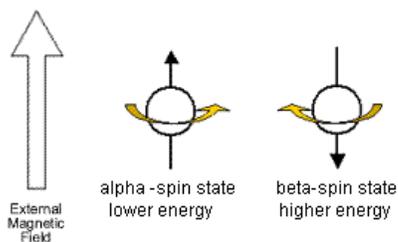


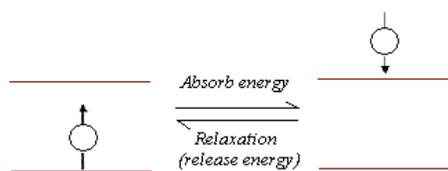
# Proton Nuclear Magnetic Resonance ( $^1\text{H-NMR}$ ) Spectroscopy

## Theory behind NMR:

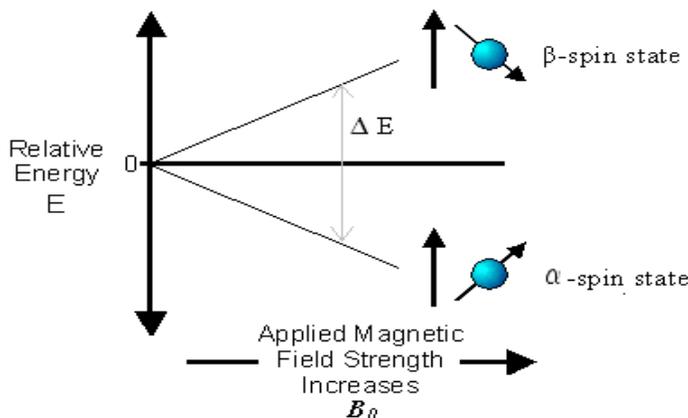
In the late 1940's, physical chemists originally developed NMR spectroscopy to study different properties of atomic nuclei, but later found it to be useful in determining the molecular structure of organic compounds. The theory behind NMR comes from the **spin,  $I$**  of a nucleus. Just as electrons have a  $+1/2, -1/2$  spin, certain nuclei also experience charged spins that create a magnetic field (called the **magnetic moment**), which allows chemists to study them using NMR. Nuclei with even numbers of both neutrons and protons experience NO spin and nuclei with odd numbers of both neutrons and protons have integer spins. Nuclei that have the sum of protons and neutrons equal to an odd number (like  $^1\text{H}$  and  $^{13}\text{C}$ ) have half-integer spins. When there is no external or **applied magnetic field ( $B_0$ )**, the nuclear spins orient randomly; however, when there is an applied magnetic field, the nuclei orient themselves with or against the larger applied field. The  $\alpha$ -spin state is parallel to the applied force and has lower energy than the  $\beta$ -spin state that is antiparallel to the applied force. The energy difference ( $\Delta E$ ) between the  $\alpha$ - and  $\beta$ -spin states depends on the strength of the applied magnetic field. The greater the strength of the applied magnetic field, the greater is the  $\Delta E$  between the  $\alpha$ - and  $\beta$ -spin states<sup>2</sup>. The  $\Delta E$  between the  $\alpha$ - and  $\beta$ -spin state is  $\sim 0.02 \text{ cal mol}^{-1}$ , which lies in the radio frequency region. The emitted energy in this region produces an NMR signal.



- Diagram 1<sup>3</sup>  
\*Addition of energy results in a spin flip



- Diagram 2  
\*nuclei shed excess energy in a process called **relaxation**



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<sup>1</sup> <http://www.chemistry.uoguelph.ca/driguana/NMR/SPIN.HTM> (11/7/06)

<sup>2</sup> p. 527, P.Y. Bruice, *Organic Chemistry* (4<sup>th</sup>)

<sup>3</sup> <http://faculty.kutztown.edu/betts/html/NMR.htm> (11/7/06)

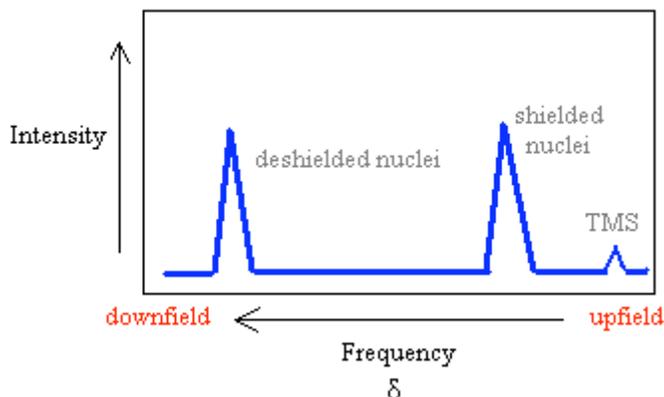
- <sup>1</sup>Diagram 3<sup>4</sup>

\*As the applied magnetic field increases, so does the energy difference between  $\alpha$  - and  $\beta$ -spin states<sup>3</sup>

<http://www.chemistry.uoguelph.ca/driguana/NMR/ENERGIES.HTM>

## NMR Spectrum

\*The NMR Spectrum is a plot of the intensity of NMR signals versus the magnetic field (frequency) in reference to TMS. The intensity is measured by the integration of the area under the triangles.



## Interpreting <sup>1</sup>H NMR Spectra

*Four types of Information from NMR:*

- 1. Number of signals:** Protons within a compound experience different magnetic environments, which give a separate signal in the NMR spectrum

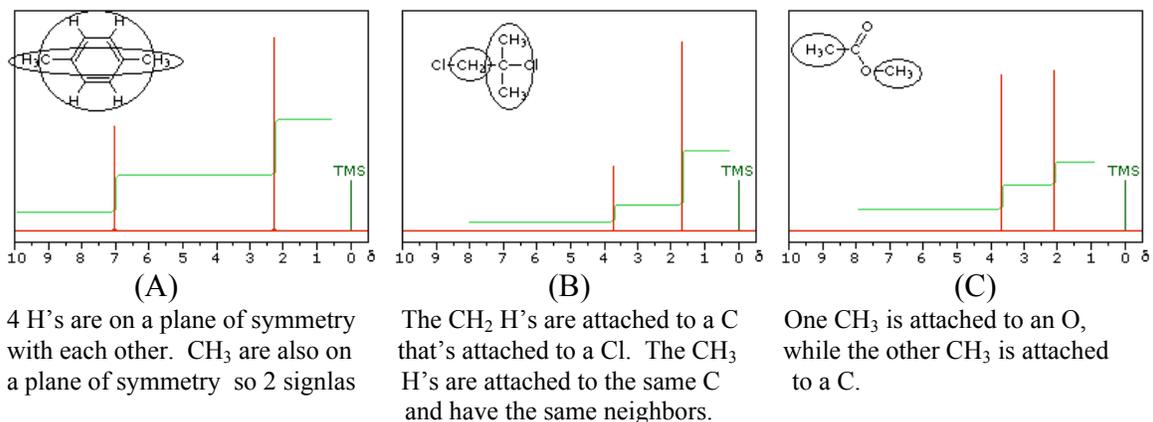
**Equivalent:** Protons that reside in the same magnetic environment are termed *chemically equivalent protons*<sup>5</sup>. As a general rule of thumb, H's in CH<sub>3</sub> and CH<sub>2</sub> groups are usually equivalent. Symmetrical compounds, such as benzene, are also equivalent; however, since many compounds are not symmetrical, it is important to know how to identify nonequivalent protons. Protons that are different in *any* way (even in their stereochemistry) are not equivalent and will absorb at different frequencies (give a separate signal on the NMR spectra).

Examples<sup>6</sup>: All of these compounds have 2 signals in their NMR spectrum

<sup>4</sup><http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm> (11/10/06)

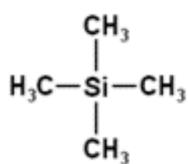
<sup>5</sup>p. 527, P.Y. Bruice, *Organic Chemistry* (4<sup>th</sup>)

<sup>6</sup><http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm> (11/10/06)



2. **Position of signals (chemical shift):** The position on the horizontal frequency scale at which the equivalent proton signals occur ( $\delta$  ppm) is called a **chemical shift**<sup>7</sup> (measured in ppm). Protons generally sense 3 different magnetic fields: magnetic field of the Earth, the NMR spectra, and different protons in the molecule. Since the magnetic fields of the Earth and NMR spectra are felt similarly by all the protons in the molecule, the chemical shift depends only on the varying local magnetic fields from the neighboring protons.

**Reference compound: Tetramethylsilane (TMS)**



In order to standardize the NMR spectra, the chemical shifts are positioned in relation to a reference proton set at 0.00 ppm. Tetramethylsilane, (CH<sub>3</sub>)<sub>4</sub>Si, is the standard for H<sup>1</sup> NMR. TMS is practical as a reference compound because of its inert quality that prevents it from reacting with the sample and its highly volatile nature that makes it easy to evaporate out of samples. Few compounds have a lower frequency reading than TMS and it has 12 equivalent protons that read strongly on the NMR spectra.

*What influences a chemical shift?*

**Shielding effects:** Under an applied magnetic field, circulating electrons in the electron cloud produce a small opposing magnetic field, ultimately decreasing the effective magnetic field felt by the proton, shifting the signal to the right (or **upfield**). This effect, in which the electron cloud “shields” the proton from the applied magnetic field is called **local diamagnetic shielding**<sup>8</sup>.

**Electronegativity and deshielding :** H's that are attached to more electronegative atoms experience higher chemical shifts. Electronegative atoms also remove electrons from the

<sup>6</sup> P 278 IR Mohriro *Techniques in Organic Chemistry (2<sup>nd</sup>)*

electron cloud, which decreases their density and results in less shielding; hence electronegative atoms are said to **desield** the proton and cause it to have a higher chemical shift, moving it to the left (or **downfield**). The **magnitude of the deshielding** effect, however, rapidly decreases as the distance between the proton and electronegative atom increases (*refer to NMR spectrum diagram above*).

Example<sup>9</sup>: Literature values of the methyl chemical shift as it moves away from bromine

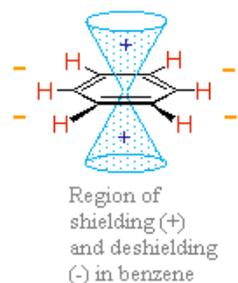
$\text{CH}_3\text{Br}$   
2.69 ppm

$\text{CH}_3\text{CH}_2\text{Br}$   
1.66 ppm

$\text{CH}_3\text{CH}_2\text{CH}_2\text{Br}$   
1.06 ppm

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{Br}$   
0.93 ppm

**Magnetic Anisotropy ( $\pi$ -system ring currents)**<sup>9</sup>: In molecules containing  $\pi$ -orbitals, **anisotropy** (having a different effect along different axes) is responsible for different shielding effects on a proton relative to the applied magnetic field since  $\pi$ -orbitals aren't spherically symmetrical.



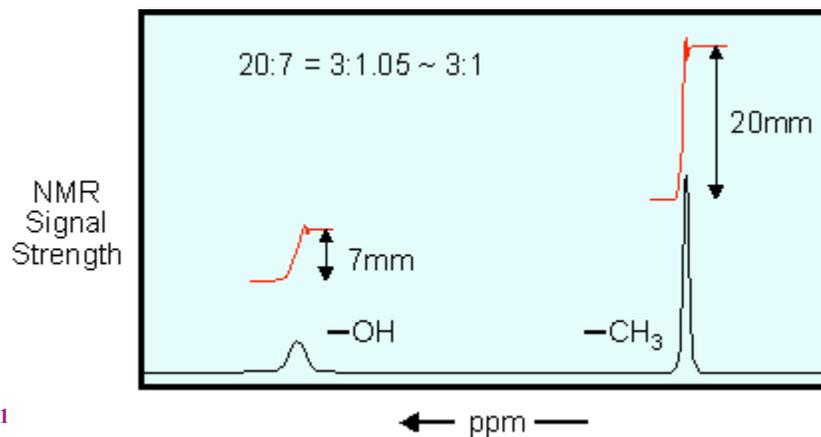
**Characteristic Chemical Shifts**<sup>10</sup>: tables of typical chemical shifts can be made since similar functional groups experience similar chemical shifts; however, due to the variability between molecules, one cannot assume a certain frequency corresponds to one type of proton. An exception occurs with a range of 6.5-8.0 ppm, which usually indicates benzene ring protons.

- 3. Relative Intensity of Signals (Integration):** The area under the signals (**integration**<sup>11</sup>) corresponds to the number of protons responsible for that signal. Therefore, the relative intensities of the signal are proportional to the relative number of proton equivalents. It is important to remember that integration only provides *ratios* of protons, not the *absolute* number. For convenience in calculating the relative signal strengths, the smallest integration is set to 1 and the other values are converted accordingly.

<sup>7</sup> p530, P.Y. Bruice, *Organic Chemistry* (4<sup>th</sup>)

<sup>8</sup> <http://bouman.chem.georgetown.edu/nmr/interaction/chemshf.htm> (11/13/06)

<sup>9</sup> p530, P.Y. Bruice, *Organic Chemistry* (4<sup>th</sup>)



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• Diagram 4<sup>12</sup>

\*Integrals appear as lines on the spectra above the signals, in which their heights correspond to the integration ratios. In this spectra, the -OH H is correctly determined to be in a 3:1 ratio with the 3 CH<sub>3</sub> H's

4. **Splitting of signals (spin-spin coupling):** NMR signals are not usually single triangles, but a complex pattern of split triangles labeled as doublets (2 peaks), triplets (3 peaks), quartets (4 peaks), etc. The distance between the split peaks are called **coupling constants**, denoted by  $J^{13}$ . The interaction between nearby protons produce different spin flip energies ( $\Delta E$ ) as they can orient themselves in a pattern of parallel or antiparallel to the applied magnetic force. This phenomenon, where the spin of the nucleus of one proton is close enough to affect the spin of another, is called **spin-spin coupling**. Splitting is always reciprocated between the protons—if Ha splits Hb, then Hb must split Ha—and provides information on the *neighbors* of a proton within the molecule.

**N+1 Rule:** For a proton with n neighbors, its signal will be split into n+1 lines

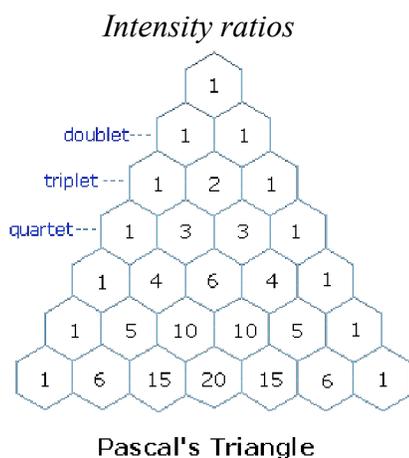


Diagram 5<sup>13</sup>

\*Pascal's triangle gives the intensity ratios between the split signals

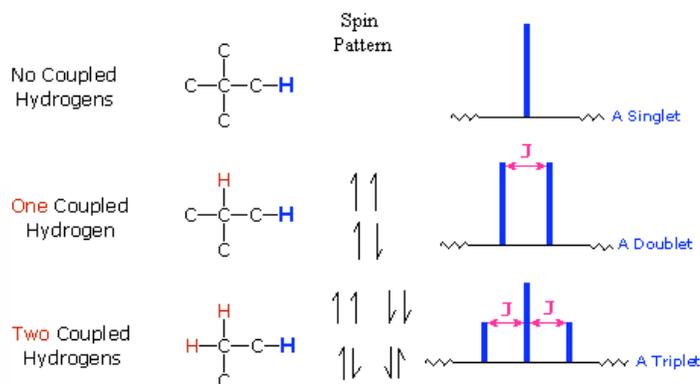


Diagram 6<sup>14</sup>

\*1 neighbor  $\rightarrow$  doublet; 2 neighbors  $\rightarrow$  triplet; 3 neighbors  $\rightarrow$  quartet  
Splitting patterns that are too difficult to analyze are called **multiplet**

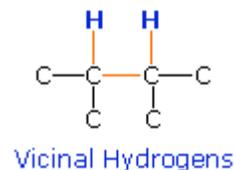
<sup>10</sup>p58, Prof. Steven Hardinger, *Chem 14C Thinkbook (version 4)*

<sup>11</sup>p538, P.Y. Bruice, *Organic Chemistry (4<sup>th</sup>)*

<sup>12</sup><http://www.chemistry.uconn.edu/driouana/NMR/INTEGR1.HTM> (11/13/06)

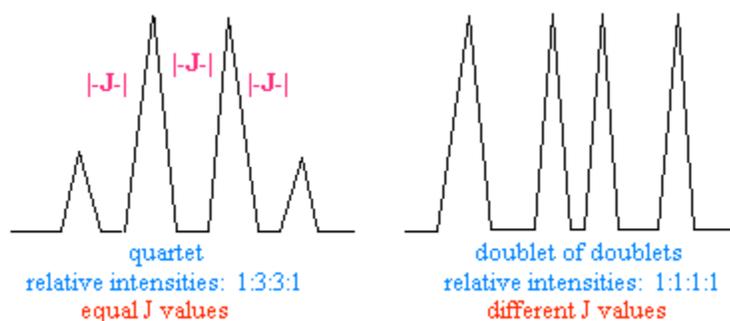
### 3 Rules/Restrictions for Proton coupling<sup>15</sup>

- 1.) Nuclei with the same chemical shift (*isochronous*) do not couple with each other: the protons must be nonequivalent in order to couple.
- 2.) *Vicinal* protons (protons separated by 3 bonds) can couple with each other. Protons that are more than 3 bonds away cannot because the signal they feel from their neighbor is too small to affect their spin. There is also *geminal coupling*—coupling through 2 bonds) and *allylic coupling*<sup>16</sup>—coupling through 4 bonds, if one is a pi bond. Pi bonds do not follow the 3 bond rule because the electron density around a pi bond is higher than in a single bond; hence, pi bonds can be counted as a free spacer. All hydrogens on the benzene ring couple with each other and the ring itself can be counted as a free spacer; however, H's on the benzene ring only couple with each other and not with H's attached to other atoms even if they are within the 3 bond max limit (“coupling club”)<sup>17</sup>.
- 3.) Hydrogens bonded to a Nitrogen or Oxygen usually do not couple with other protons and appear as singlets on the NMR spectra.



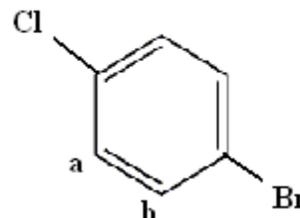
**Non-first order splitting:** the N+1 rule cannot predict the exact splitting patterns of non-first order splitting. First order splitting produces “normal” splitting patterns that have equal J values. Non-first order splitting occurs when a nucleus spin-couples with 2 or more sets of nearby nuclei that have different J values.

#### Example of First Order Splitting and Non-First Order



### **2<sup>nd</sup> Order Coupling Effects**<sup>18</sup>

First order theory is sufficient when describing NMR signals of coupled nuclei that are far enough apart from each other; however, when the



<sup>13</sup><http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm>

<sup>14</sup><http://www.cem.msu.edu/~reusch/VirtualText/Spectrpy/nmr/nmr1.htm>

<sup>15</sup>p61, Prof. Steven Hardinger, *Chem 14C Thinkbook (version 4)*

<sup>16</sup>P.302, J.R. Mohrig, *Techniques in Organic Chemistry (2<sup>nd</sup>)*

<sup>17</sup>p62, Prof. Steven Hardinger, *Chem 14C Thinkbook (version 4)*

chemical shifts come closer, other effects (second order coupling effects) begin to take over. Two things occur as a result of these weaker interactions: spin state energies shift and the intensities of the peak change and no longer adhere to the pascal triangle pattern.

Hydrogen a and b are both doublet of doublets due to 2<sup>nd</sup> order coupling effects

## QUICK SUMMARY

### Major Pieces of Info from NMR<sup>19</sup>

- Number of signals = number of sets of nonequivalent protons
- Integration = relative number of nonequivalent protons
- Chemical shift = info about proton environment and presence of benzene rings
- Splitting = info about neighboring protons

## Technique for solving NMR Problems

*Calculate DBE first:* NMR data is interpreted after the molecular formula and functional groups are found from mass and IR spectrometry, so this information is already known. When the molecular formula is provided, it can be used to determine the DBE or double bond equivalents. DBE provides the degree of unsaturation (double bonds) and reveals the presence of rings in the molecule.

$$\text{DBE} = \text{C} - \frac{\text{H} + h}{2} + \frac{\text{N}}{2} + 1$$

<sup>20</sup>C = number of carbons  
H = number of Hydrogens  
h = number of halogens  
N = number of Nitrogens

*Organize Spectral Information*<sup>21</sup>: Looking at all of the NMR Spec data at once can get too overwhelming so it is a good idea to organize all of the information into a table and work with the pieces individually. A table with the following headings is recommended:

- Chemical Shift (ppm)
- Splitting
- Integration
- # Hydrogens
- Possible Fragment Structure

Once the information is organized, add up the number of hydrogens, carbons, and DBE's to make sure that everything has been used up. Perform an atom check and a DBE check. Checking the individual atoms before forming them into pieces will prevent mistakes in later stages that may become frustrating. After the pieces are gathered, all you have to do is put them together like pieces of a puzzle.

<sup>18</sup><http://www.chemistry.uoguelph.ca/driguana/NMR/2NDORDER.HTM> (11/20/06)

<sup>19</sup> P.276, J.R. Mohrig, *Techniques in Organic Chemistry* (2<sup>nd</sup>)

### CASE STUDY

- This example is to illustrate NMR solving techniques for a molecule that also contains atoms other than just hydrogen and carbon.

Interpret the NMR spectra and find the final structure.

Molecular formula: C<sub>4</sub>H<sub>9</sub>BrO

<sup>1</sup>H-NMR: 4.49 ppm (sextet, integral=1); 3.73 ppm (triplet, integral = 2); 3.20 ppm (singlet, integral =1); 1.95 ppm (quartet, integral=2) and 1.70 ppm (doublet, integral = 3)<sup>22</sup>

**Step 1:** The molecular formula is given to be C<sub>4</sub>H<sub>9</sub>BrO, so calculate the DBE

$$\text{DBE} = 4C - \frac{9H + 1h}{2} + 0 + 1 = 0 \text{ DBE}$$

\*0 DBE indicate that there are no pi bonds or rings. The molecule is made up entirely of alkanes

**Step 2:** Fill in all of the given information into the table.

Shift	Splitting	Integration	# H	Possible Fragment Structure
4.49	sextet	1	1	
3.73	triplet	2	2	
3.20	singlet	1	1	
1.95	quartet	2	2	
1.70	doublet	3	3	

All of the information above was given in the problem. Before going on, you should see what any of this can tell you even before filling in the possible fragments. Analyzing on paper or in your head at every step will help you remember all of the details as you go through the problem, rather than trying to fill in the gaps at the very end.

*Analysis:*

- As seen above, the NMR spectrum indicates that there are 5 signals, which means that there are 5 nonequivalent protons. There is no symmetry in this molecule.
- Also, there are 5 proton signals, but only 4 carbons. Remember that you have an oxygen and a bromine in the molecule. One proton must be attached to another

<sup>20</sup>p46, Prof. Steven Hardinger, *Chem 14C Thinkbook (version 4)*

<sup>21</sup>p.312, J.R. Mohrig, *Techniques in Organic Chemistry (2<sup>nd</sup>)*

<sup>22</sup>p67, Prof. Steven Hardinger, *Chem 14C Thinkbook (version 4)*

atom, which can only be oxygen because oxygen can have 2 attachments, whereas a halogen like bromine only has 1 center of attachment.

Now fill in the possible structures, keeping in mind the conclusions drawn above.

Shift	Splitting	Integration	# H	Possible Fragment Structure
4.49	sextet	1	1	CH in $\text{CH}_2\text{CHCH}_3$
3.73	triplet	2	2	$\text{CH}_2$ in $\text{CH}_2\text{CH}_2$ $\text{CHCH}_2\text{CH}$
3.20	singlet	1	1	OH
1.95	quartet	2	2	$\text{CH}_2$ in $\text{CH}_2\text{CH}_3$ $\text{CHCH}_2\text{CH}_2$
1.71	doublet	3	3	$\text{CH}_3$ in $\text{CHCH}_3$

*Analysis:*

- The 3.20 ppm singlet must be an OH as we already determined in the above analysis. Hydrogen-bonded molecules like NH and OH are usually singlets, so we can write it down as a fragment with confidence.
- Overall, the fragment suggested first will most likely be the correct one because molecules favor simplicity and fewer atoms/bonds; however, you should always be careful, especially when there are individual attachments like halogens because you have to remember to leave enough openings to attach them. Also, you know for a fact that there is a CH, so the possible fragments that contain a CH should be equally considered.

Choose your pieces and check

Shift	Splitting	Integration	# H	Possible Fragment Structure
4.49	sextet	1	1	CH in $\boxed{\text{CH}_2\text{CHCH}_3}$
3.73	triplet	2	2	$\text{CH}_2$ in $\text{CH}_2\text{CH}_2$ $\text{CHCH}_2\text{CH}$
3.20	singlet	1	1	$\boxed{\text{OH}}$
1.95	quartet	2	2	$\text{CH}_2$ in $\text{CH}_2\text{CH}_3$ $\text{CHCH}_2\text{CH}_2$
1.70	doublet	3	3	$\text{CH}_3$ in $\boxed{\text{CHCH}_3}$
		<b>Totals</b>	<b>9 H</b>	$\text{CH} + \text{CH}_2 + \text{OH} + \text{CH}_2 + \text{CH} = \text{C}_4\text{H}_9\text{O}$

Atom check:  $\text{C}_4\text{H}_9\text{BrO} - \text{C}_4\text{H}_9\text{O} = \text{Br}$

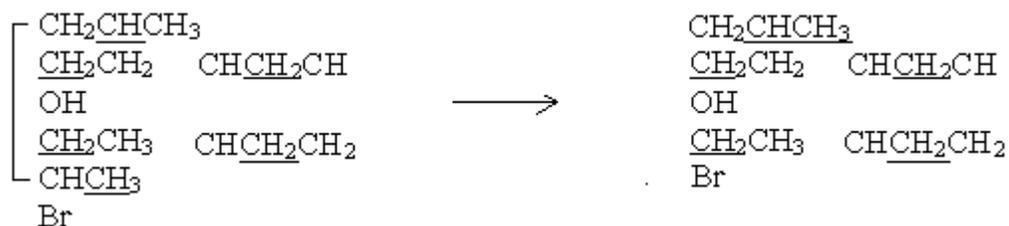
DBE check: There were no DBE's to account for so no need to check

*Analysis:*

- Everything has been used up except Br, which can be attached to the end of a carbon later on. Now all you have to do is add Br to the total number of molecular pieces you have and attach them together.

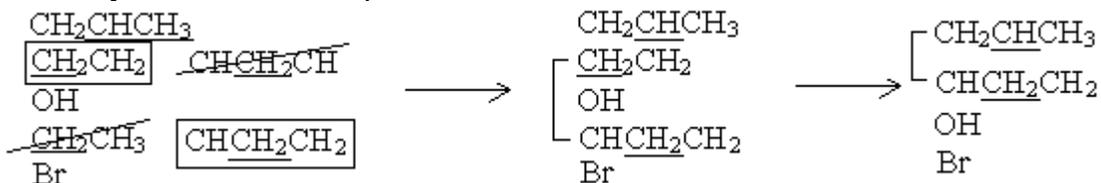
- The CH<sub>2</sub>'s weren't boxed in because they could be either the first possibility or the second.

Write out the pieces to see if you can integrate smaller pieces into a larger fragment.



Analysis: The triplet CH<sub>2</sub> is most likely next to another CH<sub>2</sub> (which would be the quartet CH<sub>2</sub>) rather than 2 CH's because there's only 1 CH we know of in this molecule. Now all we need to do is figure out the quartet CH<sub>2</sub>. In this case, the second possibility is most likely correct because it contains 1 CH, which we know is in the molecule. This quartet probably wouldn't be next to another methyl because that wouldn't leave enough room for both OH and Br attachments.

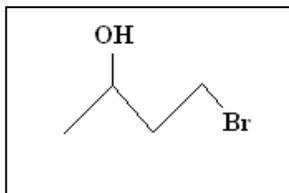
The methylenes now match up with each other



Last three pieces:



Final Structure:



In some cases when the chemical shift may still be too hard to interpret, 2 final structures may be accepted. For instance, this molecule may also be drawn with the Br and OH switched because both structures still follow all of the splitting patterns in the NMR data.