**Proton Nuclear Magnetic Resonance Spectroscopy**

Introduction:
The NMR Spectrum serves as a great resource in determining the structure of an organic compound by revealing the hydrogen and carbon skeleton. Historically, NMR was initially used to study the nuclei of Hydrogen atoms; however, any atom with an odd mass or atomic number has a nuclear spin that can be studied by NMR. Without the application of an applied magnetic field, protons are spinning in a randomly oriented manner and are generating a magnetic field (called the ***magnetic moment***)[1]. However, once an external (applied) magnetic field is present the protons either align with (parallel) or against (anti parallel) it. The parallel orientation, called the alpha spin, has a lower energy than the anti parallel (beta) spin. The stronger the applied magnetic field the greater the energy difference (ΔE) between the parallel and anti parallel states (Diagram 1)[2]. Therefore, the strength of the magnetic field determines the energy required to cause a ***nuclear spin flip***. The energy difference (ΔE) between the ground and excited states is approximately 0.02 cal/mol which correlates to radio wave photons. An NMR signal is created once the radio wave photons supplied match the (ΔE) of the nucleus.
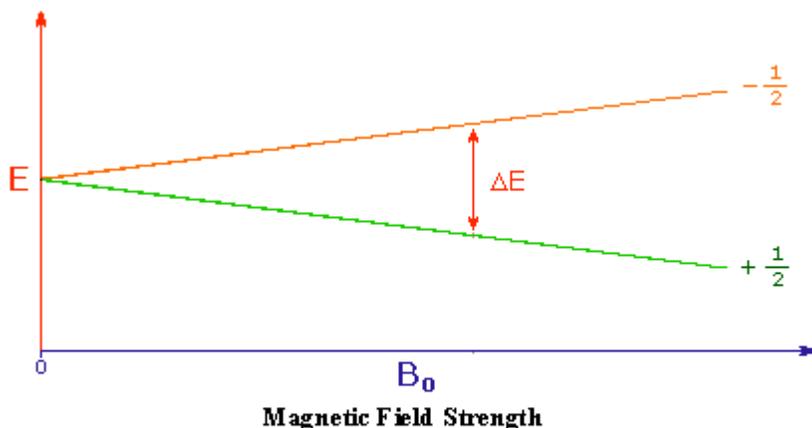
- Diagram 1:
* As the Magnetic Field increases, more energy is required for a nuclear spin flip.

Structural Information from NMR Spectrum:[3]

1. **Number of Signals:** In order to use the number of signals to gain structural information one needs to understand the concept of chemically equivalent protons.
    - **Equivalent Protons:** Identical protons, which experience the same magnetic force, will create identical and overlapping signals on the NMR spectrum. Such protons which are in the same magnetic environment are termed ***chemically equivalent***.[4] The number of signals on the NMR spectrum represents the number of equivalent sets of protons. Protons with

[1]. P.539, L.G.Wade, *Organic Chemistry (5th)*
[2]. http://www.cem.msu.edu/~reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm (08/27/06)
[3]. p.55, Steven Hardinger, PhD. *The Think Book (chem14C).*
[4]. P.552, L.G.Wade, *Organic Chemistry (5th)*

any one difference between them are no longer equivalent. For finding these differences one must begin by first looking at the atom directly attached to the proton and continue down the bonded atoms to find one difference. Protons aligned across a plane of symmetry, such as in Benzene, are equivalent. Another useful method for testing equivalency is replacing each proton with another atom, such as deuterium, to form two molecules. If the two molecules obtained are identical then the protons are equivalent.

Example 1: Indicate the expected number of signals in the H NMR spectrum for each of the following molecules. [5]
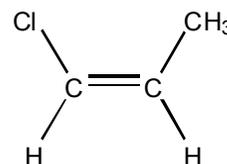
(A)   (B)

*Part A has 4 signals, one from the methyl group, one from the methoxy group, and two from the benzene ring due to the plane of symmetry. Part B has 3 different signals due to the methyl group, and one from each H due to their attachment to different carbons.

2. **Position of Signals:** As previously discussed, the ΔE required for a nuclear spin flip increases as the magnetic field strength increases (Diagram 1). The magnetic field felt by a proton is a combination of three sources; the magnetic field of the earth, the magnetic field of the NMR spectrometer, and the local magnetic field created by electrons and other nuclei. To standardize the influence of the instrument's magnet, we use a reference proton called **TMS**. Therefore, the only factor that determines the position of the signal is the magnetic field created by the other nuclei and electrons in the molecule. The **chemical shift** (ppm) represents the ΔE relative to the reference proton.

- **Tetramethylsilane, $(CH_3)_4Si$:** TMS is used as **the reference compound**[6] for multiple reasons. Firstly, there are very few compounds that have a chemical shift lower then TMS. Also, TMS is an inert compound which will not react with our sample. Finally, TMS has 12 equivalent protons which absorb at the same magnetic field and result in one intense absorption. The chemical shift of TMS is 0.00 ppm by definition and many proton chemical shifts fall between the range of 0 to 15 ppm.

- **Shielding and Deshielding:**[7] The chemical shift is also dependent upon the surrounding electron density. This factor can be influenced by the electronegativity of the neighboring atoms. The electron cloud density around an atom shields the proton from the force of the applied magnetic field.

[5]. P. 532, P. Y. Bruice, , *Organic Chemistry (4th)*
[6]. P.545, L.G.Wade, *Organic Chemistry (5th)*
[7]. P. 530, P. Y. Bruice, , *Organic Chemistry (4th)*

Electronegative neighboring atoms remove electron density from protons; causing the applied magnetic field to have a greater influence on them. Protons which are *shielded* by local electrons experience a weaker applied magnetic field and have a lower chemical shift. Such protons are on the right side of the spectrum, closer to TMS, and are referred to as being *upfield.* On the other hand, protons with low local electron density due to neighboring electronegative atoms are called *deshielded* protons (Diagram 2). They experience a strong applied magnetic field, have a high chemical shift, and are on the left side of the spectrum known as *downfield.*
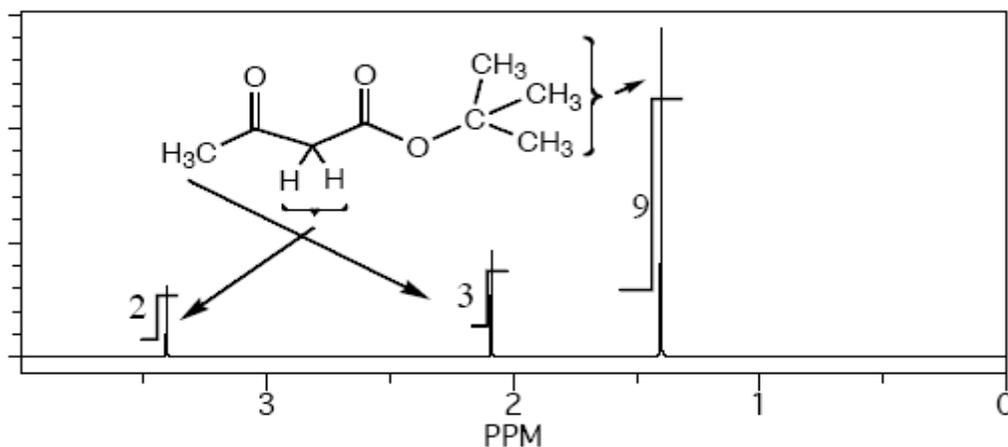

Diagram 2: [8]
* The chemical shifts of the hydrogen atoms is determined considering their relative position with respect to the electronegative oxygen atoms.

- **Magnetic Anisotropy:** [9]Other factors which influences chemical shift are pi bonds and rings which create their own magnetic fields. Pi electrons move in a circular path creating a magnetic field which has different magnetic forces at different points in space.

- **Characteristic Chemical Shifts:** Similar functional groups have similar chemical shifts which allow us to form a table of characteristic chemical shift ranges. Generally, we cannot use characteristic shifts to determine the proton types of NMR signals. The two exceptions are Benzene rings (6.5 – 8ppm) and Aldehyde groups (9.5- 11ppm).

Example 2: Predict the chemical shifts of the protons in the molecules below. Protons should be labeled from lowest to highest frequency a, b, c etc. [10]
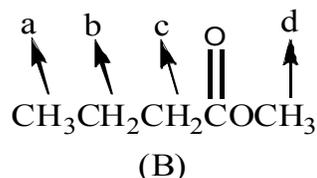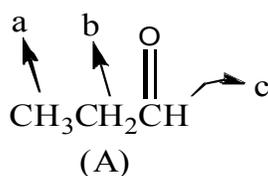
[8] . http://homepage.mac.com/tminehan/chem333.html ((08/27/06)
[9] . p.234, Steven Hardinger, PhD. *The Think Book (chem14C)*.
[10] . P. 538, P. Y. Bruice, , *Organic Chemistry (4th)*

*Part A: The Hydrogen on the CH group is closest to the Oxygen molecule. As the molecules get further from the Oxygen their chemical shifts decrease. Part B: The Hydrogens on the methyl group directly attached to the Oxygen have the highest chemical shift. As the Hydrogens get further from the electronegative Oxygen their chemical shifts decrease.

3. **Relative Intensity of Signals:** The relative intensity of each signal on the NMR spectrum provides us with additional structural information. Beer's Law states that the amount of energy absorbed is proportional to the amount of matter present. Similarly, the area under the curve of each signal is proportional to the number of equivalent protons creating the signal. Therefore, by **integrating**[11] the area under each curve the NMR spectrometer provides us with relative numbers of protons (Diagram 3). These relative integral values can then be used to determine the number of equivalent protons that cause each peak.
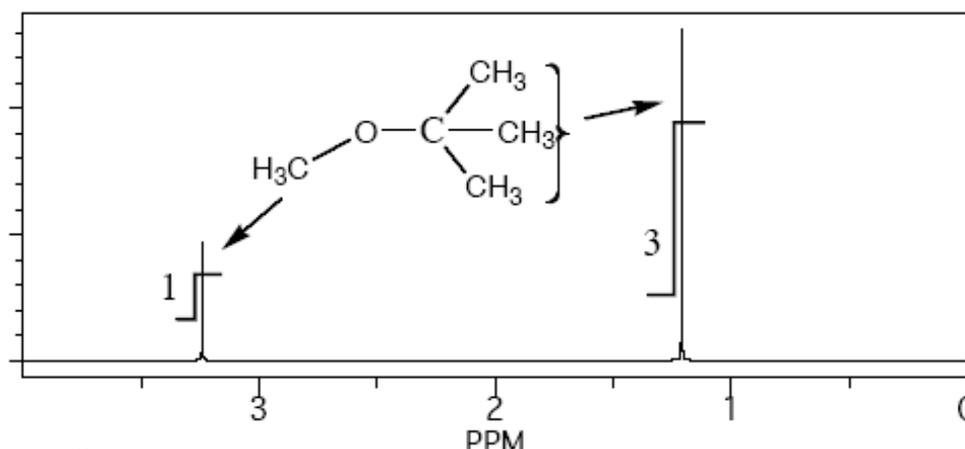

Diagram 3:[12]
* The molecule has two sets of equivalent protons in a 9:3 ratio. This integral ratio can be reduced by setting the smallest integral to 1. Thus, we arrive at the 3:1 ratio indicated.

Example 3: Use integration to distinguish the H NMR spectra of these compounds.

*Both of these compounds would show two signals. However, the ratio of integrals would be different. Molecule A would have a ratio of 9:1 where as Molecule B would have a ratio of 3:2.
*It is important to remember that the ratio of integrals may not represent the absolute number of protons

4. **Splitting of NMR Signals**: The **splitting** of a signal seen on the NMR spectrum is the result of a phenomenon known as spin-spin coupling. **Spin-spin coupling** is

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[11]. P.554, L.G.Wade, *Organic Chemistry (5th)*
[12]. http://homepage.mac.com/tminehan/chem333.html ((08/27/06)

due to the magnetic interaction of nuclear spins with the applied magnetic field. In other words, the spin of one nucleus either adds to (parallel) or subtracts from (antiparallel) the applied magnetic field. Therefore, this interaction between the nuclear spins results in more than one energy state for the system. When the magnetic field of two non equivalent protons is close enough to influence each other they are termed ***magnetically coupled***.[13] The magnetically coupled protons each split the others signal because spin-spin splitting is a reciprocal property.

- **The N+1 Rule:**[14] In the case that the proton has more then one neighbor, the signal is split into multiple lines. In general, if n represents the number of neighbors the signal is split into n+ 1 lines. If a proton has no neighbors it is a singlet, one neighbor constitutes a doublet, two neighbors is a triplet etc. The distance between the lines in splitting pattern is the ***Coupling Constant (J).*** The ratio of the lines can be determined using ***Pascal's Triangle.***[15]

Rules for Determining Neighboring Protons[16]
- **Rule 1:** Equivalent protons are in the same magnetic environment and produce the same signals. Therefore, only non equivalent protons can split signals.

- **Rule 2:** In order to couple with one another protons must be close enough to influence the magnetic fields of one another. Therefore, generally only protons seperated by three or less sigma bonds can couple with one another. Pi bonds are generally not counted towards the maximum three bonds. In addition the benzene ring has its own "coupling club" because hydrogens directly attached to it are all coupled with one another. However, hydrogens which are not directly attached cannot couple with those directly on the benzene ring even if they are within three bonds.

- **Rule 3:** Hydrogens attached directly to oxygen or nitrogen atoms are generally singlets and do not split the signals of other protons.

Non First Order Splitting[17]
- When the coupling constants (J) of neighboring protons are equal the splitting patterns we have discussed thus far are witnessed. However, in the case that the coupling constants of neighboring protons are not equal more complex splitting occur, such as doublet of doublets.

[13]. P.556, L.G.Wade, *Organic Chemistry (5th)*
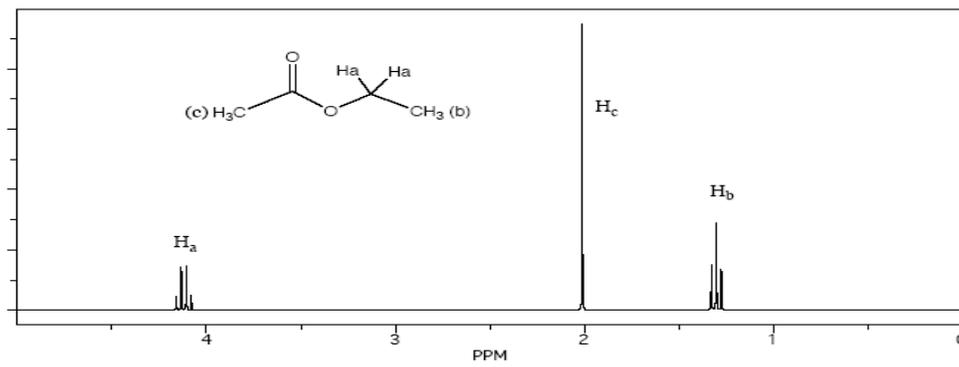[14]. p.234, Steven Hardinger, PhD. *The Think Book (chem14C).*
[15]. P. 554 P. Y. Bruice, , *Organic Chemistry (4th)*
[16]. p.61, Steven Hardinger, PhD. *The Think Book (chem14C).*
[17]. p.63, Steven Hardinger, PhD. *The Think Book (chem14C).*

Example 4: Determine the splitting patterns in the following compound.[18]

* The Hb protons of the methyl group are split by both Ha protons. Therefore the splitting pattern is a triplet (N=2). The Ha protons are equivalent and are split by the 3 methyl protons. Thus their splitting pattern is a quartet (N=3). Finally the Hc protons of the methyl group are not split by any other protons, thus their splitting pattern is a singlet.

How to use H NMR in solving spectroscopy problems:

Once the molecular formula and functional groups have been obtained from the mass spectrum and the IR spectrum we can utilize the H NMR spectrum to put together the pieces into a final structure. The following problem outlines this procedure assuming the mass spectrometry and IR spectroscopy have been completed.

Example 5:[19] The molecular formula has been determined from the Mass Spectrometry to be $C_{10}H_{14}$. The H NMR results are the following: 7.14 ppm – 7.266 ppm (multiplet, integral= 5), 2.470 ppm (doublet, integral = 2), 1.860 ppm (nonet, integral = 1), 0.910 ppm (doublet, integral = 6). Propose a structure given the following data.

Step 1: [20]First begin by calculating the DBE in order to recognize the possibilities of any rings and/or pi bonds.

DBE = C – (H/2) + (N/2) + 1 = 1, where H represents hydrogens and halogens.
DBE = 10 – (14/2) + 1 = 4.

This tells us that we have a combined four pi bonds and/ or rings. Anytime the DBE is greater than four there is a possibility for a benzene ring, although it is not certain.

*Based on the formula we also know that functional groups with C and H are the only possibilities because there are no N, O, etc in our molecular formula.

Step 2: Input the H NMR data into a table. This allows us to better organize our information in a logical manner.

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[18]. http://homepage.mac.com/tminehan/chem333.html ((08/27/06)
[19] . http://www.aist.go.jp/RIODB/SDBS/cgi-bin/direct_frame_top.cgi?lang=eng (08/29/06)
[20] . p.239, Steven Hardinger, PhD. *The Think Book (chem14C)*.

Chemical Shift	Splitting	Integral	# of H	Implication
7.14 – 7.226 ppm	Multiplet	5		
2.470 ppm	Doublet	2		
1.860 ppm	Nonet	1		
0.910	Doublet	6		

Step 3: Calculate the absolute number of hydrogens by summing up the integral for each signal. The sum of the integrals is 5 + 2 + 1 + 6= 14. We have 14 hydrogens in our molecular formula; therefore the integral represents the absolute number in this case. The ratio is 1:1 in this example. For other problems the ratio may not be equal and one must multiply by a factor to determine the correct number of hydrogens for each signal. Go back to the table and add in the new data.

Chemical Shift	Splitting	Integral	# of H	Implication
7.14 – 7.226 ppm	Multiplet	5	5	
2.470 ppm	Doublet	2	2	
1.860 ppm	Nonet	1	1	
0.910	Doublet	6	6	

Step 4: Use the number of hydrogens in the signal to determine if the group is a CH_3, CH_2, or CH. Consider all possibilities for each signal. If suggested by the IR and formula, also consider OH and NH as possible hydrogen containing groups (both of which would usually be singlets). In this case, there is no oxygen or nitrogen in the molecular formula. Additionally, check the chemical shifts for the presence of an aldehyde or benzene functional group. In this case the multiplet has a chemical shift in the range of benzene (6.5 ppm – 8.0ppm). This is also verified by our IR analysis.

Chemical Shift	Splitting	Integral	# of H	Implication
7.14 – 7.226 ppm	Multiplet	5	5	**5 Benzene H's**
2.470 ppm	Doublet	2	2	**CH$_2$ in CH$_2$CH** 2xCH in CHCH
1.860 ppm	Nonet	1	1	**CH in (CH$_3$)$_2$CHCH$_2$**
0.910	Doublet	6	6	**2x CH$_3$ in CH$_3$CH** 3x CH$_2$ in CH$_2$CH 6x CH in CHCH
Totals		**14**	**14 H's**	

Step 5: Determine the number of neighboring hydrogens for each signal. This can be done using the N + 1 rule in reverse. For example, the doublet at 2.470 ppm represents a doublet which has 2 peaks and by subtracting one we determine it has 1 neighboring hydrogen. Additionally, the nonet at 1.860 ppm represents 9 peaks and therefore has 8 neighboring hydrogens. Next, come up with different combinations of neighboring groups with the correct number of hydrogens.

Step 6: At this point, we have multiple groups fulfilling the conditions. The best decision is generally the most simple group containing the least number of atoms. For instance, we select CH_2 over 2 x CH because it contains less atoms. Additionally, in our case the chemical shifts between 6.5 ppm and 8.0 ppm indicate to us that these are benzene ring hydrogens. Also the fact that we have a DBE = 4 confirms the presence of such a benzene ring. We can also conclude that the group is a monosubstituted benzene ring due to the presence of 5 benzene H's.

Step 7: Now, add all of the atoms used from the HNMR, IR or other sources to make sure all hydrogens are accounted for and to detect any unused atoms.
$C_6H_5+CH_2+CH+CH_3+CH_3= C_{10}H_{14}$ Subtract this from the given molecular formula.

$C_7H_{14} - C_7H_{14}= 0$. Therefore our H NMR accounts for all of the atoms in our molecular formula. If at this point all hydrogens are not accounted for an error has been made. Additionally, if any other atoms remain, such as carbon, they are not bonded to any hydrogens.

Step 8: Check for any unused DBE. Subtract the DBEs accounted for by the H NMR, IR, or other sources from the DBEs calculated from the molecular formula. In this case we have 4 (calculated from molecular formula) – 4 (from the benzene ring) = 0. All DBE have been accounted for.

Step 9: We can now finally bring all of our information together to determine the structure of the compound. Make a list of all the pieces and assemble them to determine the structure.

Pieces: Benzene Ring C_6H_5
          CH_2 in $\underline{CH_2}CH$
          CH in $(CH_3)_2\underline{CH}CH_2$
          2x CH_3 in $\underline{CH_3}CH$

      In order to assemble the pieces begin by analyzing the groups and splitting patterns. A useful method is to look for similarities in the coupling patterns of various groups and assemble them together. In certain cases, the simplest groups that one choses may not give us a valid structure and one must go back to make alternate selections. In this case we see that the group in the middle requires two neighboring CH_3 groups and one neighboring CH_2 group. Thus the three groups can fit together to form one fragment and obey the splitting patterns.

Our groups have been reduced to two fragments: C_6H_5 and $(CH_3)_2CHCH_2$. There is only one way to assemble these two groups.

Final Structure: