

## 15.10 Analyzing a $^1\text{H}$ NMR Spectrum

In this section, we will practice analyzing and interpreting NMR spectra. Because a  $^1\text{H}$  NMR spectrum provides a lot of information, we must develop a systematic approach to solving the puzzle. Given below is a 5-step procedure that can guide us through the process.

1. Calculate the degrees of unsaturation (hydrogen deficiency index, HDI).
2. Determine the number of protons that correspond to each signal (peak integration).
3. Create a list of pieces (using the peak integration and molecular formula).
4. Figure out how those pieces fit together (using the chemical shift and multiplicity).
5. Confirm that our structure matches the spectral data given.

Let's consider each step in more detail.

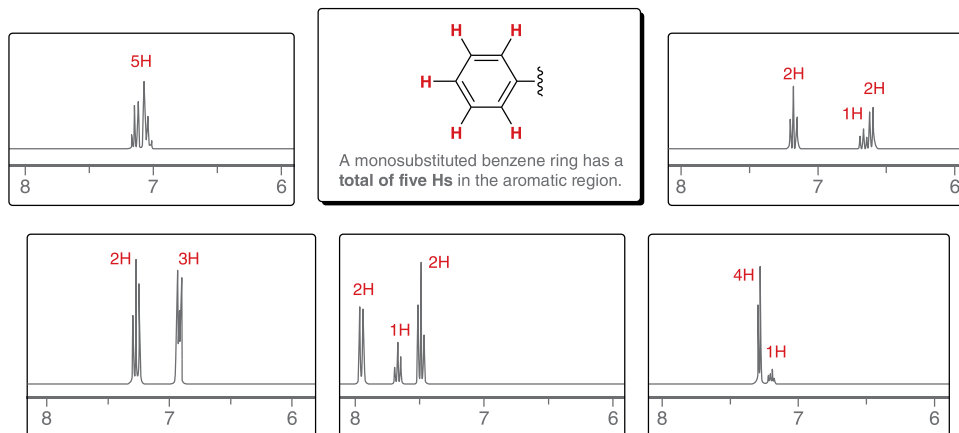
### LOOKING BACK

For a review of how to calculate and interpret the HDI of a compound, see Section 14.13.

1. Always begin by inspecting the molecular formula (if it is given), as it provides useful information. Specifically, calculating the hydrogen deficiency index (HDI) can provide important clues about the structure of the compound. An HDI of zero indicates that the compound does not possess any rings or  $\pi$  bonds. An HDI of 1 indicates that the compound has either one ring or one  $\pi$  bond. If the HDI is 4 or more, then it indicates the possible presence of a benzene ring (one ring + three  $\pi$  bonds = four degrees of unsaturation).
2. If the number of protons corresponding to each signal is not given, use the integration values to determine the number of protons for each signal.
3. Using the integration numbers, make a list of the pieces that will be used to build the molecule. During this step, we are using only the integration values. We are NOT going to worry about the chemical shift ( $\delta$  values) during this step, unless the signal is above 7 ppm. For signals above 7 ppm, the chemical shift must be taken into account, because it reveals important information. Recall that aromatic protons are expected in the general region 6.5–8 ppm. If the molecular formula has an HDI of at least four, and there are signals around 7 ppm, then a *benzene ring* is one of the pieces of your puzzle! The signals for these *aromatic protons* may be grouped closely together (as an apparent singlet or a multiplet) or they may appear as several signals in the general region. The integration values can be used to determine how many substituents are on the benzene ring. If there are a total of five protons around 7 ppm, that indicates the presence of a *monosubstituted* benzene ring (a benzene ring with just one group attached to it). Shown below are several examples of  $^1\text{H}$  NMR spectra that contain a monosubstituted benzene ring. In each example, we would consider all of these signals together (with a total of 5H) to deduce the puzzle piece shown (called a phenyl group,  $-\text{Ph}$ ).



Four degrees of unsaturation (HDI=4)

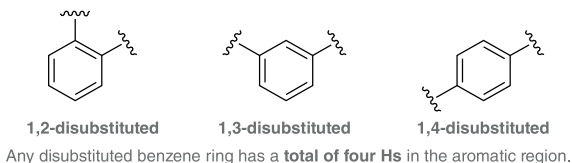


If we instead find that there are a total of four protons in the aromatic region, then the molecule contains a *disubstituted* benzene ring, and we record that as one of our pieces. The two substituents might be on adjacent positions (1,2-), or they might have a CH between them

(1,3-) or they might be on opposite sides of the ring (1,4-). The number of signals, along with the splitting patterns of the signals can often be used to differentiate between the possibilities.

### BY THE WAY

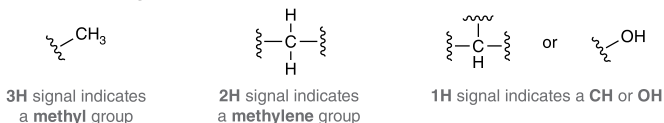
In Chapter 17, we will learn that these three substitution patterns are called *ortho*, *meta*, and *para*, respectively.



There are two more important signals above 7 ppm that give us clues about the molecular structure. A sharp signal at approximately 9.7 ppm indicates an aldehyde. Aldehyde protons usually appear as singlets, but they may exhibit very small splitting (2–3 Hz). Carboxylic acid protons typically appear as very broad singlets in the region of 10–13 ppm.



What other pieces can we look for in the rest of the spectrum (below 7 ppm), based only on integration values? Let's assume that a signal with an integration of three represents a methyl group ( $-\text{CH}_3$ ). Likewise, a signal with an integration of two most likely represents a methylene group ( $-\text{CH}_2-$ ). A 1H signal usually represents a CH, but it could be an OH. Recall that an OH signal typically appears as a broad singlet.



Two equivalent methyl groups give rise to a 6H signal, and a *tert*-butyl group produces a 9H signal. A 4H signal is likely to correspond to two equivalent  $\text{CH}_2$  groups. These assumptions are usually correct, so they are a good place to start. However, if the molecular formula contains nitrogen, then the spectrum may show a broad 2H signal ( $\text{NH}_2$ ) or 1H signal ( $\text{NH}$ ) that would have to be taken into account.

Before moving to the next step, check to make sure you have listed all the pieces of the molecule. Count up all the atoms in the pieces and compare the totals to the molecular formula. If any carbon atoms or heteroatoms (O, N, X) are missing, then they must be added to your list. If the pieces you have drawn do not already account for the calculated HDI, then you should make a note of that as well.

- Now that we have all our pieces, we are ready to assemble the fragments into a molecular structure. Start with an end piece, such as a methyl group ( $-\text{CH}_3$ ). To determine what the methyl group is attached to, we consider its chemical shift and multiplicity. We must identify the piece that provides the correct number of neighbors ( $n + 1$  rule) and also accounts for any downfield shift if there is one (*i.e.*, if  $\delta > 2$  ppm). If the methyl signal is a triplet, then it is likely to be attached to a  $\text{CH}_2$  (2 neighbors  $\rightarrow$  3 peaks). Likewise, if the signal is a singlet then there are no protons on the neighboring atoms (0 neighbors  $\rightarrow$  1 peak). Gradually, the pieces are assembled into larger fragments until a complete molecule is produced.
- Completing a jigsaw puzzle comes with the satisfaction of perfectly fitting the last piece into the last opening. A similar reward comes from solving an NMR spectrum, when we verify that the proposed structure is consistent with all of the spectral data.

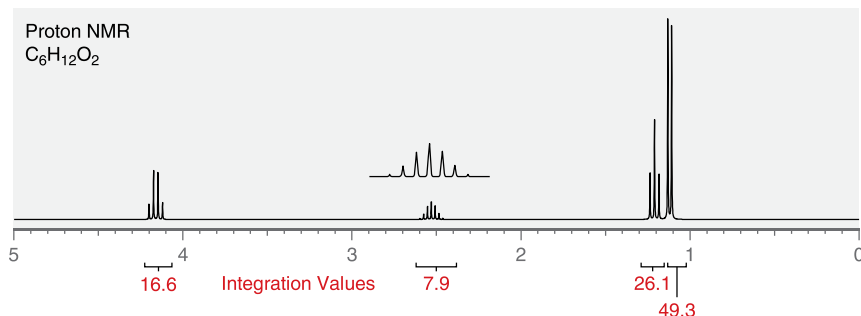
The following SkillBuilder illustrates how this is done.

## SKILLBUILDER

15.8 ANALYZING A  $^1\text{H}$  NMR SPECTRUM AND PROPOSING THE STRUCTURE OF A COMPOUND

## LEARN the skill

Identify the structure of a compound with the molecular formula  $\text{C}_6\text{H}_{12}\text{O}_2$  that exhibits the following  $^1\text{H}$  NMR spectrum:



## SOLUTION

## STEP 1

Using the molecular formula, calculate and interpret the HDI.

## STEP 2

Determine the number of protons for each signal by using the integration values.

## STEP 3

Using the integration for each signal, determine the pieces of your molecule. Confirm that the pieces “add up” to the molecular formula.

Begin by calculating and interpreting the HDI. The molecular formula ( $\text{C}_6\text{H}_{12}\text{O}_2$ ) indicates one degree of unsaturation (see Section 14.13), which means that the compound has either one  $\pi$  bond or one ring (but not both).

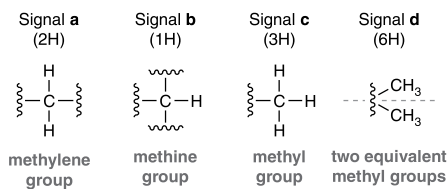
Next, we determine the number of protons for each signal by using the integration values. We divide each of the given integration values by 7.9 (the smallest integration value), giving the following approximate ratio:

$$2 : 1 : 3 : 6$$

The molecular formula indicates that the compound has twelve protons, so these integration values represent the actual number of protons giving rise to each signal:

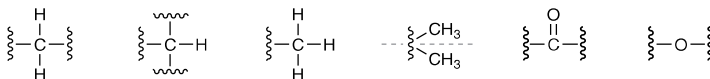
$$2\text{H} + 1\text{H} + 3\text{H} + 6\text{H} = \text{H}_{12}$$

Next, we generate a list of molecular pieces (fragments) by analyzing the integration value of each signal. For clarity, we label the four signals from left to right as **a–d** (the signal above 4 ppm is labelled **a**, and the signal closest to 1 ppm is labelled **d**). Signal **a** has an integration value of 2H, highly suggestive of a methylene group ( $\text{CH}_2$ ). Signal **b** has an integration of 1H, which corresponds with just one proton (either OH or CH). There is generally no coupling across an oxygen atom so an OH signal would be singlet. This signal is not a singlet, so it must represent a CH (methine) group rather than an OH group. Signal **c** has an integration value of 3H, indicating a methyl group. And finally, signal **d** has an integration value of 6H, suggesting two equivalent methyl groups:



Before moving on to the next step, we must confirm that the fragments “add up” to the molecular formula ( $\text{C}_6\text{H}_{12}\text{O}_2$ ). The fragments above account for five carbon atoms and twelve hydrogen atoms. We still need to account for one more carbon atom and two oxygen atoms, and we must also account for one degree of unsaturation (either a ring or a  $\pi$  bond). A carbonyl group conveniently takes care of most of these requirements (all except for one

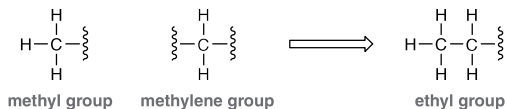
oxygen atom), so we draw a carbonyl group and an oxygen atom as the missing fragments. The following list of fragments now accounts for all atoms in the molecular formula:



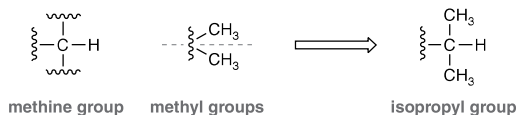
#### STEP 4

Use the splitting patterns and chemical shifts to assemble the pieces.

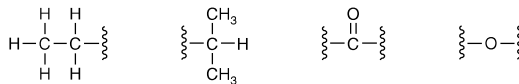
Next, we assemble these puzzle pieces by using the chemical shift values and splitting patterns as clues to determine how the fragments are connected. As a starting point, we choose one of the methyl groups (either signal **c** or signal **d**). Either is a fine starting point. We will start with signal **c**. This signal is a triplet, which means that this methyl group has two neighboring protons. Therefore, we can connect the methyl group with the methylene group to give an ethyl group:



Now let's consider signal **d** (the two equivalent methyl groups). This signal is a doublet, which means that it represents protons that have only one neighbor. That is, the two equivalent methyl groups are connected to the methine group (CH), like this:



At this point, we have the following pieces which must be assembled to complete the puzzle:

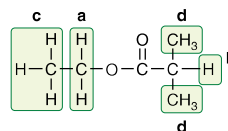


There are only two ways to connect these fragments, as shown here (**1** and **2**):



We can differentiate between these two possibilities by considering the chemical shifts of the signals. The oxygen atom of an ester will cause a significant downfield shift for any nearby protons. So we look for the signal that is shifted the most downfield (signal **a**). This signal is the  $\text{CH}_2$  group that is part of the ethyl group. That means that the ethyl group (not the isopropyl group) is connected directly to the oxygen atom of the ester, so compound **2** is the correct structure.

As a final check, we verify that our proposed structure is consistent with all spectral data:



Signal **a** (at 4.2 ppm) corresponds with the protons labelled **a**. There are two such protons (a methylene group), consistent with an integration of 2H. This signal is a quartet because this methylene group has three neighbors (labelled **c**). The chemical shift for this signal is within the range expected for protons that are alpha to an oxygen atom (3.3 – 5 ppm), as

#### STEP 5

Verify that the proposed structure is consistent with all of the spectral data.

seen in Table 15.1. A calculation using Table 15.2 leads to a more specific prediction for the chemical shift: 1.2 (methylene) + 3.0 (alpha to the oxygen atom of an ester) = 4.2 ppm. Indeed, this prediction exactly matches the observed chemical shift.

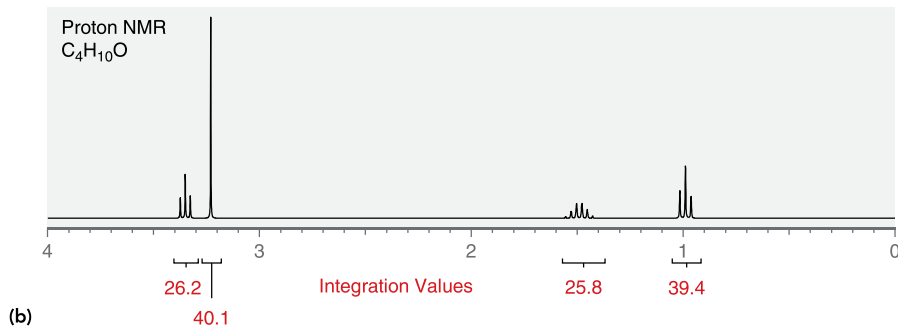
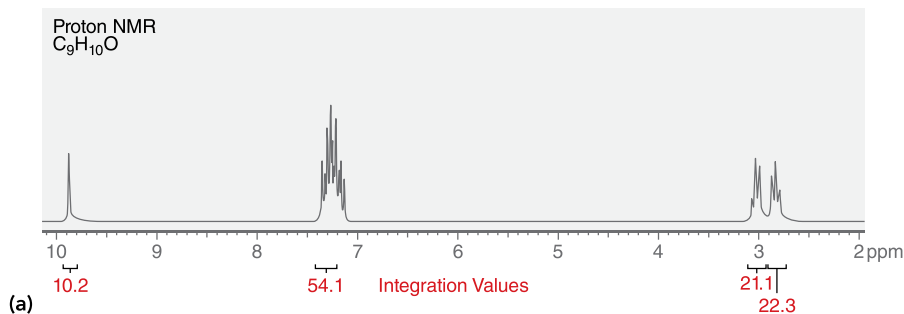
Signal **b** (at 2.5 ppm) corresponds with the proton labelled **b**. There is one such proton (a methine group), consistent with an integration of 1H. This signal is a septet, although the outermost peaks are hard to see because they are so small (which is often the case with a septet). A septet is consistent with having six neighbors (the proton labelled **b** is adjacent to two methyl groups). The chemical shift for this signal is within the range expected for a proton that is alpha to a carbonyl group (2 – 2.5 ppm), as seen in Table 15.1. A calculation using Table 15.2 leads to a more specific prediction for the chemical shift: 1.5 (methine) + 1.3 (alpha to a carbonyl group) = 2.8 ppm. Indeed, this prediction is close to the observed chemical shift (2.5 ppm).

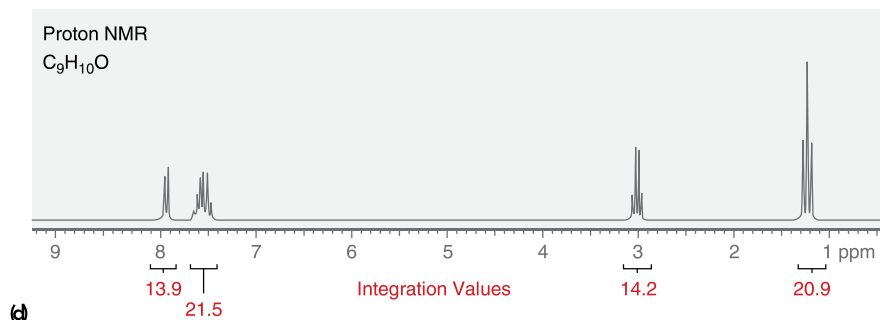
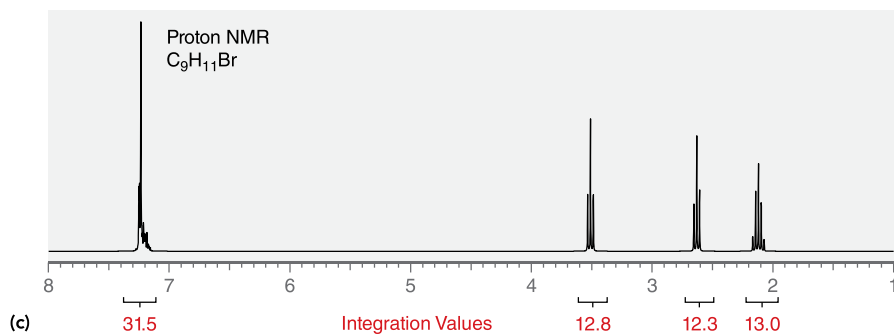
Signal **c** (at 1.2 ppm) corresponds with the protons labelled **c**. There are three such protons (a methyl group), consistent with an integration of 3H. This signal is a triplet because this methyl group has two neighbors (labelled **a**). The chemical shift for this signal is also as expected. A methyl group has a benchmark value of 0.9 ppm, and this signal is shifted a little bit downfield because of the distant electron-withdrawing effect of the oxygen atom (which is beta, rather than alpha, to this methyl group).

Signal **d** (at 1.1 ppm) corresponds with the protons labelled **d**. There are six such protons (two methyl groups), consistent with an integration of 6H. This signal is a doublet because these methyl groups have only one neighbor (labelled **b**). The chemical shift for this signal is also as expected. The benchmark value for a methyl group is 0.9 ppm, and this signal is shifted a tiny bit downfield because of the distant deshielding effect of the carbonyl group (which is beta, rather than alpha, to these methyl groups).

In summary, our proposed structure is consistent with all of the spectral data.

**15.22** Propose a structure that is consistent with each of the following  $^1\text{H}$  NMR spectra (or  $^1\text{H}$  NMR spectral data). In each case, the molecular formula is provided:





(e) Molecular formula  $\text{C}_{10}\text{H}_{14}\text{O}$

1.33 ppm (9H, singlet)  
4.98 ppm (1H, broad singlet)  
6.60 ppm (2H, doublet)  
7.37 ppm (2H, doublet)

(f) Molecular formula  $\text{C}_5\text{H}_9\text{ClO}$

1.06 ppm (3H, triplet)  
2.45 ppm (2H, quartet)  
2.73 ppm (2H, triplet)  
3.79 ppm (2H, triplet)

### APPLY the skill



Serotonin stabilizes our mood, and it also regulates sleep and wakefulness. Certain drugs that treat anxiety and depression do so by targeting low levels of serotonin.

**15.23** Neurotransmitters are small molecules that are produced by the body to send messages from one neuron to another. Noradrenaline (also called norepinephrine) and serotonin are neurotransmitters that act in the central nervous system. A synthetic compound called PMPEA has effects that are similar to both noradrenaline and serotonin in the spinal cord.<sup>8</sup> Deduce the structure of PMPEA, given its molecular formula ( $\text{C}_9\text{H}_{13}\text{NO}$ ) and the following  $^1\text{H}$  NMR spectral data:

1.1 ppm (2H, broad singlet)	3.8 ppm (3H, singlet)
2.7 ppm (2H, triplet)	6.8 ppm (2H, doublet)
2.9 ppm (2H, triplet)	7.1 ppm (2H, doublet)

need more **PRACTICE?** Try Problems 15.47, 15.62b,c, 15.63, 15.64, 15.69