PROTON NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY (H-NMR)

WHAT IS H-NMR SPECTROSCOPY?
References: Bruice 14.1, 14.2

Introduction
NMR or nuclear magnetic resonance spectroscopy is a technique used to determine a compound's unique structure. It identifies the carbon-hydrogen framework of an organic compound. Using this method and other instrumental methods including infrared and mass spectrometry, scientists are able to determine the entire structure of a molecule. In this discussion, we will focus on H NMR or proton magnetic resonance. Even though there are many other spectrometers including C-NMR and N-NMR, hydrogen (H-NMR) was the first and is the most common atom used in nuclear magnetic resonance spectroscopy.
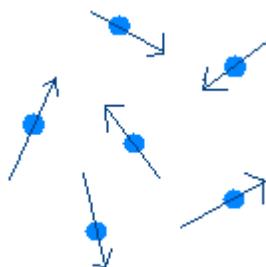
How does it work?
The atomic nucleus is a spinning charged particle, and it generates a magnetic field. Without an external applied magnetic field, the nuclear spins are random and spin in random directions. But, when an external magnetic field is present, the nuclei align themselves either with or against the field of the external magnet.
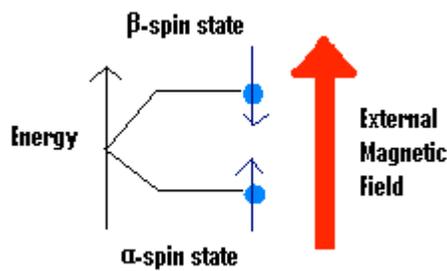
References: Bruice, Figures 14.1 and 14.2
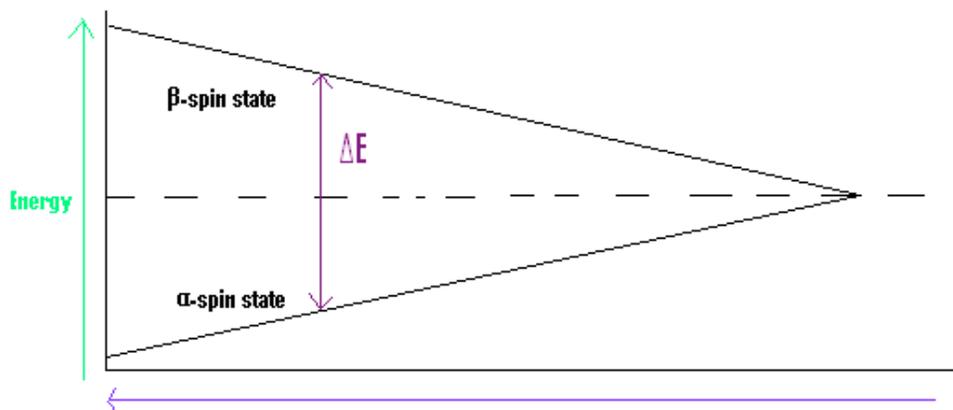*References: Thinkbook pg 54 and 55*

No External Applied Magnetic Field   External Magnetic Field is Applied

  _-spin state: Protons that align with the external magnetic field. They are in a lower energy state.

  _-spin state: Protons that align against the external magnetic field. They are in a higher energy state.

The _E is the energy difference between the _ and _ spin states. This depends on the applied magnetic field. As shown by the graph above, the greater the strength of the applied magnetic field, the larger the energy difference between the two spin states. When radiation, that has the same energy as the _E, is placed upon the sample, the spin flips from _ to _ spin states. Then, the nuclei undergoes relaxation. **Relaxation** is when the nuclei return to their original state. In this process, they emit electromagnetic signals whose frequencies depend on _E as well. The H-NMR spectrometer reads these signals and plots them on a graph of signal frequency versus intensity. **Resonance** is when the nuclei flip back and forth between _ and _ spin states due to the radiation that is placed on them. To summarize, an NMR signal is observed when the radiation supplied matches the _E. And, the energy required to cause spin flip is dependent on the magnetic environment experienced by the nucleus.

STRUCTURAL INFORMATION THAT THE NMR SPECTRUM TELLS US

References: Bruice 14.4
References: Thinkbook pg 55
1. Number of Signals
Each group of chemically equivalent protons gives rise to a signal. **Chemically Equivalent Protons** are protons that are in the same environment, and they must be identical in every way. They experience is the same magnetic force, and therefore, will create overlapping signals on the spectrum. Therefore, we can determine how many sets of equivalent protons there are in a molecule by looking at the number of signals in its H-NMR spectrum.

> *How do we determine how many equivalent protons there are?*
> There are many ways to determine how many sets of equivalent protons there are in a molecule. For example, we can see if there is a line of symmetry. Protons that are aligned on a line of symmetry are equivalent. Another way is to replace the proton with deuterium to form two molecules, and if the two molecules are the same, then the two protons are equivalent. The third way to determine how many equivalent protons there are is to look at the atom attached to the proton (usually a carbon) and observe what that atom is bonded to, and then the atom bonded to that, all the way until a difference is observed. If there is no difference, the protons are equivalent. If there is a difference, the protons are not equivalent.

> *Are protons on the same carbon always equivalent?*
> No. Usually, protons on the same carbon are equivalent. But, sometimes, they are not equivalent because they are not in the same environment. One proton could be trans and the other proton could be cis. This would create two different signals.

Practice Problem: How many signals are in the molecule chlorocyclobutane?
*References: Bruice, Example in 14.4*
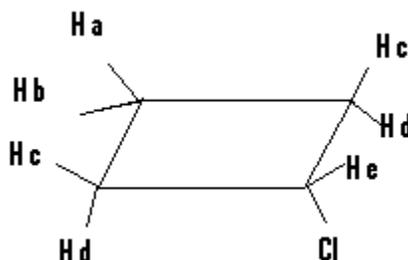
Answer: Chlorocyclobutane has five signals. Ha and Hb are not equivalent because Ha is trans to Cl while Hb is cis to Cl. Hc and Hd are not equivalent because Hc is trans to Cl while Hd is cis to Cl. The Hc and Hd protons are equivalent because they are in the same environment and are attached to the same atoms, and those atoms are attached to the same atoms, and so on. Therefore, there are 5 signals in this molecule.

Practice Problem: How many signals will the H NMR spectrum produce for this molecule?
References: Bruice, Example in 14.4
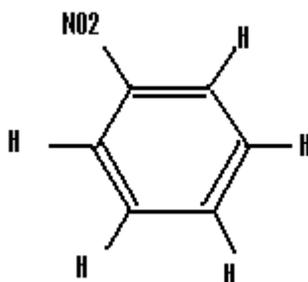
Answer: There are three signals because there are three sets of equivalent protons.
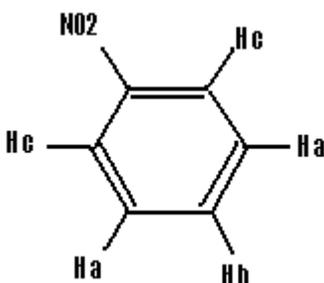
References: Bruice, 14.5, 14.6, 14.7, 14.9
References: Thinkbook pg.56-58, 234
2. Position of Signals
 The positions of the signals in an NMR spectrum are based on how far they are from the signal of the reference compound. This information tells us the kind of proton or protons that are responsible for the signal.
Reference compound: Tetramethylsilane (TMS) is usually used as the reference compound because it can easily be removed from the sample by evaporation due to its volatile properties. TMS is at a lower frequency than most other signals because its methyl protons are in a more electron dense environment than most protons are because silicon is less electronegative than carbon (which is a significant component of organic molecules.)

The position of the signals depends on the chemical shift.
Chemical Shift: It is a measure of how far the signal produced from the proton is from the reference compound signal, and it usually measured using the _ (delta) scale. The TMS or reference compound is at the zero position on the very left of the spectrum, and as it moves toward the left, the ppm values become larger. Ppm stands for parts per million, and it is the unit used to measure chemical shift. The proton chemical shifts range from 0 ppm to 15 ppm. The chemical shift is identical for a specific proton regardless of the spectrometer used. The formula for the chemical shift is

$$\_ \text{ (delta)} = \frac{\text{distance downfield from TMS (Hz)}}{\text{operation frequency of the spectrometer (MHz)}} = \text{parts per million (ppm)}$$

What is shielding and how does it affect the chemical shift?

As mentioned before, _E is determined by the strength of the magnetic field. The nucleus of the molecule is found within a cloud of electrons that partly shields it from the applied magnetic field. This shielding is different for different protons in a molecule, and that is why there are many signals in the H NMR spectrum, instead of just one. In a magnetic field, electrons go around the nuclei and induce a local magnetic field that opposes the applied magnetic field.

Effective Magnetic Field: This is what the nuclei sense through its electron filled environment.

$$B \text{ effective} = B \text{ applied} - B \text{ local}$$

B applied is the magnetic field supplied by the applied external magnetic force (NMR spectrometer) and the magnetic fields supplied by the earth. This number is the same of all the nuclei in the molecule. *B* local is the magnetic field supplied by the surrounding electrons around the nuclei. This number varies between nuclei in the molecule. According to this formula, the greater the electron density is around the nuclei, the larger the *B* local will be, and the more the proton is shielded from the applied magnetic field. This is called **diamagnetic shielding**.

Protons in **electron dense (rich) environments** sense a smaller effective magnetic field because they are more shielded by the large amount of electrons, and therefore, will require a lower frequency to come into resonance because the _E is smaller. The _ (ppm) will be smaller, and lower frequencies are located on the right side of the spectrum.

Upfield: farther to the right hand side of the spectrum

Protons in **electron poor environments** sense a larger effective magnetic field because they are less shielded due to fewer electrons, and therefore, they require a higher frequency to come into resonance because the _E is larger. The _ (ppm) will be larger, and higher frequencies are located on the left side of the spectrum.

Downfield: farther to the left side of the spectrum.

How does electronegativity affect chemical shift?

The electron cloud shields the nucleus from the applied magnetic field, and electronegativity is defined as the tendency of an atom to pull electrons toward itself. Therefore, electronegative atoms remove electron density from the proton. This causes the proton to have less electron density, and this leads to less shielding. If the proton has less shielding, it will feel the applied magnetic field more, and this leads to a higher _E and a higher chemical shift. Protons that are closer to the electronegative atom are in a less electron dense environment, which means that they're chemical shifts will be larger.

What are characteristic chemical shifts?

An important concept to understand is that similar functional groups have similar chemical shifts. Characteristic chemical shifts are the averages for the normal or typical proton. Therefore, this number varies between different molecules. We cannot use these shift numbers to assign proton types to NMR signals. On the characteristic proton NMR chemical shifts table, two molecules with the same functional group may have different chemical shifts. This could be due to many factors such as being positioned near an electronegative atom.

What is magnetic anisotropy and how does it influence chemical shifts?

Magnetic anisotropy is the magnetic field created by pi electrons or rings. This describes an environment where different magnetic fields are found at different points in space. Pi electrons are held less strongly than sigma electrons, so pi electrons are more able to move in response to the magnetic field. How this affects the chemical shift depends on the direction of the induced magnetic field relative to the direction of the applied magnetic field. In pi electrons found in the benzene ring and an alkene, the magnetic field induced is in the same direction as the applied magnetic field, so the protons feel a larger effective magnetic field. Therefore, the protons undergo resonance at a higher frequency due to the pi electrons. If the magnetic field induced is oriented in the opposite direction as the applied magnetic field, the protons will feel a smaller effective magnetic field.

References: Bruice, Example from 14.6
Practice Problem: Put the chemical shifts of the nonequivalent protons from the lowest frequency to the highest frequency.

$CH_3CH_2CH_2NO_2$

Answer: CH_3 has the lowest chemical shift because it is the furthest away from the nitro group, and the CH_2 in between the CH_3 and CH_2 has the middle chemical shift, and the CH_2 attached to the NO_2 has the largest chemical shift because it is the closest to the nitro group.

References: Bruice 14.8
References: Thinkbook pg. 59
3. Integration or intensity of NMR Signals
Integration is the area measurement that tells us the relative number of protons that give rise to each signal. Beer's Law says that the amount of energy absorbed or transmitted is proportional to a certain number of moles present. The area under each signal is proportional to the amount of radio energy and number of equivalent protons that give rise to that signal. The numbers do not always correspond to the exact or absolute number of protons. Instead, it tells us the relative number or ratio of the amount of equivalent protons.

References: Bruice, Example from 14.8
Practice Problem: Explain how this molecule produces this H-NMR spectra using number of signals, position of the signals, and the integration of the signals.
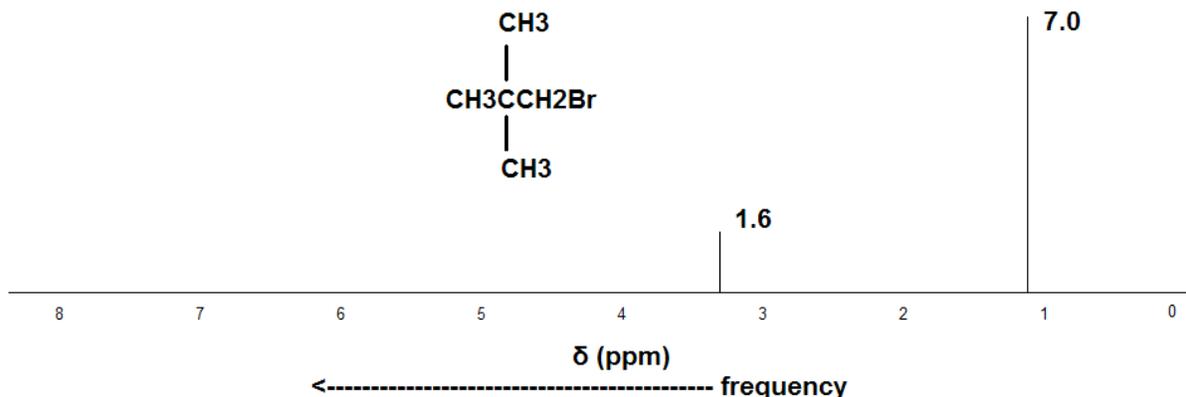
Answer: This molecule has two nonequivalent sets of protons. The protons on the three methyl groups are equivalent, and therefore produce one signal. The CH2 attached to the Br is not equivalent to the methyl groups, so those protons produce the other signal. That is why there are two signals in the spectra. According to the characteristic proton NMR chemical shifts chart, methyl groups are usually at around 0.9ppm, and CH2 groups at around 1.3ppm. The shifts shown on the charts are different than the ones shown in this example because of the electronegative bromine atom. This atom pulls the electron density toward itself, so these is less electron density around the protons, causing less shielding and higher chemical shift. The CH2 is more affected by the electronegative Br because it is closer to it when compared to the methyl groups which are further away from Br. There are 9 equivalent protons (3 groups of CH3) for one signal and 2 equivalent protons (CH2) for the other signal. Therefore, 2/9 should be about equal to 1.6/7.

References: Bruice, 14.10-14.12
References: Thinkbook pg 60-62
4. Splitting of Signals
Splitting of signals is caused by (and therefore tells us the number of) protons bonded to adjacent carbons. As shown by the picture below, the different _E (spin flip energies) for Ha due to the different spins of the Hb causes the Ha signal to be split into two lines. When they are parallel, Ha feels a stronger field (B+Hb), and when they are antiparallel, Ha feels a weaker field (B-Hb), and this results in two close signals.

References: Thinkbook pg 60
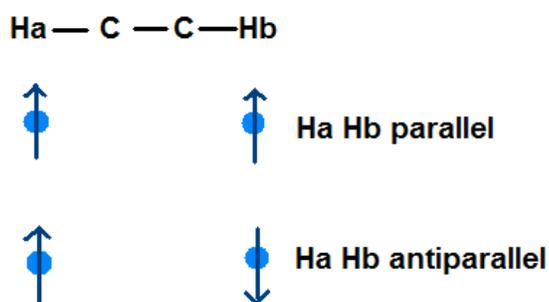
N+1 Rule: N is the number of equivalent protons that are bonded to the adjacent carbons. So, the number of splitting that occurs is one more than the number of equivalent protons bonded to the adjacent carbons.
Multiplicity: The number of peaks in a signal. The number of protons bonded to the immediately adjacent carbon determines multiplicity.
Coupled Protons: They are protons that split each other's signal. The splitting is always mutual.
Spin-spin coupling: Different kinds of protons are close enough for their magnetic fields to influence on another. The spin of one nucleus influences the spin of another nucleus.
Long-range coupling: This occurs when the protons are separated by more than three bonds and one of the bonds is a double or triple bond. A small splitting is observed.
Coupling Constant (*J*): This is the distance between two adjacent peaks of a split signal. The magnitude of J is a measure of how strongly the nuclear spins of the coupled protons influence each other. Therefore, it is dependent upon the number and type of bonds that connect the coupled protons and their geometric relationship. Therefore, for some molecules, the trans form could create a smaller coupling constant than the cis form. For nonequivalent hydrogens on the same sp2 carbon, the J is usually very small and unable to be observed. But, for nonequivalent hydrogens bonded to adjacent sp2 carbons, the J is usually large enough to be observed.

What are the different types of splitting?

Using the N+1 rule, the signal for a proton with N neighbors is split into N+1 lines. If a proton has no neighbors, it is a singlet. If it has one neighbor, it is a doublet. If it has two neighbors, it is a triplet. If it has three neighbors, it is a quartet. If it has four neighbors, it is a pentet.

What are the rules for proton-proton spin-spin coupling?

1. Only non equivalent protons couple. Equivalent protons are in the same environment, and their signals overlap, so only non equivalent protons can split signals.
2. Protons that are separated by more than three single bonds usually do not couple because they are not close enough to each other to be influenced by each other magnetic fields. Pi bonds do not count toward this, but the coupling constants may be too small to distinguish. Benzene rings have a "coupling club" in which they only couple with each other. Nonequivalent benzene ring protons can couple with each other, but the coupling constants may be too small to be significant. A benzene ring blocks coupling with other protons outside of the benzene ring. This usually causes complicated splitting patterns.
3. Signals for O-H and N-H protons are usually singlets.

What is non-first order splitting?

Throughout these notes, we have assumed "normal" splitting which is when coupling constants of neighboring protons are equal. However, when the coupling constants are not equal, the splitting is more complex. To explain non first order coupling, I will use the example below.

References: Bruice, Figure 14.7
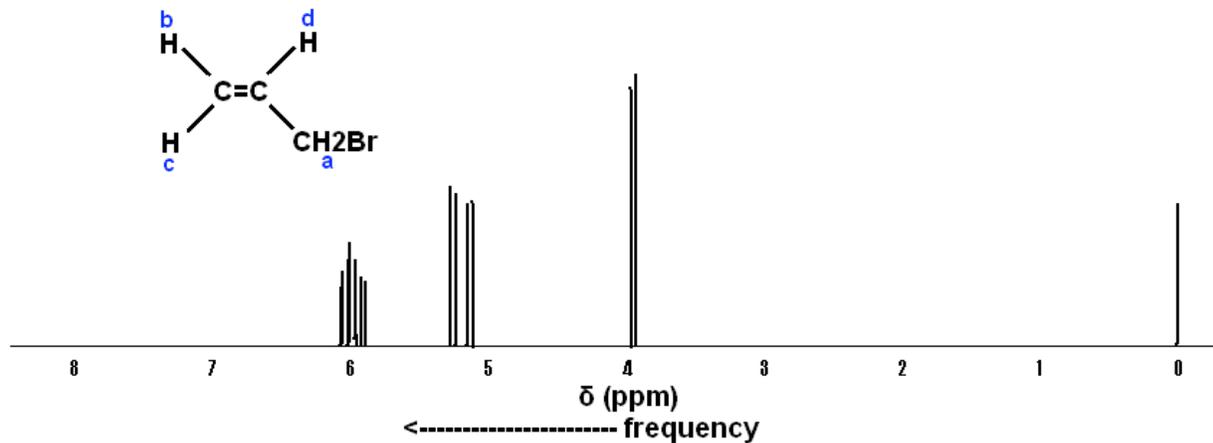
This is the H NMR spectrum for 3-bromo-1 propene. The Hb and Hc are not equivalent because one is cis and the other is trans to the bromomethyl group. The signal for the Ha proton is split into a doublet by the Hd proton. And, the signal for the Hd proton is a **multiplet** because it is split separately by the Ha, Hb, and Hc protons. Multiplet is a splitting pattern that is too complex to decipher. And, because the Hb and Hc protons are not equivalent, they split one another's signal. The Hb proton is split into a doublet by the Hd proton, and each of the peaks in the doublet is split into a doublet by the Hc proton. This is called **doublet of doublets**. Hc is also split into doublet of doublet. **Geminal coupling** is when there is the mutual splitting of the signals of two nonidentical protons bonded to the same sp2 carbon. This is usually too small to be observed.

Reference: Bruice, Figure 14.10
Practice Problem: Explain the splitting patterns of this spectrum.
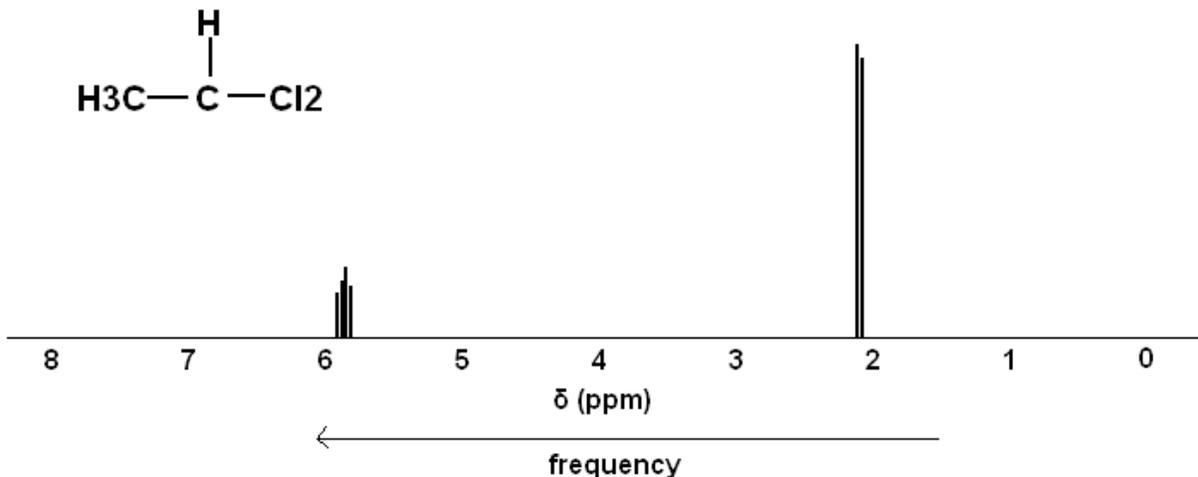
Answer: The higher frequency signal is a quartet, and the lower frequency signal is a doublet. There are two nonequivalent groups of protons- the **CH3** and the **CH**. That is why there are two signals. The H from **CH** splits the **CH3** signal and the **CH3** splits the **CH** signal. Since there are three hydrogens in CH3, using the N+1 rule, the splitting at C-**H** is a quartet. Since there is one hydrogen in CH, using the N+1 rule, the splitting at C-**H3** is a doublet.

HOW DO WE DETERMINE MOLECULAR STRUCTURE FROM THE H-NMR SPECTRA?
References: Thinkbook and Lecture, pg 65 and Example #4 pg 268

The molecular formula and functional groups are determined using the mass spectrum and the IR spectrum. The H NMR spectrum is used to put the entire structure together.

Practice Problem: Using the mass spectrum, we concluded that the molecular formula is $C_{10}H_{15}N$. The data from the H-NMR: 7.0-7.5 ppm (multiplet, integral=1.25), 3.6 ppm (quartet, integral=1.0), and 1.4 ppm (triplet, integral=1.5). Using this information, we must determine the structure of the molecule.

Answer:

Step 1: Determine the DBE using the formula DBE= $C - (H/2) + (N/2) + 1$. H is the number of hydrogens and halogens, and N is the number of nitrogens. This number tells us whether or not there are double bonds, rings, or benzene rings. If the DBE is 4 or greater than 4, there is a high possibility that there is a benzene ring. Double bonds and rings each count for 1 DBE.
  DBE= $10 - (15/2) + (1/2) + 1 = 4$ *Possible benzene ring* or 4 double bonds/rings.

Step 2: Summarize the H-NMR data in a table. This makes sure everything is organized and that we do not miss any important information.

Chemical Shift	Splitting	Integral	# of H	Implications
7.0-7.5 ppm	multiplet	1.25		
3.6 ppm	quartet	1		
1.4 ppm	triplet	1.5		
	Totals	3.75		

Step 3: To determine how many hydrogens there are, we add up the integrals to determine the total. Then we divide that number by how many hydrogens are present (determined by the molecular formula).

Total integral: 3.75
Total #H: 15
15 / 3.75 = 4   We can conclude that every 1 integral corresponds to 4 hydrogens.

Chemical Shift	Splitting	Integral	# of H	Implications
7.0-7.5 ppm	multiplet	1.25	5	
3.6 ppm	quartet	1	4	
1.4 ppm	triplet	1.5	6	
	Totals	3.75	15	

Step 4: Use the number of hydrogens in the table to decide if each signal corresponds to a CH3, CH2, or CH. We can also consider OH or NH if there are oxygen or nitrogens in the formula and if the IR spectrum suggests that a functional group containing those atoms is present. Also, we can also find more clues for determining the structure using the chemical shift numbers. By looking on the chemical shift table, we can determine whether there are characteristic proton chemical shifts. For example, benzene rings shifts between 6.5 ppm and 8 ppm.

In our example, there is a chemical shift of 7.0-7.5 ppm which most likely correlates to the benzene ring. Because there is only 5 hydrogens, it shows that it is a monosubstituted benzene ring (C6H5).

Chemical Shift	Splitting	Integral	# of H	Implications
7.0-7.5 ppm	multiplet	1.25	5	Monosubstituted benzene ring (C6H5)
3.6 ppm	quartet	1	4	2 x CH2 4 x CH
1.4 ppm	triplet	1.5	6	2 x CH3 3 x CH2 6 x CH
	Totals	3.75	15	

<u>Step 5</u>: Use the N+1 rule and the splitting patterns to determine all the possibilities that could lead to the H NMR signals.

For example, for the signal at 3.6 ppm, the splitting is the quartet (4).
Splitting=N+1
      4 = N+1
      N=3
So, there are 3 neighboring hydrogens.

For the signal at 1.4 ppm, the splitting is a triplet (3).
Splitting=N+1
      3 = N+1
      N=2
So, there are 2 neighboring hydrogens.
Make sure to list all the possibilities by using different combinations of CH, CH2, and CH3 surrounding the specific hydrogen.

Chemical Shift	Splitting	Integral	# of H	Implications
7.0-7.5 ppm	multiplet	1.25	5	Monosubstituted benzene ring (C6H5)
3.6 ppm	quartet	1	4	2 x CH2 in <u>CH2</u>CH3 2 x CH2 in CH2<u>CH2</u>CH 2 x CH2 in CHCH<u>CH2</u>CH 4 x CH in <u>CH</u>CH3 4 x CH in CH2<u>CH</u>CH 4 x CH in CHCH<u>CH</u>CH
1.4 ppm	triplet	1.5	6	2 x CH3 in <u>CH3</u>CH2 2 x CH3 in CH<u>CH3</u>CH 3 x CH2 in <u>CH2</u>CH2 3 x CH2 in CH<u>CH2</u>CH 6 x CH in <u>CH</u>CH2 6 x CH in CH<u>CH</u>CH
	Totals	3.75	15	

<u>Step 6</u>: After we have determined all the possibilities that can give rise to the signals, we choose the simplest answer. The simplest answer is the piece that uses the least number of atoms. We still must list all the possibilities because the simplest piece is not always the correct one.

Chemical Shift	Splitting	Integral	# of H	Implications
7.0-7.5 ppm	multiplet	1.25	5	Monosubstituted benzene ring (C6H5)
3.6 ppm	quartet	1	4	2 x CH2 in <u>CH2</u>CH3
1.4 ppm	triplet	1.5	6	2 x CH3 in <u>CH3</u>CH2
	Totals	3.75	15	

Step 7: Then, we add together all the atoms that are underlined in the table. This checks that we used up all the hydrogen atoms, and this also determines what atoms that did not show up on the H-NMR spectrum.

$C_6H_5 + 2 \times (CH_2) + 2 \times (CH_3) = C_{10}H_{15}$
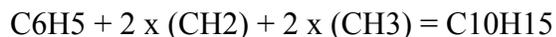
Step 8: We subtract the formula above from the molecular formula given by the mass spectrum to determine the unused atoms.

$C_{10}H_{15}N$ (given) – $C_{10}H_{15}$(H-NMR) = N (unused)

This shows that the H-NMR data accounts for all of the atoms except the nitrogen, so this nitrogen needs to be included when we assemble the pieces.

Step 9: Then, we do the DBE check. DBE (from formula) – DBE (H-NMR) = DBE (unused). If there are extra DBEs left over, we need to consider them while assembling the pieces.

4 (from formula) – 4 (benzene ring) = 0. All the DBEs are accounted for, so they are none left to consider when assembling the pieces.

Step 10: Then, we can list and assemble the pieces.
Monosubstituted benzene ring C6H5
2 x CH2 in CH2CH3
2 x CH3 in CH3CH2
N

Hint #1: When the table states 2x a certain piece, the two pieces must be equivalent.
Hint #2: Remember to include pieces suggested by the IR spectrum data.

Sometimes, trial and error is the only way to assemble the structure. But, we can also use clues provided by the spectra such as coupling patterns and equivalency. In our example, we have two sets of equivalent pieces, and they fit into one another, so they must be attached to form an ethyl group. Therefore, this forms 2 x CH2CH3. So, our new list of pieces is
Monosubstituted benzene ring C6H5
2 x CH2CH3
N
These pieces can only be assembled in one way. So, the molecular structure is:
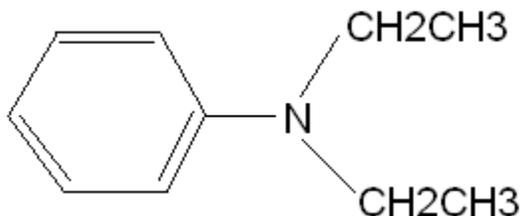
Using H-NMR, we were able to determine the structure of this molecule using the four components shown on the spectra, # of signals, chemical shift, integration, and splitting patterns. C-NMR (carbon nuclear magnetic resonance) can also be used, and this eliminates some structures that would be possible if we just had the H-NMR spectra.