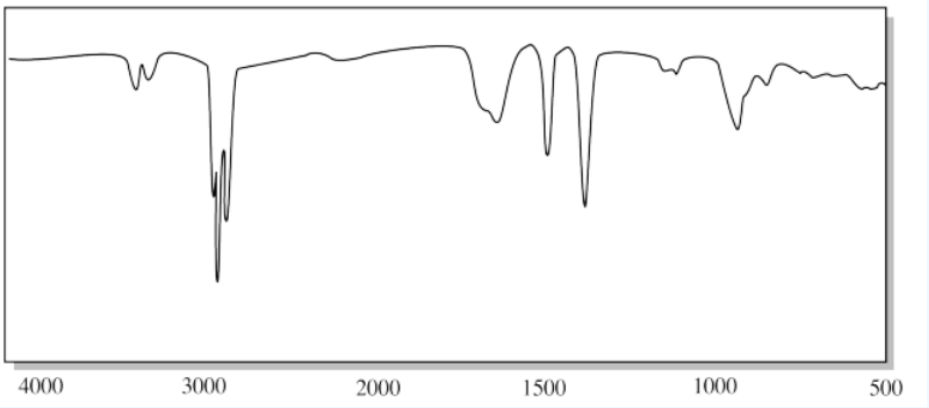
j)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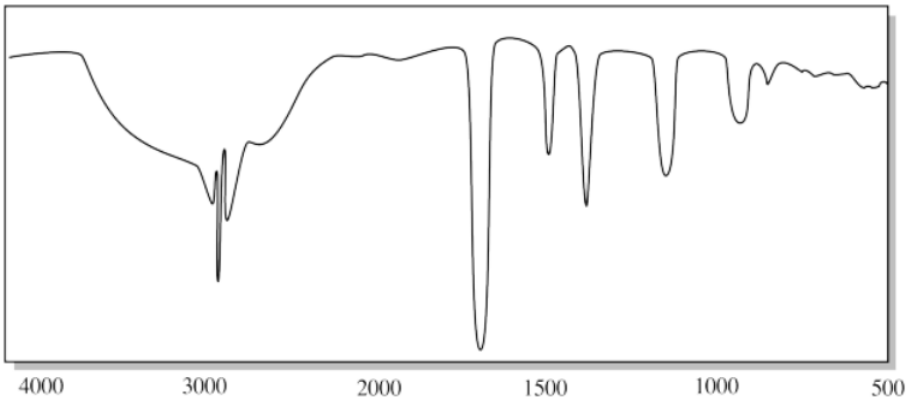
k)



Answer

a) The rounded OH peak near 3300 cm^{-1} and the strong C-O peak near 1100 cm^{-1} suggest an alcohol.

b) The sharp CH peaks below 3000 cm^{-1}, the weak CH_2 bending modes near 1500 cm^{-1} and the absence of any other features suggest an alkane.

c) The strong C=O peak near 1700 cm^{-1} and the strong C-O peak near 1100 cm^{-1} suggest an ester.

d) The strong C=O peak near 1700 cm^{-1} and the absence of additional features other than those associated with saturated hydrocarbons suggest a ketone.

e) The CH peak above 3000 cm^{-1} and the strong oop bending modes below 1000 cm^{-1} suggest an alkene. The presence of two oop bending peaks may point to a terminal alkene ($C=CH_2$).

f) The sharp N-H peaks near 3200 cm^{-1} and the strong C=O peak near 1600 cm^{-1} suggest an amide. the presence of two N-H peaks rather than one points to a primary amide ($O=C-NH_2$).

g) The small, triangular "sharktooth" peak near 3200 cm^{-1} suggests an amine. With just one N-H peak, this is probably a primary amine ($R-NH_2$).

h) The strong C-O peak near 1100 cm^{-1} suggests an ether.

i) The C-H peaks above 3000 cm^{-1} and the oop bending modes below 1000 cm^{-1} certainly suggest double bonds. The progression of tooth-like "aromatic overtones" between 1600 and 2000 cm^{-1} strongly indicates a substituted benzene.

j) The small, triangular "sharktooth" peaks near 3200 cm^{-1} suggest an amine. With two N-H peaks, this is probably a secondary amine (R_2NH).

l) The broad, deep OH peak between 3300 cm^{-1} and 2600 cm^{-1} and the C=O peak near 1700 cm^{-1} suggests a carboxylic acid. The O-H peak of a carboxylic acid is often missed; it is moved to lower frequency by hydrogen bonding.

? Exercise 3.10.3

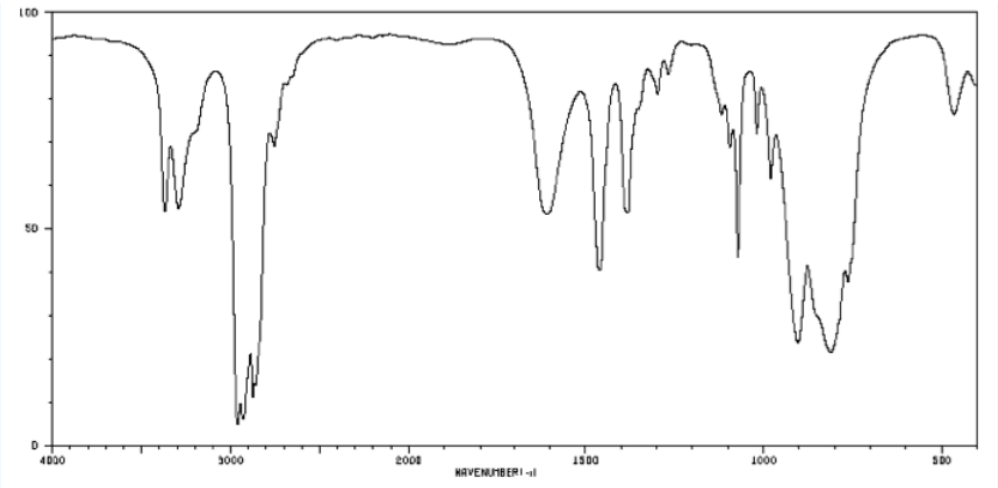
a) Identify at least three important peaks/bonds in each of the following IR spectra.

b) Identify the functional group present in each of these samples. See the Functional Group Section

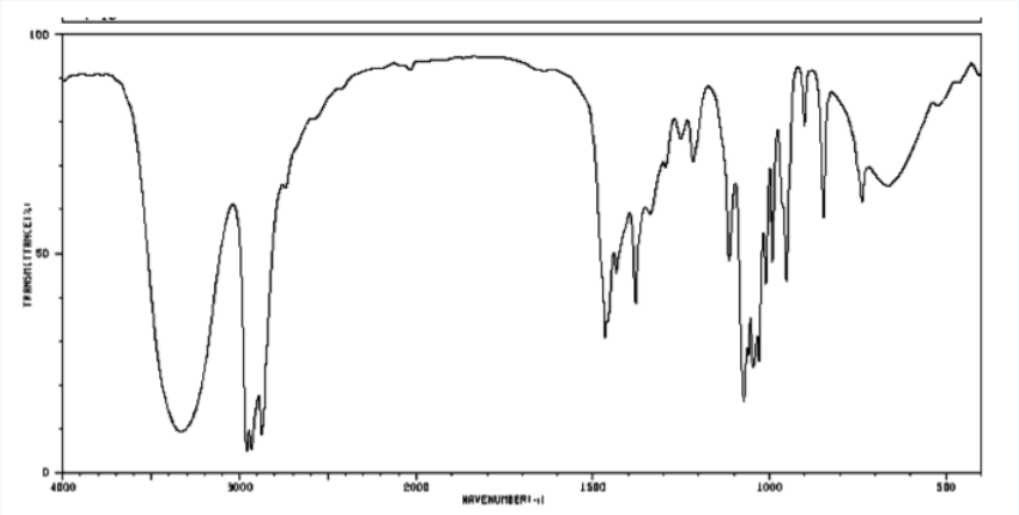
for help.

c) Draw a possible structure for each of these compounds (there may be many, many correct answers).

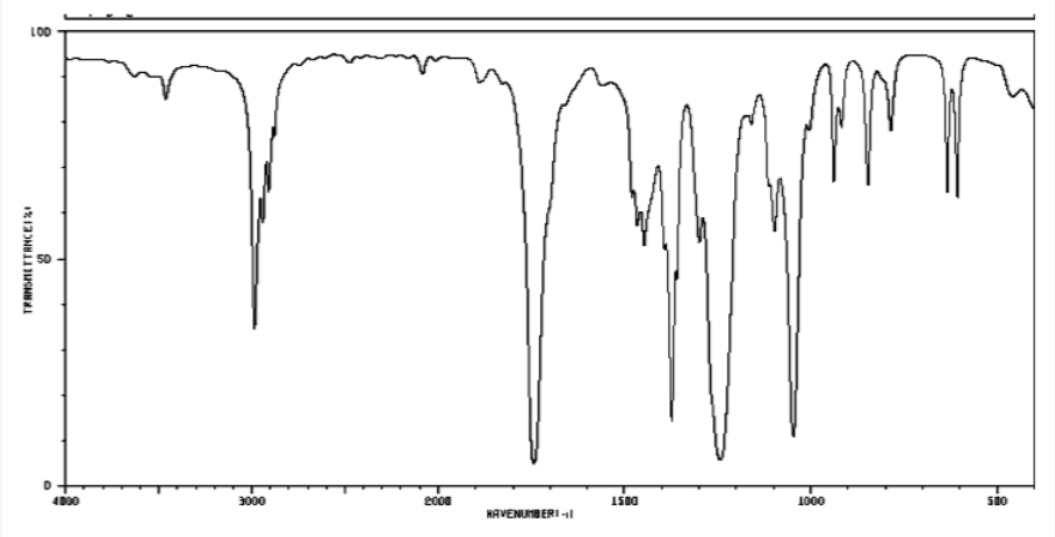
problem i)



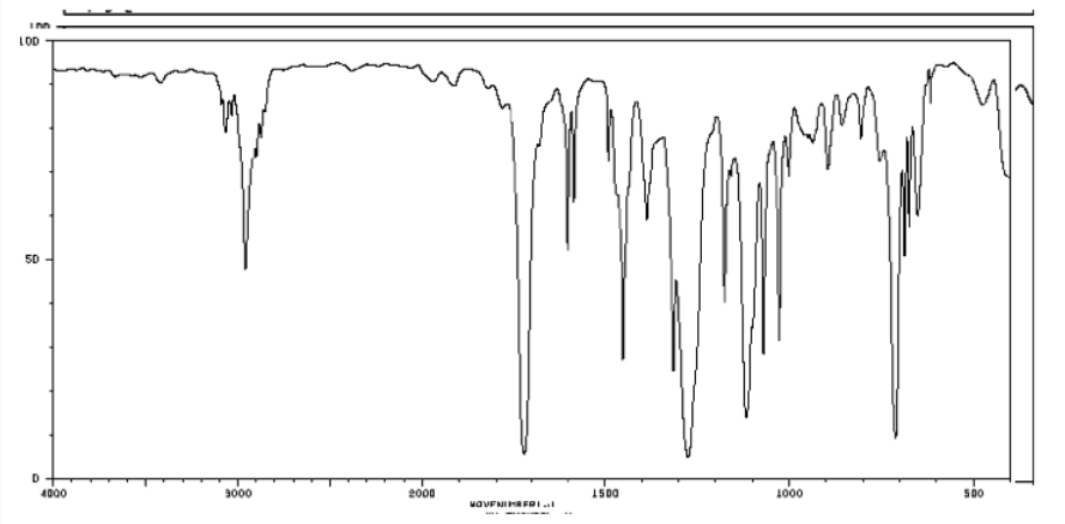
problem ii)



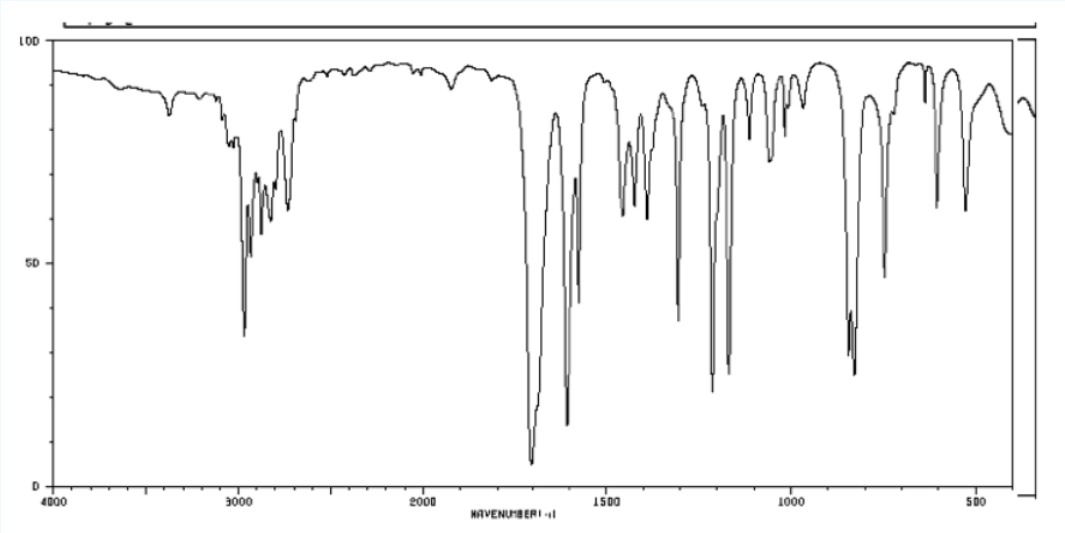
problem iii)



problem iv)



problem v)



Answer

i)

a)

3200 cm^{-1} (sharp): N-H

2900 cm^{-1} (sharp): $C_{sp}3$-H

1600 cm^{-1} (broad): probably NH_2 bending

b) A primary amine.

c)

ii)

a)

3400 cm^{-1} (strong, broad): O-H

2900 cm^{-1} (sharp): $C_{sp}3$-H

1050 cm^{-1} (strong): probably C-O

b) Alcohol.

c)

iii)

a)

2900 cm^{-1} (sharp): $C_{sp}3$-H

1700 cm^{-1} (strong): C=O

1200 and 1000 cm^{-1} (strong & medium): C-O

b) Ester

c)

iv)

a)

3050 cm^{-1} (sharp): $C_{sp}2$-H

1700 cm^{-1} (strong): C=O

1200 and 1000 cm^{-1} (strong & medium): C-O

b) Ester; probably contains an aromatic as well

c)

v)

a)

2750 and 2650 cm^{-1} (medium, sharp): C-H of an aldehyde

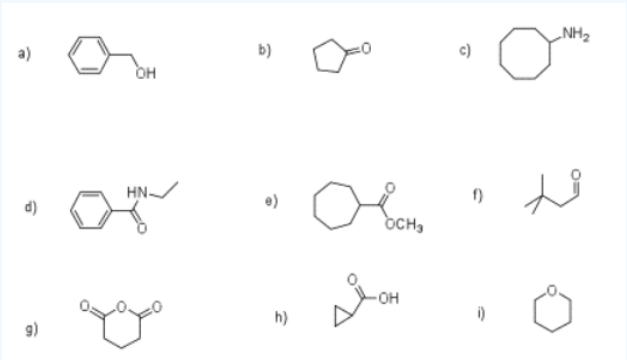
1700 cm^{-1} (strong): C=O

Below 1000 cm^{-1} (strong & medium): oop bends

b) Aldehyde; probably contains an aromatic as well

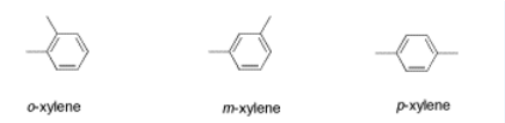
Exercise 3.10.4

Sketch an approximate IR spectrum for each of the following compounds:



Exercise 3.10.5

The oop bends are sometimes useful in distinguishing substitution pattrens around a benzene ring. Using the spectra of o-, m-, and p-xylene, formulate some guidelines about what the oop bends look like when substituents are one, two or three carbons away on a benzene ring.



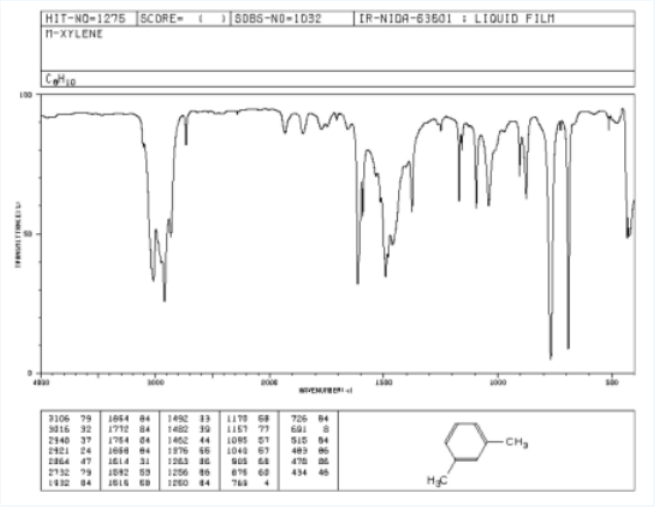


Figure 3.10.1: IR spectrum of m-xylene.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

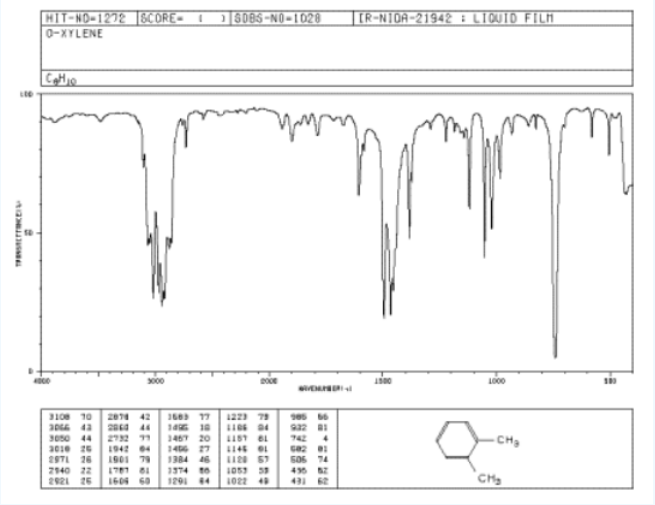


Figure 3.10.2: IR spectrum of o-xylene.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008)

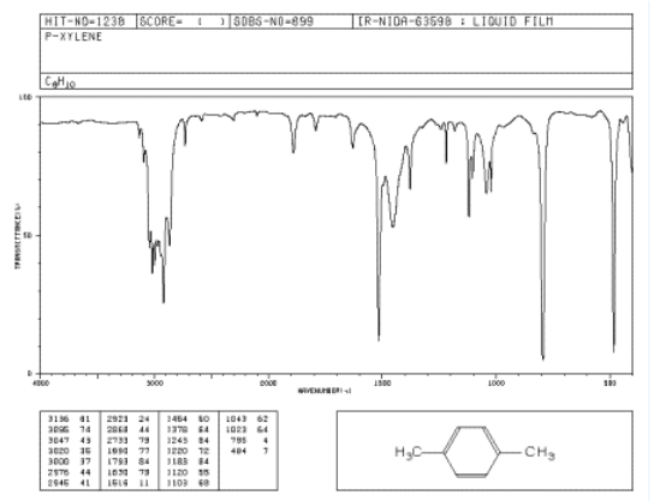


Figure 3.10.3 IR spectrum of p-xylene.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 14 July 2008

3.11: Solutions for Selected Problems

Exercise 3.3.1:

a) C-H shows up at higher wavenumber, because H is lighter than O

b) C=O shows up at higher wavenumber, because a double bond is stronger than a single

c) C≡N shows up at higher wavenumber, because a triple bond is stronger than a double

d) N-H shows up at higher wavenumber, because H is lighter than O

e) Covalent O-H shows up at higher wavenumber, because a covalent bond is stronger than a hydrogen bond

Exercise 3.4.1:

A $C_{sp}2$-H bond is stronger than a $C_{sp}3$-H bond.

Exercise 3.4.2:

The electronegative atom would polarize the nearby C=C bond. The C=C peak in the IR spectrum would become more intense; it might be a medium-sized peak instead of a weak one.

Exercise 3.4.3:

a) In the terminal alkene, in which the double bond was at the end of the chain, there were two oop bends showing at 900 and 1000 cm^{-1}. In the internal, *cis*-alkene, a single oop bend shows near 700 cm^{-1}.

b) In the *cis*-alkene, a single oop bend shows near 700 cm^{-1}. In the *trans*-alkene, that single oop bend shifts closer to 1000 cm^{-1}.

c) 1-octene: two IR bands, near 900 and 1000 cm^{-1}.

cis-2-hexene: one IR bands, near 700 cm^{-1}.

trans-2-hexene: one IR band, near 1000 cm^{-1}.

Exercise 3.4.4:

A CH_2 or H-C-H bending mode involves three atoms: two hydrogens and a carbon. A C=C-H oop bend also involves three atoms: two carbons and a hydrogen. The reduced mass of the atoms involved in the oop bend is greater than the reduced mass of the atoms involved in the CH_2 bend. The oop bend shows up at a lower frequency.

Exercise 3.4.5:

The peak at 3300 cm^{-1} is in the same region as C-H stretching peaks in other spectra. This peak must correspond to a C_{sp}-H stretch. A C_{sp}-H bond is a little stronger than either a $C_{sp}2$-H or a $C_{sp}3$-H bond, so the peak shows up at higher wavenumber.

The peak at 2100 cm-1 is not very strong. It corresponds to a relatively non-polar C≡C bond. It is a stronger bond than a C=C bond, and so it shows up at higher frequency; the C=C bond would show up around 1600 cm^{-1}. It is also stronger than a C-C bond, which would show up around 1000 cm-1 (although peaks from C-C stretch are very weak and seldom noticed in the spectrum).

Exercise 3.5.1:

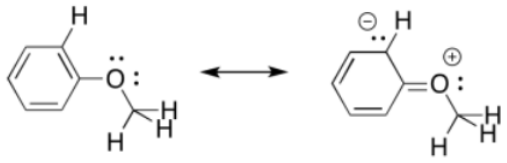
The C-O bond is much more polar than the C-H bond. More polar bonds absorb IR light much more strongly than less polar or nonpolar ones.

Exercise 3.5.2:

a) These peaks correspond to C-O stretches.

b) There are two distinguishable C-O bonds: one is a $C_{sp}2$-O bond between the oxygen and the aromatic; the other is a $C_{sp}3$-O bond between the oxygen and the aliphatic methyl group.

c) The bond to the aromatic has some double bond character because of conjugation.



d) The partial double bond character means the $C_{sp}2$-O bond is a little stronger than the $C_{sp}3$-O bond and so the $C_{sp}2$-O bond shows up at a higher frequency.

Exercise 3.7.1:

There are actually two N-H stretching bands near 3400 and 3300 cm^{-1}. This feature is common in NH_2 groups; NH groups display only one N-H stretching band.

Exercise 3.7.2:

There is just one N-H stretching band near 3300 cm^{-1}.

Exercise 3.7.3:

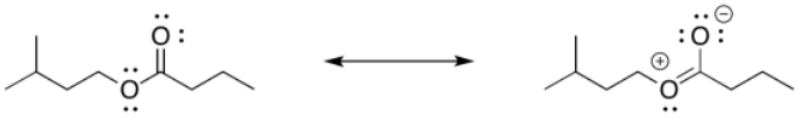
This tertiary amine has no N-H bonds. No N-H stretching frequency would appear in the IR spectrum.

Exercise 3.7.4:

The C≡N stretching frequency of the nitrile is visible near 2200 cm^{-1}. In addition, C=C-H oop bends from the aromatic group are visible below 1000 cm^{-1}. The peaks near 1500 cm-1 are likely due to C=C stretching; these peaks are more prominent than usual because of polarization by the nitrile, which is a π-acceptor. They are also at slightly low frequency because of the delocalized character of the aromatic double bonds.

Exercise 3.8.1:

The $C_{sp}2$-O bond is conjugated, so there is some double bond character, making the bond stronger and moving the IR peak to higher frequency.



Exercise 3.8.2:

OH: 3400 cm^{-1} (strong, broad)

C=O: 1700 cm^{-1} (strong)

C-O: 1050 cm^{-1} (strong)

Exercise 3.10.1:

i. a) O-H b) sp^3 C-H c) C-O

ii. a) sp^2 C-H b) sp^3 C-H c) C=C-H (oop bend)

iii. a) N-H (two of them) b) C=O c) C-N

iv. a) sp^3 C-H b) H-C-H (CH_2 bend)

v. a) sp^3 C-H b) C=O c) H-C-H (CH_2 bend)

vi. a) sp C-H b) sp^3 C-H c) C≡C

vii. a) N-H b) sp^3 C-H

viii. a) C=O b) C-O

ix. a) N-H (two of them) b) sp^3 C-H

x. a) sp^3 C-H b) aldehyde C-H c) C=O

xi. a) H-C-H (CH_2 bend) b) C-O

xii. a) O-H (very broad in CO_2H) b) sp^3 C-H c) C=O d) C-O

xiii. a) sp^2 C-H b) sp^3 C-H c) aromatic overtones d) C=C

Exercise 3.10.2:

a) The rounded OH peak near 3300 cm^{-1} and the strong C-O peak near 1100 cm^{-1} suggest an alcohol.

b) The sharp CH peaks below 3000 cm^{-1}, the weak CH_2 bending modes near 1500 cm^{-1} and the absence of any other features suggest an alkane.

c) The strong C=O peak near 1700 cm^{-1} and the strong C-O peak near 1100 cm^{-1} suggest an ester.

d) The strong C=O peak near 1700 cm^{-1} and the absence of additional features other than those associated with saturated hydrocarbons suggest a ketone.

e) The CH peak above 3000 cm^{-1} and the strong oop bending modes below 1000 cm^{-1} suggest an alkene. The presence of two oop bending peaks may point to a terminal alkene ($C=CH_2$).

f) The sharp N-H peaks near 3200 cm^{-1} and the strong C=O peak near 1600 cm^{-1} suggest an amide. the presence of two N-H peaks rather than one points to a primary amide ($O=C-NH_2$).

g) The small, triangular "sharktooth" peak near 3200 cm^{-1} suggests an amine. With just one N-H peak, this is probably a primary amine ($R-NH_2$).

h) The strong C-O peak near 1100 cm^{-1} suggests an ether.

i) The C-H peaks above 3000 cm^{-1} and the oop bending modes below 1000 cm^{-1} certainly suggest double bonds. The progression of tooth-like "aromatic overtones" between 1600 and 2000 cm^{-1} strongly indicates a substituted benzene.

j) The small, triangular "sharktooth" peaks near 3200 cm^{-1} suggest an amine. With two N-H peaks, this is probably a secondary amine (R_2NH).

l) The broad, deep OH peak between 3300 cm^{-1} and 2600 cm^{-1} and the C=O peak near 1700 cm^{-1} suggests a carboxylic acid. The O-H peak of a carboxylic acid is often missed; it is moved to lower frequency by hydrogen bonding.

Exercise 3.10.3

i)

a)

3200 cm^{-1} (sharp): N-H

2900 cm^{-1} (sharp): $C_{sp}3$-H

1600 cm^{-1} (broad): probably NH_2 bending

b) A primary amine.

c)

ii)

a)

3400 cm^{-1} (strong, broad): O-H

2900 cm^{-1} (sharp): $C_{sp}3$-H

1050 cm^{-1} (strong): probably C-O

b) Alcohol.

c)

iii)

a)

2900 cm^{-1} (sharp): $C_{sp}3$-H

1700 cm^{-1} (strong): C=O

1200 and 1000 cm^{-1} (strong & medium): C-O

b) Ester

c)

iv)

a)

3050 cm^{-1} (sharp): $C_{sp}2$-H

1700 cm^{-1} (strong): C=O

1200 and 1000 cm^{-1} (strong & medium): C-O

b) Ester; probably contains an aromatic as well

c)

v)

a)

2750 and 2650 cm^{-1} (medium, sharp): C-H of an aldehyde

1700 cm^{-1} (strong): C=O

Below 1000 cm^{-1} (strong & medium): oop bends

b) Aldehyde; probably contains an aromatic as well

c)

Problem 3.10.4

Problem 3.10.5

3.12: Appendix

Table of IR Absorptions Common in Organic Compounds

Note: strong, medium, weak refers to the length of the peak (in the y axis direction).

Note: spectra taken by ATR method (used at CSB/SJU) have weaker peaks between 4000-2500 cm^{-1} compared to reference spectra taken by transmittance methods (typical on SDBS and other sites).

Approximate Frequency (cm^{-1})	Description	Bond Vibration	Notes
3500 - 3200	broad, round	O-H	much broader, lower frequency (3200-2500) if next to C=O
3400-3300	weak, triangular	N-H	stronger if next to C=O
3300	medium-strong	≡C-H (sp C-H)	
3100-3000	weak-medium	=C-H (sp^2 C-H)	can get bigger if lots of bonds present
3000-2900	weak-medium	-C-H (sp^3 C-H)	can get bigger if lots of bonds present
2800 and 2700	medium	C-H in O=C-H	two peaks; "alligator jaws"
2250	medium	C≡N	
2250-2100	weak-medium	C≡C	stronger if near electronegative atoms
1800-1600	strong	C=O	lower frequency (1650-1550) if attached to O or N middle frequency if attached to C, H higher frequency (1800) if attached to Cl
1650-1450	weak-medium	C=C	lower frequency (1600-1450) if conjugated (i.e. C=C-C=C) often several if benzene present
1600-1450	medium	H-N-H bend	often broad
1530 and 1360	strong	N=O in $-NO_2$	two peaks
1450	weak-medium	H-C-H bend	
1300 and 1200	strong	S=O in sulfonate	two peaks
1300-1200	strong	P=O in phosphate	often double peak
1300 - 1000	medium-strong	C-O	higher frequency (1200-1300) if conjugated (i.e. O=C-O or C=C-O)
1300-1100	strong	C-F	C-F is much less common than C-O
1250-1000	medium	C-N	

1000-650	strong	C=C-H bend	often several if benzene present
800	strong	N-O	
800-600	strong	C-Cl	C-Br and C-I are below 600

CHAPTER OVERVIEW

4: Nuclear Magnetic Resonance Spectroscopy

Thumbnail: A diagram of an aromatic ring current. B_0 is the applied magnetic field, the red arrow indicating its direction. The orange ring shows the direction of the ring current, and the purple rings show the direction of the induced magnetic field. (Public Domain; Benjah-bmm27).

4.1: Introduction

Magnetic resonance imaging is a medical diagnostic technique that uses radio waves to learn about the environment of hydrogen atoms in your body. As it happens, the hydrogen atoms do not respond to the radio waves unless there is a strong magnetic field present. Looking at the hydrogen atoms in your body gives the technician and the doctor information on any of the soft tissues of the body, since they are largely composed of water and contain lots of hydrogen atoms.

Nuclear magnetic resonance (NMR) is a technique that is very closely related to magnetic resonance imaging. The term "nuclear" refers to the fact that the radio waves interact with the nucleus of the hydrogen atom, or other atoms that you might be interested in studying. NMR spectroscopy is probably the most important tool available for determining the structure of organic compounds because it tells you what atoms are present and how they are connected to each other.

4.2: ^{13}C NMR Spectroscopy

What Does the Spectrum Look Like?

Since organic compounds are largely based on carbon, ^{13}C NMR spectroscopy is a pretty important tool for studying organic compounds. The ^{13}C isotope is the only isotope of carbon that is "NMR-active"; ^{12}C and ^{14}C atoms do not absorb radio waves in a magnetic field. The ^{13}C NMR spectrum of cyclohexane is shown below.

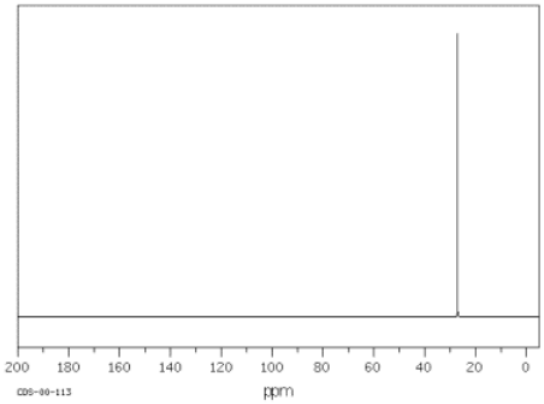


Figure 4.2.1: ^{13}C NMR spectrum of cyclohexane.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

Cyclohexane is constructed of a ring of six carbon atoms. There are two hydrogen atoms attached to each of the carbons.

Notice these features of the spectrum:

- the x axis corresponds to the energy or frequency of the radio waves that are absorbed.
- the scale on the x axis runs from roughly zero to two hundred "parts per million", abbreviated ppm.
- no scale is given on the y axis, which corresponds to the amount of radio wave "light" absorbed at a given frequency. This situation is different from IR spectroscopy, in which transmittance is plotted rather than absorbance.
- in^{13}C NMR spectroscopy, a peak looks like a spike that rises from the baseline.

There are some peculiar terms used in NMR spectroscopy that are not used in IR spectroscopy. These terms arose from the use of magnetic fields in measuring these spectra:

- the high frequency end of the spectrum, which is high ppm and is found at the left-hand end of the x axis, is termed "downfield".
- the low frequency end of the spectrum, which is low ppm and is found at the right-hand end of the x axis, is termed "upfield".
- the x-axis value is not referred to as "frequency" but rather as "chemical shift" or just "shift".

In cyclohexane, only one frequency of radio waves is absorbed by the carbon atom, and that is at about 27 ppm. Other frequencies could be absorbed by the hydrogen atoms, but hydrogen atoms absorb at very different frequencies from carbon atoms, so they wouldn't be detected in a ^{13}C NMR spectrum.

? Exercise 4.2.1

Which peak would show up farther to the right in the NMR spectrum?

a) 10 pmm or 27 ppm b) 122 ppm or 64 ppm c) 196 ppm or 158 ppm

Answer

a) 10 ppm b) 64 ppm c) 158 ppm

Exercise 4.2.2

Which peak would show up farther downfield in the NMR spectrum?

a) 17 pmm or 63 ppm b) 201 ppm or 155 ppm c) 71 ppm or 43 ppm

Answer

Which peak would show up farther downfield in the NMR spectrum?

a) 17 pmm or 63 ppm b) 201 ppm or 155 ppm c) 71 ppm or 43 ppm

---

4.3: Symmetry in Spectroscopy

Butane shows two different peaks in the ^{13}C NMR spectrum, below. Note that:

- the chemical shifts of these peaks are not very different from methane. The carbons in butane are in a similar environment to the one in methane.
- there are two distinct carbons in butane: the methyl, or CH_3, carbon, and the methylene, or CH_2, carbon.
- the methyl carbon absorbs slightly upfield, or at lower shift, around 10 ppm.
- the methylene carbon absorbs at slightly downfield, or at higher shift, around 20 ppm.
- other factors being equal, methylene carbons show up at slightly higher shift than methyl carbons.

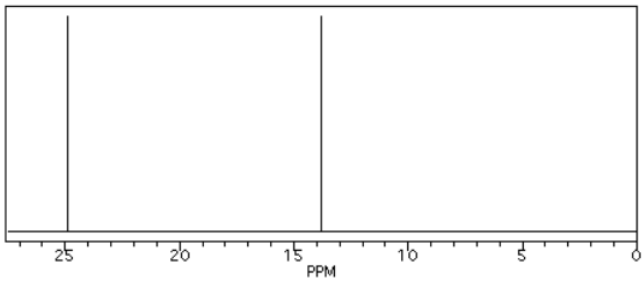


Figure 4.3.1: Simulated ^{13}C NMR spectrum of butane (showing only the upfield portion of the spectrum).

In the ^{13}C NMR spectrum of pentane (below), you can see three different peaks, even though pentane just contains methyl carbons and methylene carbons like butane. As far as the NMR spectrometer is concerned, pentane contains three different kinds of carbon, in three different environments. That result comes from symmetry.

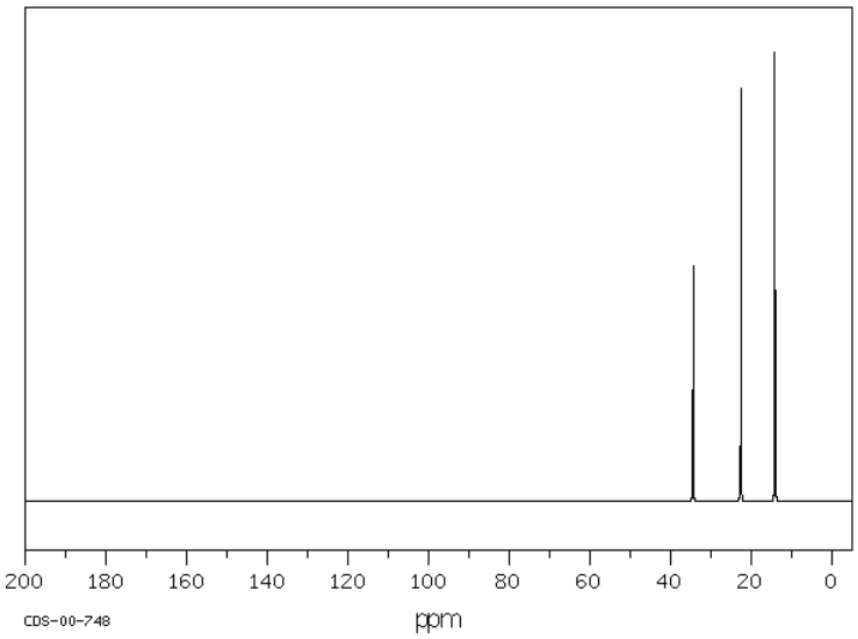


Figure 4.3.2: Simulated ^{13}C NMR spectrum of butane (showing only the upfield portion of the spectrum).

In the ^{13}C NMR spectrum of pentane (below), you can see three different peaks, even though pentane just contains methyl carbons and methylene carbons like butane. As far as the NMR spectrometer is concerned, pentane contains three different kinds of carbon, in three different environments. That result comes from symmetry.

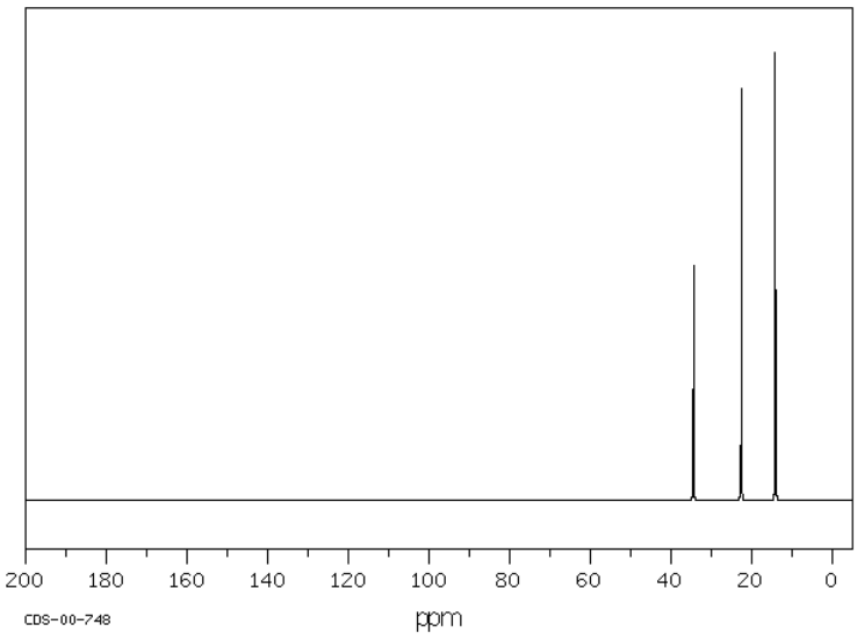


Figure 4.3.3: ^{13}C NMR spectrum of pentane. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

Symmetry is an important factor in spectroscopy. Nature says:

- atoms that are symmetry-inequivalent can absorb at different shifts.
- atoms that are symmetry-equivalent must absorb at the same shift.

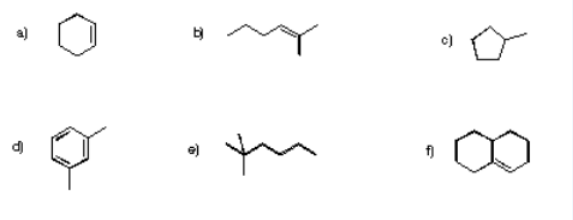
To learn about symmetry, take a model of pentane and do the following:

- make sure the model is twisted into the most symmetric shape possible: a nice "W".
- choose one of the methyl carbons to focus on.
- rotate the model 180 degrees so that you are looking at the same "W" but from the other side.
- note that the methyl you were focusing on has simply switched places with the other methyl group. These two carbons are symmetry-equivalent via two-fold rotation.

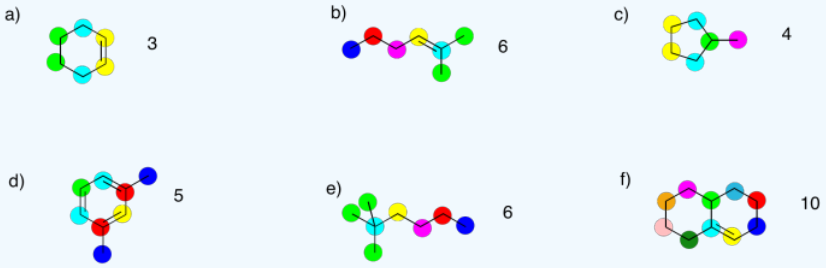
By the same process, you can see that the second and fourth carbons along the chain are also symmetry-equivalent. However, the middle carbon is not; it never switches places with the other carbons if you rotate the model. There are three different sets of inequivalent carbons; these three groups are not the same as each other according to symmetry.

Exercise 4.3.1

Determine how many inequivalent carbons there are in each of the following compounds. How many peaks do you expect in each ^{13}C NMR spectrum?



Answer



Exercise 4.3.2

Based on an IR spectrum, you have determined that your sample is a saturated hydrocarbon; it contains only C-C and C-H bonds. Assuming a straight chain structure with no branches, what could be the structure in the following cases:

a. 3 peaks in the ^{13}C spectrum
b. 4 peaks in the ^{13}C spectrum
c. 5 peaks in the ^{13}C spectrum

Answer

Based on an IR spectrum, you have determined that your sample is a saturated hydrocarbon; it contains only C-C and C-H bonds. Assuming a straight chain structure with no branches, what could be the structure in the following cases:

3 peaks in the ^{13}C spectrum 4 peaks in the ^{13}C spectrum 5 peaks in the ^{13}C spectrum

Practically speaking, there is only so much room in the spectrum from one end to the other. At some point, peaks can get so crowded together that you can't distinguish one from another. You might expect to see ten different peaks in eicosane, a twenty-carbon alkane chain, but when you look at the spectrum you can only see seven different peaks. That may be frustrating, because the experiment does not seem to agree with your expectation. However, you will be using a number of methods together to minimize the problem of misleading data.

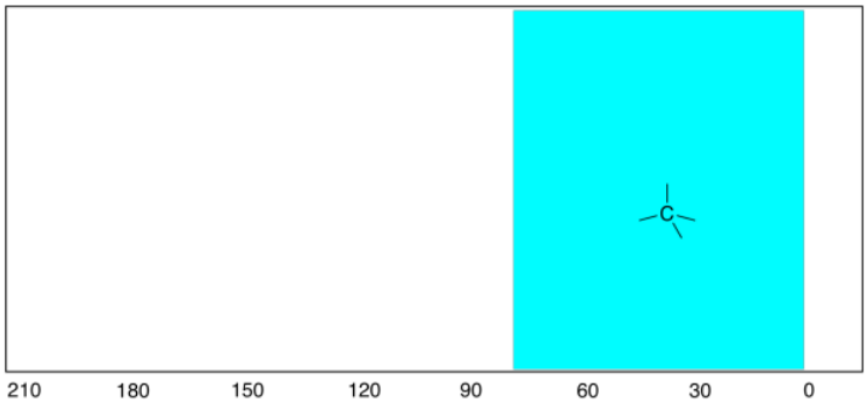
4.4: Factors in Chemical Shift- Carbon Geometry

As in IR spectroscopy, the frequency at which different carbons absorb in the NMR spectrum is pretty predictable. There are two main factors that control the shift. These two factors are :

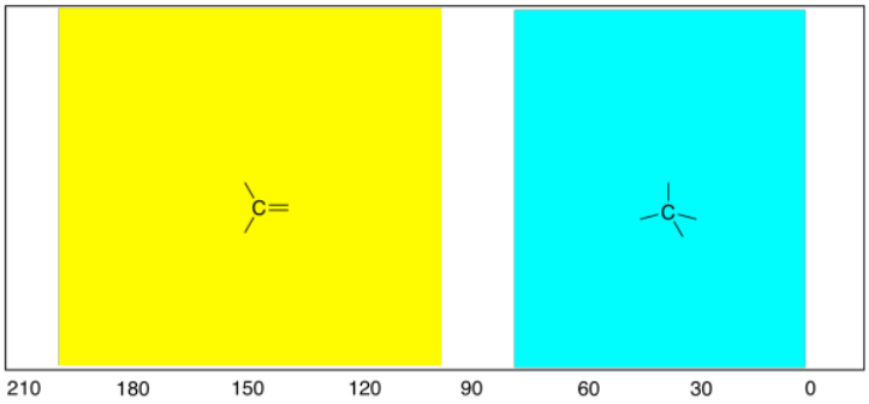
- the geometry around the carbon atom.
- the electronegativity of the other atoms attached to the carbon.

First we'll look at the influence of geometry.

In all of the hydrocarbon spectra seen above, the only peaks observed are at the right-hand end of the spectrum. The ^{13}C spectrum ranges from about 0 ppm to about 200 ppm, and all of the peaks we observed were well below 100 ppm. One of the things that those compounds had in common (cyclohexane, butane, pentane) was that they contain only tetrahedral (or sp^3) carbons. And, in fact, that kind of carbon atom generally shows up below 100 ppm (typically below 80 ppm) in the ^{13}C spectrum.



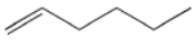
That's an important trend to know, because tetrahedral carbons are quite common in nature. Another shape of carbon atom, trigonal planar, is also pretty common. In contrast to the tetrahedral carbons, these carbons show up in the left-hand half of the spectrum, between 100 and 200 ppm.



As a *general* rule:

- sp^2 or trigonal planar carbons absorb in the left half of the spectrum (100 - 200 ppm).
- sp^3 or tetrahedral carbons absorb in the right half of the spectrum (0 - 100 ppm).

In the ^{13}C NMR spectrum of another hydrocarbon, 1-hexene, most of the peaks show up at the right-hand end, but two others show up farther to the left. A comparison of the structures will tell you that these two peaks are from the double-bonded carbons.



1-hexene

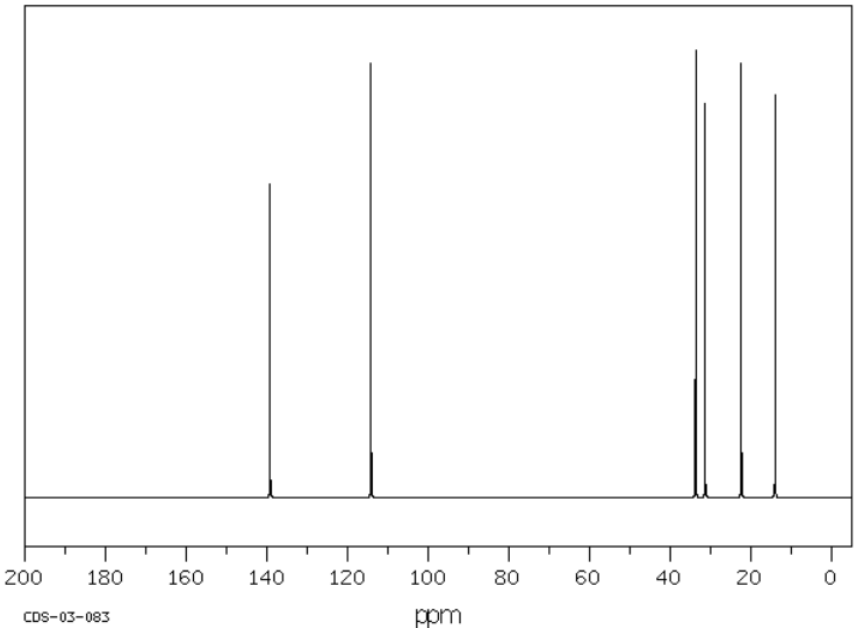
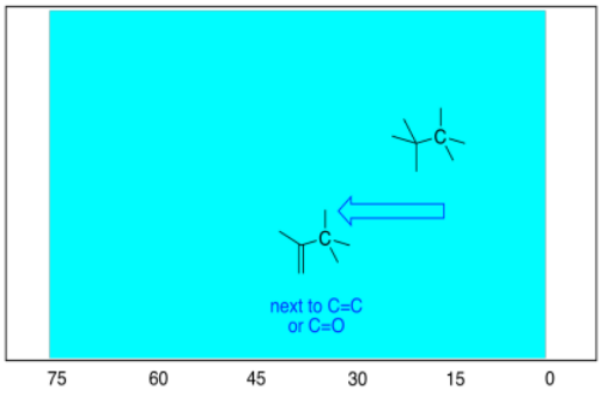


Figure 4.4.1: ^{13}C NMR spectrum of 1-hexene. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

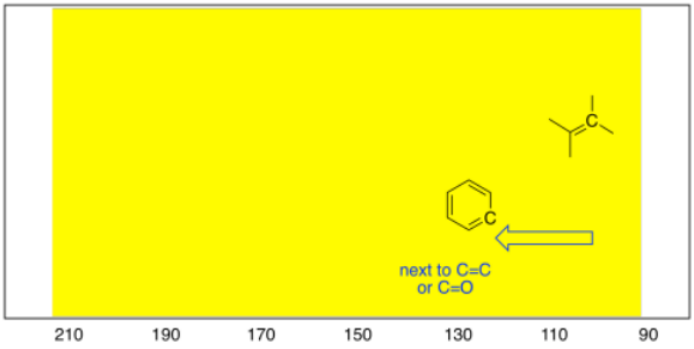
The alkene, 1-hexene, shows four peaks below 20 ppm and two near 100 ppm. The two carbons that absorb near 100 ppm are the two trigonal carbons that form the alkene functional group; the others are tetrahedral carbons.

Remember, a general rule means that there will be exceptions. You might see sp^2 carbons at 210 ppm or 95 ppm, for example. You are not likely to see them at 30 ppm, however.

There are some more subtle factors that influence the shift of a carbon atom in the spectrum, having to do with what the neighbouring groups are in the compound. For example, a tetrahedral carbon shifts a little bit downfield if it is next to a trigonal planar carbon. The reason has to do with the way the magnetic field that is used in this experiment recruits the electrons of double bonds, essentially magnetizing them, as well.

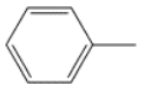


The same thing happens if trigonal planar carbons are near other trigonal planar carbons. Just as in the tetrahedral case, these sp^2 carbons can be pulled to the left under the influence of neighbouring double bonds. As a result, carbons in benzene rings show up slightly to the left of carbons in alkenes.



- sp^2 carbons in alkenes show up near the upfield end of the sp^2 half of the spectrum (usually around 100-120 ppm).
- sp^2 carbons in aromatic systems like benzene absorb a little farther downfield than alkenes (around 120-160 ppm).

Another compound that contains both sp^2 and sp^3 carbons is toluene or methylbenzene. Its ^{13}C NMR spectrum shows one peak near 30 ppm and four between 120 and 130 ppm.



toluene or methylbenzene

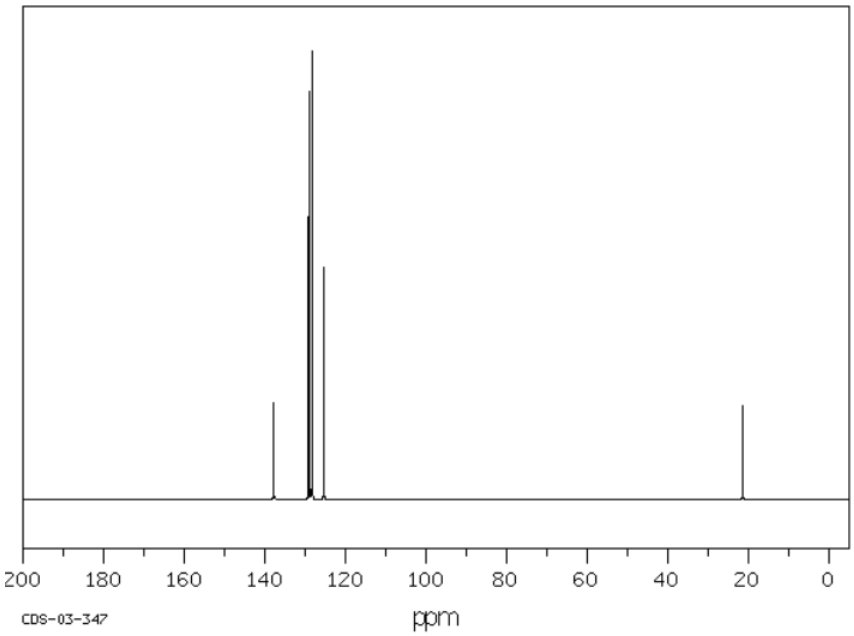
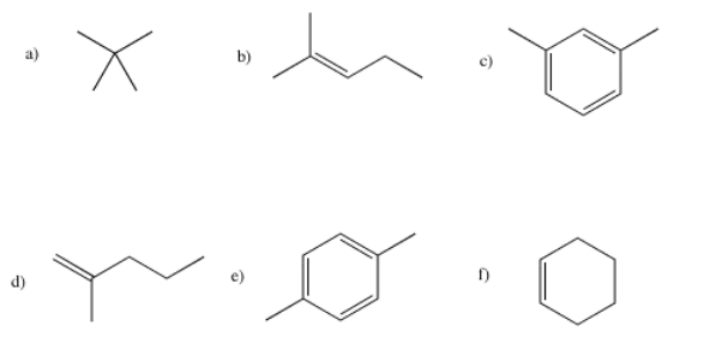


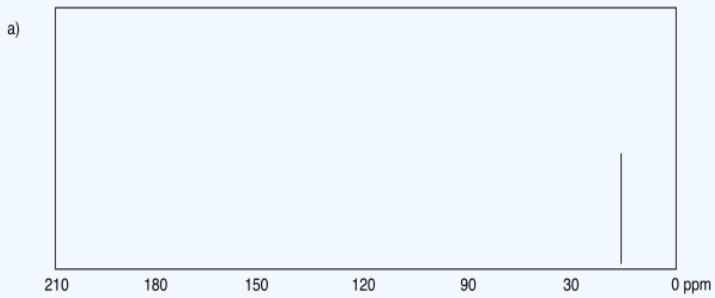
Figure 4.4.2: ^{13}C NMR spectrum of toluene. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

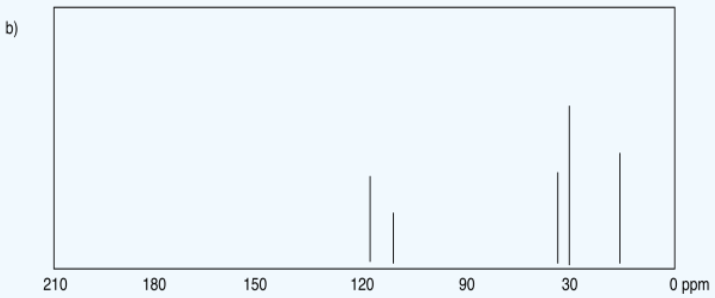
? Exercise 4.4.1

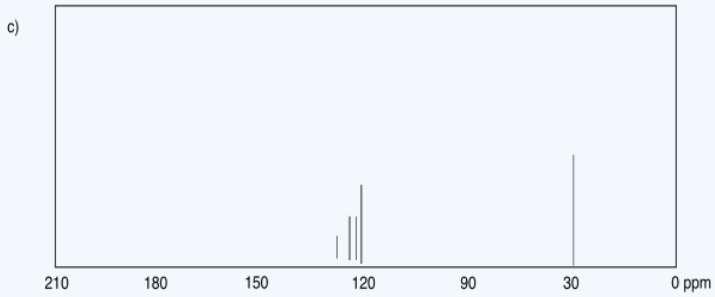
Draw an approximate ^{13}C NMR spectrum for each of the following compounds. You will need to take into account symmetry and carbon geometry.

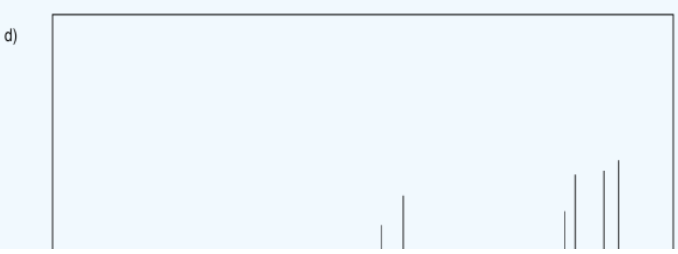

a)
b)
c)
d)
e)
f)

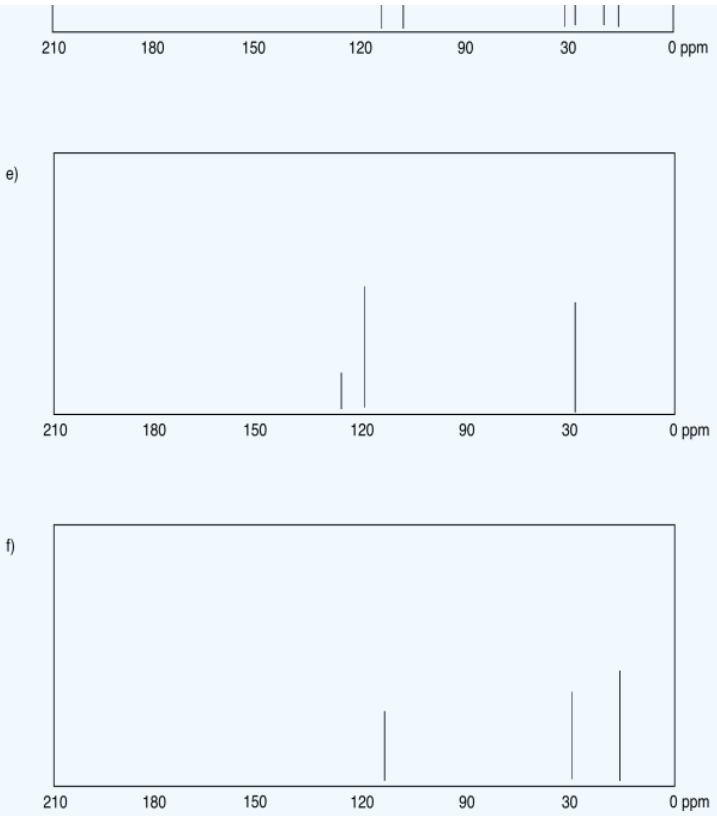
Answer


a)
210
180
150
120
90
30
0 ppm


b)
210
180
150
120
90
30
0 ppm


c)
210
180
150
120
90
30
0 ppm


d)



Exercise 4.4.2

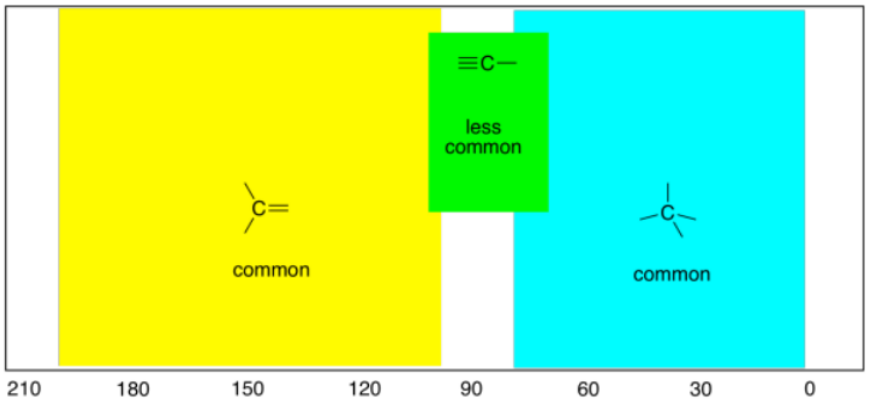
Determine whether the following peaks represent sp^2 (trigonal planar) or sp^3 (tetrahedral) carbon atoms.

a) 27 ppm b) 198 ppm c) 112 ppm d) 15 ppm e) 79 ppm f) 164 ppm

Answer

a) sp^3 b) sp^2 c) sp^2 d) sp^3 e) sp^3 f) sp^2

In addition, there are also linear carbons in organic chemistry, although they are much less common as tetrahedral and trigonal carbons. Linear or sp carbons absorb at about 60 to 100 ppm, sort of in the middle of the spectrum. Mostly they are seen around 60-80 ppm, so they overlap considerably with sp^3 carbons.



- sp or linear carbons absorb around 60-100 ppm.
- clearly, some sp^3 carbons absorb at frequencies similar to sp carbons. Be careful.

One example of a compound containing sp carbons is 1-hexyne. Its spectrum is shown below.

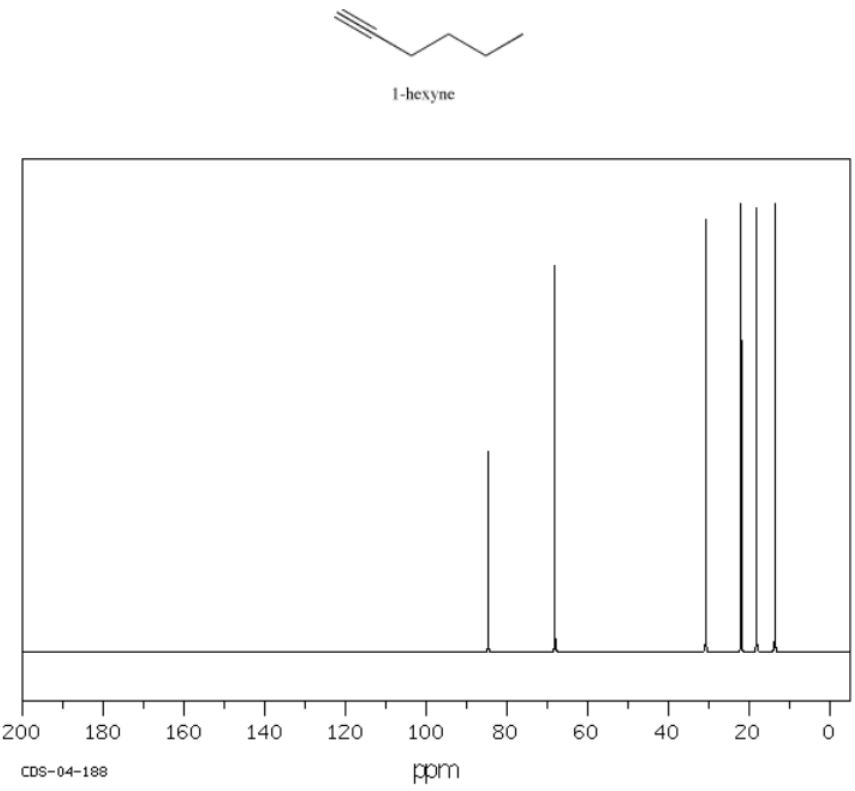


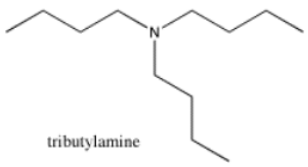
Figure 4.4.3: ^{13}C NMR spectrum of 1-hexyne. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

4.5: Factors in Chemical Shift- Electronegativity

Electronegativity is a second factor that influences NMR spectra. The frequency of radio waves absorbed by an atom depends on the magnetic field experienced at the nucleus. The magnetic field experienced at the nucleus depends on the amount of electron density around the atom. Consequently:

- the more electron density present, the further upfield the shift in the spectrum.
- the less electron density present around the atom, the further downfield the shift.

Tributylamine has an NMR spectrum with four peaks, one for each inequivalent carbon in the structure. These peaks are spread out just a little bit more than in a hydrocarbon; there are more peaks showing up further downfield. The carbon next to the nitrogen is the one that shows up furthest downfield.



tributylamine

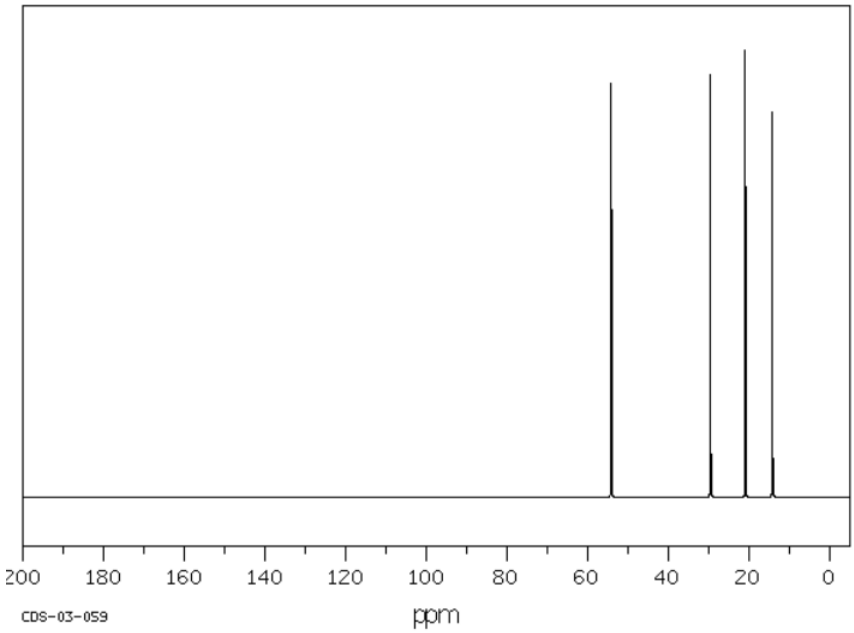
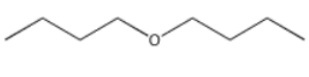


Figure 4.5.1: ^{13}C NMR spectrum of tributylamine.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

- usually, a tetrahedral carbon shows up in the upfield half of the spectrum.
- the region from about 0 to 100 ppm can be thought of as the sp^3 window.
- an electronegative atom moves a peak further downfield within the sp^3 window.

Dibutyl ether has peaks that show up even further downfield. As in tributylamine, the carbon next to the heteroatom, in this case an oxygen, shows up the furthest downfield. The other carbons in the chain also show up a little farther downfield than they would in butane, but the further from the oxygen they are, the less effect the oxygen has on them. This is a typical inductive effect. In an inductive effect, atoms have an effect on each other through sigma bonds, but the further apart the atoms are the smaller the effect.



dibutyl ether or butyl ether

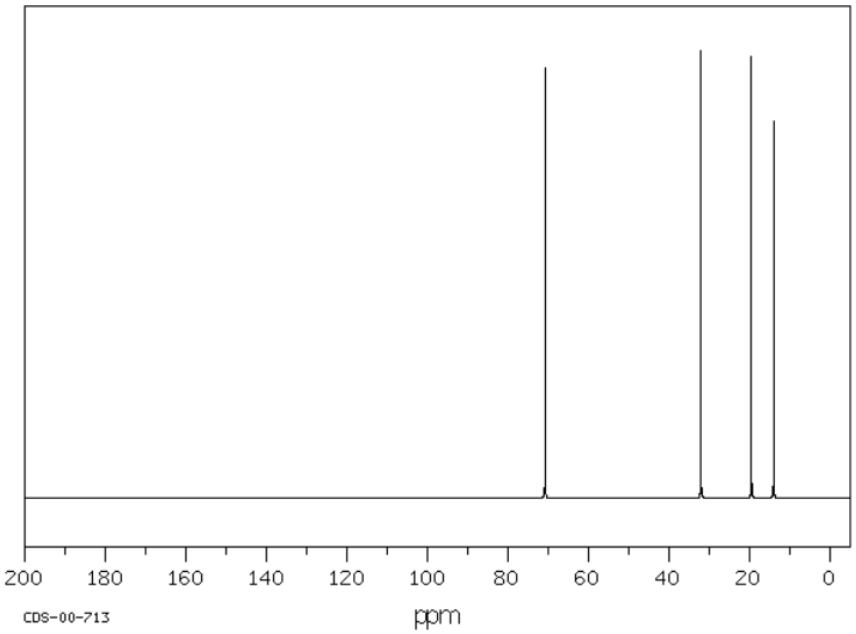
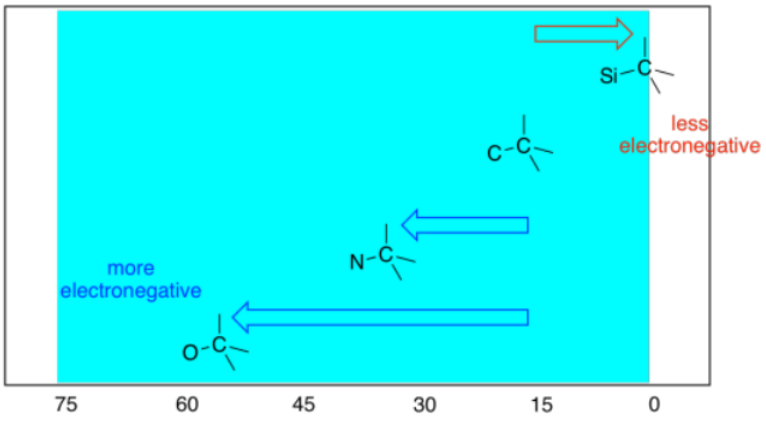


Figure 4.5.2: ^{13}C NMR spectrum of butyl ether.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

Notice that the absorbance of a carbon next to an oxygen atom was shifted even more to the left than a carbon next to a nitrogen atom. The more electronegative the neighbour, the greater the effect. You would probably expect a less electronegative neighbour than carbon will result in a shift to the right, and generally that's the case.



In summary:

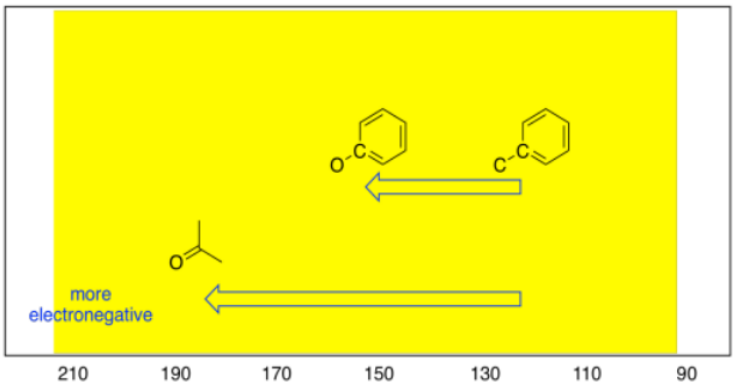
- electronegative elements draw attached carbons downfield.
- the more electronegative the element, the farther downfield the attached carbon.
- electronegative elements also have an effect on atoms further down the chain, drawing them downfield.
- the farther the atom is from the electronegative atom, the smaller the effect.
- the effect of electronegative atoms on their neighbors is called an inductive effect.

Methane (CH_4) absorbs at about 5 ppm in the ^{13}C NMR spectrum. Chloromethane absorbs at about 30 ppm. Since chlorine is about as electronegative as nitrogen, the effect of a chlorine or a nitrogen on an attached carbon are similar.

Dichloromethane or methylene chloride (CH_2Cl_2) shows up at about 55 ppm, and trichloromethane or chloroform ($CHCl_3$) at about 80 ppm. The more bonds there are to an electronegative element, the further downfield the carbon absorbs. In the case of a chlorinated carbon, each additional chlorine moves the peak about 25 ppm further downfield.

- the effect of electronegativity is additive.
- the more electronegative elements attached to a carbon, the farther downfield it absorbs.

These trends are also seen among sp^2 carbons. An oxygen atom attached to an sp^2 carbon results in a downfield shift, to about 160 ppm. On the other hand, if a trigonal planar carbon is double bonded to an oxygen atom, the shift can be much farther; it actually ranges from 160 to 210 ppm, depending on what else is attached to the carbon, and is most commonly seen around 180 ppm.

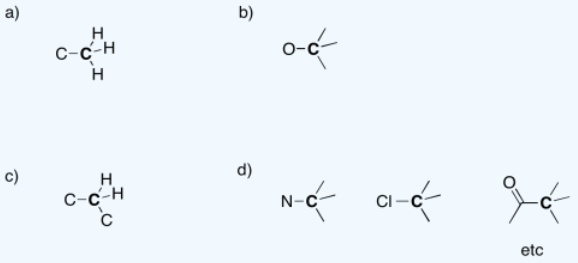


Exercise 4.5.1

Suggest an assignment for the following ^{13}C NMR peaks:

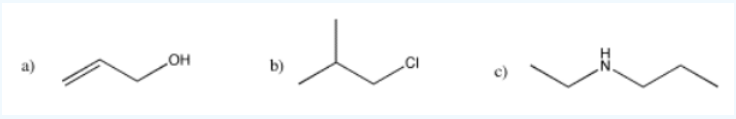
a) 12 ppm b) 58 ppm c) 22 ppm d) 41 ppm

Answer

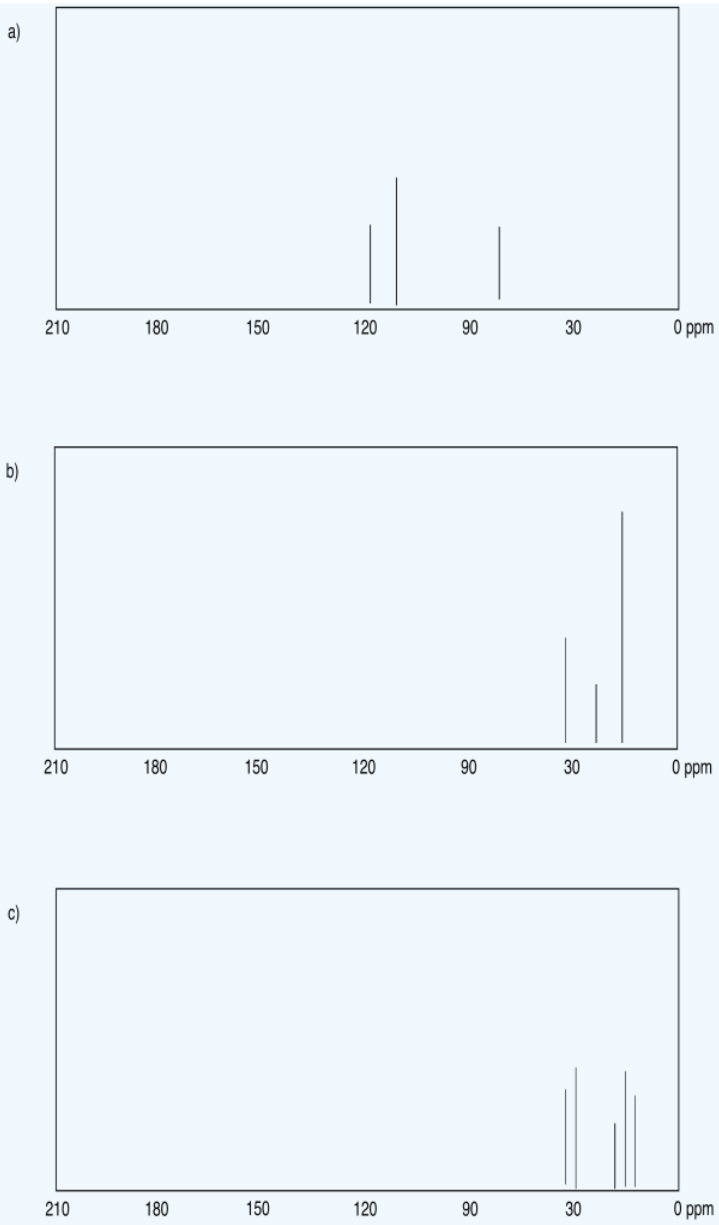


Exercise 4.5.2

Draw the predicted ^{13}C NMR spectra for the following compounds.

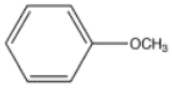


Answer



4.6: More on Electronic Effects

Methoxybenzene or anisole has six carbons, but only four peaks in the spectrum because of symmetry. These peaks are all above 100 ppm, but some peaks are as far downfield as 160 ppm.



methoxybenzene

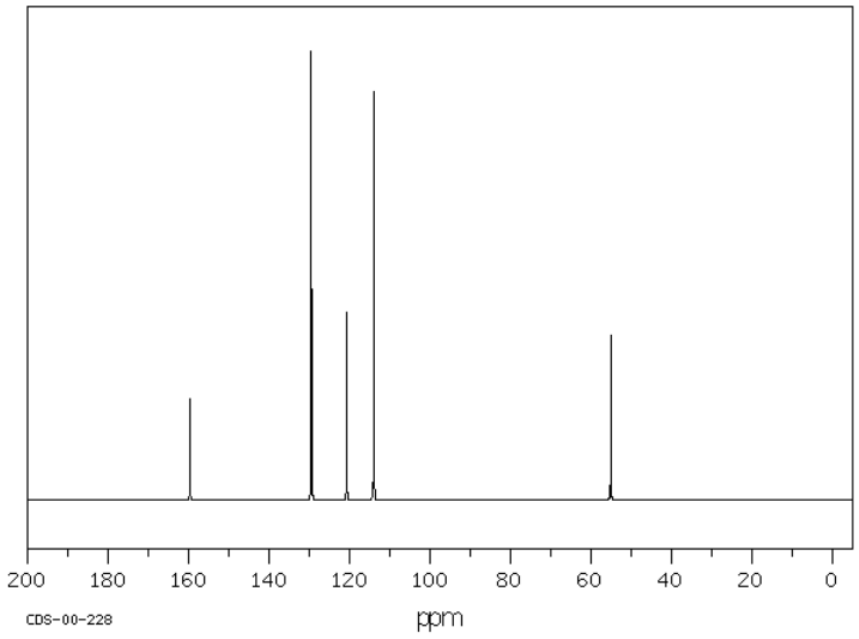
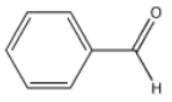


Figure 4.6.1: ^{13}C NMR spectrum of methoxybenzene (anisole).

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

- usually, a trigonal planar carbon shows up in the downfield half of the spectrum.
- the region from about 100 to 200 ppm can be thought of as the sp^2 window.
- an electronegative atom moves a peak further downfield within the sp^2 window.

Benzaldehyde has peaks between 130 and 140 ppm, as well as one near 190 ppm. Just as in the sp^3 region of the spectrum, when a carbon is attached to an electronegative element, it moves further downfield, and since the carbonyl (or C=O) carbon in the aldehyde has two bonds to oxygen, it shows up considerably downfield. The carbonyl carbon in some ketones can show up as far as 210 ppm.



benzaldehyde

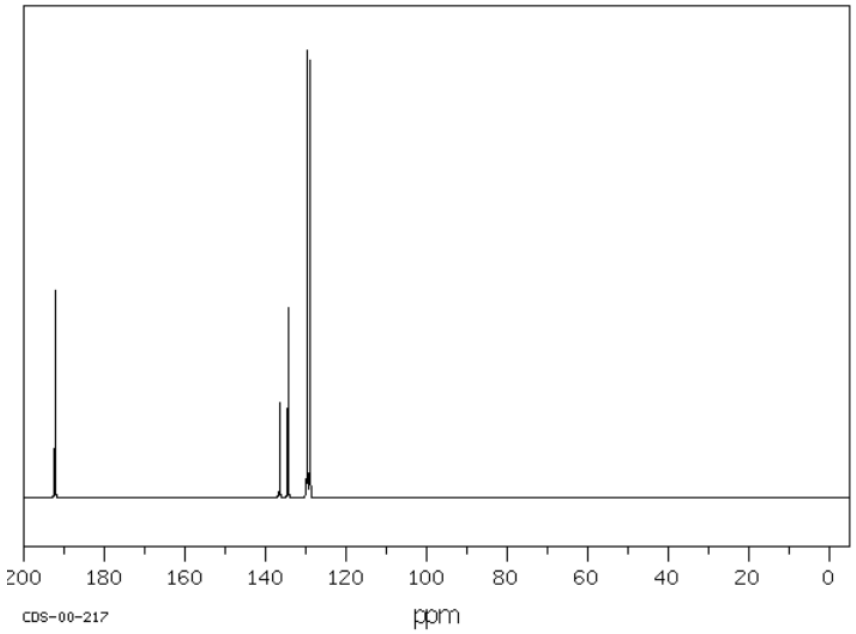


Figure 4.6.2: ^{13}C NMR spectrum of benzaldehyde.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

- Carbonyl carbons may show up even further downfield than 200 ppm.
- Carbonyl carbons have a great deal of positive charge and low electron density.

? Exercise 4.6.1

Suggests possible assignments for the following chemical shifts in a ^{13}C NMR spectrum.

a) 127 ppm b) 11 ppm c) 196 ppm d) 65 ppm e) 111 ppm

f) 154 ppm g) 210 ppm h) 28 ppm i) 170 ppm j) 42 ppm

Answer

a) 127 ppm

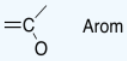
b) 11 ppm

c) 196 ppm

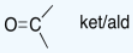
d) 65 ppm

e) 111 ppm

f) 154 ppm



g) 210 ppm



h) 28 ppm

i) 170 ppm

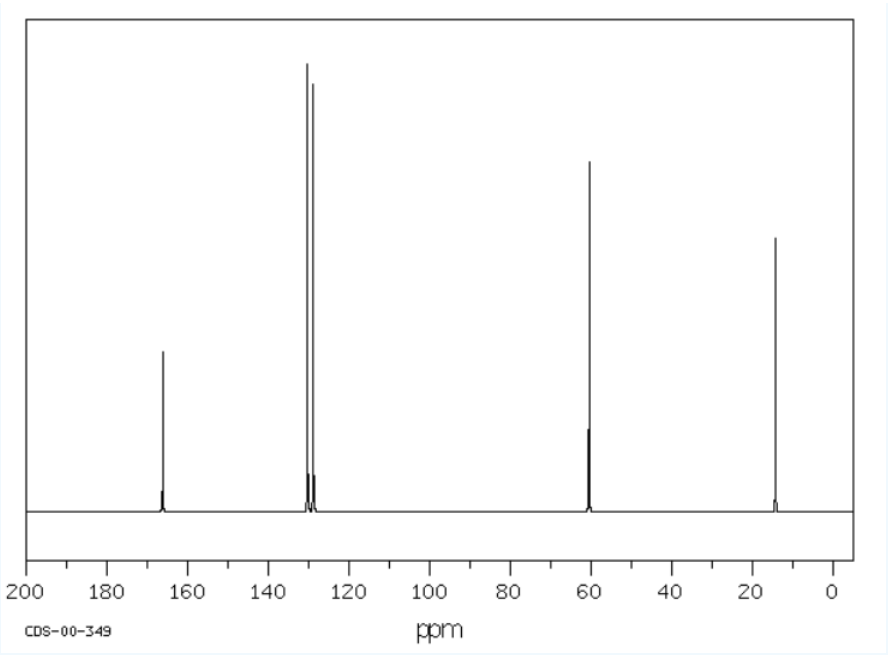
j) 42 ppm

Exercise 4.6.2

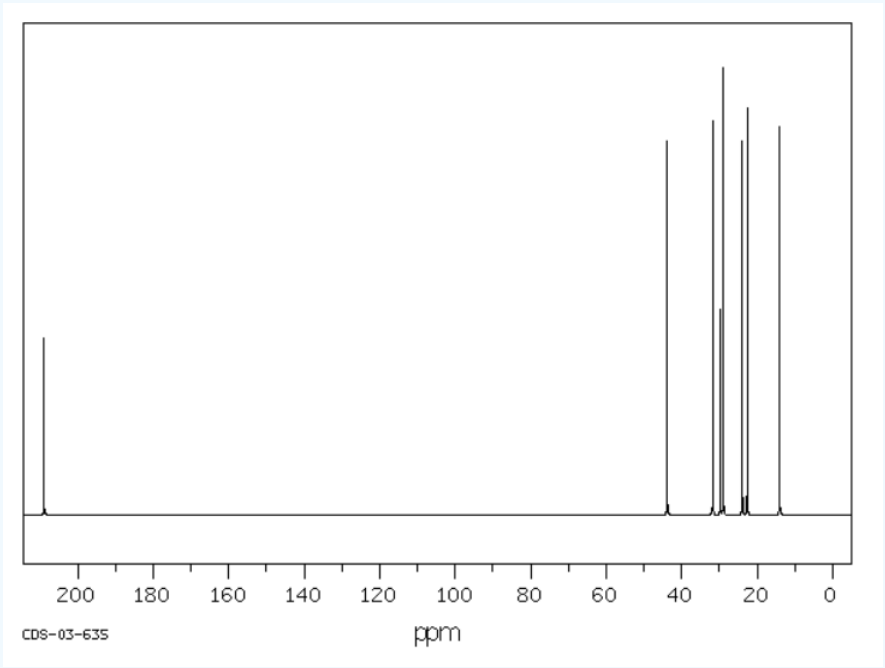
Suggest possible structures for the following spectra.

Source: SDBSWeb : riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 19 August 2008)

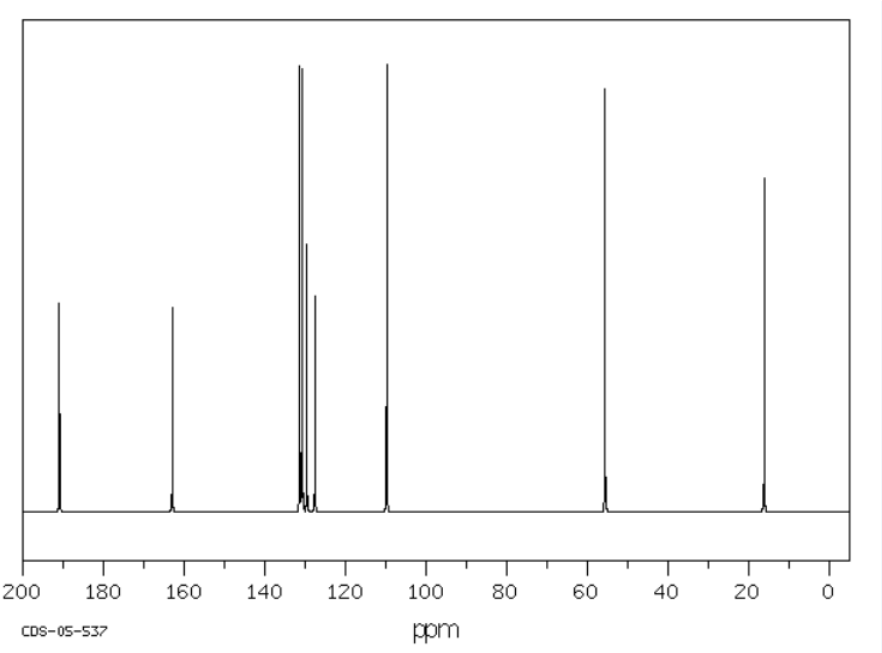
a)


200
180
160
140
120
100
80
60
40
20
0
CDS-00-349
ppm

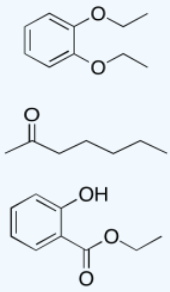
b)


200
180
160
140
120
100
80
60
40
20
0
CDS-03-635
ppm

c)



Answer



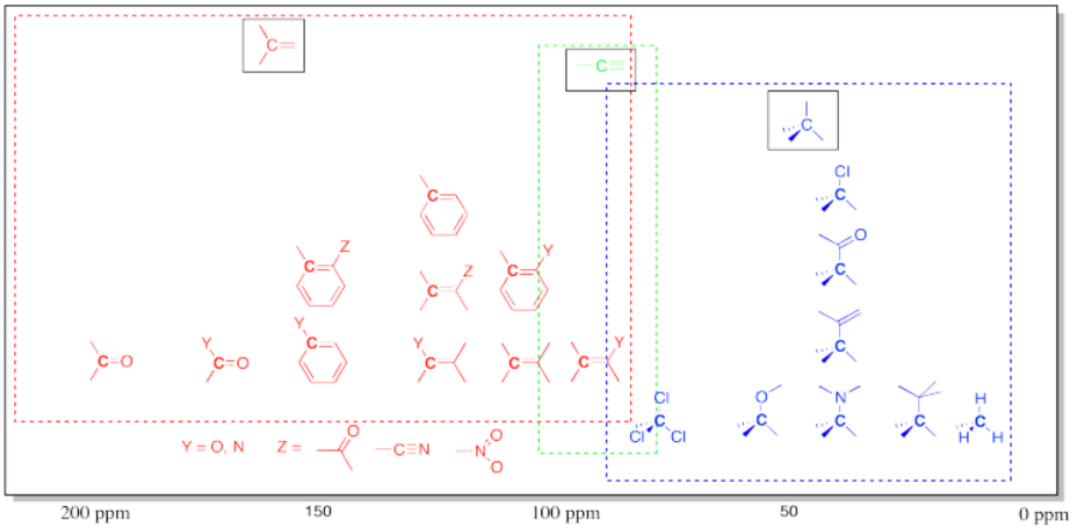
There are subtle effects of electronegativity in saturated hydrocarbons like hexane. Carbons in different positions in those compounds show up at different shifts. In general, a methyl group (CH_3) will show up farther upfield than a methylene group (CH_2), which will in turn show up further upfield from a methyne group (CH). This trend is related to the difference in electronegativity between a carbon and a hydrogen. Carbon is slightly more electronegative than a hydrogen. As a result, a carbon atom that is bonded to a number of hydrogen atoms has a very slight negative charge. That means it absorbs further upfield. A carbon that is bonded to a number of carbons is more neutral, is not quite so shielded, and shows up a little more downfield.

Unless there are bigger electronegative effects due to heteroatoms such as oxygen,

- methyl (CH_3) groups show up furthest upfield.
- methylene (CH_2) groups show up next furthest upfield.
- methyne (CH) groups show up furthest downfield.

We can use NMR spectroscopy as a diagnostic tool to determine the structure of a compound. ^{13}C NMR spectroscopy is useful in highlighting whether there are any double bonds in a molecule, whether there are any heteroatoms such as oxygen, and how many different kinds of carbons there are. That last point isn't the same as the number of carbons, but is related to the symmetry of the molecule.

Table 4.6.1: Approximate chemical shifts in ^{13}C NMR spectroscopy.



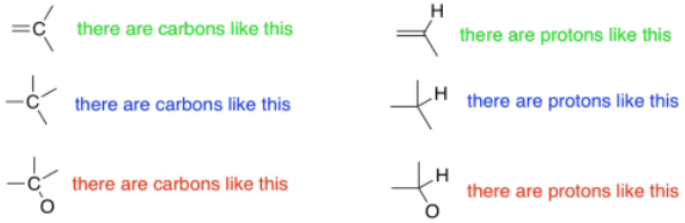
4.7: ^{1}H NMR Spectroscopy

^{1}H NMR spectroscopy is used more often than ^{13}C NMR, partly because proton spectra are much easier to obtain than carbon spectra. The ^{13}C isotope is only present in about 1% of carbon atoms, and that makes it difficult to detect. The ^{1}H isotope is almost 99% abundant, which helps make it easier to observe. Another advantage is that ^{1}H NMR spectroscopy gives more information than ^{13}C NMR, as you will find out later.

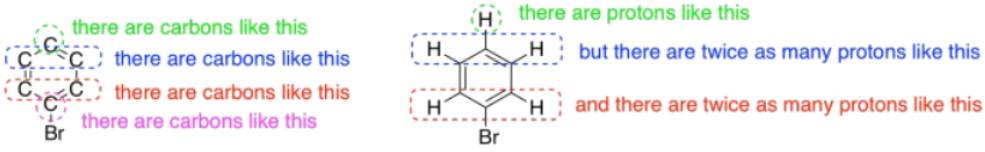
Note that in this discussion, the word "proton" is used for "hydrogen atom", because it is the proton in the nucleus of the ^{1}H isotope that is observed in these experiments. Although ^{2}H (deuterium) and ^{3}H (tritium) are also NMR-active, they absorb at frequencies that are different from the ones used in ^{1}H NMR. The ^{1}H isotope is also much more common than the other two, so ^{1}H NMR spectroscopy is more conveniently done than ^{2}H NMR spectroscopy.

^{1}H NMR spectroscopy provides more kinds of information than a typical ^{13}C NMR approach. In ^{13}C NMR spectroscopy, we get information about the environment of each unique carbon atom in a molecule. We can tell the geometry of the carbon atom by its shift, and we can also tell a little about what other atoms are nearby.

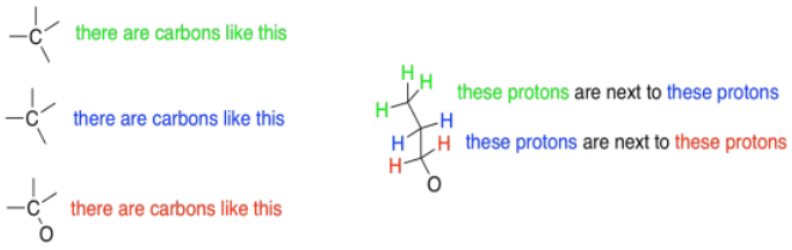
That kind of information is revealed by the chemical shift of the carbon atom -- where the peak corresponding to that carbon shows up along the x-axis of the spectrum. ^{1}H spectroscopy also gives chemical shift information, and it is very closely analogous to shift in ^{13}C spectroscopy. If you understand shift in carbon, you will understand shift in proton.



^{1}H NMR spectroscopy can be quantitative. Not only can you tell what kinds of protons are in a compound, but you can also tell how many of each you have. The spectrum might tell you that you have one proton of one kind and two identical protons of another kind. Remember in a ^{13}C spectrum, we might see two carbons that looked identical to each other because the molecule is symmetric. We might have another carbon that is different from those two. All a ^{13}C spectrum would tell you is that there were two different kinds of carbons. We would get no indication that there were actually three carbons: two of one kind and one of another. However, a ^{1}H spectrum will give that sort of detail.



^{1}H NMR spectroscopy gives us information about connectivity. In ^{13}C spectroscopy, we just know we have a bunch of different carbons in some different environments. There might be a number of different ways that those carbons could be connected together. With ^{1}H spectroscopy, it is usually much more obvious which protons go in which order throughout the molecule.



The next few sections will look at these different aspects of ^{1}H NMR spectroscopy, one at a time.

4.8: Chemical Shift in Proton Spectra

The trends here are exactly the same as in carbon spectra. Wherever the carbon goes, it takes the proton with it. Proton spectra are only around 10 ppm wide, compared to the 200 ppm of carbon spectra, so by analogy with carbon spectra,

- hydrogens on sp^3 carbons usually show up in the upfield half of the spectrum, about 0 to 5 ppm.
- hydrogens on sp^2 carbons usually show up in the downfield half of the spectrum, about 5 to 10 ppm.
- within these two halves of the spectrum, electronegative atoms attached to the same carbon as a proton will draw that proton downfield.

So, in the spectrum of hexane ($CH_3CH_2CH_2CH_2CH_2CH_3$) all of the hydrogens are on sp^3 or tetrahedral carbons. They all show up below 5 ppm. There are no electronegative atoms around, so they are even further upfield, at 1 ppm.

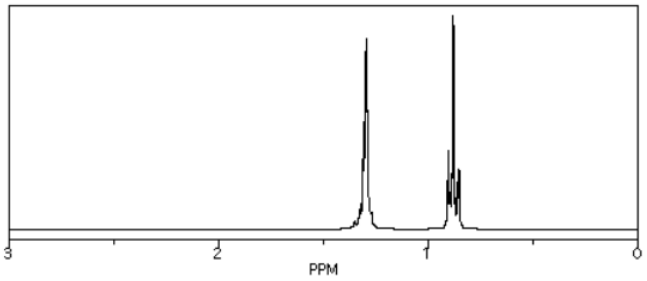
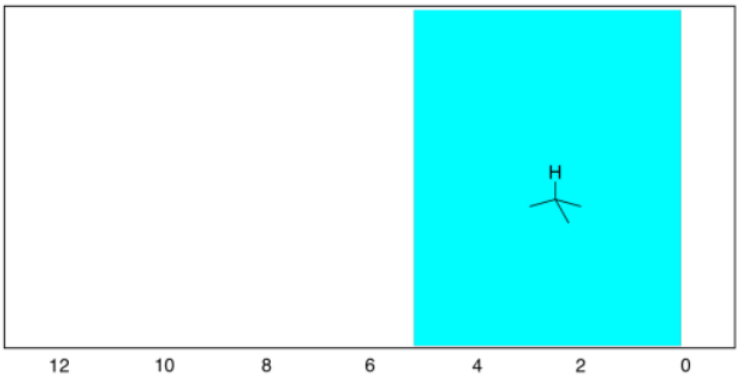


Figure 4.8.1: ^1H NMR spectrum of hexane.

Source: Simulated spectrum.

Those peaks fall well within the expected window.



If we look at 1-hexene (CH_2=$CHCH_2CH_2CH_2CH_3$), we see a similar spectrum, but two of the peaks show up above 5 ppm. These hydrogens are on sp^2 or trigonal planar carbons. There are other, more subtle changes, but that is the main one.

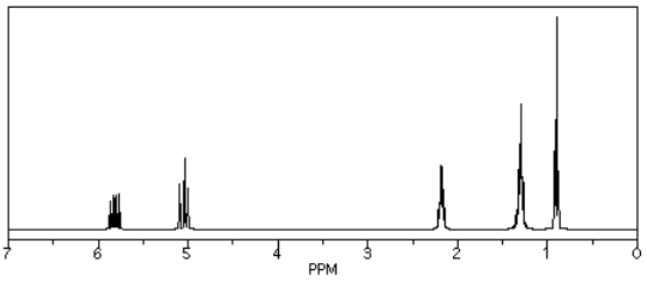
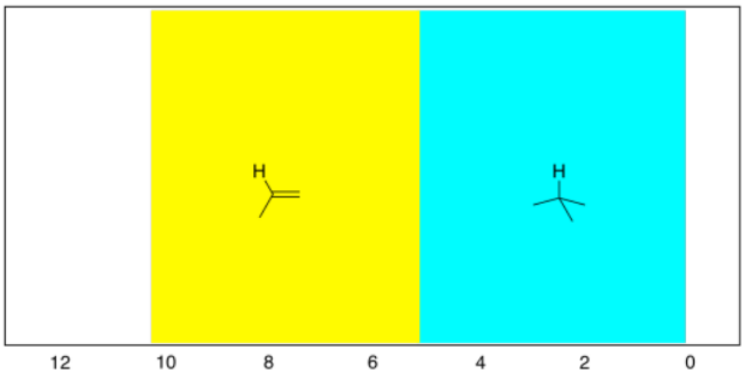


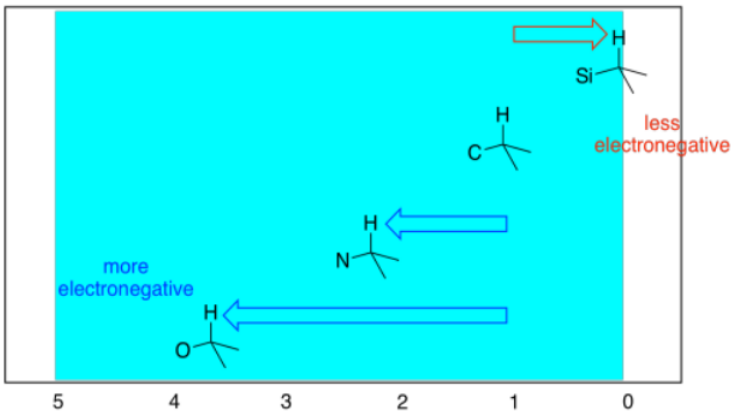
Figure 4.8.2: ^1H NMR spectrum of 1-hexene.

Source: Simulated spectrum.

Again, the new peaks fall right around where we would expect them.

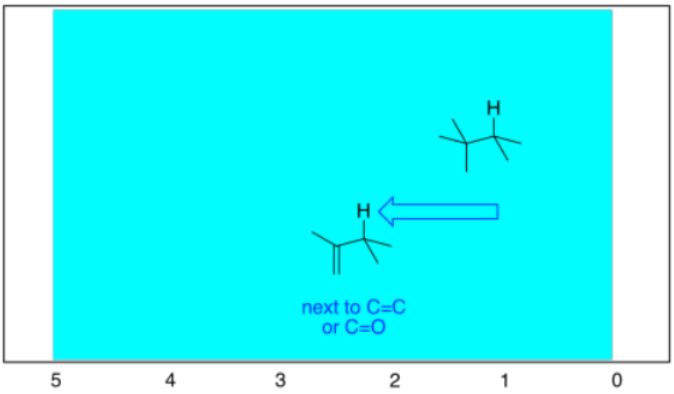


The electronegativity shifts that we saw earlier of 13C NMR spectra hold true for 1H spectra as well. The more electronegative the neighbour of the carbon on which the proton is sitting, the further the proton will be shifted to the left in the spectrum.



It can be useful to think of 1 ppm as the default position for a proton on a tetrahedral carbon, and to think of the effects of other groups as moving the peak a certain distance away from that starting point. For example, a neighbouring oxygen atom moves the peak 2.5 ppm to the left. Thinking of it that way helps you predict what will be the effect of two different attached groups. For example, if there were two oxygens attached to the carbon on which the proton is sitting, it would move 5 ppm, and end up at 6 ppm overall.

Just as in 13C NMR spectroscopy, there are more subtle effects of having sp^2 carbon neighbors nearby. Once again, that's because of the effect that the magnetic field has on the electrons in the double bond.



We see similar trends in the left-hand, sp^2 region. If we look at butanal ($CH_3CH_2CH_2CHO$), we also have several hydrogen on sp^3 carbons and one on an sp^2 carbon. The former show up below 5 ppm and the latter above 5 ppm. This time, that peak is way downfield at 10 ppm. That hydrogen is on a carbonyl carbon; being double bonded to an oxygen deshields the carbon, and its partner hydrogen a lot.

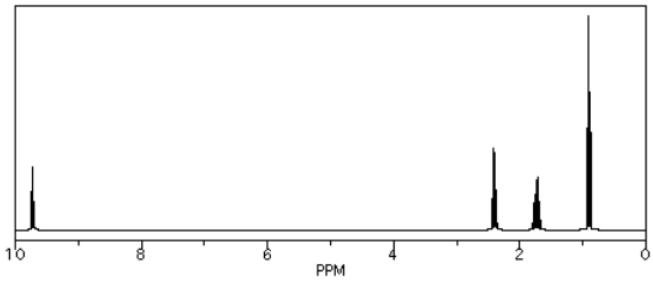
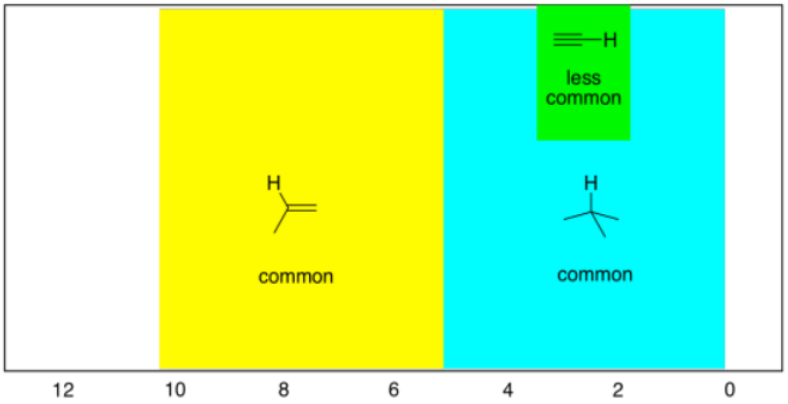


Figure 4.8.3: ^{1}H NMR spectrum of butanal.

Source: Simulated spectrum.

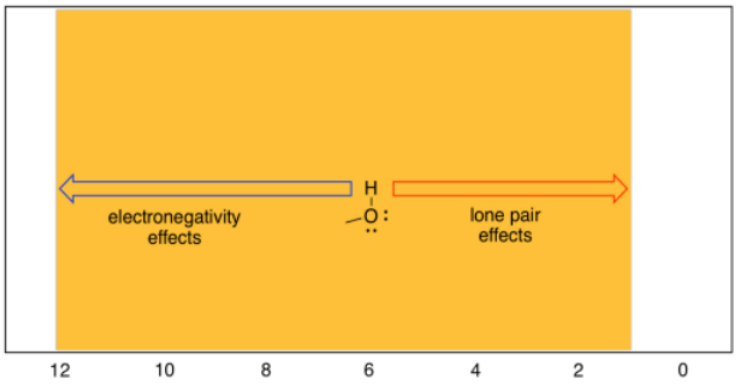
As before, there are also hydrogens on linear or sp carbons, although they are much less common than tetrahedral or trigonal carbons.

- hydrogens on sp carbons show up between 2 and 6 ppm, and most often between 2 and 3 ppm.



Remember, these are general rules that you should know. The proton in chloroform shows up at 7 ppm although it is attached to a tetrahedral carbon, because it has three different, electronegative chlorines pulling it to the left. (World-record shifts occur for hydrogens attached to transition metals: "late" metals like ruthenium or rhodium can move hydrogen peaks all the way up to -20 ppm, but "early" metals like tantalum can move them down as far as 25 ppm.)

One word of caution: students often catch on to the electronegativity rule and immediately make assumptions about OH groups that turn out not to be true. The obvious conclusion so far is that OH groups should always show up at the left hand of the spectrum, because the hydrogen is directly attached to that very electronegative oxygen. That can sometimes be true: the proton in a carboxylic acid, if it can be seen in the spectrum at all, generally shows up around 12 ppm. However, the proton in water is usually around 1.5 ppm. In fact, protons on OH groups in slightly different situations cover the entire range of the proton spectrum.



The reason for this wide range has to do with the fact that, although oxygen is very electronegative (so its neighbouring hydrogen should be electron-poor) it also posesses lone pairs. Those lone pairs have the effect of shielding the hydrogen from the magnetic

field. Thus, there are two competing effects in OH protons, and different situations tilt the balance one way or another.

Exercise 4.8.1

Indicate whether each of the following peaks in the ^{1}H NMR spectrum probably represents a hydrogen on a tetrahedral carbon (H-C_{sp}3) or a hydrogen on a trigonal planar carbon (H-C_{sp}2).

a) 1.1 ppm b) 3.4 ppm c) 7.8 ppm d) 4.2 ppm e) 5.7 ppm f) 9.9 ppm g) 2.3 ppm

Answer

a) H-C_{sp}3 b) H-C_{sp}3 c) H-C_{sp}2 d) H-C_{sp}3 e) H-C_{sp}2 f) H-C_{sp}2 g) H-C_{sp}3

Exercise 4.8.2

The following peaks in the ^{1}H NMR spectrum represent hydrogen atoms on tetrahedral carbons (H-C_{sp}3). Indicate whether that carbon is probably attached to another tetrahedral carbon, an oxygen, or a nitrogen.

a) 1.1 ppm b) 1.9 ppm c) 2.5 ppm d) 4.2 ppm e) 1.8 ppm f) 3.6 ppm g) 2.7 ppm

Answer

a) carbon b) carbon c) nitrogen d) oxygen e) carbon f) oxygen g) nitrogen

Exercise 4.8.3

Although aromatic C-H and alkene C-H are both bound to sp2 carbons the following peaks in the ^{1}H NMR spectrum probably represent hydrogen atoms on alkene carbons or aromatic carbons.

a) 7.3 ppm b) 8.3 ppm c) 5.1 ppm d) 6.2 ppm e) 5.4 ppm f) 7.8 ppm

Answer

a) aromatic b) aromatic c) alkene d) alkene e) alkene f) aromatic

Exercise 4.8.4

The following peaks in the ^{1}H NMR spectrum represent hydrogen atoms on trigonal planar carbons (H-C_{sp}2). Indicate whether that carbon is probably attached to another trigonal planar carbon in an aromatic ring, is single-bonded to a nitrogen in an aromatic ring, or is double-bonded to an oxygen.

a) 7.1 ppm b) 6.9 ppm c) 8.5 ppm d) 10.2 ppm e) 9.8 ppm f) 8.2 ppm g) 7.9 ppm

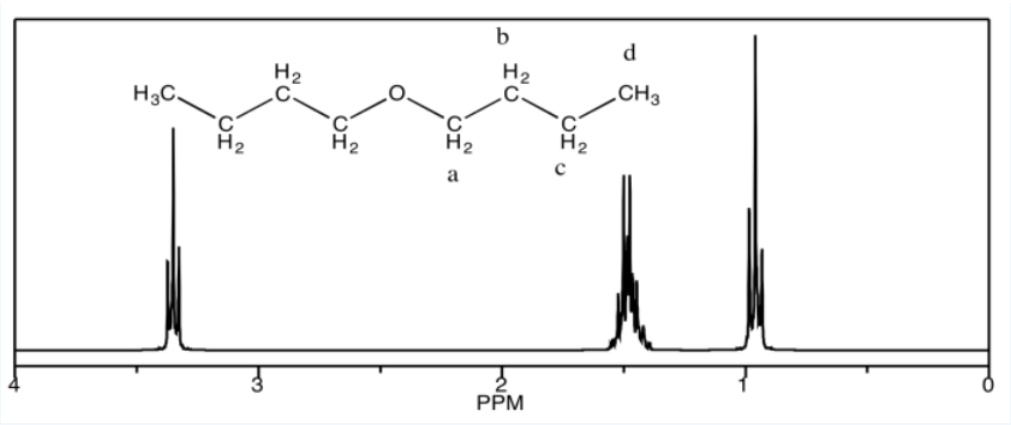
Answer

a) H-C_{Ar}-C b) H-C_{Ar}-C c) H-C_{Ar}-N d) C=O e) C=O f) H-C_{Ar}-N g) H-C_{Ar}-N

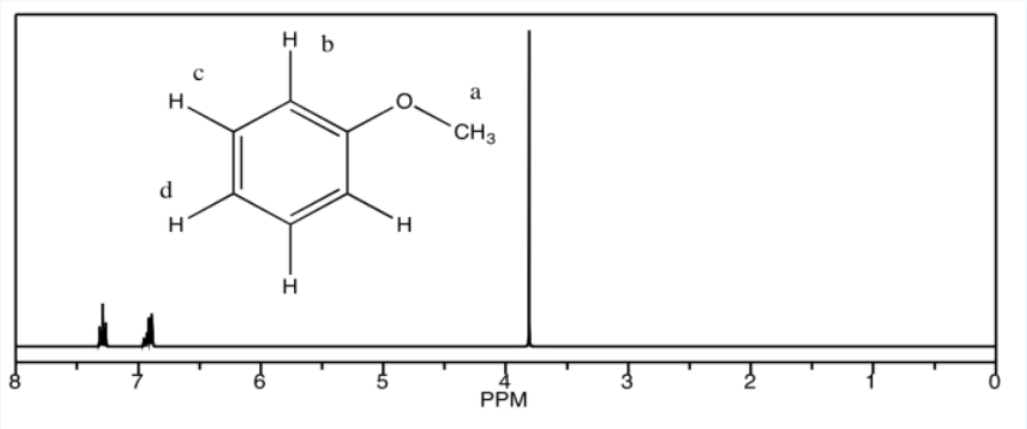
Exercise 4.8.5

Looking at the ^{1}H NMR spectra of the following compounds, indicate which peak belongs to which proton.

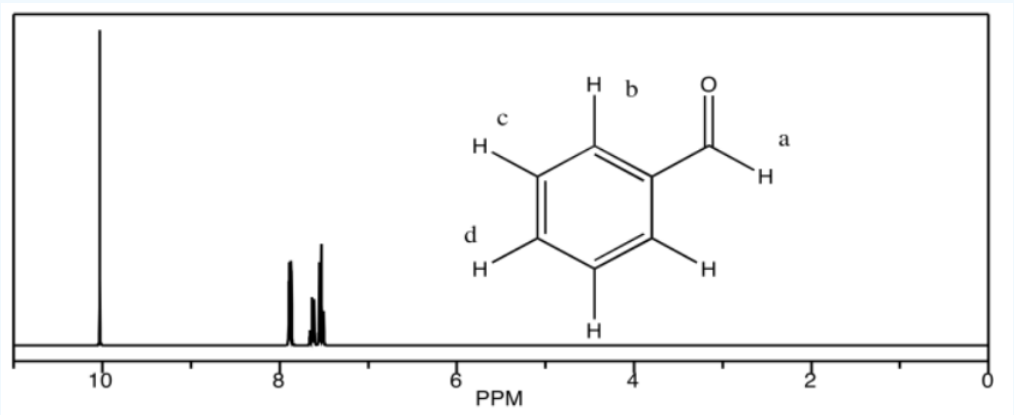
a) dibutyl ether



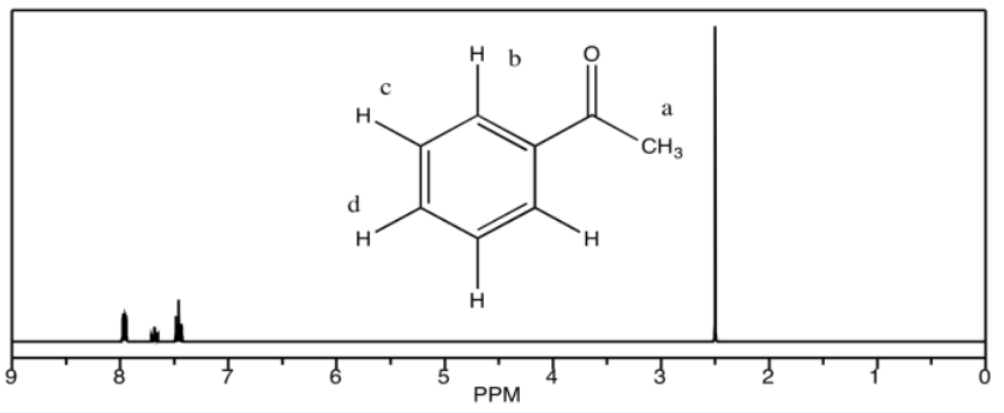
b) methyl phenyl ether



c) benzaldehyde



d) acetophenone



Answer

a) 3.4 ppm: H_a 1.5 ppm: H_b, H_c 0.9 ppm: H_d

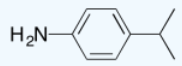
b) 7.4 ppm: H_d 6.9 ppm: H_b, H_c 3.7 ppm: H_a

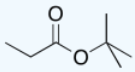
c) 10.1 ppm: H_a 7.9 ppm: H_b 7.6 ppm: H_d 7.5 ppm: H_c

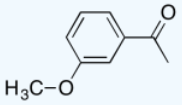
d) 7.9 ppm: H_b 7.6 ppm: H_d 7.4 ppm: H_c 2.5 ppm: H_a

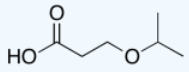
Exercise 4.8.6

Sketch a ^1H NMR spectrum for each of the following compounds, showing a simple line corresponding to the expected shift for each of the different hydrogens.

a) 

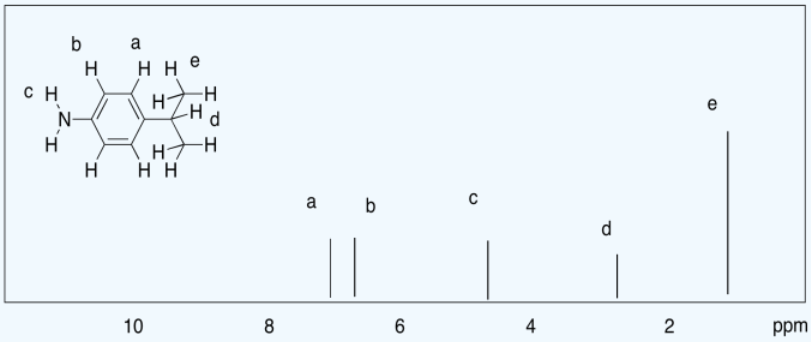
b) 

c) 

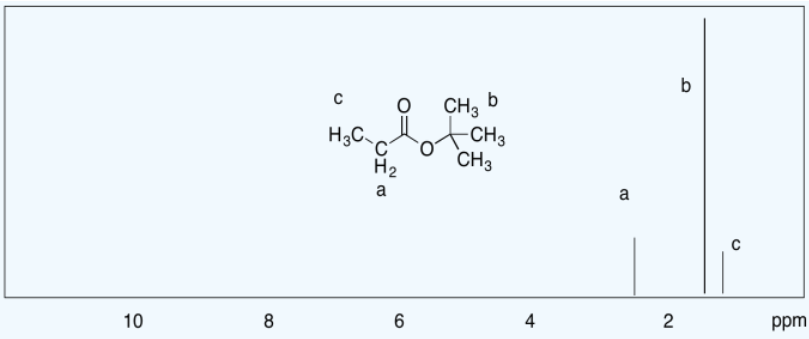
d) 

Answer

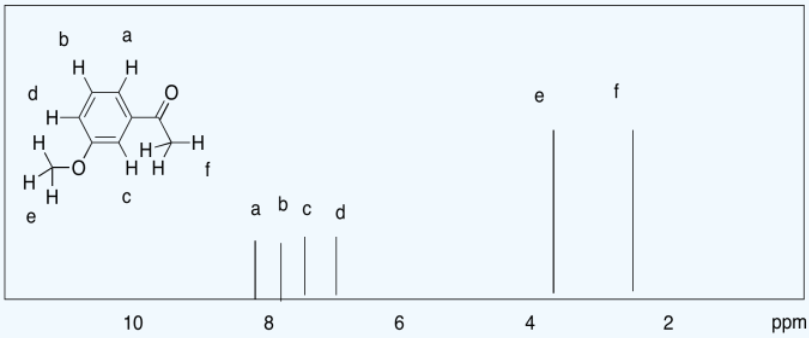
a)



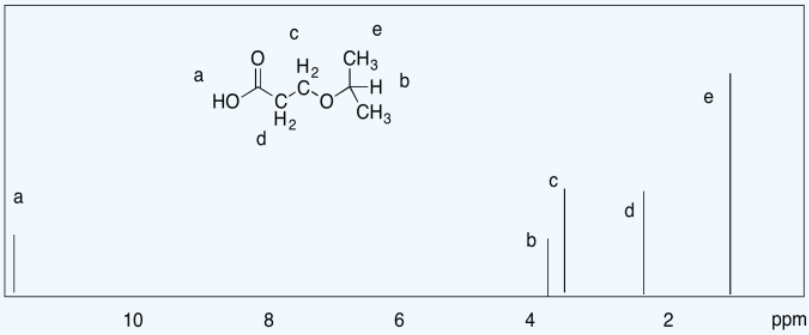
b)



c)



d)

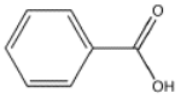


Notice that a major difference from ^{13}C NMR is that a carbon spectrum is spread out over 200 ppm, while a typical proton spectrum is compressed into about 10 ppm. There is a consequence of that difference, and it can be frustrating. It is usually easy to distinguish two different ^{13}C peaks, whereas two peaks in the ^{1}H spectrum could easily be so close together that they overlap. For example, the aliphatic hydrocarbons hexane and nonane display only two distinct peaks in the ^{1}H spectrum, one for the methyl hydrogens and one for the methylene hydrogens, because the latter are all too similar to tell apart given the limited amount of resolution in the spectrum.

- coincidental overlap of peaks in the ^{1}H spectrum is common.

There is another complication in the chemical shifts seen in ^{1}H spectroscopy, and that is the behavior of protons attached directly to heteroatoms such as oxygen and nitrogen. Oxygen is very electronegative, and hydrogen is not, so it stands to reason that an OH proton would absorb at very low field, say 10 ppm. That's completely wrong. OH protons in aliphatic alcohols show up between 2 and 6 ppm, phenolic OH protons between 5 and 9 ppm, and carboxylic acid OH protons between 11 and 12 ppm. Water shows up around 1.6 ppm when dissolved in chloroform, but if the water is present in high concentrations it can show up further downfield. Thus:

- a proton attached to oxygen shows up between 1 and 12 ppm.
- hydroxy proton shifts can vary depending on factors such as hydrogen bonding with the solvent and other molecules.
- except for carboxylic acid protons, which occur beyond the normal range of other peaks, a peak showing up at a particular shift is not strong evidence for the presence of an OH proton.



benzoic acid

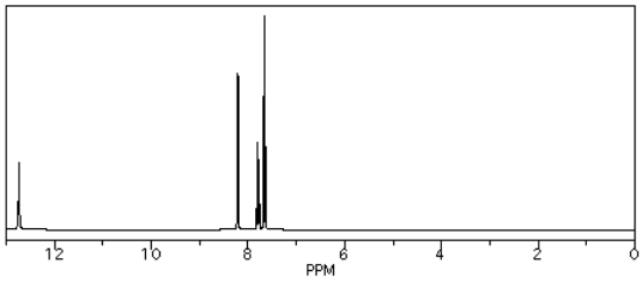


Figure 4.8.4: ^{1}H NMR spectrum of benzoic acid.

Source: Simulated spectrum.

ethanol

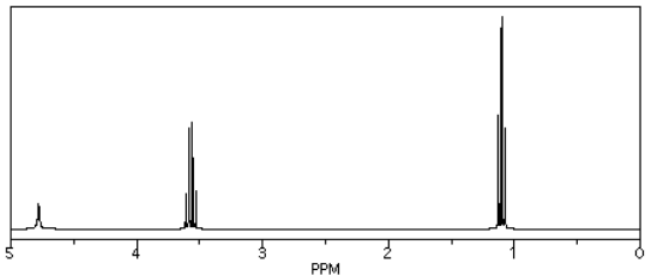


Figure 4.8.5: ^{1}H NMR spectrum of ethanol.

Source: Simulated spectrum.

Although oxygen is very electronegative, it also has two lone pairs of electrons; those lone pairs on oxygen are often crucial in understanding chemistry. The oxygen atom does pull electron density away from the hydrogen through the sigma bond between them, but the lone pairs also bathe the nearby hydrogen in the shielding effects of their electron density. Depending on how these two factors balance out, OH and NH protons don't absorb nearly as far downfield as expected.

4.9: Integration

There is additional information obtained from ^{1}H NMR spectroscopy that is not typically available from ^{13}C NMR spectroscopy. Chemical shift can show how many different types of hydrogens are found in a molecule; integration reveals the number of hydrogens of each type.

Looking at the spectrum of ethanol, you can see that there are three different kinds of hydrogens in the molecule. You can also see by integration that there are three hydrogens of one type, two of the second type, and one of the third type -- corresponding to the CH_3 or methyl group, the CH_2 or methylene group and the OH or hydroxyl group. That information helps narrow down the number of possible structures of the sample, and so it makes structure elucidation of an unknown sample much easier.

- integration reveals the ratio of one type of hydrogen to another within a molecule.

Integral data can be given in different forms. You should be aware of all of them. In raw form, an integral is a horizontal line running across the spectrum from left to right. Where the line crosses the frequency of a peak, the area of the peak is measured. This measurement is shown as a jump or step upward in the integral line; the vertical distance that the line rises is proportional to the area of the peak. The area is related to the amount of radio waves absorbed at that frequency, and the amount of radio waves absorbed is proportional to the number of hydrogen atoms absorbing the radio waves.

The following spectrum was recorded with a sample of ethanol in deuterochloroform ($CDCl_3$). Ethanol has the condensed formula CH_3CH_2OH. Its ^{1}H NMR spectrum should reflect a 3:2:1 ratio of hydrogens.

Those ratios are shown by the height that the blue integral line "hops" or "steps" as it passes each peak. There are three peaks in ethanol: a sharp peak near 4 ppm, a little blob near 1.5 ppm and another sharp peak near 1 ppm. The first step in the integral line, near 4 ppm, is pretty big. The second step, near 1.5 ppm, is only about half as big as the first one. The third step, near 1 ppm, looks a little bigger than the first. Without getting out a ruler, it's hard to judge exactly how big, but maybe it's 1.5 times bigger than the first.

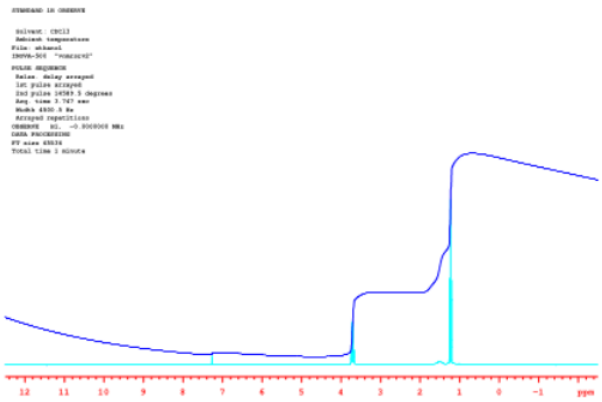


Figure 4.9.1: ^{1}H NMR spectrum of ethanol with solid integral line.

Source: Spectrum taken in $CDCl_3$ on a Varian Gemini 2000 Spectrometer with 300 MHz Oxford magnet.

That means the ratio of these peaks is 1:0.5:1.5. That's the same thing as a 2:1:3 ratio. We are probably looking at, from left to right, the CH_2, the OH and the CH_3 in the ethanol.

We'll get back to looking at that ratio within ethanol in a moment. Meanwhile, it's worth noting that there is an additional, small peak in the spectrum near 7.25 ppm. That's a little bit of regular chloroform, $CHCl_3$, in the $CDCl_3$ solvent used for the NMR spectrum. You might imagine that it's pretty difficult to separate two compounds that differ from each other only by the presence or absence of one neutron. Consequently, there is always a tiny amount of $CHCl_3$ in a bottle of $CDCl_3$. But why is that peak so tiny? nd why does the integral line barely budge upwards as it passes over the peak? If there is one H in $CHCl_3$, should its integral match the 1H in ethanol?

Let's get back to the ethanol spectrum and look at some different ways in which we can view the integration. Sometimes, the integral line is cut into separate integrals for each peak so that they can be compared to each other more easily.

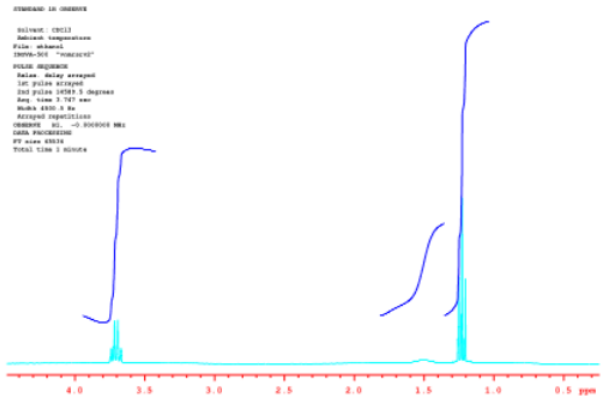


Figure 4.9.2: ^{1}H NMR spectrum of ethanol with broken integral line.

Source: Spectrum taken in $CDCl_3$ on a Varian Gemini 2000 Spectrometer with 300 MHz Oxford magnet.

In the picture above, it's easier to see the 2:1:3 ratio between the peaks.

Often, instead of displaying raw data, the integrals are measured and their heights are displayed on the spectrum.

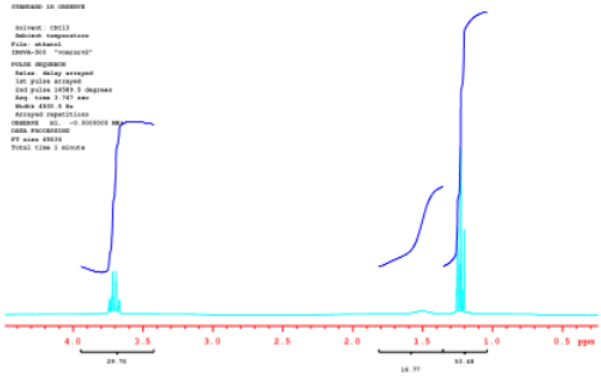


Figure 4.9.3: ^{1}H NMR spectrum of ethanol with numerical integrals.

Source: Spectrum taken in $CDCl_3$ on a Varian Gemini 2000 Spectrometer with 300 MHz Oxford magnet.

The numbers under the spectrum read, from left to right, 29.76, then 14.99 and finally 53.48. Roughly, these numbers are 30:15:54. That's close to a 2:1:3 ratio, although 30:15:45 would be an even better fit. Note that the numerical printout we get does not exactly match the ratio we expect; in fact, it seems a little worse than the ratio we roughly estimated by eye. That's because it really is worse than the ratio we roughly measured by eye.

When you compared the integrals by eye, you were looking at an entire blue integral line and comparing it to another entire blue integral line. You were performing what is called "mulivariable analysis". Each integral line is composed of dozens or hundreds of data points. Your brain takes in all of that information and weighs it carefully to come up with an idea of how high the integral steps as it passes a peak.

It's hard to find NMR software that will perform this analysis as well as you can. It may come up with much more precise numbers than you can, but it's numbers are less trustworthy than yours. That's because the computer is just doing a two-data-point analysis; it measures the change in y coordinate from the beginning of the blue line to the end of the blue line. It's still useful, but keep in mind that it won't be dead on, especially if the ends of the integral line are tilted.

Sometimes the heights are "normalized". They are reduced to a lowest common factor so that their ratios are easier to compare. These numbers could correspond to numbers of hydrogens, or simply to their lowest common factors. Two peaks in a ratio of 1H:2H could correspond to one and two hydrogens, or they could correspond to two and four hydrogens, etc.

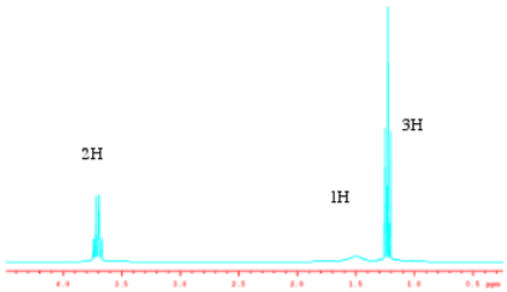


Figure 4.9.4: ^{1}H NMR spectrum of ethanol with normalized integral numbers.

Source: Spectrum taken in $CDCl_3$ on a Varian Gemini 2000 Spectrometer with 300 MHz Oxford magnet.

Note that the ratio is nothing like a comparison of the heights of the peaks. If we were to just estimate the heights of the peaks, we might come up with something like 1:0.1:3 or 10:1:30. The integrals are measuring the total area of the peak, so the width of the peak matters as well as its height.

? Exercise 4.9.1

Because the 1H NMR spectrum has relatively low resolution, the spectra of saturated, straight-chain hydrocarbons are all similar: a peak for the methyl hydrogens at 0.9 ppm and a peak for the methylene (CH_2) hydrogens at 1.0 ppm. However, different hydrocarbons can be identified by their integration values.

Predict the integrations for the following compounds:

a) pentane b) octane c) decane d) heptane e) hexane

Answer

a) 0.9 ppm, 6H; 1.0 ppm, 6H (1:1 ratio)

b) 0.9 ppm, 6H; 1.0 ppm, 12H (1:2 ratio)

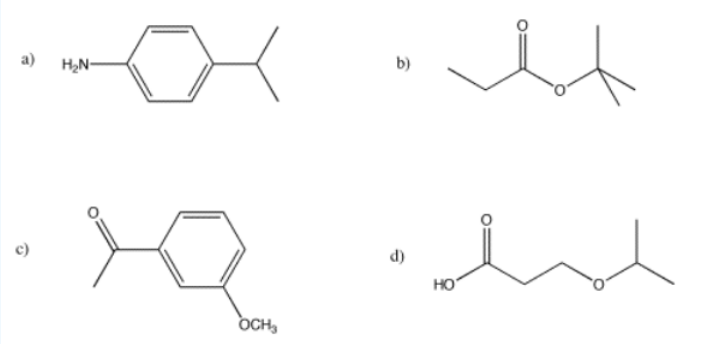
c) 0.9 ppm, 6H; 1.0 ppm, 16H (3:8 ratio)

d) 0.9 ppm, 6H; 1.0 ppm, 10H (3:5 ratio)

e) 0.9 ppm, 6H; 1.0 ppm, 8H (3:4 ratio)

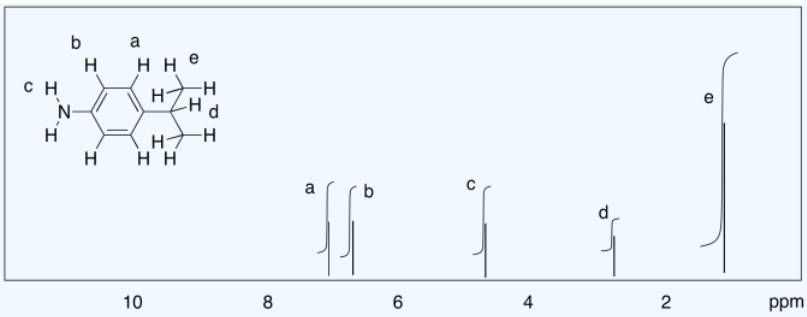
? Exercise 4.9.2

Sketch a predicted NMR spectrum for each of the following compounds, with an integral line over each peak.

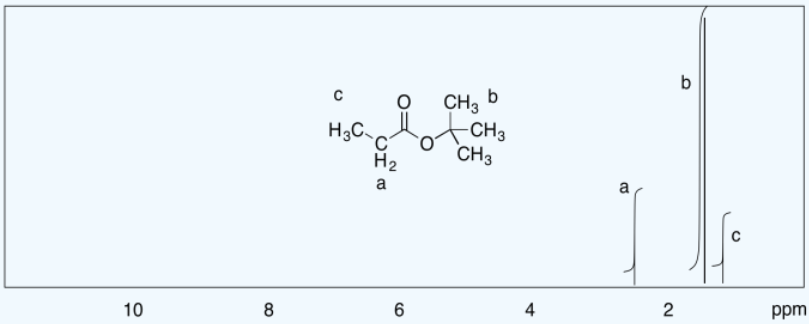


Answer

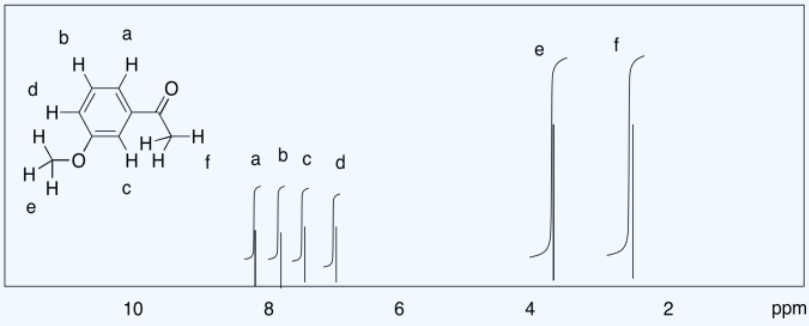
a)



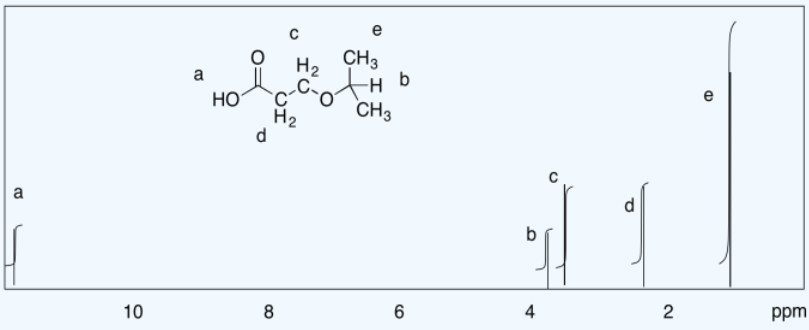
b)



c)

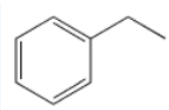


d)

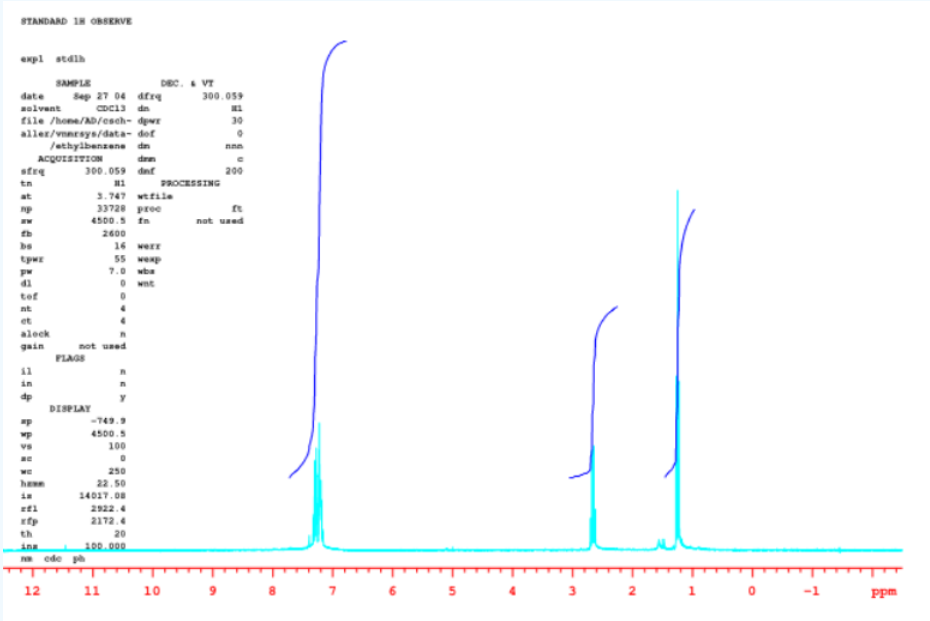


? Exercise 4.9.3

Measure the integrals in the following compounds. Given the integral ratios and chemical shifts, can you match each peak to a set of protons?



ethylbenzene



Answer

a) 5:2:3

4.10: Multiplicity

Another type of additional data available from ^{1}H NMR spectroscopy is called multiplicity or coupling. Coupling is useful because it reveals how many hydrogens are on the *next* carbon in the structure. That information helps to put an entire structure together piece by piece.

In ethanol, CH_3CH_2OH, the methyl group is attached to a methylene group. The ^{1}H spectrum of ethanol shows this relationship through the shape of the peaks. The peak near 3.5 ppm is the methylene group with an integral of 2H.

- This peak is split into four smaller peaks, evenly spaced, with taller peaks in the middle and shorter on the outside.
- This pattern is called a multiplet, and specifically a quartet. A quartet means that these hydrogens have three neighbouring hydrogens on adjacent carbons.

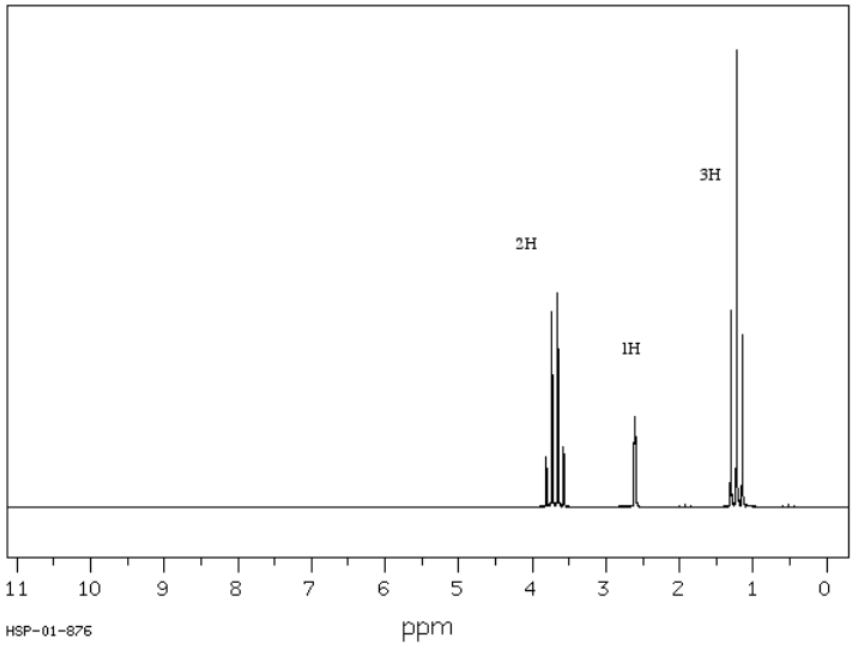
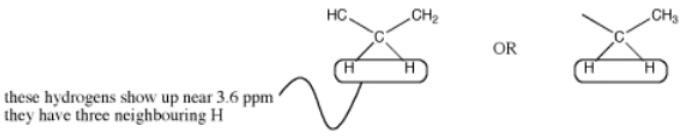


Figure 4.10.1: .^{1}H NMR spectrum of ethanol.

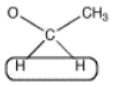
Source: Modified from SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

The integral of 2H means that this group is a methylene, so it has two hydrogens. The carbon bearing these two hydrogens can have two other bonds.

There could be two hydrogens on one neighbouring carbon and one on another. Otherwise, all three hydrogens could be on one neighbouring carbon.



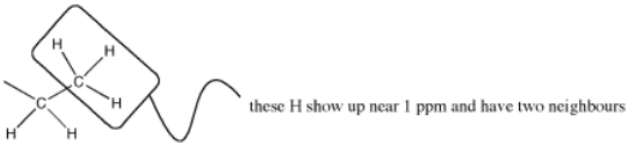
However, the shift of 3.5 ppm means that this carbon is attached to an oxygen. Mutliplicity usually only works with hydrogens on neighbouring *carbons*. If there is an oxygen on one side of the methylene, all three neighbouring hydrogens must be on a carbon on the other side.



Alternatively, look at the spectrum the other way around. The peak at 1 ppm is the methyl group with an integral of 3H.

- The peak is split into three smaller ones, evenly spaced, with a taller one in the middle and shorter ones on the outside.
- This pattern is called a triplet. A triplet means that these hydrogens have two neighbouring hydrogens on adjacent carbons.

The neighbouring H could be on two different neighbouring carbons or both on the same one.



But this group is a methyl; the carbon already has three bonds, so it can have only one neighbouring carbon. It is next to a methylene group.

The number of lines in a peak is always one more than the number of hydrogens on the neighboring carbon. The triplet for the methyl peak means that there are two neighbors on the next carbon (3 - 1 = 2H); the quartet for the methylene peak indicates that there are three hydrogens on the next carbon (4 - 1 = 3H). Table NMR 1 summarizes coupling patterns that arise when protons have different numbers of neighbors.

# of lines	ratio of lines	term for peak	# of neighbors
1	-	singlet	0
2	1:1	doublet	1
3	1:2:1	triplet	2
4	1:3:3:1	quartet	3
5	1:4:6:4:1	quintet	4
6	1:5:10:10:5:1	sextet	5
7	1:6:15:20:15:6:1	septet	6
8	1:7:21:35:35:21:7:1	octet	7
9	1:8:28:56:70:56:28:8:1	nonet	8

The third peak in the ethanol spectrum is usually a "broad singlet". This is the peak due to the OH. You would expect it to be a triplet because it is next to a methylene. Under very specific circumstances, it does appear that way. However, coupling is almost always lost on hydrogens bound to heteroatoms (OH and NH). The lack of communication between an OH or NH and its neighbors is related to rapid proton transfer, in which that proton can trade places with another OH or NH in solution. This exchange happens quite easily if there are even tiny traces of water in the sample.

In summary, multiplicity or coupling is what we call the appearance of a group of symmetric peaks representing one hydrogen in NMR spectroscopy.

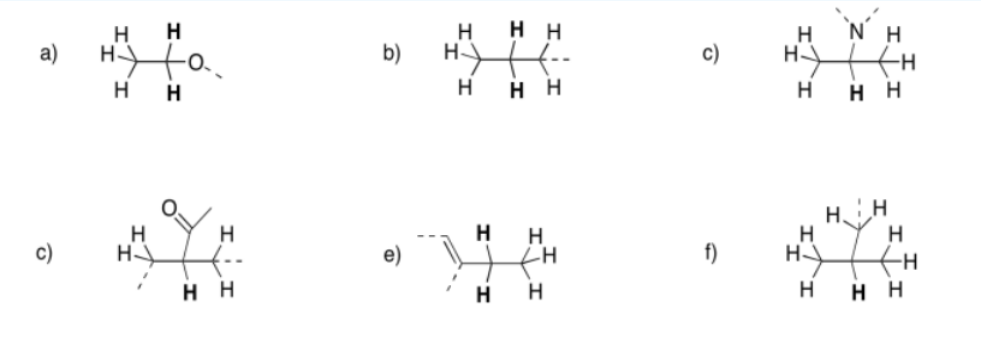
- A proton can absorb at different frequencies because of the influence of neighbouring hydrogens.
- Protons on one carbon atom are affected by different protons on the next carbon atom, provided those two carbons are directly attached to each other.
- Stated another way, these neighboring hydrogens must be three bonds away (and so this phenomenon is sometimes called "three-bond coupling").
- When a proton is coupled, the number of neighbouring hydrogens is one less than the number of peaks in the multiplet.

There are limitations on coupling:

- coupling does not occur between hydrogens of the same type ("equivalent hydrogens"). In the proton spectrum of ethane, CH_3-CH_3, you would only observe one singlet.
- coupling often does not occur across heteroatoms such as oxygen and nitrogen. The OH peak in ethanol may be a singlet instead of a triplet, although there are two hydrogens on the neighboring carbon. The methylene peak in ethanol may be a quartet instead of a quintet, even though there are actually four neighboring hydrogens: three on the attached methyl and one on the attached hydroxyl

Exercise 4.10.1

Predict the shift, integration, and multiplicity for the **bold** hydrogen in each case.



Answer

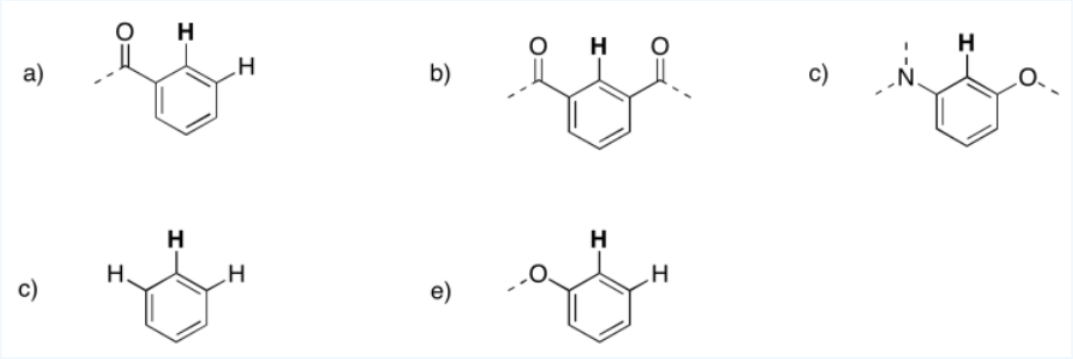
(There will be some variation in the shift depending on the rest of the structure; this is just an estimate.)

a) 3.5 ppm, quartet, 2H b) 1.5 ppm, sextet, 2H c) 2.6 ppm, septet, 1H

d) 2.3 ppm, quintet, 1H e) 2.2 ppm, quartet, 2H f) 1.7 ppm, nonet, 1H

Exercise 4.10.2

Predict the shift, integration, and multiplicity for the **bold** hydrogen in each case.



Answer

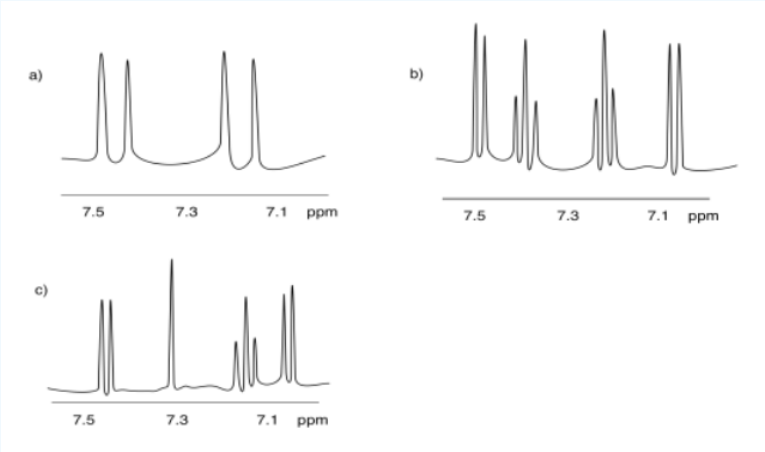
(There will be some variation in the shift depending on the rest of the structure; this is just an estimate.)

a) 7.8 ppm, doublet, 1H b) 8.4 ppm, singlet, 1H c) 6.7 ppm, singlet, 1H

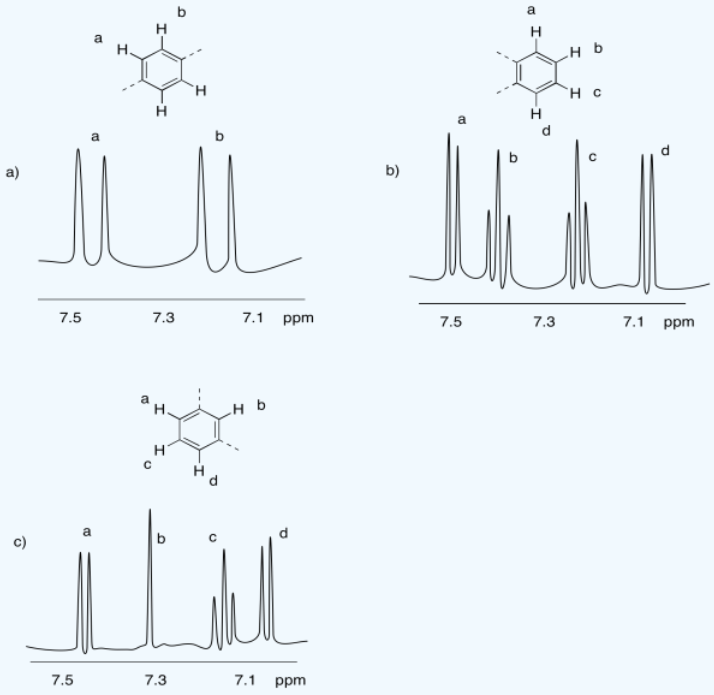
d) 7.2 ppm, troplet, 1H e) 6.9 ppm, doublet, 1H

Exercise 4.10.3

The following patterns indicate particular substitution patterns in disubstituted benzenes: 1,2-C_6H_4XY; 1,3-C_6H_4XY; or 1,4-C_6H_4XY. Match each pattern to the correct structure.

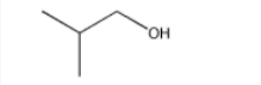


Answer

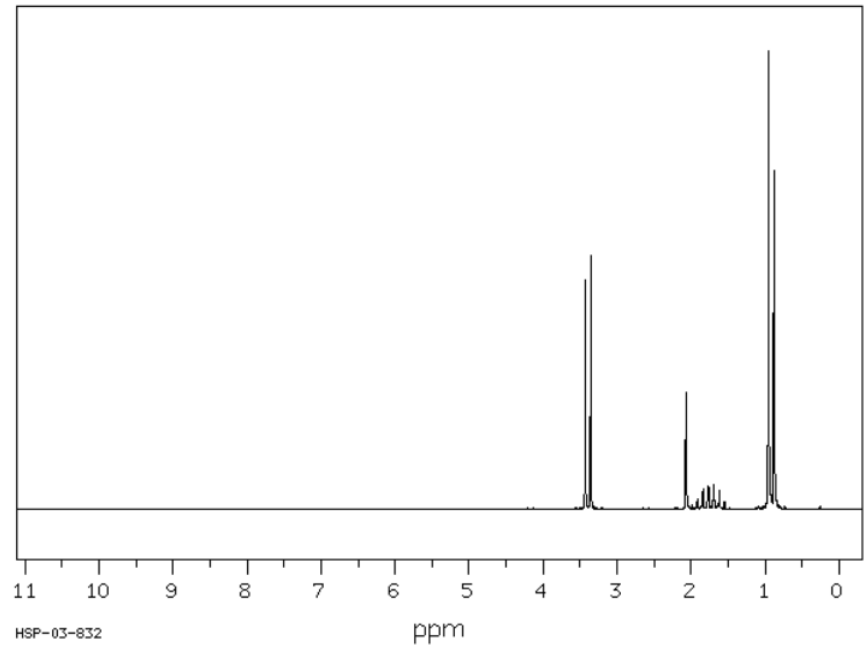


Exercise 4.10.4

The spectrum of isobutanol is shown below. Assign each peak to a different proton in the structure.



isobutanol or 2-methyl-1-propanol



Source: Modified from SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 15 August 2008)

Answer

3.4 ppm, doublet: CH-C**H**$_2$-O

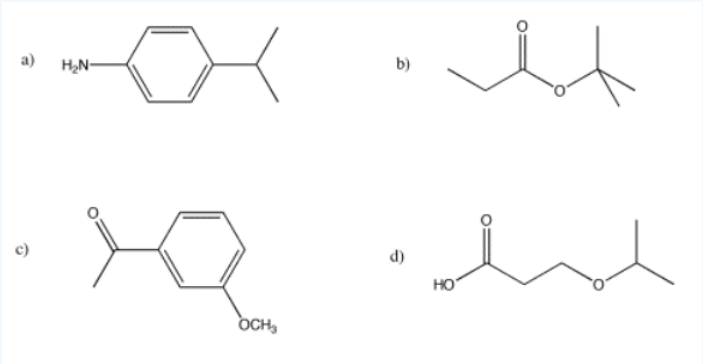
2.1 ppm, singlet: O**H**

1.7 ppm, nonet: $(CH_3)_2C\mathbf{H}CH_2$

0.9 ppm, doublet: $CH(C\mathbf{H}_3)_2$

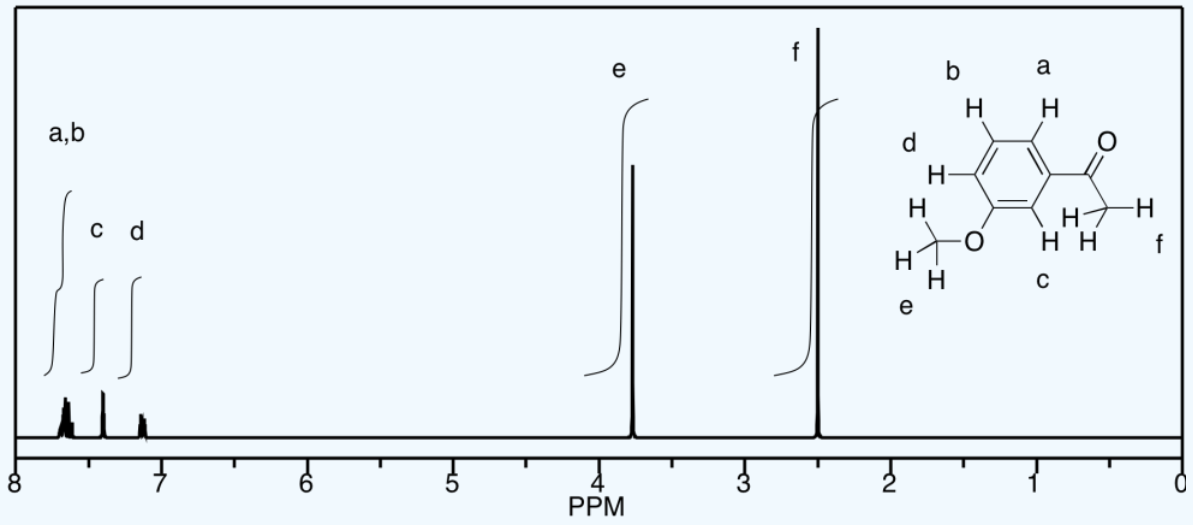
Exercise 4.10.5

Sketch predicted ^{1}H NMR spectra, complete with coupling and integration, for the following structures:

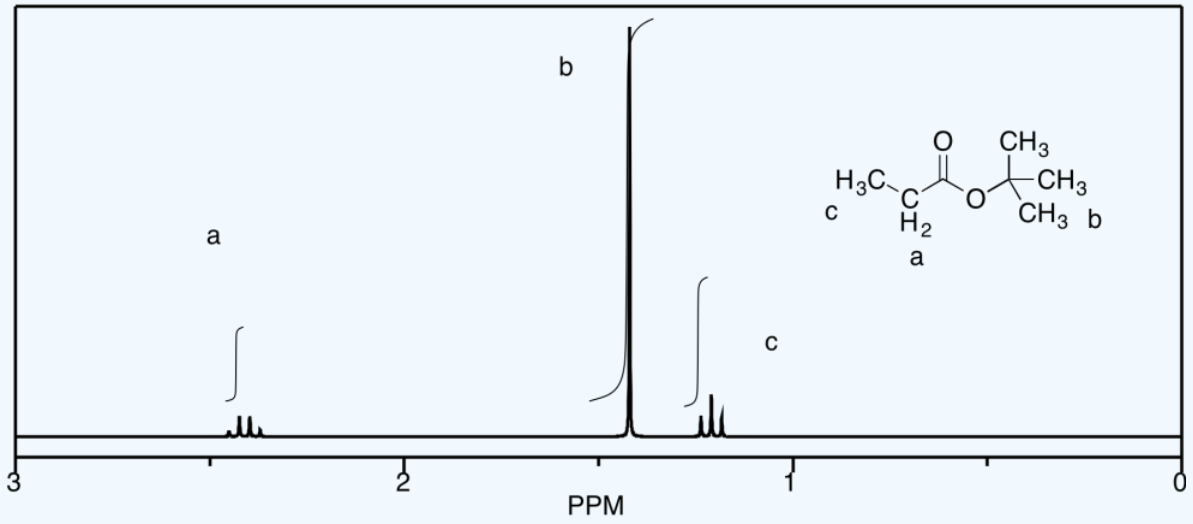


Answer

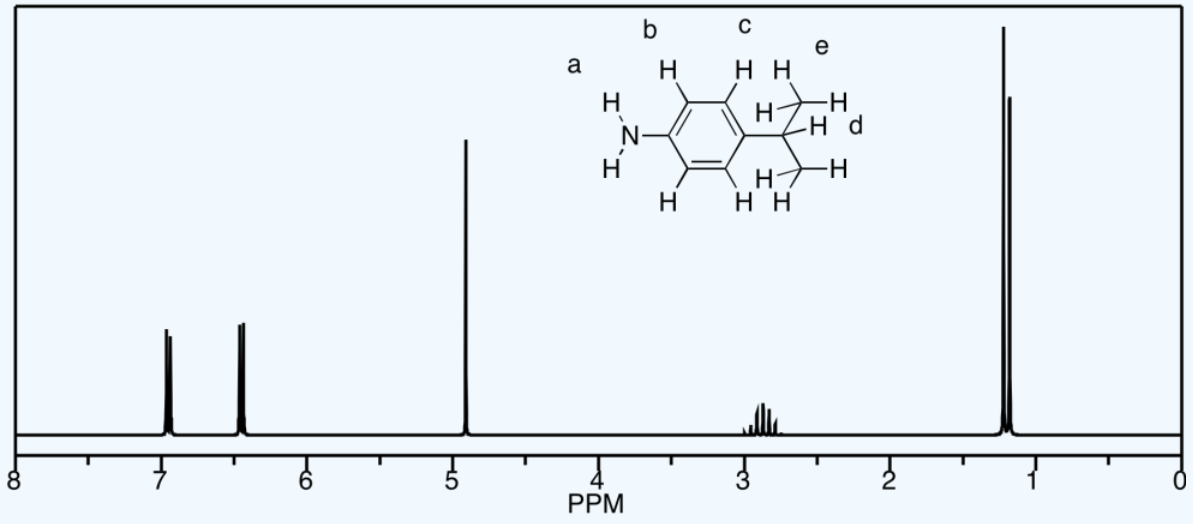
a) This is a simulated spectrum. The peaks at f, e, and c are singlets. The peak at d is a doublet. The peaks at a & b are unfortunately coincident, so their multiplicities are obscured, but they would be doublets & triplets, respectively.



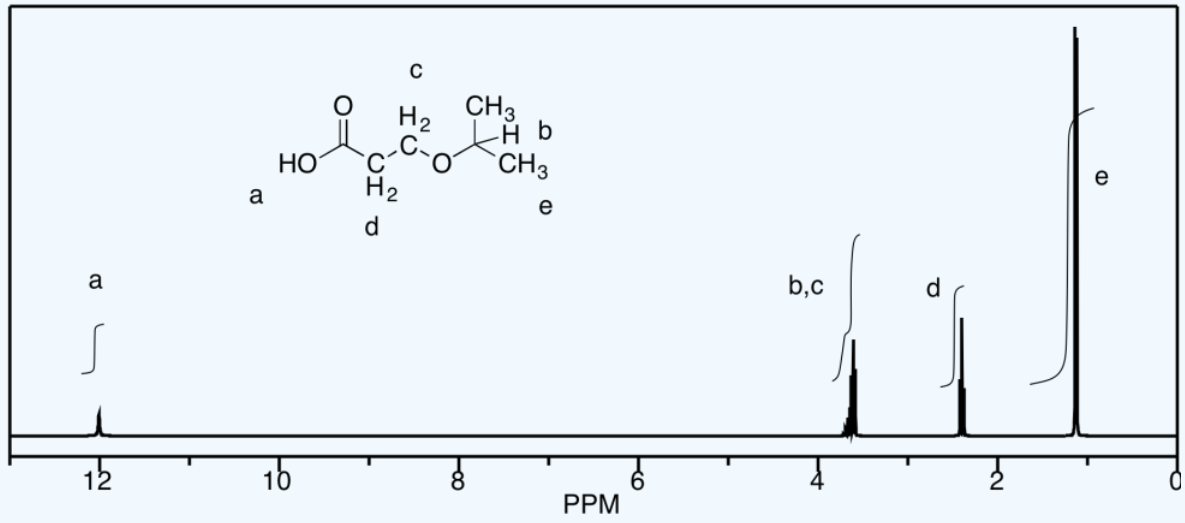
b)



c)

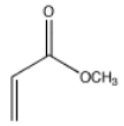


d) The peaks at b and c unfortunately coincide, but they would be a septet and a triplet, respectively. Otherwise, a is a singlet, d is a triplet, and e is a doublet.



4.11: More Complicated Coupling

The n + 1 rule (number of lines in a multiplet = number of neighbouring H + 1) will work for the majority of problems you may encounter. Occasionally, you may see more complicated coupling. The spectrum of methyl acrylate is a good example. There are a couple of points to note in this spectrum, beginning with the number of peaks.



methyl acrylate

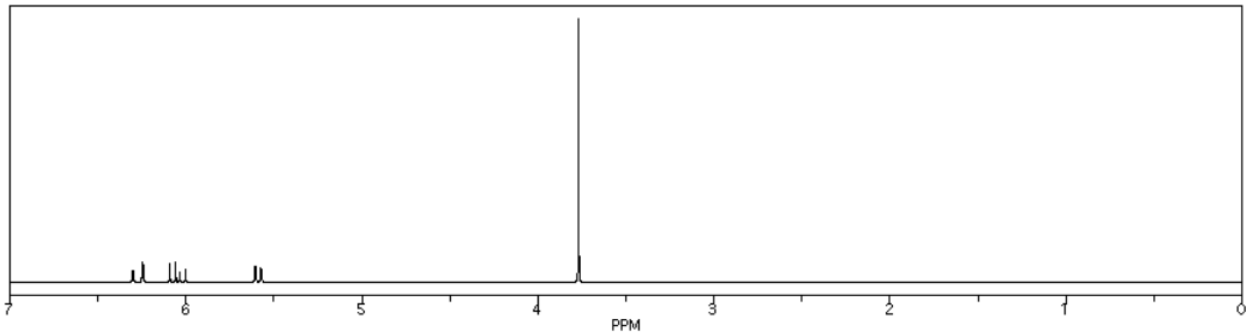


Figure 4.11.1: ^{1}H NMR spectrum of methyl acrylate.

Source: Simulated spectrum.

- the vinyl portion of the spectrum (hydrogens adjacent to the C=C double bond) shows three peaks, not just two.
- although there are two protons on one vinyl carbon, each H is different because of cis/trans relationships: one H is cis to the carbonyl and the other is trans to it.
- these hydrogens are symmetry inequivalent.

In addition, there is a problem with coupling in the vinyl region.

- the proton adjacent to the carbonyl, at 6 ppm, has two neighbors and should give a triplet.
- instead, the peak from this proton shows four lines, not three.
- this peak is not a quartet; the middle two peaks are not three times as tall as the edge ones.
- the lines within this multiplet are symmetrically spaced, but not evenly; the middle space is smaller than the spaces on the edges.

This pattern is called a "doublet of doublets". The two symmetry-inequivalent neighbors on the other end of the double bond each act as if the other one isn't there. They couple to the proton next to the carbonyl independently, each one splitting the peak for this proton into a separate doublet.

There are a few cases in which this independent coupling will occur rather than the (n+1) type coupling we saw first. Generally, independent coupling occurs when protons are not freely rotating. That can happen if one of the protons is attached to a double-bonded carbon, because we can't rotate around a double bond. It may also happen with protons that are directly attached to the carbons of a ring.

To see why this happens, you need to know more about coupling.

- in coupling, magnetic information is shared between two protons. How fully this information is shared depends on the angle between the hydrogens as you look down the connecting C-C bond.
- for (n+1) coupling, the rotational angle about the C-C bond connecting the two protons (or 'dihedral angle' between the coupled hydrogens) must be unrestricted. The bond must be able to rotate freely.
- if the bond can rotate freely, any proton on the neighbouring carbon can assume any dihedral angle with the proton being observed. That means coupling information from one neighbouring proton is indistinguishable from another, and so all the neighbouring protons affect the observed proton equally.

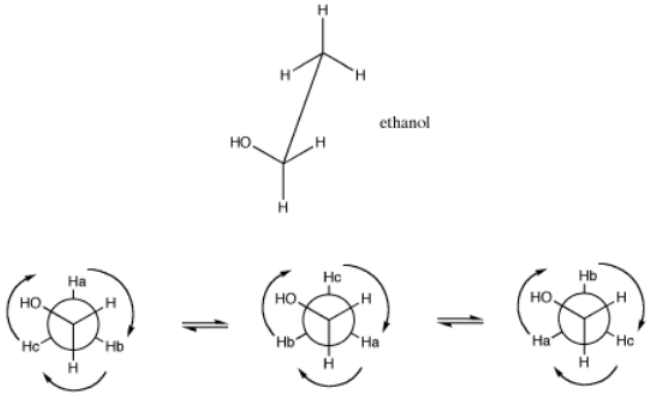
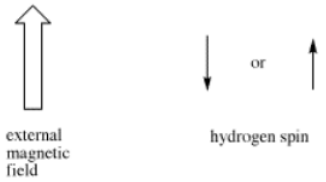
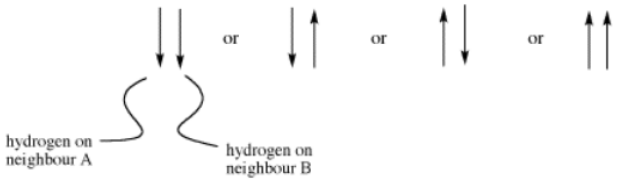


Figure 4.11.2: A sawhorse projection (top) and Newman projection of ethanol (bottom), showing the angular relationship between hydrogens on neighbouring carbons. The angle between two groups on neighbouring carbons is called the dihedral angle. Because of free rotation about the C-C bond, all three hydrogens on the methyl have an equivalent spatial relationship to the hydrogens on the CH_2 group.

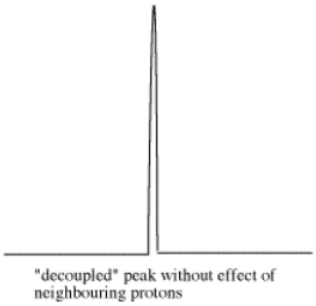
Sometimes coupling information is depicted as an arrow. This arrow stands for the coupling constant between two protons. The coupling constant is related to the spin of a hydrogen atom. The spin (related to magnetic moment) can be aligned with the external magnetic field (we will show it pointing up) or else against it; no other possibilities are allowed.



If there are two neighbouring hydrogens, both spins could be aligned with the external field, both could be aligned against it, or one could be aligned each way. That means there are three different magnetic combinations that will each have a different effect on the observed proton: increased magnetic field, decreased magnetic field, and no net effect (canceling out).



These three combinations result in the observed proton absorbing at three different frequencies, because the frequency it absorbs is sensitive to the magnetic field it experiences. Note that there are two ways to arrive at the middle possibility, with one neighbour spin up and the other spin down. Statistically this possibility is twice as likely as either both spins up or both spins down. It is thus twice as likely that the observed proton experiences that effect, and so the middle line in a triplet is twice as high as the other two lines.



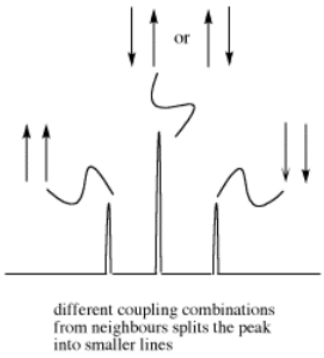
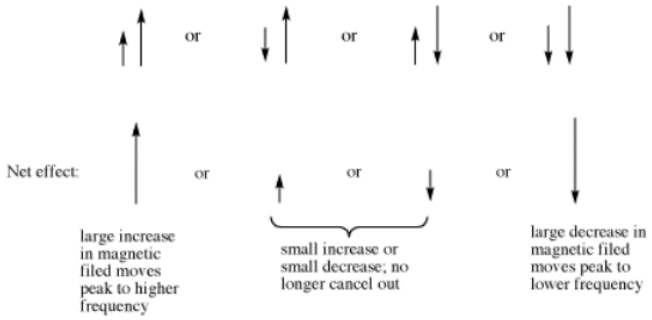


Figure 4.11.3: Effects of neighbouring protons on an observed peak. This case assumes all the neighbouring protons have an equivalent effect (they have the same coupling constant with the observed proton).

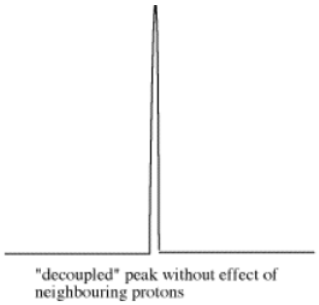
However, the size of that arrow, the coupling constant, is only the same for two neighbouring hydrogens if they have the same spatial relationship with the observed hydrogen. That isn't always true.

- if the dihedral angle is limited, complex coupling occurs.
- complex coupling occurs because one neighbouring hydrogen can only adopt a limited range of dihedral angles. Another neighbouring proton can adopt a limited range of dihedral angles as well, but these two ranges do not overlap.

As a result, the two coupling constants are different. We can depict that situation using arrows of different lengths for the two neighbouring proton spins. Each spin can be either up or down, but now two opposing spins do not cancel out. The result is four spin combinations of equal probability, not just three.



The doublet of doublets is four lines of about equal heights. The distance between the two pairs of lines on each edge



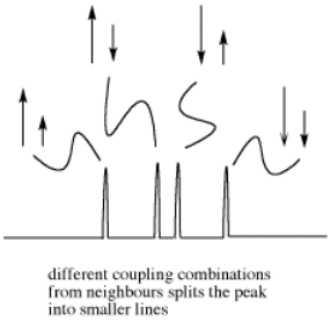


Figure 4.11.4: Effects of neighbouring protons on an observed peak. This case assumes neighbouring protons have inequivalent effects (they have differing coupling constants with the observed proton).

The dihedral angle is limited in only a few specific cases:

- there is a double bond. Double bonds cannot rotate because that would require breaking the pi bond. In a pi bond, p orbitals on the two carbons must remain coplanar in order to overlap and form a bond.
- there is a ring. In a ring, there can't be complete rotation about a bond because the ring would twist into a pretzel.
- in some cases, there can be such large groups of atoms on either end of a bond that it is difficult to rotate the bond without having these groups crash into each other.

Exercise 4.11.1

Sketch spectra for the following compounds.

a) allyl alcohol or 2-propene-1-ol, $HOCH_2CH{=}CH_2$

b) styrene or vinylbenzene, $C_6H_5CH{=}CH_2$

c) *trans*-1-chloropropene, $CH_3CH{=}CHCl$

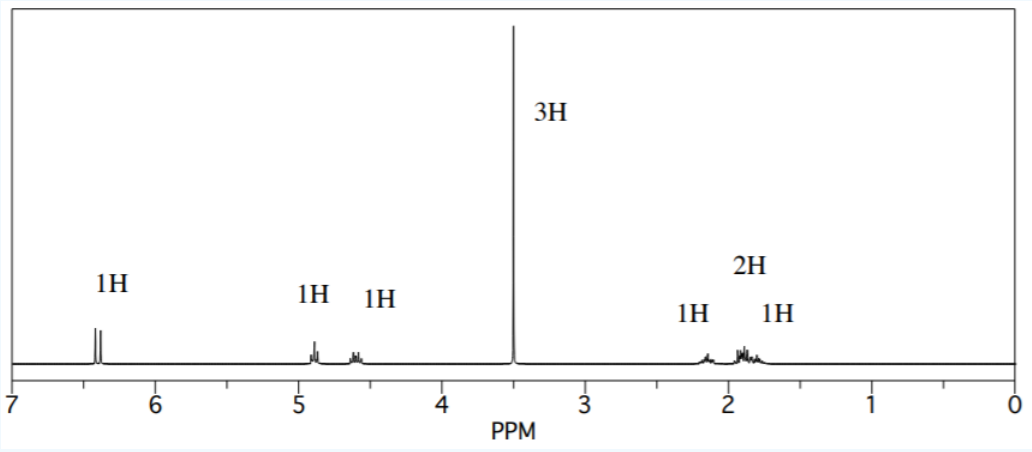
Exercise 4.11.2

A compound was shown via high-resolution mass spectrometry to have the probable formula $C_6H_{10}O_2$.

a) What is the degree of unsaturation in this compoud?

b) IR spectroscopy gave the following data: 3105 (w), 2950 (m), 1517 (m), 1235 (s), 1056 (s), 715 (m) cm^{-1}. Provide a data table with possible assignments for these peaks.

c) ^1H NMR spectroscopy provided the following spectrum. Provide a data table with partial structures for each peak.

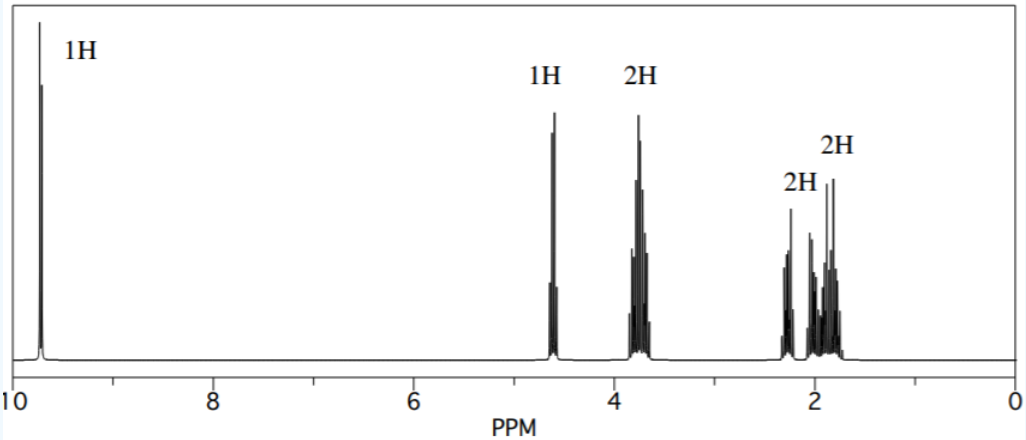


d) Suggest a likely structure for this compound

Exercise 4.11.3

A compound was shown via high-resolution mass spectrometry to have the probable formula $C_5H_8O_2$.

a. What is the degree of unsaturation in this compound?
b. IR spectroscopy gave the following data: 2950 (m), 2825 (m), 2716 (m), 1724 (s), 1505 (m), 1056 (w) cm^{-1}. Provide a data table with possible assignments for these peaks.
c. ^1H NMR spectroscopy provided the following spectrum. Provide a data table with partial structures for each peak.

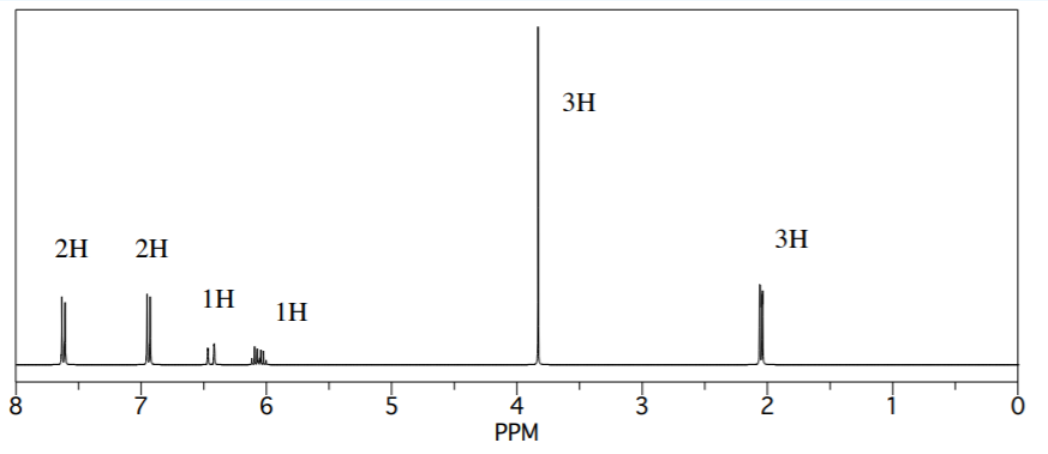


d. Suggest a likely structure for this compound.

Exercise 4.11.4

A sample of a natural product was isolated from plant material and subjected to analysis.

a. IR spectroscopy gave the following data: 3097 (m), 2975 (m), 1600 (m), 1495 (m), 1235 (s), 1056 (s), 747 (m), 705 (m) cm^{-1}. Provide a data table with possible assignments for these peaks.
b. The compound was shown via high-resolution mass spectrometry to have the probable formula $C_{10}H_{12}O$. What is the degree of unsaturation in this compound?
c. ^1H NMR spectroscopy provided the following spectrum. Provide a data table with partial structures for each peak.



d. Suggest a likely structure for this compound.

4.12: Constructing Partial Structures in NMR Spectroscopy and Combined Structure Determination

When you look at an IR spectrum, you immediately see little chunks of the structure, because you see individual bonds. You know at a glance that the compound contains a C=O bond or an O-H bond. That can be very reassuring, because you can quickly imagine what you are dealing with.

NMR spectra often take more work. You may have to put pencil to paper to come up with a structure. The work pays off, because you can get a much more detailed picture of the structure.

Let's start with a ^{13}C NMR spectrum. Suppose you had peaks in the spectrum at 200, 35 and 15 ppm. We might assign these three peaks as follows:

shift (ppm)	partial structure
200	sp^2 **C**=O
35	sp^3 **C**-C=O
30	sp^3 **C**-C=O
15	sp^3 **C**-C

We are saying that the first carbon is in the sp^2 or trigonal planar region, and that it is so far downfield because of a double bond to oxygen. The other two carbons are in the sp^3 or tetrahedral region. One of them isn't very far downfield; it is probably just attached to another sp^3 carbon. The other two, at 35 and 30 ppm, are both a little further downfield. That's around the right place for a tetrahedral carbon attached to a trigonal planar carbon; that is, these carbons are each attached to either a double bond or a carbonyl.

In the partial structure, we always **bold** or underline the carbon that corresponds to the peak we are discussing. If you don't do that, it isn't clear whether the peak at 30 comes from a carbon next to the carbonyl (C=O), or the carbon in the carbonyl itself. Also, on the peak at 15, we want to make clear that we are talking about a single carbon atom; leaving the partial structure as C-C somehow implies that this spectroscopy observes bonds, but it does not. IR spectroscopy observes bonds. ^{13}C NMR spectroscopy observes carbon atoms.

Now, suppose we look at the ^{1}H NMR spectrum for the same compound. Maybe we see three peaks this time. There is a quartet integrating for 2H at 2.3 ppm, a singlet integrating for 3H at 2.1 ppm, and a triplet integrating for 3H at 1.1 ppm. We enter those characteristics in a table. This time, there are three features to explain for each peak.

shift	integ.	multipl.	partial structure
2.3	2H	quartet	CH_3-C**H**$_2$-C=O
2.1	3H	singlet	C**H**$_3$-C=O
1.1	3H	triplet	C**H**$_3$-CH2

First of all, we need to explain the shift. All of these peaks are in the upfield end of the spectrum (below 5 ppm), so they are likely from hydrogens on sp^3 or tetrahedral carbons. The first two are slightly downfield, just past 2 ppm. That suggests that the sp3 carbons they are attached to may in turn be attached to sp^2 carbons: either double bonds or carbonyls. We already know there is a carbonyl from the ^{13}C spectrum, so let's assume that's what is causing the shift near 2 ppm. The third peak, at 1.1 ppm, is in the normal range; this hydrogen is on a tetrahedral carbon, likely attached to other tetrahedral carbons.

To demonstrate what the integration is telling us, we just show the correct number of hydrogens. There are two hydrogens responsible for the peak at 2.3 ppm. Three others are responsible for the peak at 2.1 ppm, and another three give rise to the peak at 1.1 ppm.

Finally, we need to explain the muliplicity. The peak at 2.3 ppm is a quartet, so by the "n+1" rule it must be next to a CH_3 group. The peak at 1.1 ppm is a triplet, so it must be next to a CH_2 group. (It does not take long to figure out that these two peaks represent hydrogens that are next to each other.) Finally, the peak at 2.1 ppm is a singlet. It has no hydrogen neighbors at all.

Notice we do not need to know what the structure is in order to fill in these partial structures. We are just writing down what the data is telling us. From there, it isn't very far to determine the overall structure.

Exercise 4.12.1

Fill in partial structures for the following peaks.

a) 10.1 ppm, 1H, triplet b) 3.4 ppm, 1H, septet c) 7.3 ppm, 2H, triplet

d) 5.4 ppm, 1H, quartet e) 1.4 ppm, 2H, sextet f) 8.0 ppm, 1H, singlet

g) 2.1 ppm, 3H, singlet h) 6.8 ppm, 2H, doublet i) 0.9 ppm, 6H, doublet

Answer

Aromatic (benzene etc) peaks are labeled "Ar" to distinguish from alkene peaks that show up further upfield (lower shift). Also, some peaks may be in two symmetric positions and are labeled with "x2".

a) 10.1 ppm, 1H, triplet, CH_2-C**H**=O b) 3.4 ppm, 1H, septet, O-C**H**$(CH_3)_2$

c) 7.3 ppm, 2H, triplet, CH=C**H**-CH x 2 (Ar) d) 5.4 ppm, 1H, quartet, CH_3-C**H**=C

e) 1.4 ppm, 2H, sextet, CH_3-C**H**$_2$-CH_2 f) 8.0 ppm, 1H, singlet, C=C**H**-C (Ar)

g) 2.1 ppm, 3H, singlet, C**H**$_3$-C=C or C**H**$_3$-C=O or C**H**$_3$-N; need context to choose

h) 6.8 ppm, 2H, doublet, CH=C**H**-C x 2 (Ar) i) 0.9 ppm, 6H, doublet, CH-C**H**$_3$ x 2

Exercise 4.12.2

Identify the errors in the following partial structures:

a) 3.6 ppm, 2H, triplet, C**H**$_2$-CH_2 b) 2.1 ppm, 2H, singlet, C**H**$_3$-C=C

c) 7.4 ppm, 2H, doublet, CH=C**H**$_2$-C d) 1.8 ppm, 2H, quintet, C**H**$_2$-CH_4

e) 7.8 ppm, 1H, triplet, -C**H**=CH_2 f) 1.7 ppm, 1H, nonet, NH_2-C**H**$(CH_3)_2$

Answer

Identify the errors in the following partial structures:

a) 3.6 ppm, 2H, triplet, C**H**$_2$-CH_2 the first carbon must be attached to O to have a shift at 3.6 ppm

b) 2.1 ppm, 2H, singlet, C**H**$_3$-C=C the integral says only 2H, not 3H

c) 7.4 ppm, 2H, doublet, CH=C**H**$_2$-C the shift implies aromatic, so there can only be one H per carbon; must be symmetry

d) 1.8 ppm, 2H, quintet, C**H**$_2$-CH_4 there can't be four hydrogens on one carbon; must be some hydrogens on each side

e) 7.8 ppm, 1H, triplet, -C**H**=CH_2 the shift implies aromatic, so there can only be one H per carbon; must be one one each side

f) 1.7 ppm, 1H, nonet, NH_2-C**H**$(CH_3)_2$ an attached nitrogen would shift this hydrogen past 2 ppm; also, coupling is rarely seen across O or N, so the two neighbouring H on the left are probably on a carbon.

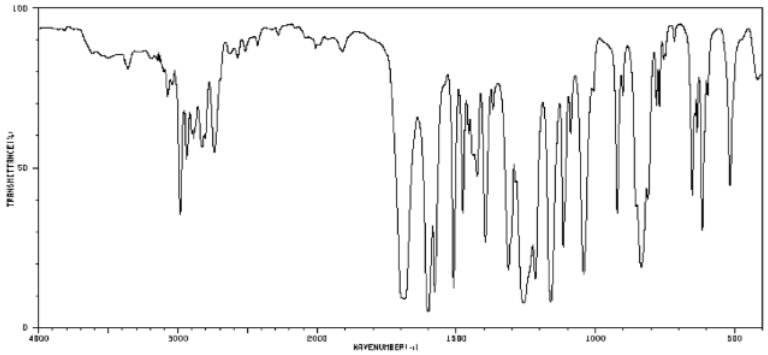
There are a many ways we can use NMR spectroscopy to analyse compounds. One common application is in determination of an unknown structure. Given the MS, IR, ^{13}C and ^{1}H NMR spectra, what might be the structure of an unknown sample?

It is often easiest to start with the IR spectrum.

- identify at least three peaks in the IR spectrum. Which peaks seem to tell you the most information about this compound?
- don't think with your head; think with your hands. Write down ideas on the spectrum.
- if you are working on a formal proof of structure, on a class test or a lab report, you may be required to enter your data in a table correlating wavenumber with peak assignment:

cm^{-1}	asst

For example, a student might obtain the following IR spectrum.



From that information, she constructs the following table. She might even write this table, by hand, directly on her spectrum. She makes useful notes on the edges, and might even include some guesses, which she later crosses out, but does not erase. She is assisted in this task by consulting an IR table, that suggests what some of these peaks might mean.

frequency (cm^{-1})	description	assignment
3400	weak, broad	OH (water?)
2990	medium, sharp	sp3 C-H
2800 & 2700	medium, sharp	aldehyde C-H 
1700	strong	C=O
1250	strong	C-O
1150	strong	(C-O ??)
825	strong	C=C-H bending

Remember:

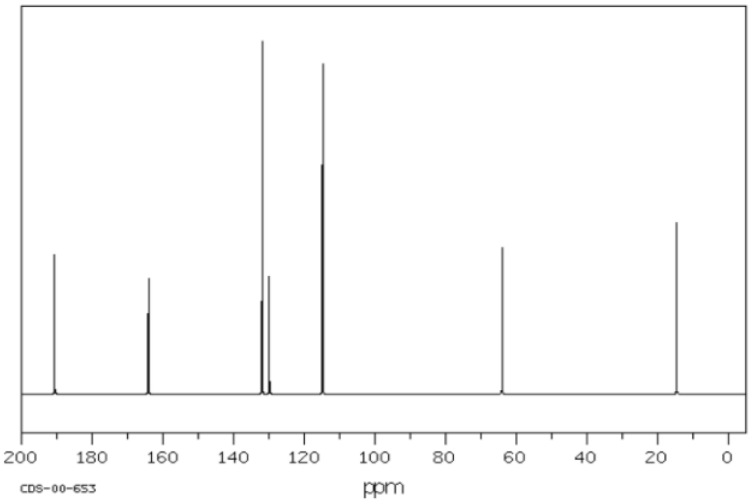
- make special note of what atoms are present in the compound: C, H, N, O...
- also note your initial ideas about specific functional groups that may be present.
- if you are unsure of an assignment, put a question mark beside it to signal this uncertainty.
- some data may need to be discarded later if it is not consistent with other data.

Look at the ^{13}C spectrum.

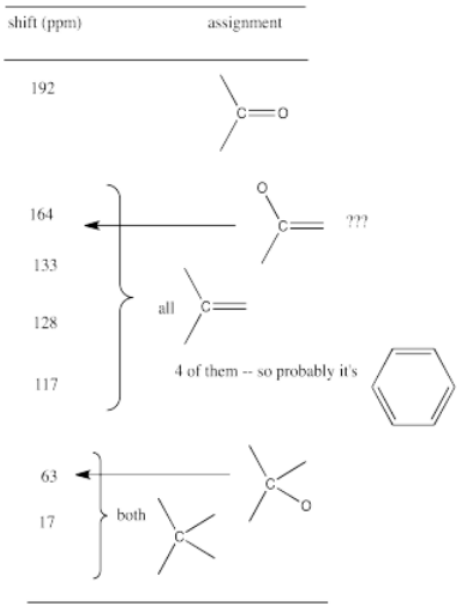
- How many different carbons are there, based on the number of peaks in the spectrum? This is the first step in estimating the molecular formula.
- Do you have reason to believe there is symmetry in the structure? In the entire compound or just part of it? Adjust the number of carbons you think you are dealing with.
- As in IR spectroscopy, begin assigning peaks, either on the spectrum or, if required, in a table:

ppm	asst

For example, a student might obtain the following ^{13}C NMR spectrum:



From that information, she puts together the following table:



Remember:

- you will be able to assign all peaks in the NMR spectrum, not just a few like in IR.

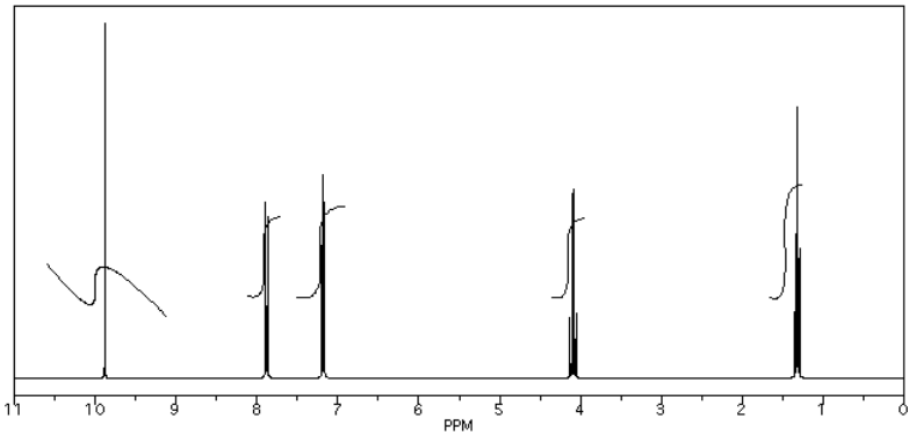
As in ^{13}C NMR, you should be able to assign all peaks in the ^{1}H NMR spectrum. You may be able to do so by making notes on the spectrum. If you think you know the structure, you may be able to draw it and note which peak belongs with which proton.

A formal proof of structure might require a table of assignments.

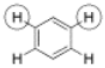
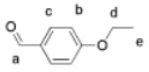
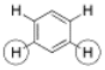
ppm	int	mult	partial structure	assignment

- This table demonstrates your ability to read the spectrum. Can you decide what ratio of protons is suggested by the integral line? Can you decide whether a peak is a quartet?
- The partial structure column should explain the shift, integration and multiplicity for the peak in that row. It should not show any other information from elsewhere in the structure. This restriction forces you to demonstrate a thorough understanding of the data in a way that "getting the right answer" does not.
- The partial structure column is best filled in with drawings, not words. The drawing is a partial structure.
- Because the partial structure will show the protons absorbing at the shift in that row as well the neighbouring protons, you need to distinguish between them in your picture. Most people circle or underline or make **bold** the protons that show up at the shift given in that row.
- When finished with the partial structure column, you should be able to link the partial structures together to make an entire structure in the assignment column.

An example of a spectrum and its accompanying data table is given below. Here is the spectrum:



Here is a data table:

	shift	integration	int(n)	multiplicity	partial structure	assignment
a	9.7 ppm	11 mm	1H	singlet		
b	7.5 ppm	23 mm	2H	doublet		
c	8.1 ppm	21 mm	2H	doublet		
d	3.8 ppm	24 mm	2H	quartet		
e	1.2 ppm	35 mm	3H	triplet		

Things to note:

- This student has used two integration columns instead of just one.

- The first column shows the integral measured from the spectrum. She probably used a ruler.
- The second column, which she called int(n), contains a convenient ratio taken from the raw data. This ratio is easier to use in her assignments.
- Also note that the peak at 9.7 ppm does not have a very good integral. There is either a "phasing" or a "level & tilt" problem here that can be corrected using the NMR software, but this is sometimes difficult to do. If she had taken an automatic printout of this integral measurement, she would have gotten a strange number; in this case, it would be about -5, because the end of the integral line is lower than the start. It clearly isn't a negative number of hydrogens, though. She has instead measured the vertical rise in the integral and recorded that; it isn't perfect, but is a fair estimate in this case.

There are a couple of additional tools that can help to confirm the structure at this point. Alternatively, if the structure is still elusive, these tools might help to produce some ideas.

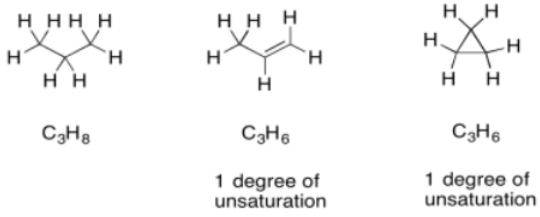
The first tool is the formula. Once we have NMR tables, we can begin guessing at the numbers of carbons and hydrogens in the structure. With the addition of an IR table, we can begin guessing at the presence of other atoms, such as oxygen or maybe nitrogen.

For example, in the ^{13}C NMR table above, there were seven peaks. That means there are probably at least seven carbons. We can start off the molecular formula as C_7. However, there may be additional carbons if there is some symmetry. There may also be a few carbons that do not show up very well in the spectrum. If you have ever obtained a real ^{13}C NMR spectrum, you will know that carbonyl peaks can be hard to find, especially if there are no hydrogens attached to the carbonyl. In the table above, it looked like there was a benzene, so maybe there werereally six carbons in the aromatic region, and not just four carbons. That would mean the formula, so far, is C_9.

In the ^1H NMR table, the integrals added up to a total of 10H. So, maybe the formula is C_9H_{10}.

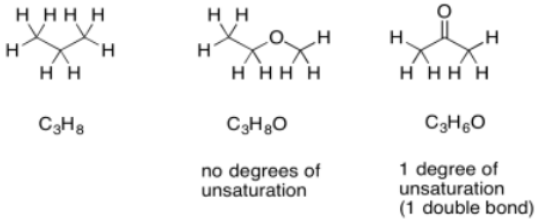
Furthermore, the IR table suggested the possible presence of two different oxygen atoms. The formula may actually be $C_9H_{10}O_2$.

Once we have a formula, we actually get a great deal of information automatically. One of the most important pieces is "units of unsaturation" or "degrees of unsaturation" (DU). The DU is the result of a formal comparison of the C/H ratio in the compound to that in a normal alkane. In a normal alkane, the formula is always C_nH_{2n+2}. If you picture a long hydrocarbon chain, there will be two hydrogens on each carbon along the chain, plus one more hydrogen at either end of the chain. However, an alkene contains one pi bond, and at the site of that pi bond there are two hydrogen atoms missing from that alkane formula. A simple alkene always has the formula C_nH_{2n}. That missing pair of hydrogens in the formula is called a degree of unsaturation.

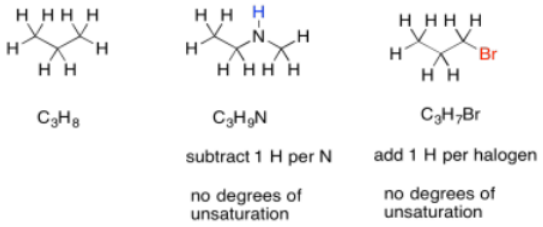


The same thing also happens to the formula if there is a ring present. One DU can correspond to the presence of a double bond or a ring. If DU=2, there may be two double bonds, two rings, or one of each.

If there are oxygen atoms present in the formula, we can just ignore them and pay attention to the hydrocarbon part. Conceptually, because oxygen forms two bonds, we can think of it as squeezing in between any two atoms in a hydrocarbon structure to form a new compound. The ratio of carbon to hydrogen is unchanged. If there is a degree of unsturation in a formula containing oxygen, it simply suggests the presence of a ring or a double bond, just like in a hydrocarbon.



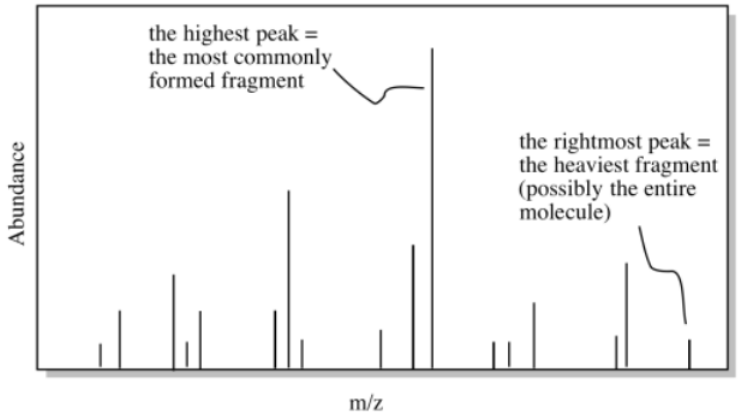
Sometimes, if there are other atoms present, we need to adjust the formula to take them into account. For example, any time a halogen is found in the structure, it conceptually replaces a hydrogen atom. In order for a halogen to be found in the structure, there would have to be one fewer hydrogen atoms in order to open up a spot for the halogen. To adjust for the presence of a halogen, we need to add one hydrogen into the formula, then compare it to the standard alkane formula.



Nitrogen, on the other hand, has three bonds. Unlike oxygen, if we squeeze it in between two other atoms, it still needs one extra bond. It always brings an extra hydrogen into the formula. To adjust for the presence of nitrogen, we need to subtract one H from the formula, then compare it to the standard alkane formula.

In the formula we just calculated, we have $C_9H_{10}O_2$. We can ignore the oxygens and look at the C9H10. If this were a saturated hydrocarbon with nine carbons, its formula would be C_9H_{20} (since 2 x 9 + 2 = 20). We are missing five pairs of hydrogens, so DU = 5. That is a lot. However, if we have one benzene in the structure, that would account for three double bonds and one ring all at once. That four degrees of unsaturation. An additional carbonyl would bring the number up to the required five. If we had not yet arrived at the idea of a benzene ring, this comparison might make us think of it. Alternatively, if we knew about the benzene but hadn't yet spotted the carbonyl, we might be on the lookout for it now.

Once we have a possible formula, another useful tool is mass spectrometry (MS). Even if you don't know much about mass spectrometry, the basic idea is simple. A mass spectrometer takes a molecules and bashes it into little pieces, then measures the molecular weights of each of those fragments. If you are lucky when you run the experiment, some of the molecules are left intact, and you get the molecular weight of the entire molecule, too.

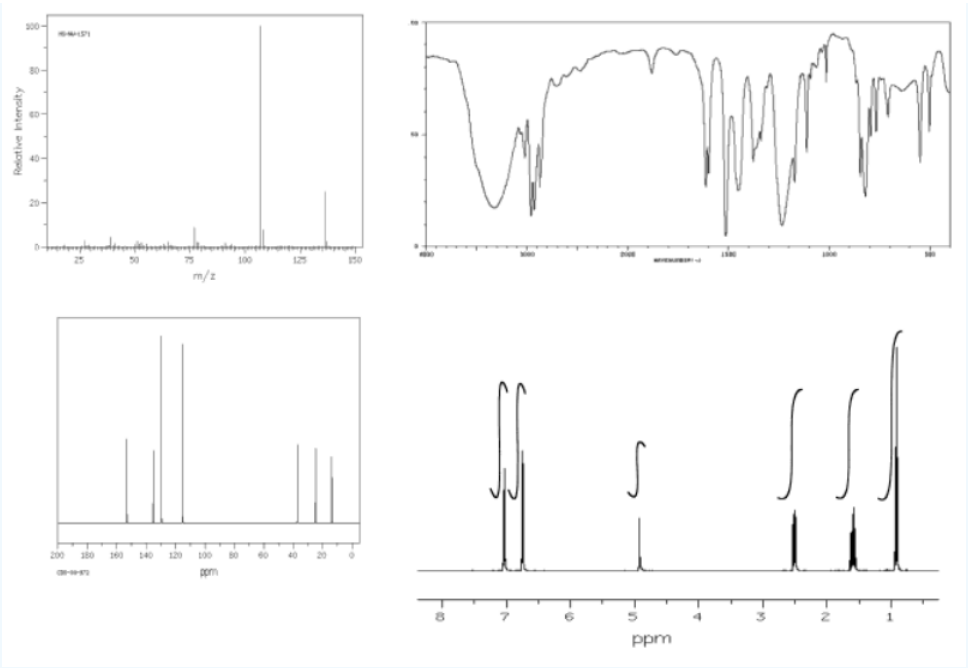


If we calculate the molecular weight based on the formula and compare it to the possible molecular weight from the mass spectrum, we might get confirmation that we are on the right track. Alternatively, maybe our calculated molecular weight will come up short. If we are off by 16, maybe we have missed an oxygen atom somewhere. If we are off by 14, maybe we have missed a carbon and a pair of hydrogens. This information might help us to correct some mistakes.

In the above example, the formula leads to a molecular weight of 150 g/mol. If the mass spectrum did not match, we would want to check our work to see if we overlooked something.

? Exercise 4.12.3

Using the approach outlined above, build a case for the structure of the compound represented by the data below.



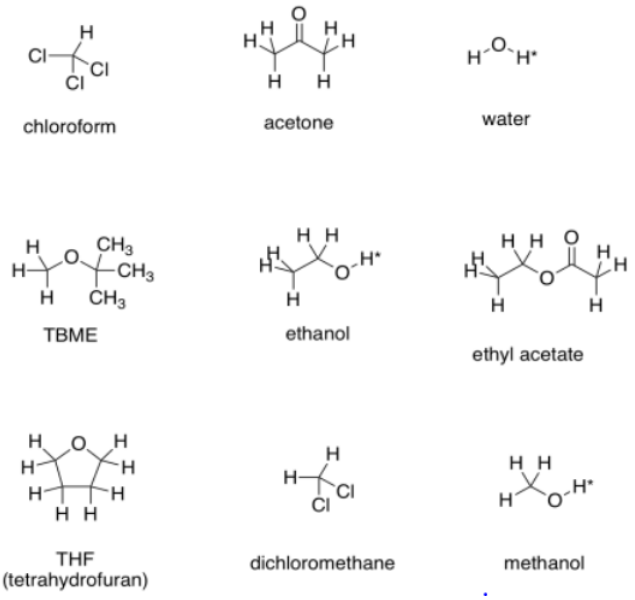
4.13: NMR in Lab- Solvent Impurities

One of the most complicated problems in lab is to deal with the analysis of a mixture. This situation is not uncommon when students run experiments in lab and analyse the data. For example, a student may have added a solvent as part of a purification procedure. Maybe the sample was recrystallized from methanol. Maybe the sample was purified by solvent extraction, and it still contains a little moisture from when it was exposed to the water. In these cases, the solvent will show up in the NMR spectrum.

- Sometimes solvents show up in the spectrum.
- In this case, you should probably make two completely separate sets of data tables for your analysis, one for each compound, or else one for the main compound and one for impurities.

As you go through a spectrum, you should think about any solvents the sample may have contacted. Look for evidence of those things in the spectrum, too.

Here are some examples of solvents that might be used in the lab. You can probably think of other ones, too.



The asterisks by the OH protons in these solvents indicate that these are "exchangeable positions". In protic solvents, or solvents capable of hydrogen bonding (any compound containing O-H or N-H bonds), the proton attached to the oxygen or nitrogen has some unusual behavior in the NMR spectrum. We do not usually observe multiplicity in peaks corresponding to these protons. Often the peaks are very broad, and sometimes they are missing altogether (especially if there is moisture in the sample).

? Exercise 4.13.1

See if you can predict what the NMR spetra of these solvents would look like.

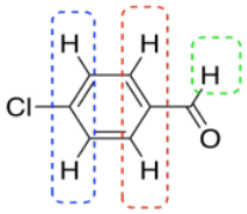
a) TBME b) acetone c) ethyl acetate d) THF e) dichloromethane f) chloroform

g) methanol h) ethanol i) water

Answer

a) TBME b) acetone c) THF d) methanol e) ethyl acetate

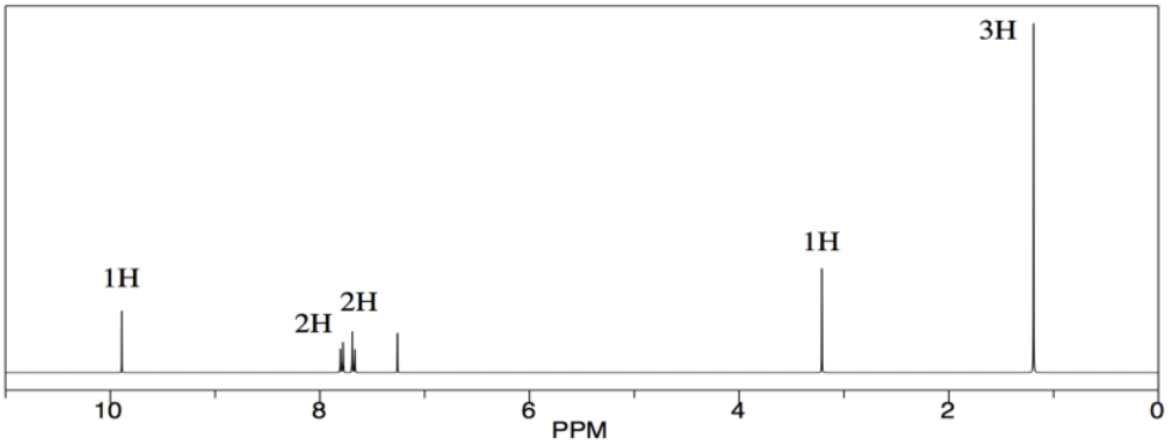
Let's look at an example. Maybe you worked with a sample of p-chlorobenzaldehyde in the lab.



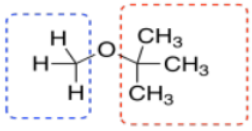
You think you know what that would look like in the NMR. All of the hydrogens are attached to sp^2 or trigonal planar carbons. They should all be somewhere in the left half of the spectrum, maybe between 5 and 10 ppm. Some of the hydrogens are symmetrically equivalent. There is a pair of hydrogens on the benzene ring that look the same as each other; they are closer to the chlorine. Another pair is closer to the carbonyl, the C=O unit. We expect to see two peaks in the NMR spectrum for these hydrogens, even though there are a total of four of them, because they are only in two groups. Because they are all on a benzene, we might even look closer to 7 ppm in the spectrum. Also, both sets of hydrogens have just one neighbour that is different from themselves. These hydrogens should both show up as doublets.

That's not all of the hydrogens in the molecule. There is also a hydrogen on the carbonyl. Because of the double bond to the electronegative oxygen, this position will be strongly deshielded. We should look for it closer to 10 ppm. It does not have any hydrogen neighbors, though. We expect to see a singlet.

The spectrum we see has all of those features. Note that this spectrum is integrated (the *area* of each peak has been measured), and it shows the peak at 10 ppm corresponds to 1H, whereas the ones closer to 7 ppm correspond to 2H each. That information corresponds to what we see in the structure.



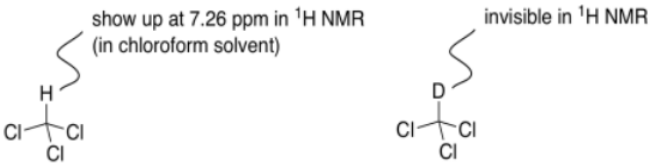
But we see other things, too. Maybe we know that the compound was once dissolved in TBME, $(CH_3)_3COCH_3$. All of the TBME probably evaporated, but you can never be too sure.



TBME has just two kinds of hydrogen, and they are both on tetrahedral or sp^3 carbons. They would probably show up in the right hand side of the spectrum, below 5 ppm. The ones on the carbon next to the other carbon would show up closer to 1 ppm. The ones on the carbon next to the oxygen would show up at 3 or 4 ppm. We do see those peaks in this spectrum.

Furthermore, there are only 3 hydrogens on the carbon next to the oxygen in TBME. There are 9 hydrogens on the methyl groups attached to the carbon. They are in a 1:3 ratio, so we should see that ratio reflected in the integration in the NMR.

There is one more peak in the spectrum, and it is an impurity of a sort, but it isn't part of the original sample. The singlet around 7 ppm is just chloroform, $CHCl_3$.



Now, the NMR solvent used here is actually deuterochloroform, $CDCl_3$. The heavy isotope of hydrogen, deuterium or ^2H, is used in this solvent. That's because we don't want the protons in the solvent to get in the way. ^2H shows up in a completely different area of the spectrum than ^1H, so it's invisible in a regular ^1H NMR spectrum. There is an awful lot of solvent in the NMR tube, and a tiny amount of the actual sample, and it has to be that way for the experiment to work. However, if we just used $CHCl_3$ as the solvent, we would see only one peak in the NMR spectrum: the $CHCl_3$ hydrogen. The sample we are interested in would show up, maybe, as tiny, tiny peaks. So instead we use $CDCl_3$, which is invisible in the hydrogen spectrum.

Well, deuterated solvents are very, very expensive, and the cost to make sure all of the hydrogen atoms in chloroform are replaced by deuteria would be prohibitive. So there is always a little bit of $CHCl_3$ still in the $CDCl_3$, and it shows up in the ^1H spectrum.

It's helpful to have a list of common solvent impurities on hand when you look at your spectrum. A few examples are provided in the following table, showing the data you would see from common solvents in an NMR spectrum taken *in chloroform*.

solvent	number of peaks	shift	multiplicity	integral ratio	assignment
water	1	1.56	br. s	-	O-**H**
acetone	1	2.17	s	-	(C=O)C**H**$_3$
chloroform	1	7.26	s	-	Cl_3C-**H**
t-butyl methyl ether	2	1.19	s	3	C(C**H**$_3$)$_3$
		3.22	s	1	O-C**H**$_3$
ethyl acetate	3	1.26	t	3	CH_2C**H**$_3$
		2.05	s	3	(C=O)C**H**$_3$
		4.12	q	2	OC**H**$_2$$CH_3$
tetrahydrofuran	2	1.85	m	1	CH_2-C**H**$_2$-CH_2
		3.76	m	1	CH_2-C**H**$_2$-O
methanol	2 (usually)	1.09	br s (may be absent)	1	O-**H**
		3.49	s	3	O-C**H**$_3$
ethanol	3 (usually)	1.25	t	1	CH_2C**H**$_3$
		1.32	br s (may be absent)	2	O-**H**
		3.72	q	3	OC**H**$_2$$CH_3$
dichloromethane	1	5.32	s	-	Cl_2C**H**$_2$
grease or alkanes	2	0.86	m	varies; smaller	CH_2C**H**$_3$
		1.26	m	varies; larger	CH_2C**H**$_2$$CH_2$ / CH_2C**H**$_2$$CH_3$

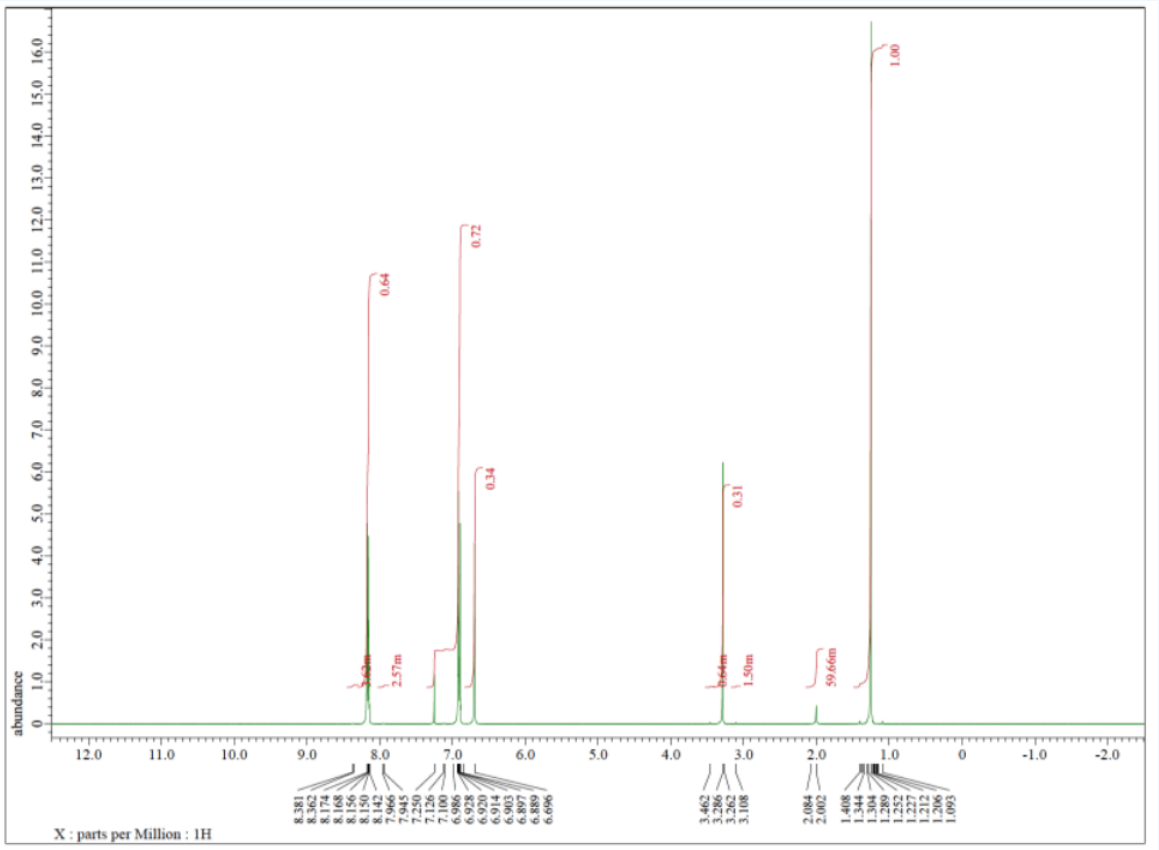
An excellent table, including shifts of a variety of impurities in different NMR solvents, can be found in the following article: Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.

Note that these compounds would show up at slightly different places if they were dissolved in something other than chloroform. Gottlieb's table lists where they would be seen in other common NMR solvents as well.

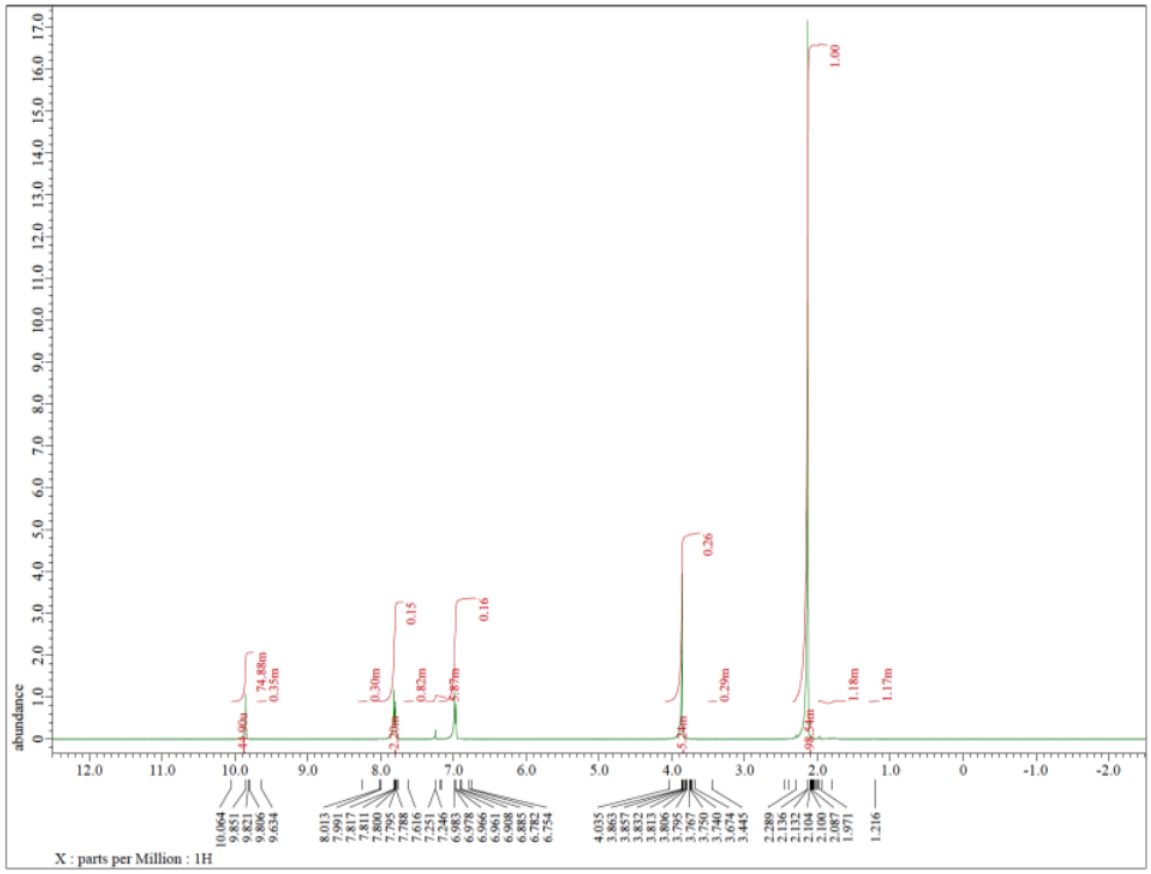
Exercise 4.13.2

Each of the following spectra contains a solvent impurity: acetone, ethyl acetate, methanol, TBME, or THF. Match the spectrum to the impurity.

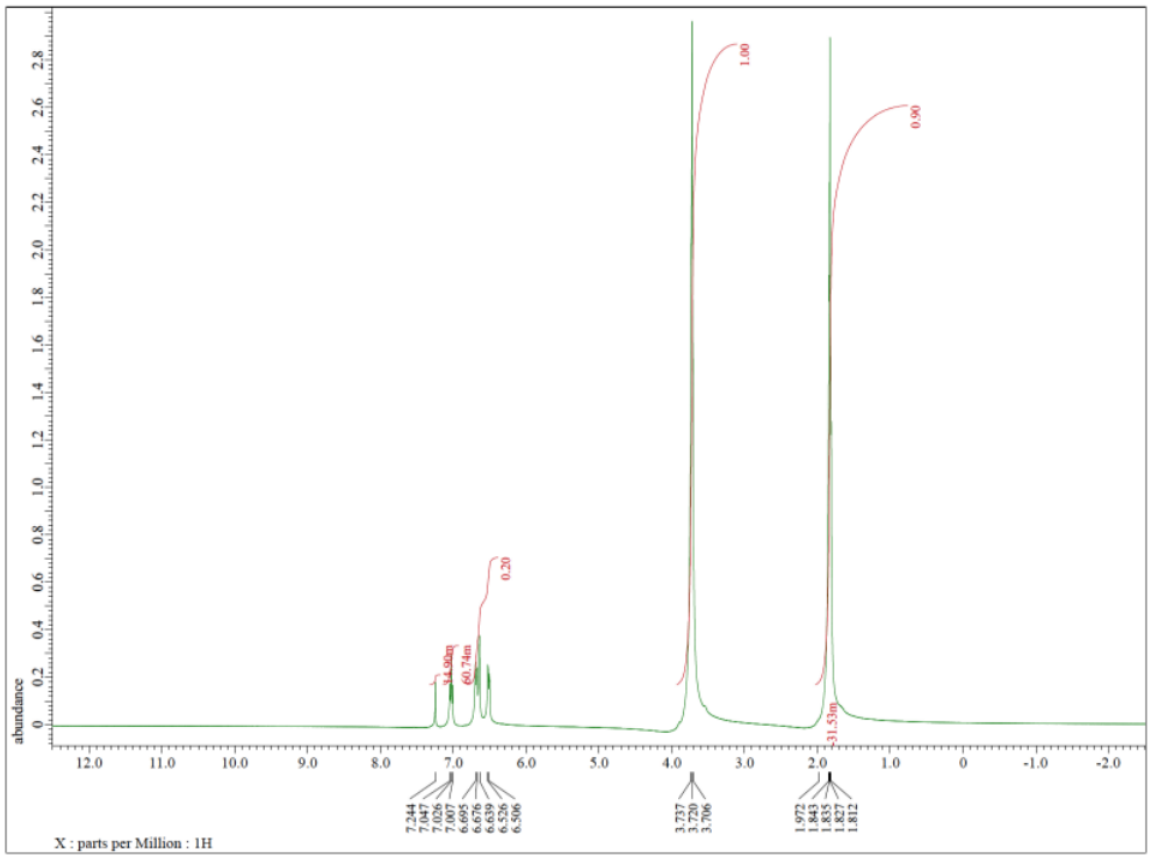
a)



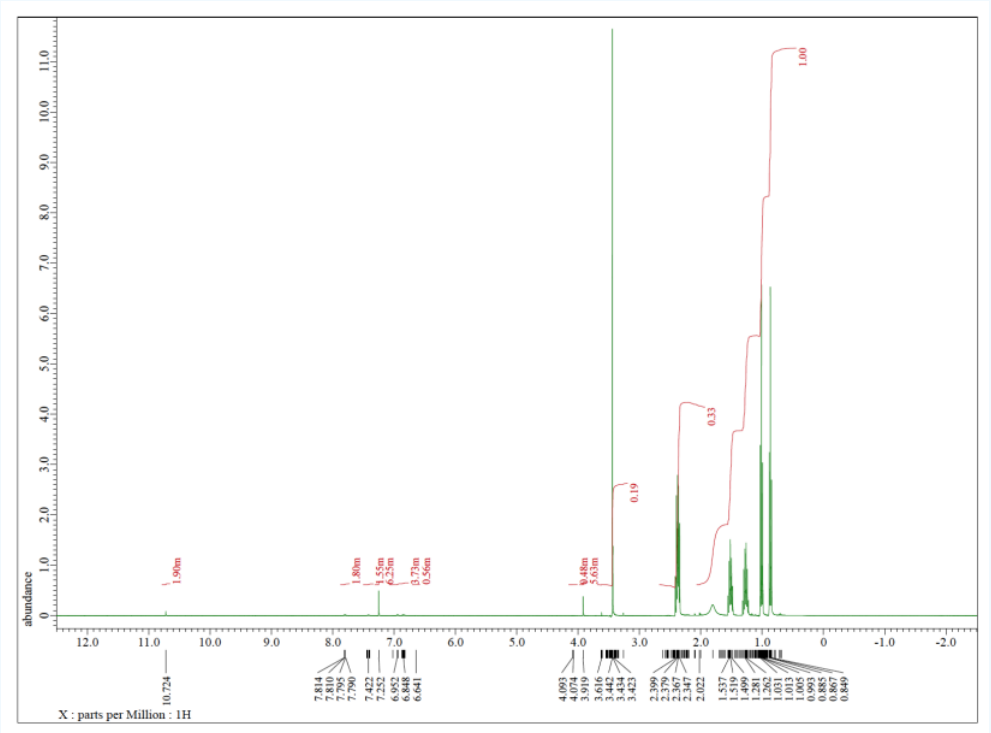
b)


abundance
X : parts per Million : 1H
1.00
0.26
0.16
0.15
74.88m
0.35m
0.30m
0.82m
0.87m
0.29m
1.18m
1.17m

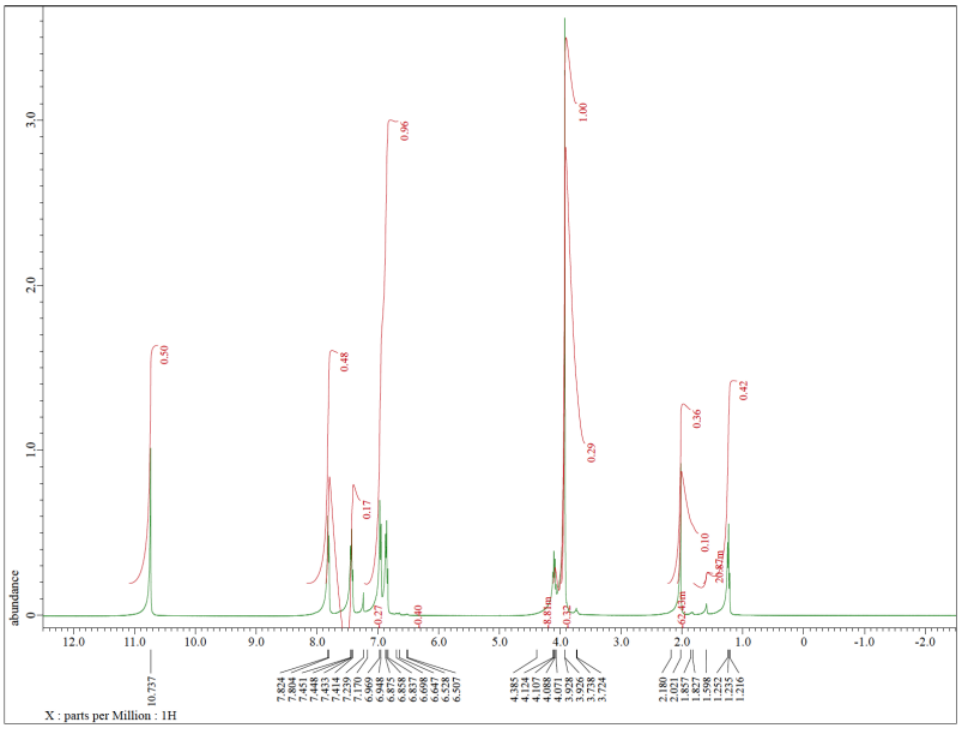
c)


abundance
X : parts per Million : 1H
1.00
0.90
0.20
14.00m
60.74m
31.53m
7.344
7.047
7.026
7.007
6.695
6.676
6.659
6.526
6.506
3.737
3.720
3.706
1.972
1.843
1.835
1.827
1.812

d)


abundance
X : parts per Million : 1H
1.00
0.33
0.19
1.90m
1.80m
1.55m
1.25m
0.73m
0.56m
0.48m
5.63m
10.724
7.814
7.810
7.798
7.790
7.422
7.252
6.952
6.848
6.641
4.093
4.073
4.019
3.616
3.442
3.434
3.423
2.399
2.379
2.367
2.347
2.022
1.537
1.519
1.499
1.281
1.261
1.031
1.013
1.005
0.993
0.885
0.867
0.849

e)



4.14: NMR in Lab- Monitoring Reaction Progress

If you are running a reaction, chances are you know what you started with. You may also have a pretty good idea of what you will be making. The big question is whether the reaction worked (or, maybe, nothing happened at all). If it worked, did you get the product you thought you would, or did you get something unexpected?

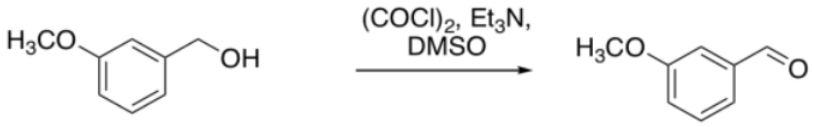
In these cases:

- You should draw attention to pieces of data that most strongly support your expected structure. This approach will demonstrate evaluative understanding of the data; that means you can look at data and decide what parts are more crucial than others.
- You should also draw attention to negative results: that is, peaks that might be there if this spectrum matched another, possible structure, but that are in fact missing.

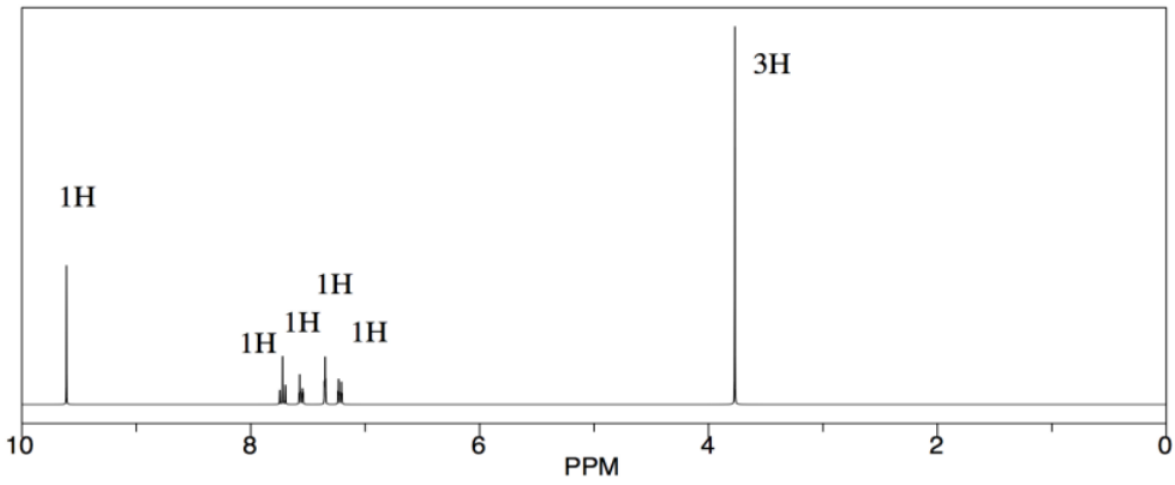
One of the most complicated problems to deal with is the analysis of a mixture. This situation is not uncommon when students run reactions in lab and analyse the data.

- Sometimes the spectra show a little starting material mixed in with the product.
- Sometimes spectra show only a little product and a lot of starting material.
- In these cases, you should probably make two completely separate sets of data tables for your analysis, one for each compound, or else one for the main compound and one for impurities.

Let's look at an example of a reaction. A student is running a type of reaction called an oxidation. She is starting with 3-methoxybenzyl alcohol and trying to convert it to 3-methoxybenzaldehyde. She follows the directions carefully, but how will she know whether she is successful?



She looks at the spectrum, and sees a group of aromatic hydrogens, and a large singlet near 4 ppm, which could be the hydrogens on the methoxy group. Those are reassuring, but they don't interest her that much, because they would appear in her spectrum whether the reaction had proceeded or not. Those peaks would all be pretty much the same in her starting material.

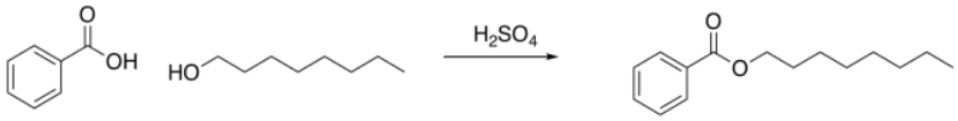


Instead, she notices the peak near 10 ppm. That's significant. Her product would have an aldehyde proton, and that would show up around 10 ppm. Maybe the reaction worked.

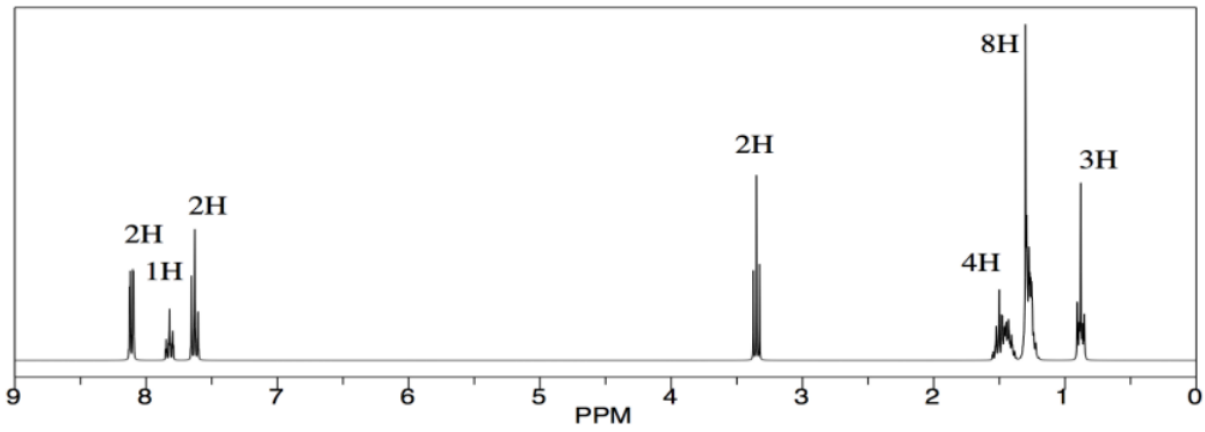
She also takes a look around 5 ppm. There is nothing there, and she thinks that's interesting, too. In her starting alcohol, she had protons on a carbon that was in between an arene and an oxygen, Ar-CH_2-OH. She knows that shift effects are additive in NMR: if a CH_2 in general shows up around 1 ppm, but next to an oxygen it gets shifted to 4 ppm and next to an aromatic it gets shifted to 2 ppm, then if it is next to both it will shift to 5 ppm. There is nothing there. She no longer has an alcohol.

She makes an argument in her report that the reaction proceeded to form an aldehyde. She does not have the hubris to call the reaction "successful" or say it went "as expected". She just points out the presence of an aldehyde proton and the absence of the protons next to the alcohol. She gets an A on the report. Three years later, she is in medical school at Harvard.

Sometimes, things are more subtle. Let's look at another reaction. A student is performing an esterification reaction. He treats 1-octanol with benzoic acid and a drop of sulfuric acid. It's a Fischer esterification. He does not realize Fischer esterifications are equilibrium quagmires that never really make it one direction or another.



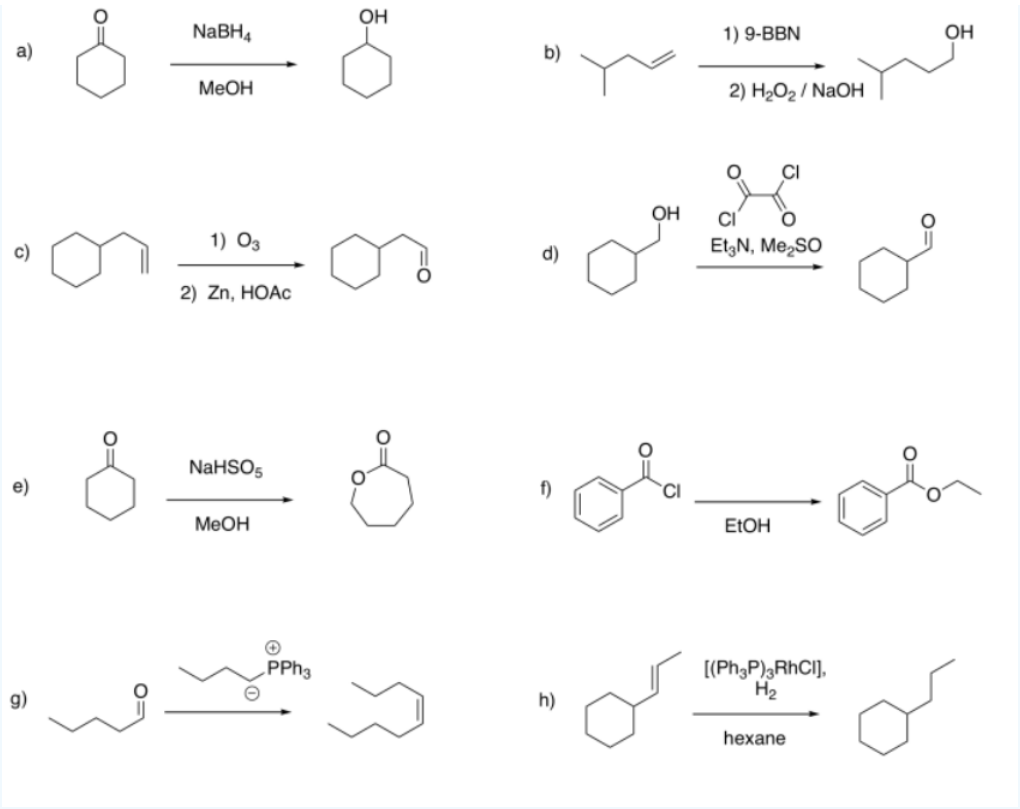
But when he sees the results, he suspects something is amiss. All the peaks are there -- the aromatics, the -CH_2-O, the long aliphatic chain -- but there is something about that methylene, that -CH_2-O, that bothers him. It shows up right around 3.5 ppm, exactly where it would in the starting alcohol. He thinks it should be just a little to the left in the ester, maybe around 4 ppm, because of the influence of the electron-withdrawing carbonyl. He thinks maybe the reaction did not proceed. It occurs to him to look for evidence of the OH protons, in both the alcohol and the benzoic acid, but he knows looking for that in the ^{1}H spectrum is usually a fool's errand, so he consults the IR evidence instead.

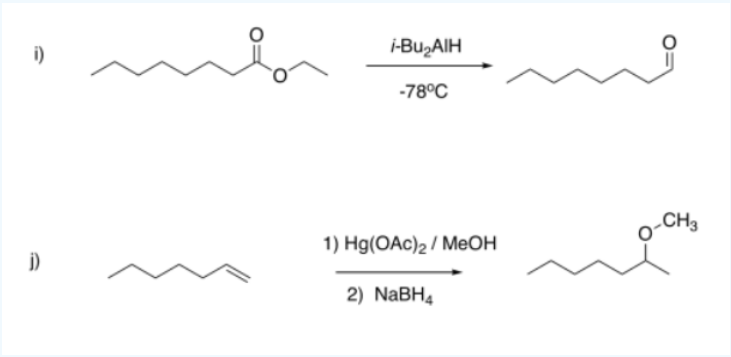


He makes an argument in the report that the reaction did not proceed, but yielded unreacted starting materials. He does not wring his hands about human error, but points out that esters can be both formed and cleaved in the presence of acid, and suggests an acid chloride route might be preferable. He still manages to get an A on the report.

? Exercise 4.14.1

Suggest diagnostic NMR peaks that could be used to determine whether each of the following reactions has proceeded.





Answer

a) appearance of CH-O near 3.5 ppm (multiplet, 1H)

b) appearance of CH_2-O near 3.5 ppm (triplet, 2H); disappearance of =CH near 5-6 ppm (mutiplets, total 3H)

c) appearance of HC=O near 10 ppm (triplet, 1H); disappearance of =CH near 5-6 ppm (mutiplets, total 3H)

d) appearance of HC=O near 10 ppm (triplet, 1H); disappearance of CH_2-O near 3.5 ppm (doublet, 2H)

e) appearance of CH_2-O near 3.5 ppm (triplet, 2H)

f) appearance of CH_2-O near 4 ppm (triplet, 2H)

g) appearance of =CH near 5-6 ppm (mutiplets, total 2H); disappearance of HC=O near 10 ppm (triplet, 1H);

h) disappearance of =CH near 5-6 ppm (mutiplets, total 2H); appearance of triplet:sextet:triplet pattern between 1-2 ppm

i) appearance of HC=O near 10 ppm (triplet, 1H); disappearance of CH_2-O near 3.5 ppm (doublet, 2H)

j) appearance of CH-O near 3 ppm (singlet, 3H) and 3.5 ppm (sextet, 1H); disappearance of =CH near 5-6 ppm (mutiplets, total 2H)

4.15: NMR in Lab- Composition of Mixtures

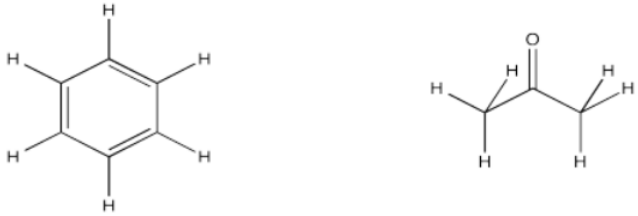
There will be cases in which you already know what the structure might be. In these cases:

- You should draw attention to pieces of data that most strongly support your expected structure. This approach will demonstrate evaluative understanding of the data; that means you can look at data and decide what parts are more crucial than others.
- You should also draw attention to negative results: that is, peaks that might be there if this spectrum matched another, possible structure, but that are in fact missing.

One of the most complicated problems to deal with is the analysis of a mixture. This situation is not uncommon when students run reactions in lab and analyse the data.

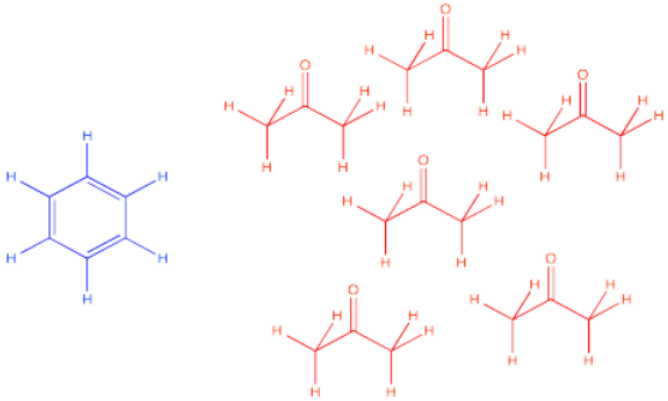
- Sometimes the spectra show a little starting material mixed in with the product.
- Sometimes solvents show up in the spectrum.
- As you might expect, the minor component usually shows up as smaller peaks in the spectrum. If there are fewer molecules present, then there are usually fewer protons to absorb in the spectrum.
- In this case, you should probably make two completely separate sets of data tables for your analysis, one for each compound, or else one for the main compound and one for impurities.

Remember that integration ratios are really only meaningful within a single compound. If your NMR sample contains some benzene (C_6H_6) and some acetone (CH_3COCH_3), and there is a peak at 7.15 that integrates to 1 proton and a peak at 2.10 ppm integrating to 6 protons, it might mean there are 6 protons in acetone and 1 in benzene, but you can tell that isn't true by looking at the structure.



There are six protons in the benzene, and they should all show up near 7 ppm. There are six protons in acetone, and they should all show up near 2 ppm. If there were 1 molecule of benzene for every molecule of acetone, then the integrations would be equal.

Assuming that small integral of 1H for the benzene is really supposed to be 6H, then the large integral of 6H for the acetone must also represent six times as many hydrogens, too. It would be 36 H. There are only six hydrogens in acetone, so it must represent six times as many acetone molecules as there are benzenes.



Integration ratio 1:6

In general, to calculate that ratio, we have to take the integral we see and correct for the number of hydrogens it is supposed to represent. If there are six hydrogens per molecule, and we divide the integral by six, then the result represents the relative amount of that molecule in the sample.

For benzene: at 7.15 ppm, integral = 1H

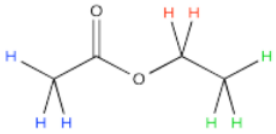
But 1H / 6H per molecule = 0.17 molecules

For acetone: at 2.10 ppm, integral = 6H

But 6H / 6H per molecule = 1 molecule

The ratio of acetone to benzene = 1 molecule acetone : 0.17 molecules benzene = 6 acetone : 1 benzene

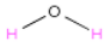
Sometimes a compound will have several peaks in an NMR spectrum because it has several unique hydrogens. For example, ethyl acetate has a few different peaks. What if you wanted to compare the amount of acetone to the amount of water?



peak near 2 ppm, integration 3H

peak near 4 ppm, integration 2H

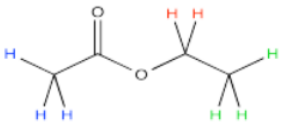
peak near 1 ppm, integration 3H



peak near 1.5 ppm, integration 2H

It might be tempting to just measure up all the integrals for the hydrogens in ethyl acetate and all the integrals for the hydrogens in water. Comparing those two numbers would tell you the ratio of ethyl acetate to water, right? Not exactly. Ethyl acetate has a lot more protons than water, so that isn't a fair comparison. Even in a 1:1 misture of water to ethyl acetate, the total integral for ethyl acetate should be much bigger than for water.

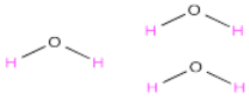
However, notice that peak near 4 ppm in ethyl acetate. It represents 2H, just like the peak for water. Comparing the integral for the peak at 4 to the integral for the peak at 1.5 would provide a pretty good ratio of ethyl acetate to water. The reason we choose the integral at 4 ppm is because it isn't close to any other peaks, so we are very confident that this integral represents only ethyl acetate and nothing else.



peak near 2 ppm, integration 3H

peak near 4 ppm, integration 2H

peak near 1 ppm, integration 3H



peak near 1.5 ppm, integration 6H

Because both peaks represent the same number of hydrogens, the integrals give a direct ratio of the number of molecules present. So, suppose the spectrum reports a raw integral of 27 for the peak at 1.5 ppm and 9 for the peak at 4 ppm. Remember, the integral is just reporting the relative area under the peak, rather than some absolute quantity, so the initial numbers we get might not sound like they correspond to a reasonable number of hydrogens. It's the ratio that matters, and the ratio of 27:9 is 3. If the integral at 1.5 ppm is three times bigger than the one at 4 ppm, there must be three times as many water molecules as ethyl acetate molecules.

For water: at 1.5 ppm, integral = 27H

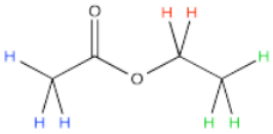
But 27H / 2H per molecule = 13.5 molecules

For ethyl acetate: at 4.2 ppm, integral = 9H

But 9H / 2H per molecule = 4.5 molecule

The ratio of water to ethyl acetate = 13.5 molecule water : 4.5 molecules ethyl acetate = 3 water : 1 ethyl acetate

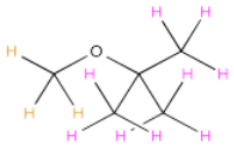
Sometimes there are several unique hydrogens in both compounds that you want to compare, so you will need to make a choice about which peaks to compare. For example, maybe you need to determine the ratio of ethyl acetate to TBME (*tert*-butyl methyl ether, sometimes alternatively called MTBE) in a sample.



peak near 2 ppm, integration 3H

peak near 4 ppm, integration 2H

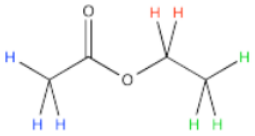
peak near 1 ppm, integration 3H



peak near 3 ppm, integration 3H

peak near 1 ppm, integration 9H

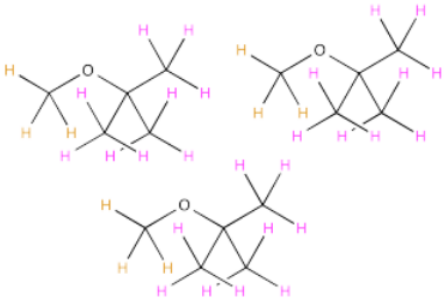
The easiest thing to do may be to compare the peak at 2 ppm in ethyl acetate with the peak at 3 ppm in TBME. They are both supposed to be 3H, so a comparison of those two integrals gives you a direct look at the ratio of molecules. For example, a 1:3 ratio between the peak at 2 ppm and the peak at 3 ppm would indicate a 1:3 ratio of molecules.



peak near 2 ppm, integration 3H

peak near 4 ppm, integration 2H

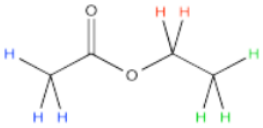
peak near 1 ppm, integration 3H



peak near 3 ppm, integration 9H

peak near 1 ppm, integration 27H

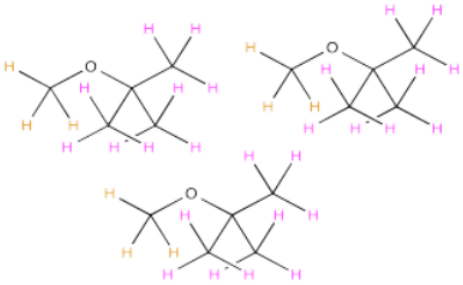
But what if, right before you made your NMR sample, you noticed a little schmutz on the NMR tube and decided to clean it with some acetone. As a result, you're pretty sure there is some acetone in your NMR sample. Unfortunately, that also shows up at 2 ppm, so you're not quite sure what part of the integral at 2 ppm is telling you about the acetone and what part is telling you about the ethyl acetate.



peak near 2 ppm, integration ???

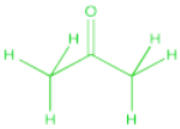
peak near 4 ppm, integration 2H

peak near 1 ppm, integration ???



peak near 3 ppm, integration 9H

peak near 1 ppm, integration ???



2 ppm, integration ???

Don't worry. You can still resort to comparing the peak at 4 ppm in ethyl acetate, which you can see very clearly, with the peak at 3 ppm in TBME, also in the clear. The only trouble is that you have to take into account that one peak represents 2H per molecule and the other peak represents 3H per molecule. You need to adjust for that by, for example, multiplying the integral at 3 ppm by 2/3. You're cutting it down so you can compare it to a peak that would only represent 2H rather than 3H. You are putting it on an

equal footing with the peak from the ethyl acetate, so that you can compare the number of molecules present, not just the number of H in each molecule.

Suppose this students measures those two raw integrals at 4 ppm and 3 ppm, and gets values of 127H and 38H.

For ethyl acetate: at 4.2 ppm, integral = 127H

But 127H / 2H per molecule = 63.5 molecules

For TBME: at 3.10 ppm, integral = 38H

But 38H / 3H per molecule = 12.67 molecule

The ratio of ethyl acetate to TBME = 63.5 molecule ethyl acetate : 12.67 molecules TBME = 5 ethyl acetate : 1 TBME

Sometimes, you may be asked to express the make-up of the sample in terms of **percent composition** rather than as a ratio. Converting ratios to percentages involves dividing one part of the ratio by the sum of both parts.

% ethyl acetate = $\frac{5}{5+1} \times 100\% = 83.3\%$ ethyl acetate

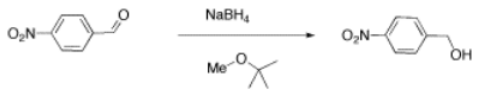
% TBME = $\frac{1}{5+1} \times 100\% = 16.7\%$ TBME

or %TBME = $100 - 83.3\% = 16.7\%$

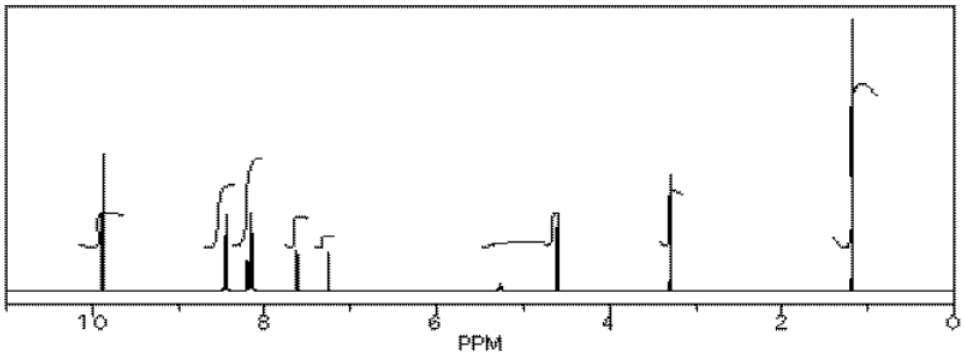
If you have decided that you can identify two sets of peaks in the 1H spectrum, analysing them in different tables makes it easy to keep the integration analysis completely separate too ; 1 H in one table will not be the same size integral as 1 H in the other table unless the concentrations of the two compounds in the sample are the same.

However, comparing the ratio of two integrals for two different compounds can give you the ratio of the two compounds in solution, just as we could determine the ratio of benzene to acetone in the mixture described above.

We will look at two examples of sample mixtures that could arise in lab. Results like these are pretty common events in the labIn the first example, a student tried to carry out the following reaction, a borohydride reduction of an aldehyde. The borohydride should give a hydride anion to the C=O carbon; washing with water should then supply a proton to the oxygen, giving an alcohol.

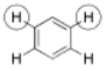
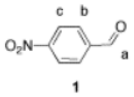
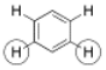
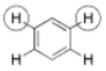
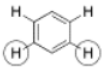
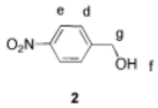
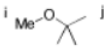


Her reaction produced the following spectrum.



(simulated data)

From this data, she produced the table below.

	shift	integration	int(n)	internal ratio	multiplicity	part structure	assignment
a	9.9 ppm	11 mm	2H	1H	singlet		
b	8.5 ppm	23 mm	4H	2H	doublet		 1
c	8.1 ppm	(20 mm?)	4H	2H	doublet		
d	8.2 ppm	(10 mm?)	2H	2H	doublet		
e	7.6 ppm	9 mm	2H	2H	doublet		 2
f	5.3 ppm	2 mm	0.4H	<1H	singlet	OH	
g	4.7 ppm	12 mm	2H	2H	singlet		
h	7.2 ppm	4 mm	0.8H	1H	singlet	$CHCl_3$	
i	3.3 ppm	8 mm	1.5H	3H	singlet		
j	1.2 ppm	24 mm	4.5H	9H	singlet		
			23.4H total				

Ratio of reactant **1** to product **2** is 2:1 based on peaks at 9.9 and 4.7 ppm (2H / 1H) : (2H / 2H); the reaction is 33% complete [2 / (2+1)]

Ratio of product **2** to TBME is 2:1 based on peaks at 4.7 and 3.3 ppm (2H / 2H) : (1.5H / 3H); the ratio of **1**:**2**:TBME is 2:1:0.5, so the sample is 57% **1** [2/(2+1+0.5)], 29% **2** and 14% TBME.

Notice how she calculated that ratio. She found a peak in molecule 1, the aldehyde, that she was pretty sure corresponded to the aldehydic hydrogen, the H attached to the C=O; in other words, the CH=O. She found another peak from molecule 2, the alcohol, that she was pretty sure represented the two hydrogens on the carbon attached to oxygen, the CH_2-O.

The integrals for those two peaks are equal. They are both 2H in her table. However, she notes that within each molecule, the first integral really represents 1H and the second represents 2H. That means there must be twice as many of molecule 1 as there are molecule 2. That way, there would be 2 x CH=O, and its integral would be the same as the 1 x CH_2-O in the other molecule.

One way to approach this kind of problem is to:

- choose one peak from each of the two compounds you want to compare.
- decide how many hydrogens each peak is supposed to represent in a molecule. Is it supposed to be a CH2, a CH, a CH3?
- divide the integral value for that peak by that number of hydrogens it is supposed to represent in a molecule.
- compare the two answers (integral A / ideal # H) vs (integral B / ideal # H).
- the ratio of those two answers is the ratio of the two molecules in the sample.

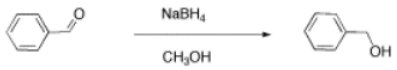
So there is twice as much aldehyde as alcohol in the mixture. In terms of these two compounds alone, she has 33% alcohol and 66% aldehyde. That's $\frac{1}{1+2} \times \%$ for the alcohol, and $\frac{2}{1+2} \times 100\%$(2/(1+2))for the aldehyde. That calculation just represents the amount of individual component divided by the total of the components she wants to compare.

There are a number of things to take note of here.

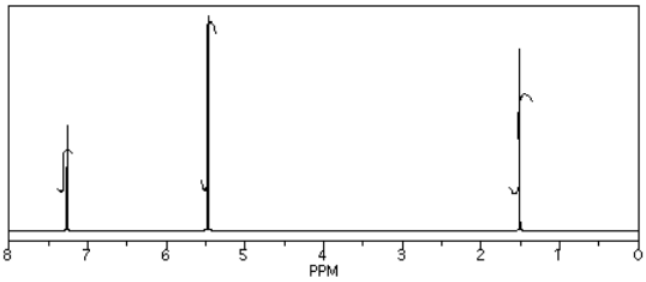
- Her reaction really didn't work very well. She still has majority starting material, not product.
- She will get a good grade on this lab. Although the experiment didn't work well, she has good data, and she has analyzed it very clearly.
- She has separated her data table into different sections for different compounds. Sometimes that makes it easier to analyze things.

- She has noted the actual integral data (she may have measured the integral with a ruler) and also converted it into a more convenient ratio, based on the integral for a peak that she felt certain about.
- She went one step further, and indicated the internal integration ratio within each individual compound.
- She calculated the % completion of the reaction using the integral data for the reactant and product, and she made clear what part of the data she used for that calculation. A similar procedure could be done if a student were just trying to separate two components in a mixture rather than carry out a reaction.
- She also calculated the overall purity of the mixture, including a solvent impurity that she failed to remove.
- However, $CHCl_3$ is not included in her analysis of purity. $CHCl_3$ really isn't part of her sample; it was just present in the NMR solvent, so it does not represent anything in the material she ended up with at the end of lab.

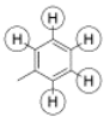
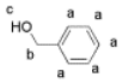
Another student carried out a similar reaction, shown below. He also finished the reaction by washing with water, but because methanol is soluble in water, he had to extract his product out of the water. He chose to use dichloromethane for that purpose.



He obtained the following data.



From this data, he constructed the following table.

	shift	integration	int(n)	multiplicity	partial structure	assignment
a	7.3 ppm	16 mm	5H	singlet		
b	5.4 ppm	64 mm	2H	singlet		
c	1.6 ppm	37 mm	1H	singlet	OH	

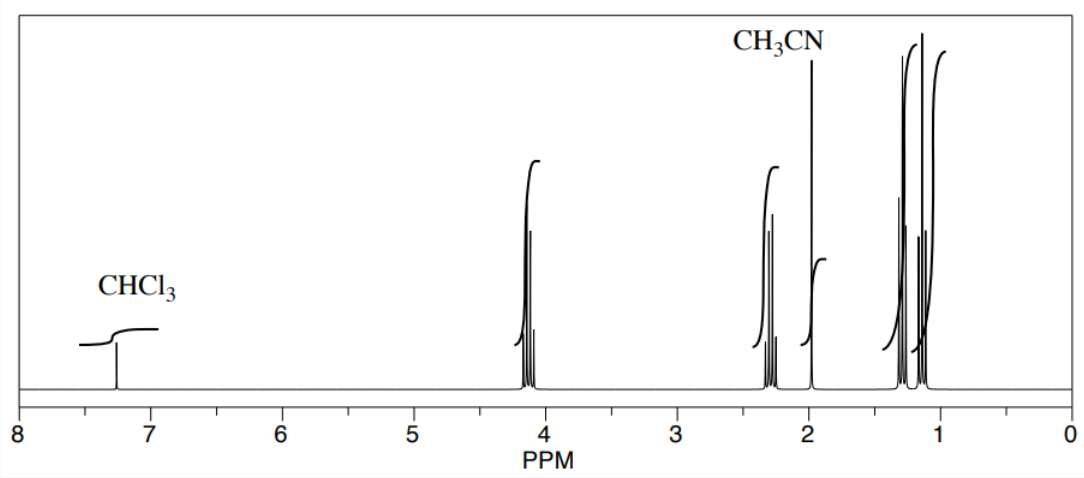
There are some things to learn about this table, too.

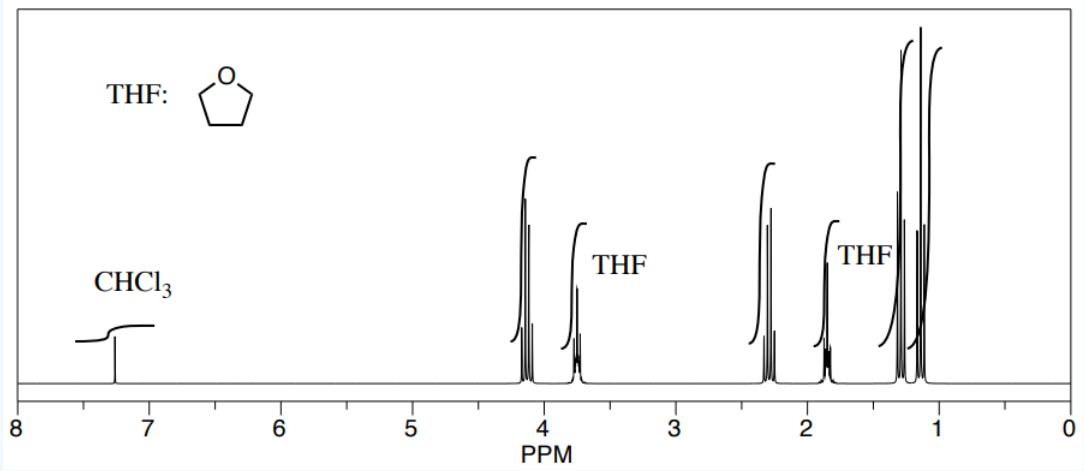
- Does the integration ratio really match the integral data? Or is this just wishful thinking?
- This table might reflect what he wants to see in the data. But what else could be in the data?
- $CHCl_3$ is often seen in NMR spectra if $CDCl_3$ is used for the NMR sample. It's there, at 7.2 ppm.
- "Leftover" or residual solvent is very common in real lab data. There it is, CH_2Cl_2 from the extraction, at 5.4 ppm.
- What about water? Sometimes people don't dry their solutions properly before evaporating the solvent. There is probably water around 1.5 to 1.6 ppm here.

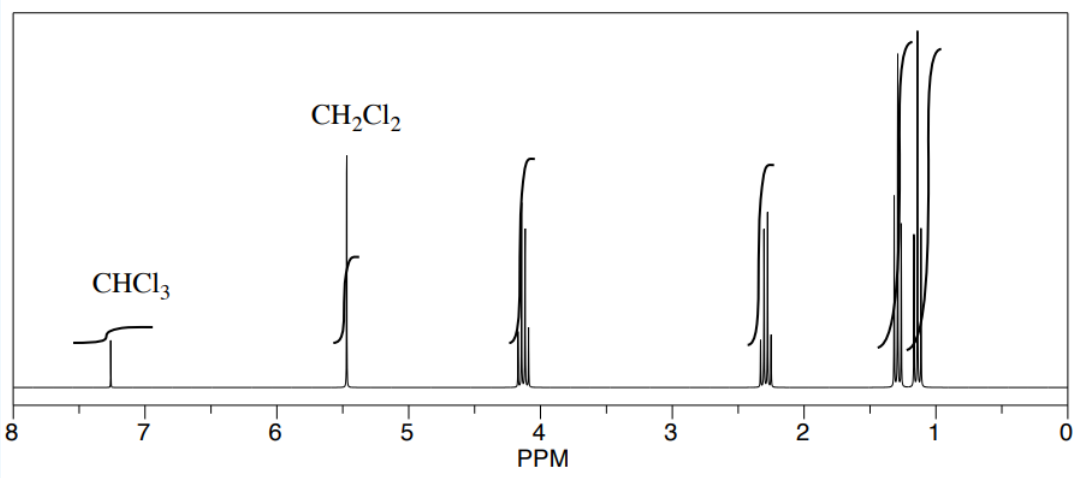
This student might not get a very good grade; the sample does not even show up in the spectrum, so he lost it somewhere. But his analysis is also poor, so he will really get a terrible grade.

? Exercise 4.15.1

Three students performed a synthesis of a fragrant ester, ethyl propanoate, $CH_3CH_2CO_2CH_2CH_3$. During their reactions, they each used a different solvent. The students were able to see peaks in the NMR spectrum for ethyl propanoate, as well as peaks for chloroform ($CHCl_3$, in the $CDCl_3$ they used to make their NMR samples).







They were also able to determine that they had some leftover solvent in their samples by consulting a useful table of solvent impurities in NMR (which they found in Goldberg et. al., *Organometallics* **2010**, *29*, 2176-2179).

a. What is the ratio of leftover solvent to ethyl propanoate in each sample?
b. What is the percent of each sample that is leftover solvent?

Answer

a) student 1: Let's use the H_2C-O peak of ethyl propanoate at 4 ppm and the acetonitrile methyl at 2 ppm. The ratio appears to be 2:1, but they represent 2 protons and 3 protons, respectively. That means the ratio of molecules is 2/2:1/3 = 3:1 ethyl

propanoate : acetonitrile.

student 2: We'll use the H_2C-O peak of ethyl propanoate at 4 ppm and the H_2C-O peak of THF at 3.5 ppm. The ratio appears to be 3:2, but they represent 2 protons and 4 protons, respectively. That means the ratio of molecules is 3/2:2/4 = 12:4 = 3:1 ethyl propanoate : THF.

student 3: Look at the H_2CCl_2 peak of dichloromethane at 5 ppm and the H_2C-O peak of THF at 4 ppm. The ratio appears to be 1:2, and they both represent 2 protons, so the ratio of molecules is 1:2 dichloromethane : ethyl propanoate.

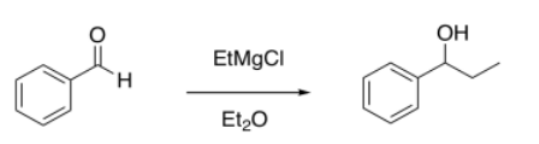
b) student 1: The sample is $[\frac{1}{1+3}] \times 100\% = 25$ acetonitrile.

student 2: The sample is $[\frac{1}{1+3}] \times 100\% = 25$ THF.

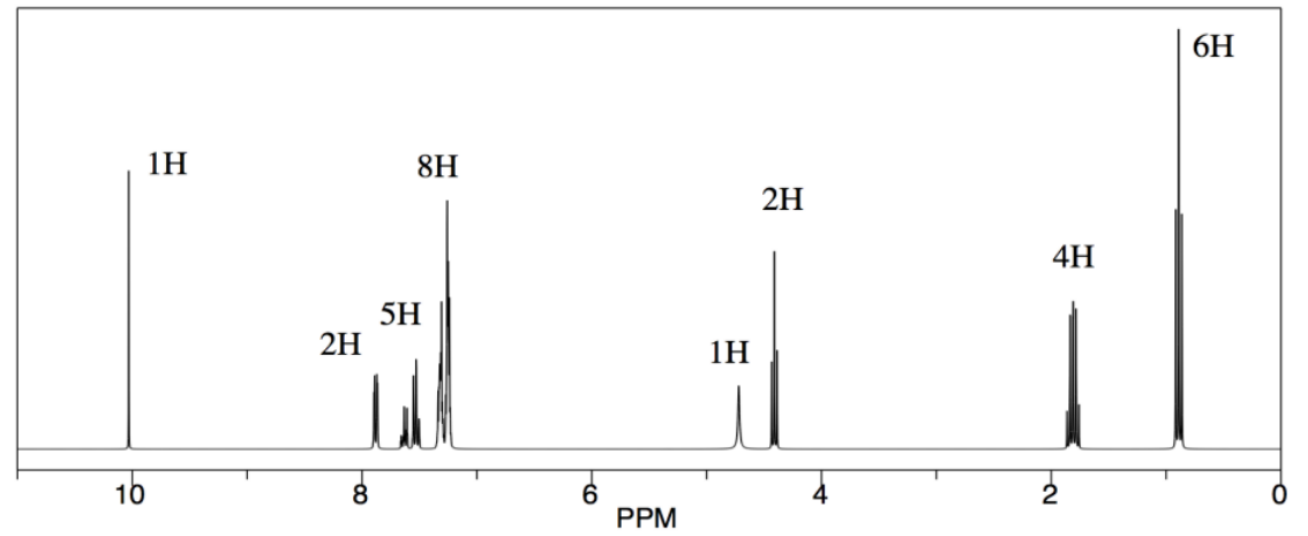
student 3: The sample is$[\frac{1}{1+2}] \times 100\% = 33$ acetonitrile.

Exercise 4.15.2

A student attempted to add a Grignard reagent to benzaldehyde.



She obtained the following data (well, this is a simulated spectrum). What was the composition of her product?



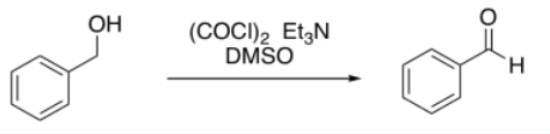
Answer

The obvious NMR handles are the H-C=O aldehyde proton at 10 ppm for benzaldehyde and the alcohol-adjacent H-C-O proton at 4.5 ppm for 1-phenylpropanol.

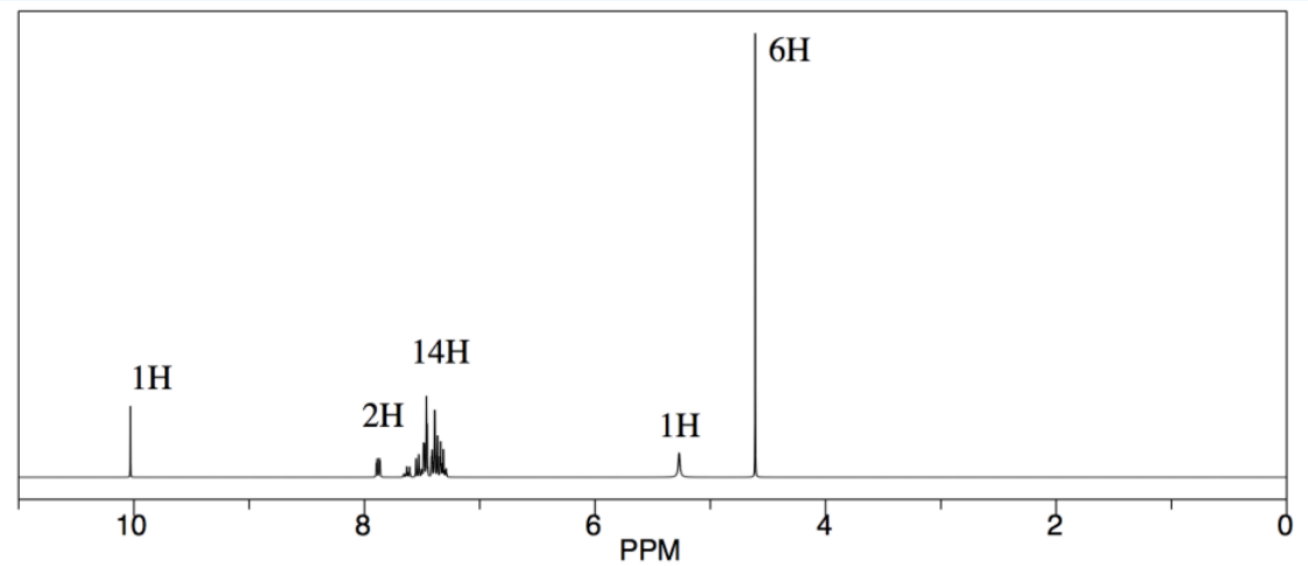
Each of those peaks represents one proton, so the integral ratio of 1:2 suggests a ratio of bezaldehyde to 1-phenylpropanol of of 1:2. That translates into 33% benzaldehyde, 67% 1-phenylpropanol.

Exercise 4.15.3

A student attempted to run a Swern oxidation on benzyl alcohol.



She obtained the following data (simulated spectrum). What was the composition of her product?



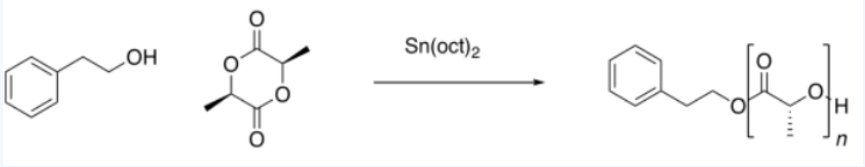
Answer

The NMR handles here are the H-C=O aldehyde proton at 10 ppm for benzaldehyde and the alcohol-adjacent H_2C-O protons near 5 ppm for benzyl alcohol.

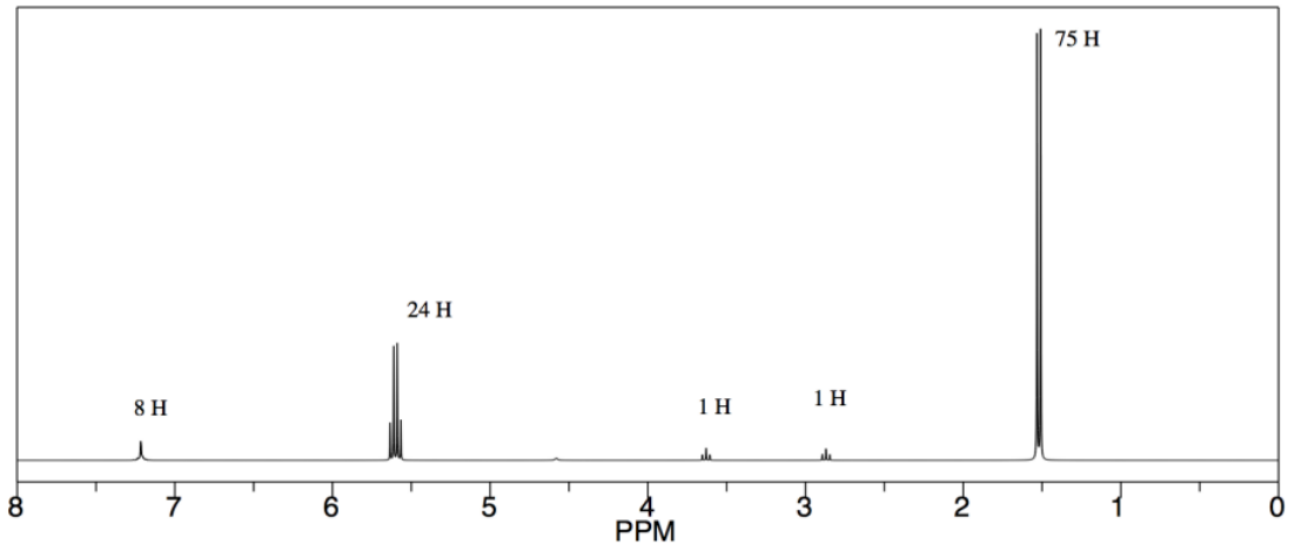
In this case, we need to correct for the differing numbers of protons represented by each peak: 1H for the aldehyde peak but 2H for the alcohol one. The integral ratio of 1:6 therefore suggests a ratio of bezaldehyde to 1-phenylpropanol of of 1:3. That translates into 25% benzaldehyde, 75% 1-phenylpropanol.

? Exercise 4.15.4

A student attempted to carry out a ring-opening trans-esterification polymerization.



She obtained the following data (simulated spectrum). She knows that the alcohol should act as the initial nucleophile and should be found at the end of the polymer chain. What is the degree of polymerization (i.e. the number of repeating units in the chain)?



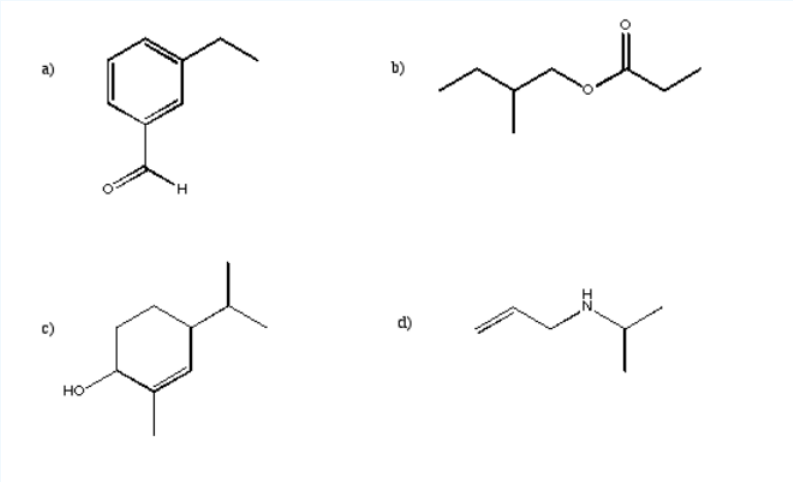
Answer

We could use the peak corresponding to the O-CH-C=O proton above 5 ppm for the repeat unit and the peak for the CH_2-O proton in the initiator/end group near 3.5 ppm. The integral ratio is 24:1, but they represent different numbers of hydrogens, so the repeat unit to end group ratio is really 24/1:1/2, or 48:1. The degree of polymerization is 48.

4.16: More Practice

Exercise 4.16.1

For each of the following structures, indicate how many peaks would be found in the ^{13}C spectrum.



Exercise 4.16.2

Sketch the expected ^{13}C spectrum for each of the structures in the previous question.

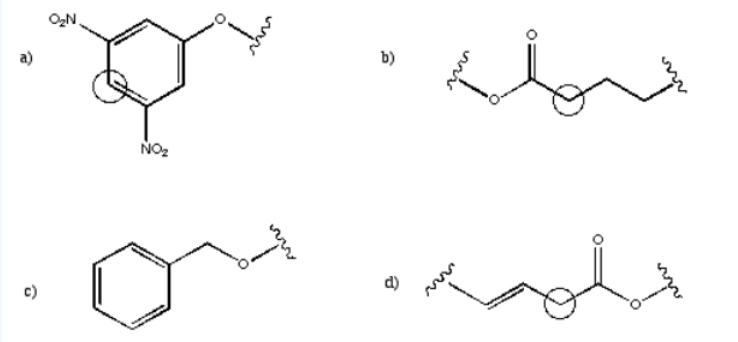
Exercise 4.16.3

Suggest possible assignments for peaks found at the following positions in the ^{13}C NMR spectrum.

a) 63 ppm b) 114 ppm c) 205 ppm d) 35 ppm e) 165 ppm f) 175 pp

Exercise 4.16.4

Suggest the approximate chemical shift for the circled carbons in the following partial structures.



Exercise 4.16.5

Explain why, in the following cases, chemical shift is slightly different from the normal range described.

a) chlorofom ($CHCl_3$): H on sp^3 carbon; normally 0-5 but here at 7.27 ppm.

b) vinyl ether ($C\mathbf{H}_2$=CHOCH=$C\mathbf{H}_2$): H on sp^2 carbon normally 5-7 but here at 4.5 ppm.

c) nitrobenzene ($C_6H_5NO_2$): H on sp^2, aromatic carbon normally 7-8 but here 8.5 ppm

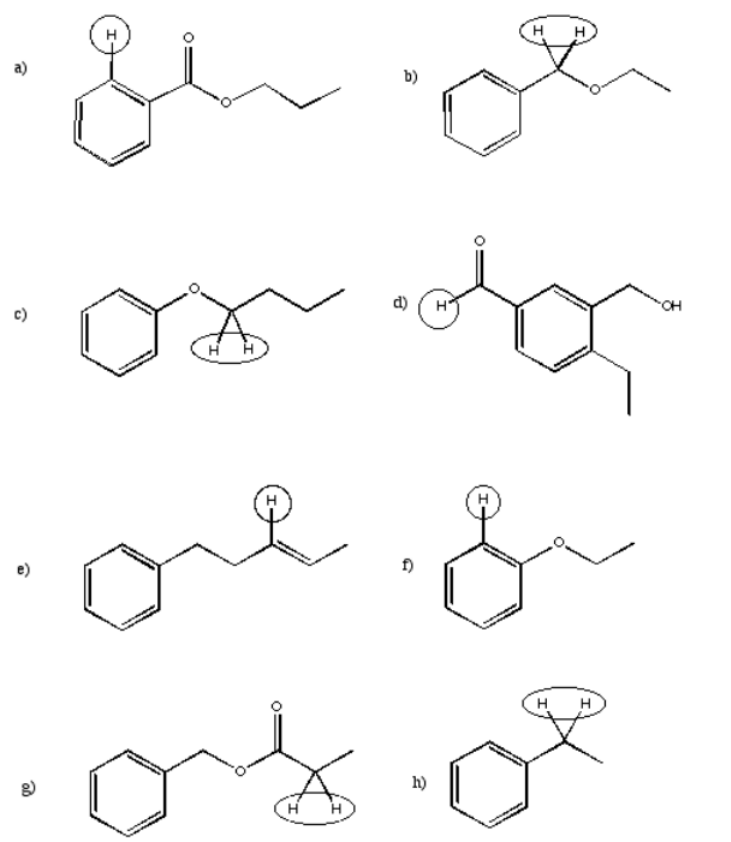
Exercise 4.16.6

Suggest possible assignments for peaks found at the following positions in the ^{1}H NMR spectrum.

a) 7.4 ppm b) 12.1 ppm c) 3.6 ppm d) 10.1 ppm e) 8.2 ppm f) 2.1 ppm g) 5.8 ppm

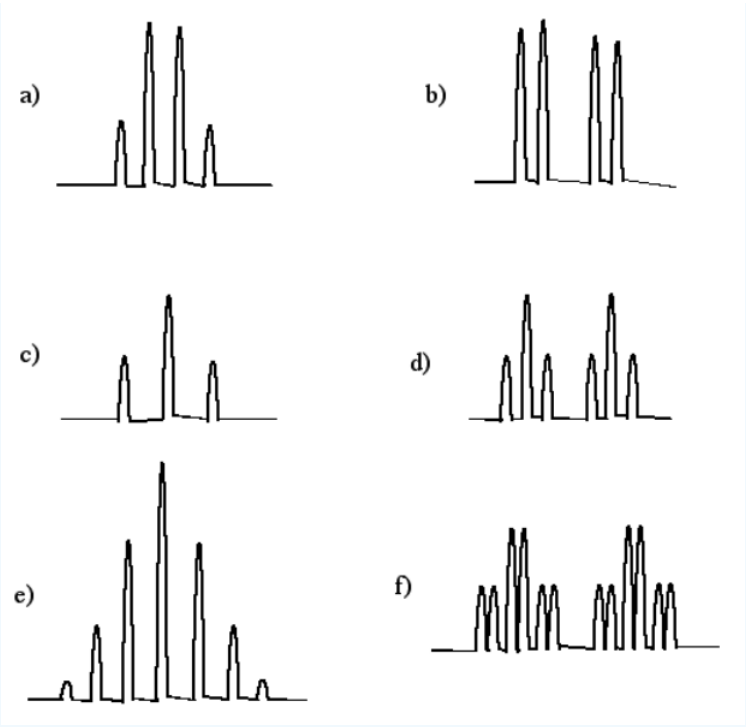
Exercise 4.16.7

Suggest the approximate chemical shift for the circled protons in the following partial structures.



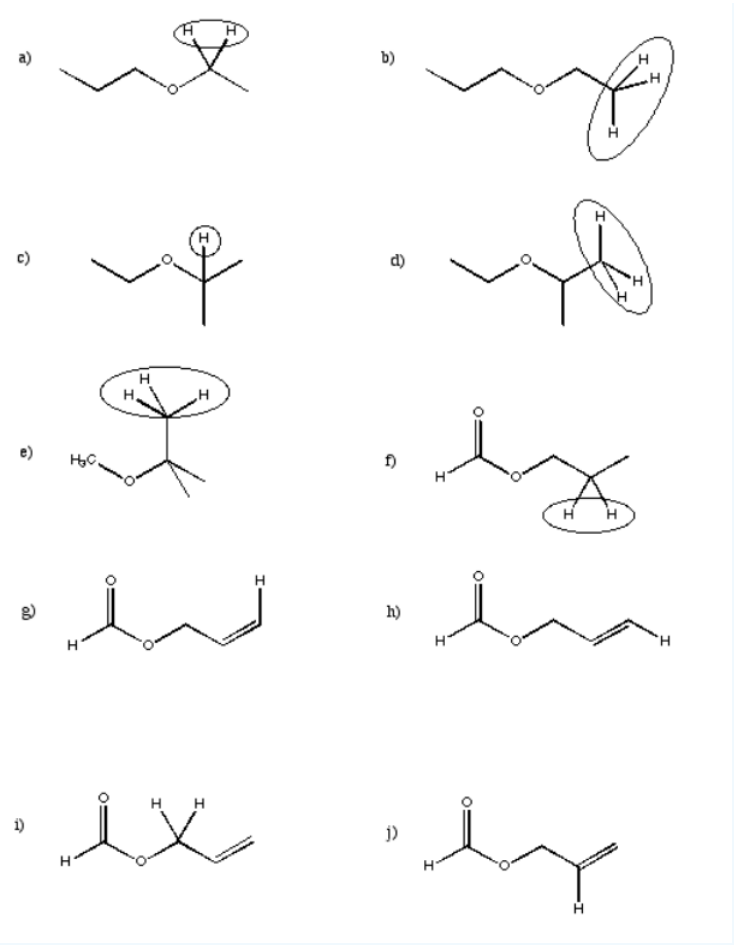
Exercise 4.16.8

Suggest the arrangement of neighbouring hydrogens for the following peaks in the ^{1}H NMR spectrum and draw a partial structure.



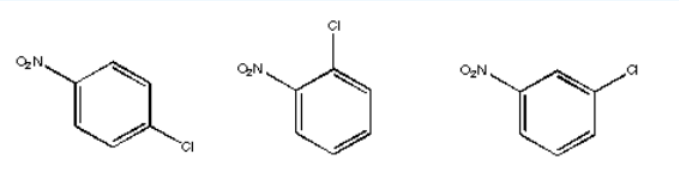
Exercise 4.16.9

Sketch peak shapes for the circled protons in the following partial structures.



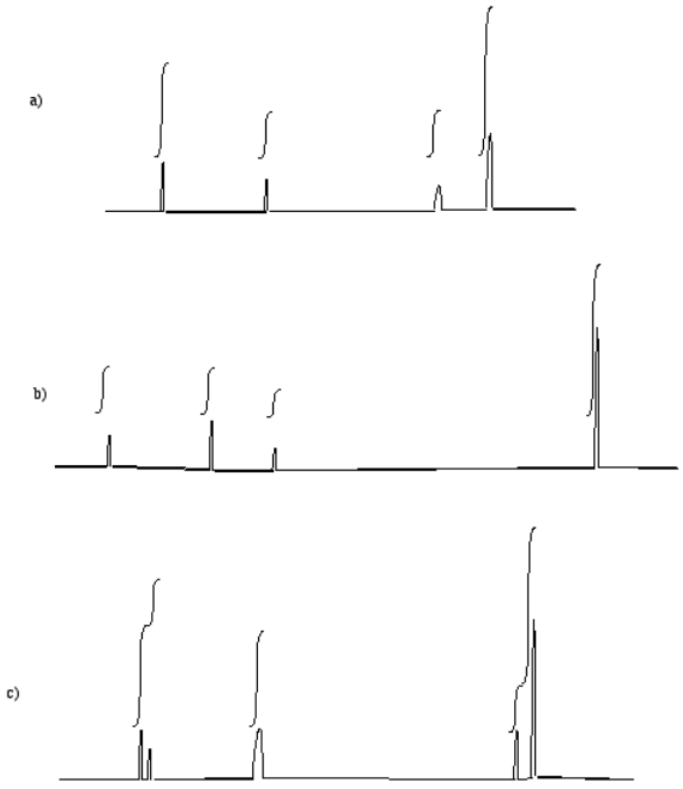
Exercise 4.16.10

Describe the different coupling patterns in the aromatic region of the ^{1}H NMR spectra of the following isomers.



Exercise 4.16.11

Assign the relative number of protons at each position based on the integral lines shown.



Exercise 4.16.12

Suggest partial structures for the following data, given in string form.

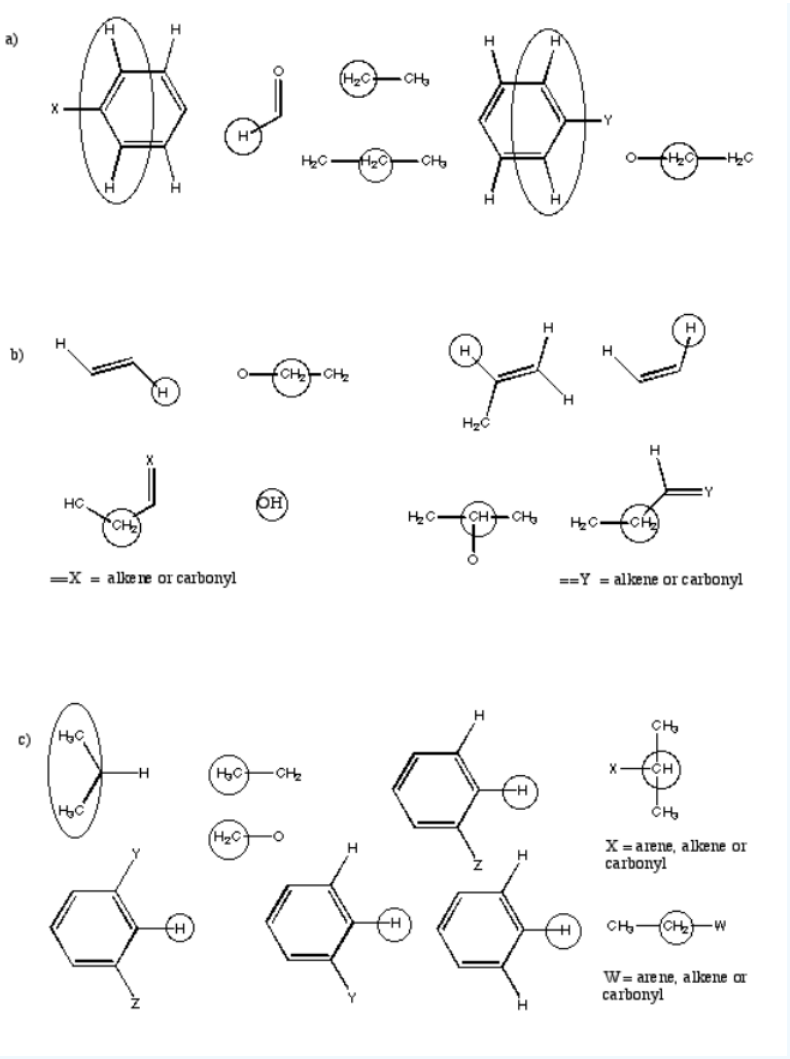
a) 8.05 ppm (doublet, 2H) b) 3.25 ppm (septet, 1H) c) 2.65 ppm (nonet, 1H)

d) 6.55 ppm (broad singlet, 1H) e) 0.94 ppm (triplet, 3H) f) 2.33 ppm (broad singlet, 2H)

g) 8.65 ppm (singlet, 1H) h) 2.05 ppm (quartet, 2H) i) 6.21 ppm (doublet of doublets, 1H)

Exercise 4.16.13

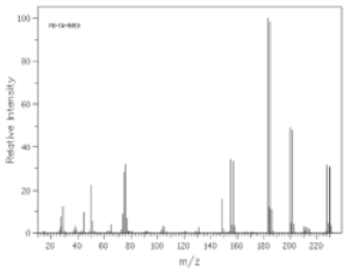
Suggest complete structures from the following sets of partial structures.

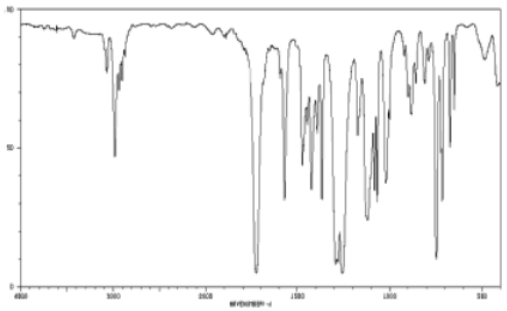


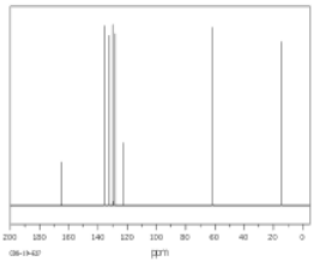
Exercise 4.16.14

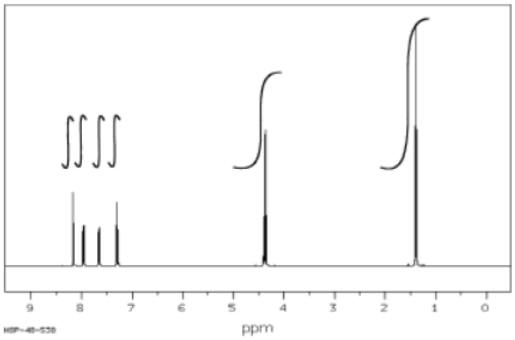
Show complete analysis of the following spectral data and propose a structure in each case.

a)

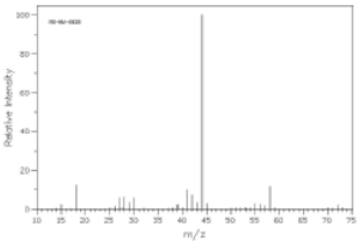




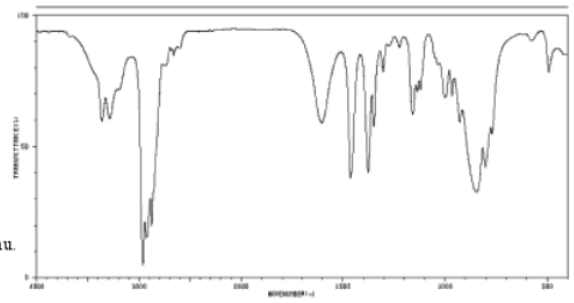


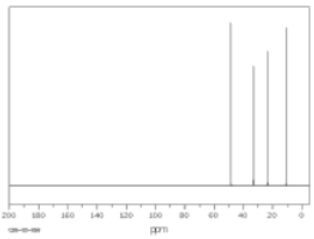


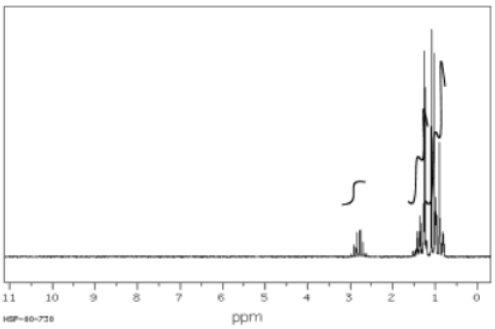
b)



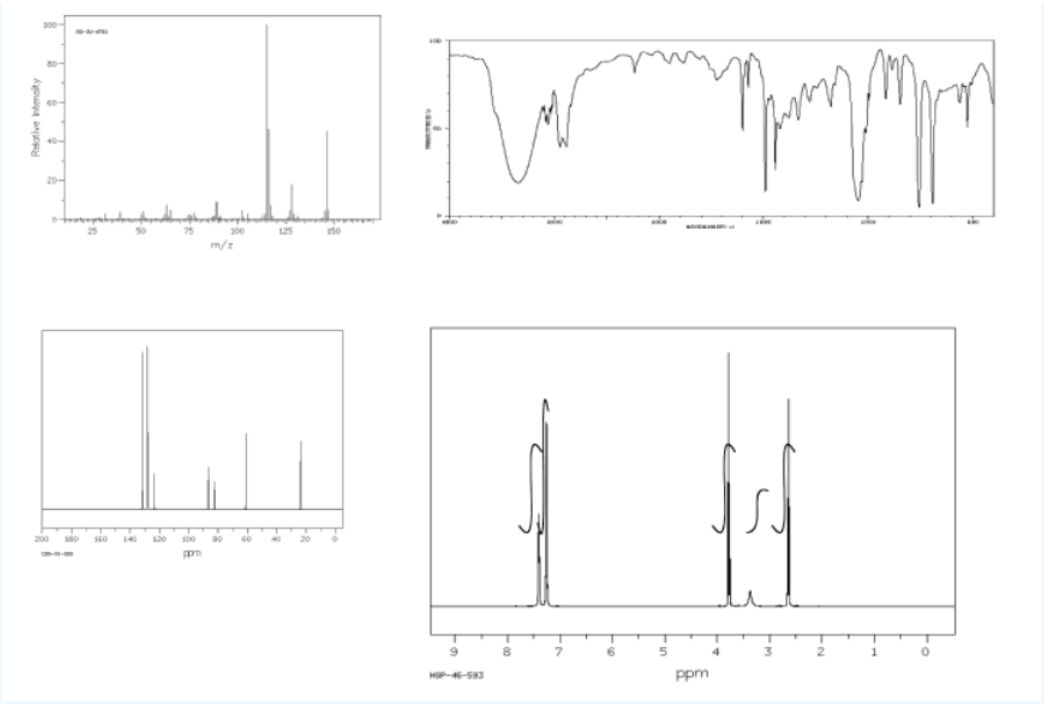
Note: there is an important peak at m/z = 73 amu.



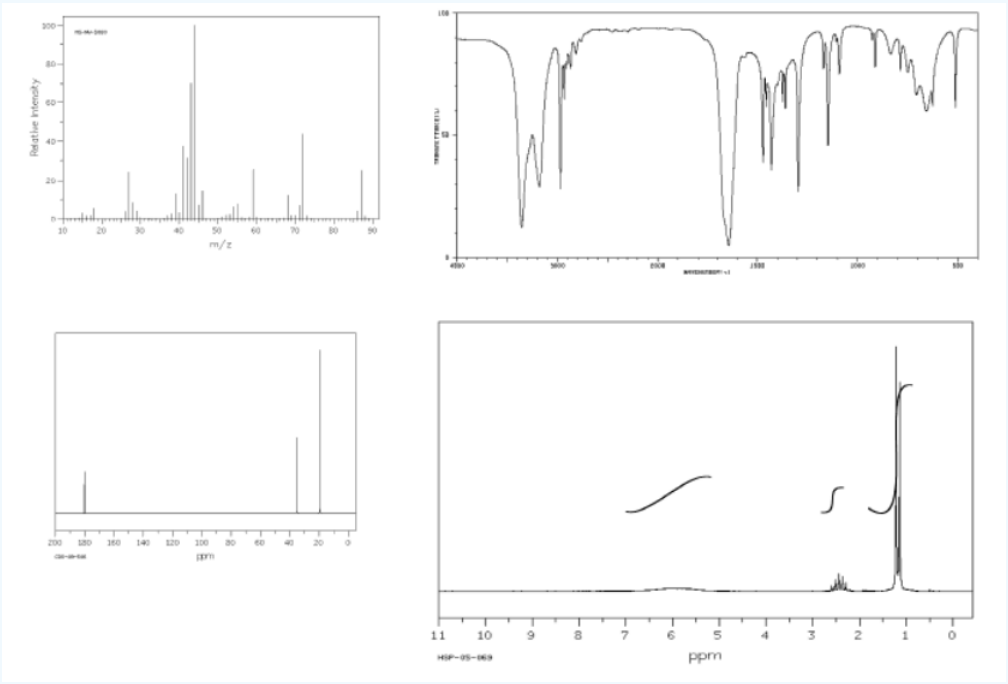




c)

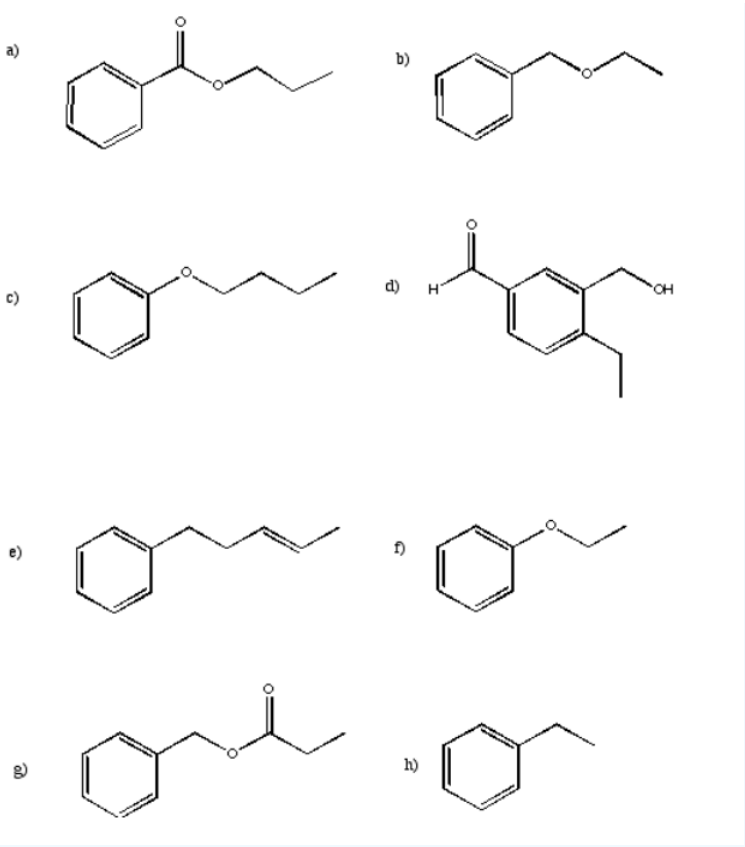


d)



Exercise 4.16.15

Sketch the expected ^{1}H spectrum for each of the following structures.

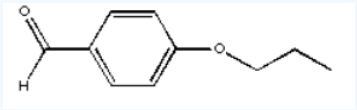


Exercise 4.16.16

Draw what the NMR spectrum of ethylbenzene, $CH_3CH_2C_6H_5$, would look like if it was contaminated with an equal amount of tert-butyl methyl ether, $(CH_3)_3COCH$

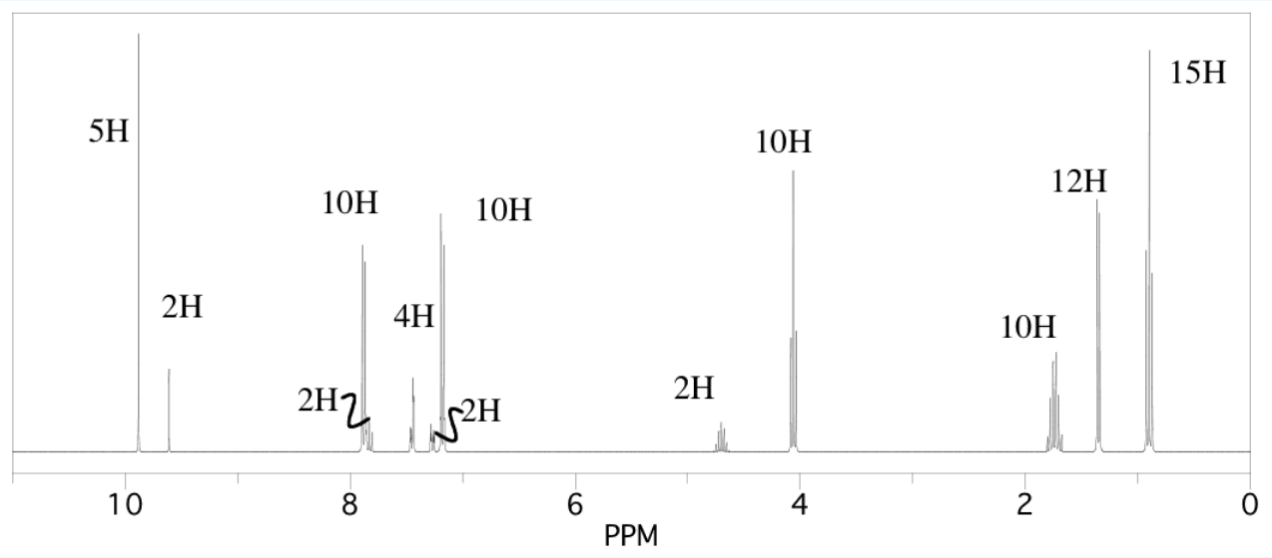
Exercise 4.16.17

The following NMR spectrum, of the aldehyde shown, is contaminated with another isomer.



a. Identify the peaks corresponding to each isomer.
b. Identify which peaks correspond to which proton in each isomer.

c. Identify the ratio of isomers in the sample.



4.17: 2D NMR

See Chapter 5

4.18: Solutions to Selected Problems

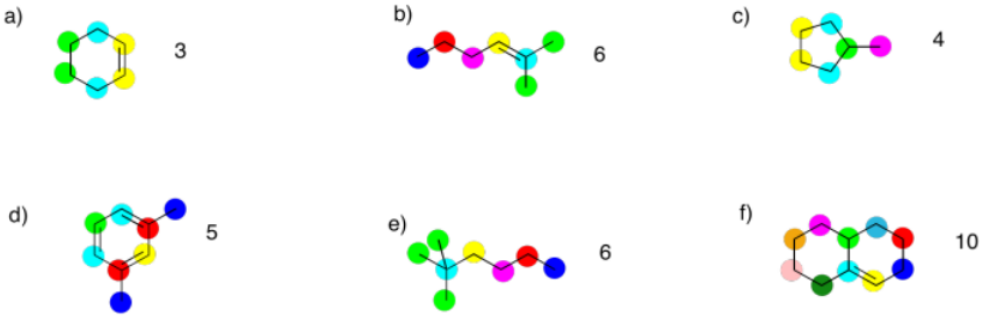
Exercise 4.2.1:

a) 10 ppm b) 64 ppm c) 158 ppm

Exercise 4.2.2:

a) 63 ppm b) 201 ppm c) 71 ppm

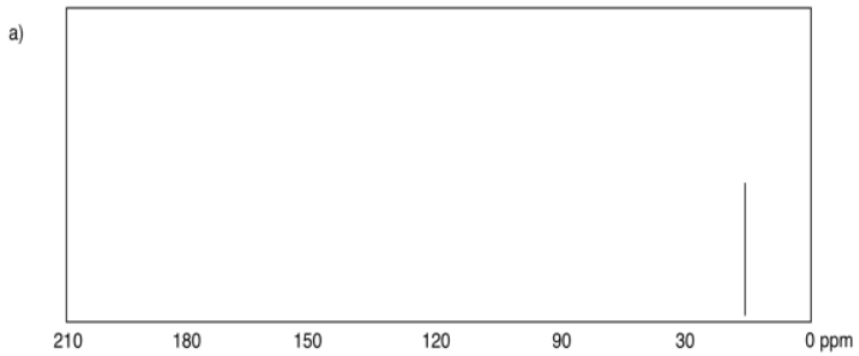
Exercise 4.3.1:

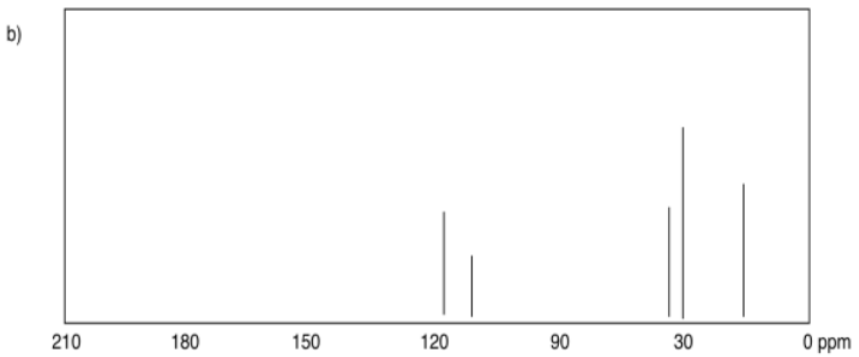


Exercise 4.3.2:

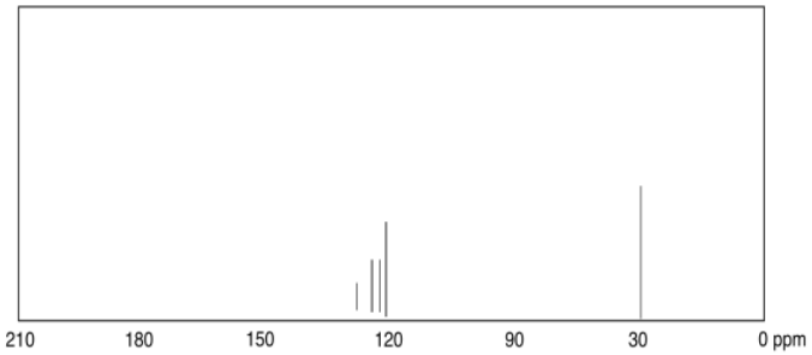
a. pentane, $CH_3CH_2CH_2CH_2CH_3$, or hexane, $CH_3CH_2CH_2CH_2CH_2CH_3$
b. heptane, $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$, or octane, $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$
c. nonane, $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$, or decane, $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$

Exercise 4.4.1:

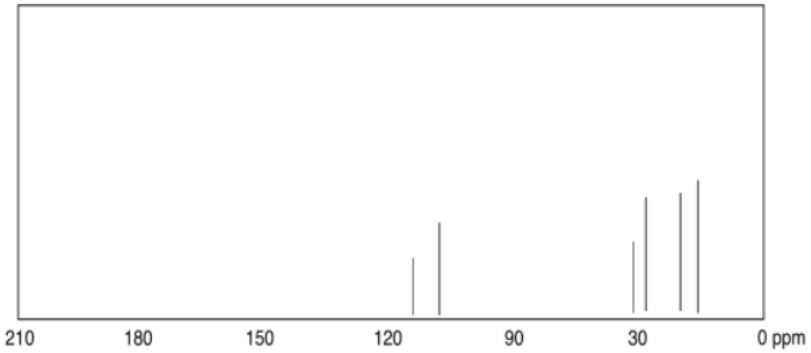




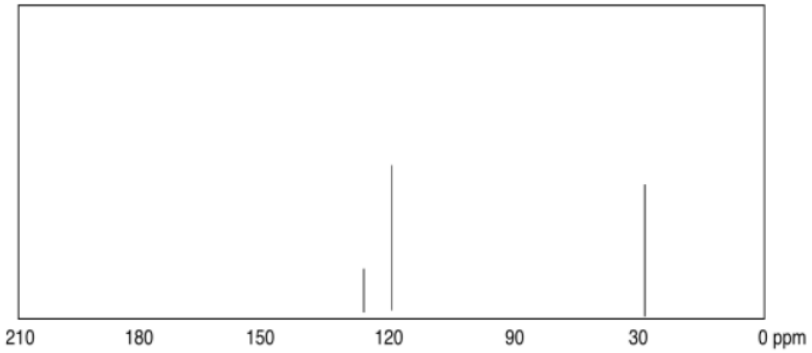
c)



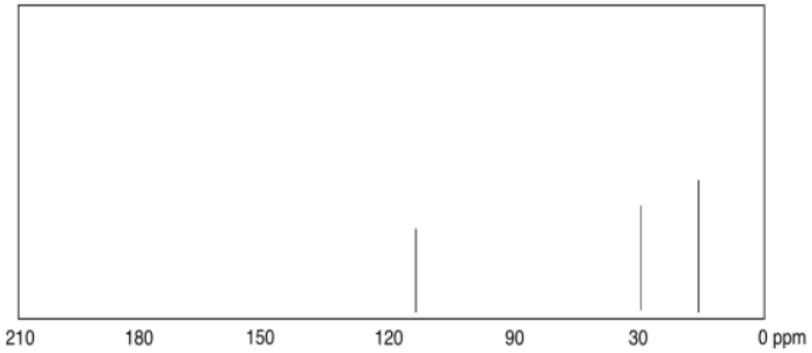
d)



e)



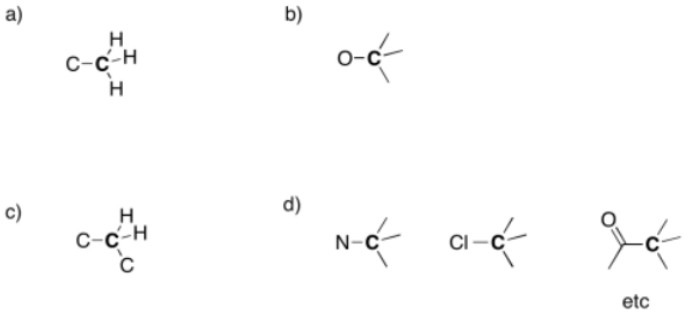
f)



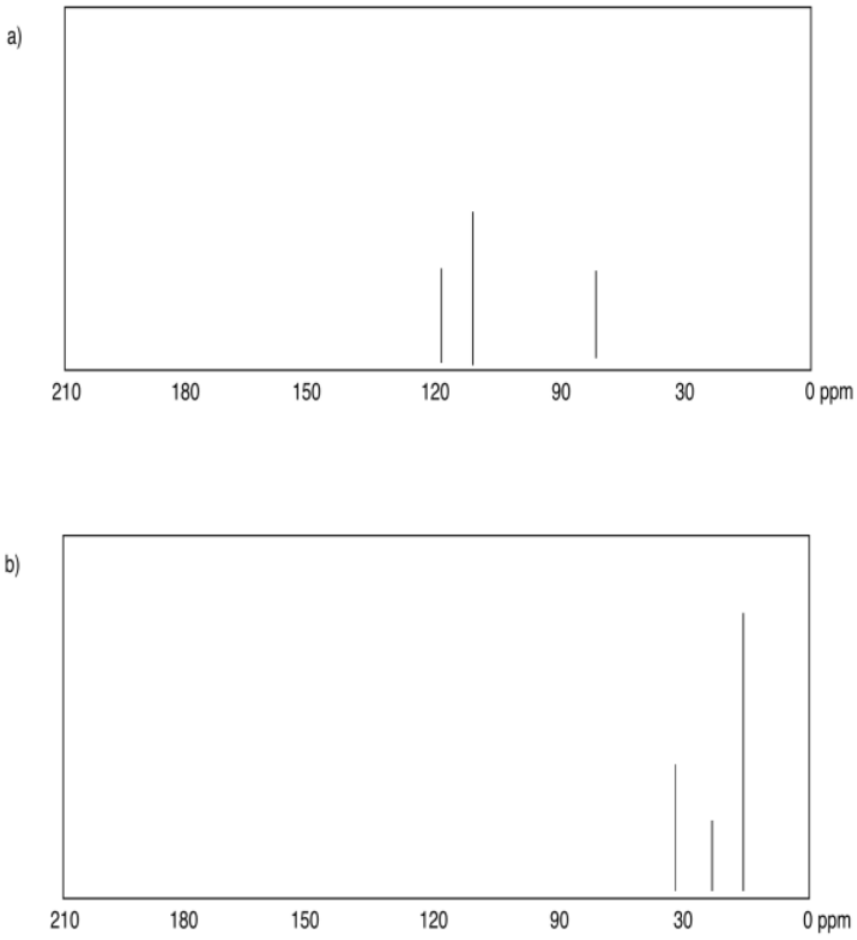
Exercise 4.4.2:

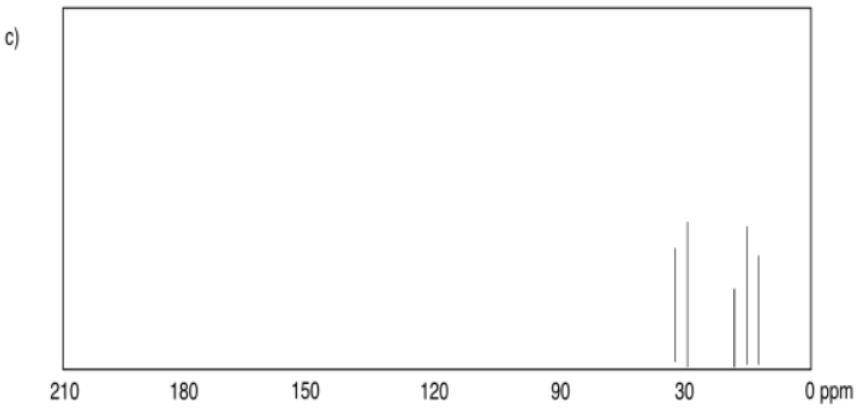
a) sp^3 b) sp^2 c) sp^2 d) sp^3 e) sp^3 f) sp^2

Exercise 4.5.1:



Exercise 4.5.2:





Exercise 4.6.1:

a) 127 ppm

Arom/Alkene

b) 11 ppm

probably Me

c) 196 ppm

ket/ald

d) 65 ppm

e) 111 ppm

f) 154 ppm

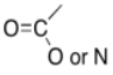
Arom

g) 210 ppm

ket/ald

h) 28 ppm

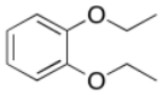
i) 170 ppm



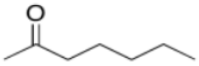
j) 42 ppm

Exercise 4.6.2:

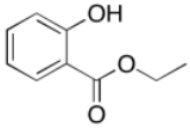
a)



b)



c)



Exercise 4.8.1:

a) H-$C_{sp}3$ b) H-$C_{sp}3$ c) H-$C_{sp}2$ d) H-$C_{sp}3$ e) H-$C_{sp}2$ f) H-$C_{sp}2$ g) H-$C_{sp}3$

Exercise 4.8.2:

a) carbon b) carbon c) nitrogen d) oxygen e) carbon f) oxygen g) nitrogen

Exercise 4.8.3:

a) aromatic b) aromatic c) alkene d) alkene e) alkene f) aromatic

Exercise 4.8.4:

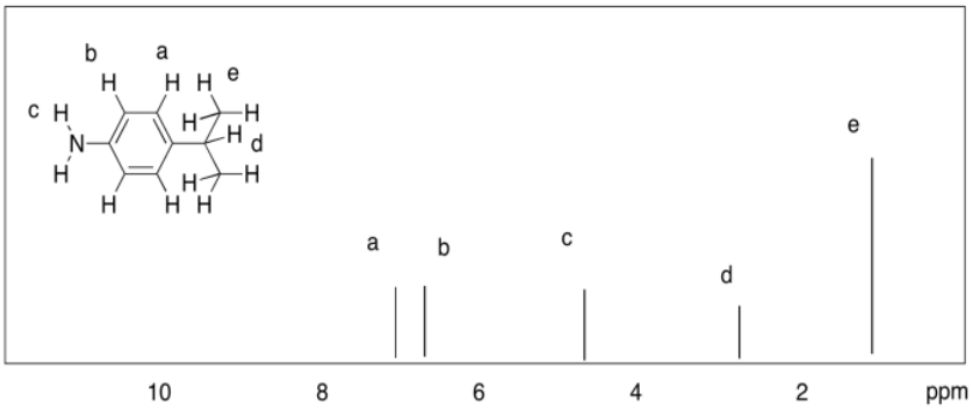
a) H-C_{Ar}-C b) H-C_{Ar}-C c) H-C_{Ar}-N d) C=O e) C=O f) H-C_{Ar}-N g) H-C_{Ar}-N

Exercise 4.8.5:

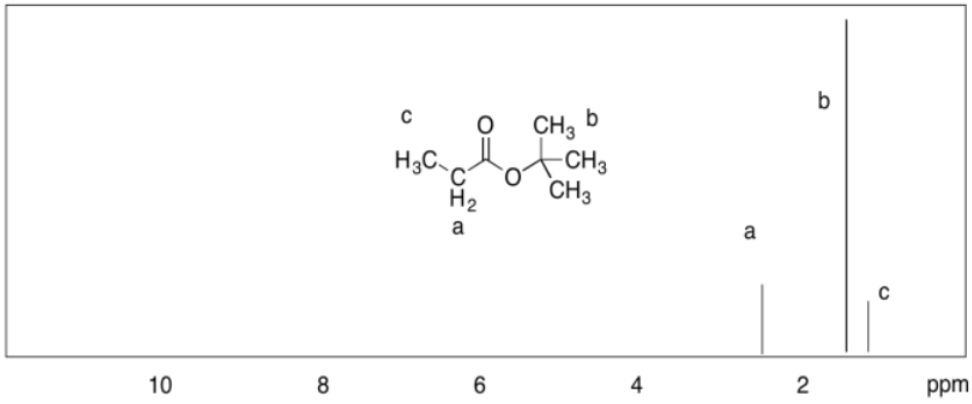
a. 3.4 ppm: H_a 1.5 ppm: H_b, H_c 0.9 ppm: H_d
b. 7.4 ppm: H_d 6.9 ppm: H_b, H_c 3.7 ppm: H_a
c. 10.1 ppm: H_a 7.9 ppm: H_b 7.6 ppm: H_d 7.5 ppm: H_c
d. 7.9 ppm: H_b 7.6 ppm: H_d 7.4 ppm: H_c 2.5 ppm: H_a

Exercise 4.8.6:

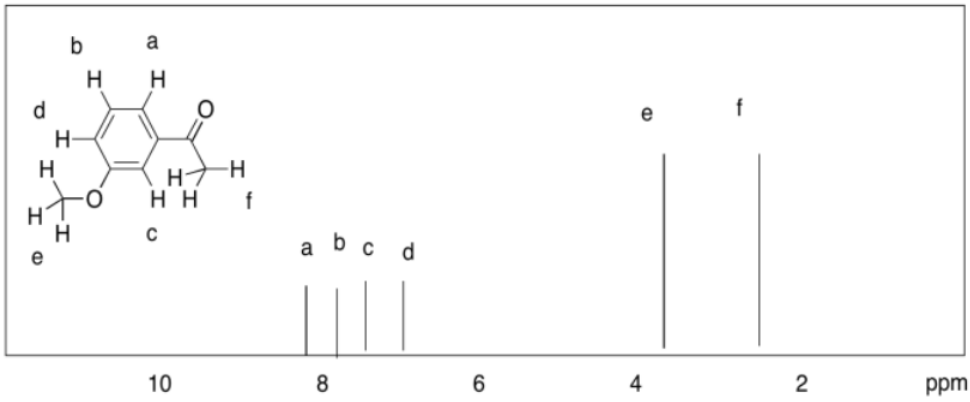
a)



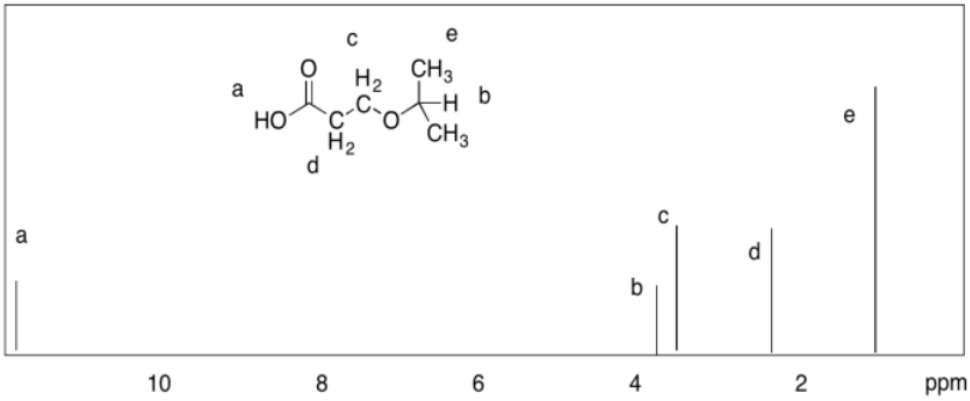
b)



c)



d)

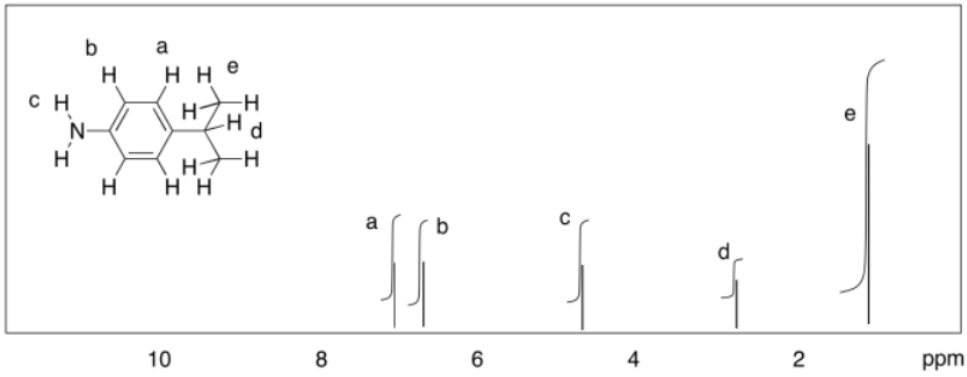


Exercise 4.9.1:

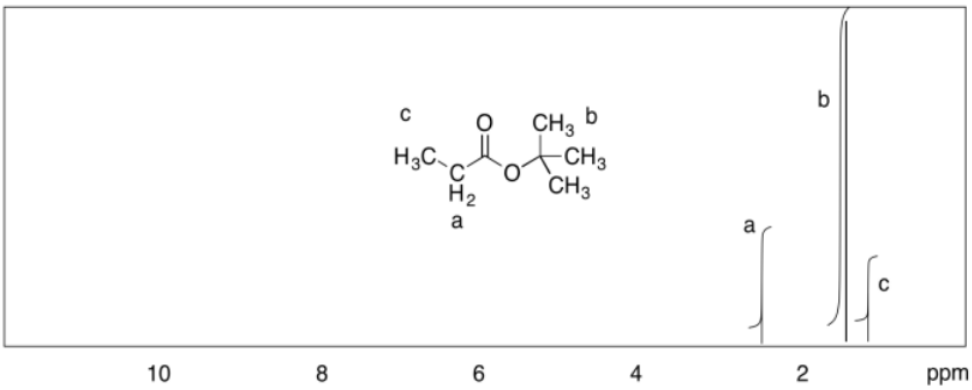
a. 0.9 ppm, 6H; 1.0 ppm, 6H (1:1 ratio)
b. 0.9 ppm, 6H; 1.0 ppm, 12H (1:2 ratio)
c. 0.9 ppm, 6H; 1.0 ppm, 16H (3:8 ratio)
d. 0.9 ppm, 6H; 1.0 ppm, 10H (3:5 ratio)
e. 0.9 ppm, 6H; 1.0 ppm, 8H (3:4 ratio)

Exercise 4.9.2:

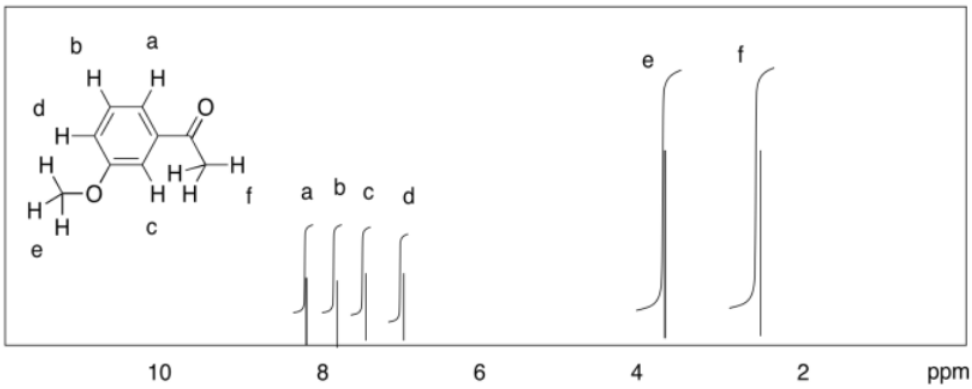
a)


b
a
e
c
d
a
b
c
d
e
10
8
6
4
2
ppm

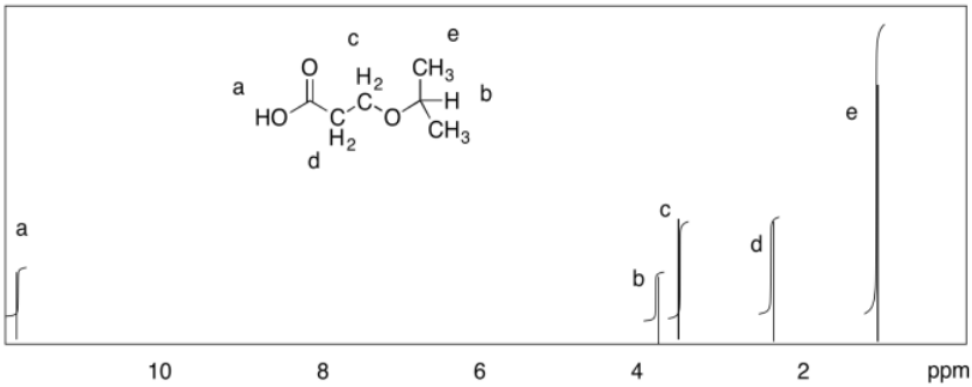
b)


c
O
CH3
b
H3C
C
O
CH3
H2
CH3
a
b
a
c
10
8
6
4
2
ppm

c)


b
a
d
O
H
H
H
H
H
f
O
H
H
e
c
a
b
c
d
e
f
10
8
6
4
2
ppm

d)



Exercise 4.9.3:

a) 5:2:3

Exericse 4.10.1:

(There will be some variation in the shift depending on the rest of the structure; this is just an estimate.)

a) 3.5 ppm, quartet, 2H b) 1.5 ppm, sextet, 2H c) 2.6 ppm, septet, 1H

d) 2.3 ppm, quintet, 1H e) 2.2 ppm, quartet, 2H f) 1.7 ppm, nonet, 1H

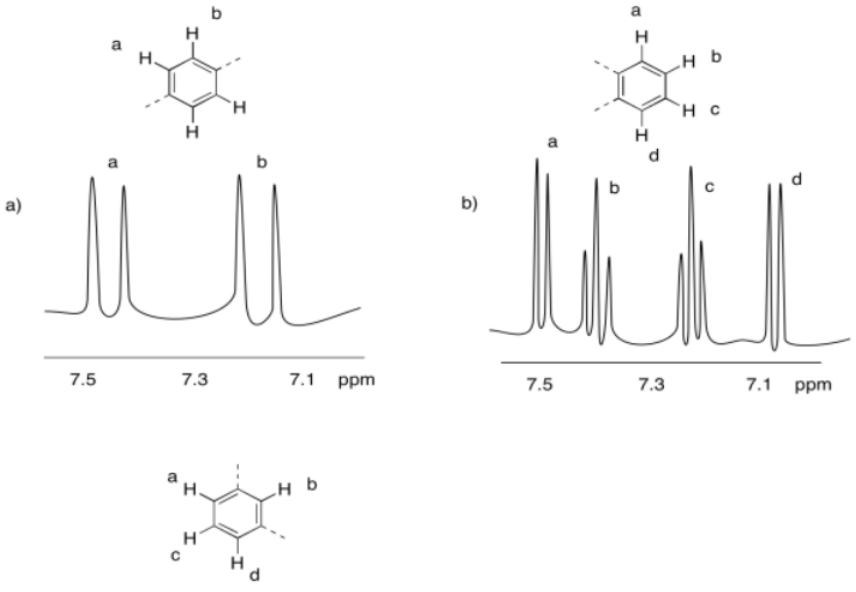
Exercise 4.10.2:

(There will be some variation in the shift depending on the rest of the structure; this is just an estimate.)

a) 7.8 ppm, doublet, 1H b) 8.4 ppm, singlet, 1H c) 6.7 ppm, singlet, 1H

d) 7.2 ppm, troplet, 1H e) 6.9 ppm, doublet, 1H

Exercise 4.10.3:



Exercise 4.10.4:

3.4 ppm, doublet: CH-C**H**$_2$-O

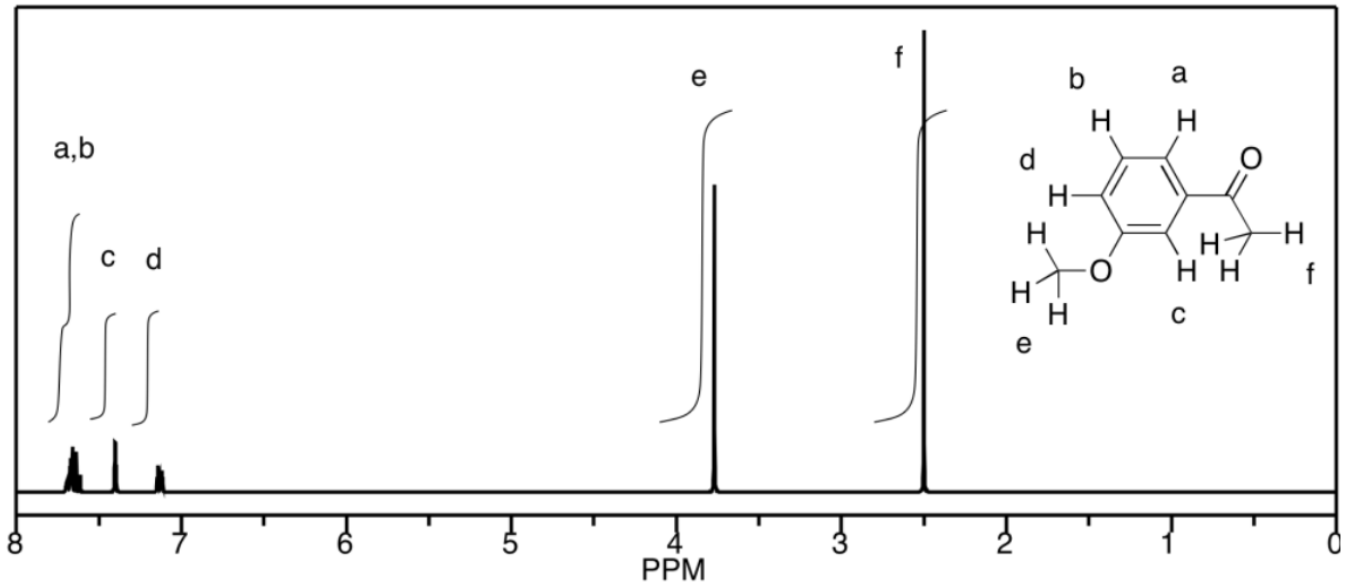
2.1 ppm, singlet: O**H**

1.7 ppm, nonet: $(CH_3)_2$C**H**CH_2

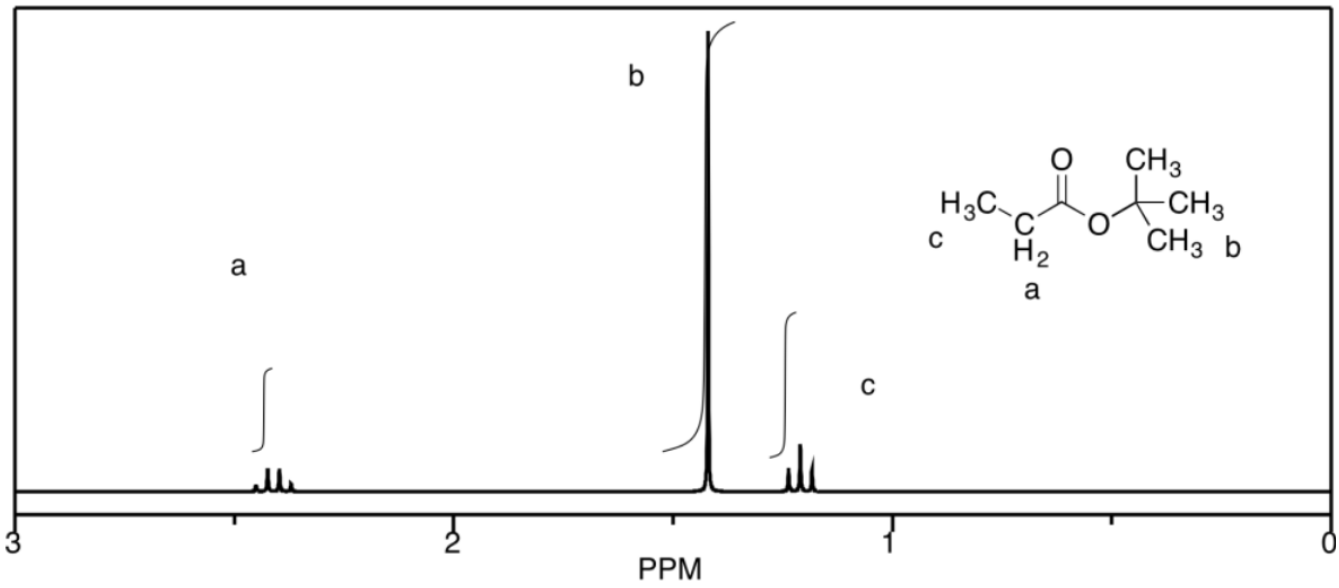
0.9 ppm, doublet: CH(C**H**$_3)_2$

Exercise 4.10.5:

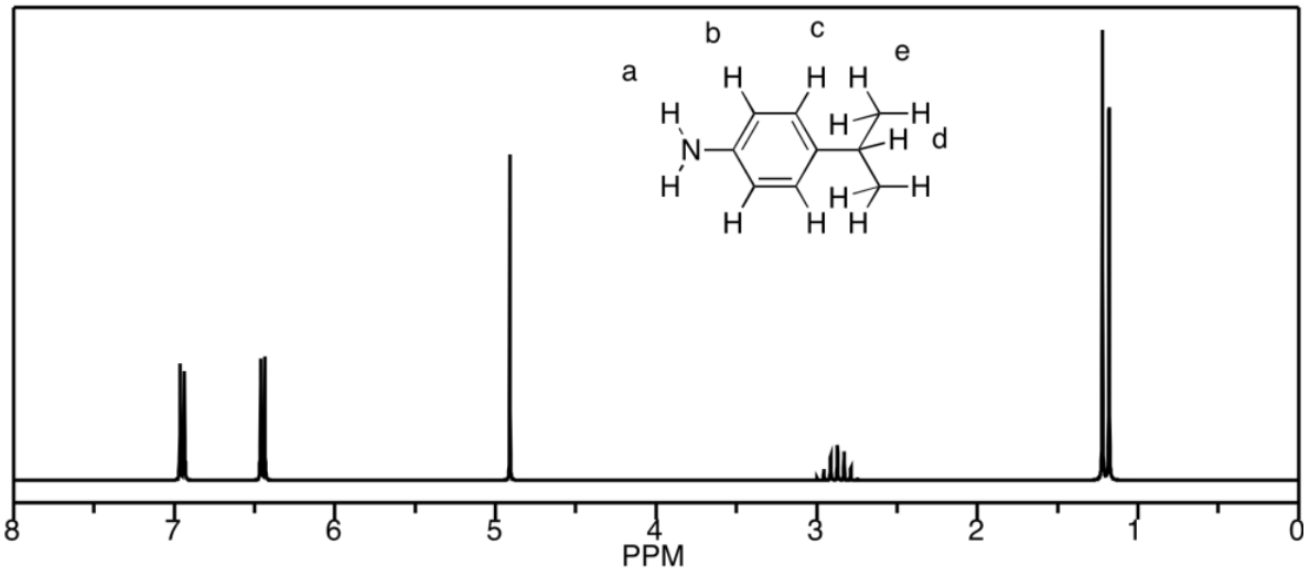
a) This is a simulated spectrum. The peaks at f, e, and c are singlets. The peak at d is a doublet. The peaks at a & b are unfortunately coincident, so their multiplicities are obscured, but they would be doublets & triplets, respectively.



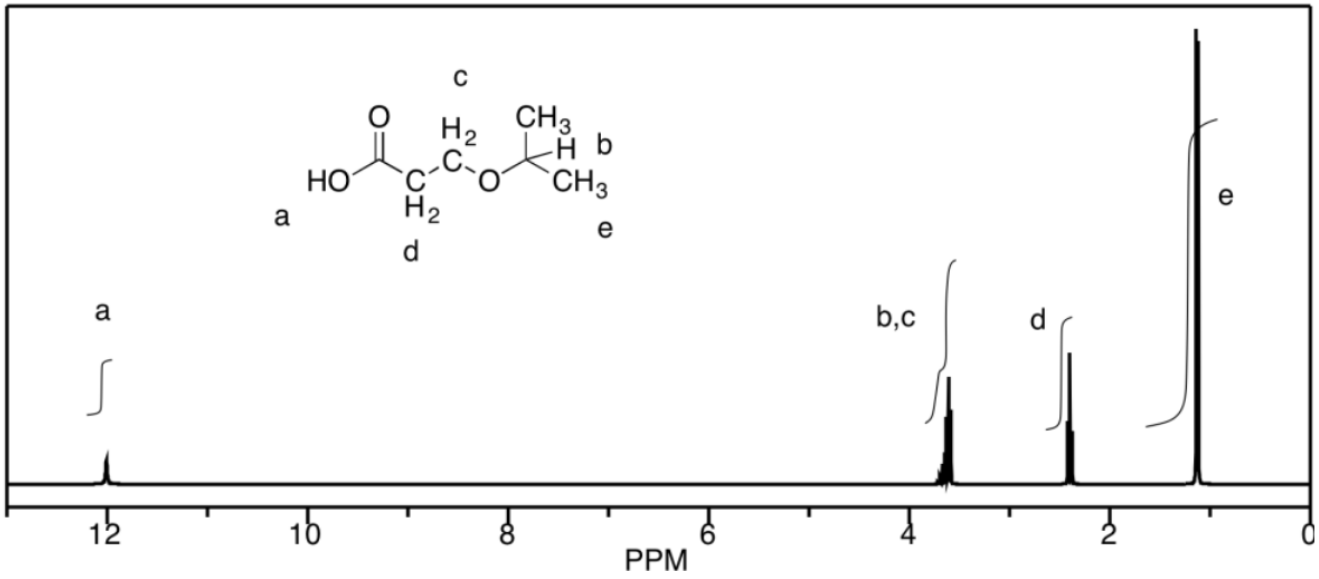
b)



c)



d) The peaks at b and c unfortunately coincide, but they would be a septet and a triplet, respectively. Otherwise, a is a singlet, d is a triplet, and e is a doublet.



Exercise 4.12.1:

Fill in partial structures for the following peaks.

Aromatic (benzene etc) peaks are labeled "Ar" to distinguish from alkene peaks that show up further upfield (lower shift). Also, some peaks may be in two symmetric positions and are labeled with "x2".

a) 10.1 ppm, 1H, triplet, CH_2-C**H**=O b) 3.4 ppm, 1H, septet, O-C**H**$(CH_3)_2$

c) 7.3 ppm, 2H, triplet, CH=C**H**-CH x 2 (Ar) d) 5.4 ppm, 1H, quartet, CH_3-C**H**=C

e) 1.4 ppm, 2H, sextet, CH_3-C**H**$_2$-CH_2 f) 8.0 ppm, 1H, singlet, C=C**H**-C (Ar)

g) 2.1 ppm, 3H, singlet, C**H**$_3$-C=C or C**H**$_3$-C=O or C**H**$_3$-N; need context to choose

h) 6.8 ppm, 2H, doublet, CH=C**H**-C x 2 (Ar) i) 0.9 ppm, 6H, doublet, CH-C**H**$_3$ x 2

Exercise 4.12.2:

Identify the errors in the following partial structures:

a) 3.6 ppm, 2H, triplet, C**H**$_2$-CH$_2$ the first carbon must be attached to O to have a shift at 3.6 ppm

b) 2.1 ppm, 2H, singlet, C**H**$_3$-C=C the integral says only 2H, not 3H

c) 7.4 ppm, 2H, doublet, CH=C**H**$_2$-C the shift implies aromatic, so there can only be one H per carbon; must be symmetry

d) 1.8 ppm, 2H, quintet, C**H**$_2$-CH$_4$ there can't be four hydrogens on one carbon; must be some hydrogens on each side

e) 7.8 ppm, 1H, triplet, -C**H**=CH$_2$ the shift implies aromatic, so there can only be one H per carbon; must be one one each side

f) 1.7 ppm, 1H, nonet, NH$_2$-C**H**(CH$_3$)$_2$ an attached nitrogen would shift this hydrogen past 2 ppm; also, coupling is rarely seen across O or N, so the two neighbouring H on the left are probably on a carbon

Exercise 4.13.1:

a) TBME b) acetone c) THF d) methanol e) ethyl acetate

Exercise 4.14.1:

a. appearance of CH-O near 3.5 ppm (multiplet, 1H)
b. appearance of CH$_2$-O near 3.5 ppm (triplet, 2H); disappearance of =CH near 5-6 ppm (mutiplets, total 3H)
c. appearance of HC=O near 10 ppm (triplet, 1H); disappearance of =CH near 5-6 ppm (mutiplets, total 3H)
d. appearance of HC=O near 10 ppm (triplet, 1H); disappearance of CH$_2$-O near 3.5 ppm (doublet, 2H)
e. appearance of CH$_2$-O near 3.5 ppm (triplet, 2H)
f. appearance of CH$_2$-O near 4 ppm (triplet, 2H)
g. appearance of =CH near 5-6 ppm (mutiplets, total 2H); disappearance of HC=O near 10 ppm (triplet, 1H);
h. disappearance of =CH near 5-6 ppm (mutiplets, total 2H); appearance of triplet:sextet:triplet pattern between 1-2 ppm

i) appearance of HC=O near 10 ppm (triplet, 1H); disappearance of CH$_2$-O near 3.5 ppm (doublet, 2H)

j) appearance of CH-O near 3 ppm (singlet, 3H) and 3.5 ppm (sextet, 1H); disappearance of =CH near 5-6 ppm (mutiplets, total 2H)

Exercise 4.15.1:

a) student 1: Let's use the H$_2$C-O peak of ethyl propanoate at 4 ppm and the acetonitrile methyl at 2 ppm. The ratio appears to be 2:1, but they represent 2 protons and 3 protons, respectively. That means the ratio of molecules is 2/2:1/3 = 3:1 ethyl propanoate : acetonitrile.

student 2: We'll use the H$_2$C-O peak of ethyl propanoate at 4 ppm and the H$_2$C-O peak of THF at 3.5 ppm. The ratio appears to be 3:2, but they represent 2 protons and 4 protons, respectively. That means the ratio of molecules is 3/2:2/4 = 12:4 = 3:1 ethyl propanoate : THF.

student 3: Look at the H$_2$CCl$_2$ peak of dichloromethane at 5 ppm and the H$_2$C-O peak of THF at 4 ppm. The ratio appears to be 1:2, and they both represent 2 protons, so the ratio of molecules is 1:2 dichloromethane : ethyl propanoate.

b) student 1: The sample is $\frac{1}{1+3} \times 100\% = 25\%$ acetonitrile.

student 2: The sample is $\frac{1}{1+3} \times 100\% = 25\%$ THF.

student 3: The sample is $\frac{1}{1+2} \times 100\% = 33\%$ acetonitrile.

Exercise 4.15.2:

The obvious NMR handles are the H-C=O aldehyde proton at 10 ppm for benzaldehyde and the alcohol-adjacent H-C-O proton at 4.5 ppm for 1-phenylpropanol.

Each of those peaks represents one proton, so the integral ratio of 1:2 suggests a ratio of bezaldehyde to 1-phenylpropanol of of 1:2. That translates into 33% benzaldehyde, 67% 1-phenylpropanol.

Exercise 4.15.3:

The NMR handles here are the H-C=O aldehyde proton at 10 ppm for benzaldehyde and the alcohol-adjacent H$_2$C-O protons near 5 ppm for benzyl alcohol.

In this case, we need to correct for the differing numbers of protons represented by each peak: 1H for the aldehyde peak but 2H for the alcohol one. The integral ratio of 1:6 therefore suggests a ratio of bezaldehyde to 1-phenylpropanol of of 1:3. That translates

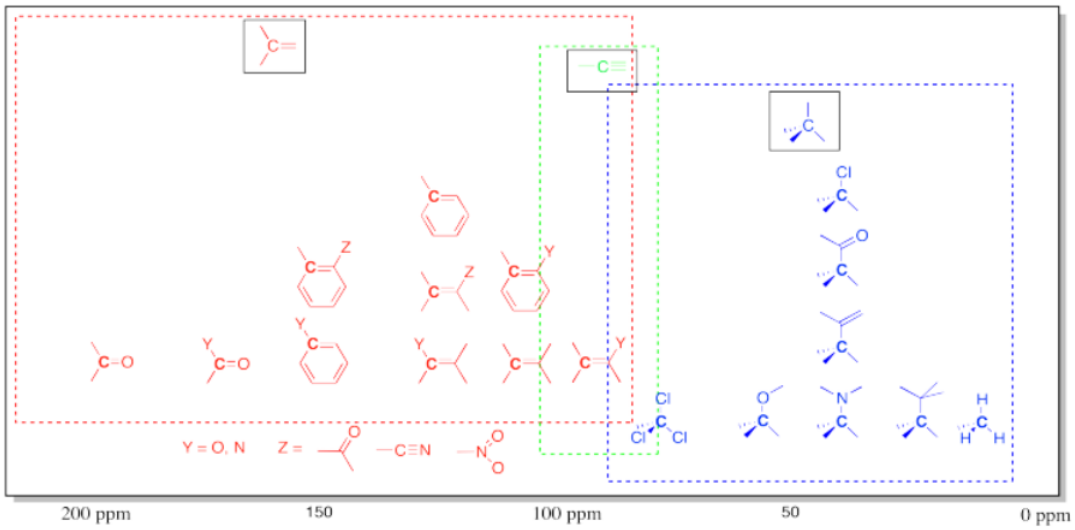
into 25% benzaldehyde, 75% 1-phenylpropanol.

Exercise 4.15.4:

We could use the peak corresponding to the O-CH-C=O proton above 5 ppm for the repeat unit and the peak for the CH_2-O proton in the initiator/end group near 3.5 ppm. The integral ratio is 24:1, but they represent different numbers of hydrogens, so the repeat unit to end group ratio is really 24/1:1/2, or 48:1. The degree of polymerization is 48.

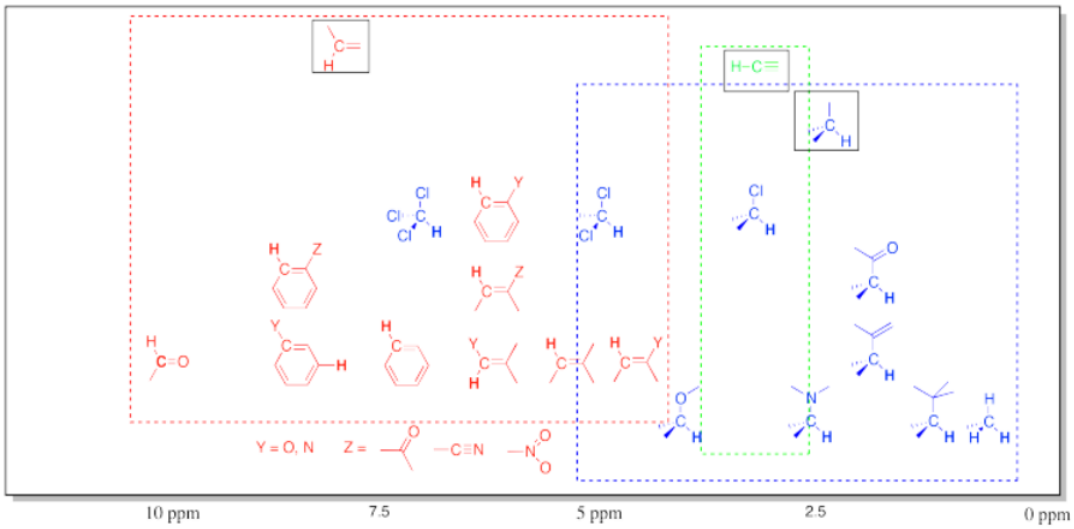
4.19: Appendix

Table of ^{13}C NMR Frequencies Common in Organic Compounds.



Note that effects are additive: two or more electron-withdrawing groups move the absorbance further to the left than just one group.

Table of ^{1}H NMR Frequencies Common in Organic Compounds.



This chart shows the frequancies of protons that are attached to carbons. In general, protons follow the trend seen in the carbon to which they are attached. Note again the additive effects of multiple attached groups.

This table does not include OH (or NH) protons. Protons attached to heteroatoms are more difficult to pinpoint because their locations in the spectrum are much less specific. Instead, they may be found across a very broad range.

Table of ^{1}H NMR Frequencies of OH Common in Organic Compounds.

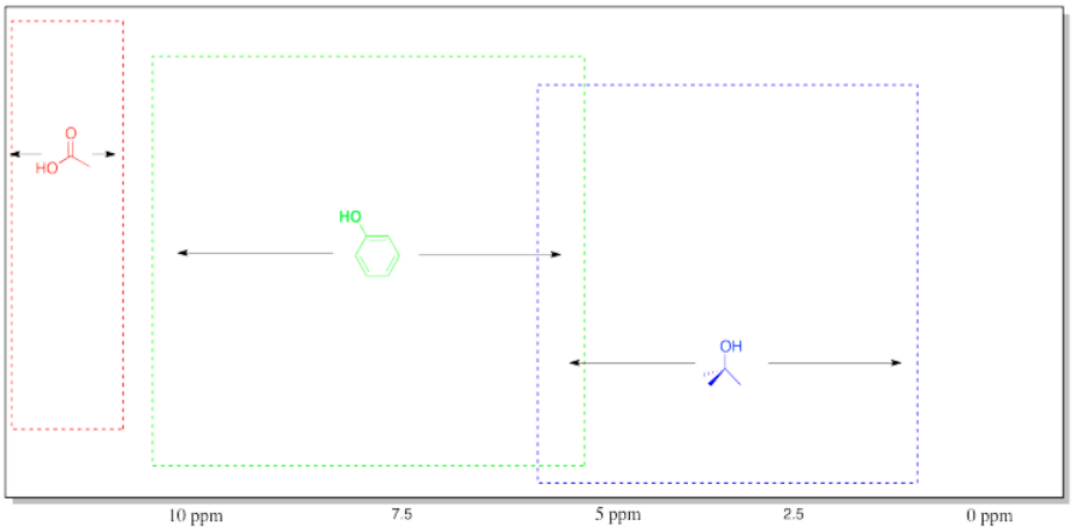


Table of Some Common Impurities in NMR Samples.

Minor impurities in the NMR spectrum are often the result of solvents used during a reaction or sample purification. A few examples are provided in the following table, showing the data you would see from common solvents in an NMR spectrum taken in chloroform.

solvent	number of peaks	shift	multiplicity	integral ratio	assignment
water	1	1.56	br. s	-	O-**H**
acetone	1	2.17	s	-	(C=O)C**H**$_3$
chloroform	1	7.26	s	-	Cl$_3$C-**H**
t-butyl methyl ether	2	1.19	s	3	C(C**H**$_3$)$_3$
		3.22	s	1	O-C**H**$_3$
ethyl acetate	3	1.26	t	3	CH$_2$C**H**$_3$
		2.05	s	3	(C=O)C**H**$_3$
		4.12	q	2	OC**H**$_2$CH$_3$
grease or alkanes	2	0.86	m	varies; smaller	CH$_2$C**H**$_3$
		1.26	m	varies; larger	CH$_2$C**H**$_2$CH$_2$ / CH$_2$C**H**$_2$CH$_3$

An excellent table, including shifts of a variety of impurities in different NMR solvents, can be found in the following article: Gottlieb, H. E.; Kotlyar, V.; Nudelman, A. *J. Org. Chem.* **1997**, *62*, 7512-7515.

Table of Solvent

Residual Peaks

Because an NMR sample is mostly solvent (with a small amount of dissolved solute that you are really interested in), there is usually a peak in the spectrum that comes from atoms in the solvent. Usually the use of deuterated solvents (enriched in ^{2}H instead of ^{1}H) minimizes the size of solvent peaks in ^{1}H NMR. However, there is always a trace of ^{1}H left in the solvent, which shows up as a small peak in the spectrum. ^{13}C residual peaks are often much larger than the peaks arising from the solute.

Solvent	^{1}H Shift	Multiplicity	^{13}C Shift	Multiplicity*
Acetone-d_6	2.05	pent	206.68	sing

			29.92	sept
Acetonitrile-d_3	1.94	pent	118.69	sing
			1.39	sept
Benzene-d_6	7.16	sing	128.39	trip
Chloroform-d	7.27	sing	77.23	trip
D_2O	4.80		--	
Dichloromethane-d_2	5.32	trip	54.00	pent
DMF-d_7	8.03	sing	163.15	trip
	2.92	pent	34.89	sept
	2.75	pent	29.76	sept
DMSO-d_6	2.50	pent	39.51	sept
Methanol-d_4	4.87	sing	49.15	sept
	3.31	pent		
THF-d_8	3.58	sing	67.57	pent
	1.73	sing	25.37	sing

*Note that coupling to ^2H produces different patterns than coupling to ^1H.

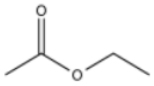
CHAPTER OVERVIEW

5: 2D NMR

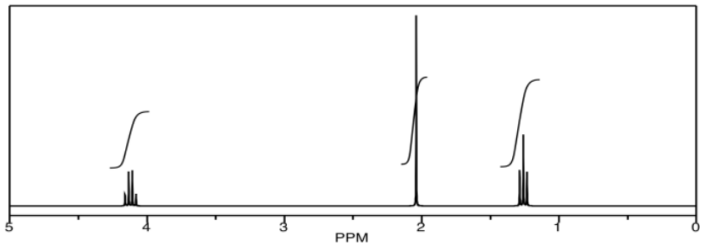
5.1: COSY Spectra

In 2D NMR, correlation peaks are used to help establish the structure.

Let's start with a simple compound, ethyl acetate.

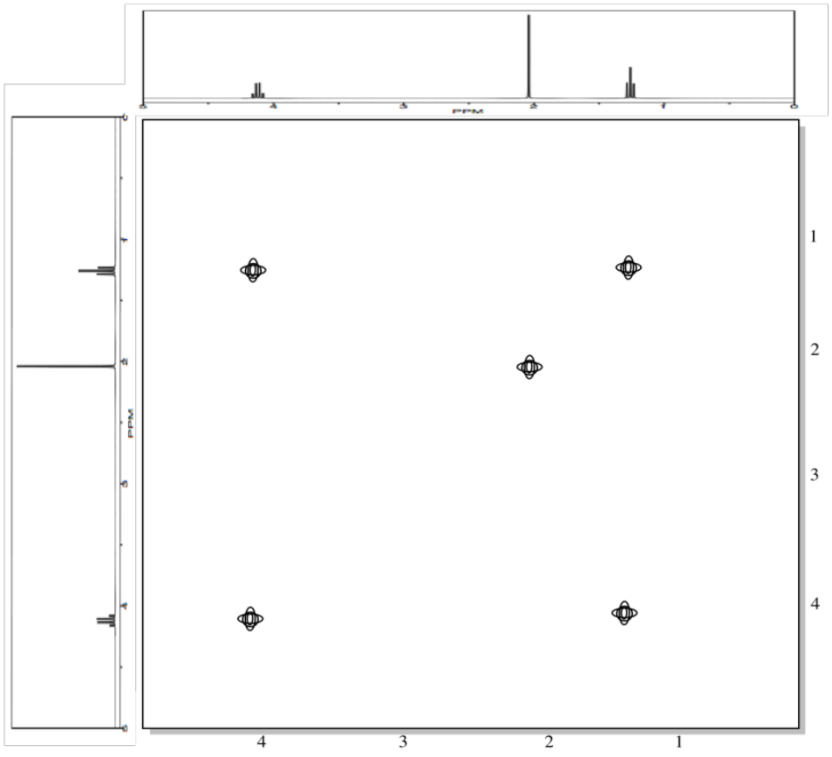


The ^{1}H NMR spectrum is not very complicated.



In **homonuclear correlation spectroscopy (COSY)**, we can look for hydrogens that are coupled to each other. In ethyl acetate, it's pretty clear where they are. There is a quartet and a triplet; the hydrogens corresponding to those two peaks are probably beside each other in the structure.

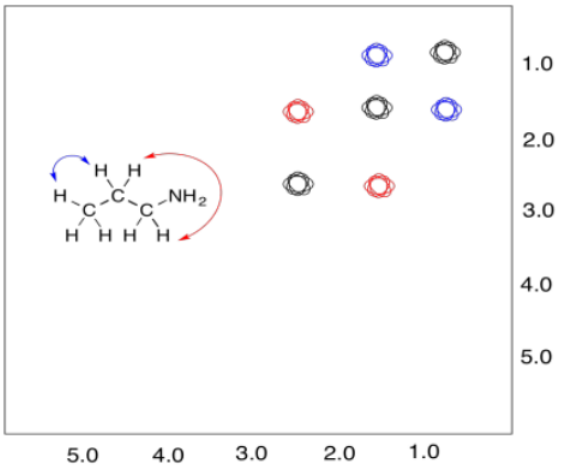
The COSY spectrum simply takes that ^{1}H spectrum and spreads it out into two dimensions. Instead of being displayed as a row of peaks, the peaks are spread out into an array. In the following simulated COSY spectrum, the peaks are displayed along one axis. The same peaks are also displayed along the other axis. In the middle of the plot, the peaks are shown plotted against each other -- that is, there is a peak at 1.25 ppm on the y axis and along the x axis, so there is a data point on the plot at (1.25, 1.25). Other such peaks appear along the diagonal stretching from the upper right to the lower left through the middle of the plot. There are three peaks appearing along that diagonal line; these three peaks basically show us what we already saw in the regular ^{1}H NMR spectrum.



The interesting peaks are the ones that do not appear along the diagonal. Those peaks indicate which hydrogens are coupled to which other hydrogens. The hydrogens at 1.25 ppm are coupled to the ones at 4.2 ppm, and that gives a "cross-peak" at (1.25, 4.20). There is also a cross-peak at (4.20, 1.25), because that relationship goes both ways.

What does it mean to be coupled? It means that magnetic information is transmitted between the atoms. How can we tell? Essentially, we can send a pulse of electromagnetic radiation into one set of hydrogens and look for a response somewhere else. Of course, if we send a pulse of radio waves at a frequency that will be absorbed by a particular hydrogen, we will see a response in that hydrogen itself. That's why we see the peaks on the diagonal. However, we also see responses from other hydrogens that are magnetically linked to the original one.

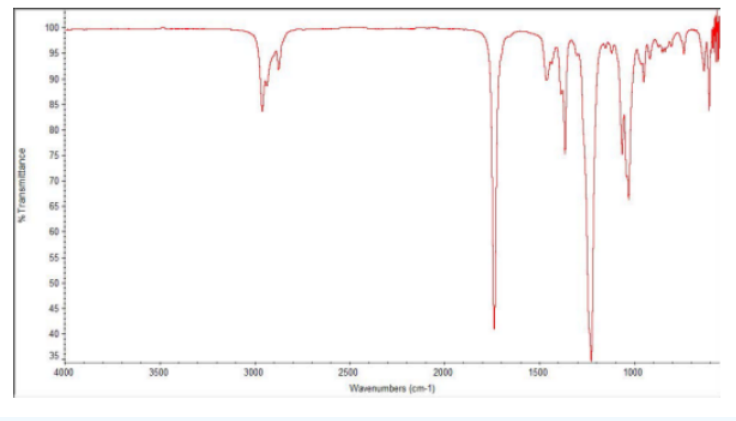
A second example is shown below. This time, the compound is propanamine. In propanamine, there would again be a diagonal set of peaks, shown in black, corresponding to the peaks in the regular proton spectrum. In addition, two different sets of protons are coupled. The methyl group is coupled to the methylene in the middle of the molecule; that cross-peak is shown in blue. The methylene in the middle is also coupled to the methylene next to the nitrogen; that cross-peak is shown in red.

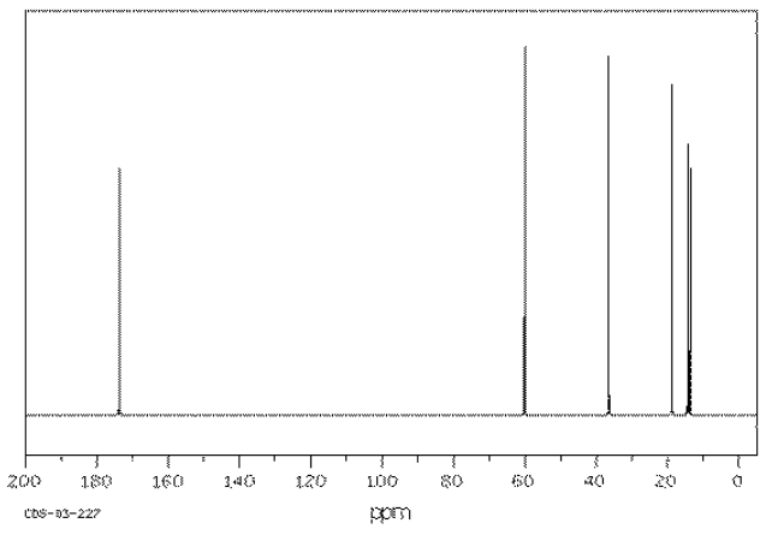


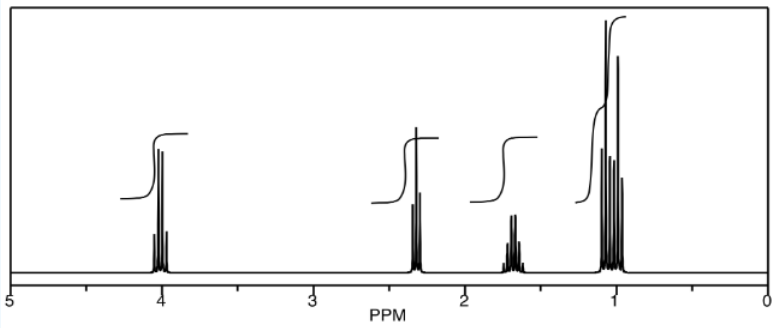
	^{13}C	^{1}H	COSY
a	10	0.9	1.5
b	28	1.5	0.9, 2.6
c	43	2.6	1.5

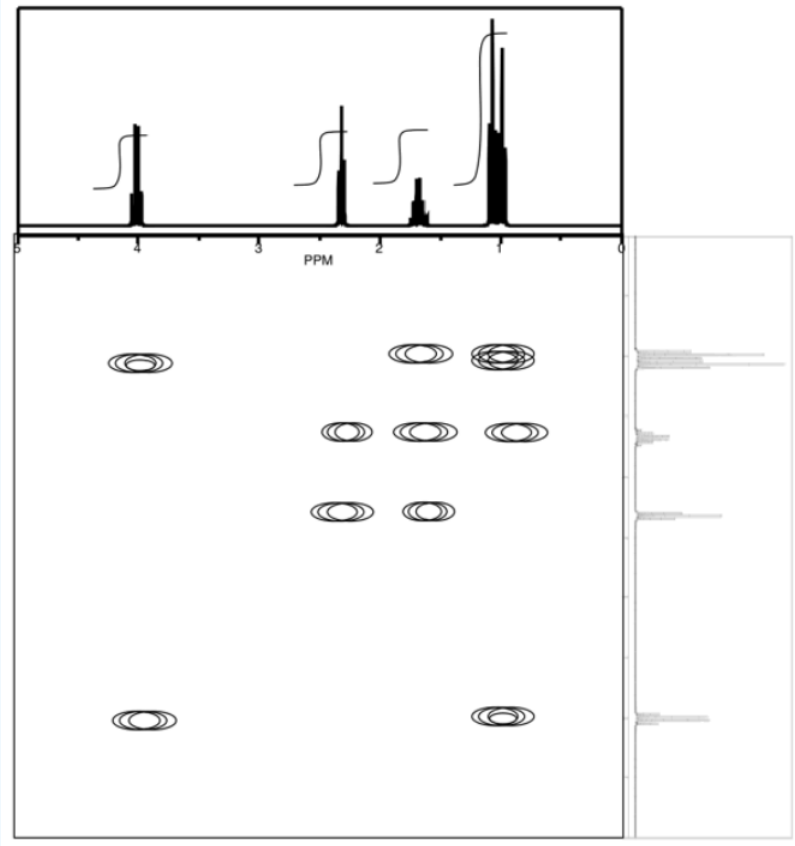
Exercise 5.1.1

Provide analyses of the following spectra and propose a structure for the compound.




200
180
160
140
120
100
80
60
40
20
0
CDS-03-227
ppm


5
4
3
2
1
0
PPM

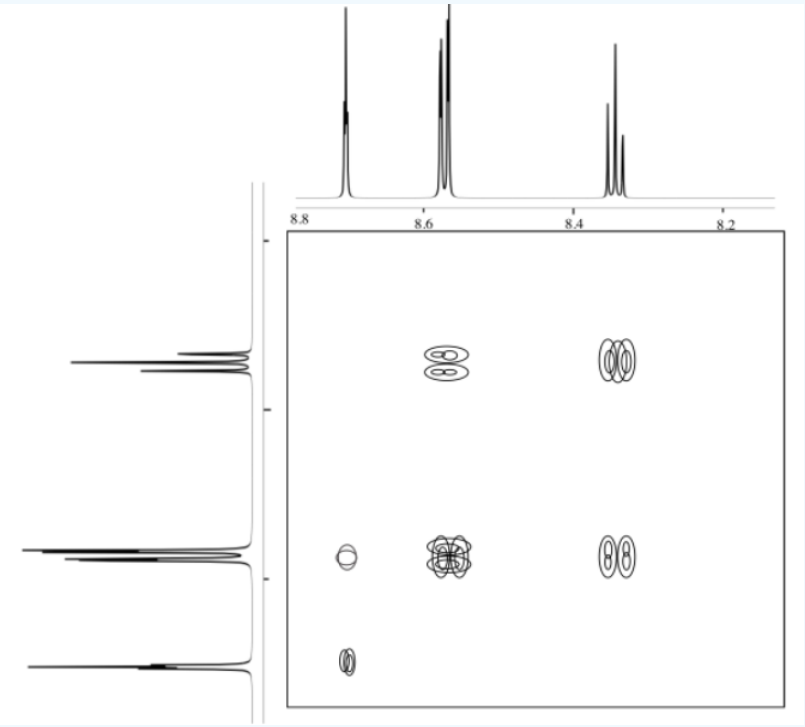

PPM

Answer

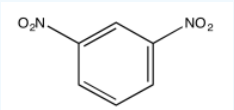
ethyl butanoate

Exercise 5.1.2

The following COSY spectrum is for an isomer of dinitrobenzene. Which isomer is it?

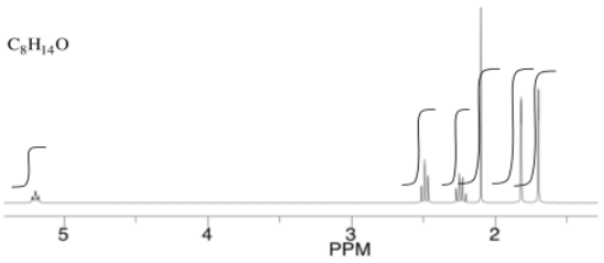


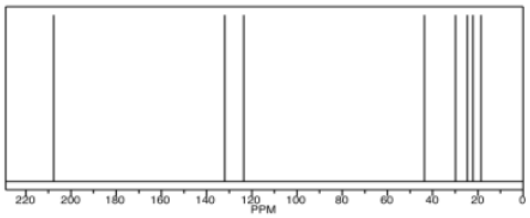
Answer

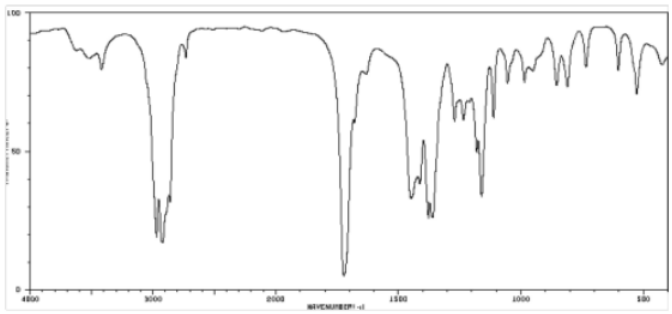


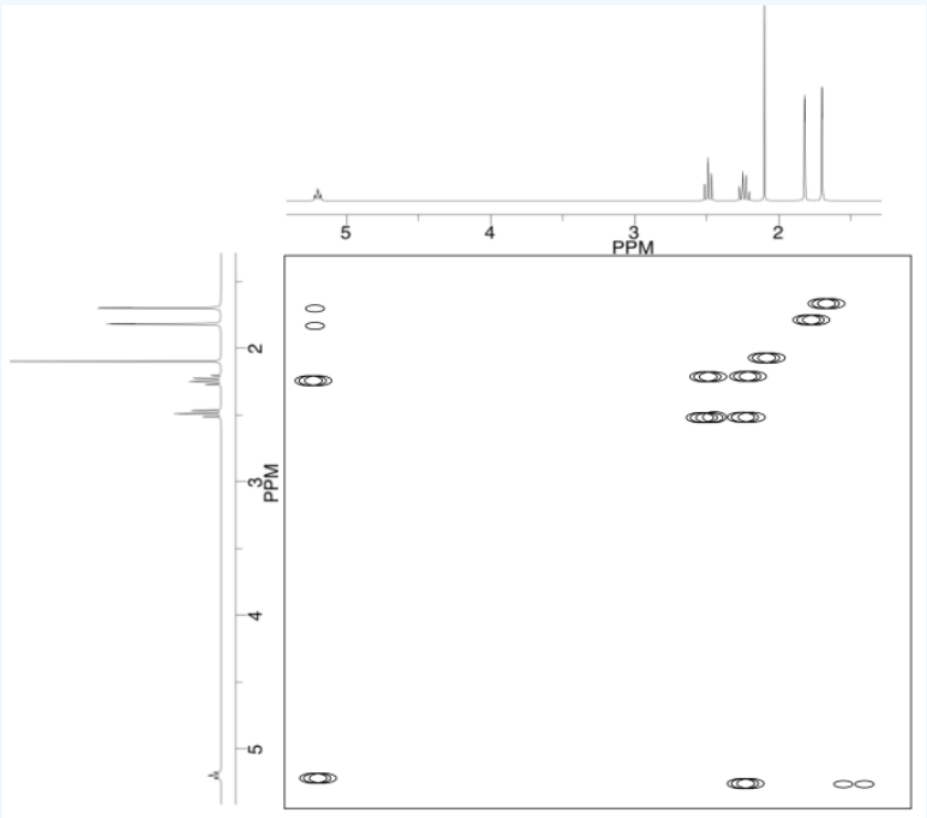
Exercise 5.1.3

Analyse the data in the following spectra and propose a structure for the compound.

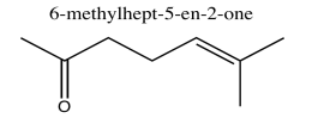

C8H14O
5
4
3
2
PPM


220
200
180
160
140
120
100
80
60
40
20
0
PPM




5
4
3
2
PPM
2
3
4
5
PPM

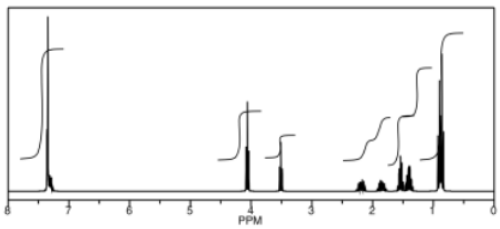
Answer

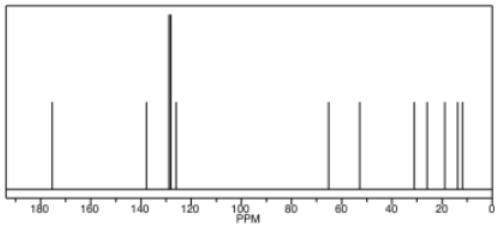

6-methylhept-5-en-2-one
O

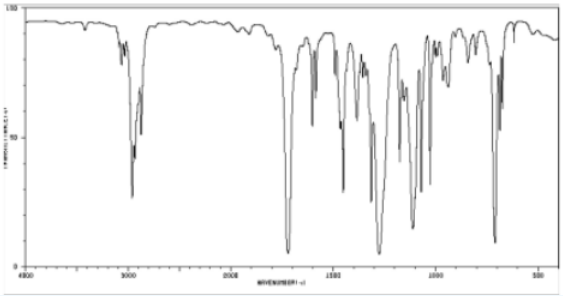
Exercise 5.1.4

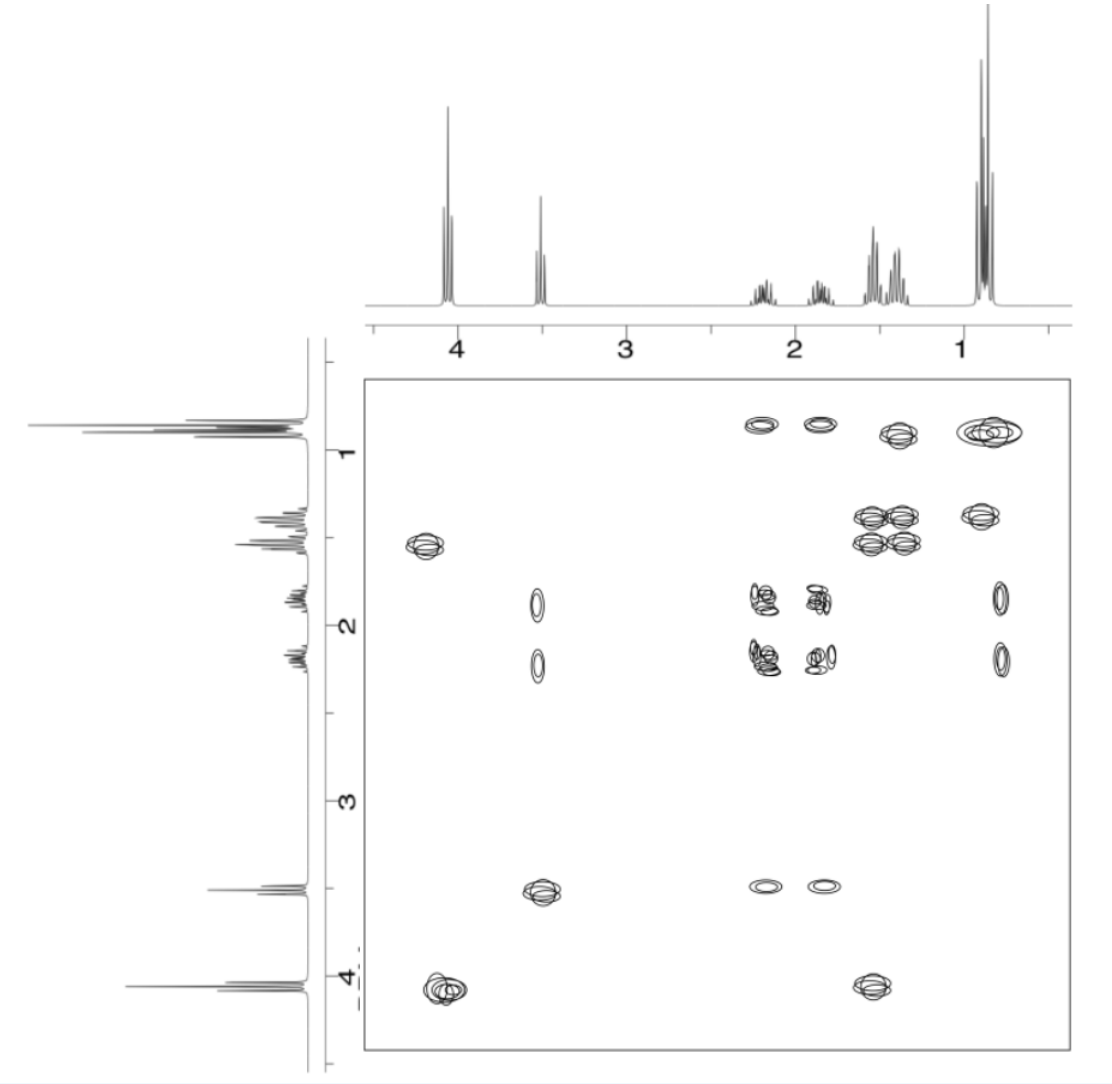
Analyse the data in the following spectra and propose a structure for the compound.

$C_{14}H_{20}O_2$

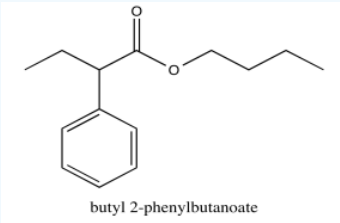








Answer

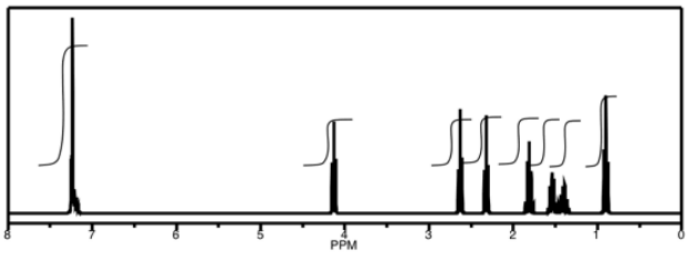


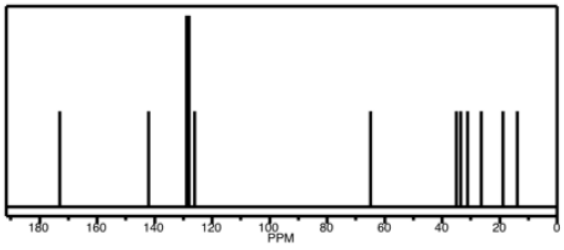
butyl 2-phenylbutanoate

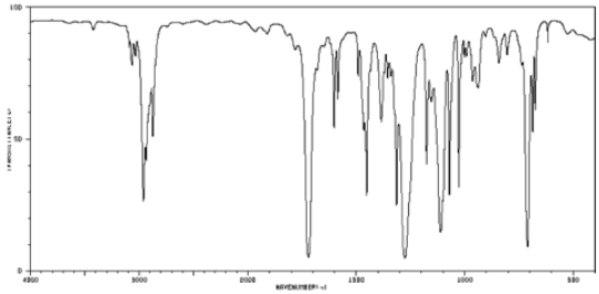
Exercise 5.1.5

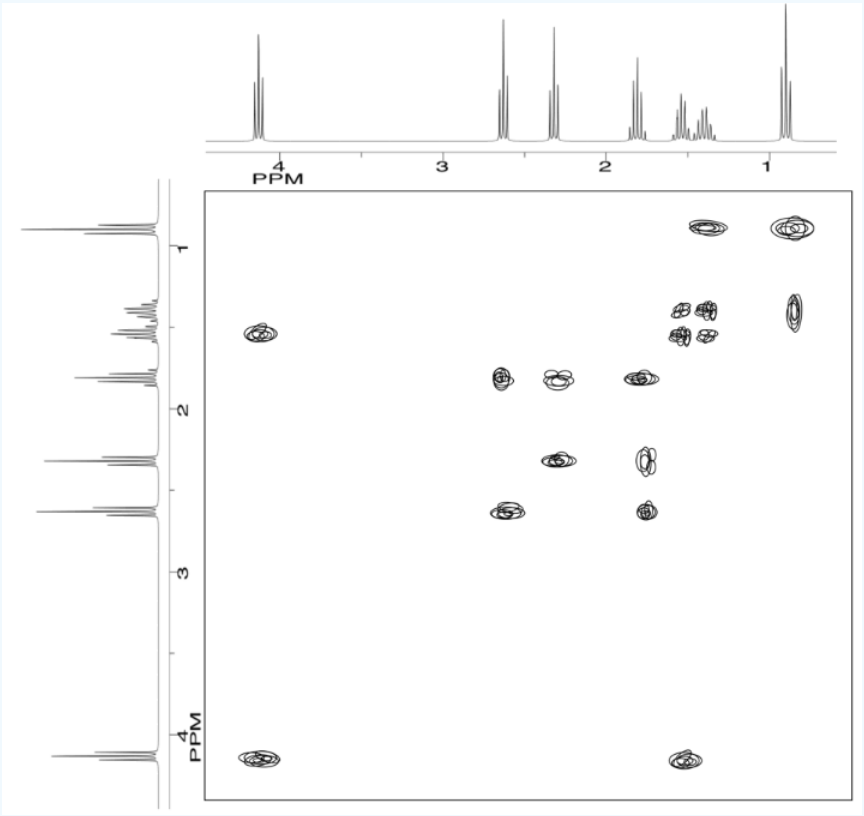
Analyse the data in the following spectra and propose a structure for the compound.

$C_{14}H_{20}O_2$

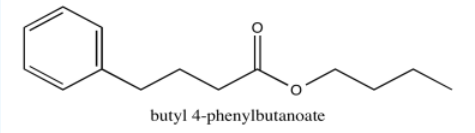








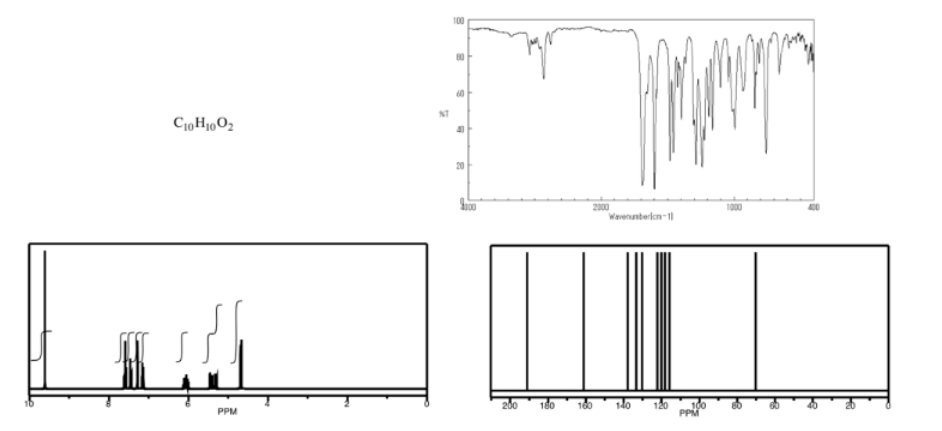
Answer

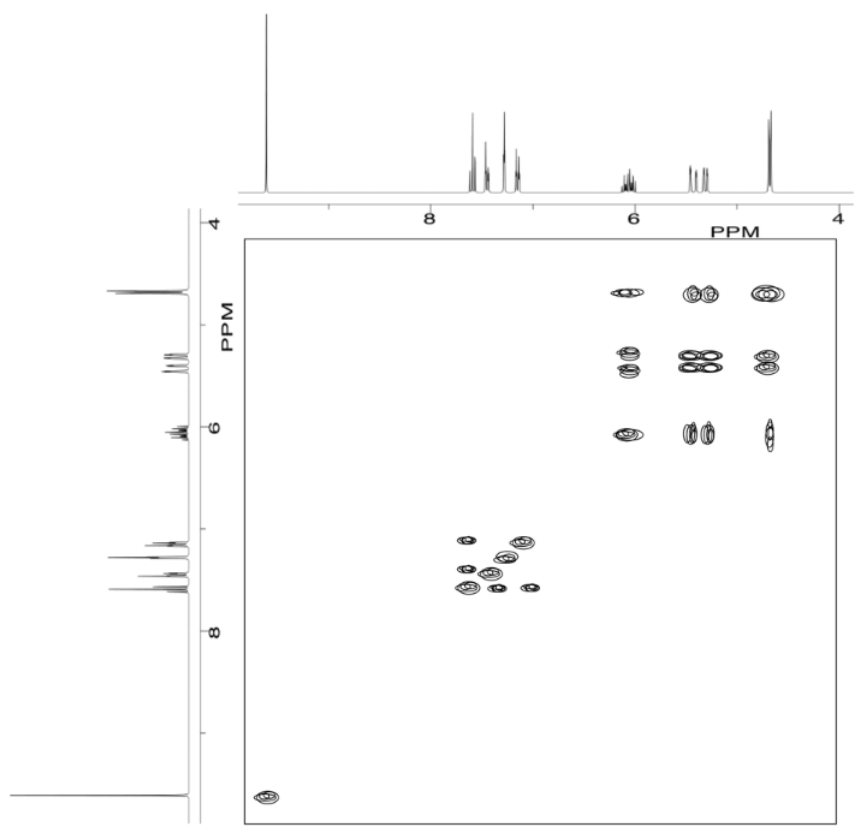


butyl 4-phenylbutanoate

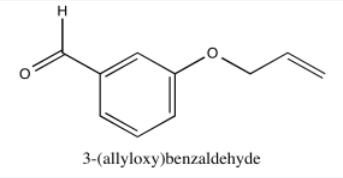
Exercise 5.1.6

Analyse the data in the following spectra and propose a structure for the compound.





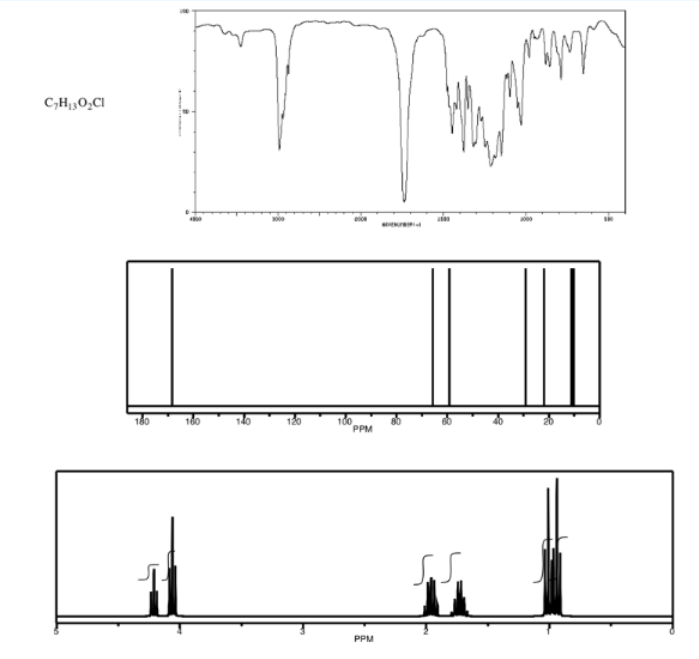
Answer

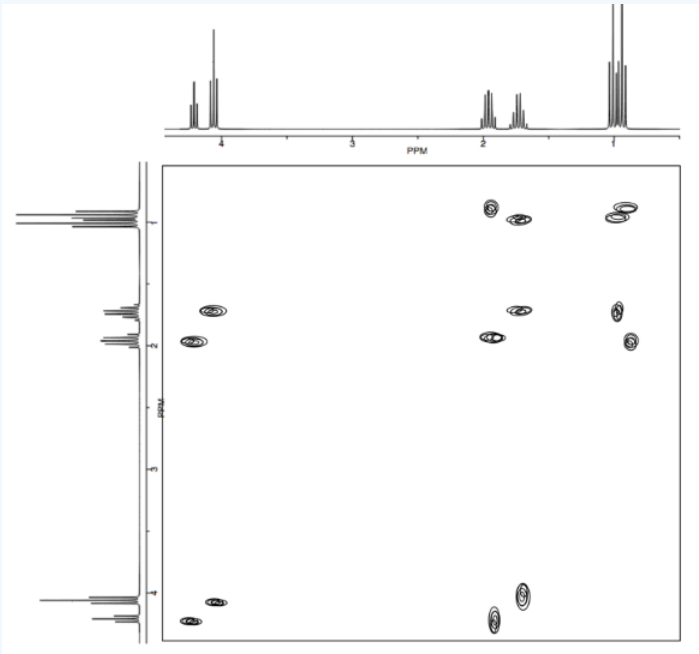


3-(allyloxy)benzaldehyde

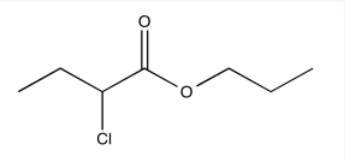
Exercise 5.1.7

Analyse the data in the following spectra and propose a structure for the compound.



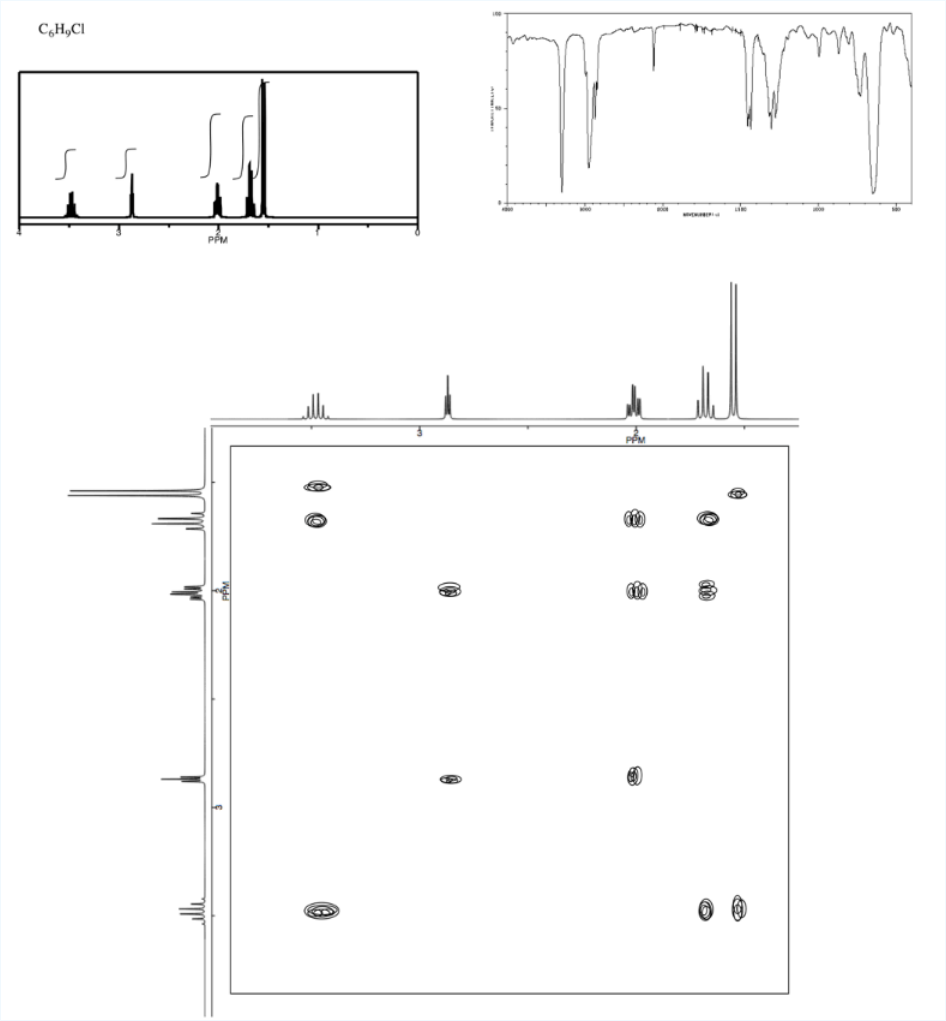


Answer

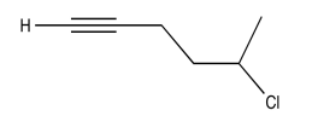


Exercise 5.1.8

Analyse the data in the following spectra and propose a structure for the compound.

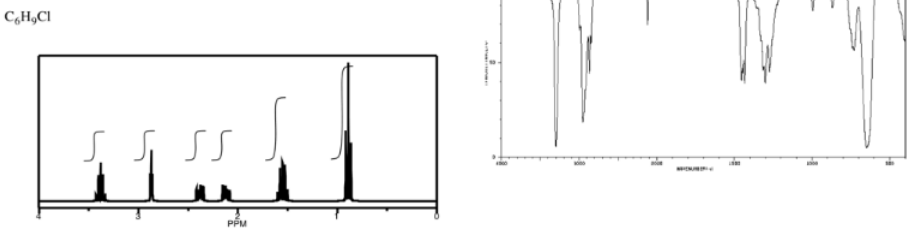


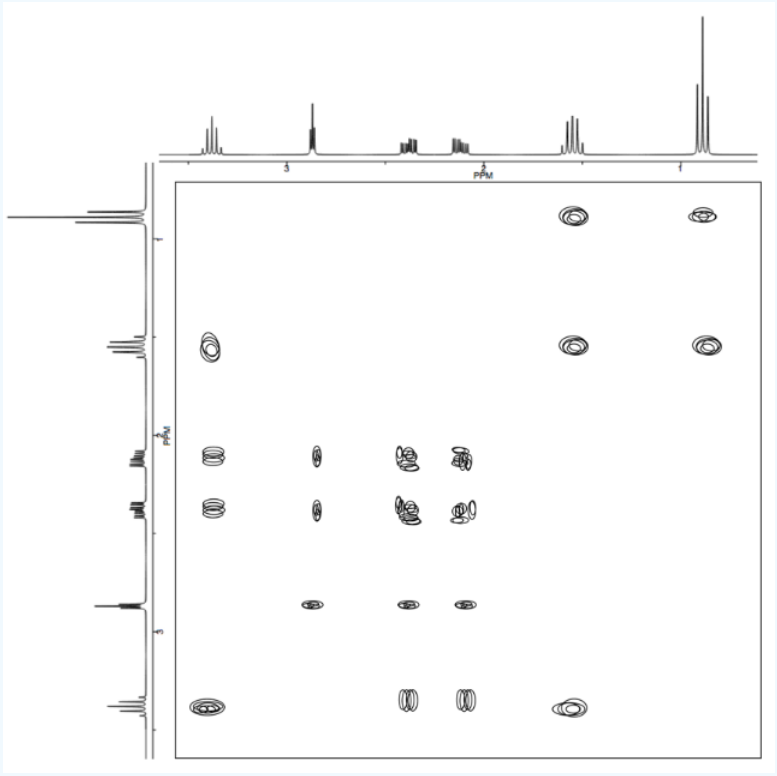
Answer



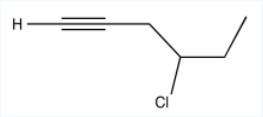
Exercise 5.1.9

Analyse the data in the following spectra and propose a structure for the compound.





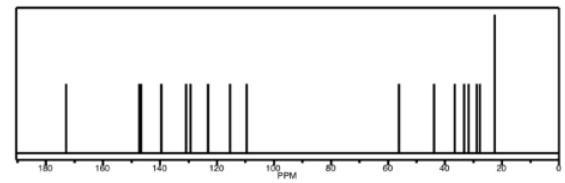
Answer

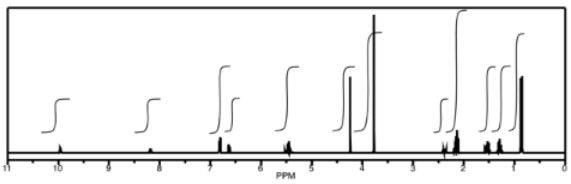


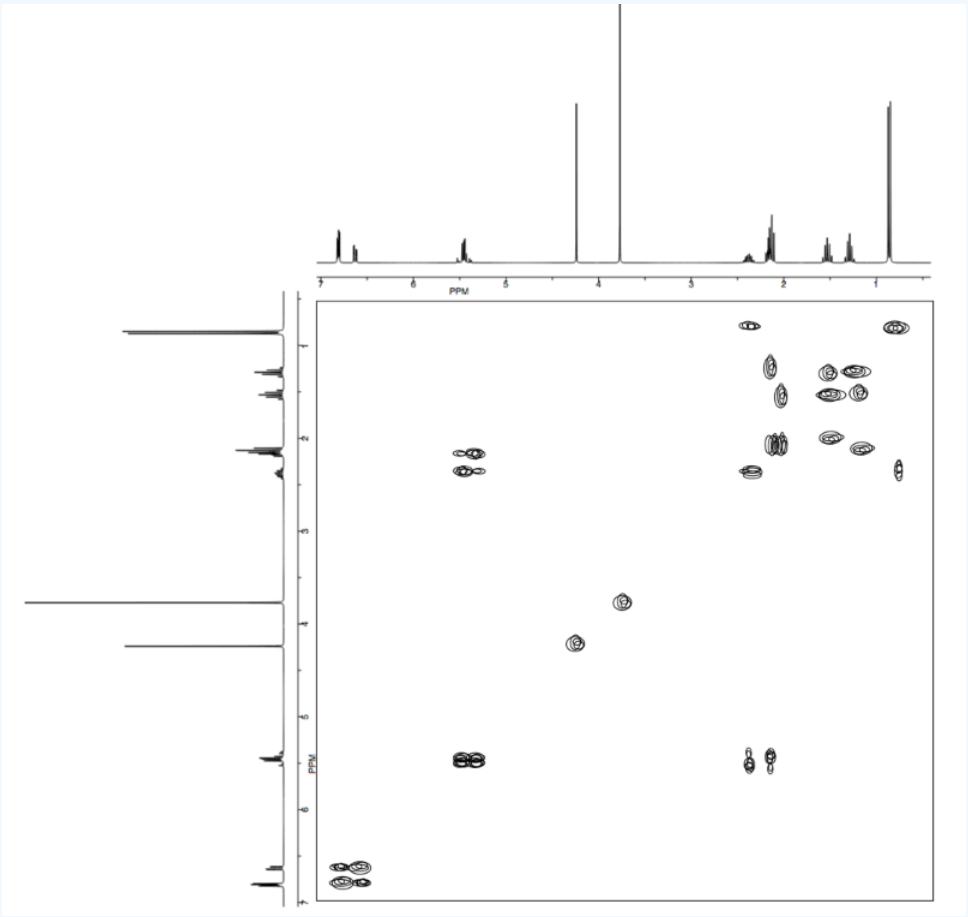
Exercise 5.1.10

Analyse the data in the following spectra and propose a structure for the compound.

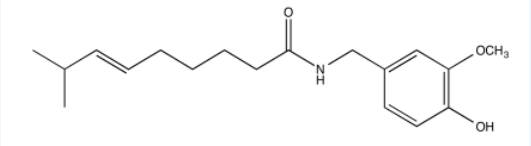
Capsaicin $C_{18}H_{27}NO_3$





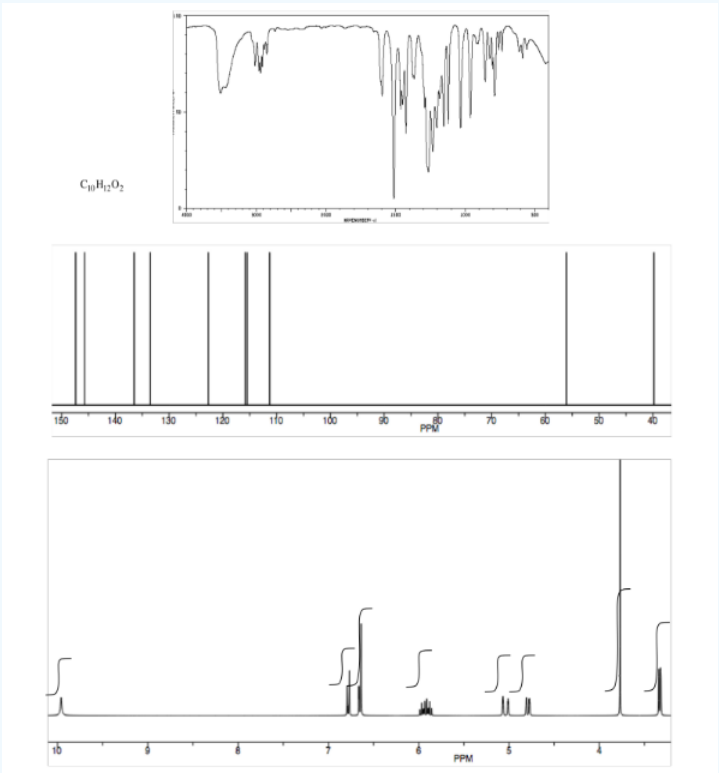


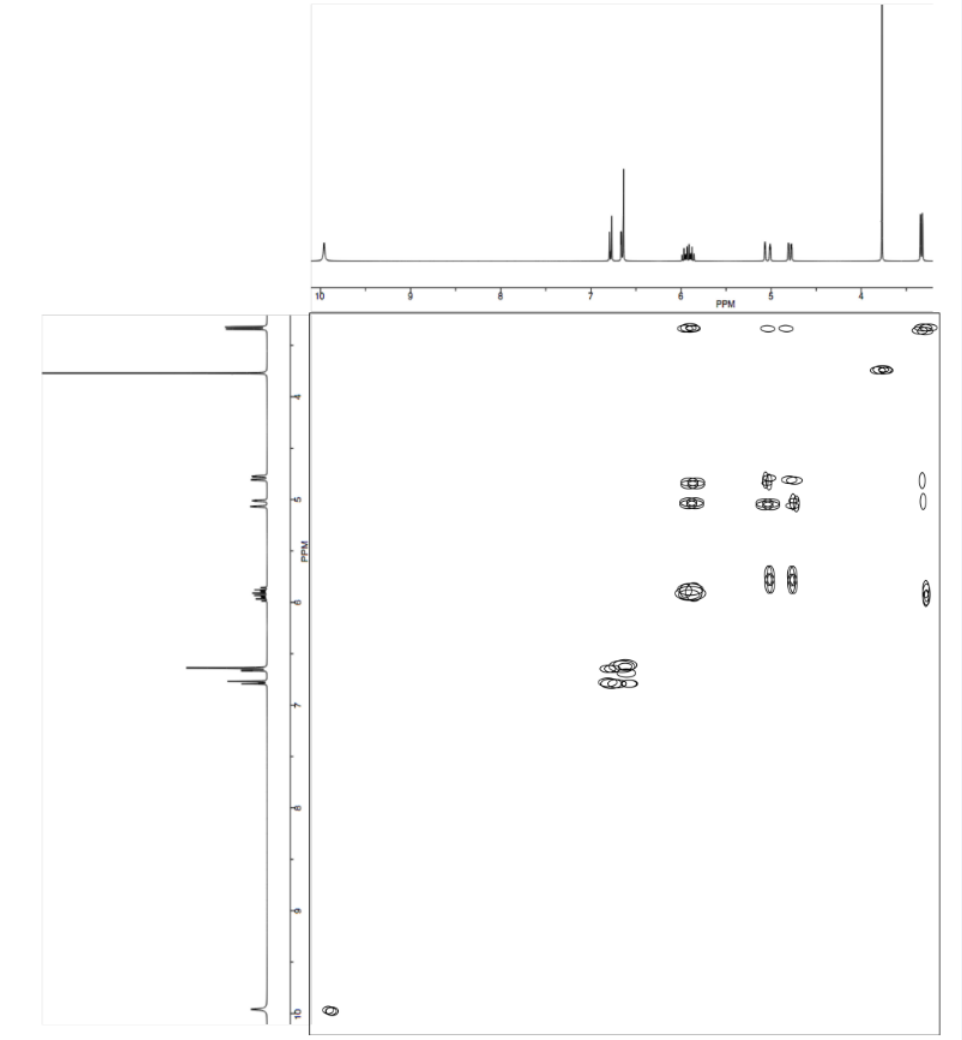
Answer



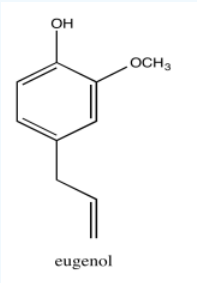
Exercise 5.1.11

Analyse the data in the following spectra and propose a structure for the compound.





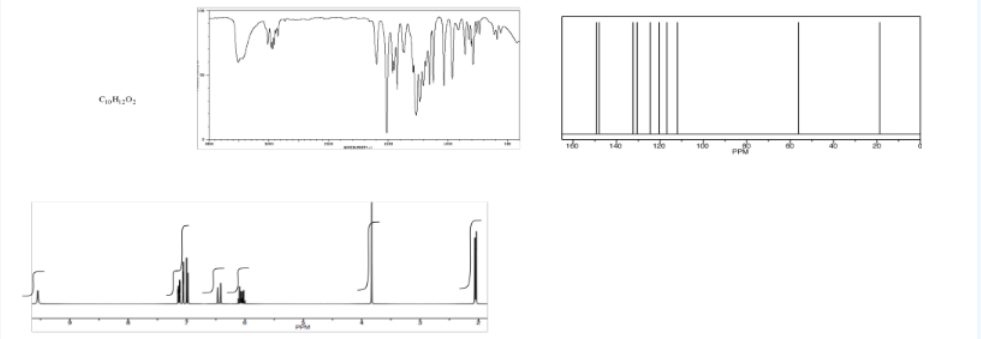
Answer

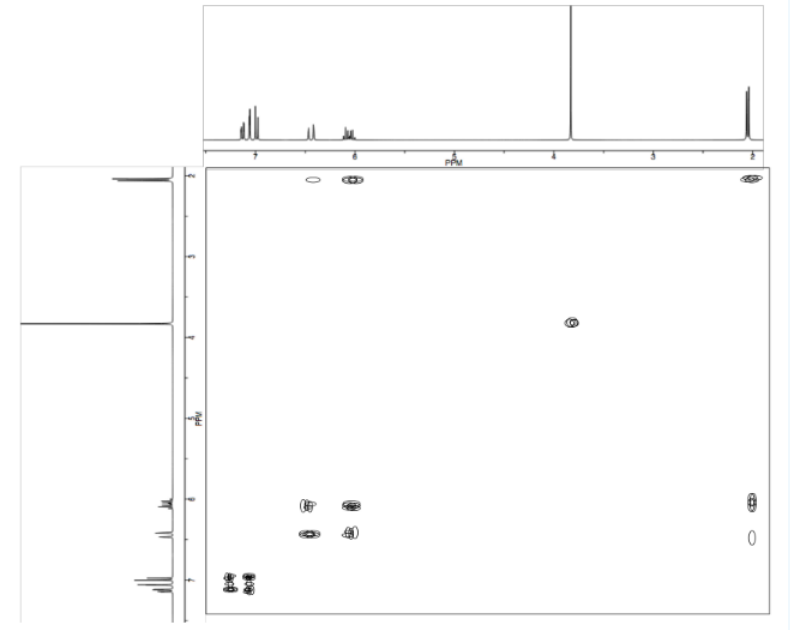


eugenol

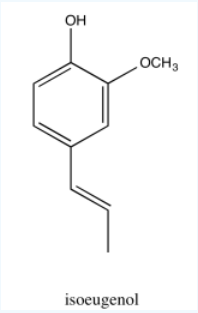
Exercise 5.1.12

Analyse the data in the following spectra and propose a structure for the compound.





Answer



isoeugenol

* Sources:

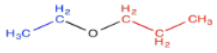
Selected IR and ^{13}C NMR spectra from SDBS (National Institute of Advanced Industrial Science and Technology, Japan, Spectral Database for Organic Compounds, http://sdbs.db.aist.go.jp/sdbs/cgi-bin/cre_index.cgi, accessed December, 2015).

^{1}H NMR and COSY spectra simulated.

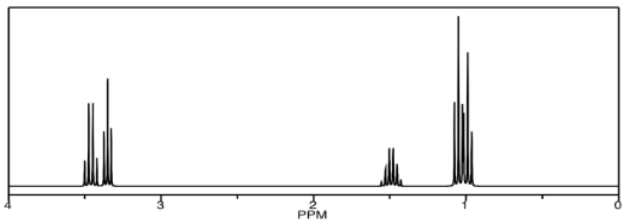
5.2: TOCSY Spectra

Total Correlation Spectroscopy, or **TOCSY**, is almost exactly the same as regular COSY. However, instead of just showing that two protons are coupled, it shows an entire spin system together. That means it shows this proton is connected to that proton, but that proton is connected to this other one, which is connected to that one over there. A TOCSY spectrum displays an entire chain of protons, each of which is coupled to the next.

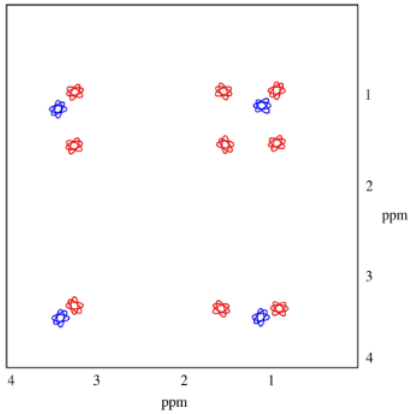
As an example, we'll look at ethoxypropane. It has a two-carbon chain and a three-carbon chain, but the two chains are separated from each other by an oxygen atom.



The ^{1}H NMR spectrum is shown below. It isn't all that complicated. However, if we wanted to know exactly which peak belonged to which hydrogen, we may have some trouble. In particular, how could we conclusively tell those two triplets apart near 1 ppm? An educated guess would put the methyl of the ethyl chain downfield, farther to the left. Can we confirm that suspicion?



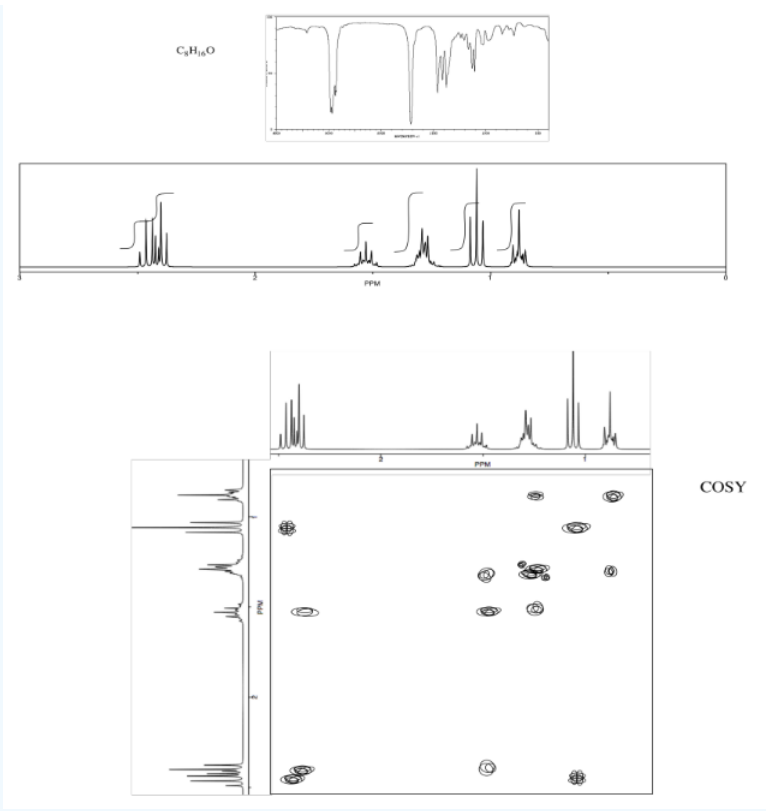
The TOCSY spectrum shows what we need to see in order to be sure. These spectra don't really show up color-coded, but red and blue have been added to make things more clear. The blue part is exactly what we would see in a COSY spectrum. The hydrogen at 1.1 is coupled to the one at 3.4. The red part is slightly different from the COSY; not only does it show the coupling between the hydrogen at 1.0 and the one at 1..5, but it also includes the hydrogen at 3.3, because that one is also coupled to the one at 1.5. The entire chain of coupled hydrogens is linked together.

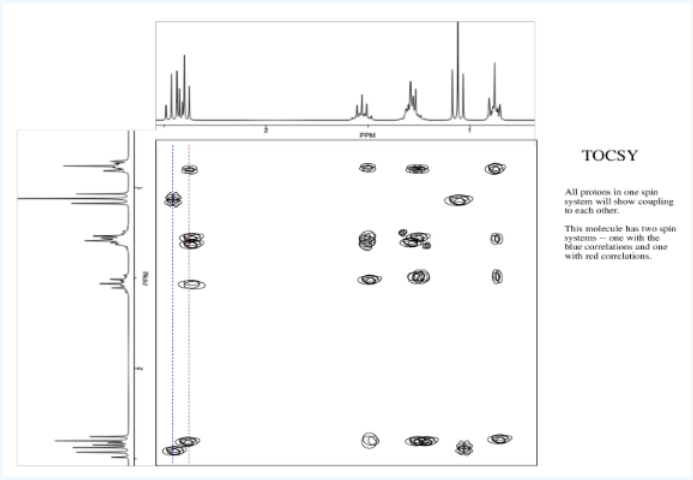


At a glance, the TOCSY spectrum tells us we have a two-carbon chain because we see two peaks in a row (or, really, a two by two array). It also tells us we have a chain of three peaks because we can see three peaks in a row (or a three by three array).

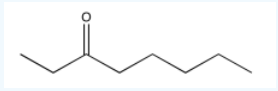
Exercise 5.2.1

Identify the compound.



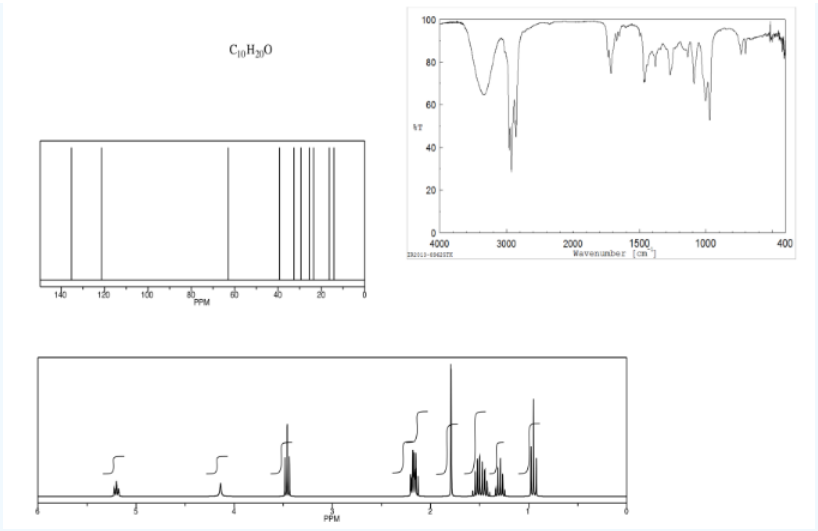


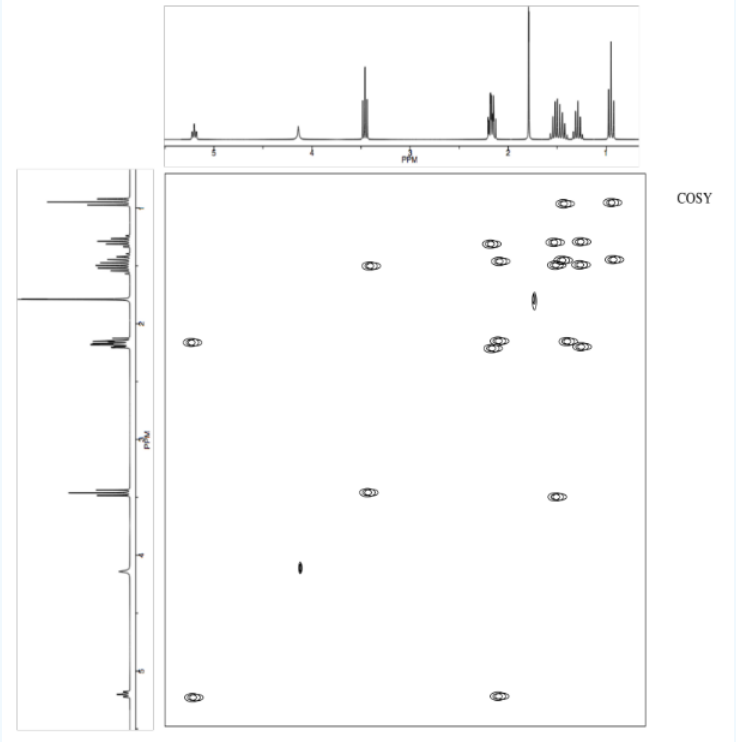
Answer

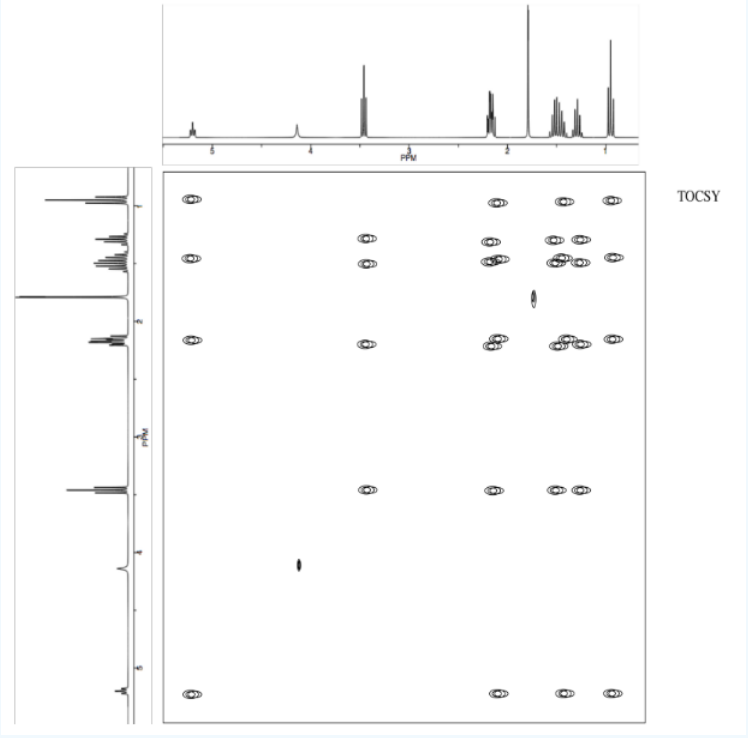


Exercise 5.2.2

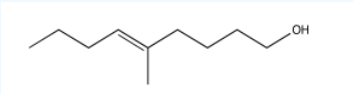
Identify the compound.





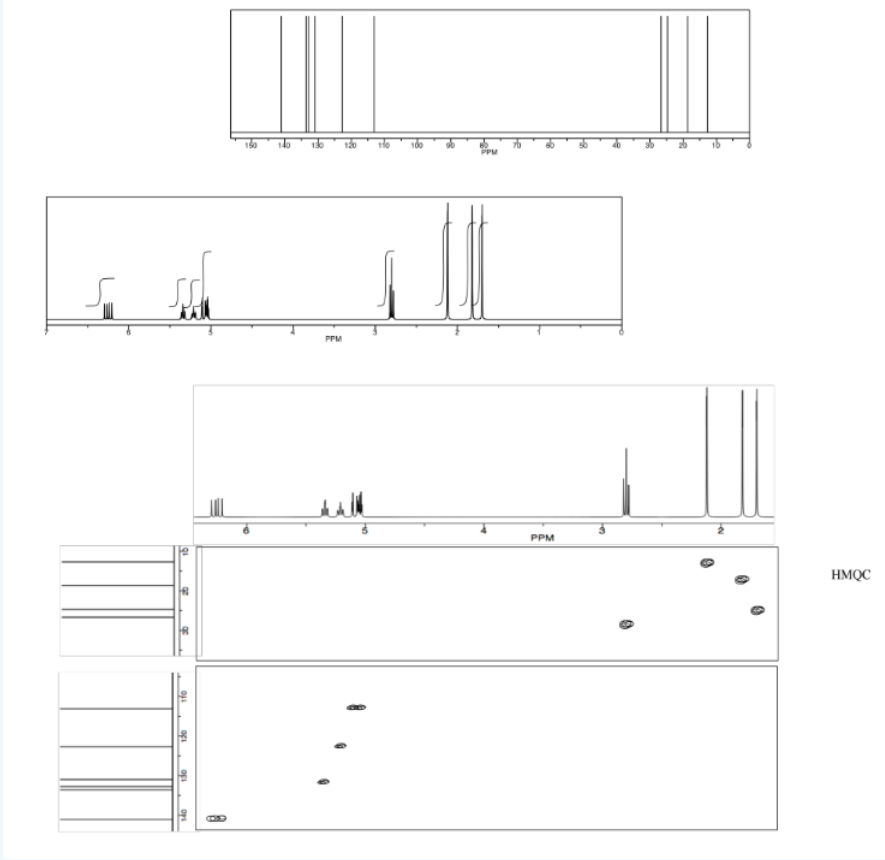


Answer

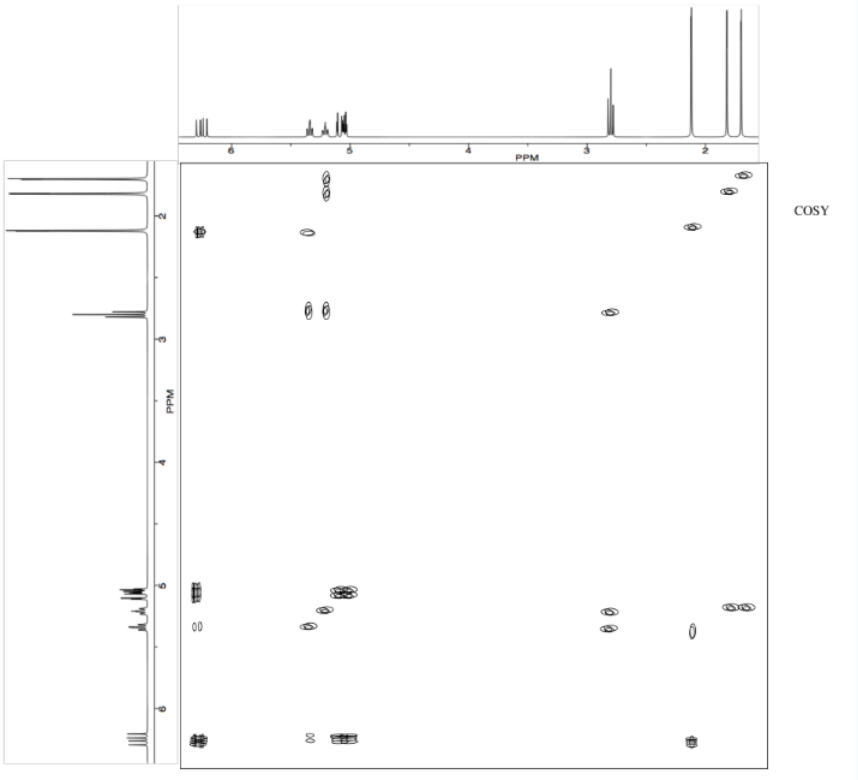


Exercise 5.2.3

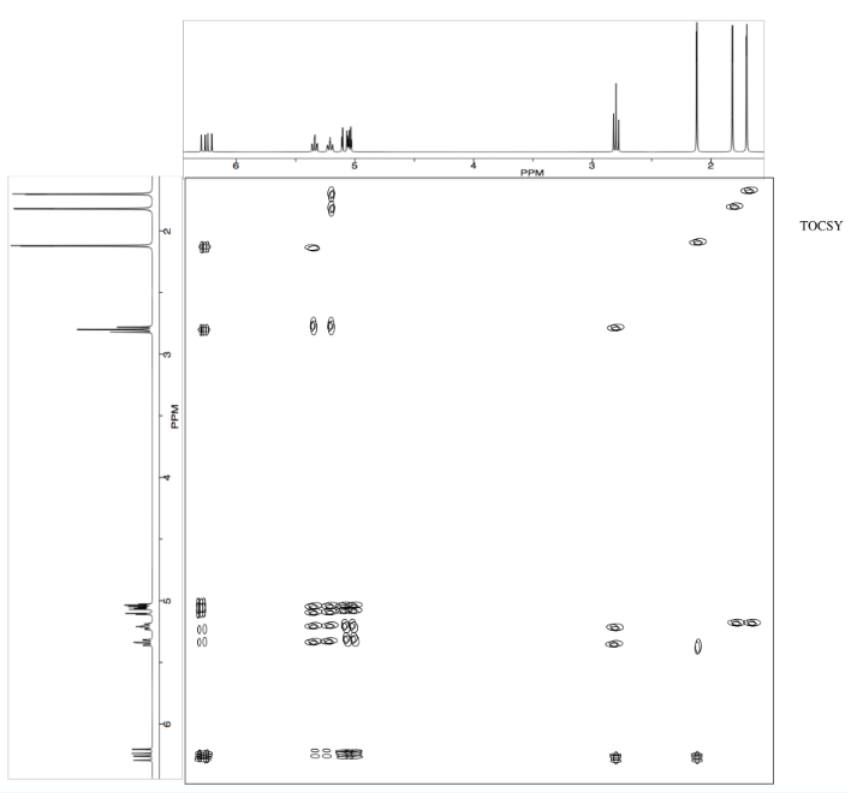
Identify this compound



HMQC

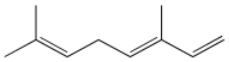


COSY



Answer

Ocimene



*Sources:

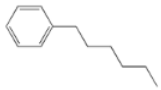
Selected IR spectra from SDBS (National Institute of Advanced Industrial Science and Technology, Japan, Spectral Database for Organic Compounds, http://sdbs.db.aist.go.jp/sdbs/cgi-bin/cre_index.cgi, accessed December, 2015).

^{1}H NMR, ^{13}C NMR, TOCSY and COSY spectra simulated.

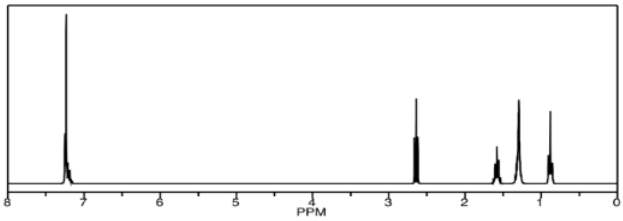
5.3: HMBC and HMQC Spectra

Just as COSY spectra show which protons are coupled to each other, HMBC (and the related HMQC) give information about the relative relationships between protons and carbons in a structure. In an HMQC spectrum, a ^{13}C spectrum is displayed on one axis and a ^{1}H spectrum is displayed on the other axis. Cross-peaks show which proton is attached to which carbon. COSY spectra show 3-bond coupling (from H-C-C-H), whereas HMQC shows a 1-bond coupling (just C-H).

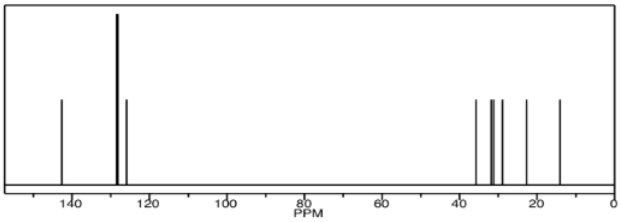
Take a look at n-hexylbenzene. There are lots of similar positions in this structure, so it may be hard to tell peaks apart in either the proton or carbon NMR spectrum.



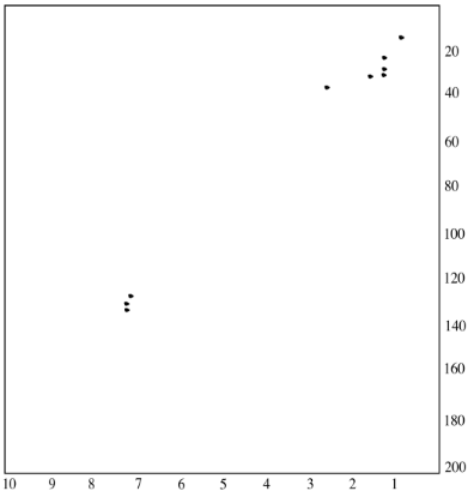
Indeed, the ^{1}H spectrum has some unique peaks but also a couple of large multiplets.



Similarly, there are a couple of carbons that show up at the same place in the ^{13}C NMR spectrum.



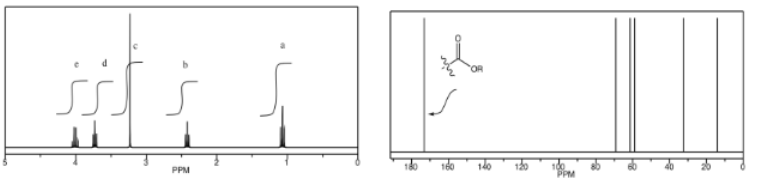
An HMQC experiment will help spread things out into two dimensions. Looking along the x axis, we can see that several peaks were clustered together near 7 ppm and near 1.3 ppm. Even looking along the y axis, we can see a couple of carbon peaks have separated out from each other around 33 ppm.

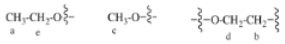


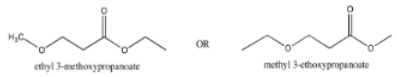
An HMBC spectrum looks very similar to an HMQC spectrum, except that it shows 2-bond, 3-bond or sometimes even 4-bond coupling (not H-C, but H-C-C or H-C-C-C or even H-C-C-C-C). Instead of seeing which carbon is directly attached to a hydrogen, we see which carbon is next to that one, so that we begin to see how the molecule connects.

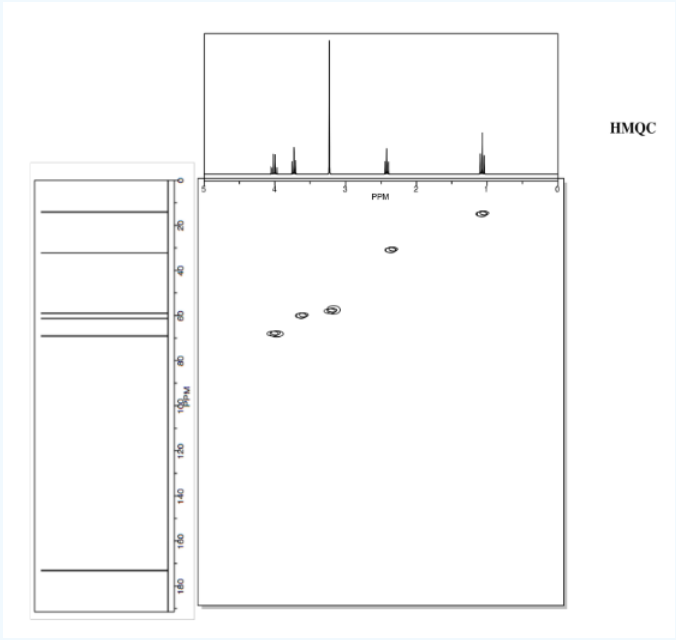
Exercise 5.3.1

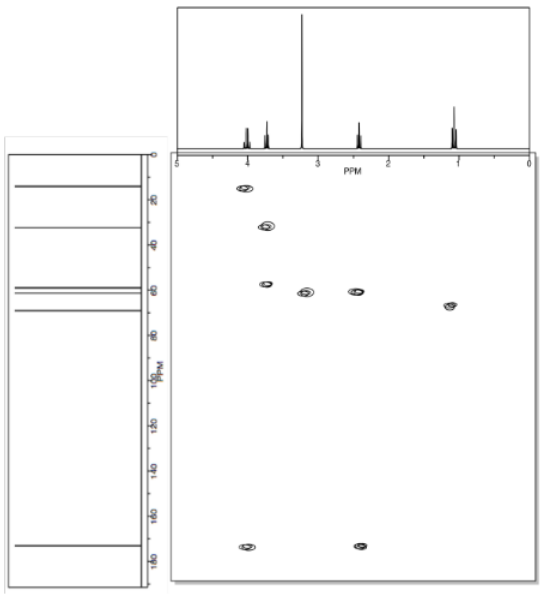
Analyse the data to determine which of the two isomers (below) we are dealing with.





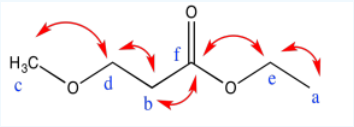






HMBC

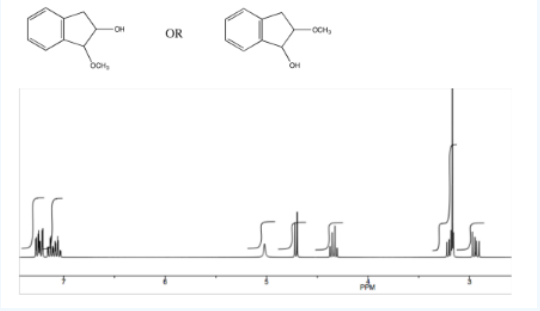
Answer

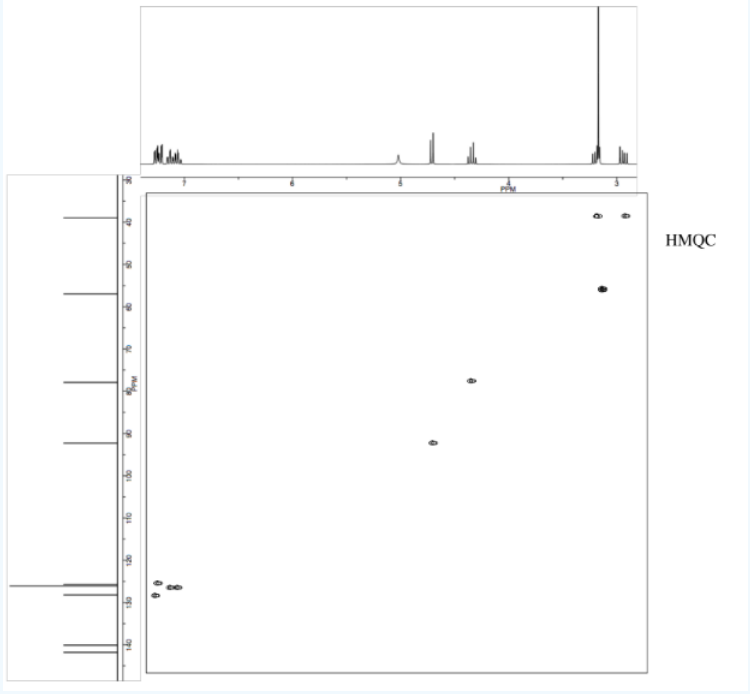


	^{1}H	^{13}C	HMBC
a	1.1	15	e
b	2.4	32	d, f
c	3.2	58	d
d	3.7	63	b, c
e	4.0	69	a, f
f	-	172	b, e

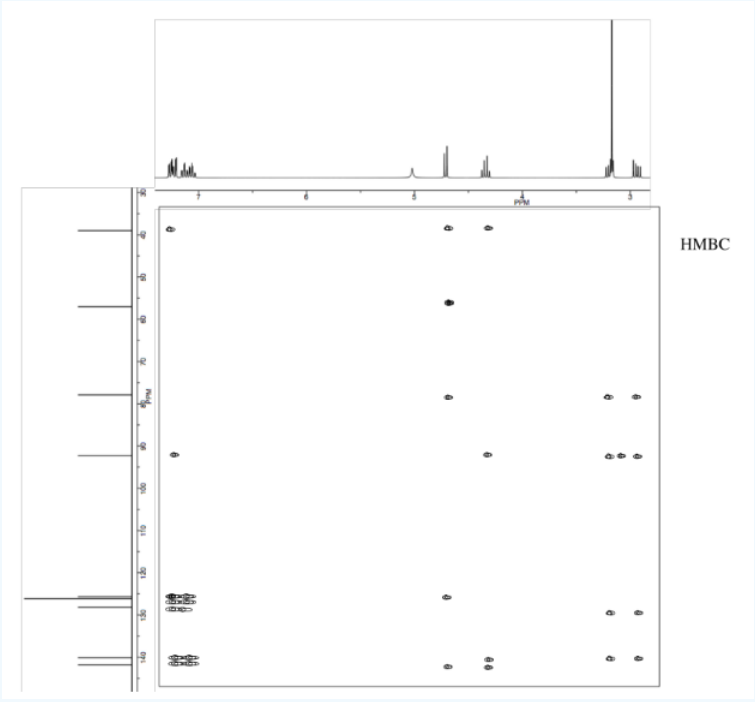
Exercise 5.3.2

Analyze the data to determine which of the two isomers (below) we are dealing with.



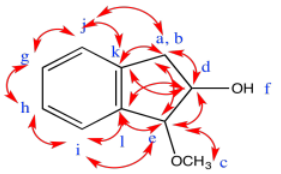


HMQC



HMBC

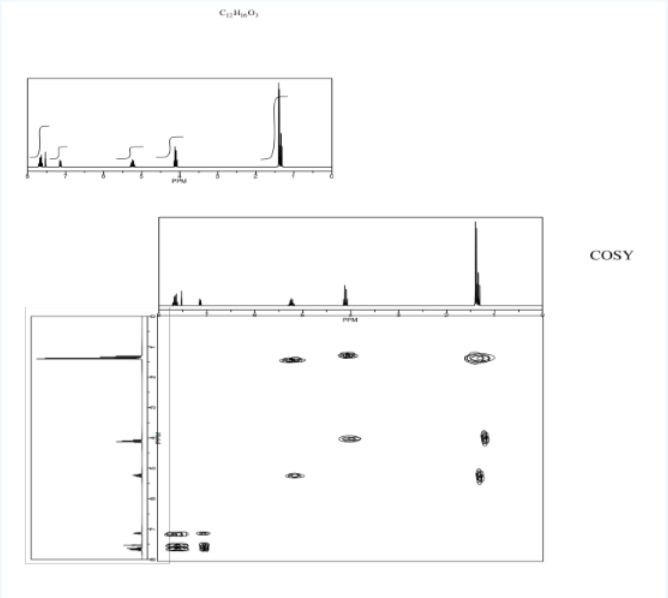
Answer



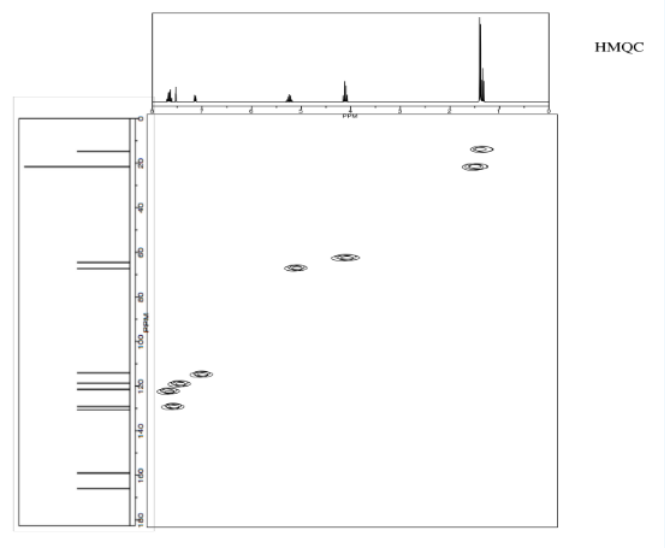
	^{1}H	^{13}C	HMBC
a	2.8	38	d, e, j, k
b	3.2		
c	3.2	57	e
d	4.4	78	a/b, e, k, l
e	4.7	92	a/b, c, d, i, l
f	5.0	-	-
g	7.1	127	h, i, j, k, l
h	7.2	127	g, i, j, k, l
i	7.3	126	e, g, h, j, k, l
j	7.4	129	a/b, g, h, i, k, l
k	-	140	a/b, d, g, h, i, j, l
l	-	142	d, e, g, h, i, j, k

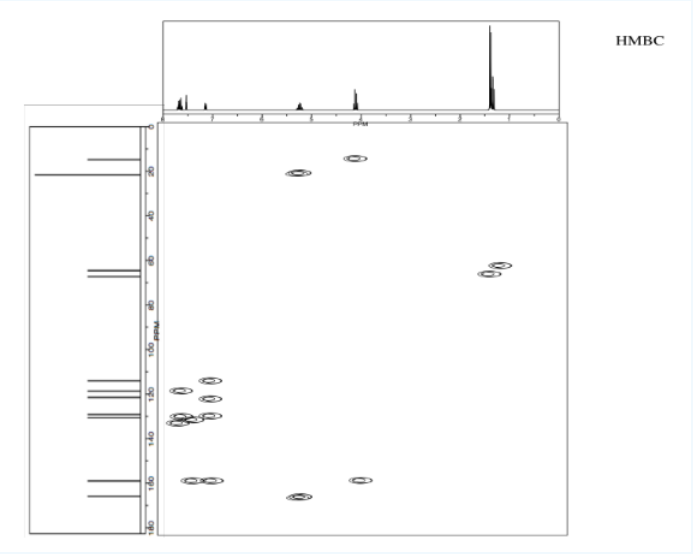
Exercise 5.3.3

Analyse the data to determine the structure of the compound.

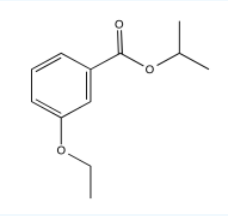


COSY

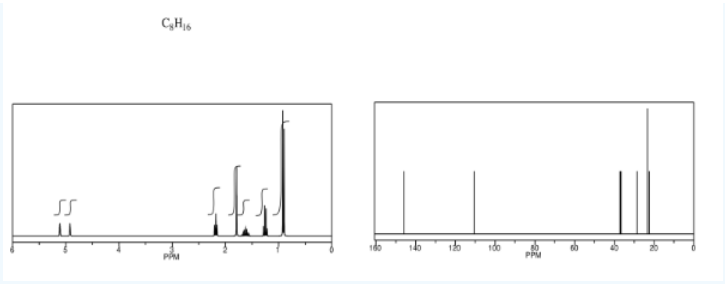


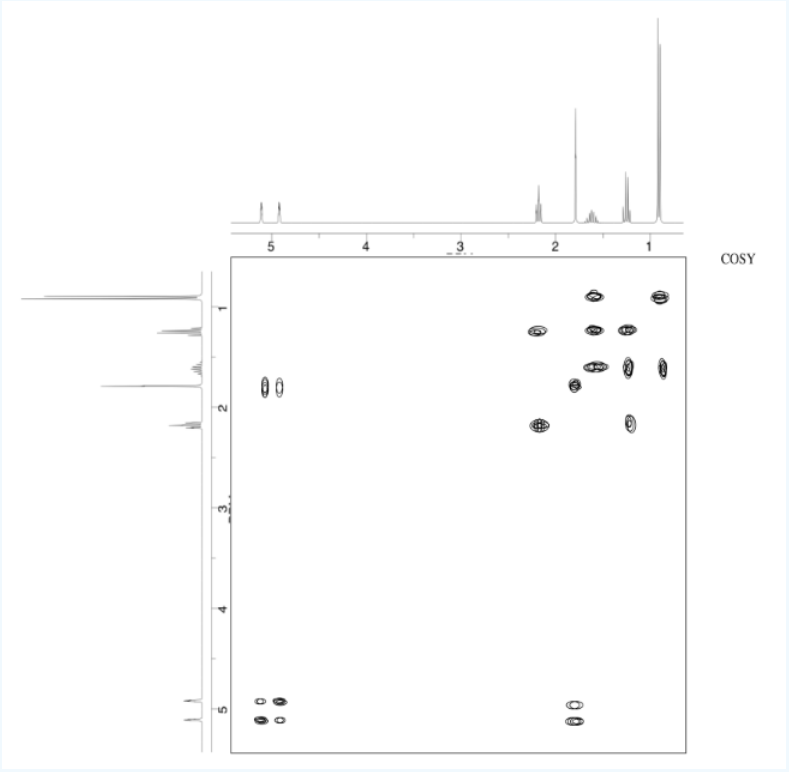


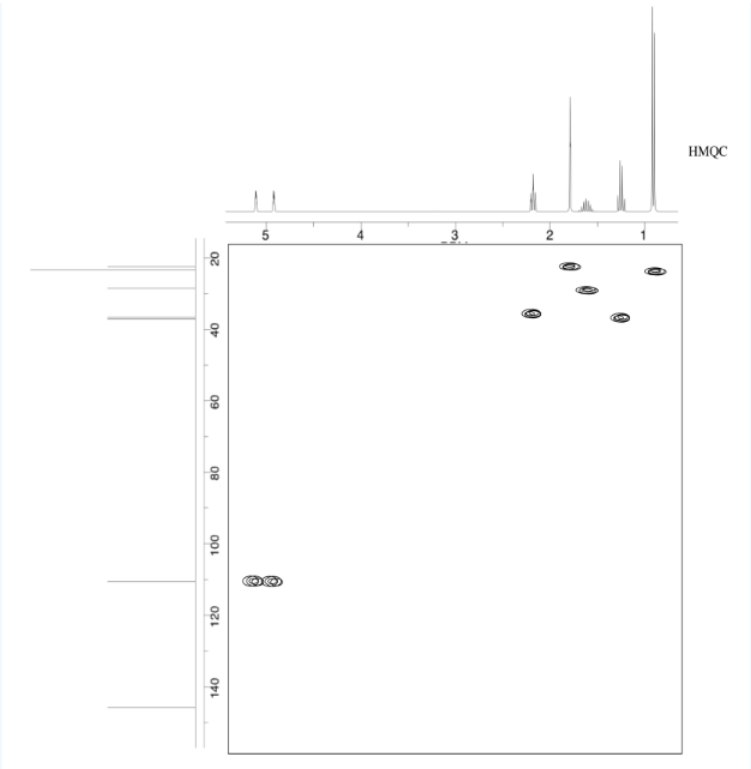
Answer

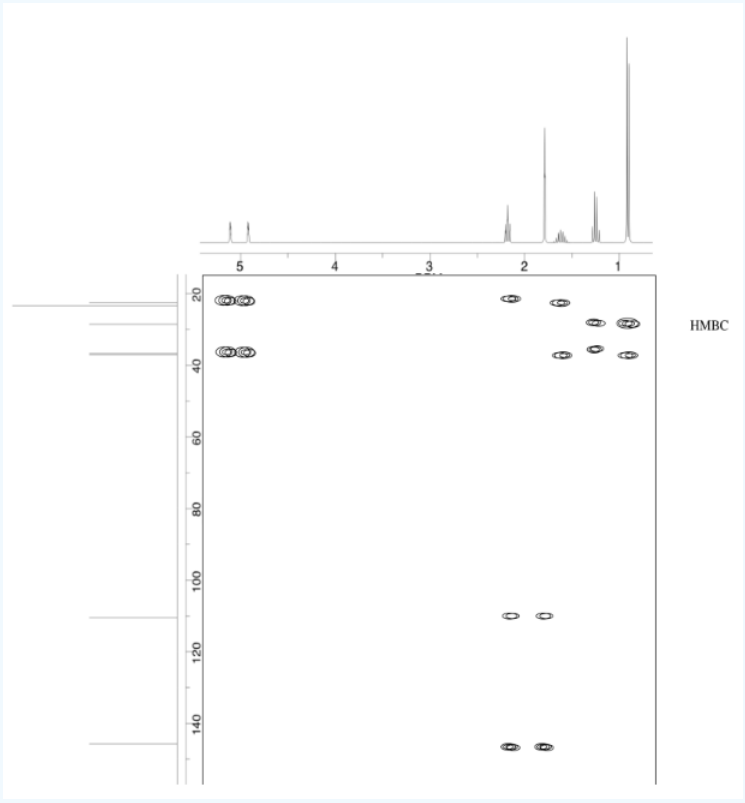


Exercise 5.3.4

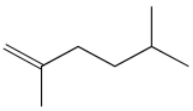

C_8H_{16}
PPM
PPM


5
4
3
2
1
COSY



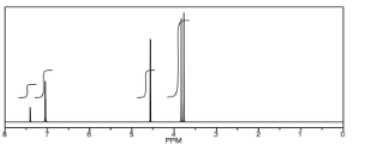


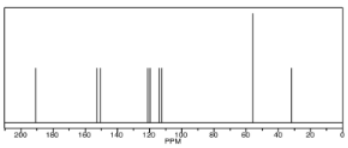
Answer

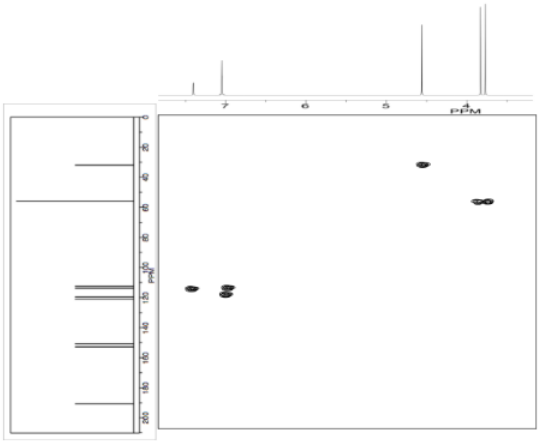


2,5-dimethylhex-1-ene

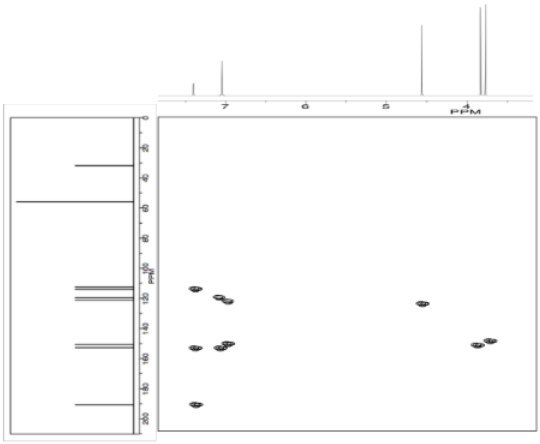
Exercise 5.3.5





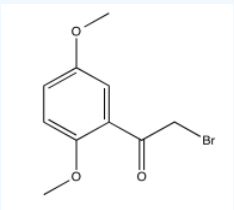


HMQC

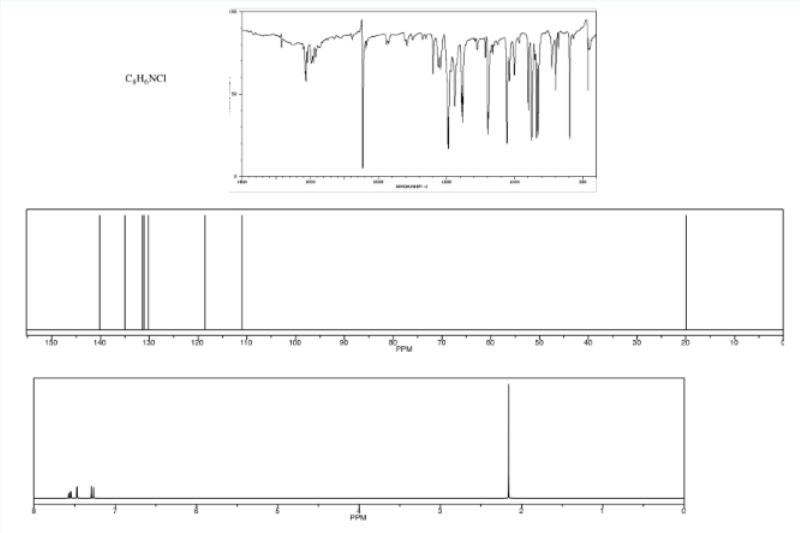


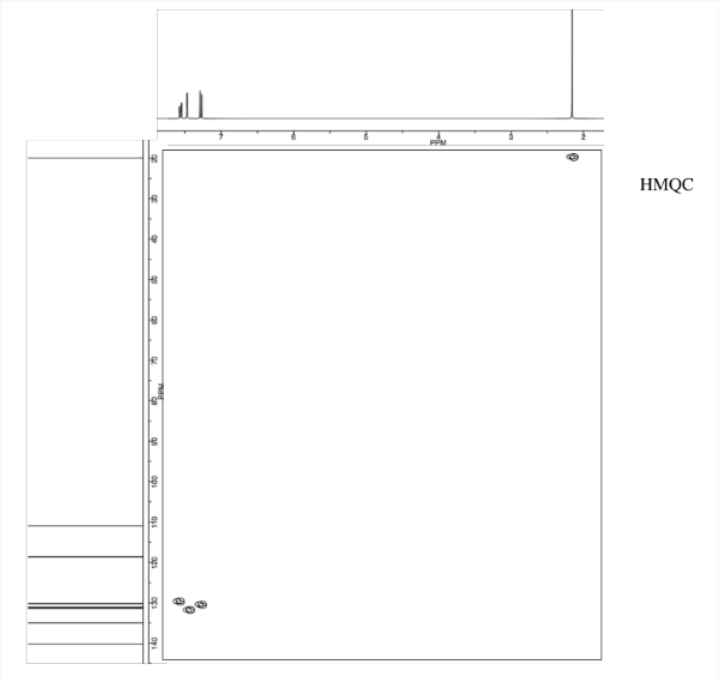
HMBC

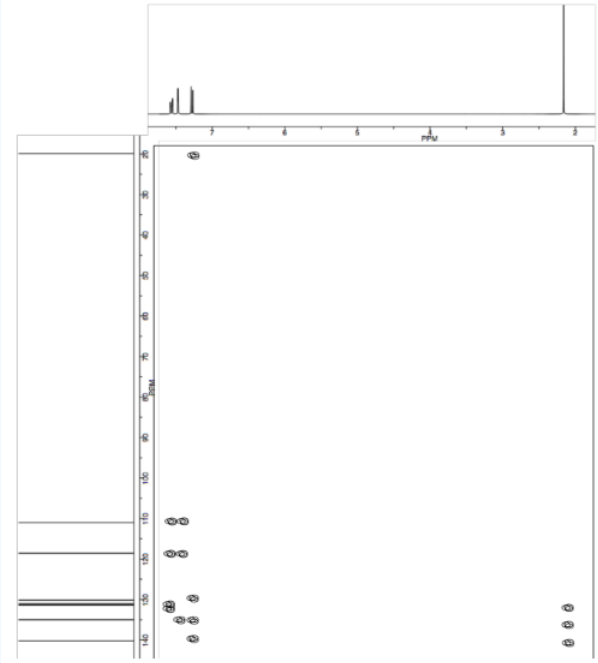
Answer



Exercise 5.3.6

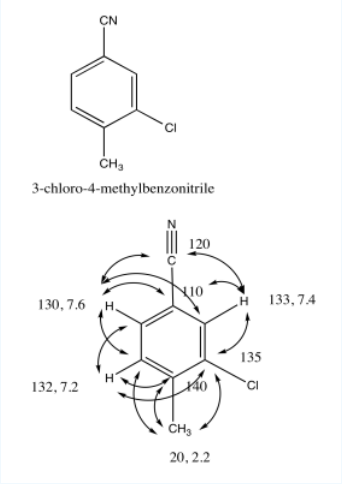




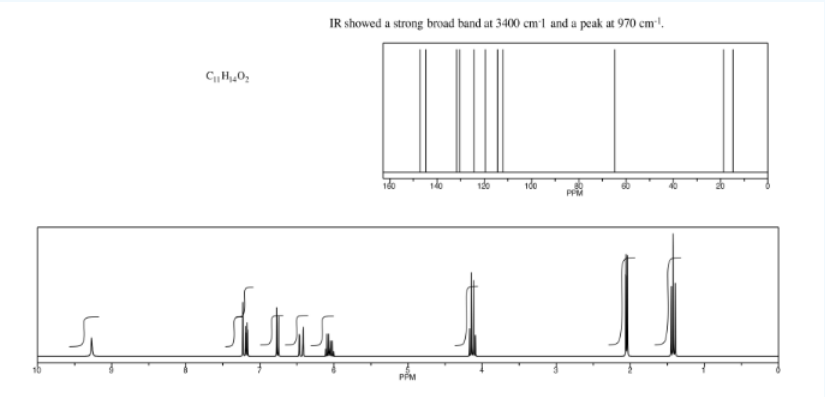


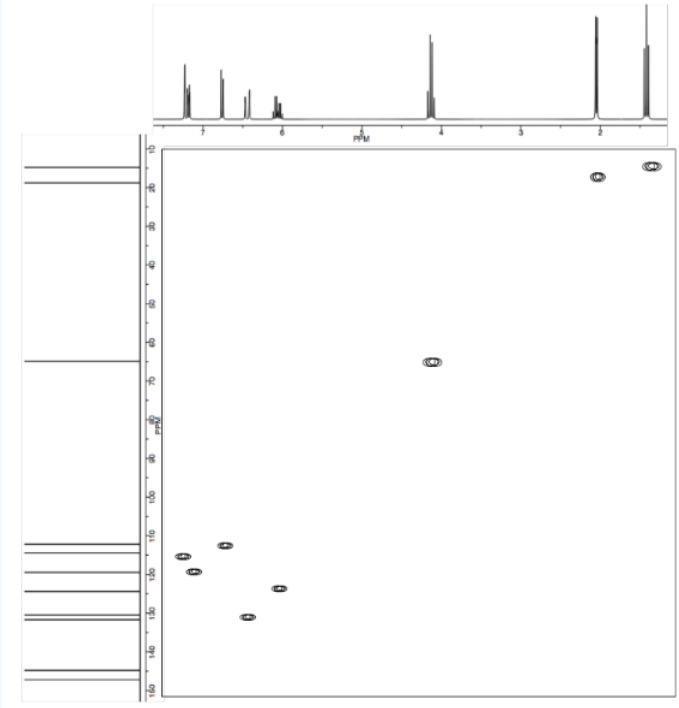
HMBC

Answer

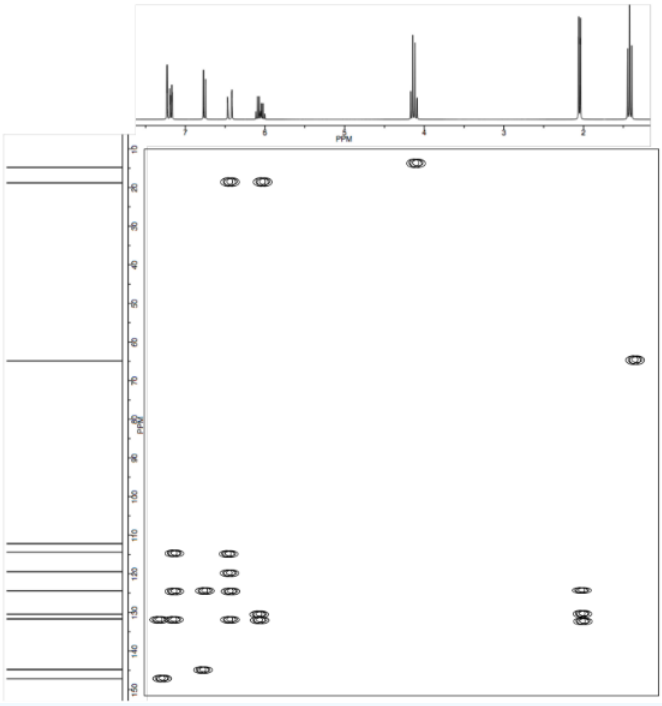


Exercise 5.3.7



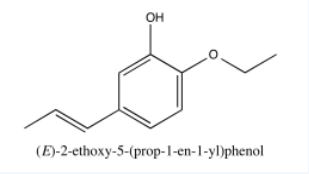


HMQC



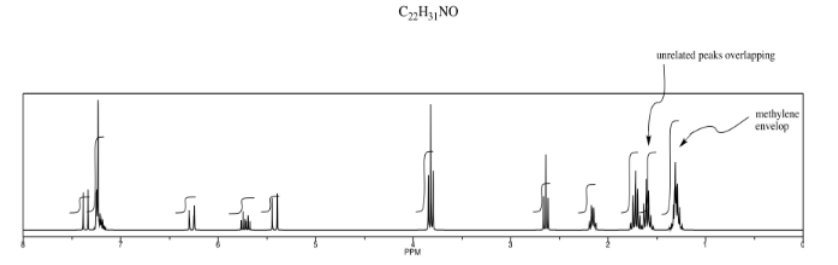
HMBC

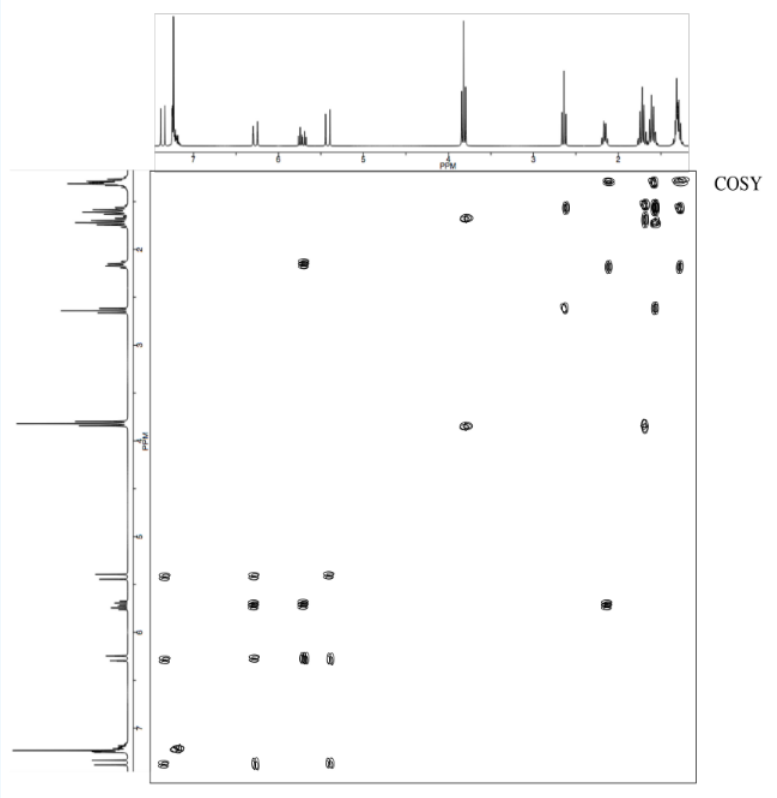
Answer

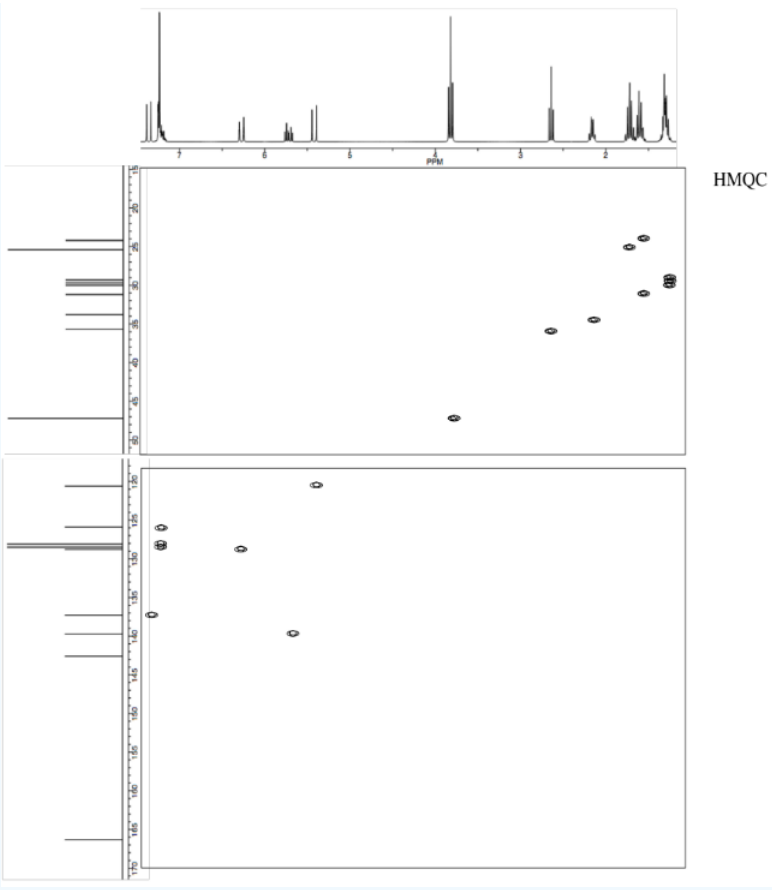


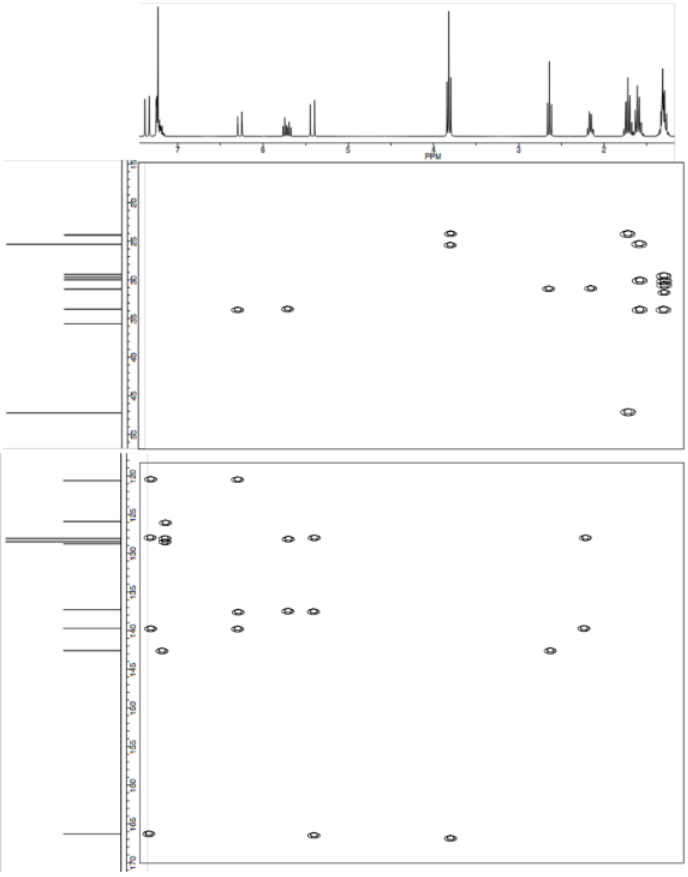
(*E*)-2-ethoxy-5-(prop-1-en-1-yl)phenol

Exercise 5.3.8

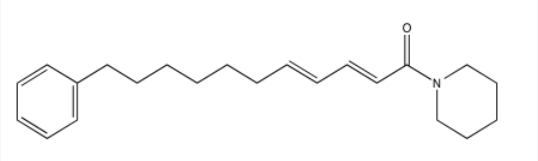








Answer



*Sources:

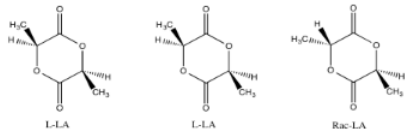
Selected IR spectra from SDBS (National Institute of Advanced Industrial Science and Technology, Japan, Spectral Database for Organic Compounds, http://sdbs.db.aist.go.jp/sdbs/cgi-bin/cre_index.cgi, accessed December, 2015).

^{1}H NMR, ^{13}C NMR, HMBC and HMQC spectra simulated.

5.4: NOESY Spectra

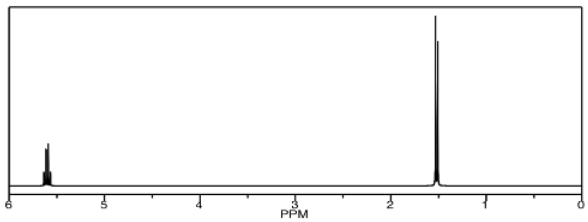
Nuclear Overhauser Effect Spectroscopy, or **NOESY**, shows through-space interactions within the molecule, rather than the through-bond interactions seen in the other methods. This method is especially useful for determining stereochemical relationships in a molecule. In two stereoisomers, the atoms are all connected in exactly the same order, through exactly the same bonds. A COSY or an HMBC spectrum wouldn't be able to distinguish between these isomers.

However, in a relatively rigid conformer, one hydrogen in one stereoisomer may be locked on the same side of the molecule as another group. If information could be transmitted from that group to that proton, we would know that they were near each other in space, and we would know which stereoisomer we have. For example, there are three different stereoisomers of lactide. Lactide is a product of the fermentation of corn and soybeans; it can be polymerized to make a sort of brittle plastic, PLA. PLA is used for food packaging because it can be composted in industrial and municipal waste management sites.

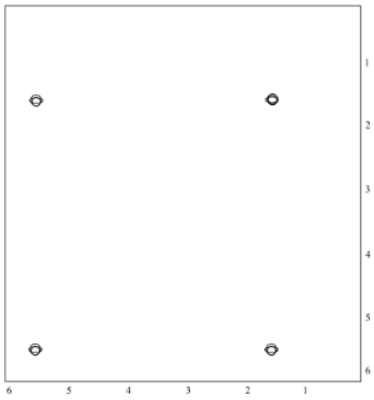


How would we know which isomer we were dealing with? Telling L-LA and D-LA apart may be difficult. They are enantiomers of each other and so they have the same physical properties. However, provided someone else has already figured out which is which, we could use optical rotation and compare the value we measure to the reported one.

On the other hand, we could easily tell the rac-LA from either the D-LA or the L-LA, because it would be the diastereomer of either of them. It would have different physical properties, including different NMR spectra. We could carefully compare the spectrum below to reported spectra for rac-LA and L-LA (or D-LA) to see which isomer we have.



On the other hand, we could just take a NOESY spectrum. In rac-LA, the methyl on one end of the molecule is on the same face of the ring as the hydrogen on the on the other end. We may be able to see that through-space relationship. We wouldn't see it in L-LA or D-LA, though.

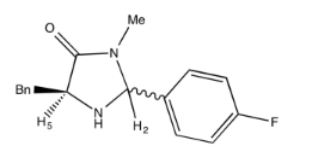


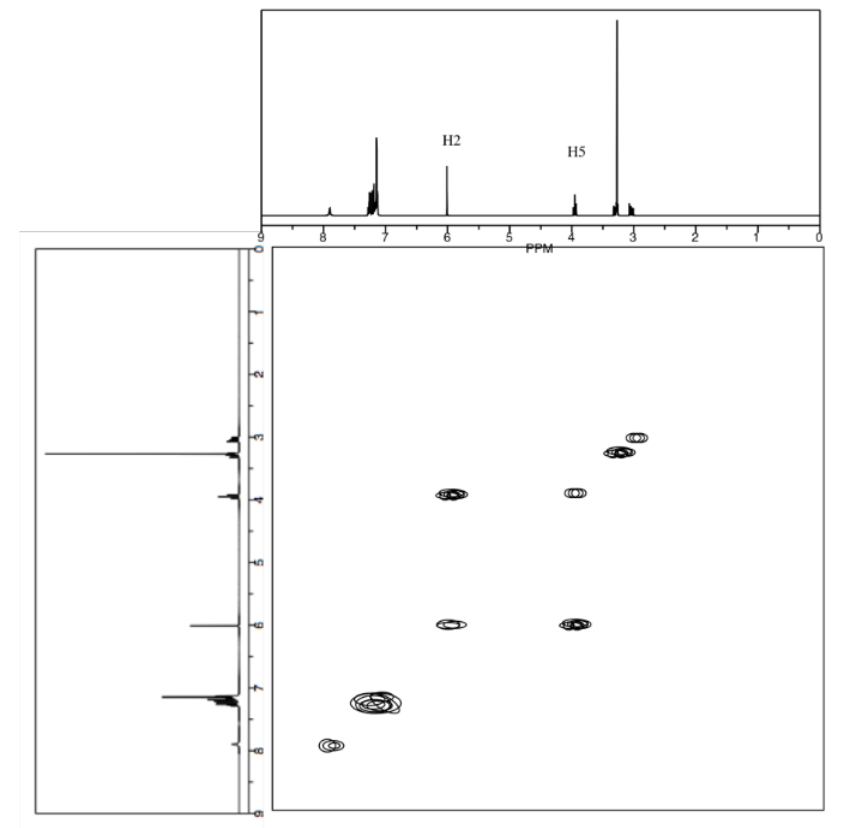
Just like in a COSY spectrum, all of the peaks that show up along the diagonal of a NOESY spectrum are simple the ones we would see in a regular ^{1}H spectrum. The peaks that show up off the diagonal tell us about through-space relationships. In this case, the relationship between the methyl hydrogen and the alpha hydrogen suggest we have a sample of rac-LA.

ROESY is a similar method that works better in some cases.

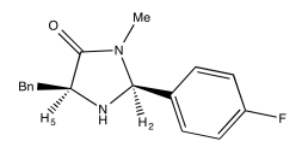
Exercise 5.4.1

Draw the relative stereochemistry of this compound based on the NOESY spectrum.



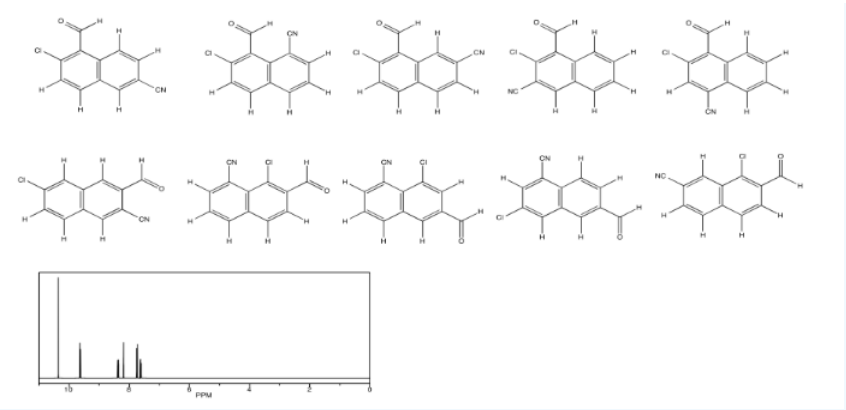


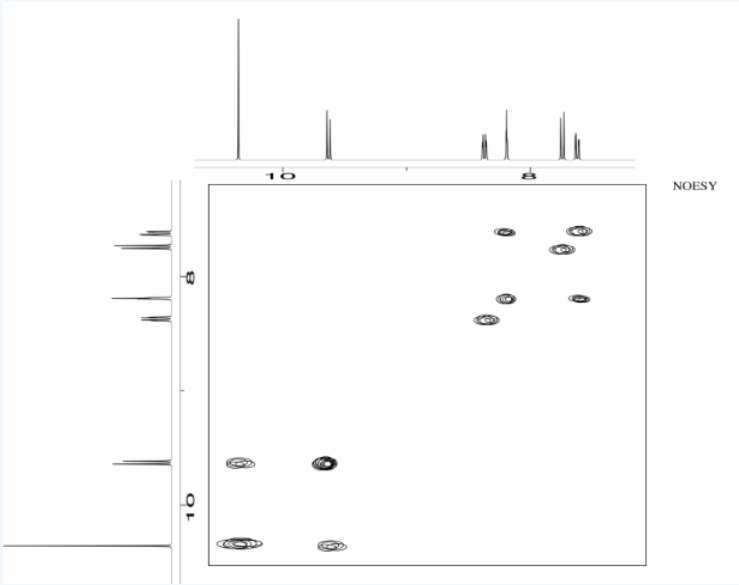
Answer



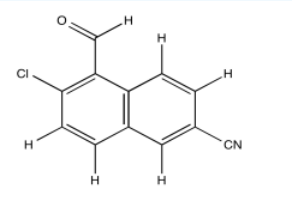
Exercise 5.4.2

Use NOESY to determine which isomer below is present.



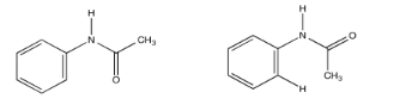


Answer

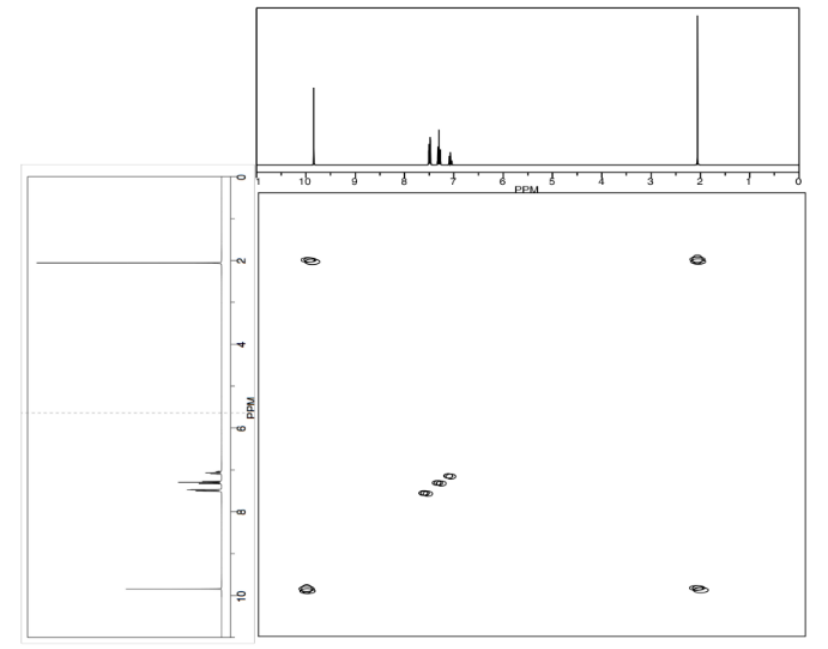


Exercise 5.4.3

Acetanilide has two different conformers. They do not easily interconvert.

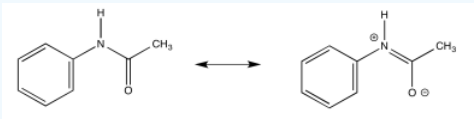


a. Explain (using pictures) why there isn't free rotation around the amide bond.
b. Use double headed arrows to predict nOe correlations.
c. Use the NOESY spectrum to determine which conformer is observed at room temperature.

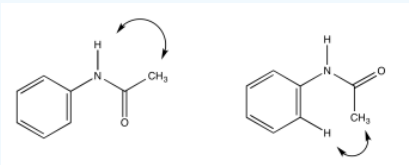


Answer

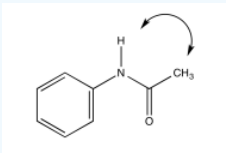
Answer a



Answer b

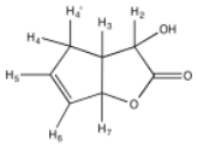


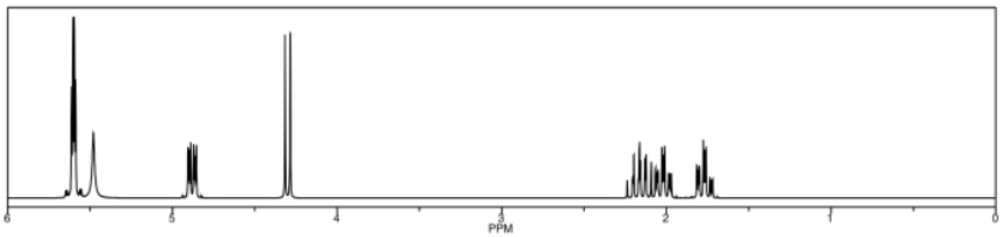
Answer c



Exercise 5.4.4

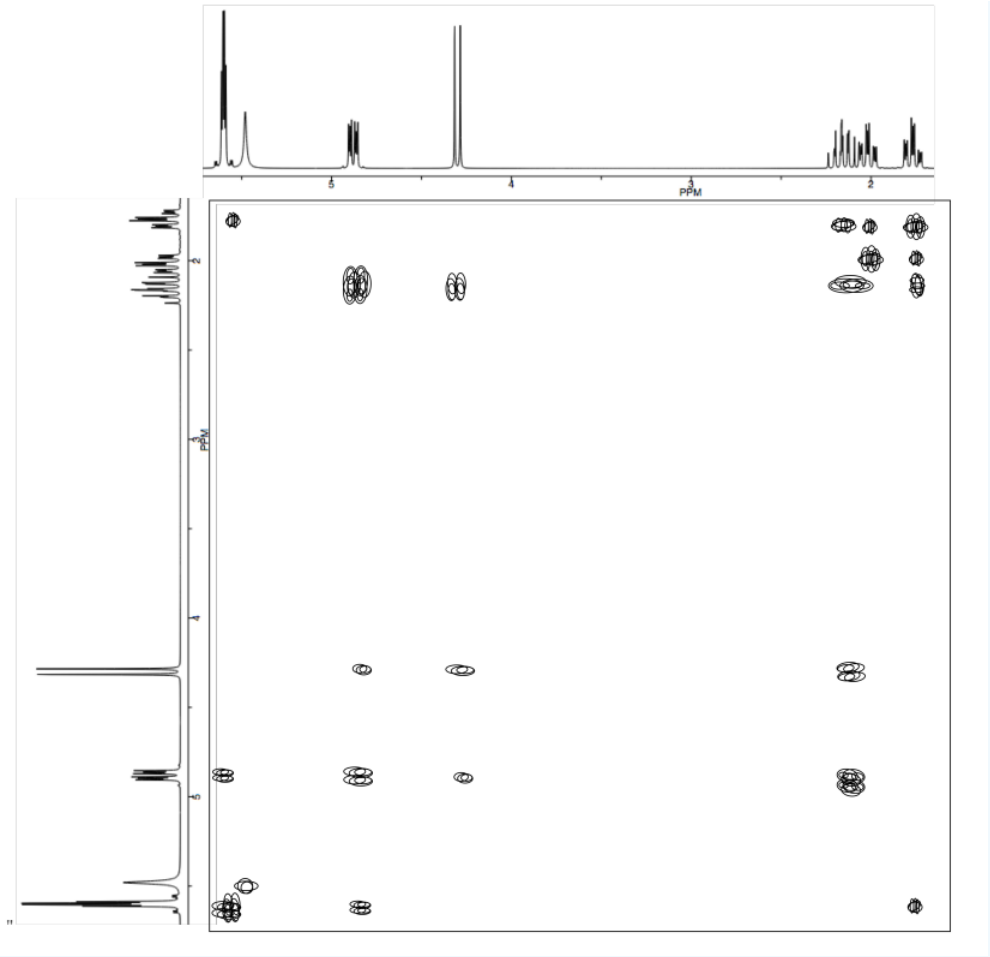
a) Complete the table of ^{1}H assignments for the following compound:



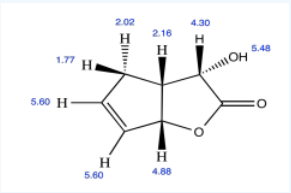


Proton	δ ppm
OH	5.48
H2	
H3	
H4	
H4'	2.02
H5	
H6	
H7	

b) Use the NOESY to assign the relative configuration.

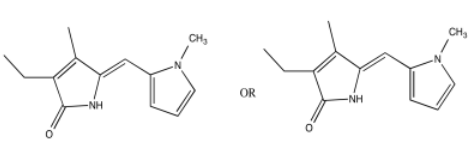


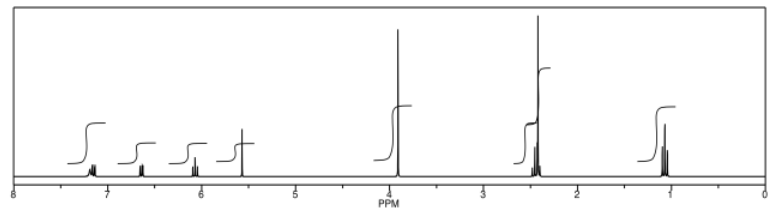
Answer
Answer b

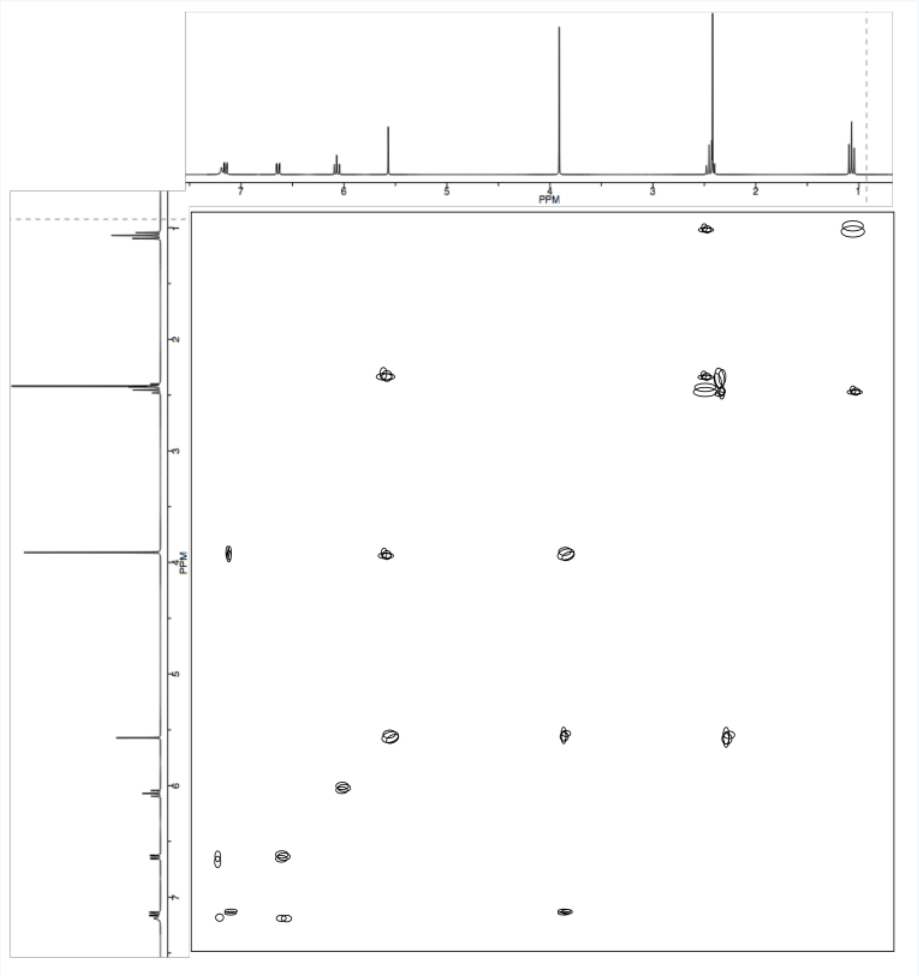


Exercise 5.4.5

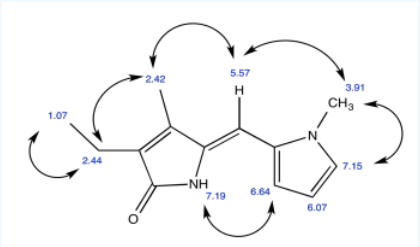
Draw the relative stereochemistry of this compound based on the NOESY spectrum.


CH3
N
NH
O
OR
CH3
N
NH
O


8
7
6
5
4
PPM
3
2
1
0


7
6
5
4
PPM
3
2
1
PPM
1
2
3
4
5
6
7

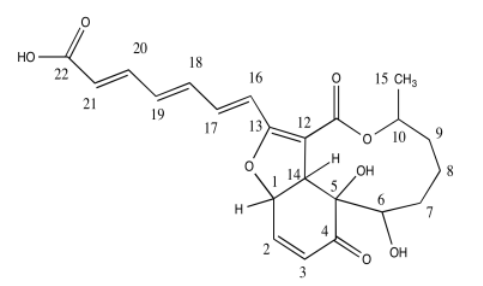
Answer


2.42
5.57
H
3.91
CH3
1.07
N
2.44
7.15
NH
7.19
6.64
6.07
O

Exercise 5.4.6

Dictyosphaeric Acid A is an antimicrobial compound isolated from an undescribed *Penicillium sp.* in an alga *Dictyosphaeria versluyii* collected in Fiji.
(Bugni, Janso, Williamson, Feng, Bernan, Greenstein, Carter, Maiese and Ireland, *J. Nat. Prod.* **2004**, *67*, 1396-1399.)

a) Circle all the chiral centers.



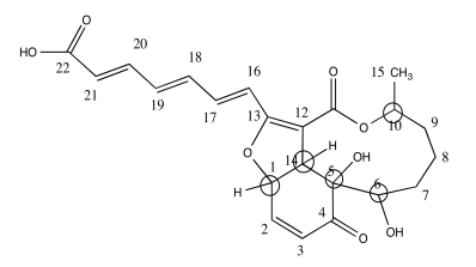
The researchers used nOe (ROESY) to determine stereochemical relationships.

H	ROESY
1	2, 14
2	1, 3
3	2
4	
5	
6	8b, 9b
7a	7b
7b	7a, 14
8a	
8b	6
9a	10, 15
9b	6, 10, 15
10	9a, 9b, 15
11	
12	
13	
14	1, 7b
15	9a, 9b, 10

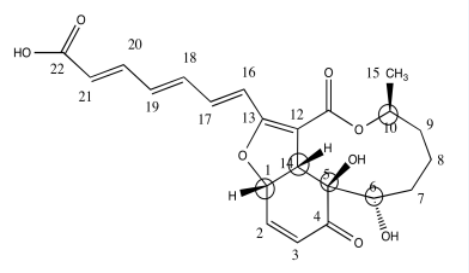
b) Use the data to put the substituents on this structure with wedges/dashes

c) Include key nOe correlations with the curved arrows.

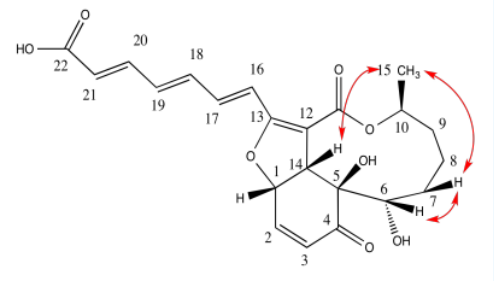
Answer
Answer a



.Answer b

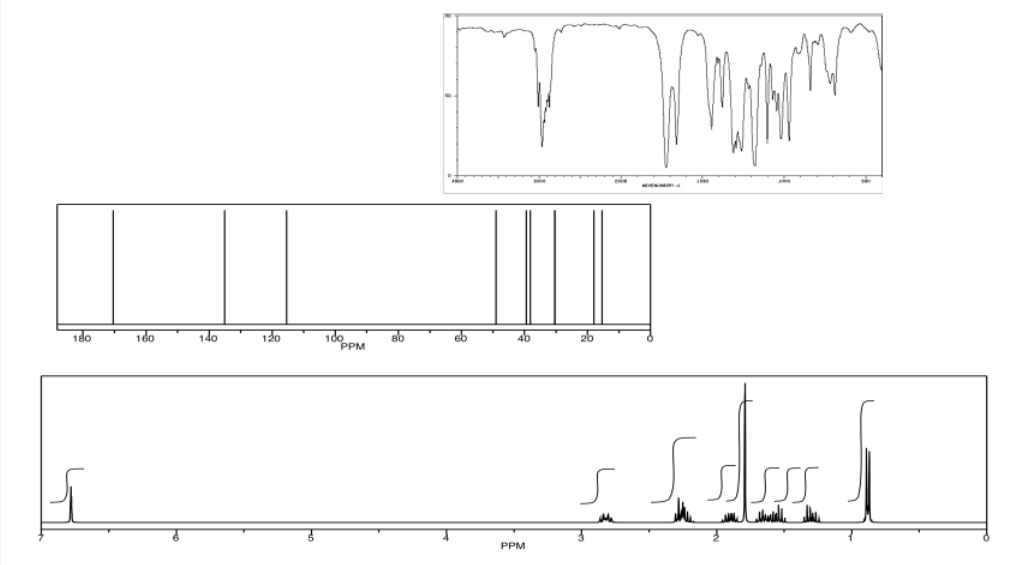


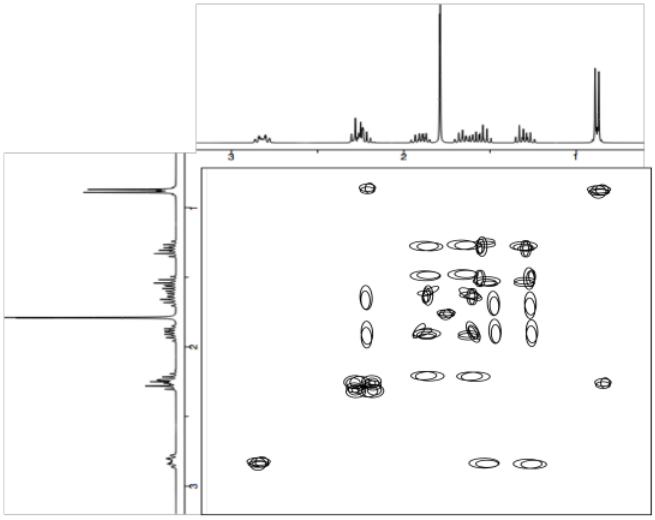
Answer c



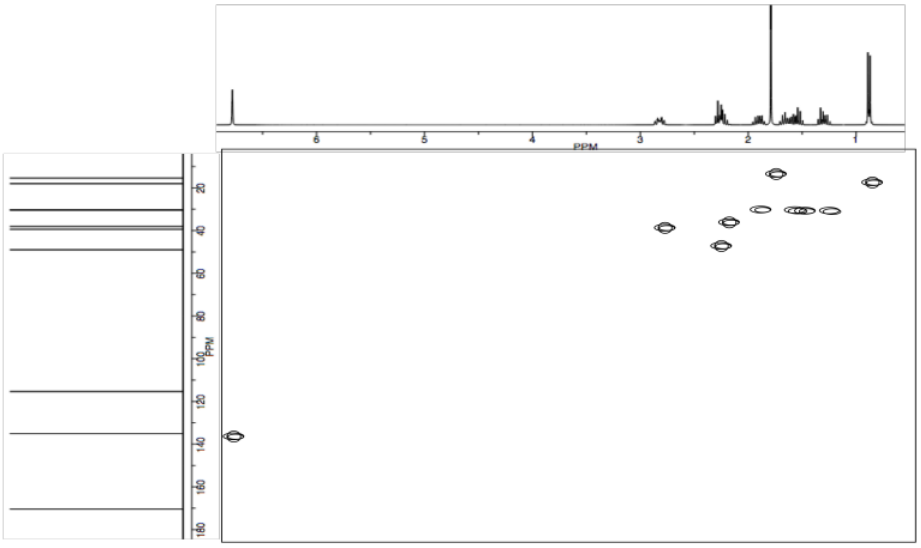
Exercise 5.4.7

Analyse the following data and propose a structure for the compound, formula $C_{10}H_{14}O_2$.

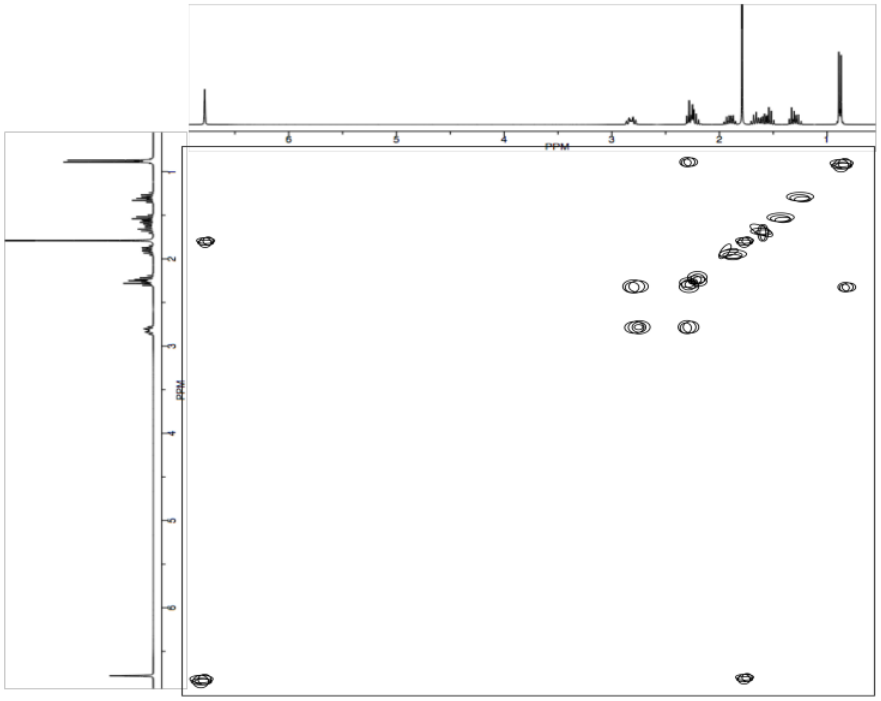




COSY

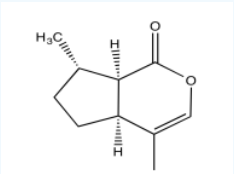


HMQC



NOESY

Answer



Catnip (nepetalactone)

*Sources:

Selected IR spectra from SDBS (National Institute of Advanced Industrial Science and Technology, Japan, Spectral Database for Organic Compounds, http://sdbs.db.aist.go.jp/sdbs/cgi-bin/cre_index.cgi, accessed December, 2015).

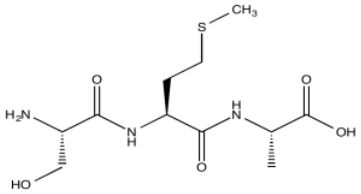
^{1}H NMR, ^{13}C NMR and NOESY spectra simulated.

5.5: Proteins

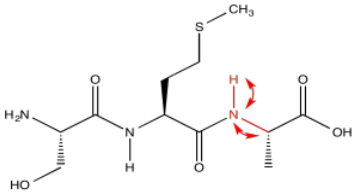
Protein structures can be complicated. Their NMR spectra can be very complicated. For that reason, multi-dimensional NMR techniques are often used to determine protein structures. On this page, we will look at just a few of the techniques, including COSY, TOCSY and HNCA.

Note that HNCA is not an example of 2D NMR. It is an example of 3D NMR. It shows a correlation between an amide proton, the amide nitrogen to which it is attached, and the carbons that are attached to the amide nitrogen. HNCA data are viewed in slices, in which we just look at one nitrogen at a time. One axis shows the shift of the proton attached to that nitrogen, and the other axis shows the shifts of the carbons attached to the nitrogen.

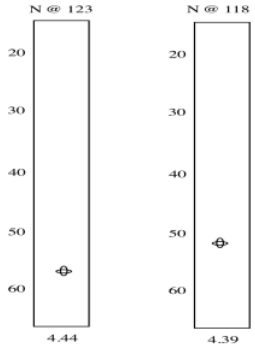
Consider a simple tripeptide.



HNCA exploits a magnetization transfer, similar to the process used in a COSY or HMBC experiment. In this case, the experiment involves three different kinds of nuclei. An amide proton is irradiated (H); it transfers information to the attached nitrogen (N) and then to the alpha carbon (CA).



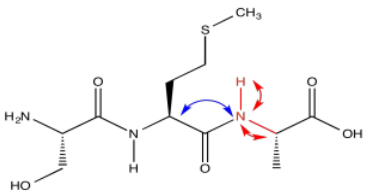
The results of the HNCA experiment display the relationship between these three nuclei. We have seen how a two-dimensional experiment can be displayed, but displaying a three-dimensional experiment would require a z axis. That might be difficult. Instead, HNCA results are displayed as "slices". A slice shows only the ^{13}C and ^{1}H data related to a particular ^{15}N resonance.



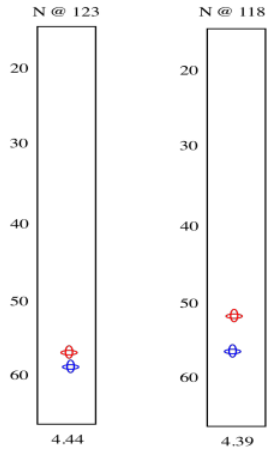
So we see there is an amide nitrogen that shows up at 123 ppm in the ^{15}N spectrum. It is attached to a carbon that shows up at 57 ppm in the ^{13}C spectrum and a proton that shows up at 4.44 ppm in the ^{1}H spectrum. A second slice shows similar results for the second amide H-N-Cα group in the tripeptide.

HNCA experiments are complicated. The way the experiment is run allows different kinds of information to be obtained, much like an HMBC and HMQC show different information from fundamentally similar methods.

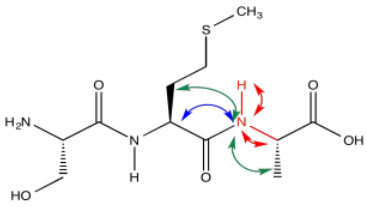
Running the HNCA in another way, we can actually see the alpha carbon on the other side of the carbonyl, in addition to the alpha carbon adjacent to the amide position we are looking at.



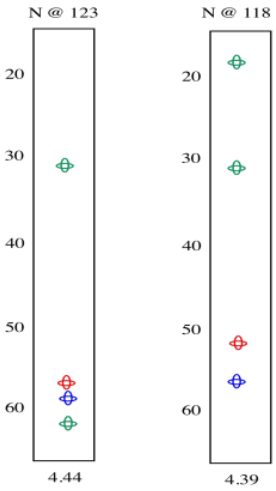
The red peaks below are the ones we had from the previous experiment. They show that relationship between the amide proton, the amide nitrogen and the alpha carbon. The blue peak shows the alpha carbon on the other side of the carbonyl. Notice that the blue peak in the slice on the right is the same as the red peak in the slice on the left. Of course, in a tripeptide, one of the amino acids is right next to the other one.



It still may not be clear which slice comes from which amide nitrogen. However, there is another variation on this experiment that can help. This one shows not only the alpha carbons on both sides of the amide nitrogen, but the beta carbons as well.



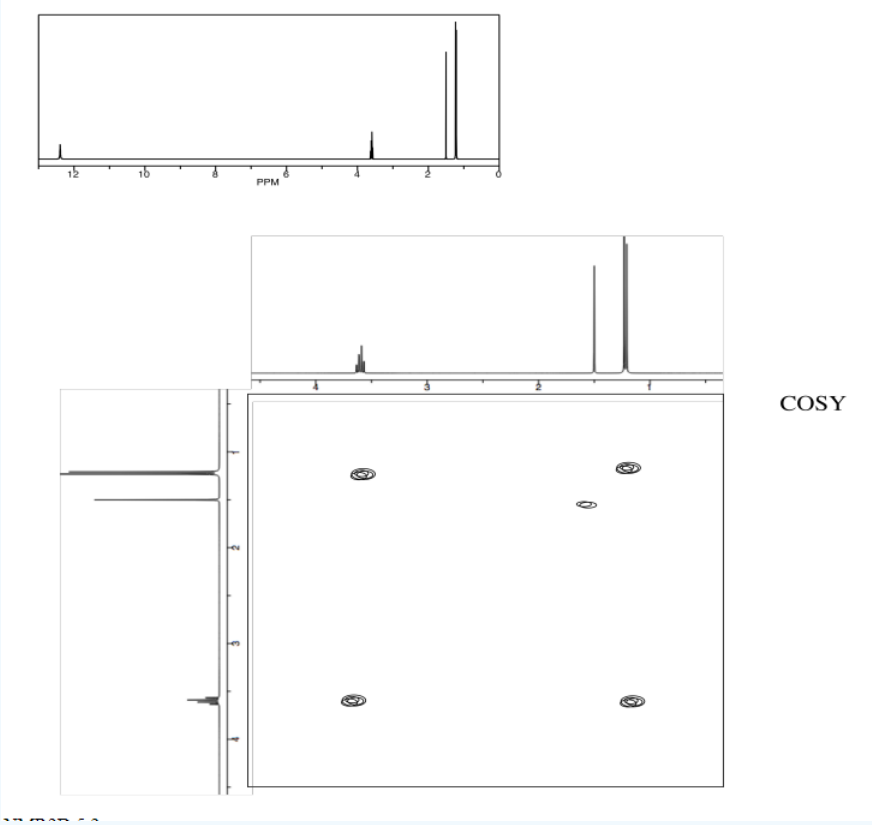
In the slices below, in addition to the red peaks and the blue peaks we had before, we now have a couple of green peaks. Those green peaks show the beta carbons on either side.



On the left slice, there is a green peak at 30 and one at 62. The peak at 62 must be the beta carbon of serine, since it is next to an oxygen. The peak at 30 is probably the beta carbon in methionine. In the right slice, the peak at 20 must be the methyl carbon in alanine. The beta carbon of methionine shows up again, because methionine is in the middle of this tripeptide -- it is next to both amide positions. Now we can see that the left slice came from the left amide position in the tripeptide, as drawn above, whereas the slice on the right came from the right amide position.

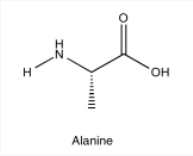
Exercise 5.5.1

Identify the following amino acid.



COSY

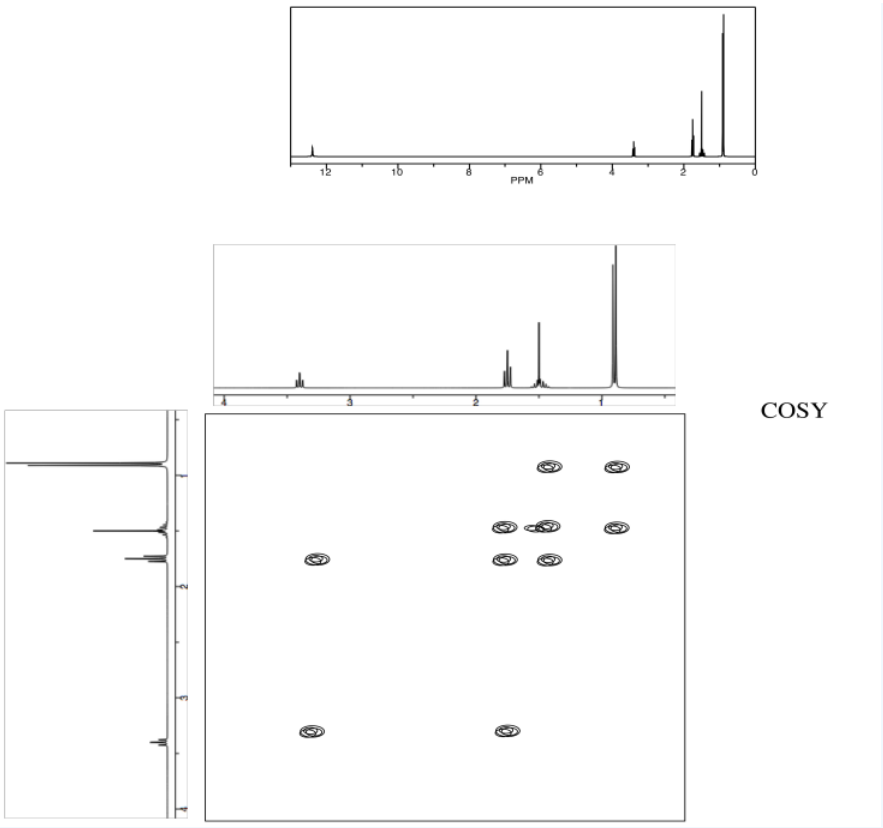
Answer



Alanine

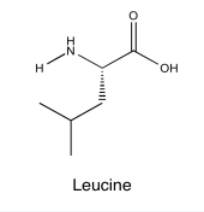
Exercise 5.5.2

Identify the following amino acid.



COSY

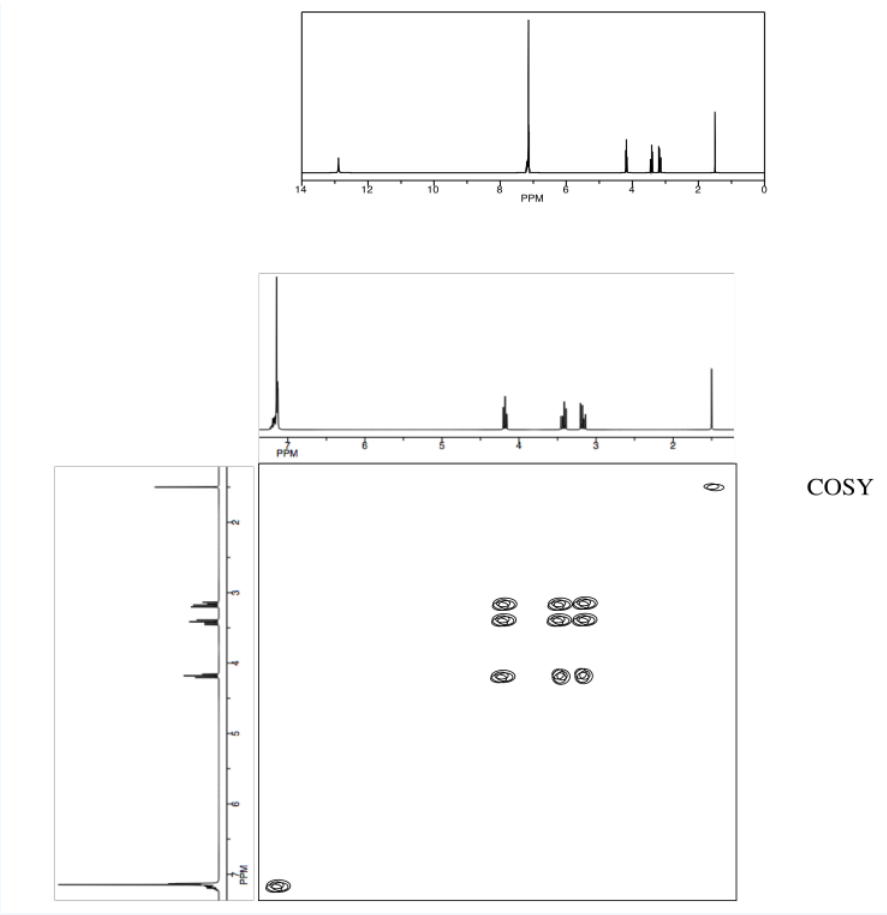
Answer



Leucine

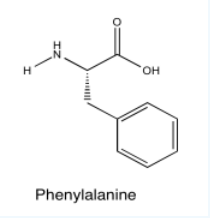
Exercise 5.5.3

Identify the following amino acid.



COSY

Answer



Phenylalanine

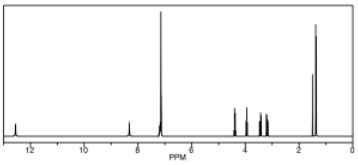
Exercise 5.5.4

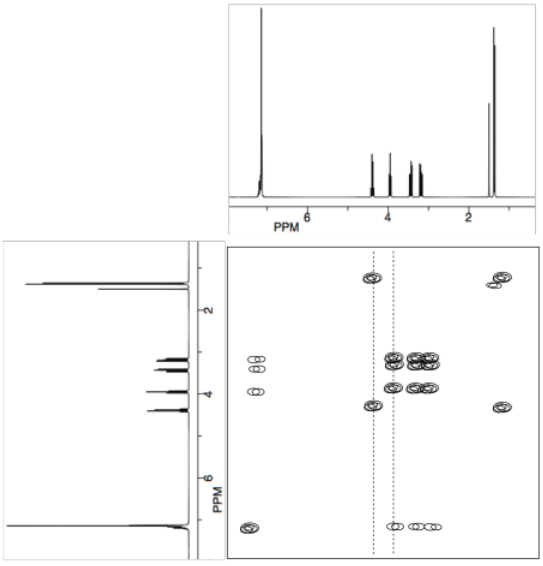
Identify this dipeptide.

a. Use the TOCSY to identify the two amino acids involved.
b. Use HNCA to determine the connectivity.

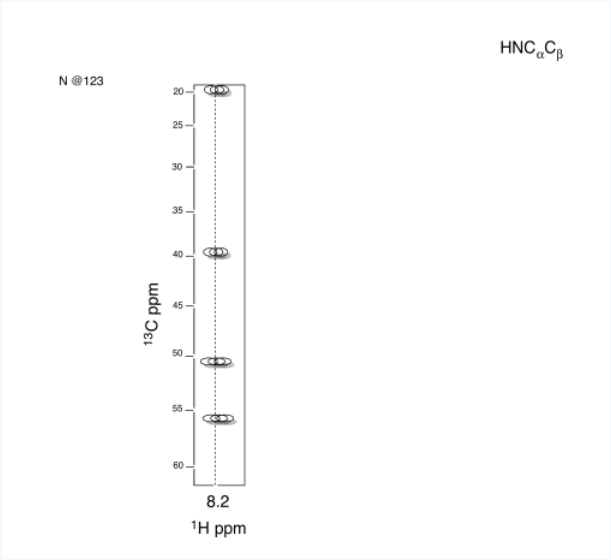
Useful References

- TOCSY/COSY of amino acids: http://www.bp.uni-bayreuth.de/NMR/nmr_aminotocsy.html
- TOCSY of all AA: http://www.bp.uni-bayreuth.de/NMR/nmr_alltocsy.html
- Standard Shifts for AA: http://www.bmrb.wisc.edu/ref_info/statsel.htm

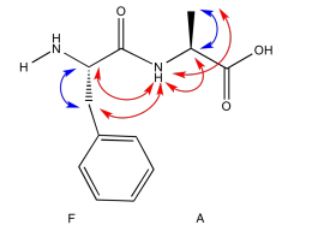




TOCSY



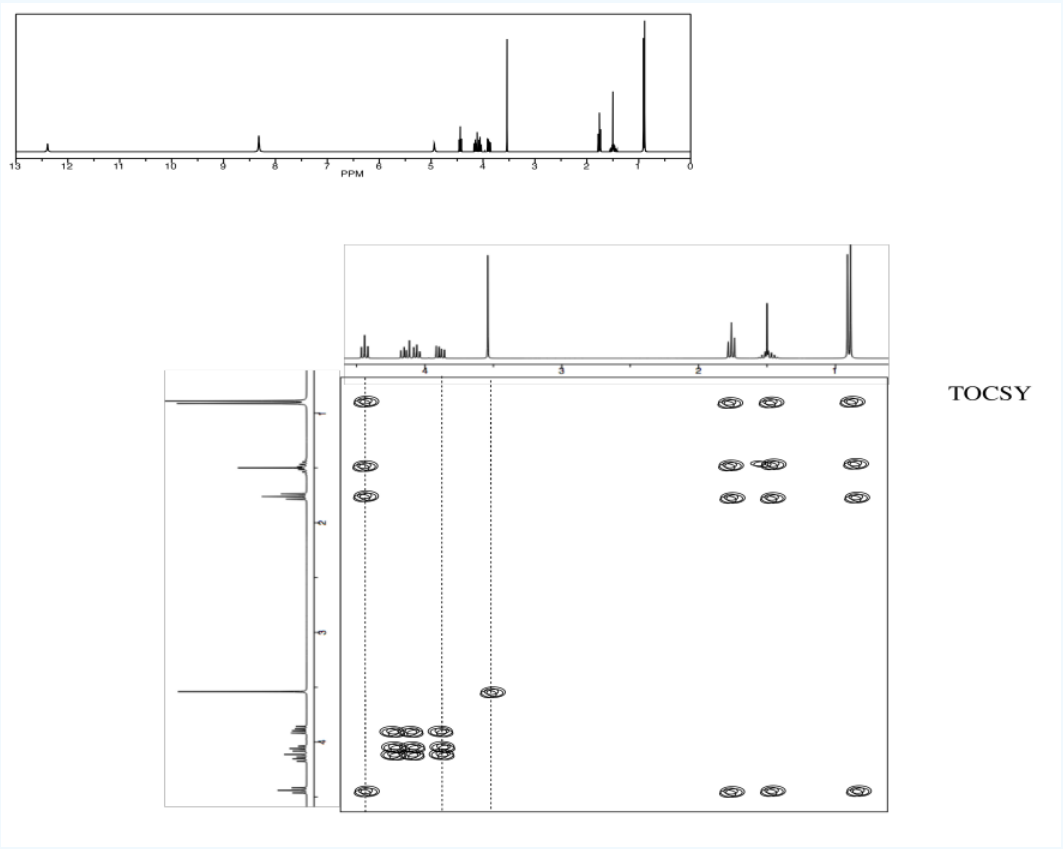
Answer

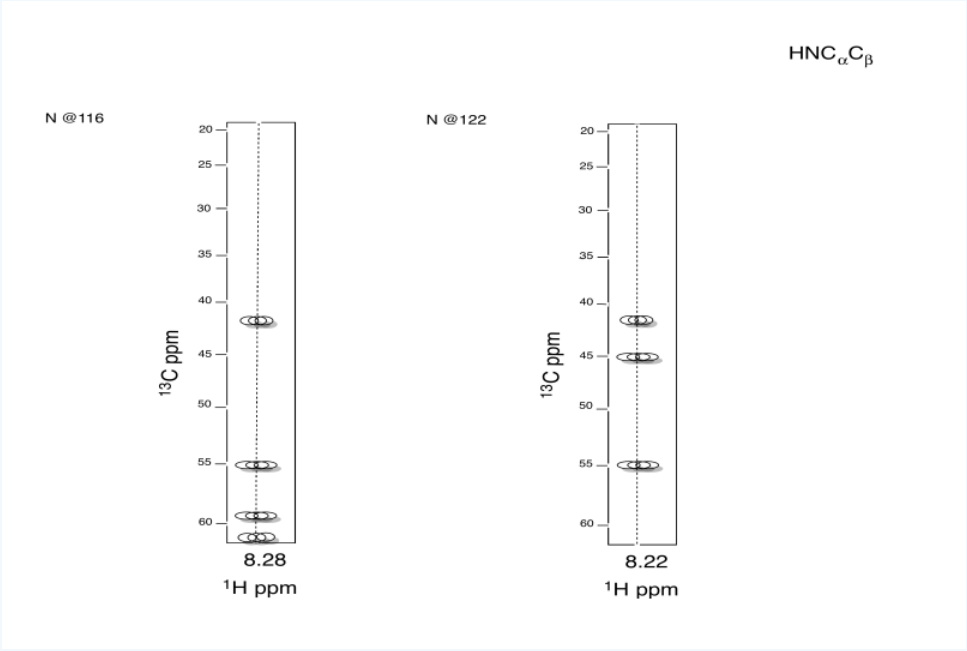


Exercise 5.5.5

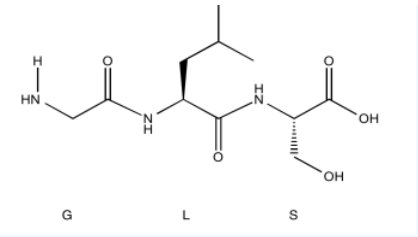
Identify this tripeptide.

a. Use the TOCSY to identify the two amino acids involved.
b. Use HNCA to determine the connectivity.





Answer



Sources

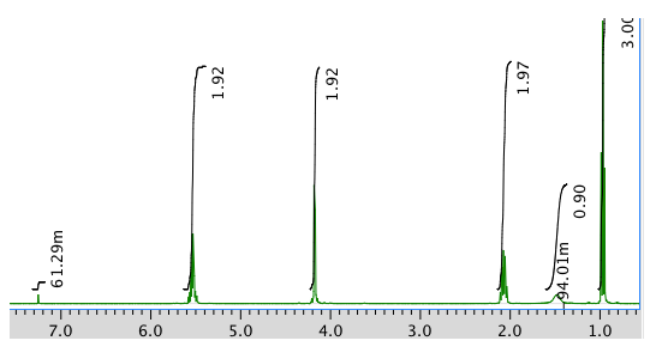
^{1}H NMR, TOCSY, HNCA and COSY spectra simulated.

5.6: More Practice with 2D

The following problems involve real samples. Note that you may need to check for peaks due to solvent. Helpful tables may be found here.

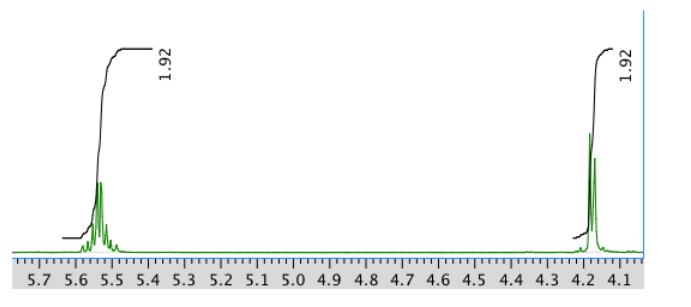
Exercise 5.6.1

The following problems involve real samples. Note that you may need to check for peaks due to solvent. Helpful tables may be found here.

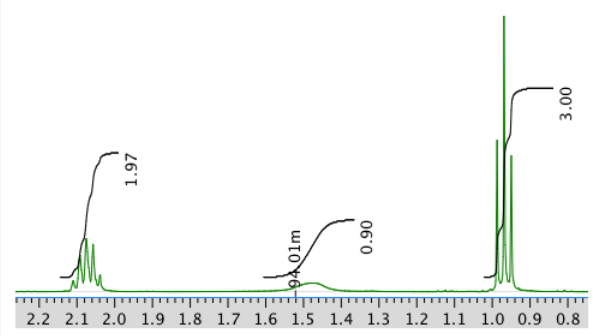


Note that the m beside one of the integral values stands for milli (one thousandth). 61.29m = 0.06129 units.

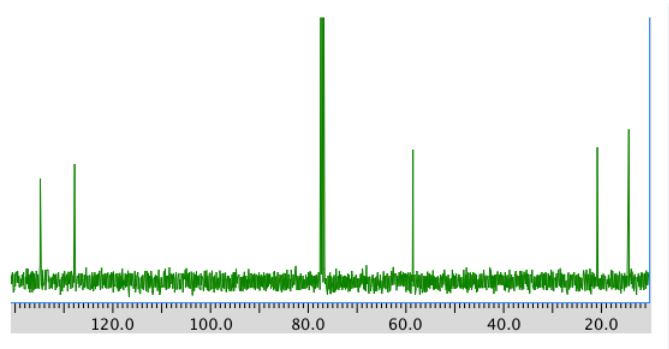
An expansion of the ^{1}H NMR spectrum:



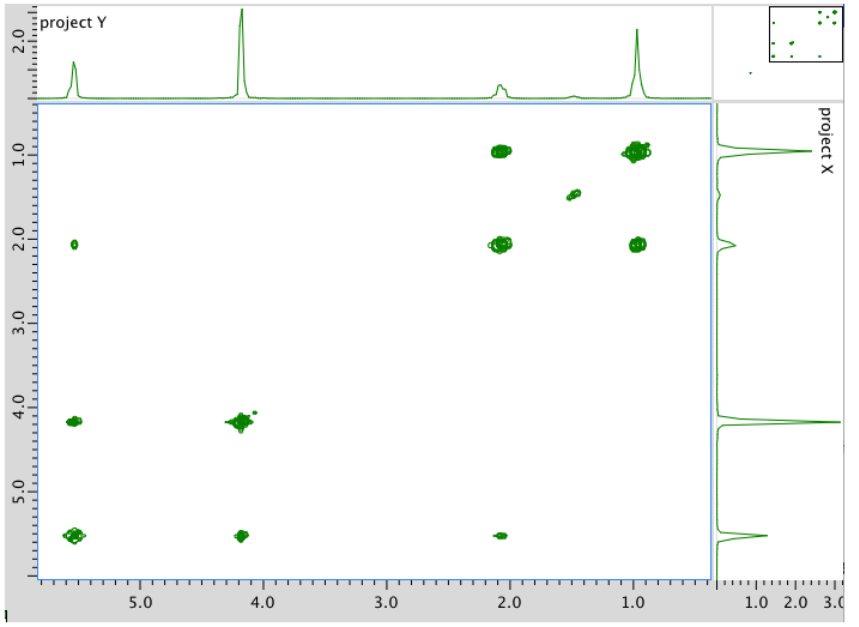
Another expansion:



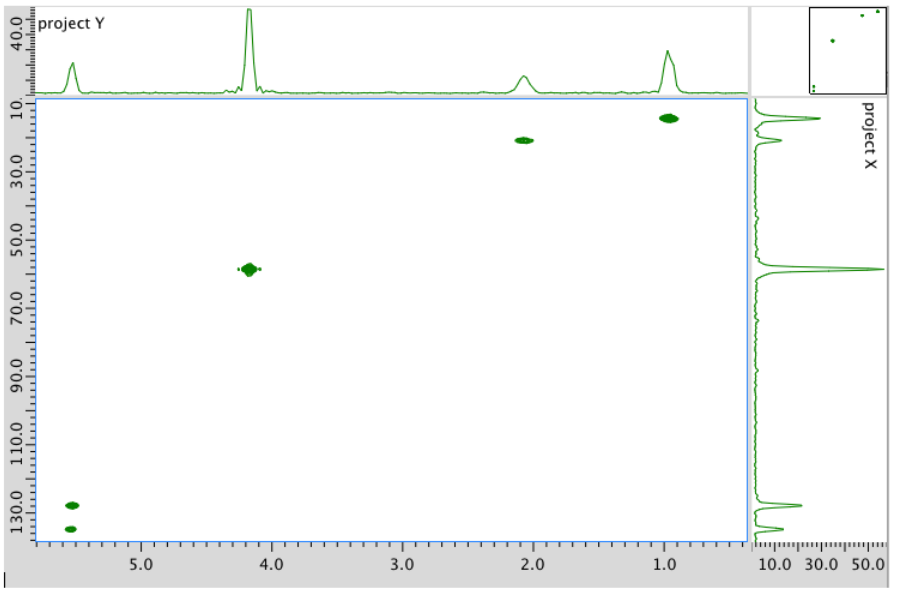
A ^{13}C NMR spectrum:



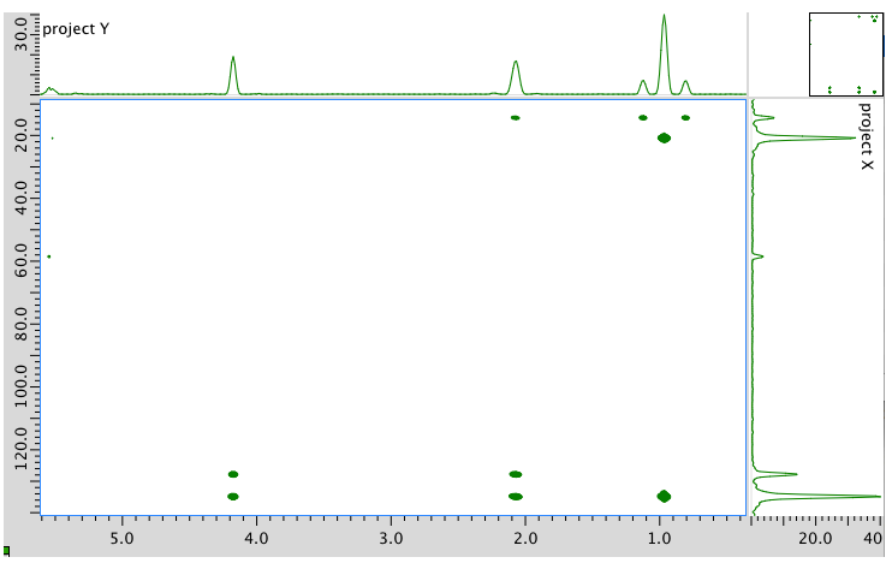
COSY spectrum:



HMQC spectrum:



HMBC spectrum:



Answer

^{1}H NMR

Chemical shift (ppm)	Integration	Multiplicity	Partial Structure
5.54	2H	multiplet	C**H**=C (x 2)
4.17	2H	doublet	O-C**H**$_2$-CH
2.08	2H	quintet	CH-C**H**$_2$-CH$_3$
1.47	1H	boad singlet	OH
0.95	3H	triplet	CH$_2$-C**H**$_3$

* total # H: 10

^{13}C NMR

Chemical shift (ppm)	Type of carbon
134	sp^2
128	sp^2
58	sp^3-O
21	sp^3
14	sp^3

*total # C: 5

COSY

Assignment	^{1}H	COSY
A	0.95	2.08
B	2.08	0.95, 5.54
C	4.17	5.54

D	5.54	2.08
E	5.54	4.17

*HMQC indicates two hydrogens at 5.54 are in two different environments

HMQC

Assignment	**^{13}C**	**^{1}H**
A	14	0.95
B	21	2.08
C	58	4.17
D	128	5.54
E	134	5.54

Formula:

$C_5H_{10}O$ (1 O indicated from shift in ^{13}C, ^{1}H NMR)

FW = $5 \times 12) + (10 \times 1) + (1 \times 16) = 86$

Compare C_5H_{10} ratio to C_5H_{12} in hydrocarbon

Degrees of unsaturation = \(\frac{(2 \times 5) + 2 - 10}{2} = 1 unit (1 double bond)

The data tables should be consitent with this structure:

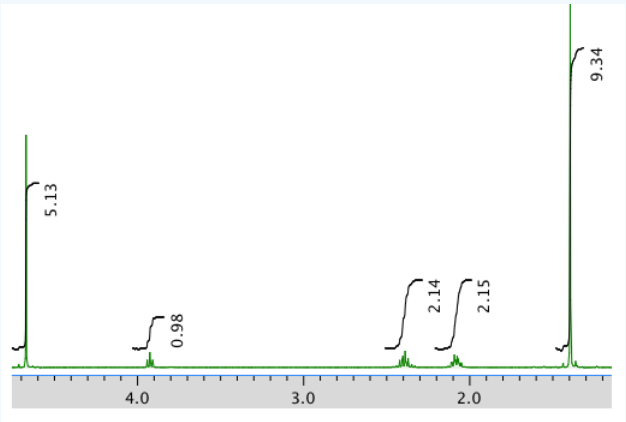
pent-2-en-1-ol (could be *cis* or *trans* based on this analysis)

Exercise 5.6.2

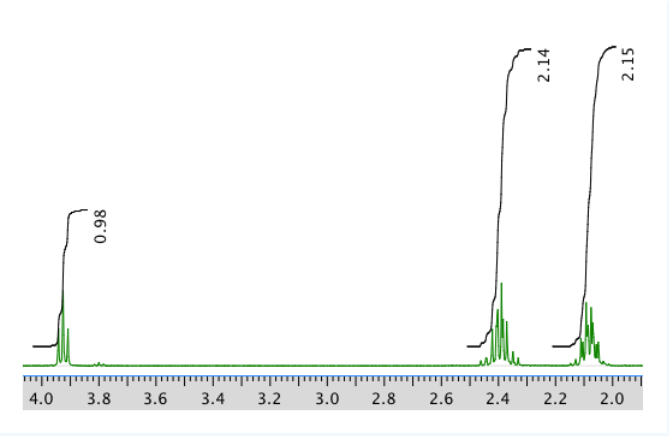
Present an analysis of the following data and propose a structure.

MW: 202 amu

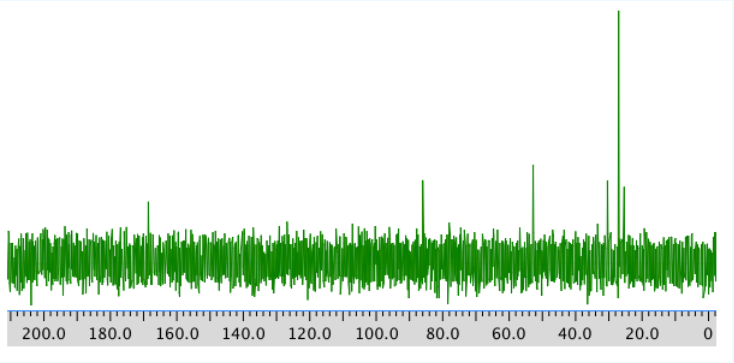
The full ^{1}H NMR spectrum in D_2O:



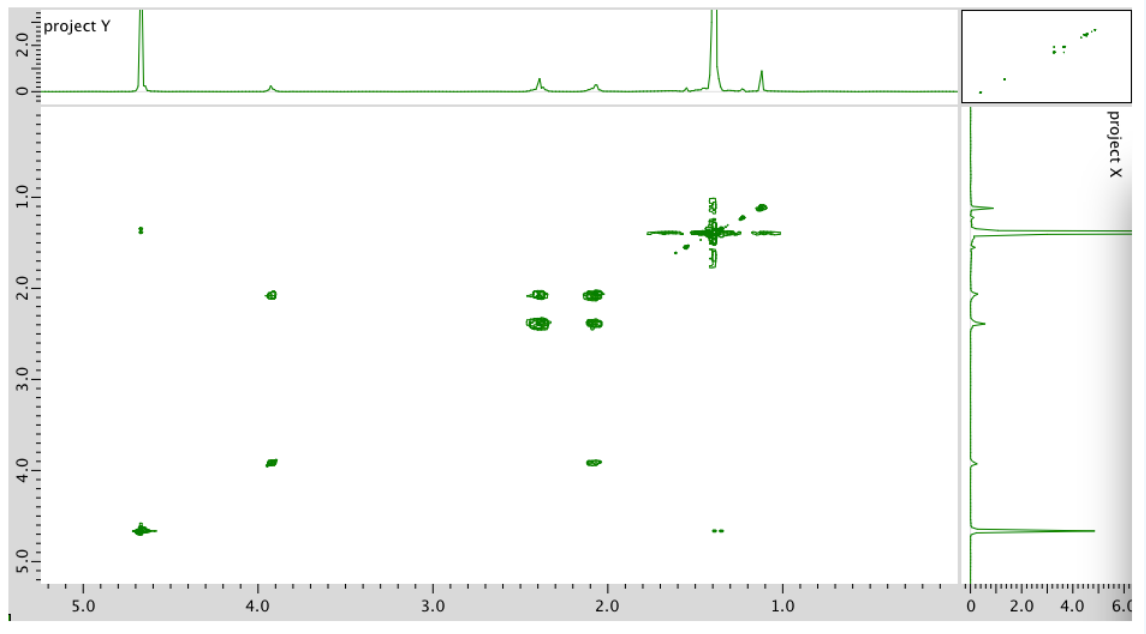
An expansion:



^{13}C NMR:



COSY:



Answer

^{1}H NMR:

Chemical shift (ppm)	Integration	Multiplicity	Partial structure

4.7	5H	singlet	solvent
3.93	1H	triplet	CH_2-C**H**-N
2.40	2H	multiplet	CH_2-C**H_2**?
2.09	2H	multiplet	C**H_2**-CH_2?
1.4	9H	singlet	C(C**H_3**)$_3$

*Total number of H: 19 H

^{13}C NMR:

Chemical shift (ppm)	**Type of carbon**
170	sp^2 (C=O)
80	sp^3 (C-O)
52	sp^3 (C-N)
32	sp^3
28	sp^3
26	sp^3

*Total number of C: 6 apparent, but two more suggested by symmetry (3 methyl groups in ^{1}H NMR) for 8 C; a third extra suggested by MW fit for 9 C

COSY:

Assignment	**^{1}H**	**COSY**
Solvent	4.7	--
B	3.93	2.40
D	2.40	2.09
C	2.09	2.40, 2.09
A	1.4	--

Formula:

$C_9H_{18}O_3N_2$ (extra O indicated from shift in ^{13}C, ^{1}H NMR; second O suggested by C=O in ^{13}C NMR; additional CO needed to fit MW)

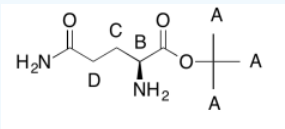
FW = $(9 \times 12) + (18 \times 1) + (3 \times 16) + (2 \times 14) = 202$

FW = ((9 \times 12) + (18 \times 1) + (3 \times 16) + (2 \times 14) = 202\)

Compare C_9H_{18} to C_9H_{22} for the corresponding hydrocarbon corrected for two nitrogens (therefore two extra hydrogens)

Degrees of unsaturation = $\frac{(2\times9)+2+2-10}{2} = 2$ units (2 double bonds)

The data tables should be consistent with this structure:

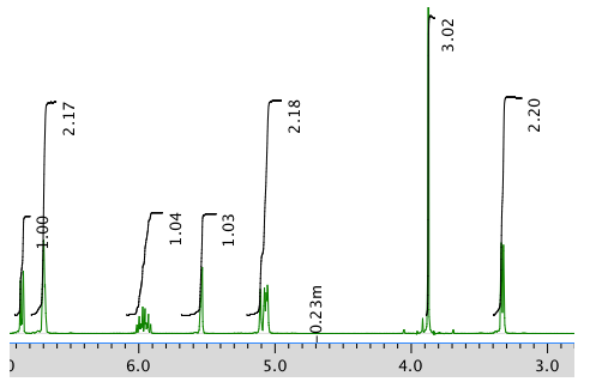


Exercise 5.6.3

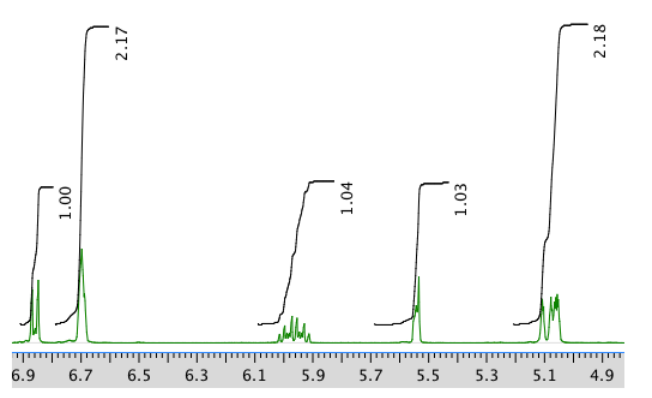
Present an analysis of the following data and propose a structure.

MW: 164 amu

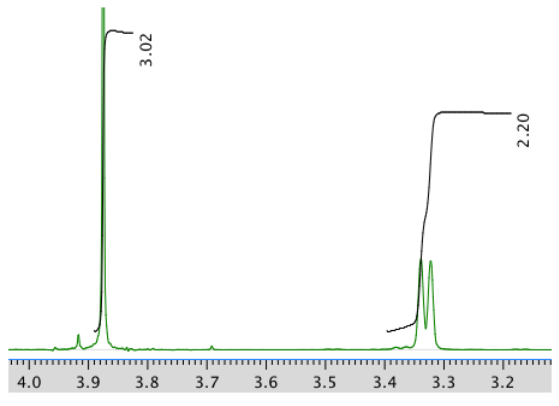
The full ^{1}H NMR spectrum in $CDCl_3$:



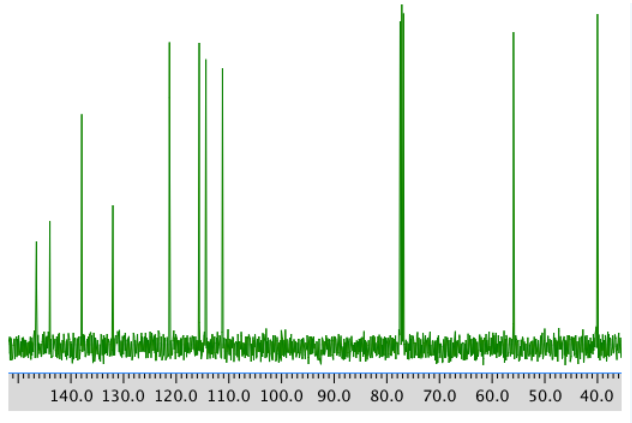
An expansion of the ^{1}H NMR spectrum:



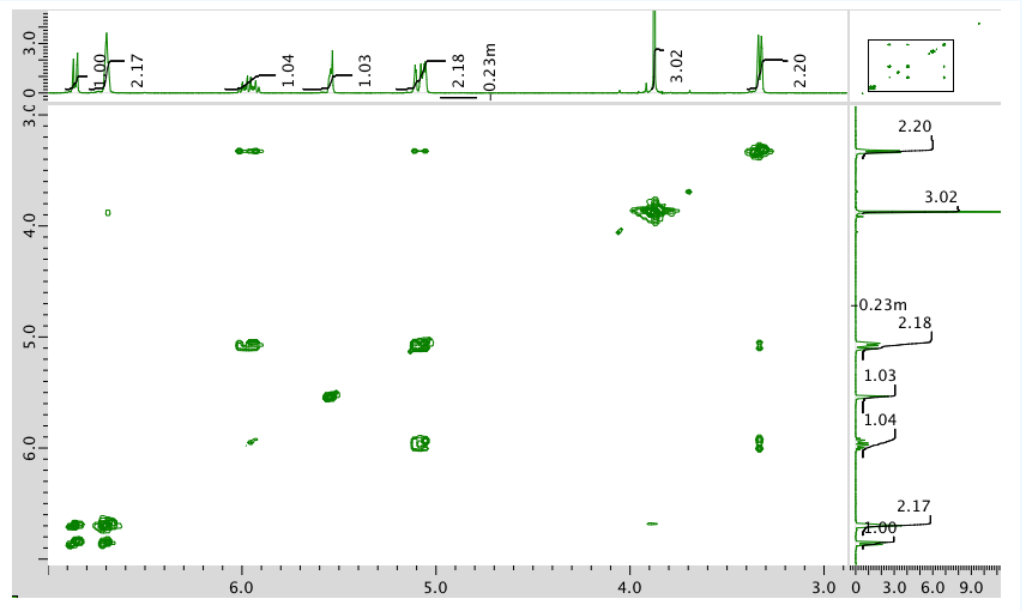
Another expansion:



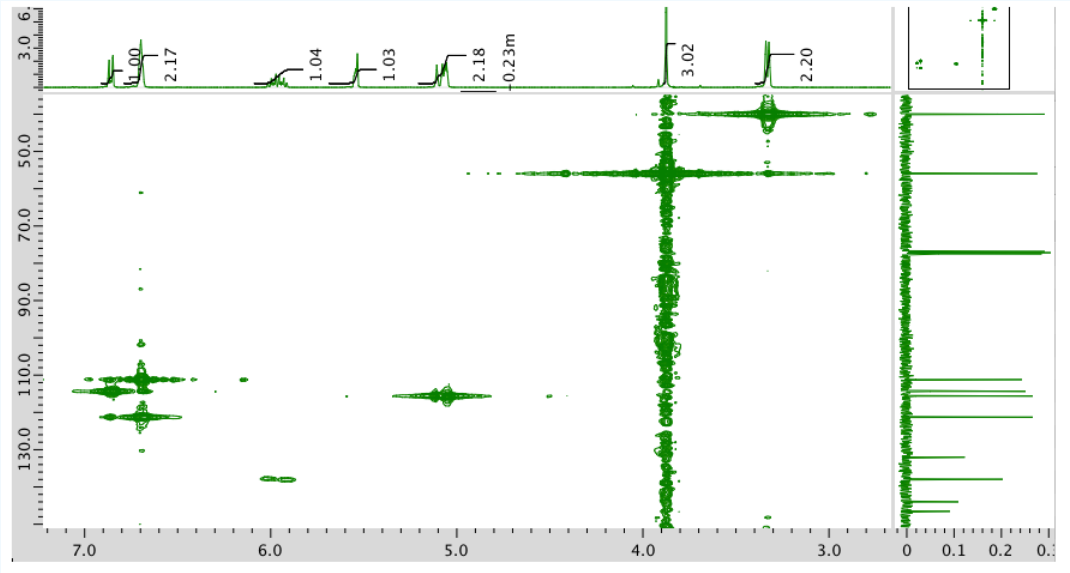
^{13}C NMR spectrum:



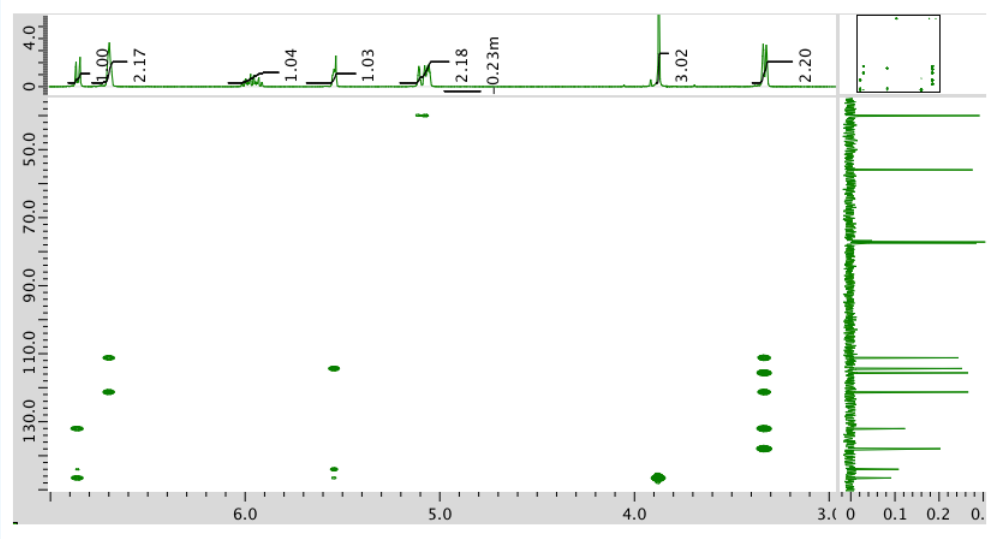
COSY spectrum:



HMQC:

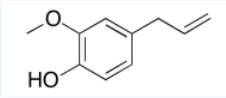


HMBC:



Answer

The data should be consistent with this structure:

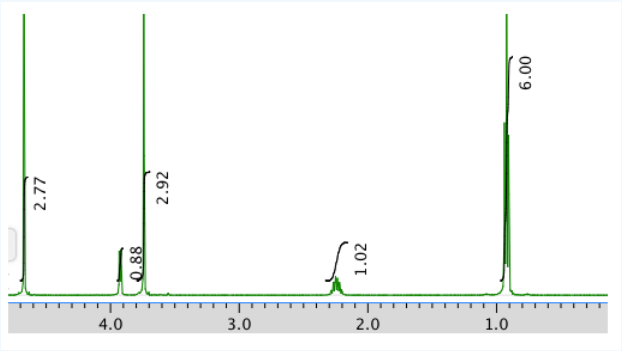


Exercise 5.6.4

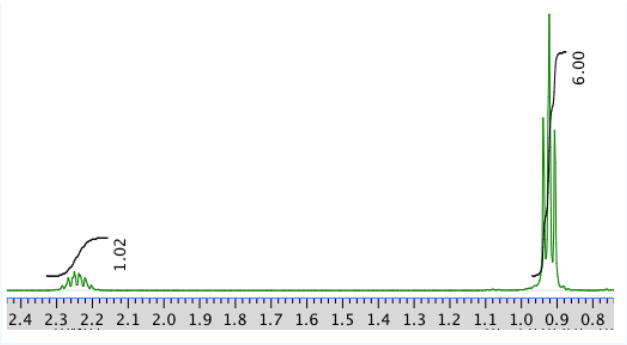
Present an analysis of the following data and propose a structure.

MW: 131 amu

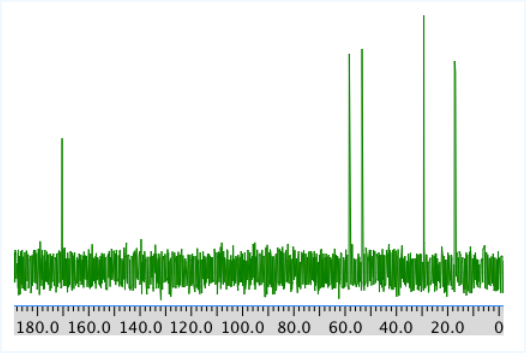
The full ^{1}H NMR spectrum in D_2O:



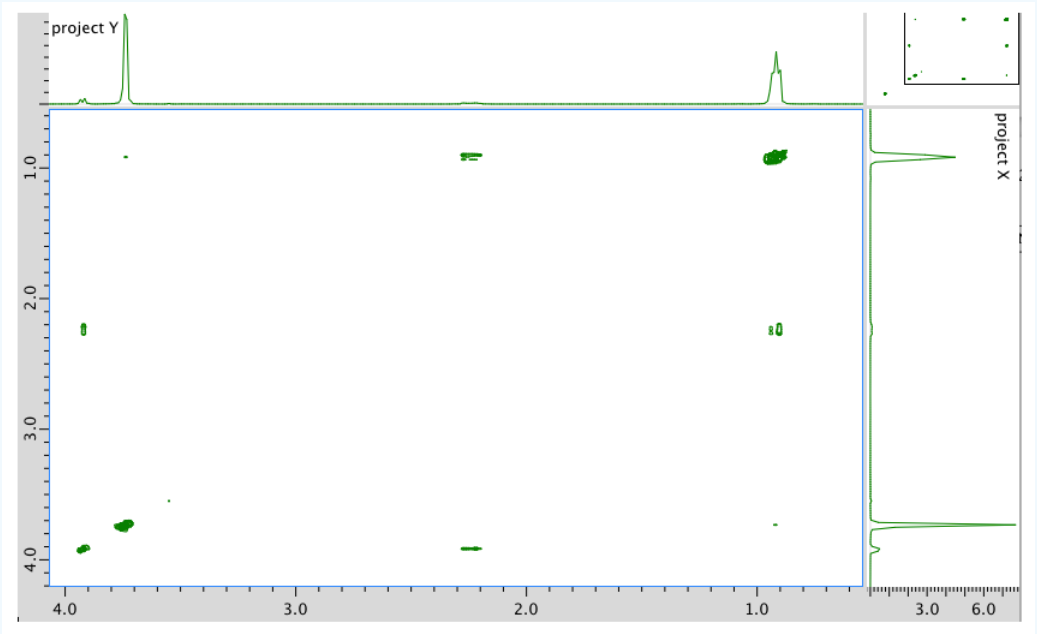
An expansion:



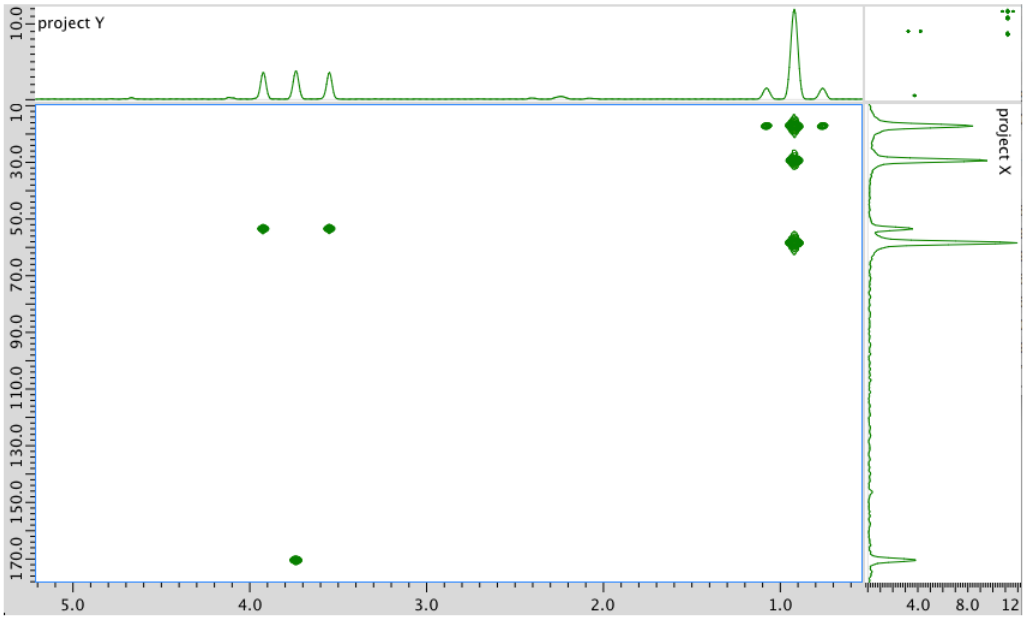
13C NMR:



COSY:



HMBC:



Answer

^{1}H NMR:

Chemical shift (ppm)	Integration	Multiplicity	Partial Structure
4.71	--	singlet	solvent
4.17	1H	doublet?	CO-C**H**-N
3.75	3H	singlet	O-C**H**$_3$
2.25	1H	multiplet	CH-C**H**-(CH$_3$)$_2$
0.92	6H	triplet?	2 x C**H**$_3$

^{13}C NMR:

Chemical shift (ppm)	Type of carbon
170	sp^2 C=O
60	sp^3 C-N
52	sp^3 C-O
30	sp^3 C
19	sp^3 C

COSY:

Assignment	^{1}H	COSY
A	4.17	2.25
B	3.75	--
C	2.25	4.17
D	0.92	2.25

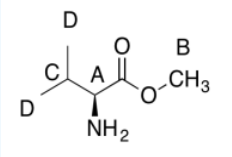
Formula:

$C_6H_{13}O_2N$ (1 O indicated from shift in ^{13}C, ^1H NMR)

FW = $(6 \times 120 + (13 \times 1) + (2 \times 16) + (1 \times 14) = 131$

Degrees of unsaturation = $\frac{(2\times6)+2+1-13}{2} = 1$ unit (1 double bond)

The data should be consistent with this structure:

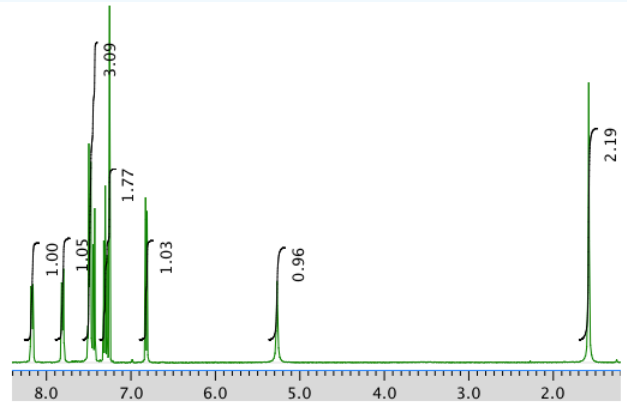


Exercise 5.6.5

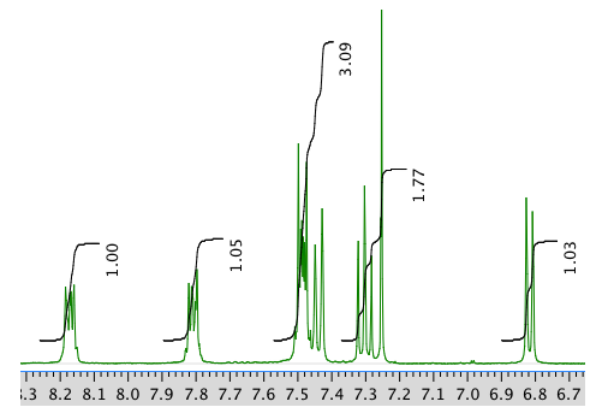
Present an analysis of the following data and propose a structure.

MW: 144 amu

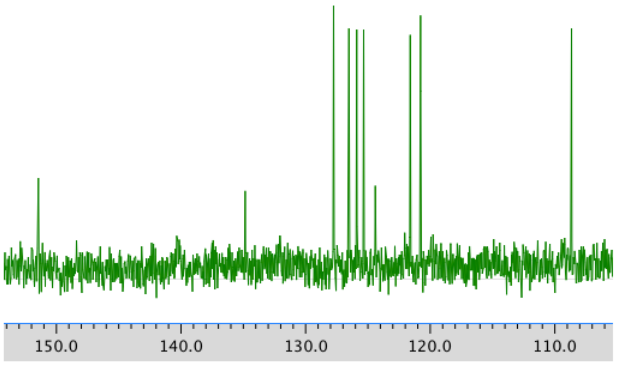
The ^1H NMR spectrum in $CDCl_3$:



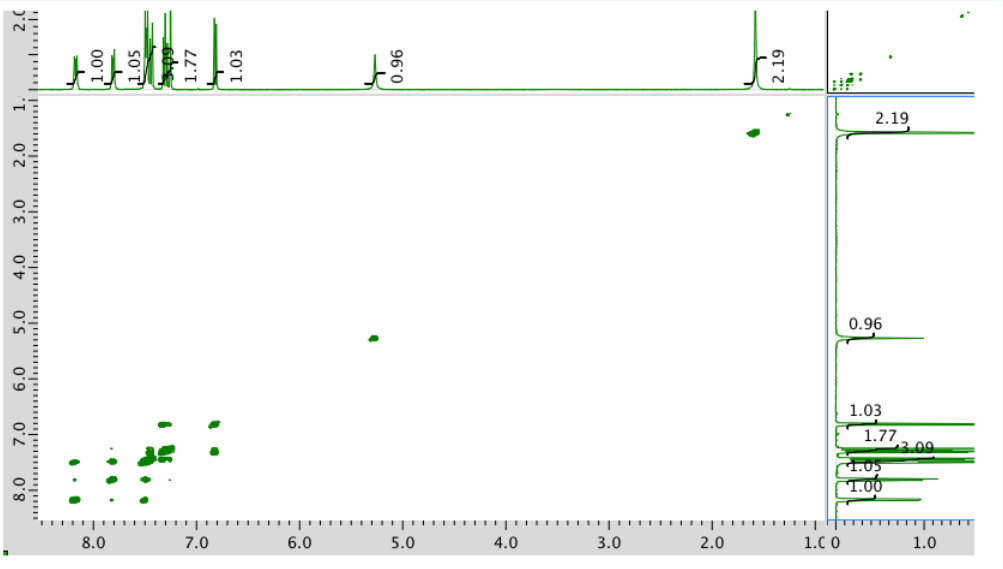
An expansion of the ^1H NMR spectrum:



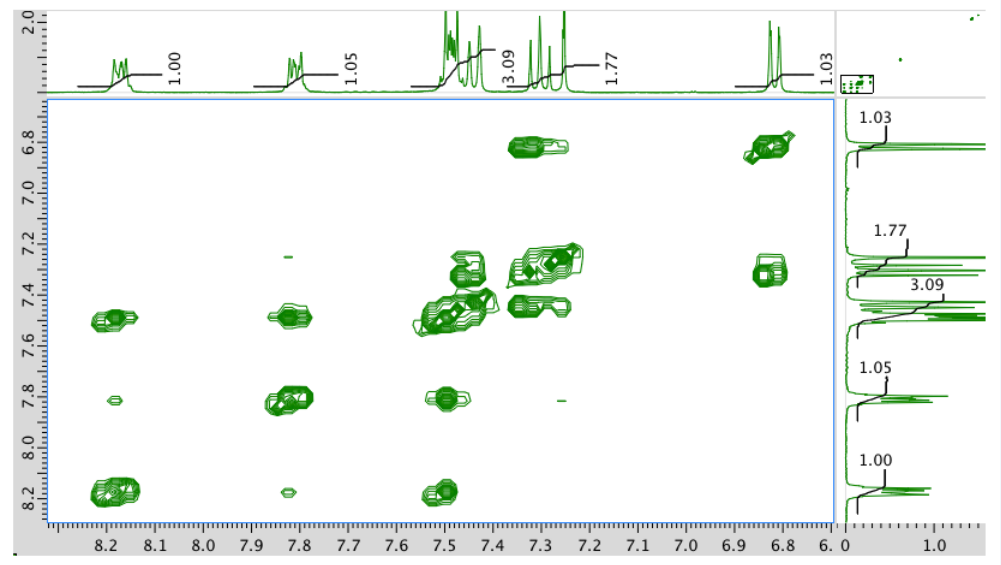
^{13}C NMR spectrum:



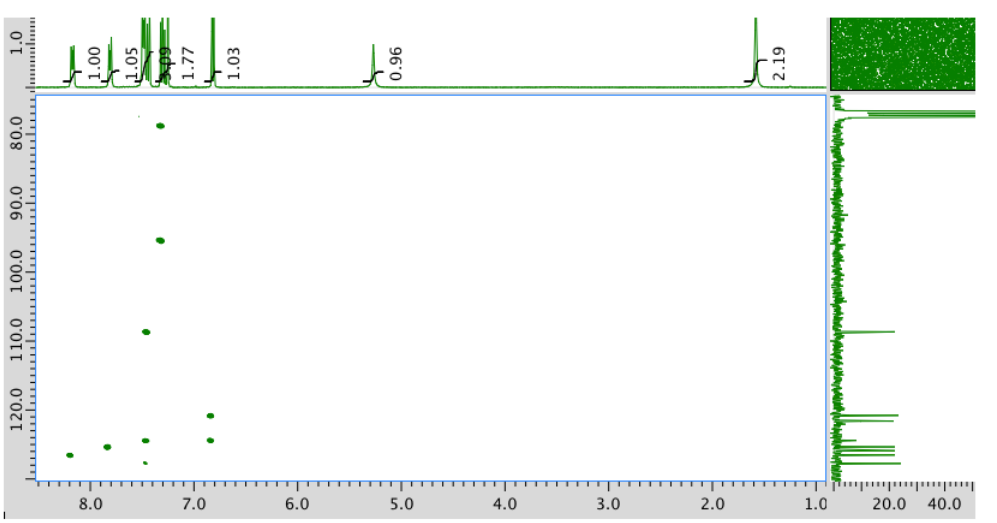
COSY:



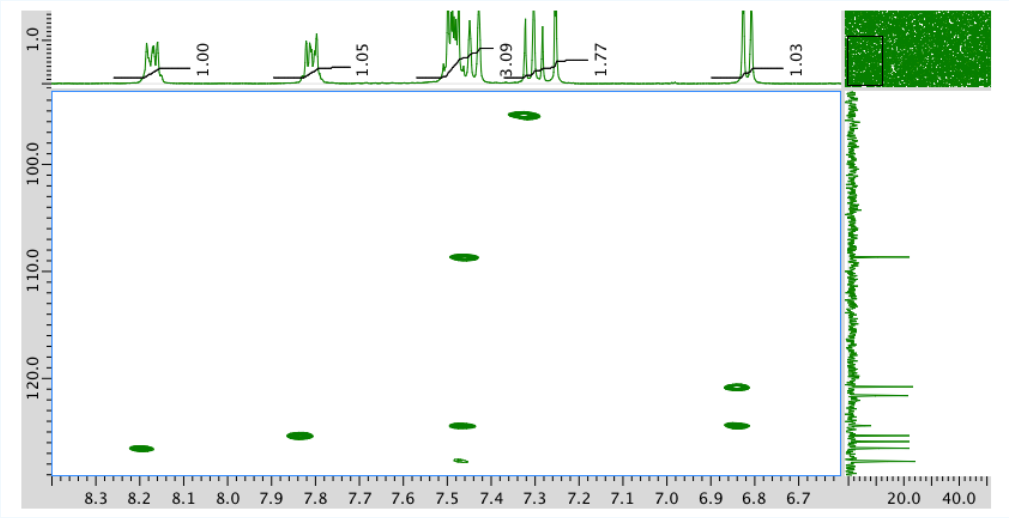
An expansion of the COSY spectrum:



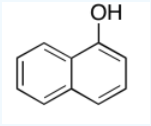
HMBC:



An expansion of the HMBC spectrum:



Answer

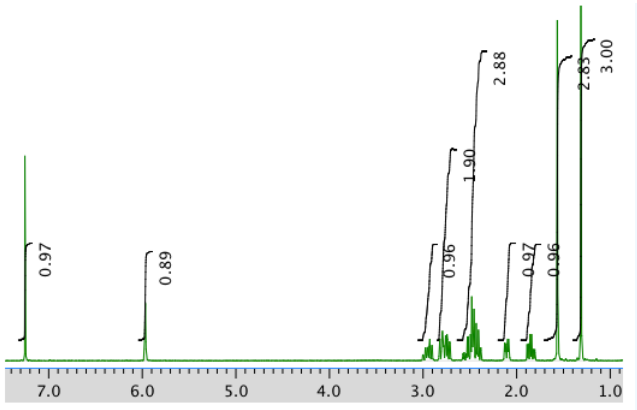


Exercise 5.6.6

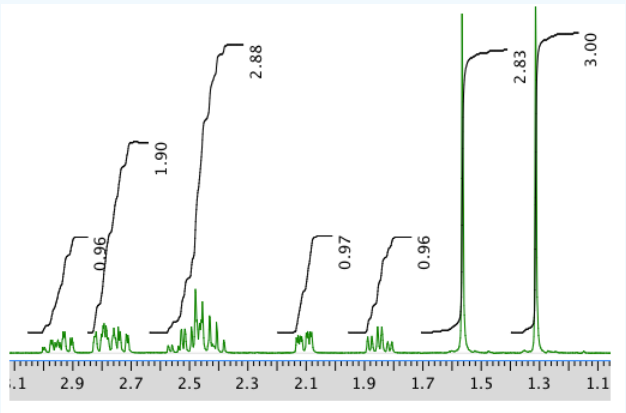
Present an analysis of the following data and propose a structure.

MW: 164 amu

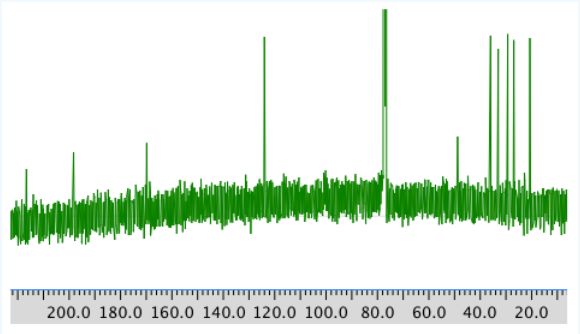
The full ^{1}H NMR spectrum in $CDCl_3$:



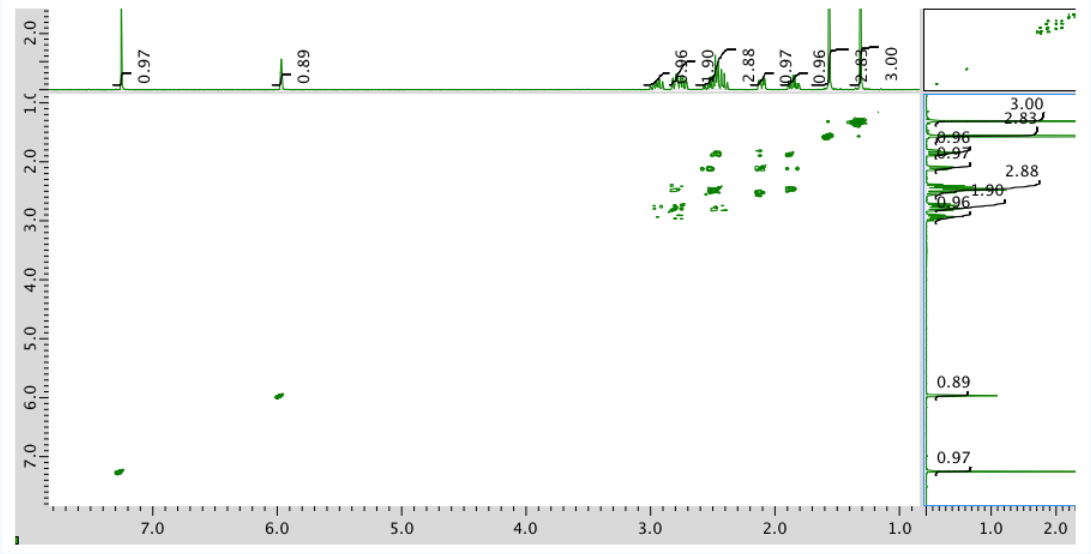
AN expansion:



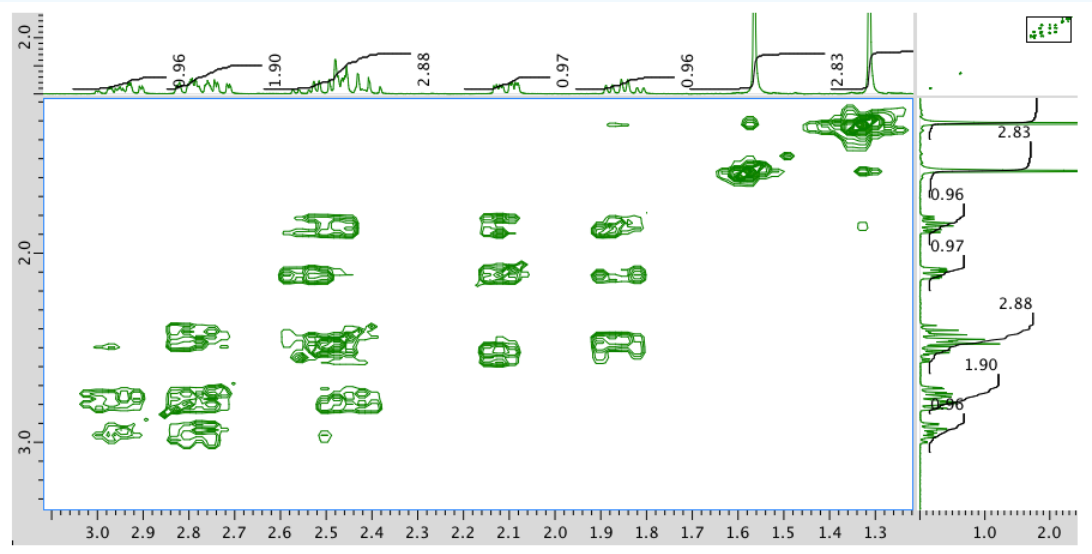
13C NMR:



COSY:

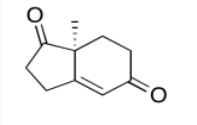


Expansion of COSY spectrum:



Answer

The data should be consistent with this structure:

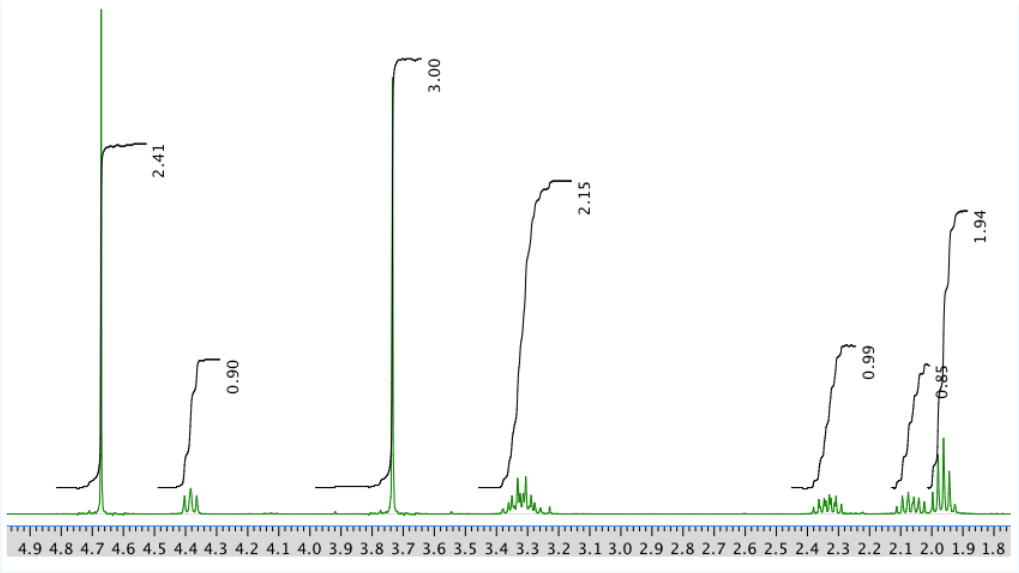


Exercise 5.6.7

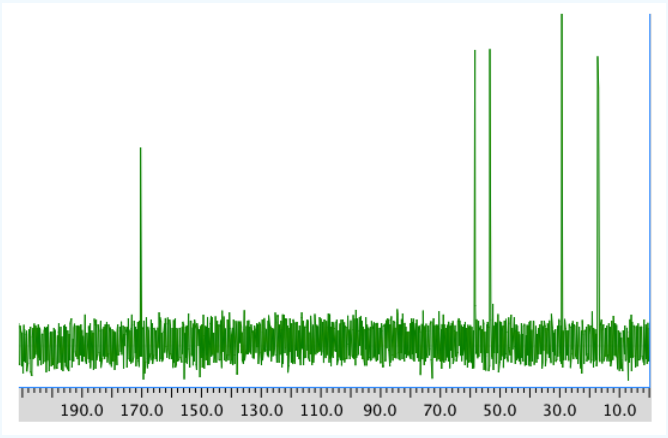
Present an analysis of the following data and propose a structure.

MW: 129 amu

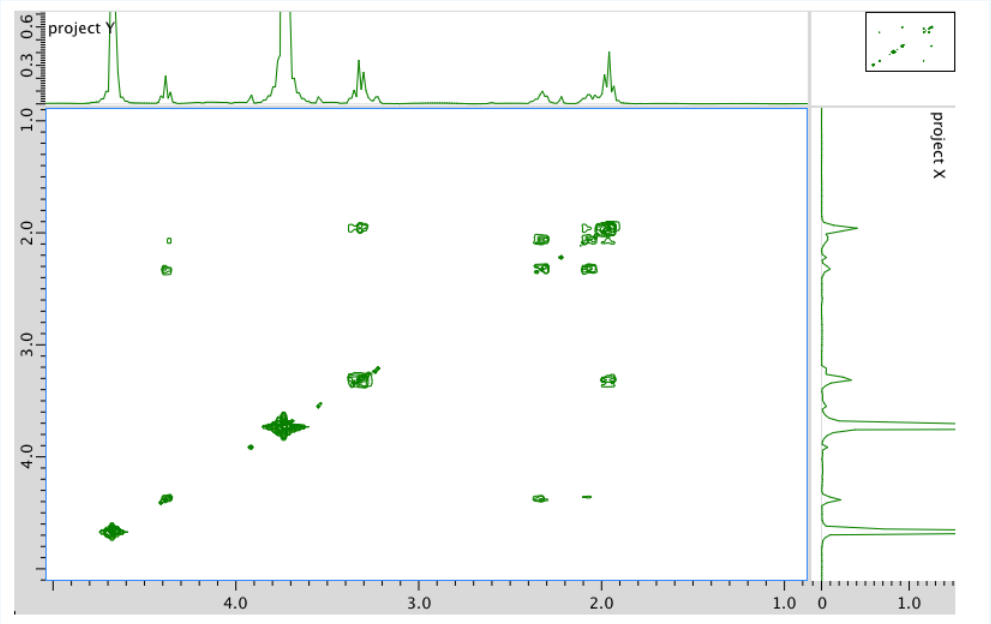
The full ^{1}H NMR spectrum in D_2O:



^{13}C NMR spectrum:

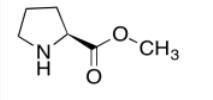


COSY spectrum:



Answer

The data should be consistent with this structure:

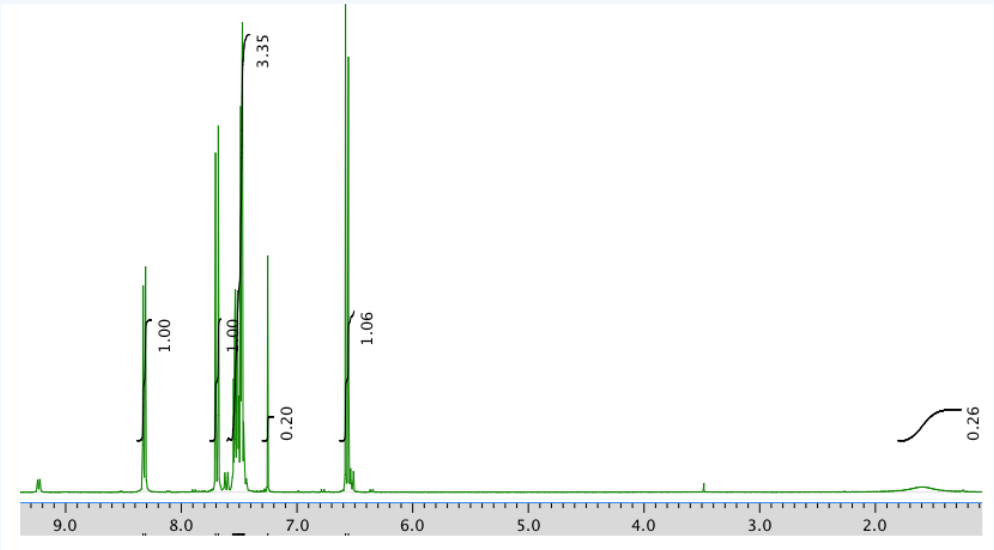


Exercise 5.6.8

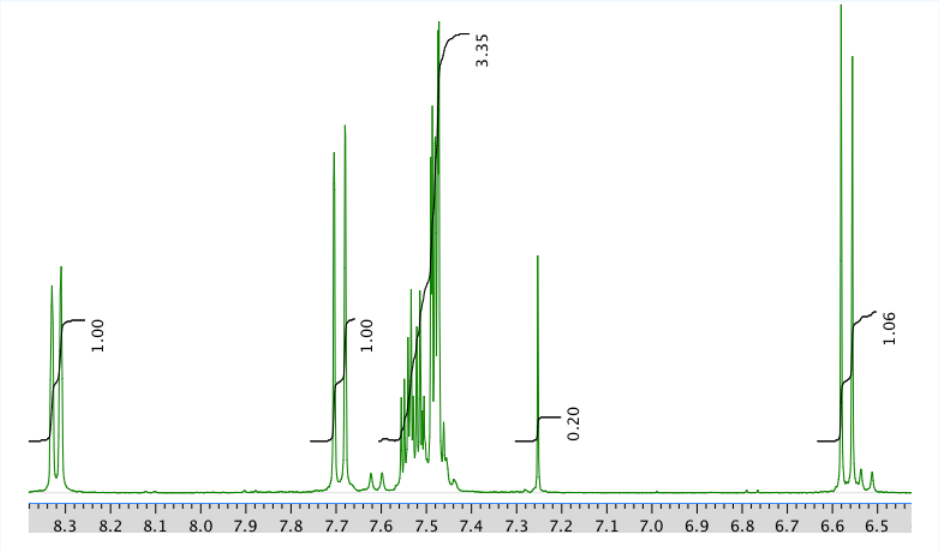
Present an analysis of the following data and propose a structure.

MW: 173 amu

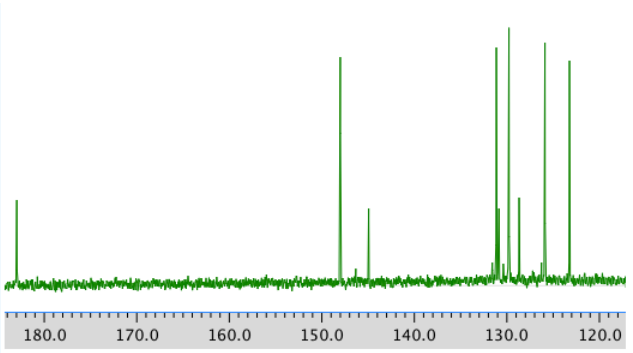
The full ^{1}H NMR spectrum in $CDCl_3$:



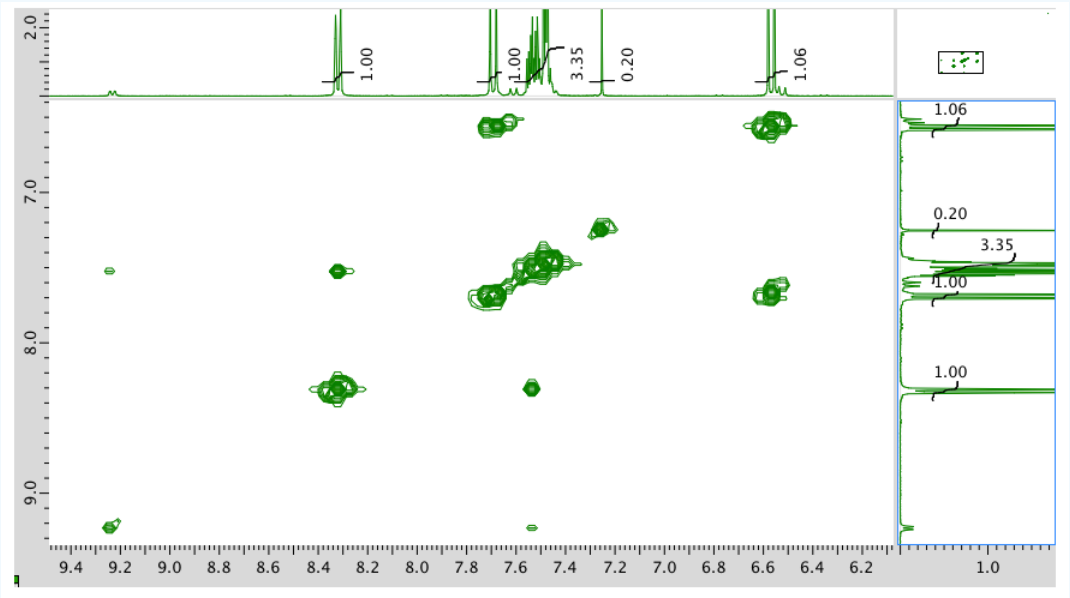
An expansion of the ^{1}H NMR spectrum:



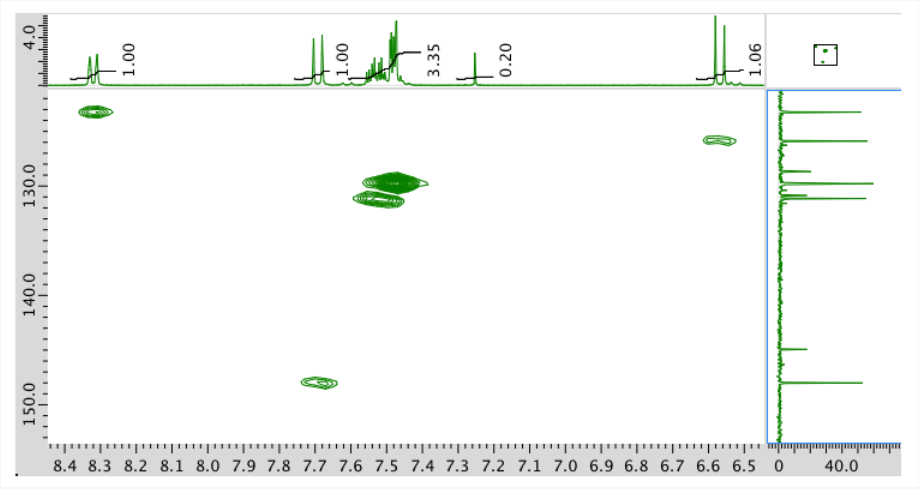
13C NMR spectrum:



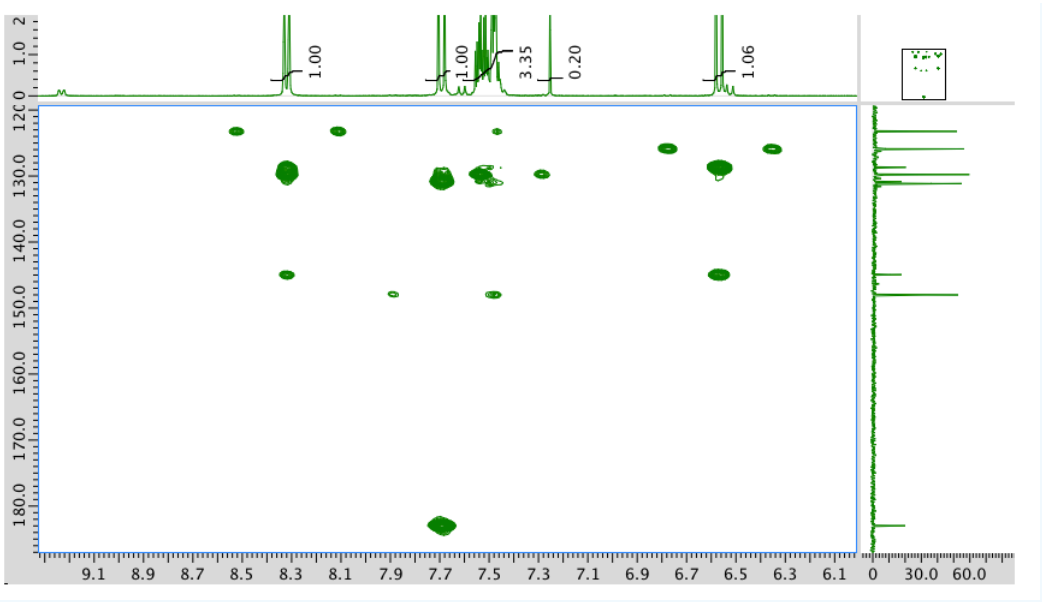
COSY:



HMQC:

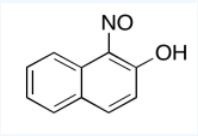


HMBC:



Answer

The data should be consistent with this structure:

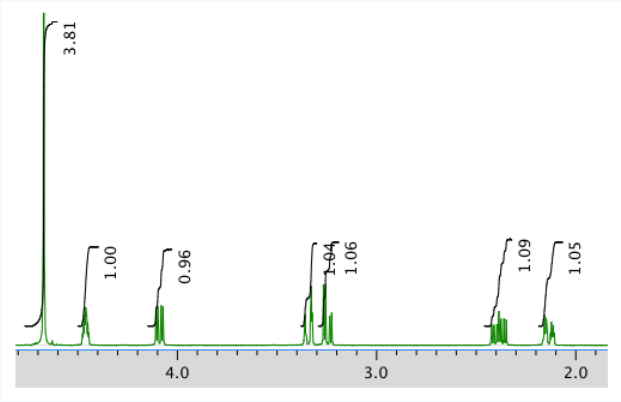


Exercise 5.6.9

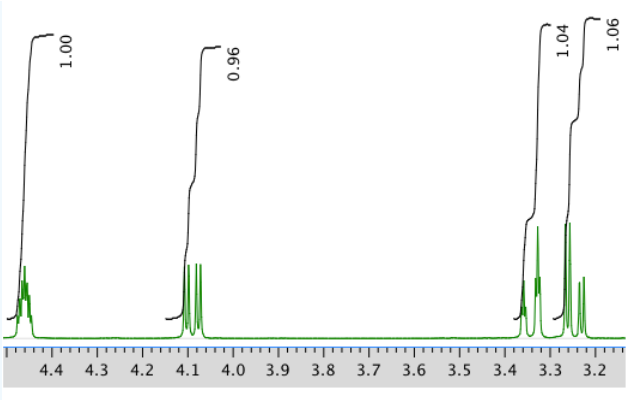
Present an analysis of the following data and propose a structure.

MW: 145 amu

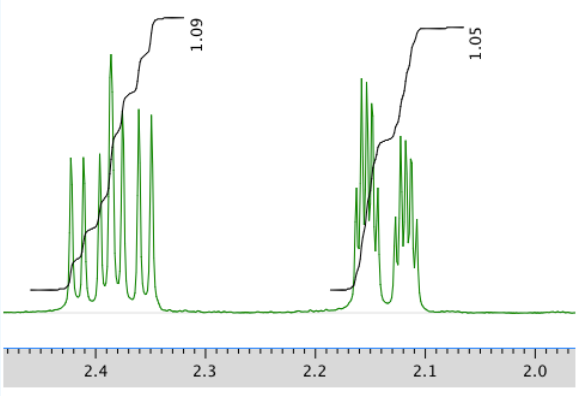
The full ^{1}H NMR spectrum in D_2O:



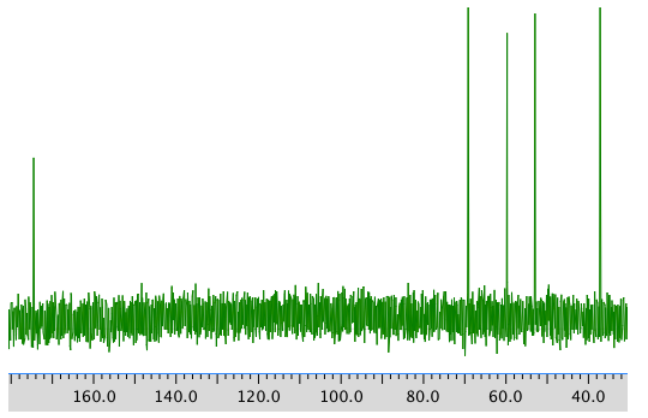
An expanded view of ^{1}H NMR spectrum:



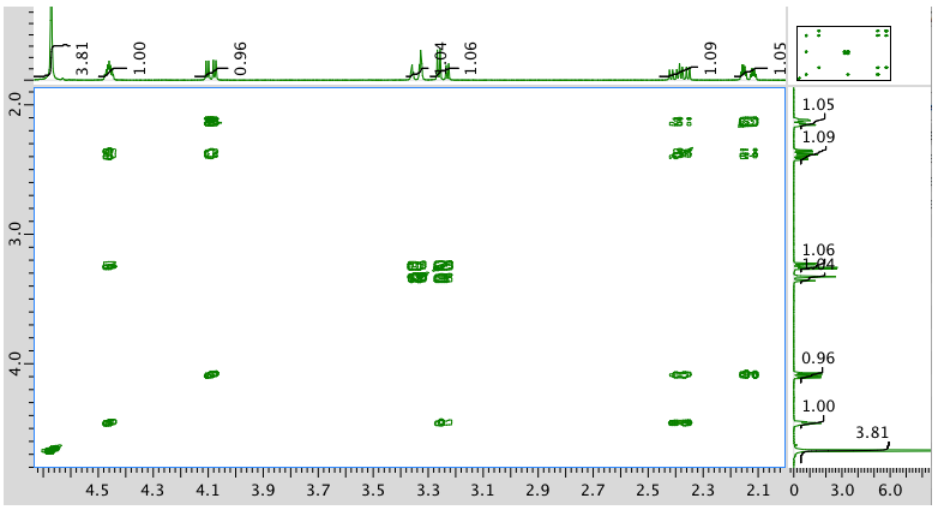
Another expanded view:



^{13}C NMR spectrum:

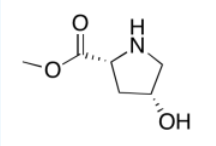


COSY spectrum:



Answer

The data should be consistent with this structure:

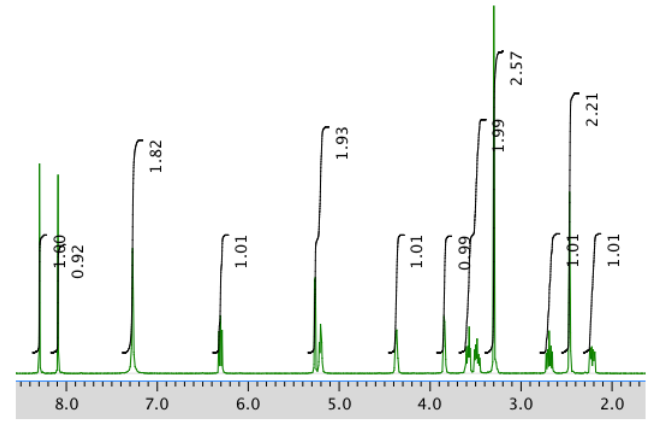


Exercise 5.6.10

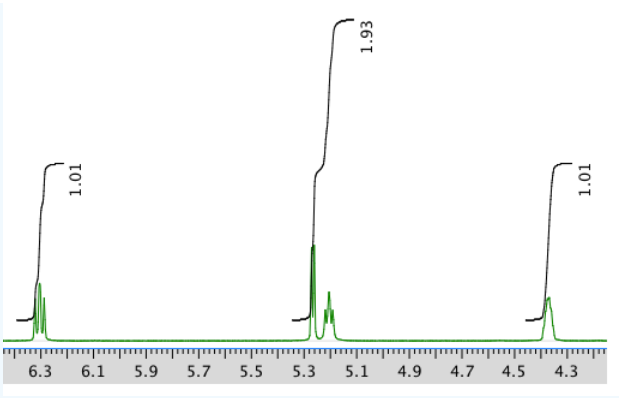
Present an analysis of the following data and propose a structure.

MW: 251 amu

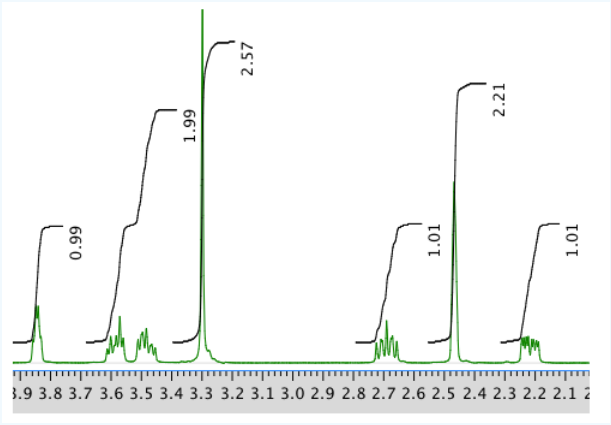
The full ^{1}H NMR spectrum in DMSO-d_6:



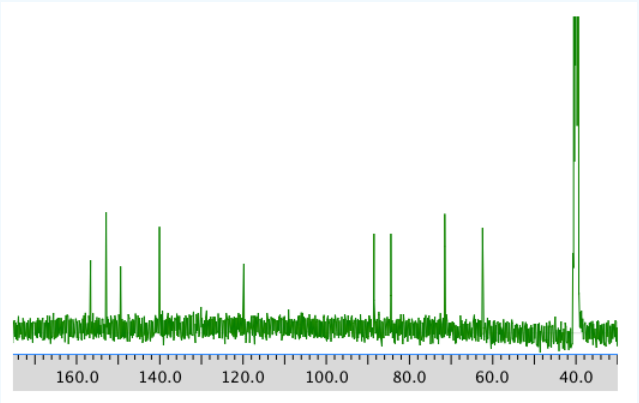
An expanded view of the ^{1}H NMR spectrum:



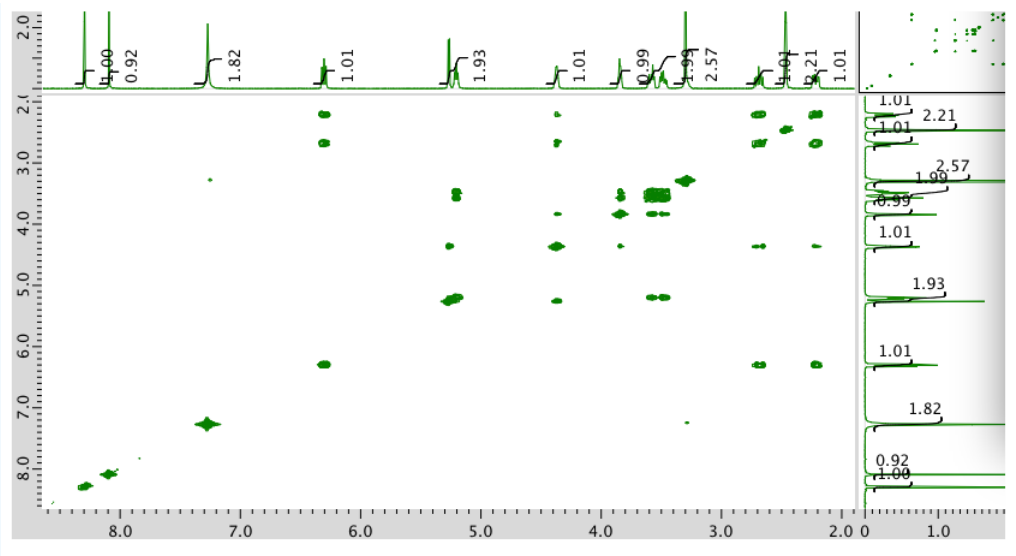
Another expansion:



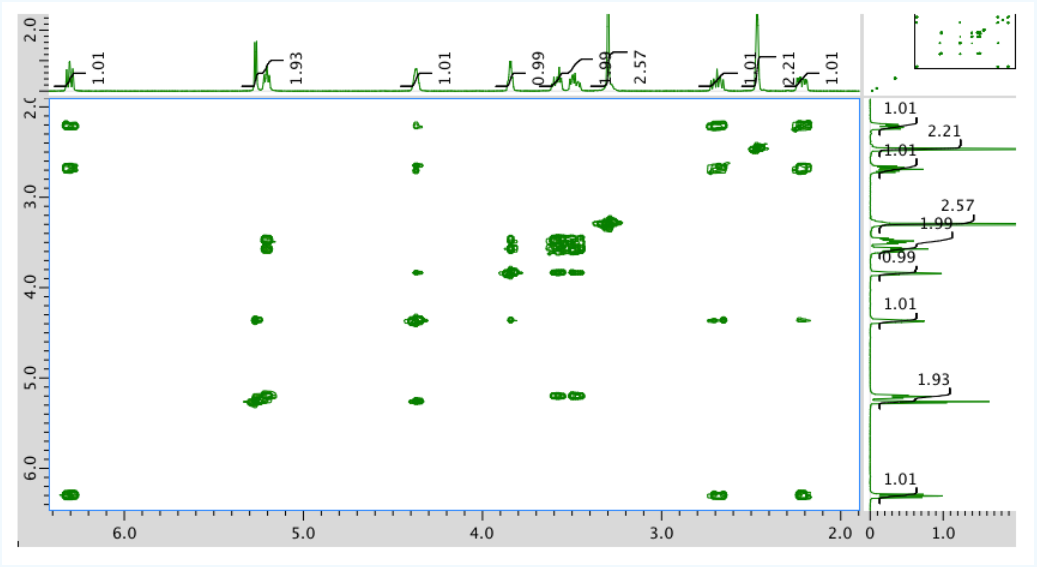
^{13}C NMR spectrum:



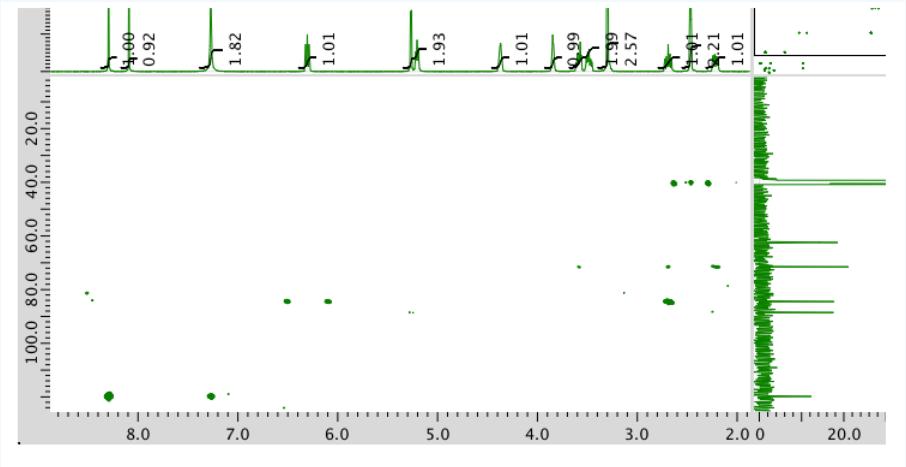
COSY spectrum:



Expansion of COSY:

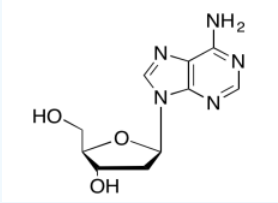


HMQC spectrum:



Answer

The data should be consistent with this structure:

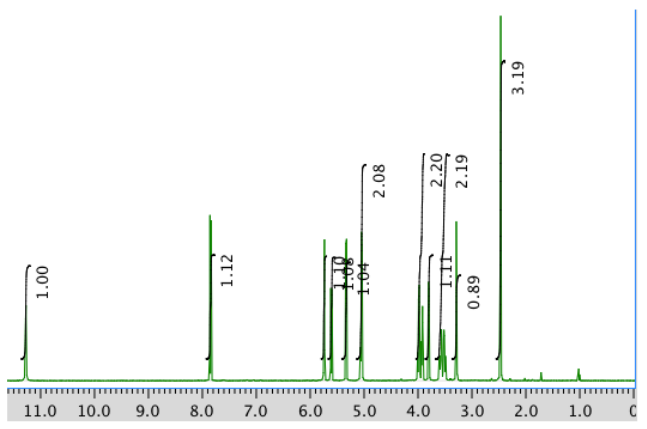


Exercise 5.6.11

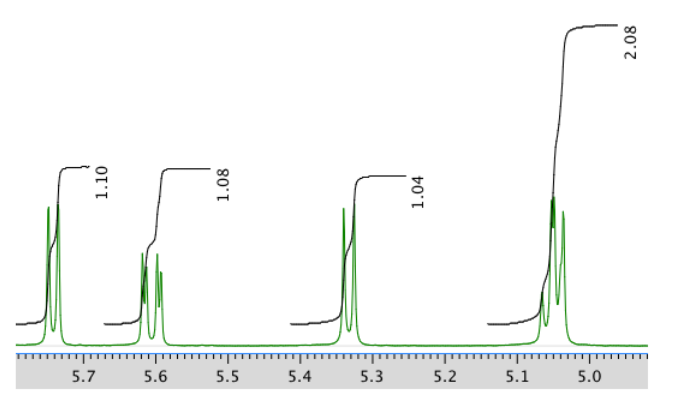
Present an analysis of the following data and propose a structure.

MW: 244 amu

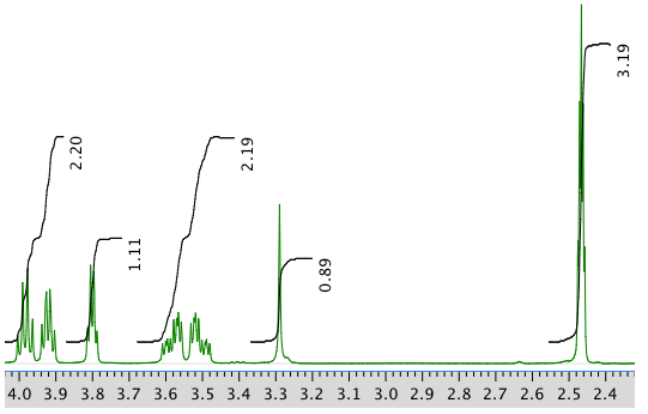
The full ^{1}H NMR spectrum in DMSO-d_6:



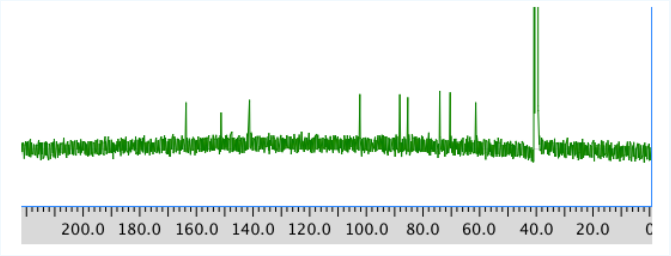
An expanded view of the ^{1}H NMR spectrum:



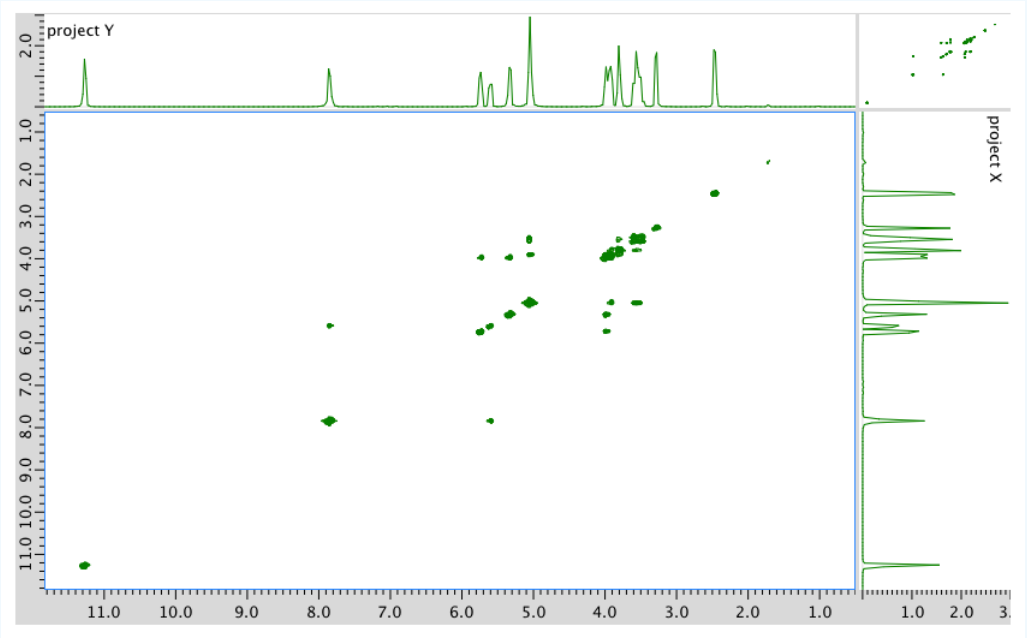
Another expansion of the 1H NMR spectrum:



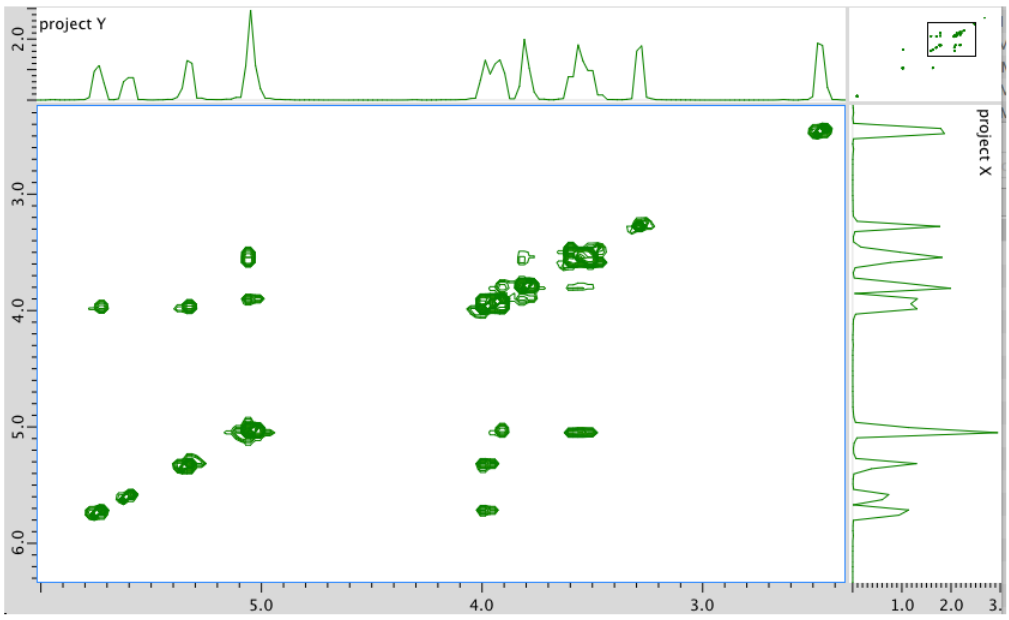
^{13}C NMR spectrum:



COSY:

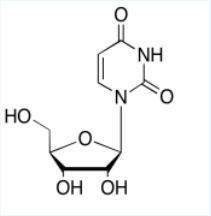


An expanded view of the COSY spectrum:



Answer

The data should be consistent with this structure:

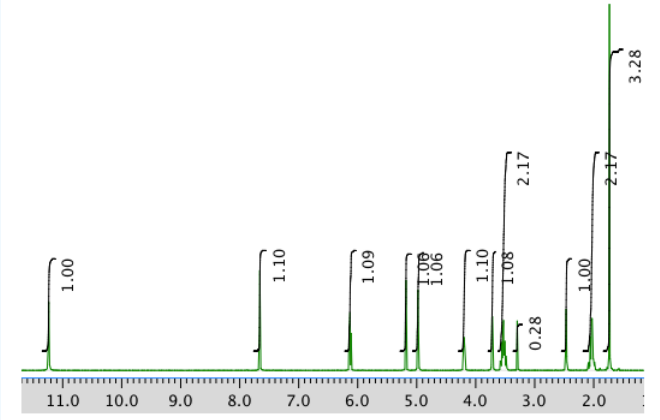


Exercise 5.6.12

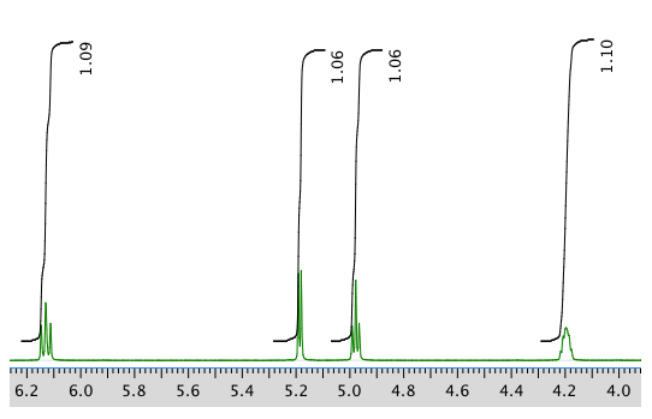
Present an analysis of the following data and propose a structure.

MW: 242 amu

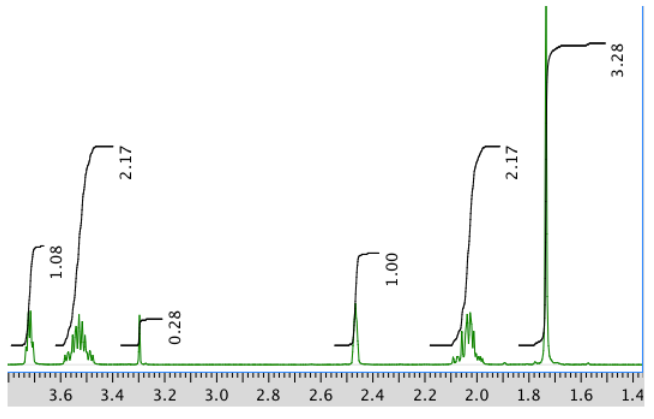
The full ^{1}H NMR spectrum in DMSO-d_6:



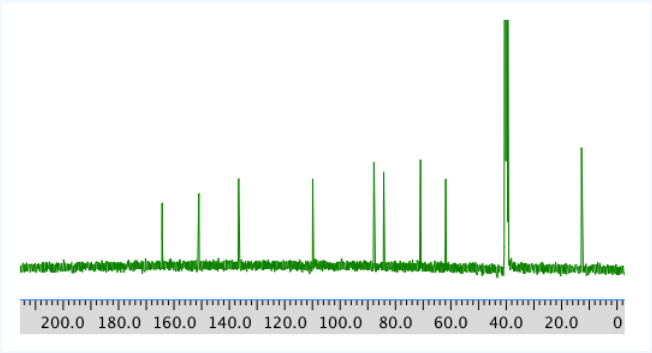
Expansion of the ^{1}H NMR spectrum:



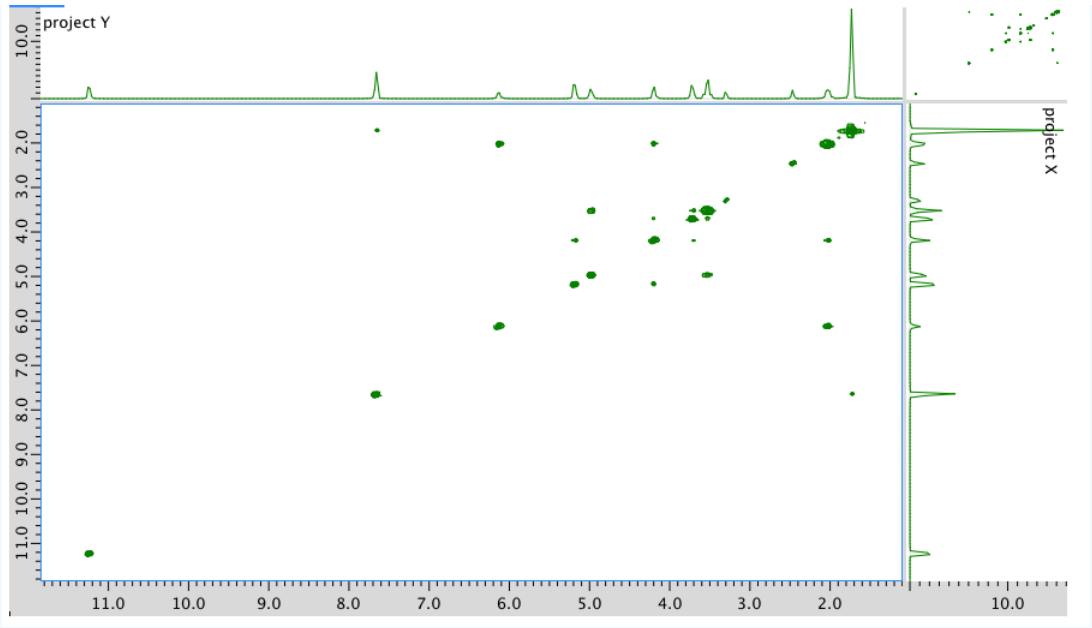
Another expansion:



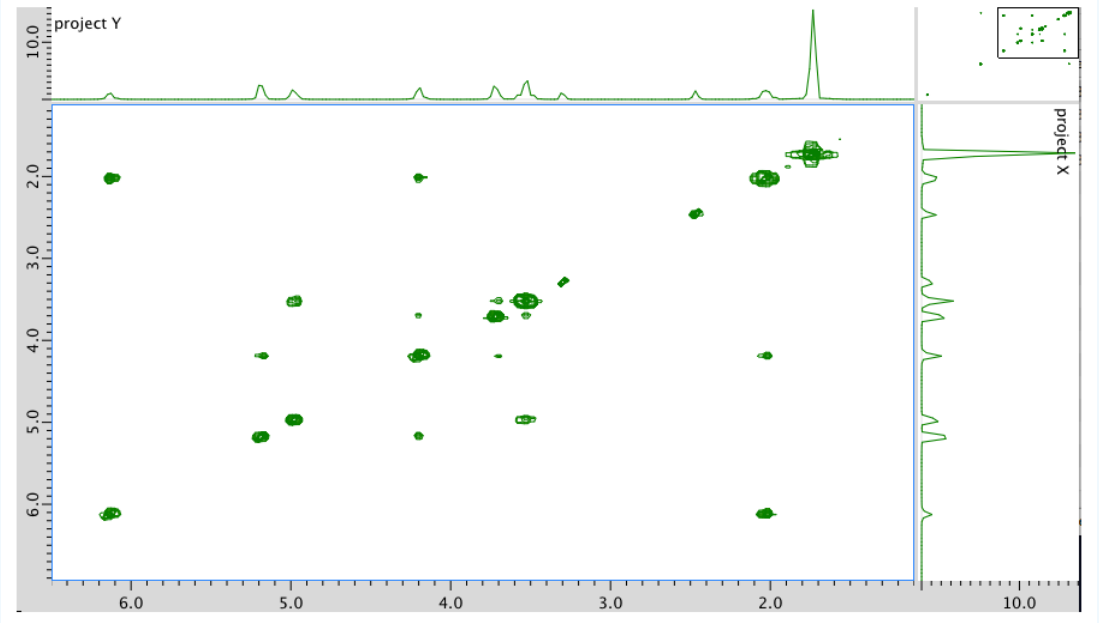
^{13}C NMR spectrum:



COSY:

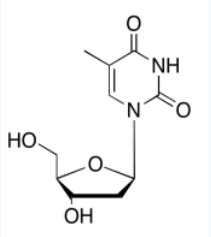


An expansion of the COSY spectrum:



Answer

The data should be consistent with this structure:

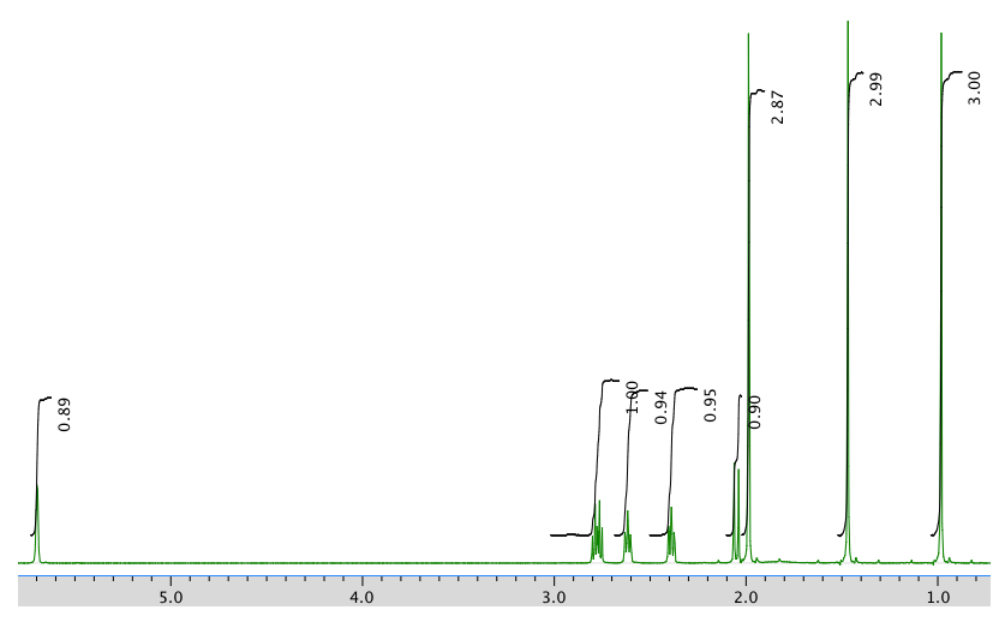


Exercise 5.6.13

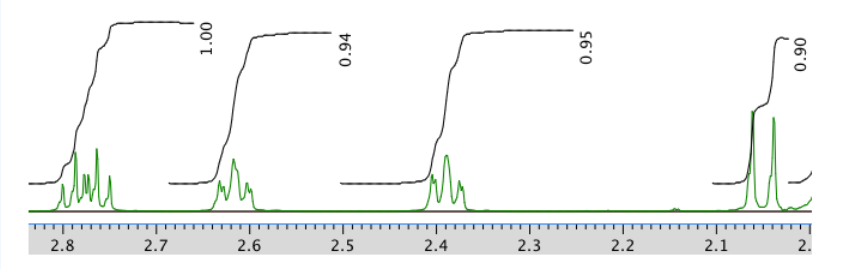
Present an analysis of the following data and propose a structure.

MW: 152 amu

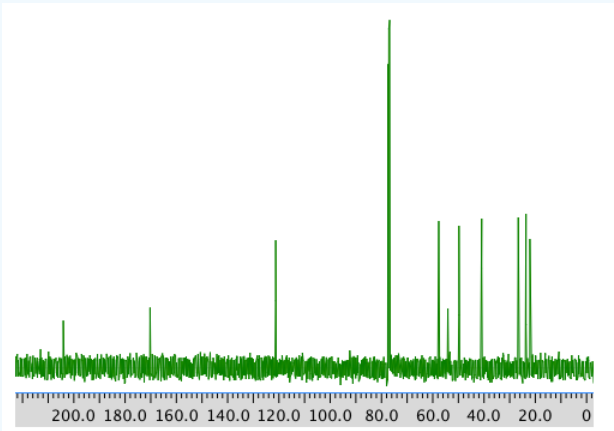
The full ^{1}H NMR spectrum in $CDCl_3$:



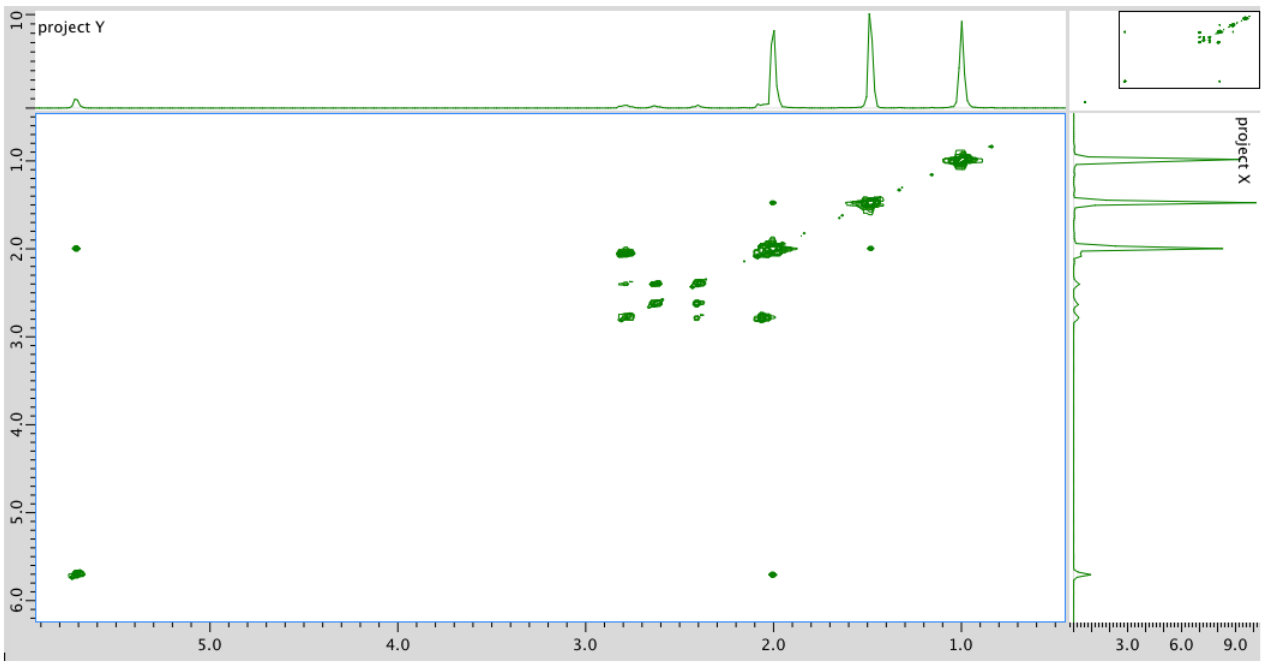
An expansion of the ^{1}H NMR spectrum:



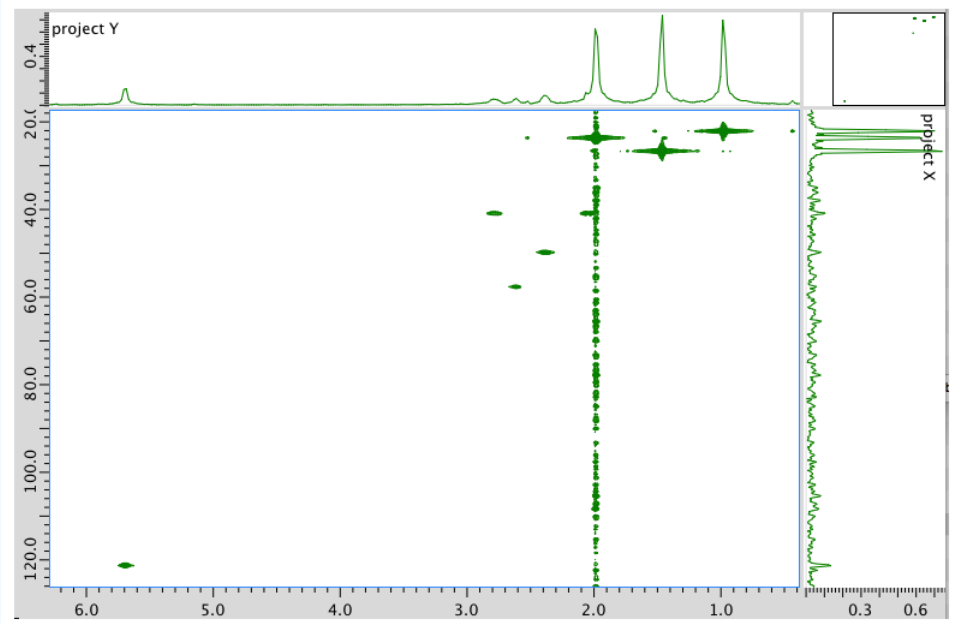
^{13}C NMR spectrum in CDCl3:



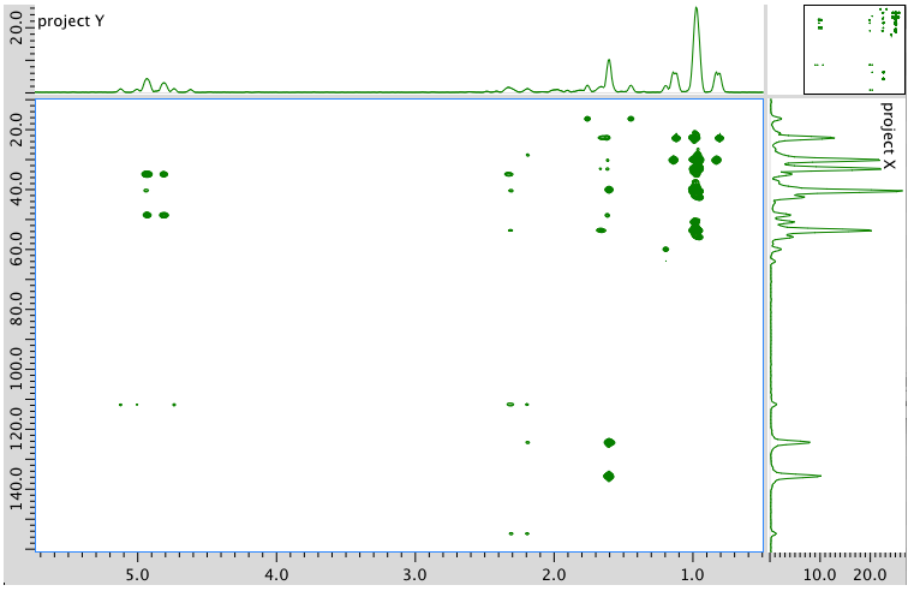
COSY spectrum:



HMQC spectrum:



HMBC spectrum:



Answer

^{1}H NMR:

Chemical shift (ppm)	Integration	Multiplicity	Partial structure
5.7	1H	singlet	C=C**H**-CO
2.77	1H	multiplet	CH_2-C**H**-CO
2.62	1H	multiplet	C-C**H**-C
2.39	1H	multiplet	C-C**H**-C
2.05	1H	doublet?	C-C**H**-CH?
1.96	3H	singlet	C-C**H**$_3$
1.48	3H	singlet	C-C**H**$_3$
0.98	3H	singlet	C-C**H**$_3$

^{13}C NMR:

Chemical shft (ppm)	Type of carbon
204	sp^2 C=O
170	sp^2
121	sp^2
59	sp^3
55	sp^3
50	sp^3
41	sp^3
28	sp^3
24	sp^3

22	sp^3

COSY:

Assignment	^1H	COSY
1	2.39	2.77, 2.62?
3	5.7	2.05?
5	2.62	2.62?
7a	2.77	2.05
7b	2.05	2.77
8	1.48	--
9	0.98	--
10	1.96	--

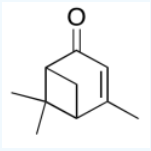
Formula:

$C_{10}H_{14}O$ (1 O indicated from shift in ^{13}C, ^1H NMR)

FW = $(10 \times 12) + (14 \times 1) + (1 \times 16) = 150$

Degrees of unsaturation = \(\frac{(2 \times 10) + 2 - 14}{2} = 4 units (e.g. 2 rings, 2 double bonds)

The data should be consistent with this structure:

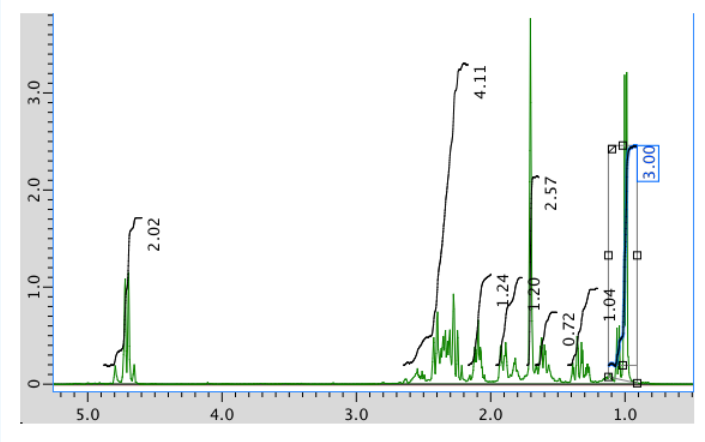


Exercise 5.6.14

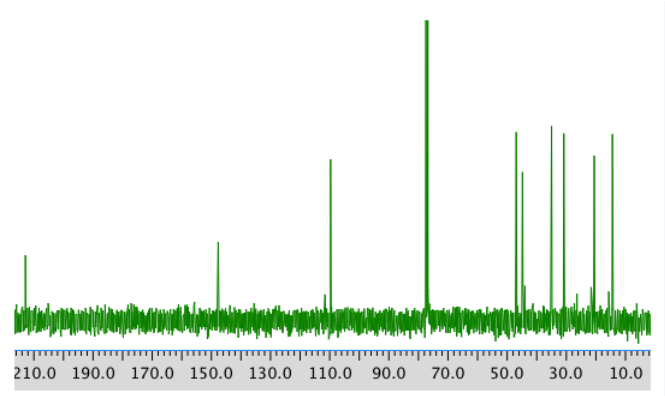
Present an analysis of the following data and propose a structure.

MW: 152 amu

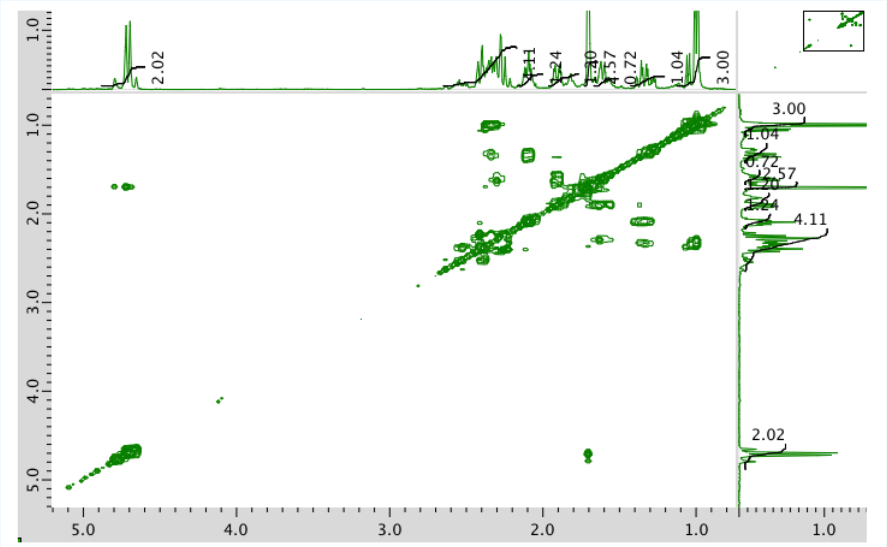
The full ^1H NMR spectrum in $CDCl_3$:



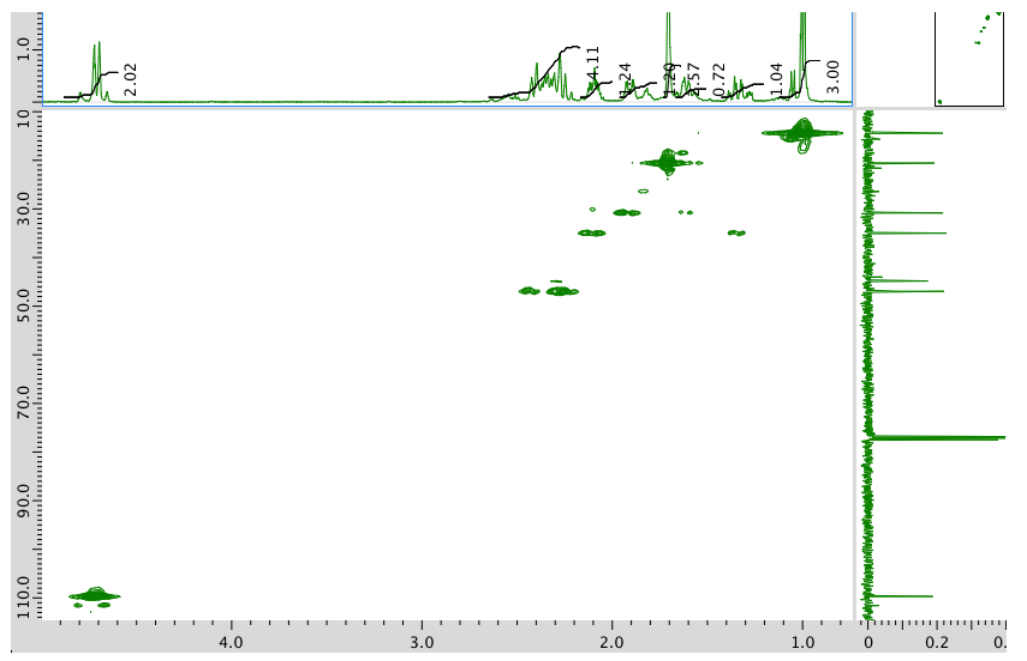
13C NMR spectrum:



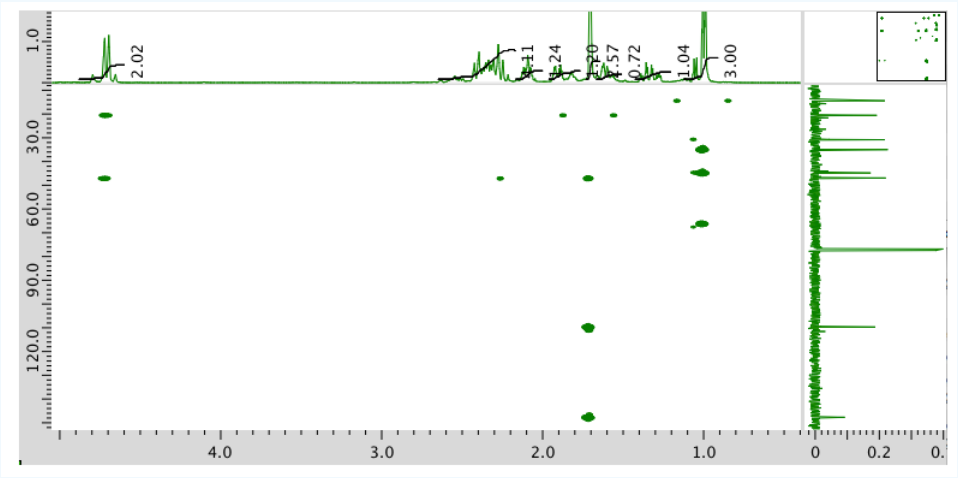
COSY spectrum:



HMQC spectrum:

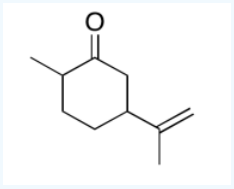


HMBC spectrum:



Answer

The data should be consistent with this structure:

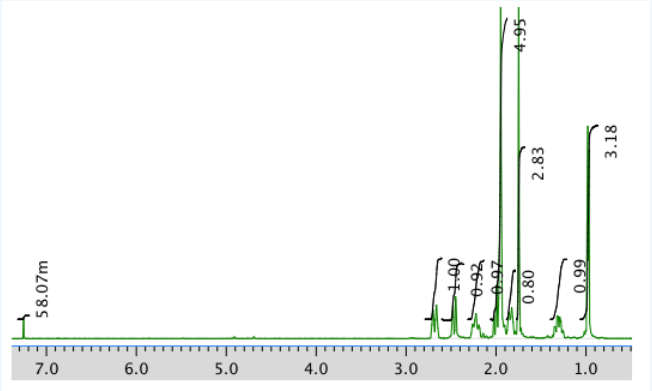


Exercise 5.6.15

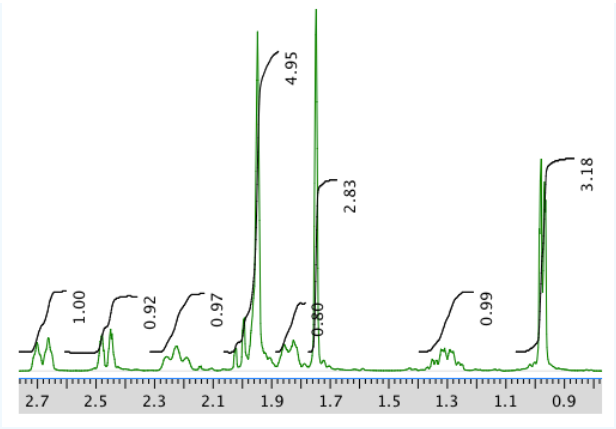
Present an analysis of the following data and propose a structure.

MW: 150 amu

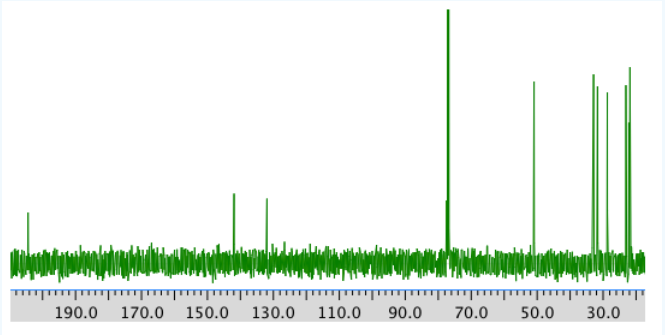
The full ^{1}H NMR spectrum in $CDCl_3$:



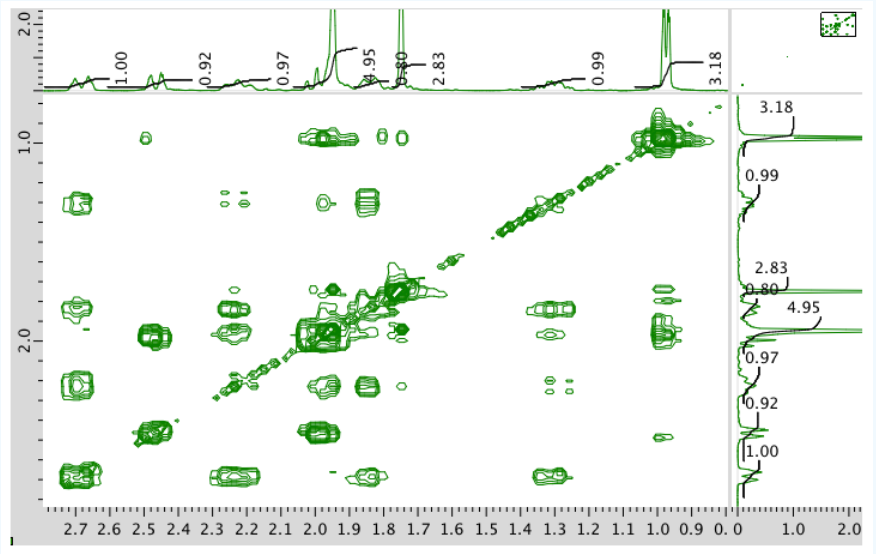
An expansion of the ^{1}H NMR spectrum:



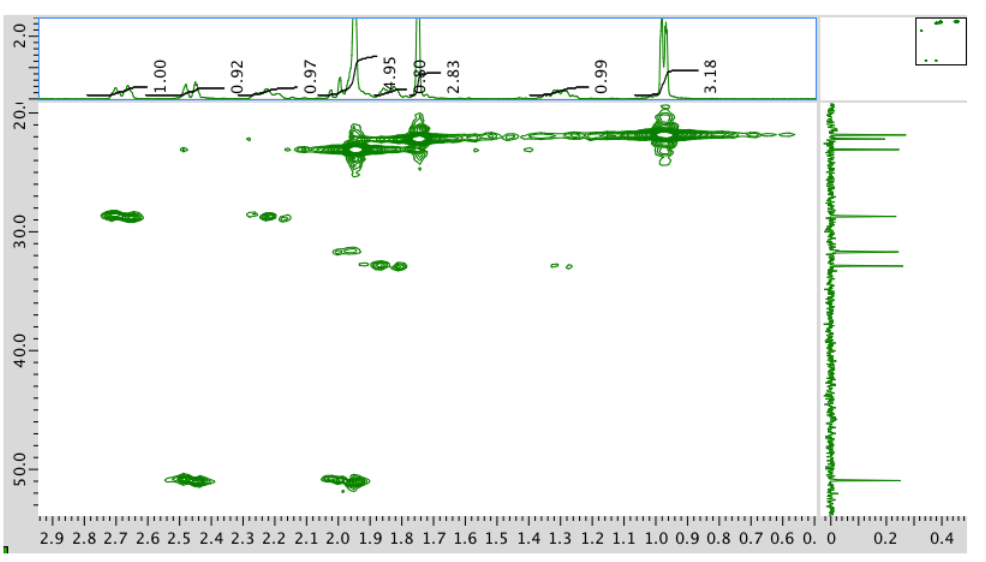
^{13}C NMR spectrum:



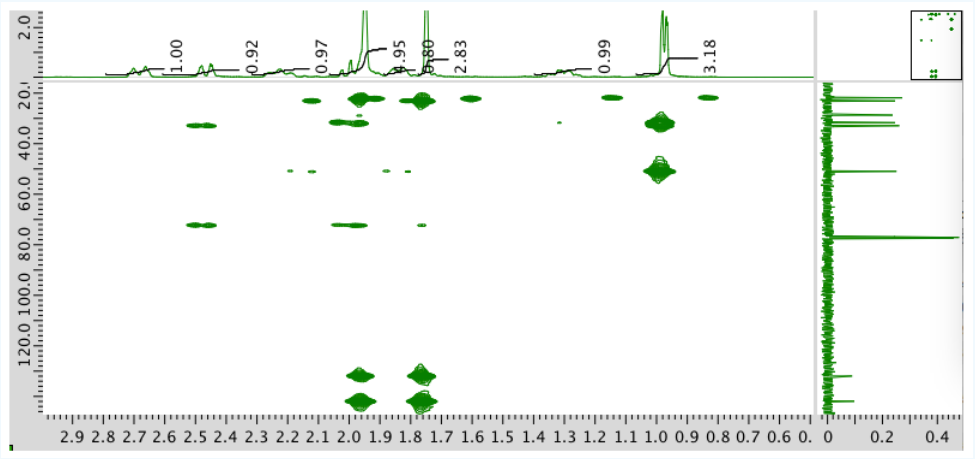
COSY spectrum:



HMQC spectrum:

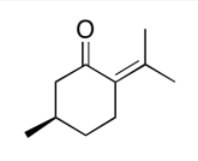


HMBC spectrum:



Answer

The data should be consistent with this structure:



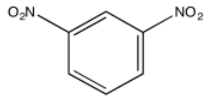
NMR spectra obtained on a JEOL 400 MHz NMR spectrometer.

5.7: 2D NMR Solutions

Exercise 5.1.1:

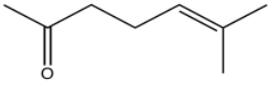
ethyl butanoate

Exercise 5.1.2:

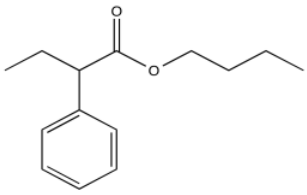


Exercise 5.1.3:

6-methylhept-5-en-2-one

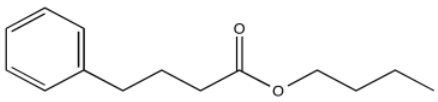


Exercise 5.1.4:



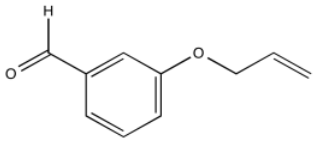
butyl 2-phenylbutanoate

Exercise 5.1.5:



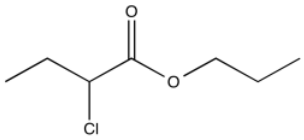
butyl 4-phenylbutanoate

Exercise 5.1.6:

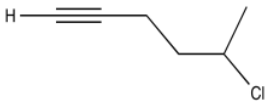


3-(allyloxy)benzaldehyde

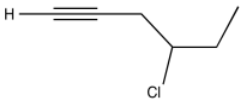
Exercise 5.1.7:



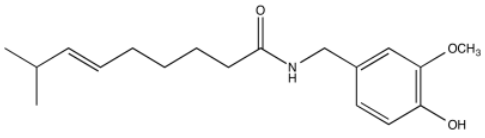
Exercise 5.1.8:



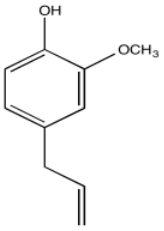
Exercise 5.1.9:



Exercise 5.1.10:

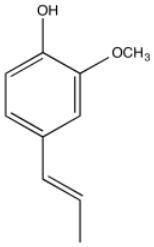


Exercise 5.1.11:



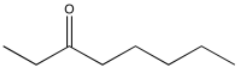
eugenol

Exercise 5.1.12:

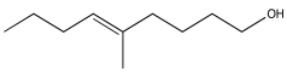


isoeugenol

Exercise 5.2.1:

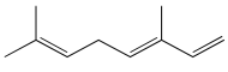


Exericse 5.2.2:

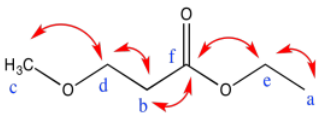


Exercise 5.2.3:

Ocimene

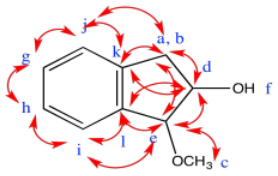


Exercise 5.3.1:



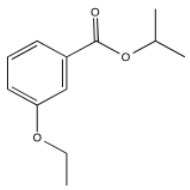
	^{1}H	^{13}C	HMBC
a	1.1	15	e
b	2.4	32	d, f
c	3.2	58	d
d	3.7	63	b, c
e	4.0	69	a, f
f	-	172	b, e

Exercise 5.3.2:

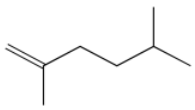


	^{1}H	^{13}C	HMBC
a	2.8	38	d, e, j, k
b	3.2		
c	3.2	57	e
d	4.4	78	a/b, e, k, l
e	4.7	92	a/b, c, d, i, l
f	5.0	-	-
g	7.1	127	h, i, j, k, l
h	7.2	127	g, i, j, k, l
i	7.3	126	e, g, h, j, k, l
j	7.4	129	a/b, g, h, i, k, l
k	-	140	a/b, d, g, h, i, j, l
l	-	142	d, e, g, h, i, j, k

Exercise 5.3.3:

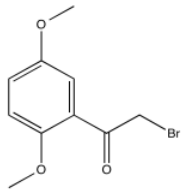


Exercise 5.3.4:

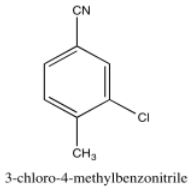


2,5-dimethylhex-1-ene

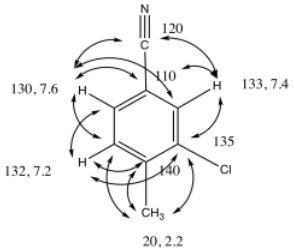
Exercise 5.3.5:



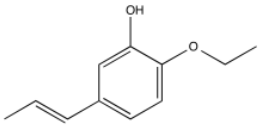
Exercise 5.3.6:



3-chloro-4-methylbenzonitrile

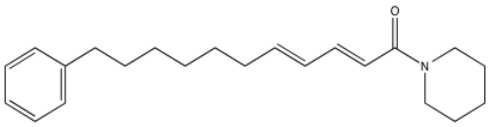


Exercise 5.3.7:

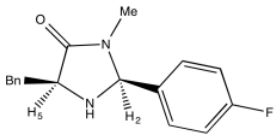


(*E*)-2-ethoxy-5-(prop-1-en-1-yl)phenol

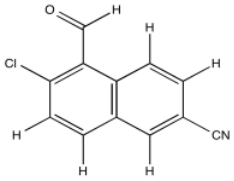
Exercise 5.3.8:



Exercise 5.4.1:



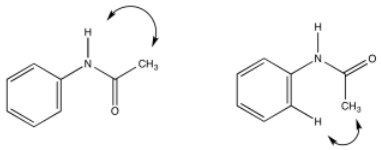
Exercise 5.4.2:



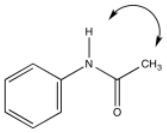
Exercise 5.4.3:

a) Due to resonance, there is substantial pi character to the amide bond which restricts free rotation around that bond.

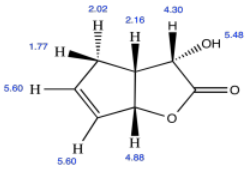
b)



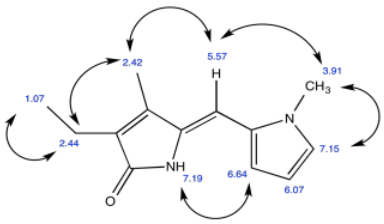
c)



Exercise 5.4.4:

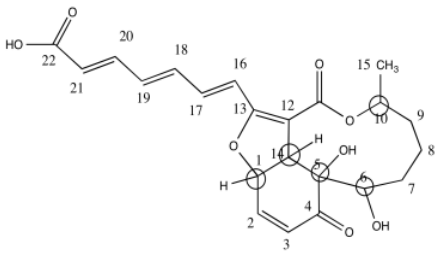


Exercise 5.4.5:

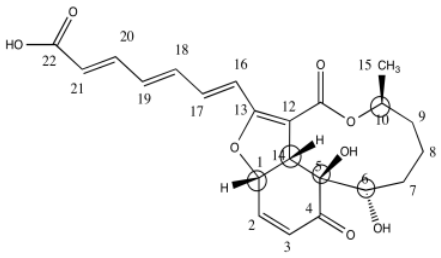


Exercise 5.4.6:

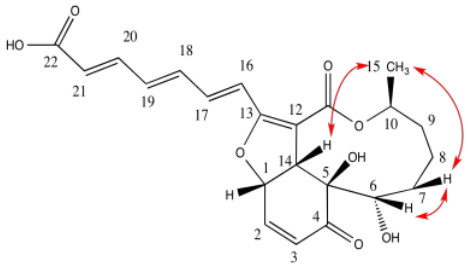
a)



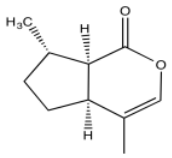
b)



c)

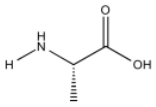


Exercise 5.4.7:



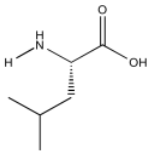
Catnip (nepetalactone)

Exercise 5.5.1:



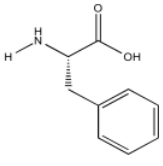
Alanine

Exercise 5.5.2:



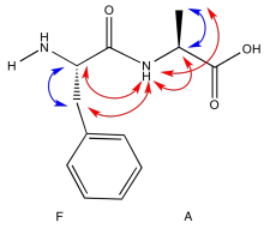
Leucine

Exercise 5.5.3:

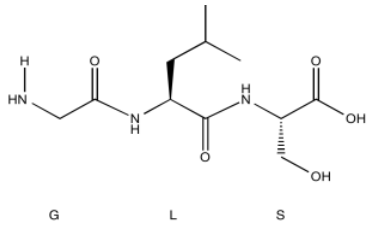


Phenylalanine

Exercise 5.5.4:



Exercise 5.5.5:



Exercise 5.6.1:

^{1}H NMR

Chemical shift (ppm)	Integration	Multiplicity	Partial Structure
5.54	2H	multiplet	C**H**=C (x 2)
4.17	2H	doublet	O-C**H**$_2$-CH
2.08	2H	quintet	CH-C**H**$_2$-CH$_3$
1.47	1H	boad singlet	OH
0.95	3H	triplet	CH$_2$-C**H**$_3$

* total # H: 10

^{13}C NMR

Chemical shift (ppm)	Type of carbon
134	sp^2
128	sp^2
58	sp^3-O
21	sp^3
14	sp^3

*total # C: 5

COSY

Assignment	^{1}H	COSY
A	0.95	2.08
B	2.08	0.95, 5.54
C	4.17	5.54
D	5.54	2.08

E	5.54	4.17

*HMQC indicates two hydrogens at 5.54 are in two different environments

HMQC

Assignment	**^{13}C**	**^{1}H**
A	14	0.95
B	21	2.08
C	58	4.17
D	128	5.54
E	134	5.54

Formula:

$C_5H_{10}O$ (1 O indicated from shift in ^{13}C, ^{1}H NMR)

FW = $5 \times 12) + (10 \times 1) + (1 \times 16) = 86$

Compare C_5H_{10} ratio to C_5H_{12} in hydrocarbon

Degrees of unsaturation = \(\frac{(2 \times 5) + 2 - 10}{2} = 1 unit (1 double bond)

The data tables should be consitent with this structure:

pent-2-en-1-ol (could be *cis* or *trans* based on this analysis)

Exercise 5.6.2:

^{1}H NMR:

Chemical shift (ppm)	**Integration**	**Multiplicity**	**Partial structure**
4.7	5H	singlet	solvent
3.93	1H	triplet	CH_2-C**H**-N
2.40	2H	multiplet	CH_2-C**H_2**?
2.09	2H	multiplet	C**H_2**-CH_2?
1.4	9H	singlet	C(C**H_3**)$_3$

*Total number of H: 19 H

^{13}C NMR:

Chemical shift (ppm)	**Type of carbon**
170	sp^2 (C=O)
80	sp^3 (C-O)
52	sp^3 (C-N)
32	sp^3
28	sp^3
26	sp^3

*Total number of C: 6 apparent, but two more suggested by symmetry (3 methyl groups in ^{1}H NMR) for 8 C; a third extra suggested by MW fit for 9 C

COSY:

Assignment	^{1}H	COSY
Solvent	4.7	--
B	3.93	2.40
D	2.40	2.09
C	2.09	2.40, 2.09
A	1.4	--

Formula:

$C_9H_{18}O_3N_2$ (extra O indicated from shift in ^{13}C, ^{1}H NMR; second O suggested by C=O in ^{13}C NMR; additional CO needed to fit MW)

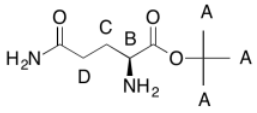
FW = $(9 \times 12) + (18 \times 1) + (3 \times 16) + (2 \times 14) = 202$

FW = ((9 \times 12) + (18 \times 1) + (3 \times 16) + (2 \times 14) = 202\)

Compare C_9H_{18} to C_9H_{22} for the corresponding hydrocarbon corrected for two nitrogens (therefore two extra hydrogens)

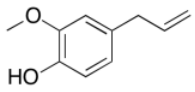
Degrees of unsaturation = $\frac{(2\times9)+2+2-10}{2} = 2$ units (2 double bonds)

The data tables should be consistent with this structure:



Exercise 5.6.3:

The data should be consistent with this structure:



Exercise 5.6.4:

^{1}H NMR:

Chemical shift (ppm)	Integration	Multiplicity	Partial Structure
4.71	--	singlet	solvent
4.17	1H	doublet?	CO-C**H**-N
3.75	3H	singlet	O-C**H**$_3$
2.25	1H	multiplet	CH-C**H**-(CH$_3$)$_2$
0.92	6H	triplet?	2 x C**H**$_3$

^{13}C NMR:

Chemical shift (ppm)	Type of carbon
170	sp^2 C=O

60	sp^3 C-N
52	sp^3 C-O
30	sp^3 C
19	sp^3 C

COSY:

Assignment	**^{1}H**	**COSY**
A	4.17	2.25
B	3.75	--
C	2.25	4.17
D	0.92	2.25

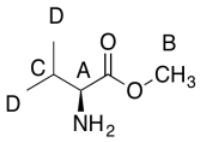
Formula:

$C_6H_{13}O_2N$ (1 O indicated from shift in ^{13}C, ^{1}H NMR)

FW = $(6 \times 120 + (13 \times 1) + (2 \times 16) + (1 \times 14) = 131$

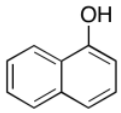
Degrees of unsaturation = $\frac{(2\times6)+2+1-13}{2} = 1$ unit (1 double bond)

The data should be consistent with this structure:



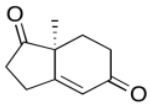
Exercise 5.6.5:

The data should be consistent with this structure:



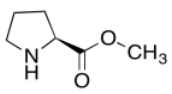
Exercise 5.6.6:

The data should be consistent with this structure:



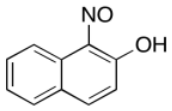
Exercise 5.6.7:

The data should be consistent with this structure:



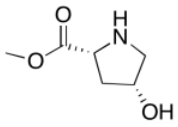
Exercise 5.6.8:

The data should be consistent with this structure:



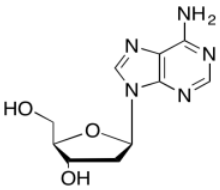
Exercise 5.6.9:

The data should be consistent with this structure:



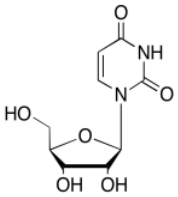
Exercise 5.6.10:

The data should be consistent with this structure:



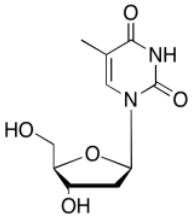
Exercise 5.6.11:

The data should be consistent with this structure:



Exercise 5.6.12:

The data should be consistent with this structure:



Exercise 5.6.13:

^{1}H NMR:

Chemical shift (ppm)	Integration	Multiplicity	Partial structure
5.7	1H	singlet	C=C**H**-CO
2.77	1H	multiplet	CH_2-C**H**-CO
2.62	1H	multiplet	C-C**H**-C
2.39	1H	multiplet	C-C**H**-C

2.05	1H	doublet?	C-C**H**-CH?
1.96	3H	singlet	C-C$\mathbf{H}_3$
1.48	3H	singlet	C-C$\mathbf{H}_3$
0.98	3H	singlet	C-C$\mathbf{H}_3$

^{13}C NMR:

Chemical shft (ppm)	**Type of carbon**
204	sp^2 C=O
170	sp^2
121	sp^2
59	sp^3
55	sp^3
50	sp^3
41	sp^3
28	sp^3
24	sp^3
22	sp^3

COSY:

Assignment	**^{1}H**	**COSY**
1	2.39	2.77, 2.62?
3	5.7	2.05?
5	2.62	2.62?
7a	2.77	2.05
7b	2.05	2.77
8	1.48	--
9	0.98	--
10	1.96	--

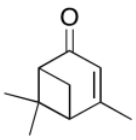
Formula:

$C_{10}H_{14}O$ (1 O indicated from shift in ^{13}C, ^{1}H NMR)

FW = $(10 \times 12) + (14 \times 1) + (1 \times 16) = 150$

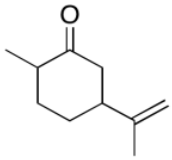
Degrees of unsaturation = \(\frac{(2 \times 10) + 2 - 14}{2} = 4 units (e.g. 2 rings, 2 double bonds)

The data should be consistent with this structure:



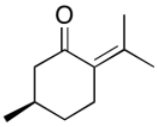
Exercise 5.6.14:

The data should be consistent with this structure:



Exercise 5.6.15:

The data should be consistent with this structure:



CHAPTER OVERVIEW

6: Introductory Mass Spectrometry

6.1: Introduction to Mass Spectrometry

Through mass spectrometry we can learn the molecular mass of a compound (more commonly called the molecular weight). Knowing the molecular weight helps us to determine a structure by limiting the possibilities for the molecular formula.

Individual molecules often fall apart during the mass spectrometry experiment. As a result, in addition to measuring the mass of an entire molecule, we also obtain the weights of various smaller pieces of the molecule. That may add some confusion to the data. However, these fragments provide an idea about what parts make up the whole molecule.

A mass spectrum of hexane (molecular weight 86) illustrates what the data looks like.

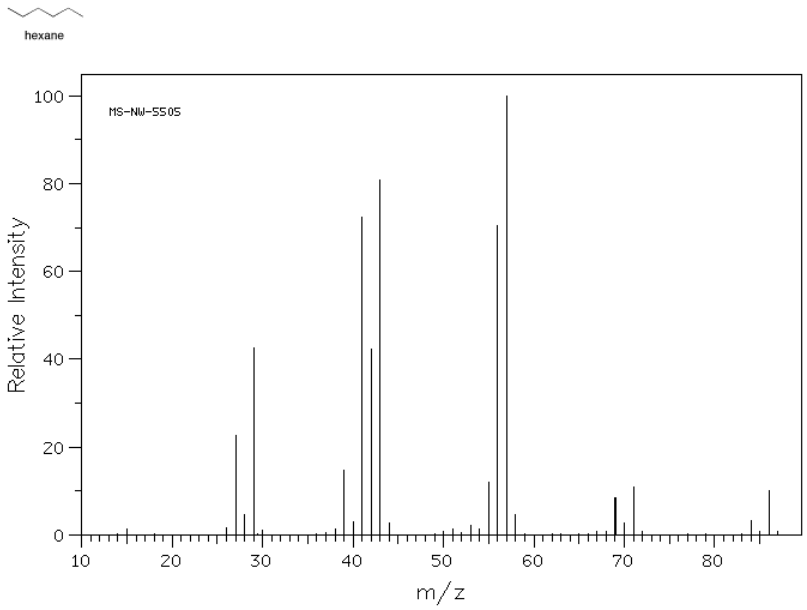


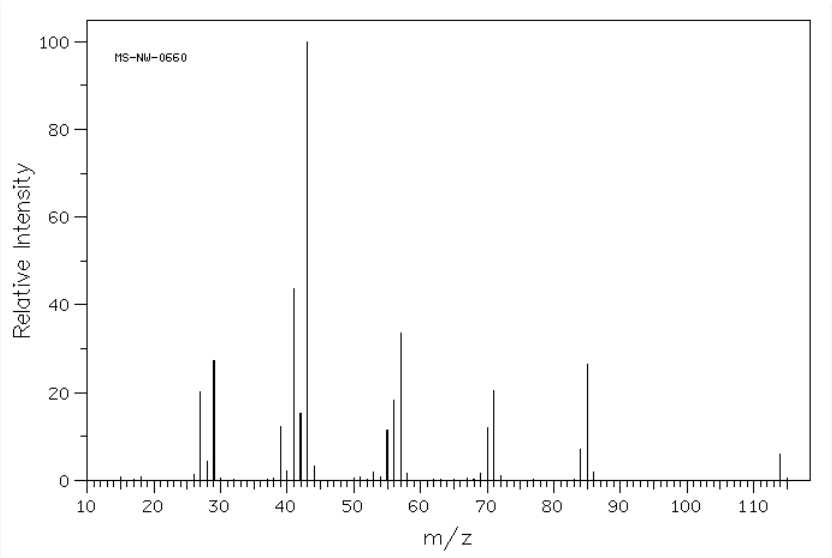
Figure 6.1.1: Mass spectrum of hexane.

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 22 August 2008)

- The y-axis is usually labeled "abundance" or "relative intensity". This axis shows how the relative ratios of molecules in the sample that have a particular mass.
- The x-axis is labeled "m/z" and corresponds to molecular mass. The designation m/z refers to the fact that this technique really measures the ratio of an ion's mass to its charge.
- A mass spectrum does not show the results from one molecule, but from millions of molecules. Because it is displaying results for a population of molecules, more than one mass is shown
- Many of the molecules in the sample fall apart during the experiment.
- A mass spectrum is a bar graph showing the weights of entire molecules as well as smaller pieces of molecules. The entire molecule must have the largest mass, the one farthest to the right, because if a molecule falls into pieces the pieces would be smaller than the whole.

? Exercise 6.1.1

The following figure shows the mass spectrum of a saturated hydrocarbon (containing only carbon and hydrogen with only single bonds between carbons, not double bonds).



a. Draw five different structures that would have the molecular weight of this compound.
b. Choose four smaller m/z values from the spectrum and draw one structure for each of them. Note that these fragments will not have complete Lewis structures.

6.2: The Mass Spectrometry Experiment

How can we "weigh" something as small as a molecule? In mass spectrometry, the balance between two different physical phenomena can be used to measure mass.

- One of these phenomena is inertia; a moving object with more mass can't slow down or turn as quickly as an object with less mass.
- The second phenomenon is the interaction of a charged particle with a magnetic field.

When placed in a magnetic field, a charged particle (such as an electron or proton) will be attracted toward one end of the field. When coupled with the phenomenon of inertia, this magnetic attraction can be used to differentiate between particles with different mass.

- Because an ion moving very fast has inertia, it tends to keep moving in a straight line.
- If a magnetic field is placed across the path of the ion, the ion will deviate from its path because of magnetic attraction.

Suppose two particles moving parallel to each other enter into a magnetic field at the same time. One of these particles is heavier than the other. Both are deflected a little bit from their original path, but one of the particles -- the heavier one -- does not turn as easily and so it is not deflected as much. If we can measure how far each particle is deflected, we may be able to get an idea of the mass in each case.

- The heavier the ion, the less it will deviate from its path, because its inertia keeps carrying it forward.
- The lighter the ion, the more sharply it will deviate from its path, because it hasn't much inertia to keep it going straight.

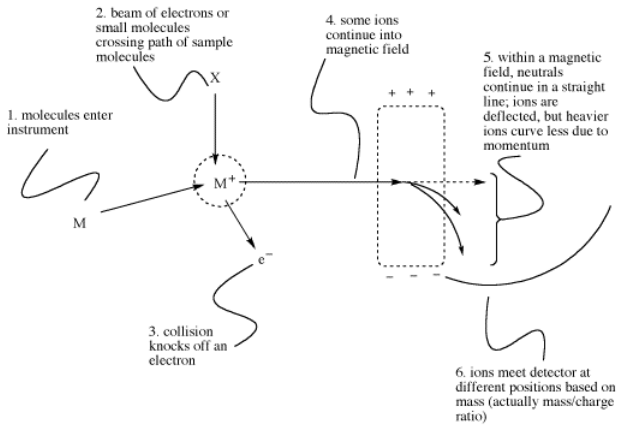


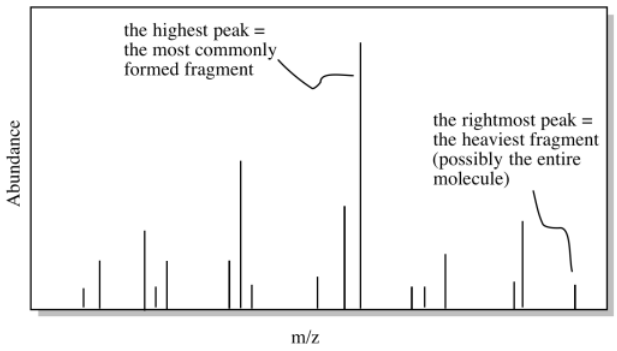
Figure 6.2.1: A very approximate schematic of a typical mass spectrometry experiment.

Mass spectrometry only works with ions, not with neutral molecules. That means a neutral molecules must become charged in order to do this experiment. It is common to generate a cation from the molecule by removing one electron. The electron is knocked off the molecule in a collision. The collision can be caused in two different ways:

- The molecule can be sent through a stream of high-energy electrons. This method is called electron ionization.
- The molecule is sent through a stream of small molecules, such as ammonia or methane. This method is called chemical ionization.
- Electron ionization frequently results in the molecule falling to pieces because of the high energy of the electrons.
- Chemical ionization results in a "softer" collision because momentum can be dissipated through various bonds in both colliding molecules. Chemical ionization results in less fragmentation of the target molecule.
- However, after chemical ionization, the ionizing molecule sometimes sticks to the target molecule, leading to a greater "molecular" mass. For example, if ammonia is used for ionization, an extra mass may be observed at 17 amu higher than expected.

The data from a mass spectrum shows the abundance of ions of different masses in the spectrometer. Because molecules tend to fall apart under these conditions, many different masses are observed for one molecule. Most of these masses correspond to smaller pieces of the molecule after it has fallen apart. However, because we are always working with very large numbers of molecules when we look at a sample, there is a statistical chance that at least some of the molecules remained intact during the experiment. Also, because we are looking at a population of molecules, we get a graph that tells us the likely fate of the molecule under these

conditions. Maybe the molecule has a high probability of falling apart in a certain way to produce a fragment of a certain mass. In that case, we see a high abundance of ions in the spectrometer with that mass. The results look something like the simulated data below.



Of course, if the molecule does manage to hold together, then it will be bigger than any of the fragments that would result if it falls apart. The intact molecule will show up at the highest molecular weight, to the right in the graph. All the peaks to the left of it would represent different ways in which the molecule falls apart.

The reason the x-axis on a mass spectrum is labeled m/z (mass-to-charge ratio) is to acknowledge that there are really two factors contributing to the experiment. The "mass" or molecular weight that is measured really is the ratio of the molecular weight of the ion to its charge. In small molecules, the instrument usually measures ions with a charge of +1. In that case, the x axis really shows the mass of the molecule or of a fragment.

However, large molecules such as proteins have many, many sites where ions might form. Most obviously, they have lots of amino groups that might pick up extra protons. In that case, the charge is not just +1. What is often observed is a cluster of peaks representing different charges but related by the molecular weight of a protein.

6.3: GC-MS and LC-MS

There are other aspects of this experiment that have been left out of this description. For example, the experiment is done in a vacuum with a low concentration of sample. Among other reasons, these steps are taken to lower the population of molecules in the instrument; that decreases the chance that ions and molecules will bump into each other and undergo reactions with each other, which might lead to the formation of larger ions with all sorts of different masses.

However, there is one important instrumental consideration to discuss. In mass spectrometry, the sample can be purified immediately after it is introduced into the instrument to make sure that only one kind of molecule is being analysed at a time. This purification is accomplished through chromatography, and so mass spectrometry when done in this way is often referred to as "GC-MS" or "LC-MS", depending on the type of chromatography used.

GC-MS employs gas chromatography, sending components through a chromatography column that is heated in an oven so that compounds can be separated out largely based on their boiling points. LC-MS uses liquid chromatography, in which components are most often separated because of polarity differences, although other criteria can be utilized as well, based on the type of packing material that is used in the chromatography column.

The other advantage of this approach is that several different components of one mixture can be analysed one by one.

The GC part of a GC-MS, termed the chromatograph, generates a plot called a chromatogram.

- The chromatogram is a graph showing amount of molecules on the y axis and time on the x-axis.
- Retention time is the amount of time it takes a compound to move through the GC.
- Different compounds have different retention times based on their physical properties.

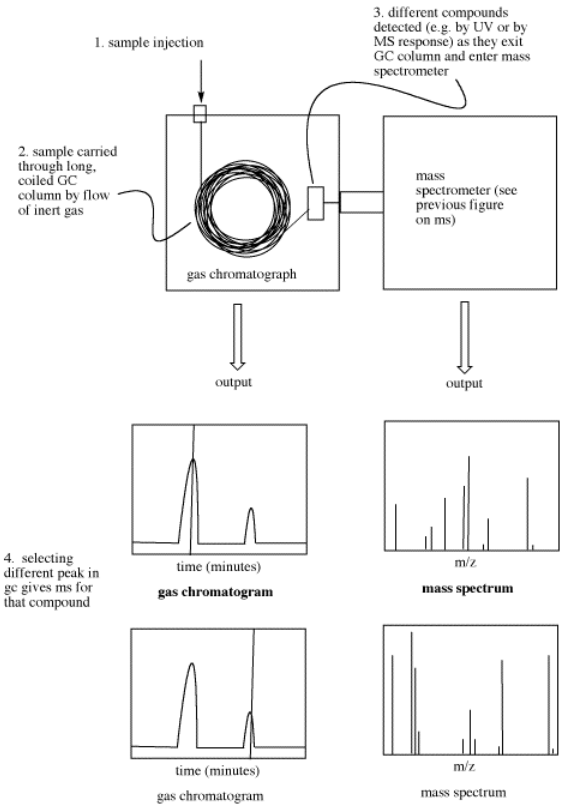
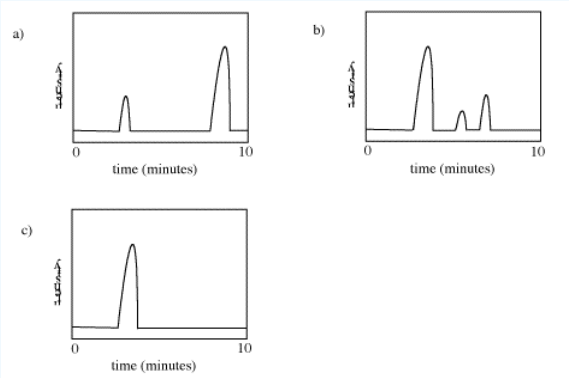


Figure 6.3.1: Approximate schematic of a GC-MS system, with representative data.

Retention time refers to how long it takes different compounds to emerge from the chromatography column. Peaks are seen on this plot whenever a compound enters the mass spectrometer. The mass spectrometer runs continuously and records whatever masses it detects at any time, so if a student selects a peak in the chromatogram on the computer screen, the corresponding mass spectrum can be shown.

Exercise 6.3.1

How many compounds appear to be present in each of the following gas chromatograms?



6.4: Molecular Ions

The ion that results from the loss of an electron is called the molecular ion. The molecular ion is an example of a radical cation. It is a cation because of its plus charge, and a radical because not all of its electrons are found in pairs.

Because an electron is so light compared to the mass of all the protons and neutrons in the molecule, the mass of the molecular ion is essentially the same as that of the original molecule.

The molecular ion, of course, has the same structure as the original molecule, minus one electron. But where does the lost electron come from? Usually the following trend is seen:

- Electrons are most easily lost from non-bonded pairs, since bonding electrons are at lower energy and are more stable (that is the whole point of forming a bond) and so they would be more difficult to remove.
- If there are no non-bonded pairs, electrons are most easily lost from pi bonds, because pi bonds are generally at higher energy than sigma bonds.
- If there are no non-bonded pairs and no pi bonds, electrons are most easily lost from sigma bonds.

Thus, in 2-pentanone the electron would most easily be lost from a lone pair; in hexene it would be lost most easily from the pi bond, and in heptane it would be lost most easily from a sigma bond.

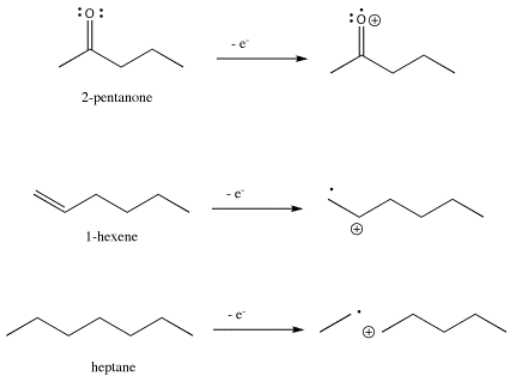
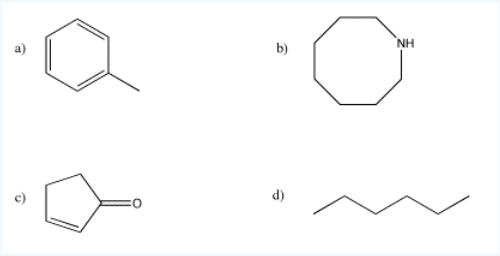


Figure 6.4.1: Ionization in three different organic compounds.

? Exercise 6.4.1

Draw an equation for the formation of a molecular ion from each of the following compounds.



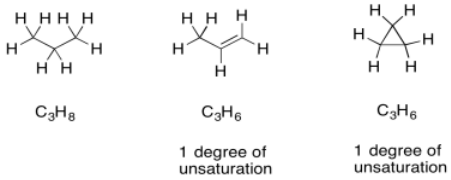
6.5: Molecular Weight, Molecular Formula and Degrees of Unsaturation

Finding the molecular weight of a compound in the mass spectrum can provide valuable evidence for a structure. This information is especially valuable if we already have an idea of what the structure might be. In that case, we could simply compare the observed molecular weight to the one that was expected.

If we do not know what the structure is, knowing the molecular formula does limit the possibilities. There will be only so many combinations of atoms that add up to a certain molecular weight. In combination with other information, such as NMR and IR spectroscopy, we might be able to work out a formula that fits the observed molecular weight.

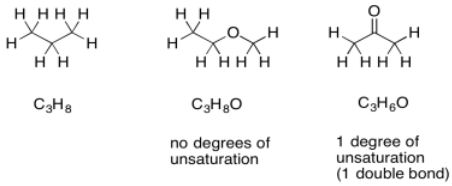
There are mass spectrometers that are designed to measure the value of m/z so accurately that the possible molecular formulae decrease to only a handful. These "high resolution" mass spectrometers rely on the fact that the atomic masses of different atoms are not exact integers. The atomic mass of a ^{1}H atom (the isotope that just has a proton in the nucleus, and no neutron) is actually 1.0078 amu, not 1.0000 amu. The atomic mass of a ^{10}B atom is actually close to 10.0129 amu, rather than the 10.0000 amu that you might expect. These are the masses of individual atoms, not average masses that take into account different isotopes. A high resolution mass spectrometer will measure the mass of the molecule so accurately that it can compute the very few combinations of atoms that could combine to produce that mass.

Once we have a formula, we actually get a great deal of information automatically. One of the most important pieces is "units of unsaturation" or "degrees of unsaturation" (DU). The DU is the result of a formal comparison of the C/H ratio in the compound to that in a normal alkane. In a normal alkane, the formula is always C_nH_{2n+2}. If you picture a long hydrocarbon chain, there will be two hydrogens on each carbon along the chain, plus one more hydrogen at either end of the chain. However, an alkene contains one pi bond, and at the site of that pi bond there are two hydrogen atoms missing from that alkane formula. A simple alkene always has the formula C_nH_{2n}. That missing pair of hydrogens in the formula is called a degree of unsturation.



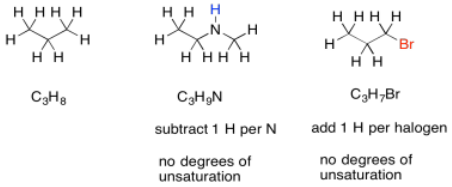
The same thing also happens to the formula if there is a ring present. One DU can correspond to the presence of a double bond or a ring. If DU=2, there may be two double bonds, two rings, or one of each.

If there are oxygen atoms present in the formula, we can just ignore them and pay attention to the hydrocarbon part. Conceptually, because oxygen forms two bonds, we can think of it as squeezing in between any two atoms in a hydrocarbon structure to form a new compound. The ratio of carbon to hydrogen is unchanged. If there is a degree of unsturation in a formula containing oxygen, it simply suggests the presence of a ring or a double bond, just like in a hydrocarbon.



Suppose the formula is $C_9H_{10}O_2$. We can ignore the oxygens and look at the C_9H_{10}. If this were a saturated hydrocarbon with nine carbons, its formula would be C_9H_{20} (since 2 x 9 + 2 = 20). We are missing five pairs of hydrogens, so DU = 5. That is a lot. However, if we have one benzene in the structure, that would account for three double bonds and one ring all at once. That is four degrees of unsaturation. An additional carbonyl or other double would bring the number up to the required five. If we had not yet arrived at the idea of a benzene ring, this comparison might make us think of it.

Sometimes, if there are other atoms present, we need to adjust the formula to take them into account. For example, any time a halogen is found in the structure, it conceptually replaces a hydrogen atom. In order for a halogen to be found in the structure, there would have to be one fewer hydrogen atoms in order to open up a spot for the halogen. To adjust for the presence of a halogen, we need to add one hydrogen into the formula, then compare it to the standard alkane formula.



Nitrogen, on the other hand, has three bonds. Unlike oxygen, if we squeeze it in between two other atoms, it still needs one extra bond. It always brings an extra hydrogen into the formula. To adjust for the presence of nitrogen, we need to subtract one H from the formula, then compare it to the standard alkane formula.

6.6: Isotopomers

If you look closely at the mass spectrum of an organic compound, 2-butanone, you see a line at m/z 72, which corresponds to 4 carbons, an oxygen and 8 hydrogens.

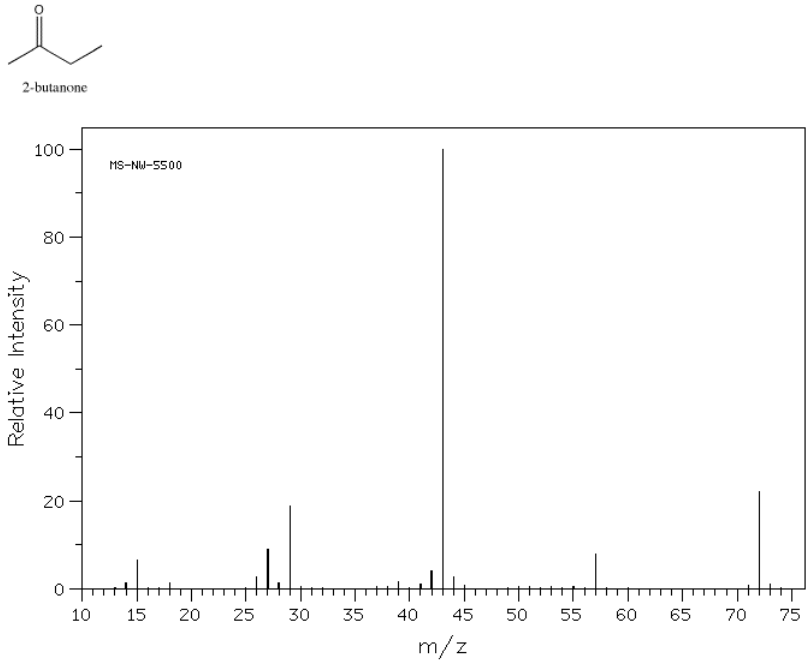


Figure 6.6.1: Mass spectrum of 2-butanone. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 22 August 2008)

- Usually, whole numbers are used for molecular weights in mass spectrometry.
- The atomic masses in the periodic table, out to 4 decimal places, are the average masses including different possible isotopes.
- Because mass spectrometry examines individual molecules, individual atomic masses are needed, not average ones. Usually that means using a whole number.

In addition, there are a number of other lines at lower values of m/z; these correspond to the masses of smaller pieces of those 2-butanone molecules that fall apart during the experiment. We won't look too closely at how those arise until we get to radical reactions later in the course. However, we will look at some factors that make cations stable later in this chapter.

If you look closely at the mass spectrum of 2-butanone, you'll also see another little peak at m/z 73. This is referred to as the M+1 peak (one greater than the molecular ion), and it arises because of ^{13}C. This compound is referred to as an isotopomer; that means the same compound with a different isotope.

- 12C is about 99% abundant; 99% of carbon atoms have a mass of 12 amu.
- 13C is about 1% abundant; 1% of carbon atoms have a mass of 13 amu.
- Compounds that contain a 13C atom have a mass one larger than expected.

The chance that a molecule in a sample contains a ^{13}C atom is related to the number of carbons present. If there is just one carbon atom in the molecule, it has a 1% chance of being a ^{13}C. That means the M+1 peak would be only 1/100th as tall as M+, the peak for the molecular ion.

- The M+! peak from a ^{13}C atom is very small.
- The more carbons there are in a molecule, the bigger the M+1 peak.
- If there are 10 carbon atoms in the molecule, there is a 10% chance of a ^{13}C atom being present. The M+1 peak is about 1/10th the size of the M+ peak.
- If there are 100 carbons in the molecule, there is a very good chance that a ^{13}C atom is present. At that point, the M+1 peak is actually much larger than the M+. peak

6.7: Other Important Isotopes- Br and Cl

There are other cases in which knowledge of isotopes can be crucial. For example, bromoethane should display a peak for the molecular ion at m/z = 109. However, the farthest large peak to the right in its mass spectrum is at 110. There is another large peak at 108.

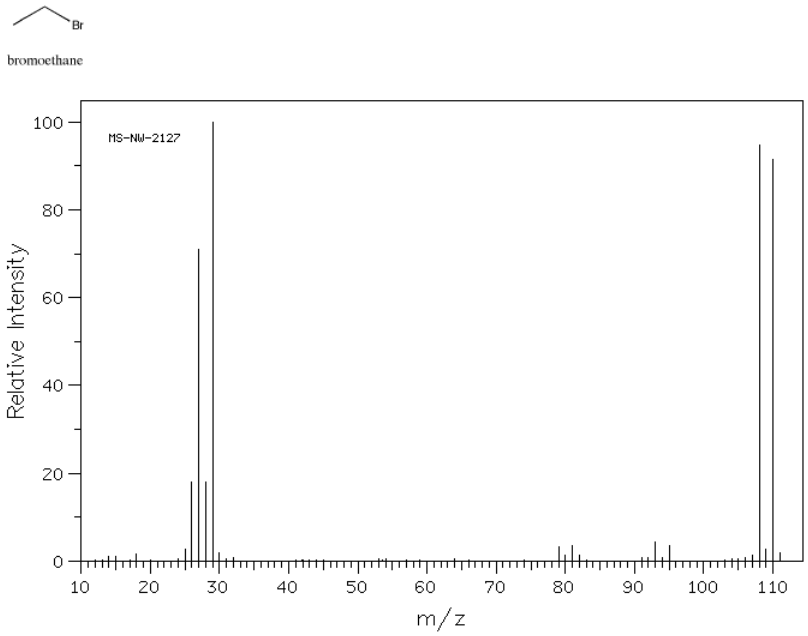
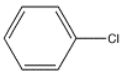


Figure 6.7.1: Mass spectrum of bromoethane

Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 22 August 2008)

- In the periodic table, the atomic mass of bromine is listed as 80, but that is just an average.
- Bromine is really about 50% ^{79}Br and 50% ^{81}Br.
- As a result, two molecular ion peaks of equal intensity two units apart, M+ and M+2, are observed.
- This pattern of molecular ions is a good indication that there is a bromine present in the molecule.

Similarly, chlorobenzene should display M+ at m/z =112, provided you take into account that most chlorine atoms have an atomic weight of 35 amu. The periodic table lists an atomic weight for chlorine of 35.453 amu, though. That's because about 25% of chlorine atoms are actually ^{37}Cl. The mass spectrum of chlorobenzene actually shows an additional molecular ion at 114 amu.



chlorobenzene

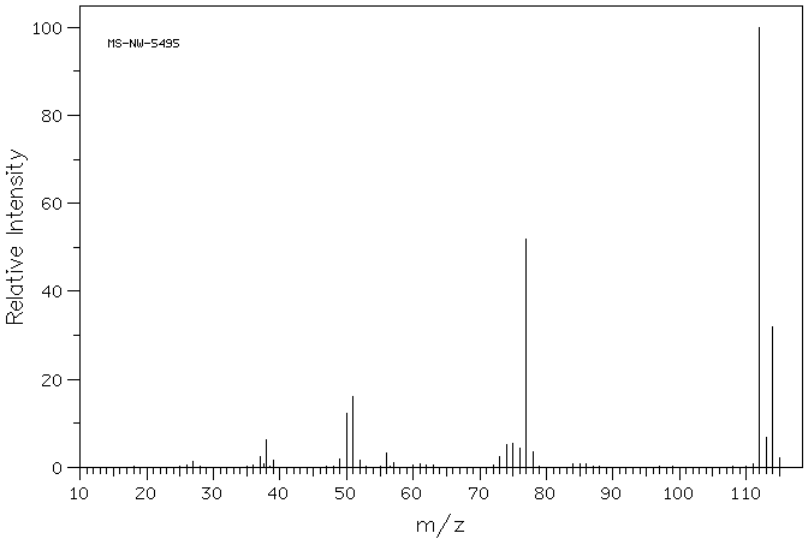


Figure 6.7.2: Mass spectrum of chlorobenzene.

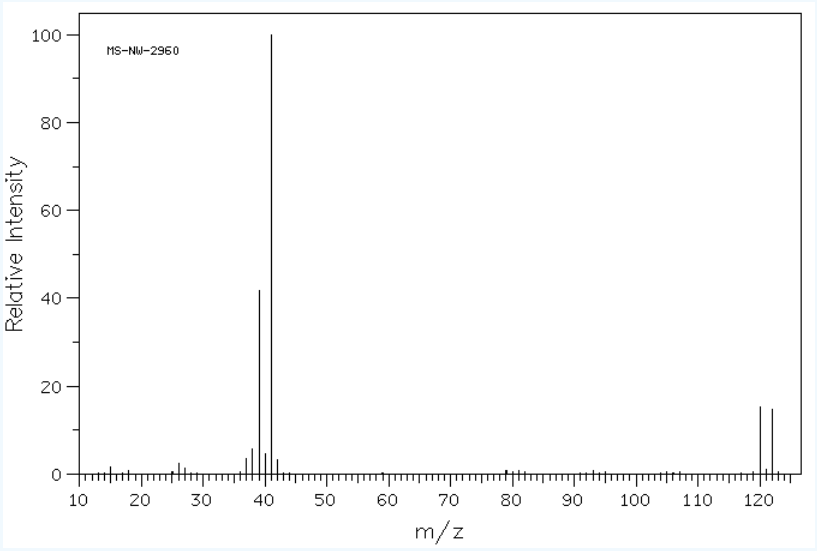
Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 22 August 2008)

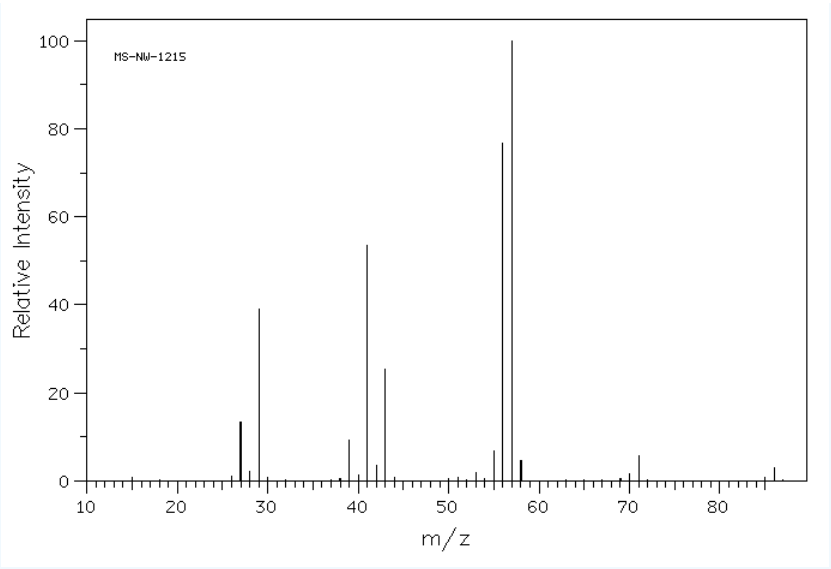
- Chlorinated compounds show an M+2 peak that is 1/3 as large as the M+ peak.

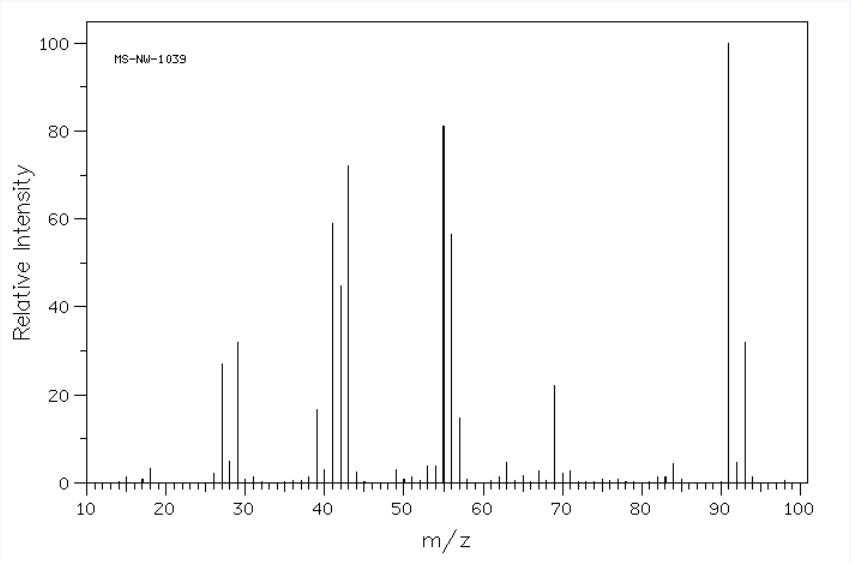
Note also that halogens are easily lost during mass spectrometry. If you subtract the mass of the halogen from the molecular ion mass, you will often find a peak that corresponds to the remainder of the structure.

? Exercise 6.7.1

Draw one possible structure for the compound in each of the following mass spectra.



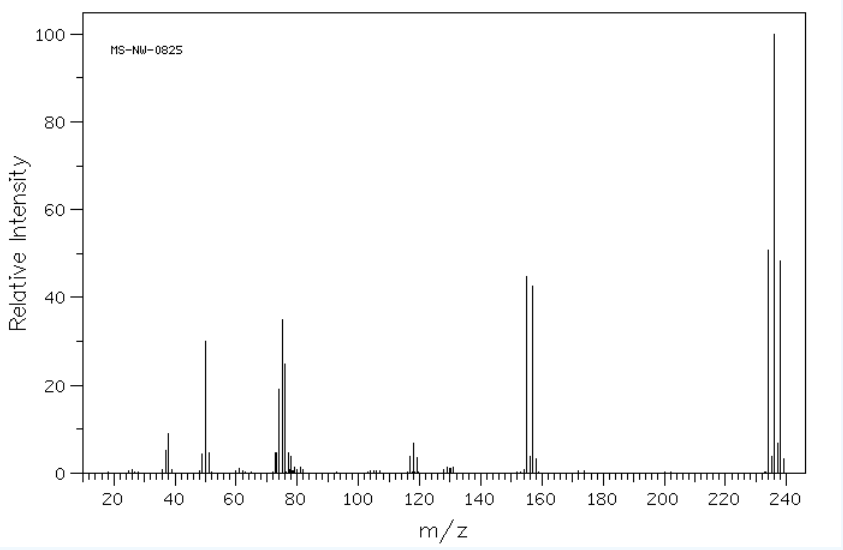




Exercise 6.7.2

In the following mass spectrum, more than one halogen atom is present.

a. What is a possible structure of the compound?
b. Show why this pattern of molecular ions is observed.



6.8: Molecular Weight- Even or Odd?

There is one other element that can be detected easily just by looking at the molecular ion: nitrogen. Usually if there is a nitrogen present in the molecule, the molecular weight is odd, as you can see in the mass spectrum of triethylamine. That isn't true with other compounds.

- Molecular weights of organic compounds are almost always even.
- Odd molecular weights result when there is nitrogen in the compound.

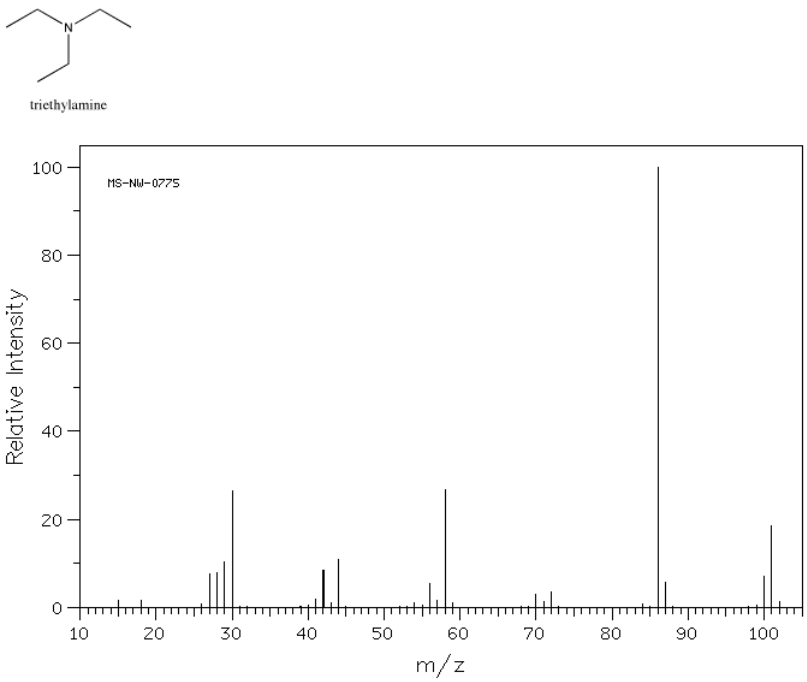


Figure 6.8.1: Mass spectrum of triethylamine. Source: SDBSWeb : http://riodb01.ibase.aist.go.jp/sdbs/ (National Institute of Advanced Industrial Science and Technology of Japan, 22 August 2008)

This phenomenon is a result of the fact that the most common elements in organic compounds, carbon and oxygen, have even atomic weights (12 and 16, respectively), so any number of carbons and oxygens will have even weights. The most common isotope of hydrogen has an odd molecular weight, but because carbon and oxygen both have even valences (carbon forms four bonds and oxygen forms two), there is always an even number of hydrogen atoms in an organic compound containing those elements, so they also add up to an even numbered weight.

Nitrogen has an even atomic weight (14), so any number of nitrogen atoms will add up to an even molecular weight. Nitrogen, however, has an odd valence (it forms three bonds), and as a result there will be an odd number of hydrogens in a nitrogenous compound, and the molecular weight will be odd because of the presence of an extra hydrogen.

Of course, if there are two nitrogens in a molecule, there will be two extra hydrogens, so the molecular weight will actually be even. That means the rule about molecular weight and nitrogen should really be expressed as:

- odd numbers of nitrogen atoms in a molecule in an odd molecular weight.

What about those other atoms that sometimes show up in organic chemistry, such as the halogens? Halogens all have odd molecular weights (19 amu for fluorine, 35 or 37 for chlorine, 79 or 81 for bromine, and X for iodine). However, halogens all have a valence of 1, just like hydrogen. As a result, to add a halogen to methane, we would need to erase one of the hydrogen atoms and replace it with the halogen. Since we are just substituting one odd numbered atomic weight for another, the total weight remains even.

? Exercise 6.8.1

Calculate molecular weights for the following compounds.

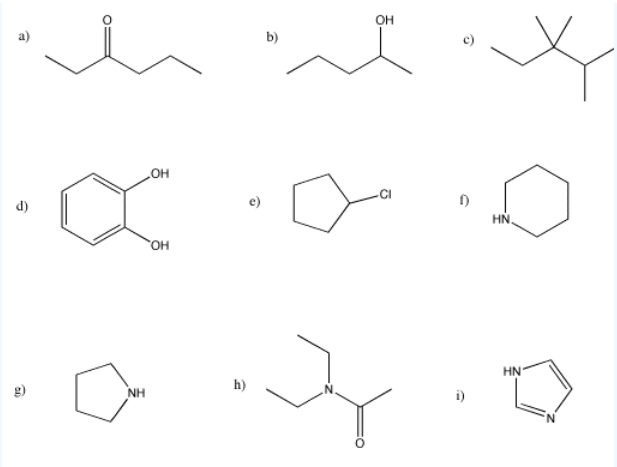


Figure 6.8.2:

6.9: High vs Low Resolution

Two common categories of mass spectrometry are high resolution mass spectrometry (HRMS) and low resolution mass spectrometry (LRMS). Not all mass spectrometers simply measure molecular weights as whole numbers. High resolution mass spectrometers can measure mass so accurately that they can detect the minute differences in mass between two compounds that, on a regular low-resolution instrument, would appear to be identical.

The reason is because atomic masses are not exact multiples of the mass of a proton, as we might usually think.

- An atom of ^{12}C weighs 12.00000 amu.
- An atom of ^{16}O weighs 15.9949 amu.
- An atom of ^{14}N weighs 14.0031 amu.
- An atom of ^{1}H weighs 1.00783 amu.

As a result, on a high resolution mass spectrometer, 2-octanone, $C_8H_{16}O$, has a molecular weight of 128.12018 instead of 128. Naphthalene, $C_{10}H_8$, has a molecular weight of 128.06264. Thus a high resolution mass spectrometer can supply an exact molecular formula for a compound because of the unique combination of masses that result.

- In LRMS, the molecular weight is determined to the nearest amu. The type of instrument used here is more common because it is less expensive and easier to maintain.
- In HRMS, the molecular weight in amu is determined to several decimal places. That precision allows the molecular formula to be narrowed down to only a few possibilities.

HRMS relies on the fact that the mass of an individual atom does not correspond to an integral number of atomic mass units.

? Exercise 6.9.1

Calculate the high-resolution molecular weights for the following formulae.

a. $C_{12}H_{20}O$ and $C_{11}H_{16}O_2$
b. $C_6H_{13}N$ and $C_5H_{11}N_2$

Answer

Add texts here. Do not delete this text first.

6.10: Fragmentation - Stable Cations

When molecules go through a mass spectrometer, some of them arrive intact at the detector, but many of them break into pieces in a variety of different ways. To establish a charge on a molecule, an electron had to be removed; removal of that electron is effected through a collision, usually with a high-energy electron. During that collision, energy is transferred from the high-energy electron to the molecule, and that energy has to go somewhere. Part of it gets partitioned into various bond vibrations, so bonds start to vibrate quite a lot, until some of them snap completely. The molecular ion breaks apart and forms a fragment ion.

Some fragment ions are very common in mass spectrometry. These ions are seen frequently for either of two reasons:

- there is not a pathway available to break the ion down.
- the ion is relatively stable, so it forms easily.

Fragmentations occur through well-defined pathways or mechanisms. A mechanism is a step-by-step series of events that happens in a reaction. It is important to understand how reactions happen, but we will look at fragmentations when we study radical reactions.

However, it is useful to know what factors make cations stable.

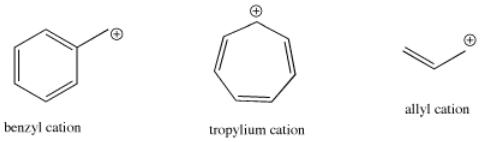
Some Common Ions

There are a number of ions commonly seen in mass spectrometry that tell you a little bit about the structure. Just like with anions, there are a couple of common factors influence cation stability:

- Electronegativity plays a role. More electronegative atoms are less likely to be cations.
- Polarizability also plays a role. More polarizable atoms are more likely to be cations.

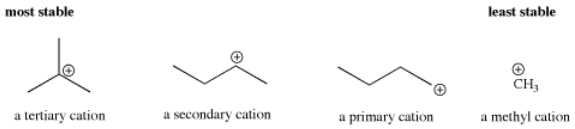
However, in most cases, we will be looking at carbon with a positive charge, and there are additional factors to distinguish between them

- Delocalization stabilizes a cation by spreading out the charge onto two or more different atoms.
- In Lewis structure terms, the easiest way to delocalize charge is via resonance.
- Resonance can involve other carbons, like in allyl and benzyl cations.



- Resonance can also involve other atoms, like in acylium or iminium cations.

- Delocalization can also be accomplished through inductive effects. The trend in carbocations is that the more substituents on teh carbocation, the greater the stability.
- Tertiary cations, with three substituents on the carbocation, are more stable than secondary cations, with two substituents on the carbocation. Secondary cations are more stable than primary ones. Primary cations are more stable than methyl cations.



Molecular orbital calculations suggest that the cation is stabilized through interaction with neighboring C-H bonds in the alkyl groups. Specifically, a C-H sigma bonding orbital has symmetry similar to the empty p orbital on the positive carbon. The lobes on the two orbitals can overlap such that they are in phase, and that allows electrons to be donated from the C-H bond to the central,

electron-deficient carbon. Formally, there is a bonding interaction and an antibonding interaction between these two orbitals. Since one of these orbitals is empty, the antibonding combination remains unoccupied. The bonding combination is populated, however, and since it is lower in energy than either the p orbital or the C-H sigma bond (all bonding combinations are lower in energy than the orbitals that combine to form them), there is a net decrease in energy.

? Exercise 6.10.1

Draw as many resonance structures as you can that help explain the stability of the following cations:

a. allyl cation
b. benzyl cation
c. tropylium cation
d. an acylium ion
e. an iminium ion

Answer

Add texts here. Do not delete this text first.

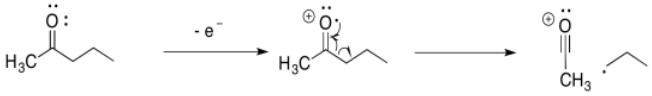
6.11: Fragmentation Pathways

When molecules go through a mass spectrometer, they break into pieces in a variety of different ways. There are many ways in which the molecules might break apart, but a few of these pathways are especially useful to know.

Alpha Fragmentation

An alpha fragmentation is driven by both bond formation and cation stability. Upon loss of an electron, which is most commonly a non-bonding electron or lone pair, a single electron is left behind on a heteroatom. That single electron is called a radical. By stealing one electron from a neighbouring bond, that radical can become paired. A new bond forms.

For example, suppose the oxygen atom in a ketone loses an electron. That leaves the oxygen atom without an octet. The atom has seven electrons in its valence shell instead of eight. If the neighbouring carbon atom had a single electron to share, then the two atoms could each contribute an electron to form a new bond. Both atoms would have octets.



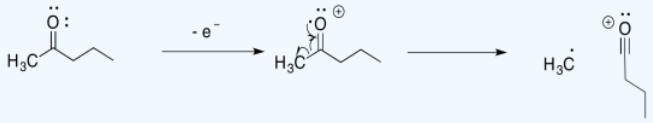
In the alpha fragmentation, a bond coming from the carbon alpha to the oxygen is broken in half. One electron remains behind, but the other electron pairs up with the radical to make a new bond.

Remember, a common term for a neighbouring atom is the alpha position. In a carbonyl, the alpha position is just the carbon next to the carbonyl. In mass spectrometry, the alpha position is the atom next to the atom that has the single electron or radical. In an alpha fragmentation, something breaks off that neighbouring atom, freeing up an electron to make a new bond. When it does so, it makes a new radical or unpaired electron; this is an example of a "propagation step" in a "radical chain reaction".

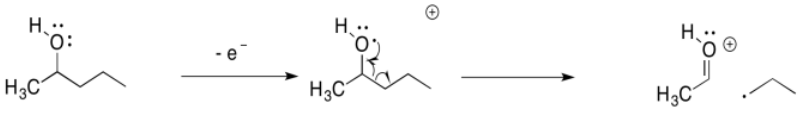
? Exercise 6.11.1

The alpha fragmentation shown above for 2-pentanone is just one of two such reactions. Show the other one.

Answer



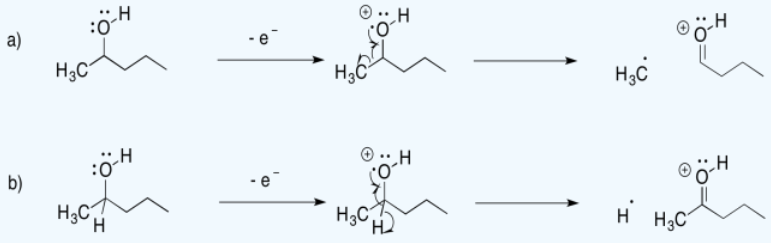
Other compounds undergo similar fragmentations. Alpha fragmentations are very common in oxygen- and nitrogen-containing compounds such as alcohols and amines. Here is the pathway in 2-pentanol:



Exercise 6.11.2

The alpha fragmentation shown above for 2-pentanol is just one of three such reactions for that radical cation. Show the other two.

Answer



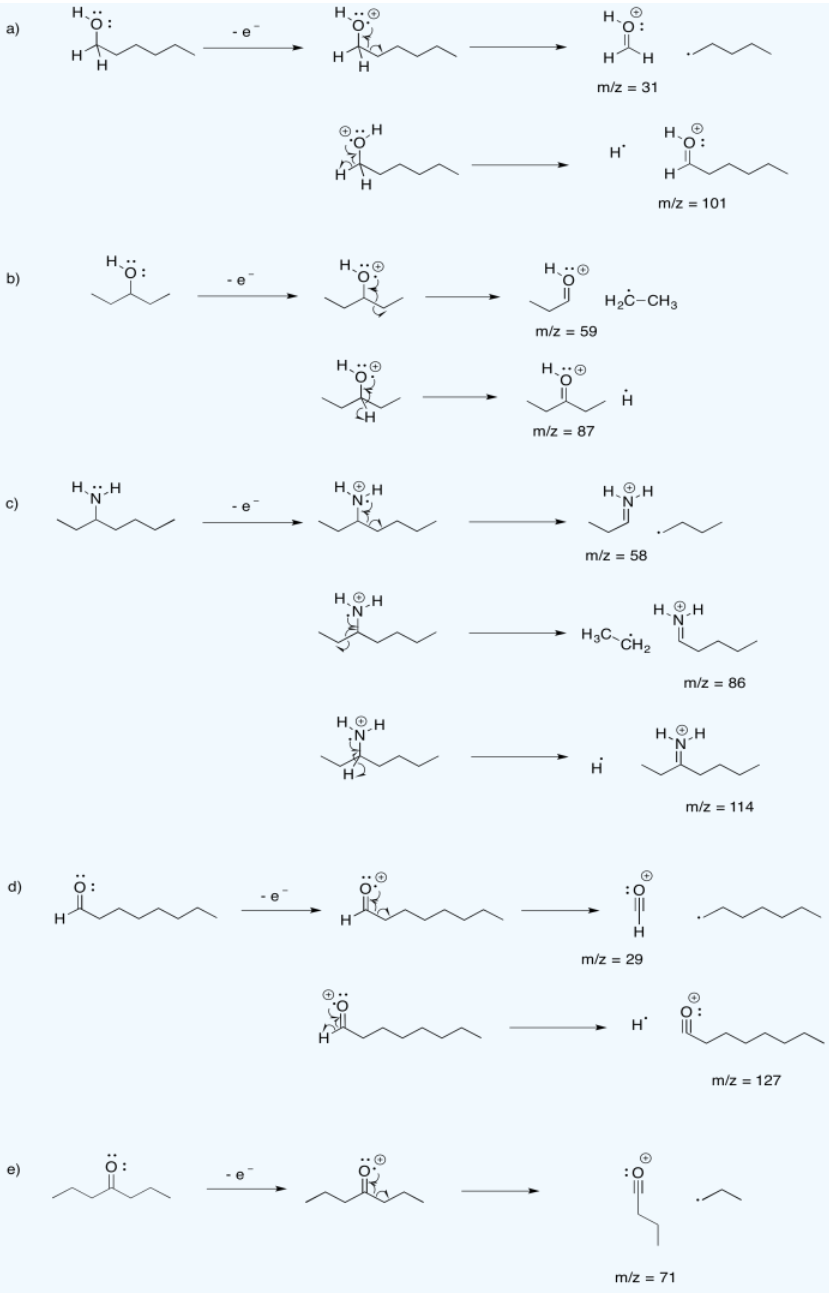
Now, the key feature of mass spectrometry is that it can detect the mass of cations. That means that if a molecule is cleaved into two pieces, only the part with the positive charge is detected by the mass spectrometer. The other part is invisible. In the example with 2-pentanone, above, the acyl cation, CH_3CO^+, would be detected at m/z = 43 amu.

Exercise 6.11.3

Draw the possible alpha fragmentations that would result after loss of a non-bonding electron from each of the following molecules, and indicate the m/z value of the fragments that would be detected:

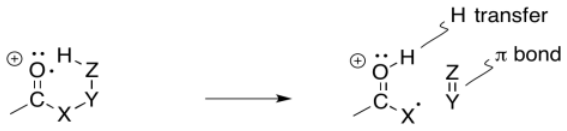
a) 1-hexanol b) 3-pentanol c) 3-aminoheptane d) octanal e) 4-heptanone

Answer



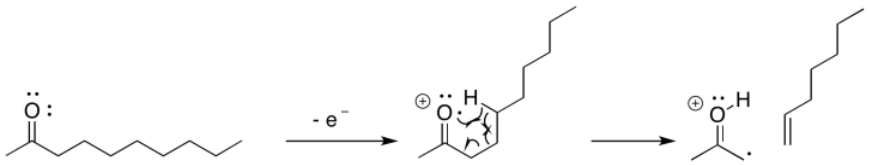
McLafferty Rearrangement

Another common pathway is called a **McLafferty rearrangement**. It happens in slightly longer chains. That's because it depends on a chain wrapping around until it loops; then, one end of the chain can react with another. The end result is the loss of an alkene from the original radical cation; however, unlike the alpha-fragmentation, both the cation and the radical remain in the same molecule after the Mclafferty rearrangement.

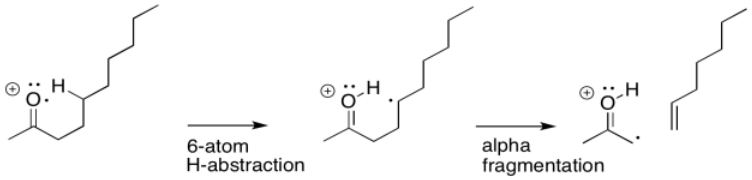


If you know anything about conformational analysis or about transition states, it might not be surprising to hear that a six-atom interaction is a key feature of this event. In the following example, involving 2-decanone, if the think of the oxygen as atom

number 1, we can see a hydrogen being abstracted from atom 5; the hydrogen is the sixth atom in a row, extending from the oxygen.



Sometimes it is helpful to break down complicated things into simpler parts. That lets us focus on one aspect of the reaction at a time. In this case, there is a hydrogen atom abstraction that occurs between the site of the initially-formed radical and a hydrogen atom that is the sixth atom along. At the same time, as that new radical forms, it begins to pull an electron out of a neighbouring bond so that it can be paired up. That aspect is like an alpha fragmentation.



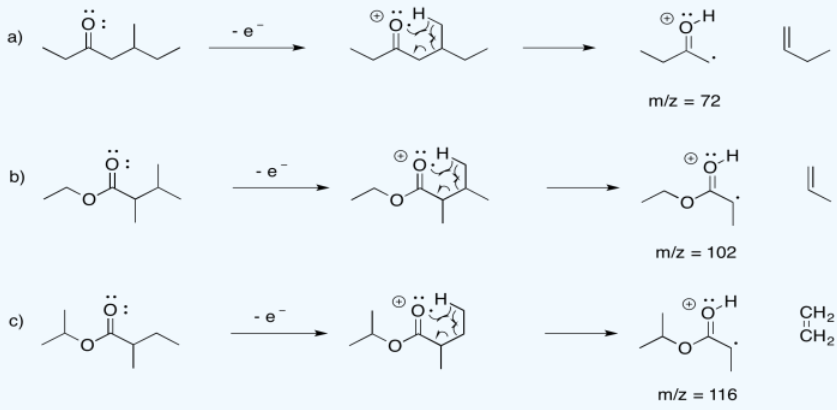
The actual reaction happens all at once, however, rather than one step at a time. As the hydrogen atom is abstracted, the remaining electron pairs up with a partner that comes from a neighbouring bond. That neighbouring bond is part of the six-membered ring transition state.

? Exercise 6.11.4

Provide mechanisms for McLafferty rearrangements for each of the following esters. Also, include the m/z values of the corresponding peaks in the mass spectrum.

a. 5-methylheptan-3-one
b. ethyl 2,3-dimethylbutanoate
c. isopropyl 2-methylbutanoate

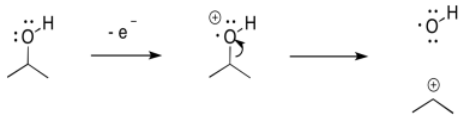
Answer



Inductive Cleavage

Inductive cleavage may be the simplest mechanism of all. If an electron is lost from an electronegative atom, the simplest way to manage cation stability is to completely transfer the positive charge to a less electronegative atom.

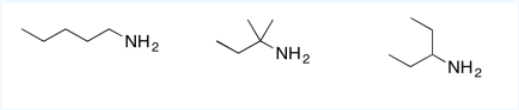
If, for example, and oxygen or a nitrogen is attached to a carbon, then once the positive charge forms on the oxygen, it can pull a pair of electrons away from the carbon.



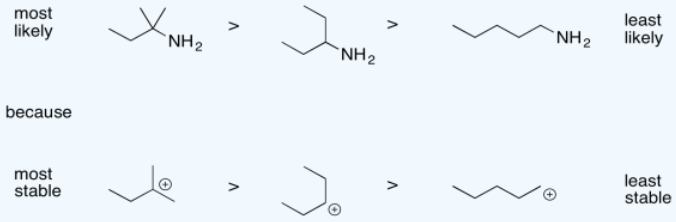
In that one, heterolytic bond cleavage, the oxygen has rid itself of the positive charge. Now it is carbon's problem. Carbon is less electronegative than oxygen, so the reaction is favored in this direction.

? Exercise 6.11.5

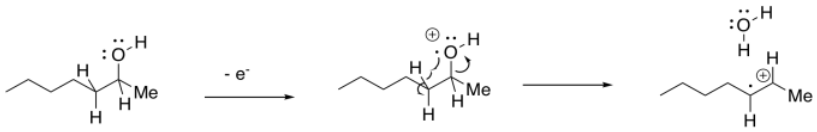
Order the following compounds from most likely to undergo inductive cleavage to least likely to undergo inductive cleavage.



Answer



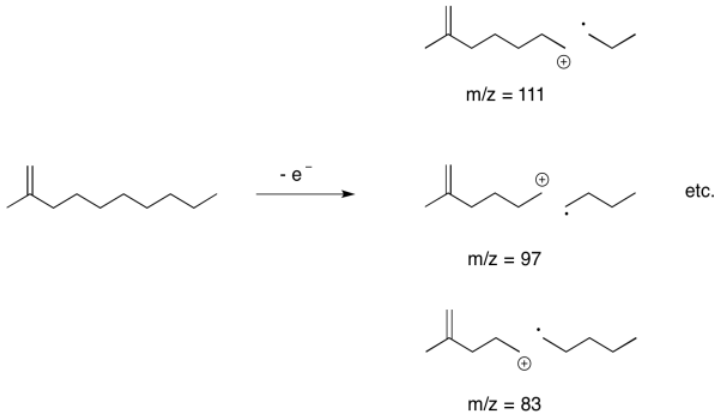
There is an added variation of this pathway that occurs specifically with alcohols. The departing OH radical can abstract a hydrogen atom from the next position in the molecule. This step is driven by formation of an OH bond, which is relatively strong. Overall, the result is the loss of a water molecule from the molecular ion.



Sigma Cleavage

What if there are no obvious places for the initial ionisation to occur? A saturated hydrocarbon, for example, has no lone pairs. It does not even have any pi bonds. There are no clear positions where a cation would form.

Nevertheless, under ionising conditions, an electron can be knocked free from a hydrocarbon, and it has to come from a sigma bonding orbital; there isn't anywhere else. When that happens, the sigma bond has already been broken, or at least greatly weakened, in one step. We have gone from a two-electron bond to a one-electron bond; the stabilisation energy is only half what it started out as, and so the bond breaks easily.



It's very common in the mass spectra of hydrocarbon chains to see a series of peaks 14 units apart. That difference corresponds to one CH_2 unit in the hydrocarbon chain.

? Exercise 6.11.6

Predict the peaks that would be observed arising from sigma cleavage in the following compounds.

a. hexane
b. butylbenzene

Answer
Answer a

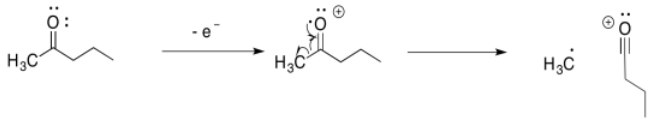
m/z = 71, 57, 43, 29

Answer b

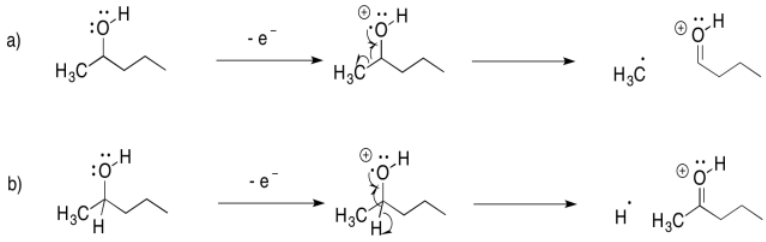
m/z = 119, 105, 91, 77

6.12: Solutions for Selected Problems

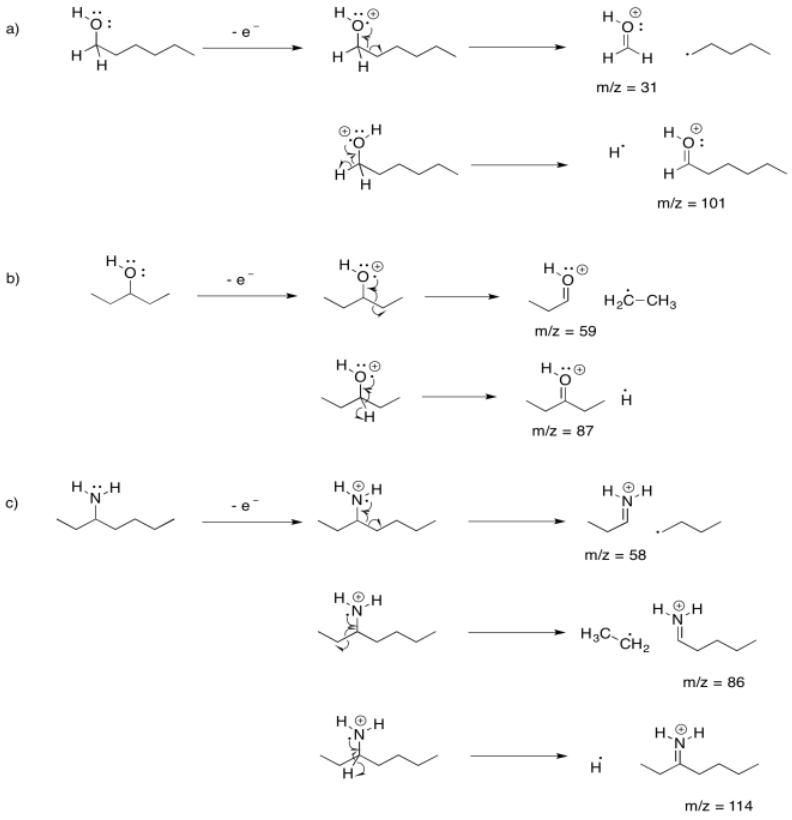
Exercise 5.11.1:

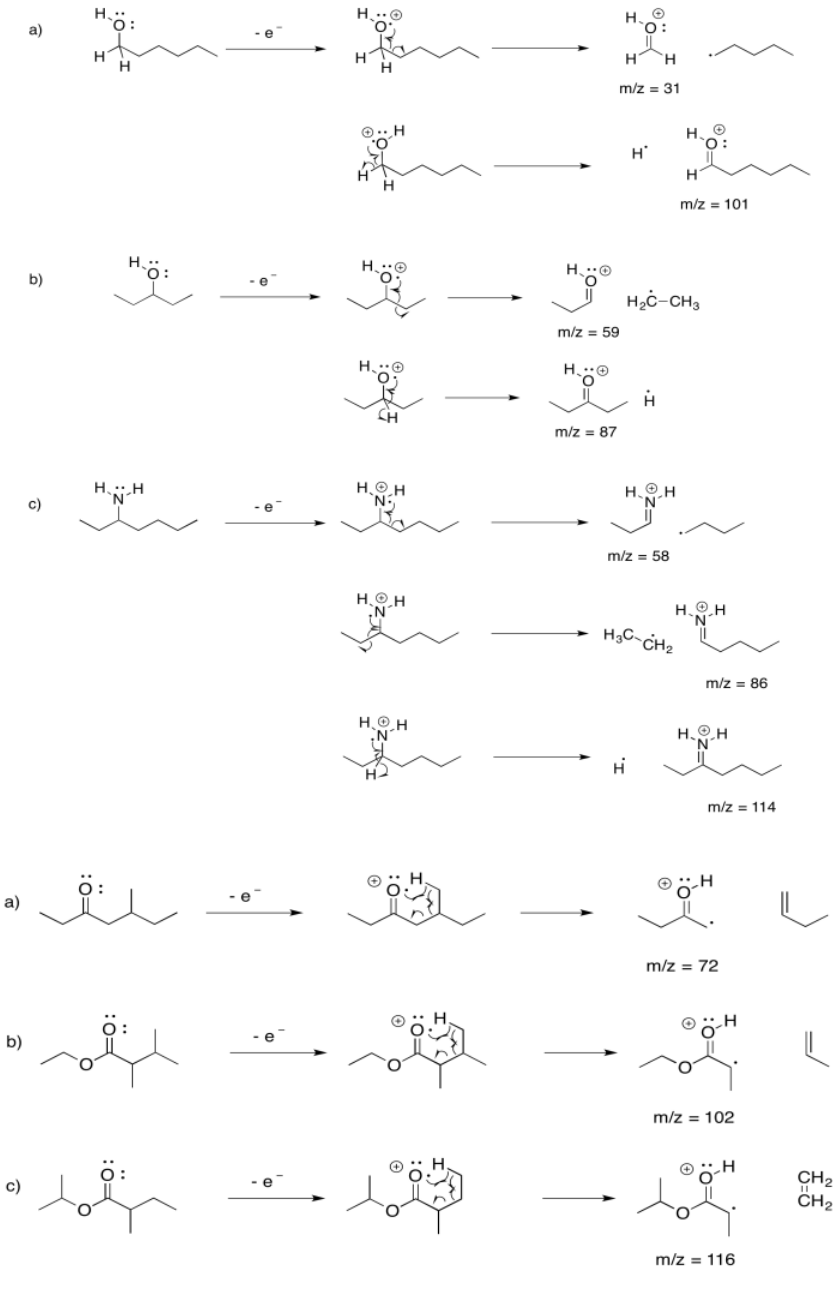


Exercise 5.11.2:

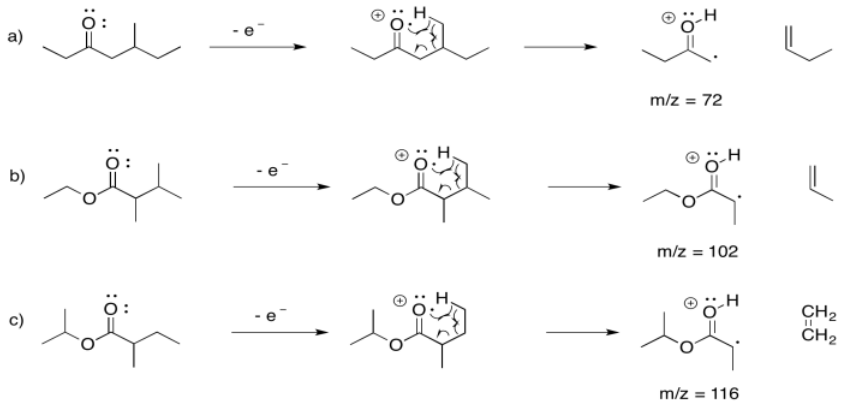


Exercise 5.11.3:

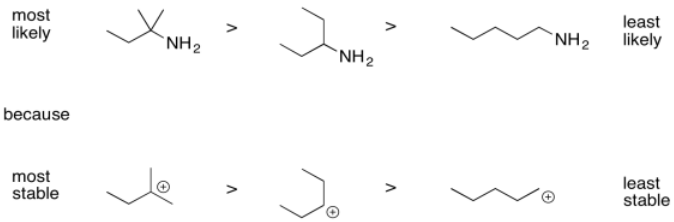




Exercise 5.11.4:



Exercise 5.11.5:



a. m/z = 71, 57, 43, 29
b. m/z = 119, 105, 91, 77

CHAPTER OVERVIEW

7: Purification of Molecular Compounds

7.1: Evaporation

There are a couple of very basic purification methods that are used routinely in the laboratory, and that are actually key steps in other methods. Evaporation is one of them.

Evaporation starts with a solution. In a solution, one compound is dissolved in another. For example, sugar water and saltwater are solutions. The sugar molecules can dissolve in the water because of hydrogen bonding; these strong intermolecular attractions allow the water molecules to pull sugar molecules apart from one another. The sugar molecules interact with the water molecules instead of with each other.

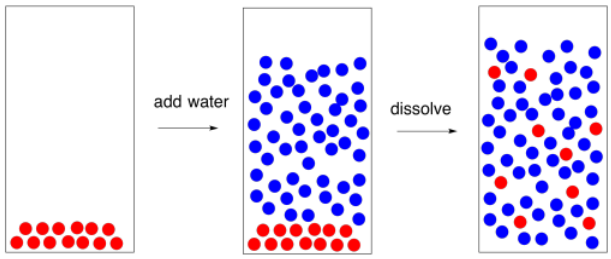


Figure 7.1.1: A cartoon representing the dissolution of sugar in water.

In saltwater, ion-dipole interactions pull the sodium ions apart from the chloride ions in the salt. Instead of interacting directly with each other, the ions interact with the partial charges on the polar water molecules.

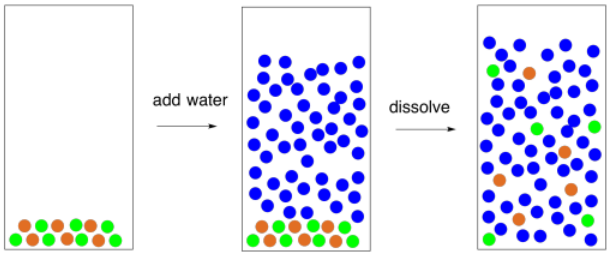


Figure 7.1.2: A cartoon representing the dissolution of salt in water.

In a solution, there is always a liquid compound that dissolves the other compound. This liquid compound is called the "solvent". Water is a very common solvent, but there are other ones, too. The compound that gets dissolved is called the "solute". This compound could be a solid, a liquid, or even a gas. Life in the oceans depends on gas-phase oxygen from the atmosphere dissolving in the water so that respiration is possible in marine organisms. Life on earth depends on solid minerals dissolving in water so that they can be taken up by plants and other organisms.

In evaporation, we are undoing the dissolving process. We are removing the solvent so that the solute is left by itself. That would be pretty hard to do if the solute were a gas, but it can be relatively easy if the solute is a liquid or solid.

The most straightforward case would be if the solvent had a very low boiling point. To isolate the solute, it would be a simple matter of waiting while the solvent molecules all move from the liquid phase to the gas phase. The change from liquid phase to gas phase is called evaporation. Once the solvent had gone into the gas phase and escaped, we would be left with only the solute.

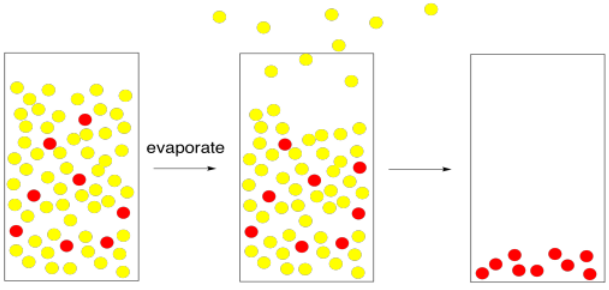


Figure 7.1.3: A cartoon representing evaporation, leaving the solute behind.

Today, sea salt is sometimes used by cooks because they feel it tastes better than regular salt. Regular table salt comes from salt mines; miners remove it from mineral deposits in the ground. Sea salt, of course, comes directly from the sea. To get the salt out of the seawater requires evaporation. The trouble is, water does not have a very low boiling point. It does not evaporate all that quickly.

To get around this problem, seawater is usually heated in pans until the water evaporates, leaving the salt behind. The added heat helps to give the water molecules enough energy to get into the gas phase. The heat may come from peat or wood fires, or even from sunlight.

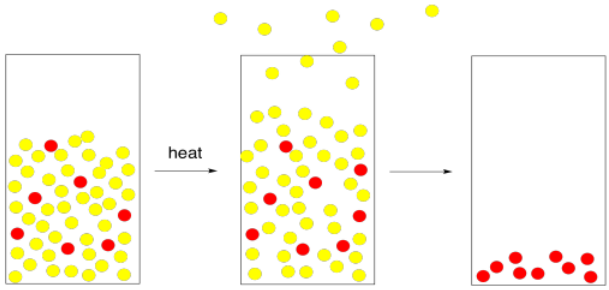


Figure 7.1.4: The addition of heat can speed up evaporation.

Adding heat is a perfectly good way to produce sea salt from seawater. In the laboratory, however, we don't always want to heat things that we wish to evaporate. There are a couple of reasons for that. First, the solute that we wish to isolate may be sensitive to heat. It may decompose if we heat it up. Second, the solvent that we wish to remove may be flammable. It may catch fire if we heat it up. In short, we may prefer not to use heat because we don't want to burn things.

How do we solve this problem? A physical chemist would tell you to think about pressure. Pressure is an ever-present factor in chemistry, but we don't often think about it because we are used to spending our lives under a fairly constant atmospheric pressure. To understand how pressure plays a role in evaporation, we need to get a more complete picture of evaporation.

In our previous pictures of evaporation, we ignored the atmosphere above the solution. The air is important here. All of those nitrogen and oxygen molecules whizzing around in the air exert a pressure on us, and on the solution. If a solvent molecule begins to move out of the liquid phase and into the gas phase, what is likely to happen? It will probably collide with one of those oxygen or nitrogen molecules in the atmosphere above the solution. When it collides, chances are that it could get knocked down into the liquid phase again.

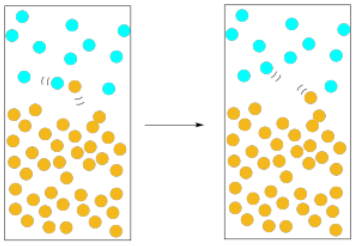


Figure 7.1.5: Atmospheric pressure can slow down evaporation.

The solvent would have a greater chance of escaping if there were many molecules moving into the gas phase at once. Statistically, if there are many molecules emerging from the liquid, the chances are pretty good that a substantial number of them will escape without being knocked down. Furthermore, the more molecules we have escaping the liquid, the more likely that we reverse the picture: instead of nitrogen molecules knocking solvent molecules back into the liquid, solvent molecules are knocking nitrogen molecules out of the way, clearing a path for others to follow.

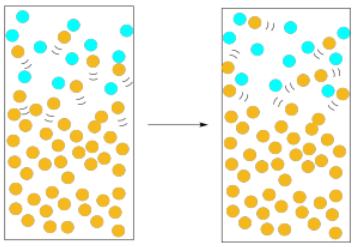


Figure 7.1.6: A higher presence of the solvent molecules in the gas phase (vapour pressure) increases evaporation.

This idea leads us to the concept of vapour pressure. Vapour pressure is the pressure exerted by the solvent molecules in the gas phase above the liquid. The higher the vapour pressure, the more easily the liquid evaporates. When the vapour pressure of the liquid exceeds the atmospheric pressure, the liquid comes to a boil and rapidly evaporates.

The way to increase the vapour pressure is to heat up the liquid. The energy imparted to the solvent molecules will put more of them into the gas phase, and those molecules in the gas phase will exert more pressure above the liquid.

- Boiling point is a function of vapour pressure.
- Vapour pressure is a function of temperature.

Now, we can use the concept of vapour pressure in an opposite way. We can heat the liquid up until it reaches its boiling point -- that is, until its vapour pressure is greater than the atmospheric pressure. Alternatively, we could lower the atmospheric pressure until it is lower than the vapour pressure of the liquid. Once the vapour pressure of the liquid exceeds that of the atmosphere, the liquid will boil.

- Boiling point is a function of pressure.

To accomplish that task, all we need is a vacuum pump. The vacuum pump sweeps the gas phase molecules away, lowering the atmospheric pressure. At some point, there are so few nitrogen and oxygen molecules that their vapour pressure becomes lower than that of the solvent. The solvent boils, even though its tempreature has not been raised.

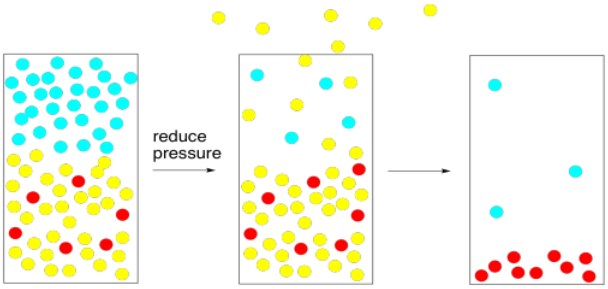


Figure 7.1.7: Reducing the local atmospheric pressure can speed up evaporation.

This approach is usually taken in the laboratory using a rotary evaporator. A rotary evaporator uses some method of lowering the atmospheric pressure above the solution that is meant to be evaporated. It may require a vacuum pump or an aspirator. Working with reduced pressure can be difficult. The most common problem is that, when the atmospheric pressure is reduced, the solution rapidly over-boils, making a mess everywhere. Use of a rotary evaporator requires that the user is aware of a few steps to avoid problems.

First, the solution is placed in a dry, round-bottom flask, and it is important that the flask is always *less than half full* of the solution. One quarter full is fine; one third full is OK. Half full may lead to problems. The fuller the flask, the more likely that, if the solution comes to a full boil, it will need to expand all the way out of the flask (it will overboil).

Second, a rotary evaporator has a motor that spins the flask on its axis. It is usually a good idea to spin the flask very rapidly. The resulting centripetal force can help to keep the solution in the flask where it belongs, rather than overboiling. Also, that centripetal force will keep the solution spread out over the walls of the flask. That will maximize the surface area of the liquid, maximizing the rate of evaporation.

Third, rotary evaporators have a water bath that allows the solution to be warmed. This capability offsets the fact that evaporation is an energy-consuming process. If the solvent starts to evaporate, the evaporating molecules will draw heat in from their surroundings. The flask and the solution will start to get colder. The vapour pressure will drop. The solvent will stop evaporating.

To cut that process off, we place the flask in a water bath. Water has a high heat capacity, so it can store lots of heat without much temperature change. It can also release some heat to the flask without getting much colder. It stabilizes the temperature, so that the vapour pressure of the solvent does not drop, and evaporation can continue. In many cases, a room-temperature water bath is all that is required for steady evaporation. If needed, the water can be heated up, but heat and vacuum should always be combined very cautiously. You don't want to overdo it and have the solution overboil.

? Exercise 7.1.1

Indicate the order in which the following liquids would evaporate, from most quickly to most slowly.

a. hexane, bp = 69°C; dichloromethane, bp = 39°C; water, bp = 100°C
b. toluene, bp = 111°C; dimethylsulfoxide, bp = 189°C; acetone, bp = 56°C
c. benzene, bp = 101°C; ethyl acetate, bp = 89°C; pentane, bp = 35°C

Answer a

Fastest: dichloromethane > hexane > water: slowest

Answer b

Fastest: acetone > toluene > dimethyl sulfoxide: slowest

Answer c

Fastest: pentane > ethyl acetate > benzene: slowest

7.2: Filtration

There are a couple of very basic purification methods that are used routinely in the laboratory, and that are actually key steps in other methods. Filtration is one of them.

Suppose you have a mixture that contains both a solid and a liquid. There are a couple of ways you could separate one from the other. Decanting is one way. In decanting, the liquid is sitting nicely on top of the solid, so you can just pour off the liquid and leave the solid behind. However, usually that leaves some of the liquid behind in the solid, so you haven't completely separated them.

Filtration is a more thorough way of separating a solid from a liquid. The most familiar example might be a coffee maker. A coffee maker filters coffee from the ground coffee beans. The coffee falls through a filter paper, powered by gravity, and the coffee grounds remain on top of the filter paper.

Filtration relies on a porous material. In a porous material, there are pores or openings in the material that will allow small molecules pass through. You can think of the pores as tunnels. Small molecules, such as water and the organic molecules responsible for the properties of coffee, can easily move through the pores in the filter paper. Other materials, such as coffee grounds, cannot.

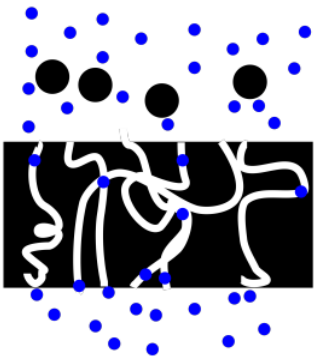


Figure 7.2.1: A cartoon representing filtration.

In the laboratory, filtration can be done just as in the coffee filter. A filter paper is placed in a funnel and the mixture is poured in, and the liquid drips out under gravity. The liquid that drips through the filter paper is called the "filtrate".

Usually the funnel is a simple glass cone with a hole in the bottom, most often with a glass tube or stem leading from the hope to help guide the liquid to the vessel below. Sometimes, the funnel may have a flat bottom with holes in the bottom, or even a seemingly solid, but porous material. This last type is called a fritted funnel. The frit in the fritted funnel is porous material, just like filter paper, but it may be made of glass or plastic.

One of the advantages of a fritted funnel is that it is easy to use a vacuum to speed up filtration. By reducing pressure on the bottom side of the frit, the atmospheric pressure above the frit helps to push the solution through the frit more quickly.

The trouble is, frits can easily get clogged. Suppose there are particles suspended in the solution that are just small enough to get into the pores, but not small enough to move all the way through. They get stuck. Now we have a problem.

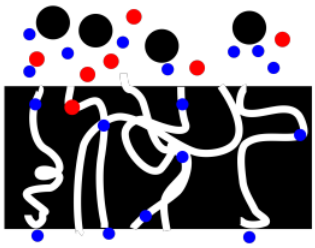


Figure 7.2.2: A cartoon showing how a frit can get clogged during filtration.

The most common way to prevent this problem is to just put a piece of filter paper over the frit. The paper may prevent those particles from getting to the frit in the first place. The filter paper may get clogged in the same way, but you can just throw it out. Disposable filter paper may seem like a waste, but it is a much smaller waste than a disposable fritted funnel.

For really sticky situations, other filter aids include celite, a powder made from diatomaceous earth. A layer of celite is simple placed on top of the filter paper. Like the filter paper, the celite is disposable, but it protects the frit and allows the filtration to proceed more smoothly.

Note that filtration might allow isolation of either the solid phase or the liquid phase. In the former case, we would simply collect the solid that was held on the filter paper (we wouldn't use a filter agent like celite, which would contaminate the solid. The solid is usually allowed to dry before it is weighed and characterized.

If we are interested in the liquid, we might have more work to do. Maybe the liquid is pure, in which case we are finished. If it is a solution, we may wish to evaporate the solvent so that we could isolate the solute that we want.

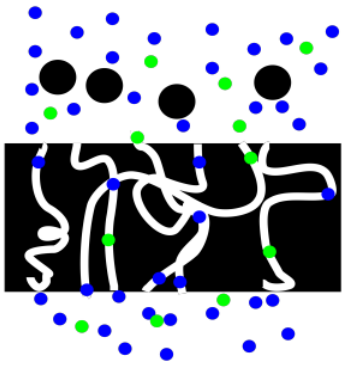


Figure 7.2.3: A cartoon showing filtration of a solution.

? Exercise 7.2.1

In the following cases, indicate which compounds would be found on the filter paper and in the filtrate.

a. A mixture of sodium carbonate and heptanal is stirred in diethyl ether and filtered.
b. A mixture of lithium chloride and benzophenone is stirred in water and filtered.
c. A mixture of anthracene and potassium benzoate is stirred in water and filtered.
d. A mixture of ethylenediamine and tris(ethylenediamino)cobalt(III) chloride is stirred in diethyl ether and filtered.

Answer
Answer a

Filter: sodium carbonate; filtrate: heptanal

Answer b

Filter: benzophenone; filtrate: lithium chloride

Answer c

Filter: anthracene; filtrate: potassium benzoate

Answer d

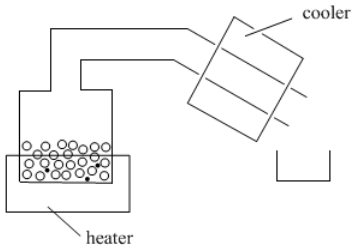
Filter: tris(ethylenediamino)cobalt(III) chloride; filtrate: ethylenediamine

7.3: Distillation

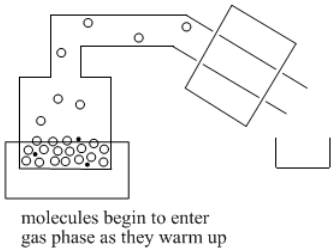
Distillation is a method of purifying organic compounds. It takes advantage of the fact that two different compounds probably have two different boiling points. Suppose two different liquids are present in a homogeneous mixture (they are completely miscible, or they mix completely together, like water and alcohol). If they have two different boiling points, one of the compounds will evaporate before the other one does. The more volatile compound (the one that evaporates easily) will leave the less volatile compound behind.

Distillation is probably a familiar word. Distilleries are factories that produce alcoholic beverages, such as whiskey, from the fermentation of grains, such as corn or rye. At the heart of the distillery is a large distillation apparatus. This "still' is used to purify the alcohol/water mixture by evaporation, leaving behind most of the other components of the grain. That process is slightly more complicated than the one described here, but it is similar.

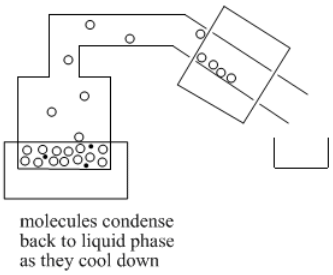
In distillation, a mixture is put into a container and the container is placed on a heat source. A tube leads away from the container. Sometimes this tube is cooled by cold, running water or ice; sometimes it is just left to cool in the air. There is also a second container to collect the liquid that distills.



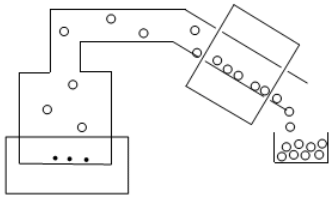
As the container or "pot" is heated, the volatile liquid begins to evaporate. Molecules enter the gas phase and begin to float through the tube leading away from the pot. In the lab, the tube above the pot is called the "still head".



Once molecules get past the still head, they reach the "condensor". Often the condensor is cooled by cold water that flows along outside of it. When molecules reach the cold condenser, they give up some heat energy and condense back into the liquid phase.



As enough molecules condense into the liquid phase, they begin to form drops of liquid. This liquid collects in a "receiver flask".



molecules collect in a receiver;
molecules with a higher boiling
point remain behind

Exercise 7.3.1

Decide whether the following mixtures are good candidates for distillation.

a. You have a sample of pentane (mp: -129°C; bp: 36°C) contaminated with 1-octanol (mp: -16°C; bp: 195°C).
b. You have a sample of 1-hexanol (mp: -50°C; bp: 145°C) contaminated with 2-hexanol (mp: -16°C; bp: 140°C).
c. You have a sample of benzene (mp: 5°C; bp: 80°C) contaminated with benzoic acid (mp: 122°C; bp: 250°C).
d. You have a sample of 2-butanone (mp: -86°C; bp: 80°C) contaminated with toluene (mp: -95°C; bp: 111°C).
e. You have a sample of naphthalene (mp: 78°C; bp: 218°C) contaminated with 2-naphthol (mp: 120°C; bp: 285°C).
f. You have a sample of 1-hexanol (mp: -50°C; bp: 145°C) contaminated with 1-hexene (mp: -140°C; bp: 63°C).

Answer

Answer a

Yes, these compounds are both liquids and the boiling point difference is large.

Answer b

No, these compounds are both liquids but the boiling point difference is small.

Answer c

Yes, the compound you want to purify is a liquid and the boiling point difference is large. However, you would have to be very careful not to char the remaining material in the flask.

Answer d

Yes, these compounds are both liquids and the boiling point difference is large.

Answer e

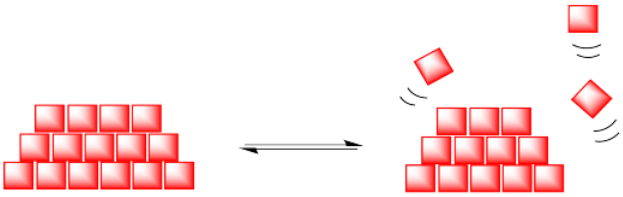
No, these compounds are both solids. Distillation is not a good idea.

Answer f

Yes, these compounds are both liquids and the boiling point difference is large. However, you would have to be careful not to char the desired material; as it distills (after the contaminant is removed), its volume will get smaller. At some point, heat dissipation will become a problem for the remaining material.

7.4: Sublimation

Sublimation is conceptually similar to distillation. It is a method in which an impure sample is heated and a purer sample collects someplace cooler nearby. Instead of relying on an equilibrium between the liquid phase and the gas phase, sublimation involves an equilibrium between the solid phase and the gas phase.



At lower temperatures, a solid material is expected to be crystalline and ordered. However, at higher temperatures, enough energy may be gained by the molecules in the solid so that they can escape into the gas phase.

Your normal experience tells you that is you heat up a solid, it just melts into liquid. To obtain a gas, you need to heat up that liquid. However, if you have ever spent time in a cold, snowy place on a sunny day, you may realize that idea isn't always true. On sunny, cold days, a snow bank will shrink and shrink without leaving any puddles. Where do all of the water molecules go? Into the gas phase. They float away into the air.

- In sublimation, molecules in the solid phase escape directly into the gas phase.

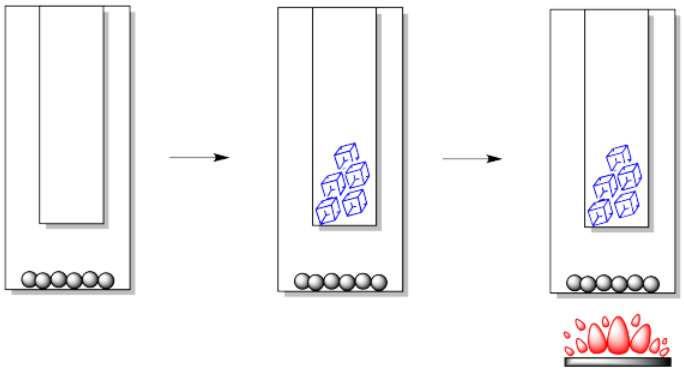
However, in a purification method, we typically want to obtain a material back in its original form, only without the impurities. We want those gas phase molecules to form a solid again.

Of course, on winter days, that happens all the time. Water vapour in the air routinely forms crystalline ice again, which then falls as snow. The trick is to let the gas phase molecules rise up to a place that is cold enough to strip a little energy away and shift that equilibrium back towards the solid.

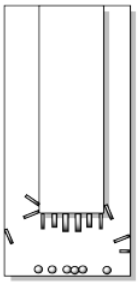
In the laboratory, we can construct a simple sublimation apparatus in a number of different ways, but there are always two key components. We need an outer vessel or lower vessel. This is the place where we would put the impure sample. We also need an inner vessel or upper vessel. This is the place where we want the pure solid to form again.

- To purify by sublimation, molecules in the solid phase are heated so that they go into the gas phase, then cooled to form a solid again.

Usually the cooling is provided by plain old ice or cold water. Occasionally, dry ice may be used. The heat is not usually provided by an open flame, but by a hot plate or heating bath.



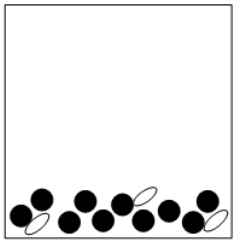
After the sample is heated for some time, crystals begin to form higher in the apparatus. Usually, they form on the cold finger, but they may also form higher up the walls of the outer vessel. The crystals may first appear in different forms or habits: they may be light and feathery, round and scaly, needles or blocks.



Very carefully, the cold finger must be separated from the outer vessel. Sometimes the crystals are barely hanging on to their perch, so the slightest movement will cause them to fall. Other times, they may be very firmly attached and it might take some effort to scrape them off.

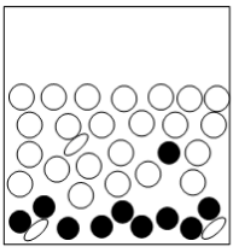
7.5: Recrystallization

Recrystallization is used to purify solids. Usually this method works best when there is only a small amount of impurity in the solid.



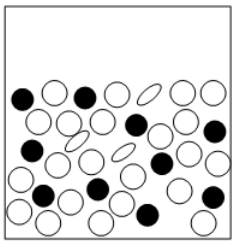
an impure solid

The method involves addition of a cold solvent to the material.



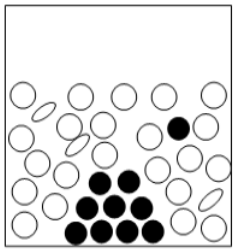
some of the solid dissolves
when solvent is added

The mixture that results is heated until the solids dissolve.



all of the solid dissolves
when the solvent is heated

The mixture is slowly cooled again until a pure solid is obtained.



some materials
remain dissolved

when cooled, one of the solids
slowly packs together in an
organized, crystalline form.

Recrystallization depends on different solubilities of the target compound and other compounds present in the impure mixture. The goal of this method is to have one compound dissolved in a solvent while the other compound is not dissolved. If one compound is an undissolved solid, it can be filtered out of the solution in order to separate it from all the other things that are in solution.

Solubility in a solvent is a physical property of a material, just like its boiling point or melting point. Sodium hydroxide (lye) has a particular solubility in cold water (40 g will dissolve in 100 mL) while sodium oleate (found in some soaps) has a different solubility in cold water (2 g per 100 mL). That difference can be exploited to separate these two compounds.

Exercise 7.5.1

Suppose you were trying to go into the soap business. Maybe you find you can easily produce a mixture of equal parts (weight:weight) of sodium hydroxide and sodium oleate. Describe how you could get pure sodium oleate.

Answer

It's possible that a mixture of sodium hydroxide and sodium oleate could be purified through the addition of water. If the right amount of water were added and the resulting slurry were stirred together and filtered, much of the sodium hydroxide would be removed because it is more soluble in water than is sodium oleate. Sodium oleate is less soluble in water than is sodium hydroxide, so most of it would not dissolve. It could be gathered or "isolated" by filtration.

Exercise 7.5.2

Look at the structures of sodium hydroxide and sodium oleate. Can you qualitatively explain the difference between their solubilities in water?

Answer

Sodium oleate has a long, non-polar hydrocarbon chain. Hydrocarbon chains are not very soluble in water. That's beacuse they get in between the water molecules and prevent the water molecules from hydrogen bonding to each other.

It's possible that a mixture of sodium hydroxide and sodium oleate could be purified through the addition of water. If the right amount of water were added and the resulting slurry were stirred together and filtered, much of the sodium hydroxide would be removed because it is more soluble in water than is sodium oleate. Sodium oleate is less soluble in water than is sodium hydroxide, so most of it would not dissolve. It could be gathered or "isolated" by filtration.

The technique described above is not recrystallization. It is referred to as "washing". The sodium oleate was washed with water to remove sodium hydroxide. Washing is simple to do. Sometimes it can increase the purity of a compound, but it is not always very effective.

Sometimes in a mixture the two compounds are mixed very tightly together. Suppose there is a pile of powder that contains sodium oleate and sodium hydroxide. Instead of having individual grains of sodium hydroxide and individual grains of sodium oleate, the grains of powder contain both compounds. There might be a small nugget of sodium hydroxide surrounded by a coating of sodium oleate. This situation is very common, especially when the two compounds have formed together. Washing might remove most of the exposed sodium hydroxide, but it wouldn't touch the hidden or "occluded" sodium hydroxide that was surrounded by sodium oleate molecules.

Exercise 7.5.3

How can you get all of the sodium hydroxide out of this mixture? In other words, how can you make sure there is no sodium hydroxide covered by sodium oleate?

Answer

The solution contains water, lots of sodium hydroxide, and a little sodium oleate.

It would be convenient if there were a switch that could be turned on and off to control dissolution. When the switch is on, all the sodium oleate dissolves, and any sodium hydroxide trapped inside can get dissolved, too. When the switch is off, the sodium oleate comes out of solution again so that you can filter it out.

This switch exists. It is found on the front of your hot plate in the organic lab. Solubility is temperature-dependent. For example, the solubility of sodium hydroxide is different in cold water (40 g per 100 mL at 0 °C) than in hot water (330 g per 100 mL at 100

°C). In comparison, the solubility ofsodium oleate also depends on temperature (2 g per 100 mL at 20 °C, vs. 30 g per 100 mL at 30 °C).

It's possible that, in the right amount of hot water, all the sodium oleate and all the sodium hydroxide dissolves. If the resulting solution is cooled to room temperature, the sodium oleate is no longer soluble. The sodium oleate forms a solid again. This solid can be filtered away from the water.

Exercise 7.5.4

After filtration, list the contents of the solution.

Answer

No. If the water were evaporated, the sodium hydroxide would still be stuck in the sodium oleate.

Exercise 7.5.5

Instead of filtering, can the solution be allowed to evaporate to leave the sodium oleate behind?

There is one more part of this process that would make it a complete recrystallization. If the sodium oleate forms an amorphous solid when it comes back out of solution, we have precipitation. If the sodium oleate forms a crystalline solid when it comes back out of solution, we have recrystallization. An amorphous solid contains molecules that are packed together in random ways. A crystalline solid contains molecules that are ordered in a specific way.

An amorphous solid is like a pile of boxes that were thrown across the room and piled in the corner. A crystalline solid is like a set of boxes that were stacked neatly in the corner.

There are many open spaces between the boxes in the "amorphous" pile. Impurities could get trapped in those spaces; in that case we are back where we were at the beginning.

There are not really spaces between the boxes in the "crystalline" pile. No impurities can be trapped. Crystallization safeguards against the inclusion of impurities in the material.

Exercise 7.5.6

There are many variations on most purification techniques. One problem that could happen in a recrystallization is that there is a very insoluble impurity. How could this very insoluble impurity be separated from the rest of the sample? What precautions must be taken in doing so?

Answer

You might have to filter out this impurity while everything else is still dissolved. You might have to make sure everythings stays warm while you do this. If things get too cold, the solubility will get lower, and compounds might solidify before you want them too. Sometimes, when filtering an aqueous solution, it helps to put some hot water in the filter flask and keep everything warm using steam.

Exercise 7.5.7

Suppose you are trying to recrystallize a sample of borneol. You think it should be recrystallized from methanol. You add a couple of mL of cold methanol and the sample all dissolves. Evaluate the prognosis of your recrystallization: is it working well? If not, what do you need to do?

Answer

The borneol seems too soluble in the methanol. If you don't have anymore borneol, you will have to evaporate the methanol again. This time, add less methanol; maybe you only need a quarter mL or ten drops or something. For a recrystallization to work, you want to see partial solubility; you want the compound to dissolve when hot but not when cold.

Exercise 7.5.8

Suppose you are trying to recrystallize a sample of borneol. You think it should be recrystallized from methanol. You add a couple of mL of cold methanol and only about half the sample dissolves. Evaluate the prognosis of your recrystallization: is it working well? If not, what do you need to do?

Answer

This is a good sign. Try heating the methanol to see whether more dissolves. If it dissolves when hot, try cooling it down and see whether the solid appears again.

Exercise 7.5.9

Suppose you are trying to recrystallize a sample of borneol. You think it should be recrystallized from methanol. You add a couple of mL of hot methanol and only about half the sample dissolves. Evaluate the prognosis of your recrystallization: is it working well? If not, what do you need to do?

Answer

This is still a good sign, but you might need to add more methanol to get it all dissolved. Don't forget to shake or stir it, too; that will help to get it dissolved.

7.6: Solvent Partitioning (Liquid-Liquid Extraction)

This method is often called "extraction". Extraction means drawing a compound out of a mixture using a solvent. Solvent partitioning is more specific. It means compounds have a "choice" of two solvents that they can dissolve in. Some compounds dissolve in one solvent. Some compounds dissolve in the other solvent. That way the compounds in the mixture become separated into two groups.

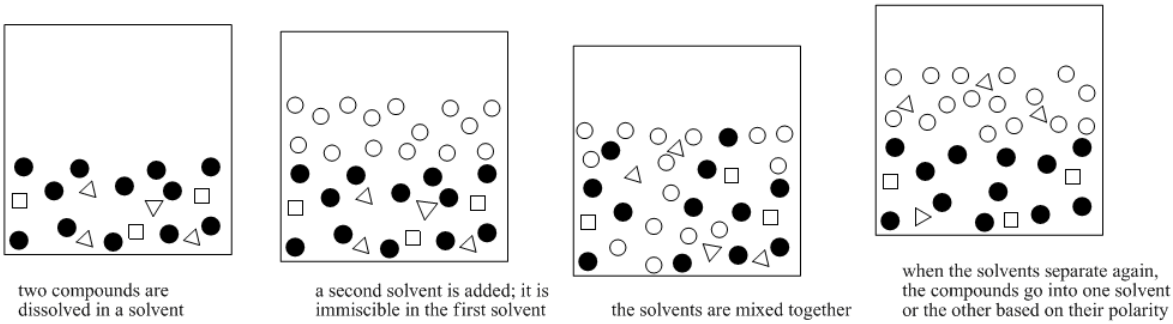


Figure 7.6.1: A cartoon showing the basic idea of solvent partitioning.

Solvent partitioning depends on solubility. It depends on the solubility in two different solvents, though. It depends on an equilibrium: does the compound dissolve more in solvent A, or solvent B?

Solvent partitioning requires two solvents that are not miscible in each other. Usually one of the solvents is water. The other solvent is a liquid that does not dissolve very well in water, such as diethyl ether (this is the most common type of ether, and it is often called simply "ether"). If you look closely at a mixture of ether and water, you will see two layers because the two compounds do not dissolve very well in each other.

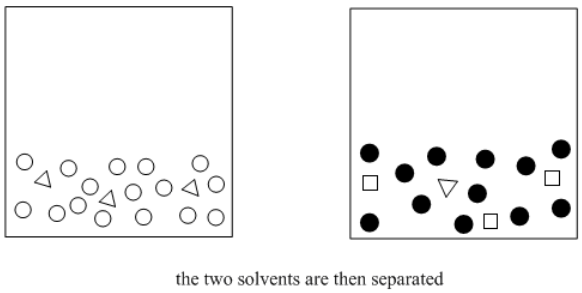


Figure 7.6.2: The next step in solvent partitioning.

It's important that the two solvents are immiscible, because then it is easy to separate them from each other. The top liquid can be drawn off with a pipet, or the bottom layer can be drained out via a stopcock. The compounds that dissolved in the ether have thus been separated from the water-soluble compounds. Because ether evaporates very easily, the compounds that dissolved in the ether can also be separated from the ether (see "distillation"). As a result, purer compounds can be obtained.

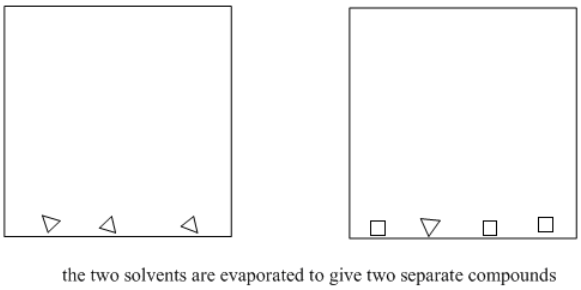


Figure 7.6.3: The end result of solvent partitioning.

Now let's take another look at the whole process and fill in some details. A solvent partitioning almost always involves the use of water and an organic solvent (based on carbon & hydrogen). In most cases, the organic solvent is not polar enough to dissolve in

water. The few exceptions are instructive to look at. Methanol, ethanol, and 2-propanol -- that is, CH_3OH, CH_3CH_2OH, and $(CH_3)_2CHOH$ -- dissolve very well in water. Butanol does not, and neither does common ether -- $CH_3CH_2CH_2CH_2OH$ and $CH_3CH_2OCH_2CH_3$. That comparison gives rise to a very rough rule of thumb about water solubility. That is, the carbon : oxygen ratio should be below 4:1 in order for an organic compound to dissolve in water. There are exceptions, but this is a good rule to keep in mind.

If the two solvents do not dissolve in each other, then when they are mixed together, they will form two different layers. That's exactly what we want. If we have a mixture of polar and nonpolar compounds, and we mix them together with water and, say, diethyl ether, then the polar compounds should migrate to the water layer and the nonpolar compound should migrate to the ether layer.

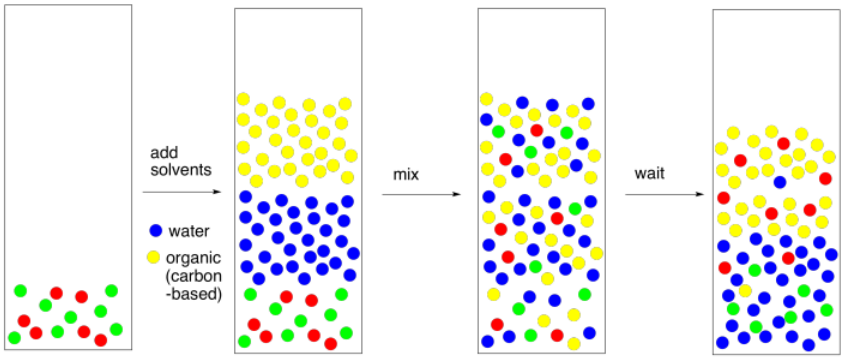


Figure 7.6.4: The basic idea of solvent partitioning.

There are a couple of different ways to carry out this step. If we are working with a very small amount of material (such as a couple of hundred milligrams) and need only a small amount of solvents (maybe a couple of millilitres), we might do all of this in a test tube. We would use a pipet to mix the two layers up by flushing one layer repeatedly through the other.

On a larger scale, we would use a separatory funnel. It has an opening on each end, with a stopper at the top and a stopcock at the bottom. We just close the stopcock, pour the stuff in the top, put the stopper on, and shake it up; typically we shake it up three times, and vent it after each time. To vent, we just open it up to let the air out, because the mixture gets a little gassy. That's because when we mix two liquids together there are always heat and volume changes as a result; the mixture may get a little warmer, or it may expand a little, so it needs more room. Most people turn it upside down and open the stopcock to vent it. Usually you can hear a little hiss when you do this.

After venting for the third time, we wait for the layers to separate.

At this point, we can separate the two layers. We take the stopper off, open the stopcock a little, and carefully drain each layer into its own flask. Usually we transfer them into two Erlenmeyer flasks (the cone-shaped ones). It's always a good idea to label the flasks. Alternatively, if we are on a test-tube scale, we can use a pipet to transfer the organic layer into a dry test tube.

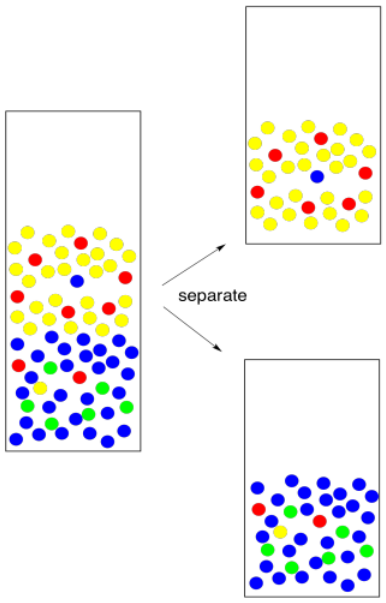


Figure 7.6.5: Separating the two layers.

How do we know which layer is which? The fact that two layers form depends on differences in intermolecular attractions, but which layer is on the bottom depends on density. That's something you should look up in a table. However, there are some rough rules of thumb here, too. Most organic solvents are less dense than water, so they float on the top. A few organic solvents are more dense than water, so they sink to the bottom. Usually these solvents contain heavy atoms such as halogens, like chlorine.

If you're looking closely at the pictures, you will notice here is something wrong with them. The red molecules were supposed to go into the yellow solvent and the green molecules were supposed to go into the blue solvent. In reality, it never works out perfectly. Someone always gets left behind. This isn't because of "human error", the mainstay of high school lab reports. It's because of nature. When we expect a compound to dissolve in one solvent rather than another, we are seldom rewarded with perfection. Instead, the compound is more likely to dissolve in one layer; there is an equilibrium constant that governs how much of the compound goes in one layer and how much goes in the other. Maybe 95% goes in the right layer, and the equilibrium constant forces the other 5% into the wrong one.

So we go back and try again. We take the water layer and extract with fresh solvent. If we are able to extract 95% of the remaining 5%, that leaves just 0.25% behind this time. That's pretty good.

By the way, that term "extract" is usually used to indicate that we are removing what we want from something we did not want. We just extracted the remaining compound from the water. Now we need to keep it safe. We combine it with the first fraction that we extracted so that all of the compound we want is in one place.

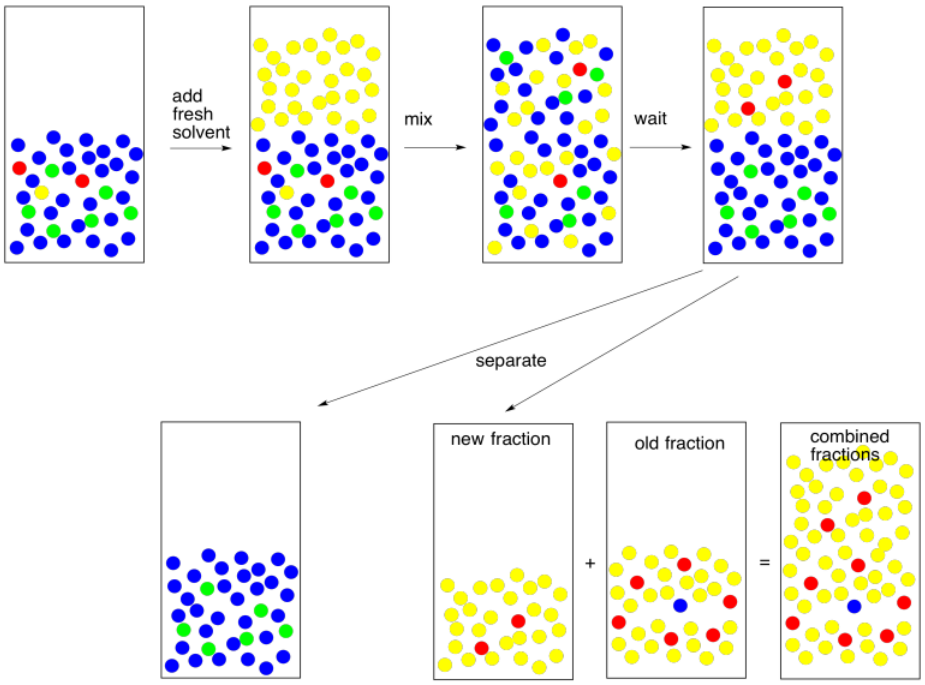


Figure 7.6.6: A second extraction: making sure to get every bit.

Now for another practical problem. Usually when we do an extraction, we like to see a good separation between two clear layers. Sometimes that does not happen. Things are cloudy, they are messy, the laters are not separating well. This is not always about human error. This could be more nature. Maybe the two layers are not separating because they are not different enough from each other.

One way to make the layers more different is to add brine (saltwater). That brine takes a polar water layer and makes it even more polar. Now there is a clearer choice about phase separation.

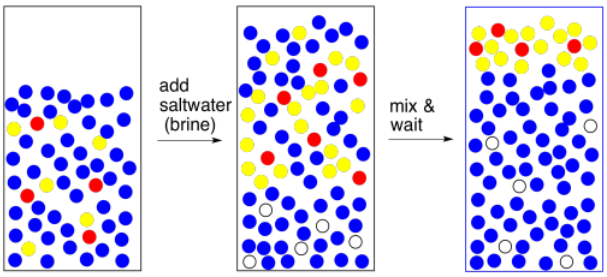


Figure 7.6.7: Adding brine to force better separation between layers.

Incidentally, if you are worried that there is polar impurity in the organic layer, we can handle it the same way. Add brine to the organic layer to coax that polar impurity out. You will get two layers and will need to separate them again but the organic layer may be purer as a result. This step is called washing; washing is like extraction, but we are removing something we do not want rather than keeping something we do want.

We are getting close to the end of a successful experiment but there is still another detail we need to deal with. Most organic solvents can dissolve a little bit of water. Usually it's an amount that is significant enough to contaminate the compound we are trying to isolate. We need to get that water out.

To remove water, we add a drying agent. A drying agent is just a salt containing a Lewis acidic metal ion; anhydrous sodium sulfate, magnesium sulfate, or calcium chloride are the most common examples. These salts have been dried to remove any traces of water, but they have a natural affinity for it, and will sponge it out of solution for us.

The method of using a drying agent is simple. You need to put a very thin layer of it on the bottom of the flask containing your combined extracts. Stir it up and wait five minutes. That's 5 minutes. Wait until the big hand moves to the next number.

At the end of that time, swirl the flask and look at the drying agent. The thing you need to know about drying agent is that when it gets wet the grains stick together in little clumps. Some of them should be stuck together now, because your organic layer came into contact with water recently and it certainly picked up a little bit of moisture. The question is, are some of the grains free? They did not stick to anybody else? When you swirl the flask, do they fly up freely like a snow globe? If so, they must be dry. If they are dry, so is your solution. Good job!

What if all of your grains of drying agent are stuck in little clumps at the bottom of the flask? They all got wet. Maybe all of the water is gone, but maybe there was too much water for the drying agent that you added. In that case, add another layer of drying agent. Wait five minutes. You get the idea.

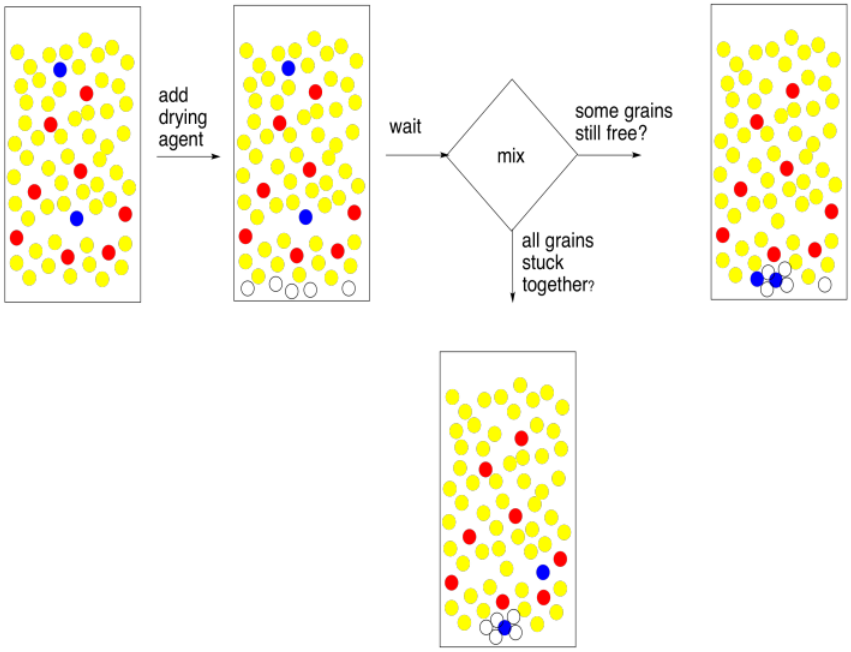


Figure 7.6.8: Removing traces of moisture from an organic layer ("drying").

If you're a lab genius, you will find a shortcut to this drying business. Forget the little layer. Just add lots. That will get rid of all the water quickly. And you're right, it will. It will probably get rid of anything else you want, too. The problem is, the drying agent is a Lewis acid. It sticks to lone pairs on the oxygen atoms in the water molecules. Unless the compound you are trying to extract is a hydrocarbon, chances are it contains oxygen atoms, too; most compounds in nature do. That means it sticks to the drying agent. Too much drying agent, and you've lost all of the compound you needed. In science, this could be described as a non-ideal situation. In layman's terms, it's a complete and utter failure.

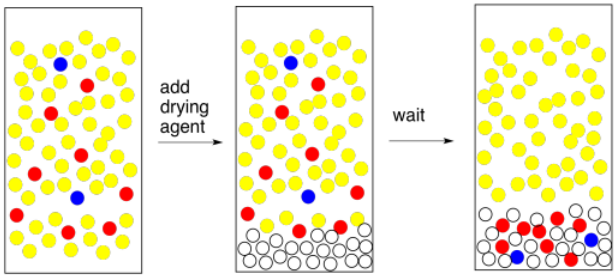


Figure 7.6.9: Drying agent disasters: when you add too much drying agent.

There's another common problem that can appear when you add the drying agent. If the organic layer is really, really wet, and you add a drying agent, which is a salt, you make saltwater. Now you have an organic layer mixed with brine. The brine layer separates from the organic layer. This is an easy problem to solve. Just separate the two layers and go back to drying the organic layer. But wait -- is the TA looking? Maybe you can just add a bunch of drying agent and absorb all of that water. If you think that sounds like a good idea, go back and read the previous paragraph.

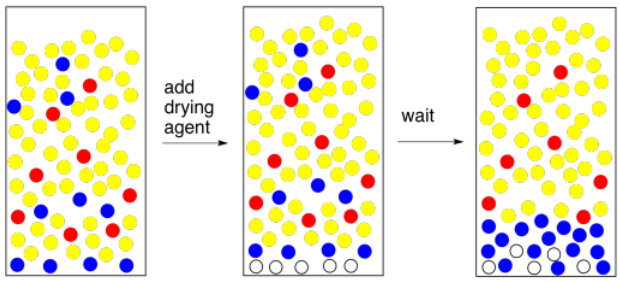


Figure 7.6.10: Drying agent disasters: when you form a briny layer.

If all goes well, and you have a nice, clear organic layer, you can just filter out the drying agent and evaporate the solvent. Finished.

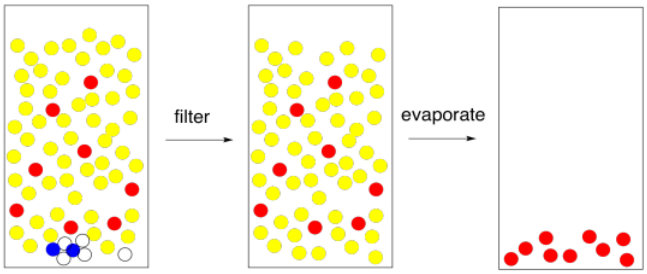


Figure 7.6.11: The end result of solvent partitioning.

Exercise 7.6.1

List reasons why ether and water SHOULD and SHOULD NOT dissolve in each other. In this case, what factors prevail in determining whether these two compounds are miscible?

Answer

Both water and ether (a common nickname for diethyl ether) contain electronegative oxygen atoms. Because both oxygens are bonded to less electronegative hydrogen or carbon atoms, each molecule will have a dipole. We may expect dipole-dipole interactions and miscibility.

Both oxygen atoms have lone pairs. Either one could act as a hydrogen bond acceptor. Because ether also contains a very polar O-H bond (remember, hydrogen bonding involves F,O,N), we may expect hydrogen bonding interactions and miscibility.

However, a C-O bond in ether is less polar than a H-O bond in water. In order for the two liquids to be miscible, stronger dipole-dipole interactions between the water molecules would have to be given up and traded in for weaker dipole-dipole interactions between the water and the ether molecules. The two liquids might not mix.

Ether has an oxygen atom with a lone pair, but it does not have a very polar O-H bond. The possibility for hydrogen bonding between water and ether is lower than between water molecules alone. The two liquids might not mix.

Ether has two hydrophobic hydrocarbon chains, although they are rather short. When mixing, these chains must be accommodated between neighbouring water molecules, which are thereby prevented from hydrogen bonding with each other. The two liquids might not mix.

Exercise 7.6.2

Ether and water have different densities. Water has a density of 1.000 g/mL and specific gravity of 1.000. Specific gravity is the ratio of a compound's density to that of water. It is no surprise that water has a specific gravity of 1.000. If ether has a specific gravity of 0.977, which compound is heavier? Which compound will float to the top and which will sink to the bottom?

Answer

The lighter ether would be on the top. The heavier water would sink to the bottom.

Exercise 7.6.3

a. Methanol has a specific gravity of 0.980. When methanol and water are mixed, which compound should float to the top?
b. However, only one layer of liquid is observed, not two. Why?

Answer
Answer a

Given two separate layers, the lighter methanol would be on the top. The heavier water would sink to the bottom.

Answer b

Methanol and water are miscible. Both are fully capable of hydrogen bonding; they are each hydrogen-bond donors and acceptors. Although the methanol has a non-polar hydrocarbon component, the methyl groups are not large enough to significantly disrupt hydrogen bonding between neighbouring water molecules.

Exercise 7.6.4

a) Draw three compounds that you think will dissolve better in water than in ether. Explain your answer.

b) Draw three compounds that you think will dissolve better in ether than in water. Explain your answer.

Answer
Answer a

Maybe the compounds are salts, containing an anion and a cation. The anions and cations could be simple inorganic ones such as Li^+ and F^-, but either the anion or the cation could also be organic (containing hydrocarbon portions). If the compounds are organic and not ionic, either the molecules would be fully capable of hydrogen bonding (containing O-H or N-H bonds), or they would contain highly polar bonds such as C=O. Also, the compounds should not contain too great a proportion of hydrocarbon compared to the polar part; for neutral compounds, that means a carbon:oxygen ratio below about 4:1, although the ratio can be significantly higher for ionic compounds.

Answer b

The compounds should be neutral, not ionic. Although they may contain polar bonds, the compound should be mostly non-polar; a rough rule is that the carbon:oxygen ratio should be greater than 4:1.

Exercise 7.6.5

State whether the following organc solvents would be form the top or bottom layer when mixed with water (d = 1.0 g/mL).

a) dichloromethane, d = 1.33 g/mL b) hexane, d = 0.66 g/mL c) toluene, d = 0.87 g/mL

d) tert-butyl methyl ether, d = 0.7404 g/mL e) chlorobenzene, d = 1.11 g/mL

f) ethyl acetate, d = 0.902 g/mL g) chloroform, d = 1.489 g/mL h) cycopentane, d = 0.75

Answer
Answer a

bottom

Answer b

top

Answer c

top

Answer d

top

Answer e

bottom

Answer f

top

Answer g

bottom

Answer h

top

Exercise 7.6.6

In general, most neutral, organic compounds will dissolve better in ether than in water. Most ionic compounds dissolve better in water than in ether. Benzoic acid dissolves better in ether than in water, but sodium benzoate dissolves better in water than in ether. Why do you think this is true?

Answer

The ionic compounds can form strong ion-dipole interactions with the water molecules. That interaction enhances their solubility in water.

Exercise 7.6.7

Describe a series of steps you could take in the lab to separate sodium benzoate from benzoic acid via solvent partitioning. By the end, you should have a sample of pure benzoic acid in one labeled vial and a sample of sodium benzoate in another.

Answer

Water and ether should be added to the mixture and the mixture should be shaken until it dissolves. The layers should be separated. The water should be extracted with additional ether and the combined ether layers should be washed with brine. The ether layers should be dried with sodium sulfate, filtered, and evaporated under vacuum.

Exercise 7.6.8

In the question above about separation of benzoic acid from sodium benzoate, why is washing the solid possibly an inadequate method?

Answer

The water molecules would have to come into contact with the sodium benzoate in order to dissolve it. If some sodium benzoate is completely surrounded by benzoic acid, it would remain undissolved.

Exercise 7.6.9

There are exceptions to the rule that most neutral, organic compounds dissolve better in ether than water. Acetic acid dissolves well in water. Why?

Answer

Acetic acid, CH_3CO_2H, contains a polar C=O bond, a hydrogen-bonding O-H group, and a carbon:oxygen ratio of 1:1. All of these factors render it relatively polar.

Exercise 7.6.10

Some organic compounds will dissolve in ether under some circumstances and water in others. For example, suppose THF is mixed with equal volumes of ether and water, and the water layer gets bigger.

In what layer is the THF? If salt is added, the water layer gets smaller and the ether layer gets bigger. In what layer is the THF now? Why does the solubility of THF vary in this way?

Answer

Answer a

The THF is in the water layer.

Answer b

The THF is in the ether layer.

Answer c

The brine makes the water layer even more polar. The THF is already on the edge of being water-soluble, because it has a carbon:oxygen ratio of 4:1. The added water polarity pushes it past the tipping point.

Exercise 7.6.11

It is useful to remember that solvent partitioning always involves an equilibrium between two solvents; compounds often do not dissolve entirely in one solvent or the other. Suppose perfluorobutanoic acid, a member of a class of compounds used for stain-resistant carpeting, is taken up in a mixture of equal parts water and ether. Imagine half the perfluorobutanoic acid ($C_3F_9CO_2H$) dissolves in the water and half in the ether (this is just a made-up number for argument's sake). What would you have to do in order to get all the perfluorobutanoic acid out of the water?

Answer

After one extraction, half the perfluorobutanoic acid would remain in the water. A second extraction would remove half the remainder, leaving only a quarter of the original amount still in the water. A third extraction would leave 12% of the original in the water; a fourth extraction would leave 6%; a fifth extraction would leave 3%; a sixth extraction would leave 1.5% a seventh extraction would leave less than 1%.

The idea here is that multiple extractions are usually necessary. However, it would be pretty unusual to choose solvent partitioning as a purification method if a compound is this soluble in water.

Exercise 7.6.12

Suppose you have a mixture of benzoic acid and sodium benzoate. You add 2 mL of ether and 2 mL of water to the mixture and it all dissolves. You forget what to do next, so you go to read Zubrick's Organic Chem Lab Survival Manual for a while. When you come back, you notice the top layer of liquid is only half as big as the bottom layer. There are also white floaties in between the two layers.

a. What has happened?
b. What are the white floaties?
c. What should you do next?

Answer

Answer a

It looks like half the ether has evaporated.

Answer b

The white floaties are probably the bezoic acid that used to be dissolved in the ether. You don't have enough ether to keep it dissolved anymore.

Answer c

> You should add more ether before this experiment gets any worse.

7.7: Acid-Base Extraction

An acid-base extraction is a type of liquid-liquid extraction. It typically involves different solubility levels in water and an organic solvent. The organic solvent may be any carbon-based liquid that does not dissolve very well in water; common ones are ether, ethyl acetate, or dichloromethane.

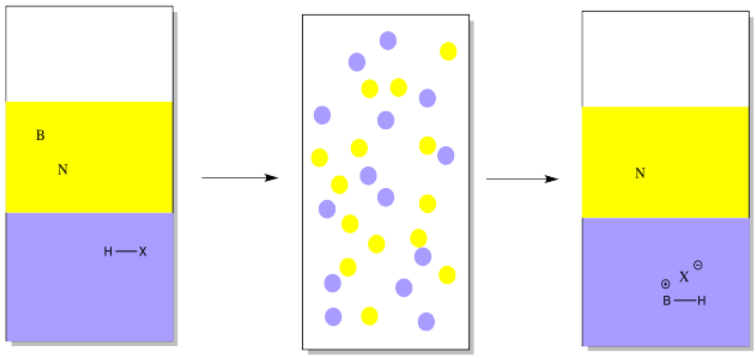
Acid-base extraction is typically used to separate organic compounds from each other based on their acid-base properties. The method rests on the assumption that most organic compounds are more soluble in organic solvents than they are in water. However, if the organic compound is rendered ionic, it becomes more soluble in water than in the organic solvent.

These compounds can easily be made into ions either by adding a proton (an H^+ ion), making the compound into a positive ion, or by removing a proton, making the compound into a negative ion.

Suppose you have a mixture of two compounds. There is a neutral one which does not react with any acids or bases. There is also a basic one, which reacts with acids by picking up a proton.

In this case, a proton might be added via reaction with a strong mineral acid (represented by HX in the drawing). Suppose an aqueous solution of mineral acid, such as HCl, were shaken vigorously with an ethereal solution of an organic base and an organic neutral. The proton would be transferred to a basic compound, but not to a neutral one. The basic compound would become ionic, and more water-soluble.

Note that in the drawing, the ether is represented in yellow, whereas the water is shown in blue. The water is on the bottom in this case because water has a higher density than ether, so it will sink to the bottom (along with anything dissolved in it). Some organic solvents do have a higher density than water, so the aqueous solution would float to the top in those case.



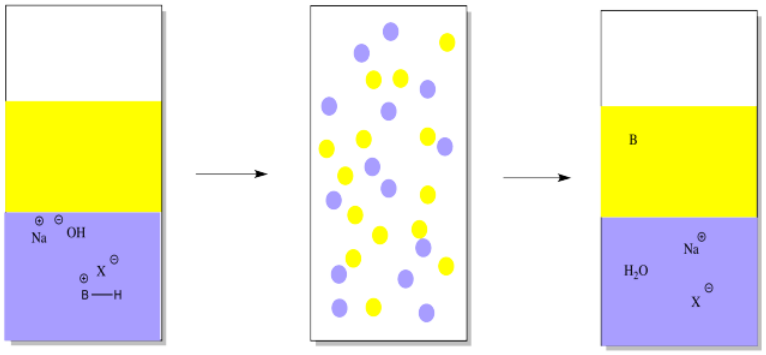
As a result, the ethereal solution would contain only the neutral compound, not the basic one. The neutral compound could be isolated simply by evaporating the ether.

However, as a practical matter, the ether would have to be dried first. What's the difference between evaporating and drying? Have you ever been to the beach or taken a shower? *Drying* refers to the removal of *water*. This step is necessary because ether tends to dissolve a lot of water in it. Once the ether has been evaporated, there would be some neutral compound, but it would be mixed with water.

Water removal is most easily done by adding a drying agent, such as magnesium sulfate or sodium sulfate. The water sticks to these solids, which are then filtered off.

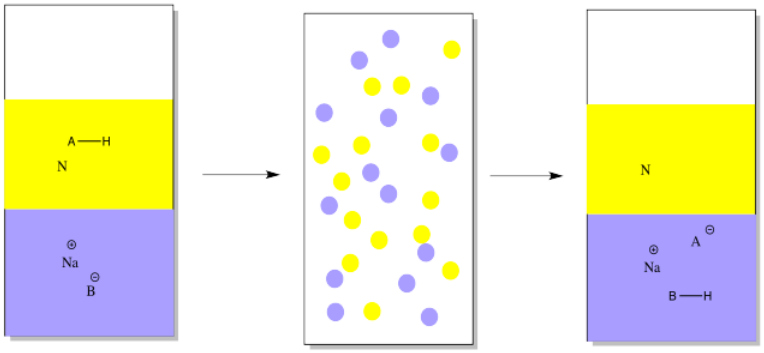
Now the neutral compound is alone in the ether. Evaporation of the ether gives the pure, neutral compound.

However, the basic compound is stuck in the water, and it isn't the same compound anymore. It's an ion, now. If we want the original compound in a pure form, we need to take that proton away. That can be done by adding a mineral base, such as sodium hydroxide.



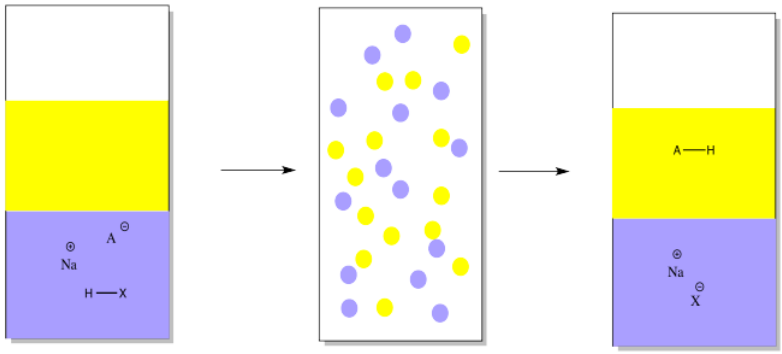
The mineral base will remove the proton, leaving the original organic compound. The organic compound is uncharged and not as soluble in water anymore. It will go back into the ether layer.

Conversely, we might have a mixture of an acidic organic compound and a neutral compound to start out with. In that case, we would add a mineral base in the first place, to take a proton away from the acidic compound. The mineral base might be something like sodium hydroxide or sodium bicarbonate. In the drawing, it is just represented as Na^+ B^-.



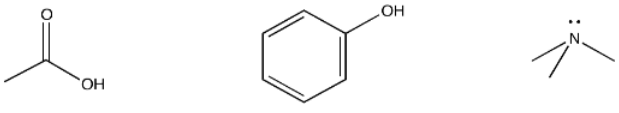
The acidic compound becomes ionic and water-soluble when it loses a proton. That leaves the neutral compound alone.

To get that acidic compound back, we would add a mineral acid such as hydrochloric acid in order to restore the missing proton.



Just as in the other case, the ether layer containing a pure compound could be separated, dried and evaporated in order to provide the pure compound.

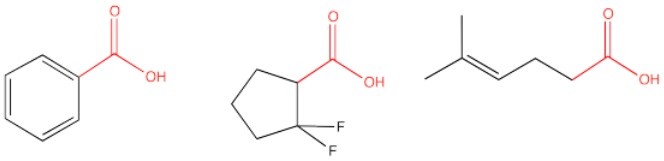
But how do we know whether something is an organic acid or a base? Common structural features of organic acids and bases are displayed below.



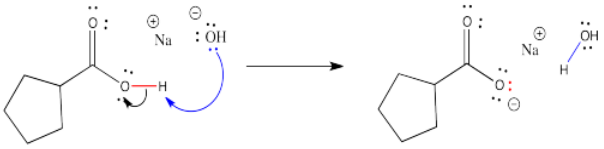
"strong acid" "weak acid" base

Note that the terms, "strong acid" and "weak acid", are relative. Sometimes, the term, "strong acid", designates a compound that completely ionizes in solution, so that it automatically gives up a H^+ ion and forms an ionic compound. Hydrochloric acid, HCl, in water is a good example. That isn't true here; none of these acids ionize very easily on their own, and they appear in solution just as they do above, with just a small minority of molecules forming H^+ and an anion. In this case, the term just compares one group of acidic compounds (called carboxylic acids) to another group of acidic compounds (called phenols). Carboxylic acids are more likely to give up protons than are phenols, so carboxylic acids are referred to in this context as "strong" and phenols as "weak".

The carboxylic acid group contains a C=O (a carbonyl) with an additional OH group attached to the carbon. Examples are shown below.

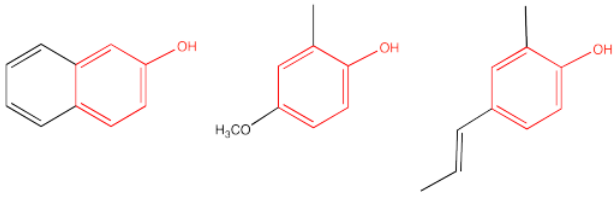


When carboxylic acids are treated with mineral bases such as sodium hydroxide, the carboxylic OH group gives up a proton to the hydroxide, forming a water molecule. The electrons in the O-H bond stay behind, putting a negative charge on the resulting carboxylate anion. The salt that forms is much more water soluble.

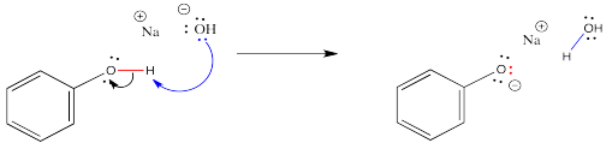


This reaction is completely reversible. A mineral acid, such as HCl, could provide protons to the carboxylate anion. The carboxylate ion would use a pair of electrons to bind to a proton, and the compound would become a neutral (as in uncharged) carboxylic acid again.

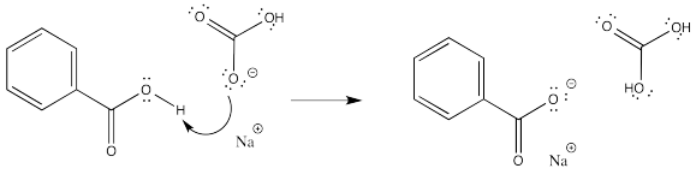
Phenols also contain an OH group, but instead of being attached to a C=O group, the OH is attached to a benzene (a six-carbon ring with three double bonds). Examples are shown below.



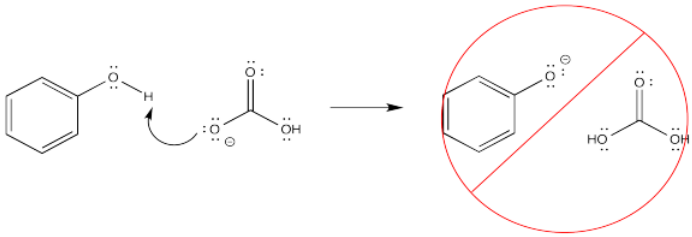
Phenols react with bases in the same way as do carboxylic acids. They just don't do so as easily.



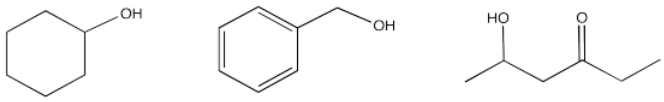
Because phenols do not react as easily as carboxylic acids, there are situations in which a carboxylic acid would react with a base but a phenol would not. For example, carboxylic acids react even with weak bases such as sodium bicarbonate (baking soda).



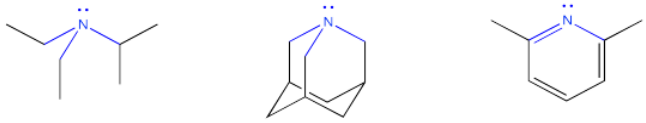
Phenols, on the other hand, do no such thing.



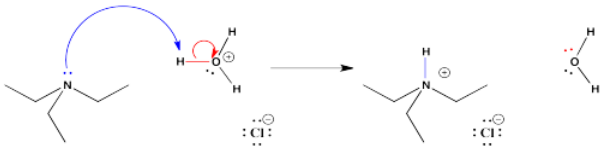
If the OH is attached to a carbon in an organic compound, but it is not attached to either a C=O or a benzene ring, it is not acidic enough to be removed to an appreciable extent. That is true even if there is a carbonyl or a benzene somewhere else in the molecule. As a result, acid-base extraction is not possible in these cases.



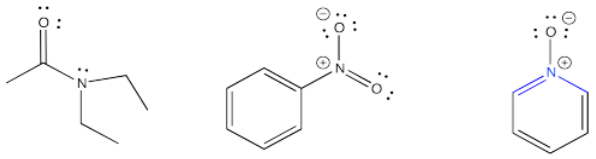
Organic bases are compounds that contain nitrogen atoms. In order to be basic, the nitrogen atom must have a lone pair. The lone pair is needed in order to make a bond with the proton.



Once the lone pair has donated to the proton to form a bond with it, the nitrogen compound becomes positively charged. It then becomes more water-soluble.

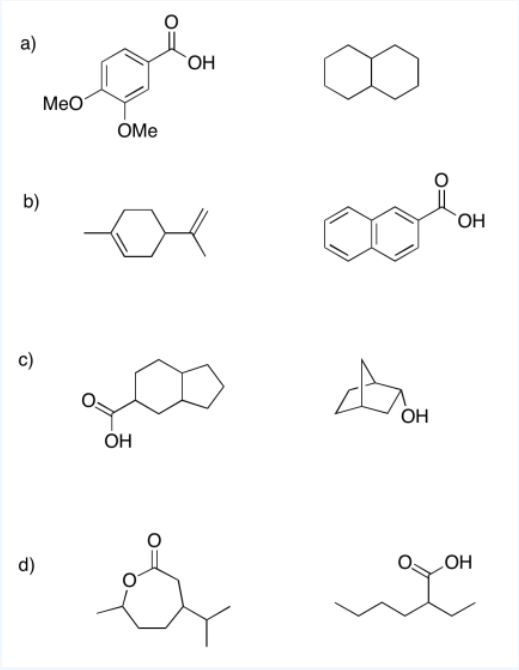


If the nitrogen does not have a lone pair, it is unable to bond to a proton. However, some compounds that do have a lone pair on the nitrogen still can't donate their lone pair to make a bond to the hydrogen. Most often that's because of a very electronegative oxygen atom nearby. The attraction of the oxygen for the lone pair makes the lone pair less able to donate to another atom. There can also be other reasons, especially involving electron delocalization or aromaticity that makes the lone pair unavailable for bonding.

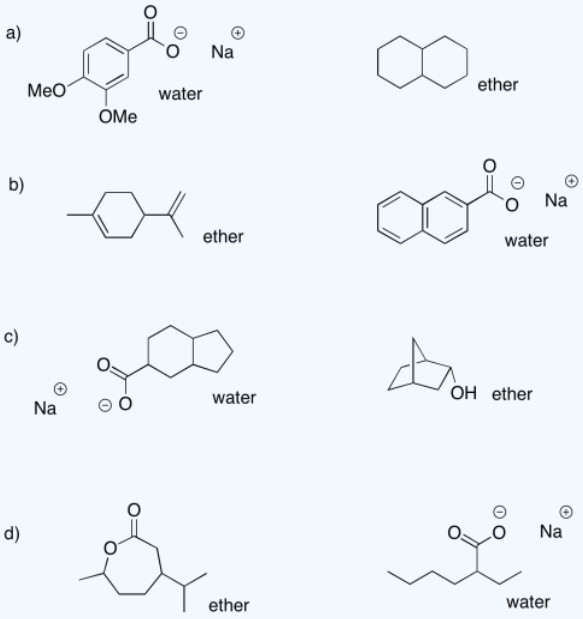


Exercise 7.7.1

If the following mixtures were taken up in ether and 1 M sodium hydroxide, indicate which compound would be found in each solvent.

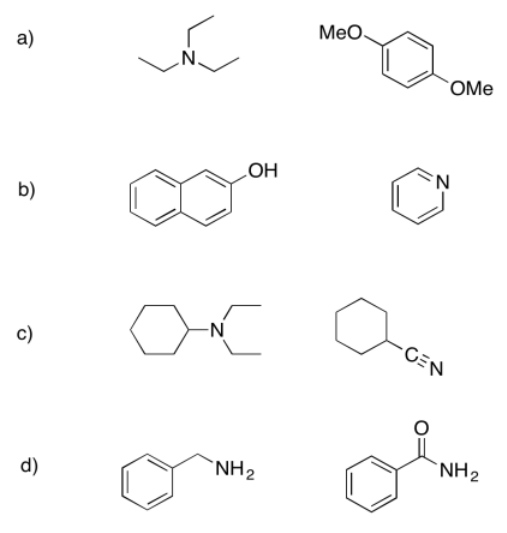


Answer

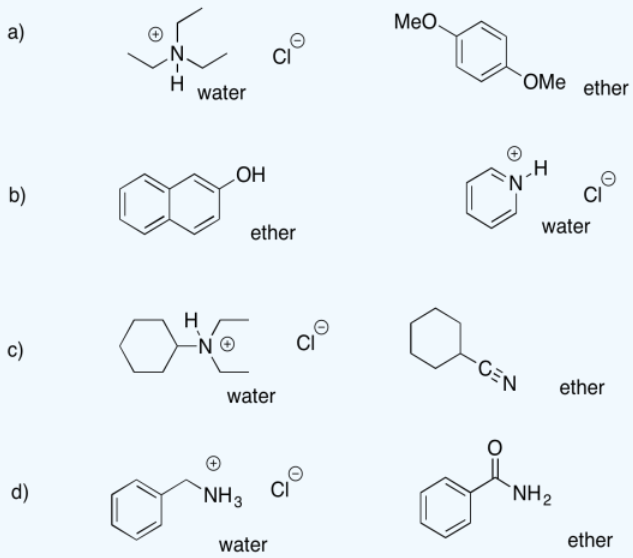


Exercise 7.7.2

If the following mixtures were taken up in ether and 1 M hydrochloric acid, indicate which compound would be found in each solvent.

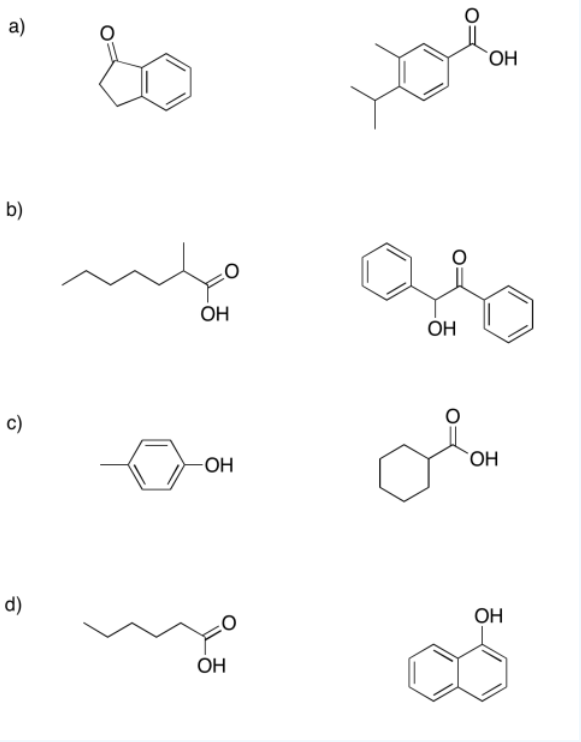


Answer

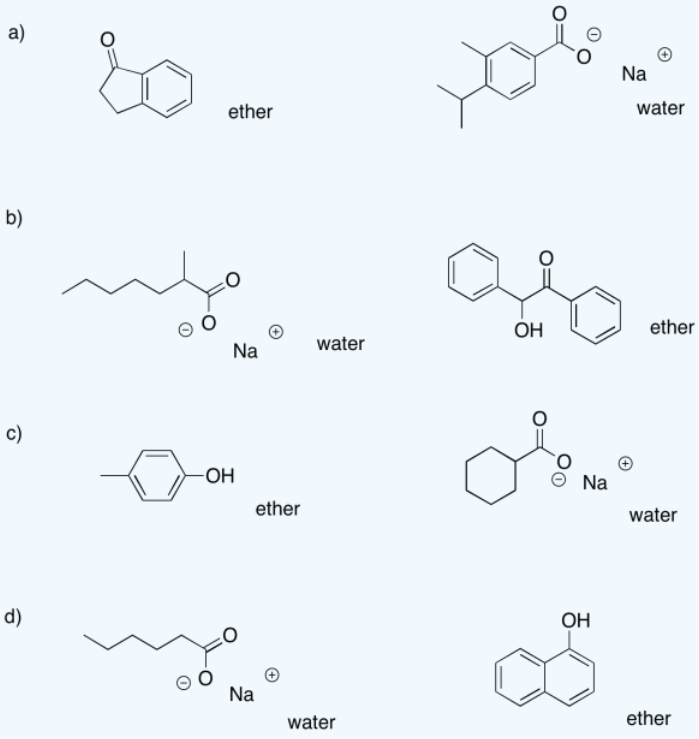


Exercise 7.7.3

If the following mixtures were taken up in ether and 1 M sodium bicarbonate, indicate which compound would be found in each solvent.



Answer



? Exercise 7.7.4

Indicate what compounds would be found in each solvent in the following cases.

a. A mixture of cyclohexanone and octanoic acid is taken up in ether / 1 M sodium hydroxide.
b. A mixture of benzylamine and dibenzyl ether is taken up in ether / 1 M hydrochloric acid.

c. A mixture of propyl heptanoate and phenol is taken up in ether / 1 M sodium hydroxide.
d. A mixture of 2-octanol and 3-bromobenzoic acid is taken up in ether / 1 M sodium hydroxide.
e. A mixture of trioctylamine and heptanal is taken up in ether / 1 M hydrochloric acid.
f. A mixture of 4-methoxyphenol and 3-nitrobenzoic acis is taken up in ether / 1 M sodium bicarbonate.

Answer
Answer a

ether: cyclohexanone; water: sodium octanoate

Answer b

ether: dibenzyl ether; water: benzylammonium chloride

Answer c

ether: propyl heptanoate; water: sodium phenolate

Answer d

ether: 2-octanol; water: sodium bromobenzoate

Answer e

ether: heptanal; water: trioctylammonium chloride

Answer f

ether: 4-methoxyphenol; water: sodium 3-nitrobenzoate

? Exercise 7.7.5

Indicate what compounds would be found in each layer (top or bottom) in the following cases.

a. A mixture of decanal and heptanoic acid is taken up in ethyl acetate / 1 M sodium hydroxide.
b. A mixture of benzyl alcohol and 4-bromophenol is taken up in dichloromethane / 1 M sodium hydroxide.
c. A mixture of 3-heptanone and N,N-dimethylbenzylamine is taken up in *tert*-butyl methl ether / 1 M hydrochloric acid.
d. A mixture of benzoic acid and 2-methylhexanoic acid is taken up in chloroform / 1 M hydrochloric acid.
e. A mixture of 2-ethylheptanoic acid and 4-chlorophenol is taken up in ether / 1 M sodium hydroxide.
f. A mixture of benzonitrile and N,N-dimethyloctanamide is taken up in dichloromethane / 1 M hydrochloric acid

Answer
Answer a

ethyl acetate (top): decanal; water (bottom): sodium benzoate

Answer b

dichloromethane (bottom): benzyl alcohol; water (top): sodium 4-bromophenolate

Answer c

ether (top): 3-heptanone; water (bottom): N,N-dimethylbenzylammonium chloride

Answer d

chloroform (bottom): benzoic acid, 2-methylhexanoic acid; water (top): nothing

Answer e

ether(top): nothing; water (bottom): sodium 2-ethylheptanoate, sodium 4-chlorophenolate

Answer f

dichloromethane (bottom): benzonitrile, N,N-dimethyloctanamide; water (top): nothing

7.8: Liquid Chromatography

Solvent partitioning involves an equilibrium between dissolving in one liquid and dissolving in another. Our first look at chromatography involves a similar equilibrium between dissolving in a liquid and sticking to a solid.

Sticking to a solid, or adhesion, occurs through intermolecular attractions between the solid and the compound adhering to it.

A grass stain on the knee of your jeans goes into the washing machine and enters into this sort of equilibrium. The equilibrium constant involving these materials (grass stain compounds such as chlorophyll, the cellulose in the cotton of the jeans, and the soapy water) determines whether your jeans will become clean or remain stained.

The great advantage of chromatography is flexibility. It does not matter whether the compound you wish to purify is a solid or liquid. Even gases can be purified by chromatography, as you will see in a later section. As long as the compound is able to dissolve in one liquid and stick to one solid, chromatography can be used to purify it.

There is a very similar type of chromatography called paper chromatography. In a typical paper chromatography demonstration, a sample of ink is spotted onto a piece of filter paper. The filter paper is made of cellulose, like jeans. The paper is dipped into a beaker of water. The water begins to wick up along the paper. As it water seeps up past the spot of ink, the spot begins to move. If the ink is made from a mixture of pigments, it separates out into different, colored compounds.

? Exercise 7.8.1

Look at the structures of paper (cellulose) and water. Why is water able to spread up through a piece of paper that is dipped into it?

Answer

The cellulose contains many OH groups and can hydrogen bond with the water molecules.

? Exercise 7.8.2

Why does the ink separate into different components as the water seeps up the paper?

Answer

Different pigments have different physical properties. Some of them will be more water-soluble than others. Some of them will adhere to the paper more strongly than others.

In liquid chromatography, there is a solid that stays put, called the stationary phase, and a liquid that moves over the solid, called the mobile phase or the eluent.

The solid is usually silica (SiO_2) or alumina (Al_2O_3). Both are polar compounds capable of hydrogen bonding. Usually they have hydroxyl groups on their surfaces.

The eluent is usually an organic solvent or mixture of solvents. The eluent can be more polar or less polar. It should not be so polar that it would dissolve the alumina or silica. If it did, the stationary phase would not stay put, but would move with the liquid phase. For that reason, methanol and water are not normally used as the eluent.

If the solid phase is stationary, then when compounds are absorbed onto the solid, they will not move either. If the liquid phase is moving, then when compounds dissolve in the liquid, they will move along, too. If there is an equilibrium between solid-phase adhesion and liquid-phase solution, compounds will spend some time moving and some time staying still.

Different compounds may have different equilibria between solution and adhesion. That means different compounds will spend different amounts of time moving or staying still. As a result, the compounds will separate from each other over time.

Schematically, chromatography works something like this. A mixture is placed at one end of the solid, stationary phase. In most cases, the stationary phase is polar; polarity is represented by arrows in the diagram. Think of the arrows as magnets. Chromatography is a little bit like a race; right now, everyone is at the starting line.

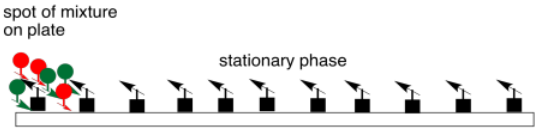


Figure 7.8.1: Loading a mixture onto the stationary phase.

A liquid, mobile phase is made to flow across the stationary phase. Although the compounds in the mixture interact with the stationary phase and spend some time sticking to it, they will also interact with the mobile phase and spend some time dissolved in it. While they are dissolved in the mobile phase, they will move along with it, because it is flowing. The race begins.

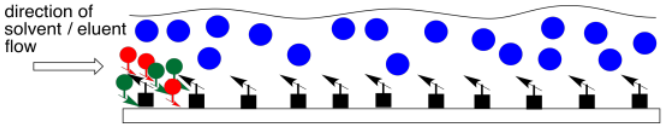


Figure 7.8.2: Introduction of a mobile phase.

The two compounds in the mixture have different properties. They have different equilibrium constants governing how much time they spend in the liquid, mobile phase and how much time they spend on the solid, stationary phase. Eventually, the less polar compound pulls ahead of the more polar one. The more polar compound is spending more time sitting on the stationary phase. The less polar compound wins the race.

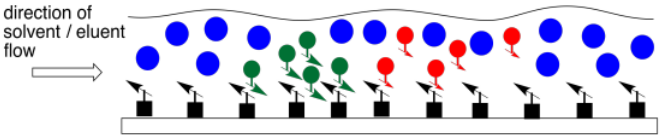
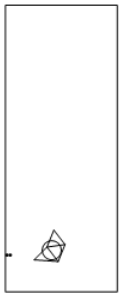


Figure 7.8.3: Elution of the mixture along the plate.

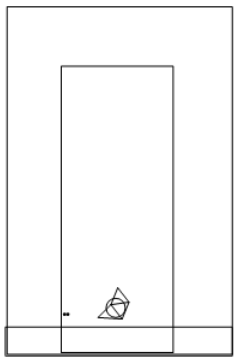
Thin layer chromatography is often done as an exploratory method to quickly see whether a mixture of compounds can be separated based on their equilibria between a stationary, solid phase and a mobile, liquid phase. Thin layer chromatography is like paper chromatography, which is sometimes demonstrated in high school. A solid sheet or plate is dipped into a solution. As the solution moves up the surface of the solid, the compounds on the plate move along to a different extent based on their polarity.

A thin layer chromatography (TLC) plate can be made of metal, glass or plastic. The alumina or silica is sprayed onto the plate and it is allowed to dry, like paint. Very often, TLC plates are purchased already prepared, with the stationary phase already "painted" onto them. Sometimes students need to make the plates themselves.

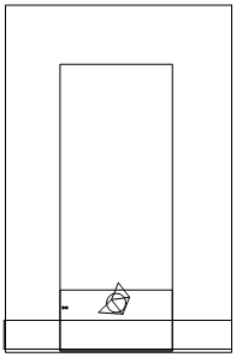
The steps in a TLC experiment are outlined below.



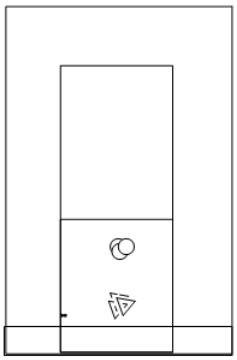
a mixture is spotted on a TLC plate



the plate is placed in a container with a small amount of solvent

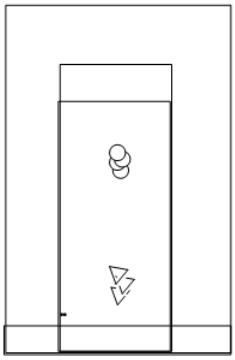


the solvent begins to wick up the plate

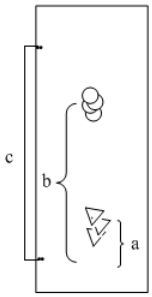


as the solvent wicks up the plate, compounds in the mixture equilibrate between adsorbing onto the surface of the plate and dissolving in the mixture

the plate and dissolving in the mixture



the farther the solvent goes, the farther the spots of compound move (unless they run out of TLC plate)



the direction of this equilibrium depends on each compound's polarity; **b** spent most of its time moving with the solvent, while **a** spent most of its time adsorbed on the plate

Figure 7.8.4: Steps in running a TLC experiment.

? Exercise 7.8.3

Suppose you place a spot of sample on a TLC plate. You have pentane and 2-butanone to use as eluent. First you try the pentane. After the pentane elutes (or wicks up) all the way to the top of the plate, none of the compounds in your mixture have moved. What is wrong? How will you fix the problem?

Answer

The pentane is not polar enough. You should add some 2-butanone to your solvent system.

? Exercise 7.8.4

Suppose you place a spot of sample on a TLC plate. You have pentane and 2-butanone to use as eluent. First you try the 2-butanone. After the 2-butanone elutes (or wicks up) all the way to the top of the plate, all of the compounds in your mixture have moved to the top of the plate, too. They have not separated from each other. What is wrong? How will you fix the problem?

Answer

The 2-butanone is too polar. You should add some pentane to your solvent system.

Exercise 7.8.5

Suppose you finally succeed in getting your mixture separated into three spots on a TLC plate. You want to isolate these three pure compounds and put them each in a labeled vial. Come up with a series of steps that you could do to accomplish this task.

Answer

Sticking with the TLC method, you would probably want to start with a much larger plate than you used for your initial tests. Instead of putting a small dot of sample on the plate, you might paint a line of sample all the way across the plate. You would use exactly the same solvent system to elute the plate as one that you found worked well on a smaller scale. After eluting the plate, you would scrape off the three lines (not spots) that had separated on the plate. You would slurry each sample in some solvent that is pretty polar but evaporates easily (maybe the 2-butanone) and filter out the silica, then evaporate the solvent. You could put the remaining sample in a vial. repeat with the two other separated samples

TLC can also be used to help confirm the identity of a compound. If we suspect a mixture contains a certain compound, and you have a sample of that known compound on hand, we can load the TLC plate with two spots, side by side. When we elute the plate, we check to see whether one of the spots from the mixture has moved the same distance as the known compound.

Of course, this method is not foolproof. It could be that one of the compounds in the mixture just happens to move the same distance as the known compound, but is actually something else. Nevertheless, it is a relatively easy way to see whether you may be right.

7.9: Column Chromatography (Normal Phase)

Thin layer chromatography (TLC) can be used to separate many different mixtures. It is very flexible because several different compounds can be separated from each other in one experiment.

Practically speaking, TLC is often used only as an analytical tool rather than as a method of purification. It is used to quickly determine if a mixture is pure, how many compounds it may contain, and what combination of eluent and stationary phase can be used to separate the compounds. However, TLC often works best with a very small amount of material. Isolating useful amounts of compound sometimes requires other kinds of chromatography.

Column chromatography is another kind of liquid chromatography. It works just like TLC. The same stationary phase and the same mobile phase can be used.

Instead of spreading a thin layer of the stationary phase on a plate, the solid is packed into a long, glass column. Usually, the solid is slurried together with the solvent and poured into the column. Sometimes these columns are several inches wide and a few feet long. A large amount of material can be purified on a chromatography column.

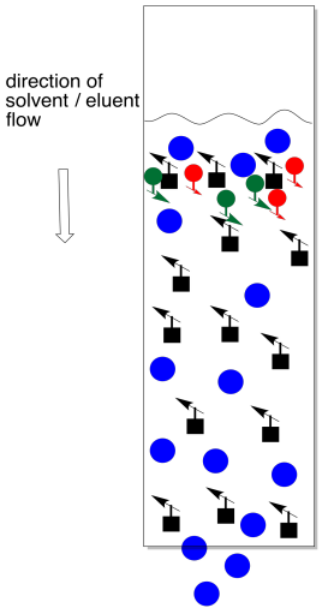


Figure 7.9.1: Introduction of a mixture to a chromatography column.

Instead of letting eluent wick up through the stationary phase, the solvent is poured into the top of the column and allowed to run through by gravity. The same factors of adhesion and solution in TLC apply here. If the same solid phase and liquid phase from TLC are used in a column, the compounds will elute through the column in the same order that they elute across a TLC plate.

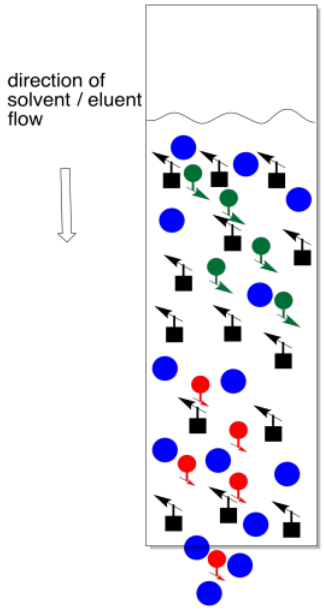


Figure 7.9.2: Elution of a mixture on a chromatography column.

To collect the separated compounds, we just collect the solution as it drips out the end of the column. Normally we can't see the compounds, so we continuously collect fractions. That might mean collecting a mL of solution in one test tube, then a mL in the next test tube, and so on.

After collecting several fractions, we would have to check to see if they contained anything. Usually this is done by TLC. We carefully take a capillary tube and spot each fraction several times on a TLC plate. We take up some solution from the first fraction in a capillary tube, tap the capillary tube on the TLC plate where we want to spot the sample, and wait for the solvent to evaporate. Then we tap the capillary again, in the exact same spot. We will repeat this cycle a few times. What we are trying to do is build up enough compound on that spot so that we will be able to detect it (usually by shining a UV light on it). Of course, the fraction may be empty, so after the solvent evaporates there may nothing there anyway, but we don't know that until we check.

We then take the next fraction and do the same thing a little bit further along the TLC plate, and the same with the fraction after that. Eventually we have a row of spots, each corresponding to a different fraction. When we elute the TLC plate, we would ideally like to see fractions containing just one spot, at an Rf value corresponding to one of the components of the original mixture.

We collect any fractions that contain pure compound and evaporate them to obtain the isolated compound.

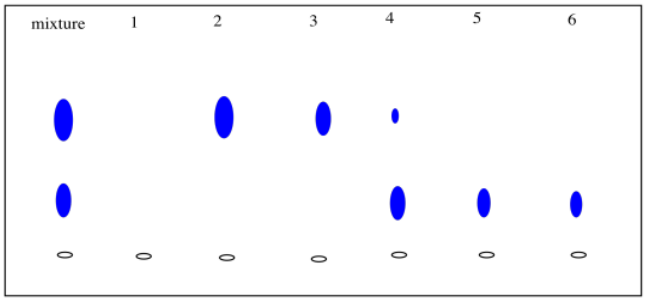


Figure 7.9.3: Checking chromatography fractions via TLC.

That's the basic idea of a chromatography column, but let's look at a few practical details.

The first thing to think about is how we set up the column. Earlier we said that we load the stationary phase as a slurry, mixed together with the mobile phase already. Alternatively, sometimes the stationary phase is carefully poured into a column already full of the mobile phase. It would be a whole lot easier to just add the solid, stationary phase first, then pour in the mobile phase. That approach comes with its own problems.

The trouble is, stationary phases such as silica usually swell when they come in contact with the mobile phase. If you pour some silica into a column, then add solvent, the grains of silica puff up and get a whole lot more crowded. They get so crowded that there isn't much room for anything to move between them. If you have a couple of months to sit around and wait for your compound to elute through the column, this method may be right for you. Otherwise, don't try it.

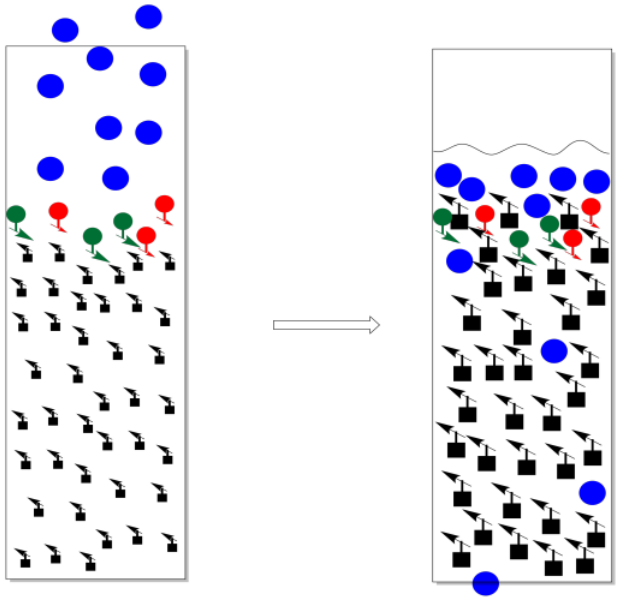


Figure 7.9.4: Swelling of the stationary phase slows down a chromatography column.

As a general rule, we want the stationary phase to always be covered in solvent. If we let the stationary phase get exposed to air (if we let it run dry and don't replace the solvent), the opposite of swelling happens. The stationary phase shrinks. When it shrinks, it gets cracks in it. Maybe we notice the problem and add more solvent, but by then it may be too late. Instead of moving through the stationary phase like it should, everything just rushes through the cracks. There is no opportunity for any of the compounds in the mixture to separate from each other.

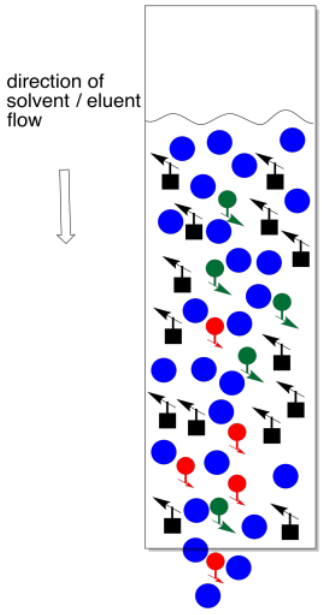


Figure 7.9.5: A crack has developed in this chromatography column.

On the other hand, you can go oveboard with solvent. This is a particular problem at the beginning, when you are introducing the mixture to be separated. What you want to do at this point is let the eluent fall exactly to the same level as the top of the stationary phase, but no further. If it falls further, the column dries out. On the other hand, if you don't let it fall far enough, you have an equally big problem.

Usually the sample is introduced as a concentrated solution in a little bit of the eluent. Sometimes it is dried onto a little bit of stationary phase by making a mix of sample, stationary phase, and a solvent, then evaporating the solvent. Either way, the idea is to get the sample in a thin layer at the top of the column. We want a thin layer because chromatography is really a race and we want all of the molecules to be at the same starting line; we can't have anybody getting head start.

The trouble with adding too much solvent at this point is that some of the sample will dissolve and move backward into the eluent. We no longer have a thin layer of sample. Not everybody is at the same starting line. It now becomes almost impossible to separate the mixture.

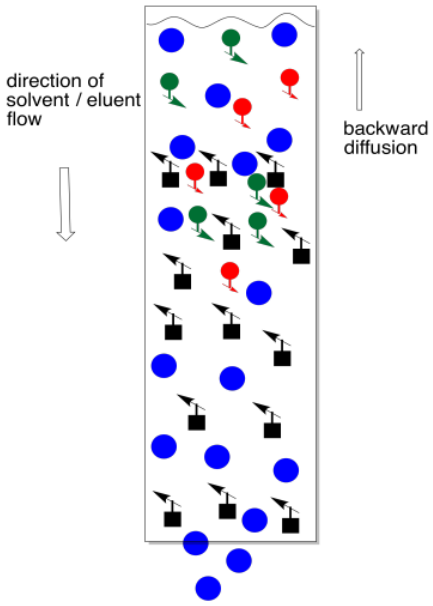


Figure 7.9.6: Too much solvent at the beginning of a chromatography column.

Instead, we add a small amount of solvent and let it drop again to the top of the stationary phase. Repeat that a couple of times (three is a magic number in the lab). At this point, we have probably drawn the compounds down into the column far enough that there is none left on the top of the stationary phase. We can safely add more solvent without washing material backward.

Eventually, you will want to add as much eluent as you can, because the column operates under gravity. The more eluent you have above the column, the more weight pushes down to move things through the column. The column speeds up.

Sometimes, instead of letting the eluent run through the column via gravity, the eluent can be pushed through more quickly using an inert gas or an air pump. This method is called flash chromatography, and it requires some special equipment. There is sometimes a trade-off between quality of separation and the time it takes to run the column, though.

? Exercise 7.9.1

Why might there be less separation between two compounds if they both move through the column faster?

Answer

The method depends on adequate time for the compounds to differentiate from each other as they move through the column. If they all move too quickly, they are probably all spending too much time in the mobile phase.

? Exercise 7.9.2

Suppose you are in the middle of separating a mixture on a chromatography column when you remember that you left the oven on in your apartment. Your apartment is a half hour from lab. You turn off the stopcock at the bottom of the column so that the eluent stops flowing. When you get back, you finish the column. You find that you didn't get very good separation between the compounds. What happened?

Answer

Without flow to keep molecules moving forward, the compounds probably diffused in all directions while they were in the mobile phase. After some time, some compounds had probably spread throughout the column.

Exercise 7.9.3

a) Suppose you are working with a chromatography column that can hold about 20 mL of solvent. You know that a sample is usually dissolved and then poured onto the top of the column before eluting with solvent. You dissolve your sample in 20 mL of solvent and proceed with the experiment. You get very poor results. What went wrong?

b) Meanwhile, the annoyingly perfect student in the next hood dissolves her sample in 1 mL of solvent and runs her column. She gets three pure compounds at the end and the instructor immediately gives her an A in the course. What did she do right?

Answer

Answer a

Instead of having a thin layer of sample at the beginning, we started with a very wide layer. As a result, by the time some molecules of one compound were emerging from the bottom of the column, others were just starting out at the beginning. Molecules of other compounds were already way ahead of them and they were not be able to catch up.

Answer b

She kept all of the molecules together at the beginning so that molecules of one compound would all stay together and arrive at the end of the comlumn at the same time.

Exercise 7.9.4

Silica and alumina are not the only possible solid phases. For example, a C18 column contains beads that have 18-carbon chains attached to them. A C18 column is an example of a "reverse phase" column, which are often used with solvents such as water, methanol or acetonitrile. In a normal column, the stationary phase is more polar than the mobile phase; is that true in a reverse phase column?

Answer

No. The solvent is more polar than the stationary phase in this case, so more polar compounds will spend more time in the mobile phase. As a result, more polar compounds will actually elute before less polar compounds.

7.10: Reverse Phase Chromatography

Silica and alumina are not the only possible solid phases. Stationary phases can be purchased that have long carbon chains bonded to silica beads. For example, a C18 column contains beads that have 18-carbon chains attached to them. These stationary phases are powders, like silica, and they can be loaded into a column just like silica can.

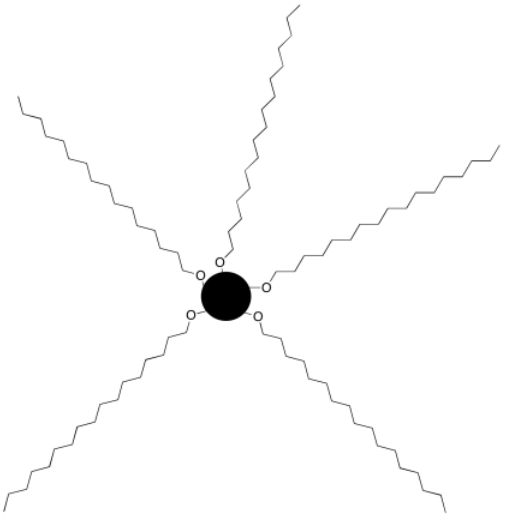


Figure 7.10.1: A cartoon of a C18 bead

A C18 column is an example of a "reverse phase" column. Reverse phase columns are often used with more polar solvents such as water, methanol or acetonitrile. The stationary phase is a nonpolar hydrocarbon, whereas the mobile phase is a polar liquid.

The same approach can also be used in TLC. If a plate is sprayed with a layer of C18 beads, then we can elute the plate in a polar solvent and separate compounds in a sample. Of course, things are reversed now. The most polar compounds will spend the most time in the mobile phase, and move most quickly. The least polar compounds will spend the most time in the stationary phase, and move most slowly.

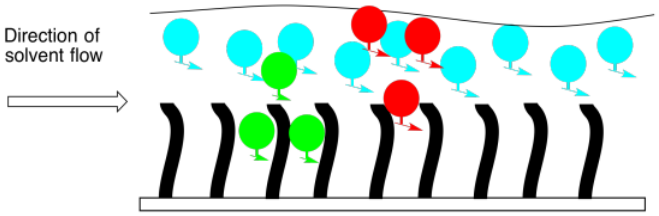


Figure 7.10.2 A cartoon of reverse phase chromatography.

? Exercise 7.10.1

On a silica (SiO2) column, three compounds were eluted in the following order using a hexanes / ethyl acetate mixture: p-dimethylbenzene, p-dimethoxybenzene, then p-methoxyphenol. What might you expect the order of elution would be on a C18 column?

Answer

p-methoxyphenol, then p-dimethoxybenzene, then p-dimethylbenzene

? Exercise 7.10.2

You are trying to elute a sample on a C18 column using 20:80 mixture of water:acetontrile, but the compounds are taking too long to come through the column. What should you do?

Answer

The compounds are not spending much time in the mobile phase, and have a much higher affinity for the non-polar stationary phase; use more acetonitrile and less water in the mobile phase.t.

One of the advantages of reverse phase chromatography is that there are many kinds of stationary phase from which to choose. By changing the kind of chain that is to the bead, we can alter how strongly it will interact with certain molecules. Maybe a completely saturated hydrocarbon packing interacts well with saturated hydrocarbons in the sample, making them elute more slowly. On the other hand, maybe a more rigid packing that contains aromatics will interact better with aromatic hydrocarbons in the sample, making those elute more slowly. We might even have some polar groups mixed in, to get a mixture of interactions.

? Exercise 7.10.3

Predict the order in which the following compounds would elute from a reverse phase column.

a. butylbenzene and benzylamine
b. 2-decanol and decanoic acid
c. 1-heptanol and 1-heptene
d. octanal and methyl octyl ether

Answer
Answer a

benzylamine then butylbenzene

Answer b

2-decanol then decanoic acid

Answer c

1-heptanol then 1-heptene

Answer d

octanal then methyl octy ether

7.11: Size Exclusion Chromatography

Size Exclusion Chromatography (abbreviated SEC), or Gel Permeation Chromatography (abbreviated GPC), uses porous plastic beads as a stationary phase. The beads are not completely uniform, and the pores or channels may be of different sizes; there may be some really tiny ones as well as larger ones.

Because the beads are porous, molecules can get caught in the pores as they travel past the beads.

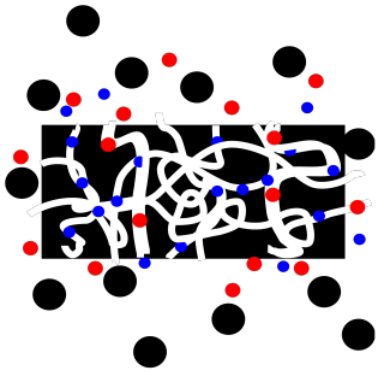


Figure 7.11.1: Molecules of different sizes interacting with a porous bead.

Smaller molecules are more likely to get caught in these pores, because small molecules can fit into these small spaces more easily. In contrast, larger molecules can't fit into the pores, and they are more likely to keep moving past the beads. The small molecules spend most of their time in the stationary phase, and elute very slowly from the column. The large molecules spend their time in the stationary phase, and elute very quickly from the column.

In between, some molecules may be able to fit into some larger pores but not the smallest ones. They will spend an intermediate time in the stationary phase.

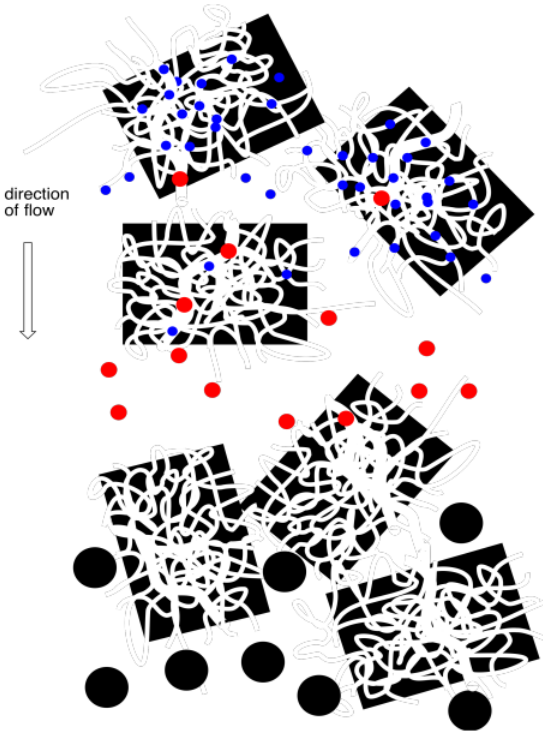


Figure 7.11.2: Molecules of different sizes flow through a column packed with porous beads.

In practice, SEC is a method of separation for macromolecules. Polymers are often separated this way, and so are proteins. You need really enormous differences between the molecules to get significant separation with this method, and that isn't likely to be the case if the molecular weights are generally low.

Exercise 7.11.1

Predict the order in which the following compounds would elute from a size exclusion column.

a. the sweet protein brazzein, MW = 6,491 D; aspartame, MW = 294 D
b. rubisco, MW = 158,300 D; trypsin, MW = 24,000 D
c. insulin, MW = 23,400 D; titin, MW = 3,800,000 D
d. polystyrene, MW = 10,000 D; polystyrene, MW = 100,000 D

Answer

Answer a

brazzein then aspartame

Answer b

rubsico then trypsin

Answer c

titin then insulin

Answer d

the MW 100,000 polystyrene then the MW 10,000 polystyrene

7.12: Ion Exchange Chromatography

In ion exchange chromatography, we can separate ions from each other, largely based on their relative charges. If one ion is more highly charged than another, it will have more affinity for the stationary phase in an ion exchange column. It will spend more time on the stationary phase and move more slowly. A compound with a lower charge will elute first.

The stationary phase would have charges opposite those of the ions that we wished to separate. For example, maybe the column is packed with a phase that contains many anions. Maybe we have some sulfate ions attached to the packing in the column, each with a negative charge.

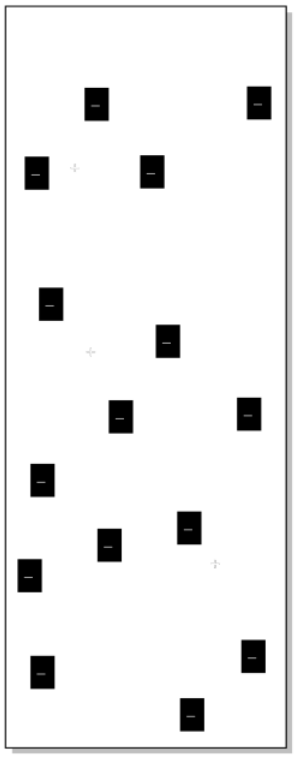


Figure 7.12.1: The packing in an ion exchange column.

Suppose we have some cationic coordination complexes that we wish to separate from each other. We can dissolve them in water and introduce them to the column. Some of them have a charge of +1 and some of them have a charge of +2. If we introduced them to a stationary phase that contained a lot of anions, they both would stick to the stationary phase. The cations with the +2 charge would stick more strongly, however, and take longer to elute from the column. They would spend more time sitting still in the stationary phase and less time moving along in the mobile phase.

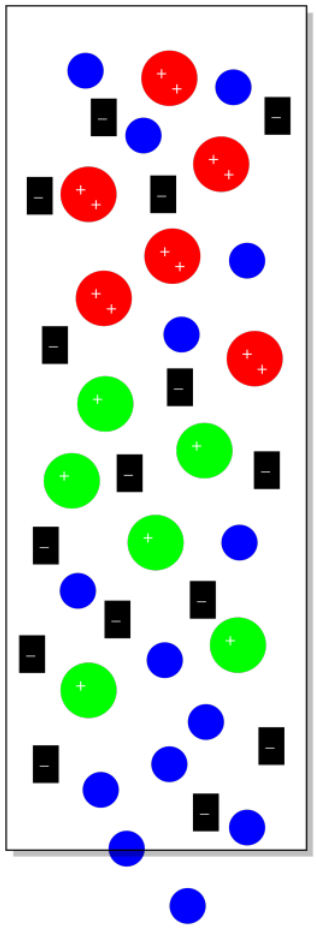


Figure 7.12.2: Ion exchange chromatography.

Of course, there are some real problems with the picture so far. First of all, we can never have just one ion without a counterion. So those sulfate ions in the original stationary phase would have sodium ions, for example, and the sodium ions would balance out the charge.

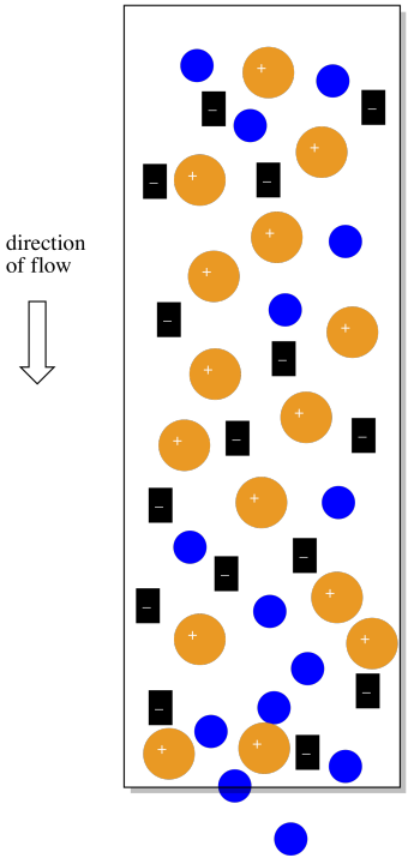


Figure 7.12.3: The counterions in an ion exchange column.

The sodium ions will be very helpful in another way. If there are no counterions, why would the cationic complexes ever come off the column? They would just stick there forever. However, if the mobile phase is a salt solution, containing more sodium ions, then eventually the sodium ions will displace the coordination complexes, which will move along in the mobile phase for awhile.

Practically speaking, the eluted fractions will not contain pure coordination complexes. They will contain the mobile phase they came with when they eluted off the column, and that mobile phase contains some sodium salts. However, each coordination complex will be separate from the other one.

7.13: Affinity Chromatography

Affinity Chromatography uses a stationary phase that is designed to bind to a specific molecule in order to isolate that molecule from a mixture. For example, this method is frequently used to purify proteins. The protein we are interested in has to have well-defined properties so that we know what to put into the stationary phase that will bind the protein. Proteins that bind to the packing spend more time in the stationary phase. Proteins that don't bind to the packing spend less time in the stationary phase and so they move through the column more quickly.

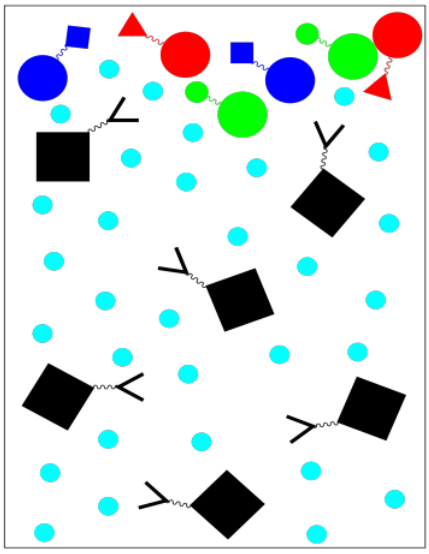


Figure 7.13.1: The stationary phase in affinity chromatography

For example, if we wish to purify a specific protein, we might use a stationary phase in which a solid resin is bonded to specific peptide chains. These peptide chains would be chosen because we know they bind well to the specific protein of interest; they are good ligands for this protein. When a mixture of proteins is loaded onto the column and washed through with a buffer, only the protein of interest will get stuck on the stationary phase. Everything else should keep moving in the mobile phase.

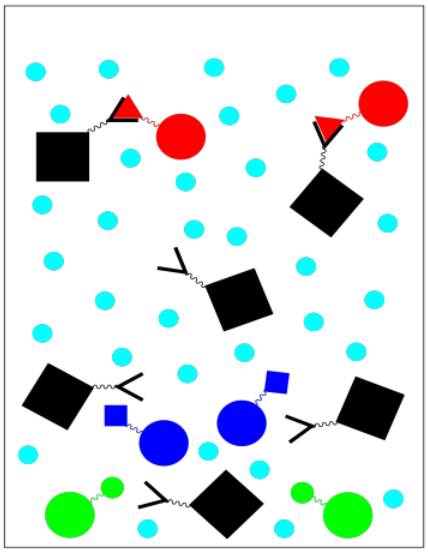


Figure 7.13.2: Washing off impurities in affinity chromatography

Unlike some other kinds of chromotography, affinity chromatography is binary. There are only two fractions: the one we want and the one we don't want. The one we don't want comes out as we wash the column with buffer.

To get the fraction we do want, we need to elute the column with an eluting solution. The eluting solution changes the conditions so that the protein we want no longer sticks to the stationary phase. For example, a change in buffer solution may result in some

conformational changes that make the protein bind less tightly to its ligand. We collect this fraction of purified protein.

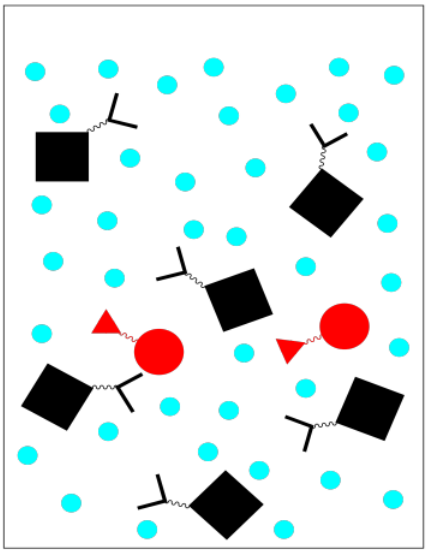


Figure 7.13.3: Releasing the desired protein in affinity chromatography

There are other variations on affinity chromatography. For example, antibodies can be purified in this way by bonding complementary antigens to the stationary phase. A peptide or nucleotide sequence might also be used because it binds to DNA or RNA.

7.14: Electrophoresis

Electrophoresis is a method of separating charged molecules from one another. In order to do so, a voltage is applied across the sample. Positively charges molecules are attracted to the negative electrode and negatively charged molecules are attracted to the positive electrode.

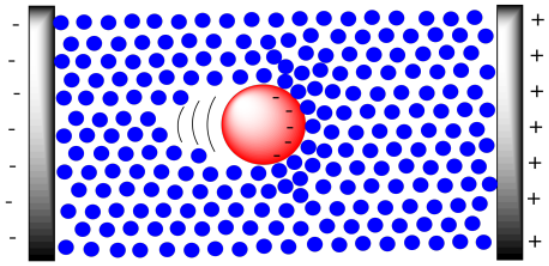


Figure 7.14.1: The electrical basis of electrophoresis.

Typically, this method is applied for the purification or analysis of very large molecules, such as proteins and DNA. These molecules are charged to begin with, so they make good candidates for movement via electric field. DNA is negatively charged because of the phosphate groups along the backbone. Of course the DNA is accompanied by counterions, but in a buffer solution the DNA molecule itself will act as a large anion, and it will move toward the positive electrode.

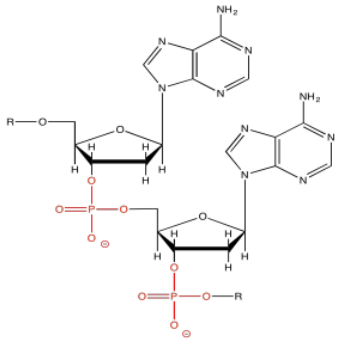


Figure 7.14.2: The phosphate group on DNA makes it anionic.

Proteins are also charged because they contain charged end groups and side chains. A buffer is chosen to give the protein net negative charge, with more anionic sites than cationic ones. That way, it will also move toward the positive electrode.

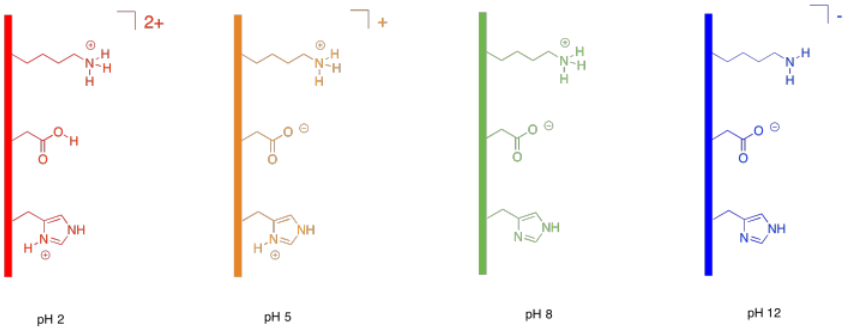


Figure 7.14.3: The effect of buffer on polar side chains in a protein.

One practical aspect of electrophoresis is that molecules must move through a stationary gel medium. A gel is composed of a solid matrix swollen with liquid. For example, the medium may be based on agar or, in a common method, a polyacrylamide gel (used in PAGE gel electrophoresis), and it is swollen with a buffer solution. The medium is not designed to bind the molecules, but it does exert drag on macromolecules as they move through it. That's true of a large molecule moving through any surroundings; think of all the water molecules that will have to get pushed out of the way to make room for a huge protein as it migrates through. That drag will slow the progress of the sample through the electric field.

The overall result is that the electric field keeps all of these anions moving in the same direction, but the drag from the medium exerts a slowing effect. The drag is really the key part of separation. The larger the molecule, the greater the drag, and the more slowly the molecule moves. In gel electrophoresis, small molecules move the fastest, and large molecules move the slowest.

Setting up electrophoresis is basically similar to chromatography, although a little more complicated. The idea is still like a race between the molecules. We start with all of the molecules at the same starting line and see who is fastest. After a gel is run through electrophoresis, the gel is usually stained with a dye (such as bromothymol blue) so that we can see how far each protein has moved.

Usually a gel is calibrated so that you get some idea of how big the proteins are in your mixture. A mixture with known components of known molecular weights is run alongside the sample that you are analysing. By comparing how far proteins in our mixture moved compared to proteins in the standard mixture, we can estimate the molecular weights of proteins in our own mixture.

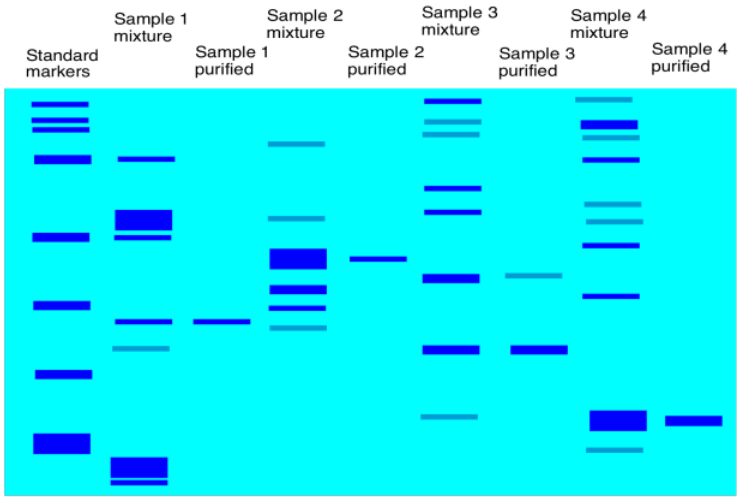


Figure 7.14.4 A cartoon showing a developed gel.

There may be different steps in electrophoresis that are designed to make things go more smoothly. For example, a protein mixture is complicated by the fact that the proteins have different secondary and tertiary structures; they have different shapes. A compact, spherical protein might move more efficiently through a gel than a more open, floppy one. As a result, a heavier protein may move farther on the gel than a lighter one simply because of its shape. To get around this problem, a surfactant (kind of like soap) may be added to the mixture; the surfactant with help to unwind the proteins so that they are all in open chains. The proteins are denatured now, but they are all more similar to each other, and it is easier to compare them based solely on molecular weight or chain length.

7.15: Instrumentation Using Chromatography

Liquid chromatography is often done with more sophisticated equipment. One kind of method is called "high performance liquid chromatography" or HPLC. Rather than packing stationary phase into a glass column, a steel column containing the stationary phase can be purchased. The column can be plumbed into a system that contains a solvent pump to push eluent through the column. After passing through the column, the liquid may go into a UV spectrometer so you can detect when compounds are eluting from the column. The whole apparatus is controlled by a computer. By clicking a button, you can change how quickly the solvent flows. You can easily change the ratio of solvents in the eluent by clicking a button, too.

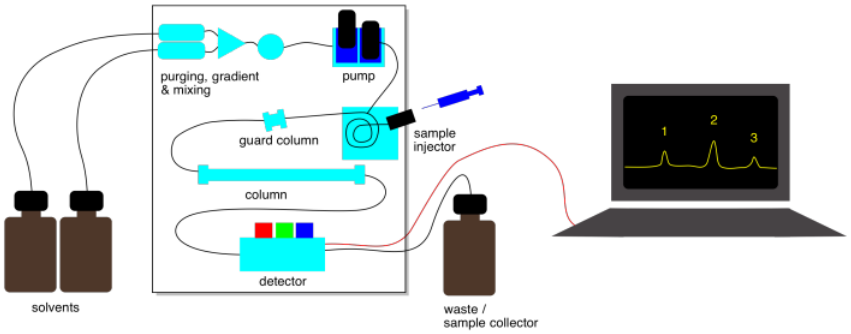


Figure 7.15.1: Schematic of an HPLC system.

In addition to a UV spectrometer, other instruments can be used with an HPLC system to get information about compounds being eluted . One of the most important is mass spectrometry (MS). Liquid chromatography-mass spectrometry (LC-MS) can be used to determine the molecular weights of the compounds as they elute. That information can be used to help identify the compound.

Gas chromatography is another important variation that you should know about. Instead of passing a liquid over the stationary phase, an inert gas moves over the stationary phase. The inert gas may be helium or nitrogen. The equilibrium here is between compounds absorbed onto the stationary phase and compounds moving in the gas phase. Intermolecular attractions with the stationary phase play a role in GC, but so does the boiling point of the compounds.

Because most compounds are not very volatile, they would spend all their time sitting on the solid phase under normal conditions. For that reason, the column in a gas chromatograph is placed inside an oven. The temperature in this oven is carefully controlled so that compounds will spend a greater fraction of time in the gas phase. A heating element in the oven can increase the temperature, and a fan is present to help cool it down when.

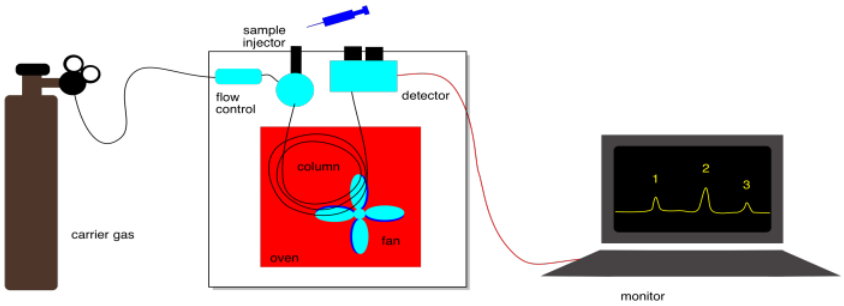


Figure 7.15.2: Schematic of a GC system.

The eluent can't be varied in GC. It is just an inert gas. To control separation of compounds in GC, we can change the pressure of the inert gas, which controls how quickly the gas flows. We can also control the temperature, which influences how much time compounds spend moving along in the gas phase . We can also choose different kinds of columns with different stationary phases.

7.16: Solutions for Selected Problems

Exercise 7.1.1:

a) Fastest: dichloromethane > hexane > water: slowest

a) Fastest: acetone > toluene > dimethyl sulfoxide: slowest

a) Fastest: pentane > ethyl acetate > benzene: slowest

Exercise 7.2.1

a) Filter: sodium carbonate; filtrate: heptanal

a) Filter: benzophenone; filtrate: lithium chloride

a) Filter: anthracene; filtrate: potassium benzoate

a) Filter: tris(ethylenediamino)cobalt(III) chloride; filtrate: ethylenediamine

Exercise 7.3.1:

a. Yes, these compounds are both liquids and the boiling point difference is large.
b. No, these compounds are both liquids but the boiling point difference is small.
c. Yes, the compound you want to purify is a liquid and the boiling point difference is large. However, you would have to be very careful not to char the remaining material in the flask.
d. Yes, these compounds are both liquids and the boiling point difference is large.
e. No, these compounds are both solids. Distillation is not a good idea.
f. Yes, these compounds are both liquids and the boiling point difference is large. However, you would have to be careful not to char the desired material; as it distills (after the contaminant is removed), its volume will get smaller. At some point, heat dissipation will become a problem for the remaining material.

Exercise 7.5.1:

It’s possible that a mixture of sodium hydroxide and sodium oleate could be purified through the addition of water. If the right amount of water were added and the resulting slurry were stirred together and filtered, much of the sodium hydroxide would be removed because it is more soluble in water than is sodium oleate. Sodium oleate is less soluble in water than is sodium hydroxide, so most of it would not dissolve. It could be gathered or “isolated” by filtration.

Exercise 7.5.2:

Sodium oleate has a long, non-polar hydrocarbon chain. Hydrocarbon chains are not very soluble in water. That's beacuse they get in between the water molecules and prevent the water molecules from hydrogen bonding to each other.

Exercise 7.5.3:

The solution contains water, lots of sodium hydroxide, and a little sodium oleate.

Exercise 7.5.4:

No. If the water were evaporated, the sodium hydroxide would still be stuck in the sodium oleate.

Exercise 7.5.6:

You might have to filter out this impurity while everything else is still dissolved. You might have to make sure everythings stays warm while you do this. If things get too cold, the solubility will get lower, and compounds might solidify before you want them too. Sometimes, when filtering an aqueous solution, it helps to put some hot water in the filter flask and keep everything warm using steam.

Exercise 7.5.7:

The borneol seems too soluble in the methanol. If you don't have anymore borneol, you will have to evaporate the methanol again. This time, add less methanol; maybe you only need a quarter mL or ten drops or something. For a recrystallization to work, you want to see partial solubility; you want the compound to dissolve when hot but not when cold.

Exercise 7.5.8:

This is a good sign. Try heating the methanol to see whether more dissolves. If it dissolves when hot, try cooling it down and see whether the solid appears again.

Exercise 7.5.9:

This is still a good sign, but you might need to add more methanol to get it all dissolved. Don't forget to shake or stir it, too; that will help to get it dissolved.

Exercise 7.6.1:

Both water and ether (a common nickname for diethyl ether) contain electronegative oxygen atoms. Because both oxygens are bonded to less electronegative hydrogen or carbon atoms, each molecule will have a dipole. We may expect dipole-dipole interactions and miscibility.

Both oxygen atoms have lone pairs. Either one could act as a hydrogen bond acceptor. Because ether also contains a very polar O-H bond (remember, hydrogen bonding involves F,O,N), we may expect hydrogen bonding interactions and miscibility.

However, a C-O bond in ether is less polar than a H-O bond in water. In order for the two liquids to be miscible, stronger dipole-dipole interactions between the water molecules would have to be given up and traded in for weaker dipole-dipole interactions between the water and the ether molecules. The two liquids might not mix.

Ether has an oxygen atom with a lone pair, but it does not have a very polar O-H bond. The possibility for hydrogen bonding between water and ether is lower than between water molecules alone. The two liquids might not mix.

Ether has two hydrophobic hydrocarbon chains, although they are rather short. When mixing, these chains must be accommodated between neighbouring water molecules, which are thereby prevented from hydrogen bonding with each other. The two liquids might not mix.

Exercise 7.6.2:

The lighter ether would be on the top. The heavier water would sink to the bottom.

Exercise 7.6.3:

a. Given two separate layers, the lighter methanol would be on the top. The heavier water would sink to the bottom.
b. Methanol and water are miscible. Both are fully capable of hydrogen bonding; they are each hydrogen-bond donors and acceptors. Although the methanol has a non-polar hydrocarbon component, the methyl groups are not large enough to significantly disrupt hydrogen bonding between neighbouring water molecules.

Exercise 7.6.4:

a. Maybe the compounds are salts, containing an anion and a cation. The anions and cations could be simple inorganic ones such as Li^+ and F^-, but either the anion or the cation could also be organic (containing hydrocarbon portions). If the compounds are organic and not ionic, either the molecules would be fully capable of hydrogen bonding (containing O-H or N-H bonds), or they would contain highly polar bonds such as C=O. Also, the compounds should not contain too great a proportion of hydrocarbon compared to the polar part; for neutral compounds, that means a carbon : oxygen ratio below about 4 : 1, although the ratio can be significantly higher for ionic compounds.
b. The compounds should be neutral, not ionic. Although they may contain polar bonds, the compound should be mostly non-polar; a rough rule is that the carbon : oxygen ratio should be greater than 4: 1.

Exercise 7.6.5:

a) bottom b) top c) top d) top e) bottom f) top g) bottom h) top

Exercise 7.6.6:

The ionic compounds can form strong ion-dipole interactions with the water molecules. That interaction enhances their solubility in water.

Exercise 7.6.7:

Water and ether should be added to the mixture and the mixture should be shaken until it dissolves. The layers should be separated. The water should be extracted with additional ether and the combined ether layers should be washed with brine. The ether layers should be dried with sodium sulfate, filtered, and evaporated under vacuum.

Exercise 7.6.8:

The water molecules would have to come into contact with the sodium benzoate in order to dissolve it. If some sodium benzoate is completely surrounded by benzoic acid, it would remain undissolved.

Exercise 7.6.9:

Acetic acid, CH_3CO_2H, contains a polar C=O bond, a hydrogen-bonding O-H group, and a carbon: oxygen ration of 1:1. All of these factors render it relatively polar.

Exercise 7.6.10:

a. The THF is in the water layer.
b. The THF is in the ether layer.

a) The brine makes the water layer even more polar. The THF is already on the edge of being water-soluble, because it has a carbon : oxygen ratio of 4:1. The added water polarity pushes it past the tipping point.

Exercise 7.6.11:

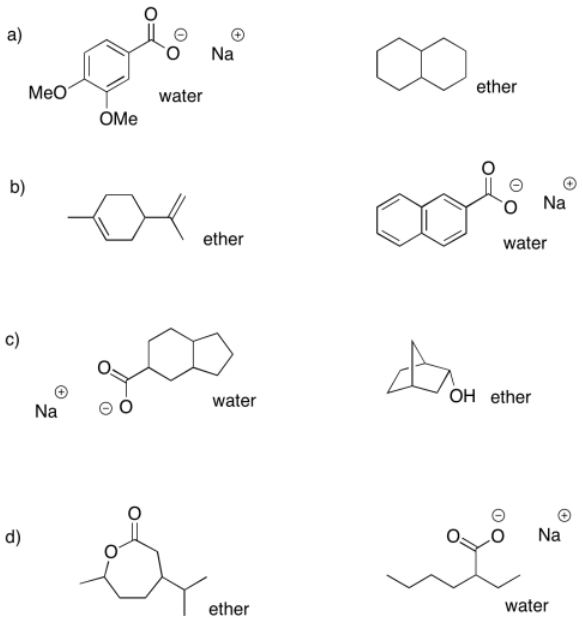
After one extraction, half the perfluorobutanoic acid would remain in the water. A second extraction would remove half the remainder, leaving only a quarter of the original amount still in the water. A third extraction would leave 12% of the original in the water; a fourth extraction would leave 6%; a fifth extraction would leave 3%; a sixth extraction would leave 1.5% a seventh extraction would leave less than 1%.

The idea here is that multiple extractions are usually necessary. However, it would be pretty unusual to choose solvent partitioning as a purification method if a compound is this soluble in water.

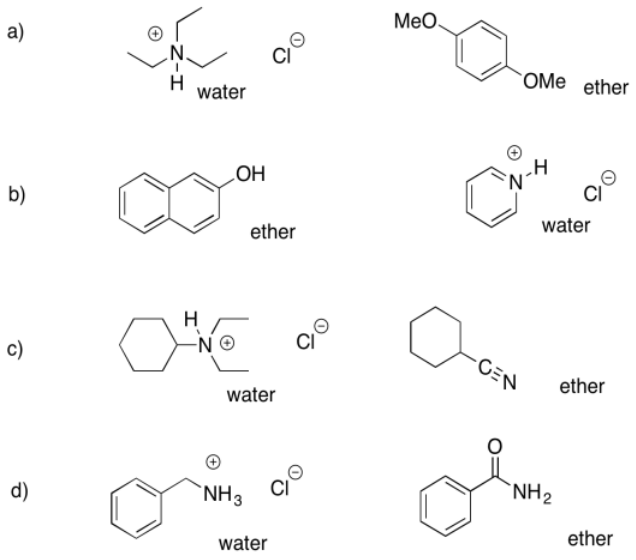
Exercise 7.6.12:

a. It looks like half the ether has evaporated.
b. The white floaties are probably the bezoic acid that used to be dissolved in the ether. You don't have enough ether to keep it dissolved anymore.
c. You should add more ether before this experiment gets any worse.

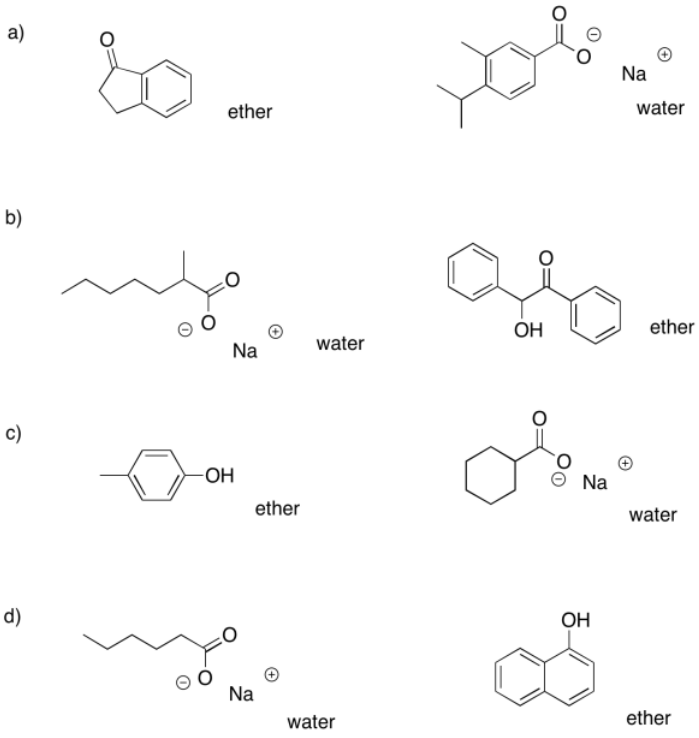
Exercise 7.7.1:



Exercise 7.7.2:



Exercise 7.7.3:



Exercise 7.7.4:

a. ether: cyclohexanone; water: sodium octanoate
b. ether: dibenzyl ether; water: benzylammonium chloride
c. ether: propyl heptanoate; water: sodium phenolate
d. ether: 2-octanol; water: sodium bromobenzoate
e. ether: heptanal; water: trioctylammonium chloride
f. ether: 4-methoxyphenol; water: sodium 3-nitrobenzoate

Exercise 7.7.5:

a. ethyl acetate (top): decanal; water (bottom): sodium benzoate

b. dichloromethane (bottom): benzyl alcohol; water (top): sodium 4-bromophenolate
c. ether (top): 3-heptanone; water (bottom): N,N-dimethylbenzylammonium chloride
d. chloroform (bottom): benzoic acid, 2-methylhexanoic acid; water (top): nothing
e. ether(top): nothing; water (bottom): sodium 2-ethylheptanoate, sodium 4-chlorophenolate
f. dichloromethane (bottom): benzonitrile, N,N-dimethyloctanamide; water (top): nothing

Exercise 7.8.1:

The cellulose contains many OH groups and can hydrogen bond with the water molecules.

Exercise 7.8.2:

Different pigments have different physical properties. Some of them will be more water- soluble than others. Some of them will adhere to the paper more strongly than others.

Exercise 7.8.3:

The pentane is not polar enough. You should add some 2-butanone to your solvent system.

Exercise 7.8.4:

The 2-butanone is too polar. You should add some pentane to your solvent system.

Exercise 7.8.5:

Sticking with the TLC method,you would probably want to start with a much larger plate than you used for your initial tests. Instead of putting a small dot of sample on the plate, you might paint a line of sample all the way across the plate. You would use exactly the same solvent system to elute the plate as one that you found worked well on a smaller scale. After eluting the plate, you would scrape off the three lines (not spots) that had separated on the plate. You would slurry each sample in some solvent that is pretty polar but evaporates easily (maybe the 2-butanone) and filter out the silica, then evaporate the solvent. You could put the remaining sample in a vial. repeat with the two other separated samples.

Exercise 7.9.1:

The method depends on adequate time for the compounds to differentiate from each other as they move through the column. If they all move too quickly, they are probably all spending too much time in the mobile phase.

Exercise 7.9.2:

Without flow to keep molecules moving forward, the compounds probably diffused in all directions while they were in the mobile phase. After some time, some compounds had probably spread throughout the column.

Exercise 7.9.3:

a. Instead of having a thin layer of sample at the beginning, we started with a very wide layer. As a result, by the time some molecules of one compound were emerging from the bottom of the column, others were just starting out at the beginning. Molecules of other compounds were already way ahead of them and they were not be able to catch up.
b. She kept all of the molecules together at the beginning so that molecules of one compound would all stay together and arrive at the end of the comlumn at the same time.

Exercise 7.9.4:

No. The solvent is more polar than the stationary phase in this case, so more polar compounds will spend more time in the mobile phase. As a result, more polar compounds will actually elute before less polar compounds.

Exercise 7.10.1:

p-methoxyphenol, then p-dimethoxybenzene, then p-dimethylbenzene

Exercise 7.10.2:

The compounds are not spending much time in the mobile phase, and have a much higher affinity for the non-polar stationary phase; use more acetonitrile and less water in the mobile phase.

Exercise 7.10.3:

a. benzylamine then butylbenzene

b. 2-decanol then decanoic acid
c. 1-heptanol then 1-heptene
d. octanal then methyl octy ether

Exercise 7.11.1:

a. brazzein then aspartame
b. rubsico then trypsin
c. titin then insulin
d. the MW 100,000 polystyrene then the MW 10,000 polystyrene

CHAPTER OVERVIEW

8: Lab Basics

8.1: Dissolution

There are a couple of very basic procedures that are used routinely in the laboratory, and that are actually key steps in other methods. The preparation of solutions, or dissolution of solutes, is one of them.

In a solution, one compound is dissolved in another. For example, sugar water and salt water are solutions. The sugar molecules can dissolve in the water because of hydrogen bonding; these strong intermolecular attractions allow the water molecules to pull sugar molecules apart from one another. The sugar molecules interact with the water molecules instead of with each other.

In salt water, ion-dipole interactions pull the sodium ions apart from the chloride ions in the salt. Instead of interacting directly with each other, the ions interact with the partial charges on the polar water molecules.

In a solution, there is always a liquid compound that dissolves the other compound. This liquid compound is called the "solvent". Water is a very common solvent, but there are other ones, too. The compound that gets dissolved is called the "solute". This compound could be a solid, a liquid, or even a gas. Life in the oceans depends on gas-phase oxygen from the atmosphere dissolving in the water so that respiration is possible in marine organisms. Life on earth depends on solid minerals dissolving in water so that they can be taken up by plants and other organisms.

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