NUCLEAR MAGNETIC RESONANCE (NMR) SPECTROSCOPY

The nuclei of some atoms exhibit magnetic behavior. The ability to behave in this way is related to the "spin quantum number", I, of the nucleus.

When such nuclei are placed in a strong magnetic field they may assume "spin" states of different levels. If the nucleus is irradiated with radio frequency energy corresponding to the energy difference between two spin states, energy is absorbed, causing a transition of the nucleus from a lower energy spin state to a higher energy spin state.

Not all nuclei are "magnetically active". Such activity is limited to nuclei in which the spin quantum number, I, is not zero. In general, the magnetically active nuclei have either an odd mass number or an odd atomic number, or both.

Some magnetically active nuclei are:

$^{1}_{1}H$ $^{13}_{6}C$ $^{10}_{5}B$ $^{19}_{9}F$ $^{31}_{15}P$ $^{15}_{7}N$

The following nuclei have spin quantum numbers of zero and are magnetically inactive. As a consequence they are "invisible" in the NMR spectrometer.

$^{12}_{6}C$ $^{16}_{8}O$ $^{32}_{16}S$

The simplest nuclei in terms of their magnetic behavior are nuclei having $I = ½$. Such nuclei exhibit two spin states. The number of spin states is equal to $2I + 1$, so when $I = ½$, $(2 \times ½) + 1 = 2$.

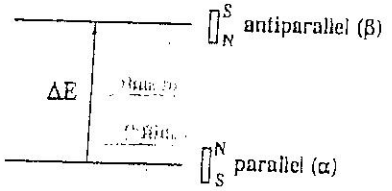
The two nuclei of central importance in the study of organic compounds are ^{1}H and ^{13}C, and both of these nuclei have $I = ½$.

At this point we will focus attention on the ^{1}H nucleus. Since the ^{1}H nucleus consists of a single proton, ^{1}H NMR spectroscopy is some times referred to as PMR or Proton Magnetic Resonance spectroscopy.

With a spin quantum number of ½, there are two magnetic spin states that a hydrogen nucleus can assume when placed in an external magnetic field.

In a vastly oversimplified analogy, it is useful to compare the behavior of a proton to that of a simple bar magnet.

When placed in an external magnetic field a bar magnet has two stable orientations, aligned parallel to the external field, or aligned antiparallel.



The energy difference ΔE between the two states depends upon the strength of the external field (typically expressed in terms of gauss, G, or tesla, T) and the strength of the nuclear magnet, which is a constant γ (gamma), defined as the magnetogyric ratio of the nucleus. The value of γ is a constant for a particular type of nucleus.

When a proton is irradiated with electromagnetic energy, energy will be absorbed by a nucleus when the energy of irradiation exactly equals ΔE, the energy difference between the two spin states.

The equation relating frequency of irradiation and magnetic field strength is:

$$\nu = \frac{\gamma}{2\pi} B_o$$

ν is frequency of irradiation (in hertz, Hz, cycles per second)
B_o is magnetic field strength (in tesla, T)
γ is the magnetogyric ratio

Since $\gamma/2\pi$ is a constant for the ^{1}H nucleus, the equation shows a direct relationship between the absorption frequency for a proton and the strength of the magnetic field in which the proton is located. The frequency at which the proton absorbs energy is called its "resonance frequency".

Thus, by measuring the absorption of radio frequency energy by a proton, we can obtain information about its magnetic environment when placed in the nuclear magnetic resonance spectrometer.

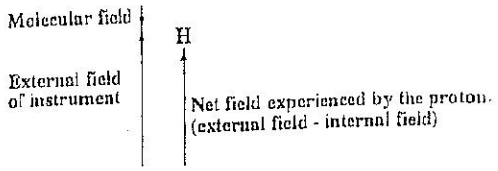
When a molecule is placed in a strong magnetic field, the motion of the electrons in the molecule responds to the external magnetic field by generating very small magnetic fields within the molecule. Since the electrons within a molecule are localized in the various bonds, the result is that the internally-generated magnetic fields within the molecule are not uniformly distributed. The result is that different hydrogen atoms situated in different locations within the same molecule may experience different magnetic environments and will have different resonance frequencies.

The PMR spectrum is a measurement of the resonance frequencies of the magnetically nonequivalent sets of protons within a molecule.

Since the magnetic environment is related to the structure of the molecule, the PMR spectrum provides information about the structure of the molecule in which the protons are located.

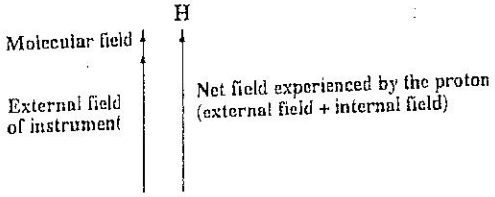
Shielding and Deshielding of Protons

In some cases a proton in a molecule may be located at position where the internally-generated molecular magnetic is oriented in the opposite direction to the direction of the external magnetic field produced by the large magnet that is a part of the instrument.



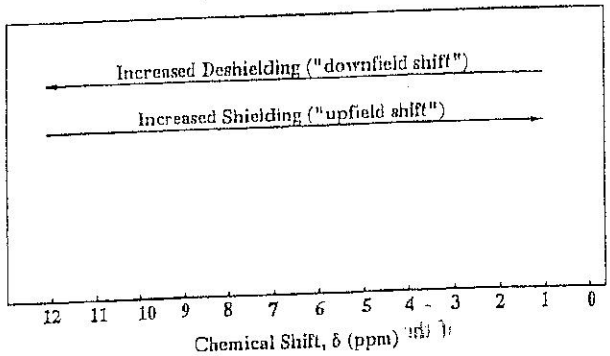
In this situation the proton will have a lower resonance frequency than it would have if it were not located in the molecular environment. The proton is said to be "shielded" by the internally generated molecular field.

Another possibility is that a proton in a molecule may be located at a position within the molecule where the internally-generated molecular magnetic field reinforces the external field. A proton in this environment experiences a slightly stronger total field, so its resonance frequency will be slightly increased from what it would be in the absence of the molecular environment.



In this case the proton is said to be "deshielded" by its molecular environment.

In reporting NMR data the scale used in designating the location of signals is not expressed in units of frequency (Hz), but in units of parts per million (ppm). The location of a signal for a proton in the NMR spectrum is called the "chemical shift", δ, for the signal in ppm. The typical PMR spectral chart has an appearance like that shown below.



The chemical shift of a signal is scale is located along the horizontal axis and is expressed in units of parts per million (ppm) relative to the chemical shift of the signal for the protons in tetramethylsilane (TMS), $(CH_3)_4Si$. TMS gives a single sharp peak in the PMR spectrum that is assigned a value of 0 ppm. Most of the ^1H atoms in organic molecules appear "downfield" (to the left) of the signal for TMS; they are "deshielded" relative to the ^1H atoms in TMS.

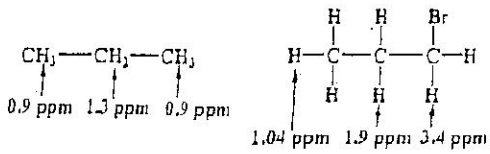
Two principal factors influence the magnetic environments of protons within molecules.

1) *Inductive effects*: effects resulting from polarization of the bonding electrons of the hydrogen atom. When a molecule is placed in the strong magnetic field of the NMR spectrometer, the bonding electrons for a hydrogen atom respond by producing a magnetic field that shields that hydrogen atom. Electron-withdrawing groups that draw electron density away from the hydrogen atom cause a decrease in the ability of the bonding electrons to shield the hydrogen atom. The effect of the electron-withdrawing group is to deshield the hydrogen atom (*i.e.*, cause a downfield shift in the signal for the proton).

The presence of atoms of electronegative elements is a very common cause of an electron-withdrawing inductive effect. Inductive effects are exerted through polarization of the sigma bond between the electronegative atom and the hydrogen atom under consideration. Two common features of inductive effects in PMR spectroscopy are:

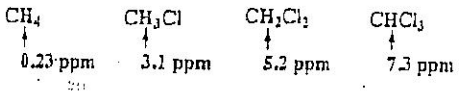
a) The strength of an inductive effect decreases as the number of intervening bonds between the electronegative atom and the hydrogen atom increases.

Consider the effect of the presence of an electron-withdrawing bromine atom on the chemical shifts of the protons in 1-bromopropane, compared with propane.



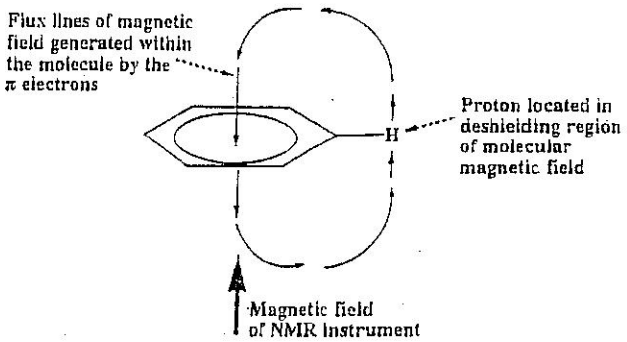
In a simple alkane, the chemical shift of a primary (1^{o}) H is typically about 0.9 ppm, while the chemical shift of secondary (2^{o}) H is slightly larger, around 1.3 ppm. In 1-bromopropane the electron-withdrawing inductive effect of the Br atom has a deshielding effect. The magnitude of the deshielding effect decreases as the number of bonds intervening between the Br atom and a hydrogen atom increases. The greatest downfield shift is seen for the hydrogen atoms located on the same carbon atom as the Br (2 intervening bonds), where a downfield shift of about 2.5 ppm from 0.9 to 3.4 ppm is seen. For an H atom on the second carbon (3 intervening bonds), the deshielding effect is much smaller, only about 0.6 ppm (from 1.3 ppm in propane to 1.9 ppm in 1-bromopropane). The effect on H at the third carbon (4 intervening bonds) the deshielding effect has decreased to only about 0.14 ppm.

b) Inductive effects are roughly additive. For example, consider the effect of successive replacement of three of the hydrogen atoms of methane by chlorine atoms.



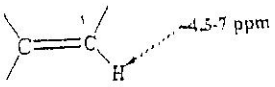
2) Magnetic fields generated by π bond systems in the molecule.

The electrons in π bonds generate particularly strong magnetic fields when the molecules are placed in the strong magnetic field in the NMR spectrometer. This is particularly true for aromatic rings such as those in benzene and benzene derivatives.

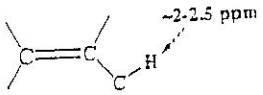


When an aromatic ring is located in the strong magnetic field of the NMR spectrometer the electrons in the cyclic π electron cloud of the ring generate an internal magnetic field. The orientation of this internal field is such that the magnetic flux lines at the center of the ring are in the direction opposite to the external field. However, if you follow the path of the flux lines of the internal magnetic field, you find that the protons attached to the ring carbons lie in a region where the flux lines are oriented in the same direction as the field of the NMR spectrometer. The result is that protons attached to aromatic rings are strongly deshielded by the aromatic ring. The chemical shift of the hydrogen atoms in benzene appear at a chemical shift of about 7.15 ppm. The signals for hydrogen atoms on substituted benzenes or other aromatic rings are usually found in the region of about 6-9 ppm.

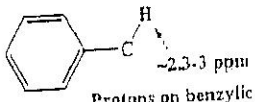
A similar situation is exhibited by protons directly bonded to the double bond carbon of an alkene, but the deshielding effect is not so strong as is the case for protons attached to aromatic rings. For vinylic protons, the typical chemical shift region is about 4.5-7 ppm.



Protons farther away from the π bond such as those attached at benzylic or allylic positions are also influenced by the magnetic field generated by the aromatic ring or the alkene, but not as strongly.

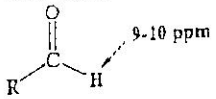


Protons on allylic carbons of alkenes

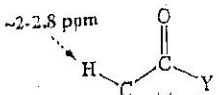


Protons on benzylic carbons of aromatic compounds

The effect of a carbonyl group (C=O) involves a combination of inductive deshielding due to the electron-withdrawing oxygen atom and the deshielding caused by the magnetic field generated by the π bond.



Aldehyde



Protons α to carbonyl group in aldehydes, ketones, carboxylic acids, carboxylic acid derivatives

Over the years an enormous number of compounds have been examined by NMR spectroscopy. Not only have the usual deshielding effects of the most commonly encountered functional groups been determined, but tables of "shielding constants" for those functional groups have been constructed. If a proton is located in an organic molecule where more than one functional group is influencing its chemical shift, the shielding constants can be used to predict what the chemical shift of the proton would be expected to be.

The most useful table of shielding constants for predicting chemical shifts was formulated by James N. Shoolery, who was employed by Varian Associates, the company which developed the earliest commercial Nuclear Magnetic Resonance Spectrometers. Shoolery constructed a table of shielding constants based upon experimental observations. He formulated an equation that could be used to estimate the approximate chemical shifts of protons on alkyl groups that are affected by the deshielding effects of more than one deshielding group.

In using Shoolery's equation to predict chemical shifts, various substituent groups are assigned "effective shielding constants", σ_{ieff} The following table shows the σ_{ieff} values for a number of common groups.

Shoolery's Effective Shielding Constants

Functional Group	σ_{ieff}
–Cl	2.53
–Br	2.33
–I	1.82
–OH	2.56
–O-Alkyl	2.36
–O-Aryl	3.23
–O–C(=O)–R	3.13
–SR	1.64
–N(Alkyl)$_2$	1.57
–CH_3	0.47
–CR^1=CR^2R^3	1.32
–C_6H_5	1.85
–C≡CR	1.44
–CR(=O)	1.70
–COR(=O)	1.55
–CNR$_2$(=O)	1.59
–CF_3	1.14
–C≡N	1.70

To predict the approximate chemical shift, δ, for the signal for the hydrogen atoms on the methylene group (CH_2) of X-CH_2-Y, simply substitute the shielding constants for X and Y into the equation below:

$$\delta = 0.23 + \sigma_X + \sigma_Y$$

In this equation 0.23 is the chemical shift of the protons in CH_4. The agreement between experimentally observed chemical shifts and those predicted using Shoolery's equation, while not perfect, is often remarkably good.

Compound	δ calculated	δ observed
ICH_2I	0.23 + 1.82 + 1.82 = 3.87	4.09
ClCH_2Br	0.23 + 2.53 + 2.33 = 5.09	5.16
$C_6H_5CH_2CH_3$	0.23 + 1.85 + 0.47 = 2.55	2.52
$C_6H_5CH_2OCH_3$	0.23 + 1.85 + 2.36 = 4.44	4.41
$C_6H_5CH_2C_6H_5$	0.23 + 1.85 + 1.85 = 3.93	3.92
C≡C-CH_2OH	0.23 + 1.32 + 2.56 = 4.11	3.91
CH_3CH_2–C(=O)–CH_3	0.23 + 0.47 + 1.70 = 2.40	2.47
C≡C-CH_2-C≡C	0.23 + 1.32 + 1.32 = 2.87	2.91

Shoolery's constants cannot be applied in predicting the chemical shifts of methine protons in $CHXYZ$. Apparently factors such as steric crowding in those cases cause unreliable correlation between observed values and values predicted from the extension of Shoolery's rules.

Other useful tables of PMR chemical shift information are found in the lab manual and shown on the next page.

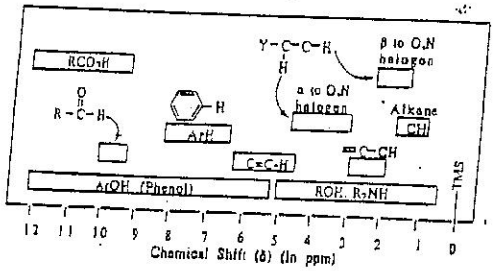
TABLE 1. TYPICAL ^{1}H NMR CHEMICAL SHIFT VALUES

A. For Hydrogen Atoms Attached to Carbon

ENVIRONMENT OF HYDROGEN	TYPICAL CHEMICAL SHIFT VALUE (δ in ppm)
Alkyl-CH$_3$	0.9
Alkyl$_2$CH$_2$	1.25
Alkyl$_3$CH	1.5
Cl-CH	3 to 4
Br-CH	2.6 to 4.1
I-CH	2.2 to 4.2
HO-CH	3.4 to 3.6
Alkyl-O-CH	3.3 to 3.8
Aryl-O-CH	3.7 to 4.1
O=C-O-CH	3.6 to 5.1
Alkyl-N-CH	2.2 to 3.0
O=C-CH (α to carbonyl group)	2 to 3
C=C-CH (Allylic)	1.6 to 2.6
Phenyl-CH (Benzylic)	2.3 to 2.9
O=C-H (Aldehyde)	9.5 to 10.1
C=C-H (Vinylic)	4.6 to 7.3
Aryl-H	6.5 to 9.0

B. Hydrogen Attached to N or O (Variable due to hydrogen bonding, conc)

ENVIRONMENT OF HYDROGEN	TYPICAL CHEMICAL SHIFT VALUE (δ in ppm)
R-OH (Alcohols)	0.5 to 5.0
Ar-OH (Phenols)	4.5 to 12
O=C-OH (Carboxylic Acids)	9 to 12
Alkyl-NH (Alkylamines)	0.6 to 1.6
Aryl-NH (Arylamines)	2.5 to 4.0
O=C-NH (Amides)	4.0 to 8.5



Some points that are worthy of note in the tables.

1) The chemical shift ranges within which signals for protons attached to oxygen or nitrogen might be found are very broad. In fact, for NH or OH protons, the chemical shifts of the signals for those protons may vary greatly in different spectra for the same compound. Protons attached to N, or especially to O exhibit hydrogen bonding interactions that influence the magnetic environments of those protons. The extent of hydrogen bonding is quite sensitive to concentration, temperature, and solvent, accounting for the variability.
2) There is considerable overlap of the normal chemical shift ranges for the signals of protons in different chemical environments. More often than not it is necessary to have more information about the compound than the PMR spectrum alone in order to assign the molecular environment of the proton which produces a signal at a particular chemical shift in the spectrum of that compound.
3) It is not uncommon for signals for structurally different sets of protons in the same molecule to give signals that overlap so that it may not be possible to recognize the appearance of the individual signals. For example, a molecule of heptane, $CH_3CH_2CH_2CH_2CH_2CH_2CH_3$, contains four structurally distinct sets of protons. However, the three structurally distinct sets of 2^0 protons all have similar molecular environments and their PMR signals are not separated, giving one unresolved signal for all ten 2^0 protons. A separate signal appears for the six 1^0 protons.

When interpreting a ^{1}H NMR spectrum, there are four types of information that might be deduced.

1) The number of structurally distinct sets of protons in the molecule.
2) The possible chemical environments of the protons giving rise to the various signals.
3) The relative numbers of protons in the sets that give rise to the various signals in the spectrum.
4) The relationship between chemically nonequivalent sets of protons that are in close proximity in the molecule.

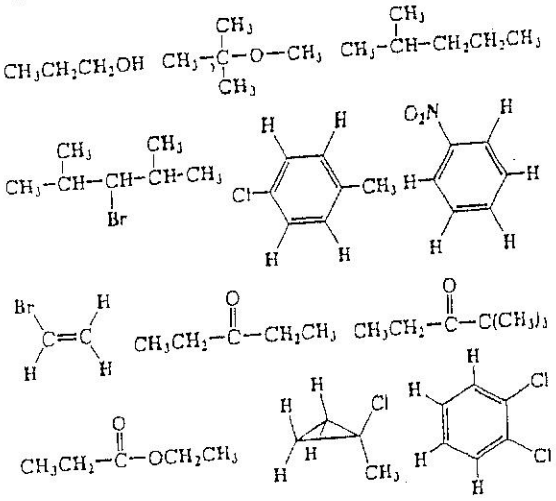
We will consider these items in order.

1) The number of structurally distinct sets of protons in the molecule:

If the spectrum of a compound contains "n" distinctly identifiable separate signals, the molecule generally must have at least "n" structurally distinct sets of hydrogens. However, since protons in different structural environments may not be different enough in their magnetic environments to give signals at different chemical shifts, there may be more structurally distinct sets of protons than "n".

Usually, in conformationally mobile systems, hydrogen atoms on the same carbon are magnetically equivalent. Hydrogen atoms on different carbons but in symmetrical locations in a molecule will be magnetically equivalent. Where conformational mobility is restricted (*e.g.* by ring systems or double bonds), protons attached to the same carbon may not be structurally or magnetically equivalent.

For example, how many structurally different sets of protons are there in the molecules below?



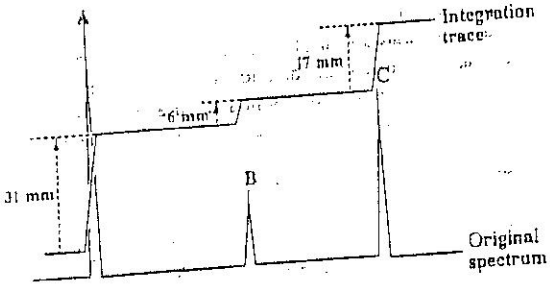
2) Possible structural environments of sets of protons: this would involve consideration of the chemical shifts of the various signals using the relationships described earlier in this discussion.

3) Relative numbers of protons represented by the various signals in the spectrum--integration of the spectrum.

There is a direct relationship between the area under a signal in the PMR spectrum of a compound. The ratio of the areas under the signals in the spectrum of a compound corresponds to the relative numbers of protons in the various sets of protons represented by those signals. The areas under the signals can be measured by the "integration" of the spectrum.

The classical method of determining the integration ratio of the peaks was to run the spectrum to obtain the pattern of peaks in the spectrum, then to change the electronic settings of the spectrometer and scan over the spectrum a second time. This second scan produced a plot in which a series of ascending steps were shown corresponding to the positions of the signals in the original spectrum. The height of the step over a signal was directly related to the number of protons in the set of protons that produced that signal. One then measured the heights of each of the steps in the integration trace and determined the whole number ratio of the various steps. This whole number ratio corresponded to the relative numbers of protons in the sets of protons in the molecule.

Suppose, for example, that the PMR spectrum of a compound showed the three signals A, B, and C.



The integration trace of the spectrum shows the series of ascending steps whose heights are in the same ratio as the numbers of protons in the sets producing the signals in the original spectrum. Suppose, in this case, that measurement of the three steps gave measurements of 31 mm:6 mm:17 mm, for A, B, and C. Notice that the measurements may show some slight deviation from a perfect whole number ratio. However, a reasonable whole number ratio for the measurements would be 5:1:3. This suggests that relative numbers of protons in the sets within the molecule are in a ratio of 5 protons in set A, 1 proton in set B, and 3 protons in set C. The ratio must be a whole number ratio, since a molecule can't contain fractions of H atoms. One word of caution, however, is that the actual numbers of protons in the molecule might not be 5, 1, and 3, but could be some multiple like 15, 3, and 9, which also reduces to a 5:1:3 integer ratio.

You cannot assume that the peak with the smallest integration has to correspond to a single proton. For example, suppose that a spectrum consisted of two signals and that the heights of the corresponding integration steps was 18 mm:27 mm. If the signal with the 18 mm integration step was assumed to represent one H atom, then the step of 27 would represent 1.5 H atoms, which is not an integer. Upon further consideration, if the step whose height is 18 represents a set of two protons, then the integration for one proton would have a height of 9 mm. Using this value, the ratio of 18:27 reduces to a 2:3 ratio in terms of the numbers of protons represented by the two signals.

5) Splitting of signals into multiplets by interaction with neighboring protons (*Spin-Spin coupling*).

Sometimes the signal for a set of protons with give a PMR signal that is a single sharp peak referred to as a "singlet".

Often, however, a signal does not appear as a single sharp line, but as a cluster of lines called a "multiplet". Multiplets result from the mutual magnetic interaction of protons that are in close proximity to each other in the molecule. This interaction is transmitted from one proton to another through the σ bonds that intervene between the two protons.

Some important points regarding the magnetic interaction, or coupling, between two protons in the same molecule are:

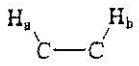
a) Coupling is <u>not</u> observed between two protons that have identical chemical shifts.

b) The magnitude of the coupling interaction drops off rapidly as the number of intervening σ bonds between the two protons increases.

Two hydrogen atoms that are attached to the <u>same</u> carbon atom are described as "*geminal*" hydrogen atoms. In the most common cases hydrogen atoms attached to the same carbon atom are in magnetically identical environments and have identical chemical shifts so that coupling between them is not observed. We will not deal with that at this point.

By far the most common relationship encountered for coupling between different sets of protons in an organic molecule is between two magnetically nonequivalent hydrogen atoms on neighboring carbon atoms. Two hydrogen atoms on adjacent carbon atoms are said to be in a "*vicinal*" relationship. The following discussion will focus on vicinal coupling.

Consider the interaction between two magnetically nonequivalent hydrogen atoms, H_a and H_b that are in a vicinal relationship.



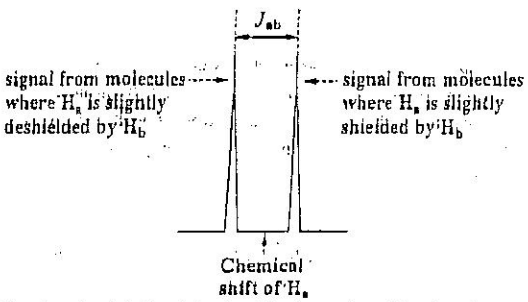
Consider the total magnetic environment of H_a. We have already discussed the effect of the external magnetic field generated by the magnet in the spectrometer instrument and magnetic fields generated within the molecule by the response of the electrons to the external magnetic field. There is one additional factor that can influence the magnetic environment of proton H_a, and that is the magnetic field of the neighboring proton H_b.

We ascribe the magnetic field generated by the ^1H nucleus as being a consequence of its nuclear spin. For a nucleus with a nuclear quantum number of ½ there are two spin states with magnetic fields oriented in opposite directions. In a first-order situation, there is equal probability of the nuclear spin being in spin state α or spin state β.

Considering H_a, the nucleus H_b may be either spinning in the same direction as H_a or the spin of H_b may be opposite that of H_a, the populations of the two situations being equal.

The result is that, at any instant, in half of the molecules the magnetic field produced by H_b is slightly shielding H_a, while in the other half of the molecules the magnetic field is slightly deshielding H_a. The NMR spectrum then contains <u>two</u> signals for H_a, a <u>doublet</u> instead of a singlet.

The appearance of the signal for H_a, which is split into a doublet by coupling with a single neighboring proton H_b.

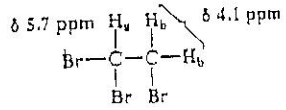


The chemical shift of the doublet is at the midpoint of the doublet. The separation between the two lines of the doublet is called the "coupling constant" and is designated as J. The magnitude of the coupling constant is always expressed in units of cycles per second, Hz. This is different from the chemical shift, δ, which is expressed in ppm.

The coupling between H_a and H_b is a mutual interaction. The signal for H_b will be split by its interaction with H_a, and the magnitude of the coupling constant, J, for the H_b signal will be exactly the same as J shown for H_a.

If a proton is coupled with <u>one</u> neighboring proton that one proton produces <u>two</u> lines, a doublet, with the two lines being equal in intensity. When determining the integration for the signal H_a, you must add together the steps for both branches of the doublet.

Next consider a situation in which there is a single hydrogen atom H_a coupled with a set of two hydrogen atoms H_b. For example, 1,1,2-tribromoethane:



This compound would be expected to give two signals in the PMR spectrum. One signal would be for H_a and would integrate for 1 proton. The two protons H_b are in equivalent structural and magnetic environments and would have identical chemical shift values, so together they would produce one signal that would integrate for 2 protons; this signal has a chemical shift of 4.1 ppm. The proton H_a, as you would expect, is more strongly deshielded and its signal has a chemical shift of 5.7 ppm.

In terms of spin-spin coupling, the two protons H_b do not exhibit splitting with each other, since they have identical chemical shifts, and protons with identical chemical shifts to not show coupling with each other. However, a proton H_b is coupled with the single proton H_a, and as we have discussed, if a proton is coupled with a single neighboring proton, its signal is split into a <u>doublet</u>, two lines of equal intensity separated by a coupling constant of 7.0 Hz.

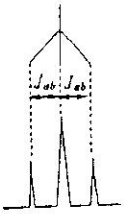
The proton H_a is coupled with <u>two</u> hydrogen atoms H_b. Each proton H_b has an equal probability of deshielding H_a or shielding H_a. For purposes of this discussion, we will distinguish the two identical protons as H_b and $H_{b'}$. In terms of their effect on the magnetic environment of H_a, there are four possible combinations:

a) One combination with both protons H_b and $H_{b'}$ deshielding H_a.

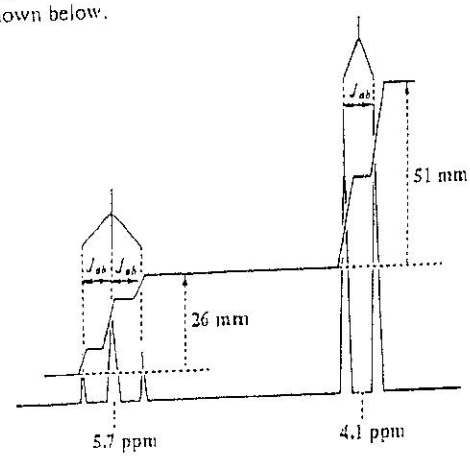
b) Two combinations in which one of the two protons is deshielding H_a and the other is shielding H_a (*i. e.*, H_b deshielding and $H_{b'}$ shielding, or H_b shielding and $H_{b'}$ deshielding).

c) One combination in which both protons H_b and $H_{b'}$ are shielding H_a.

This causes the signal for H_a to be split into three equally space lines, a triplet, with the line intensities exhibiting a 1:2:1 ratio. The coupling constant, J_{ab}, is the same when measured between any two adjacent lines.



A more complete representation of the entire spectrum is shown below.



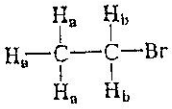
Notice some typical features in this spectrum:

i) The chemical shift of a true simple multiplet is measured at the midpoint of the multiplet.

ii) The coupling constant is measured between any two adjacent lines for a true multiplet and the magnitude of the coupling constant is the same for two multiplets that are coupled with each other. For alkane protons the value of J for protons on adjacent carbons is ~7 Hz.

iii) The integration of a multiplet is the sum of the heights of all of the steps of that multiplet. This gives a ratio of 26 mm to 51 mm, which is approximately 1:2.

A simple alkyl group that is very frequently encountered in organic molecules is the ethyl group. For example, consider bromoethane.



In this case there are two structurally distinct sets of hydrogen atoms. The signal for the set of three protons labeled H_a appear at a chemical shift of 1.68 ppm, while the set of two protons H_b are more strongly deshielded and appear at 3.42 ppm.

The multiplicity for the protons H_a is determined by the number of protons in the set of protons H_b on the adjacent carbon. We have already seen that coupling with a set of <u>two</u> protons on the adjacent carbon splits the signal for H_a into a <u>triplet</u>, three equally spaced lines in a ratio of 1:2:1.

For a proton H_b there are four possible combinations of spin states that the three protons H_a could assume. The probability ratio of these four states is 1:3:3:1.

i) All three protons H_a are deshielding H_b ↑↑↑

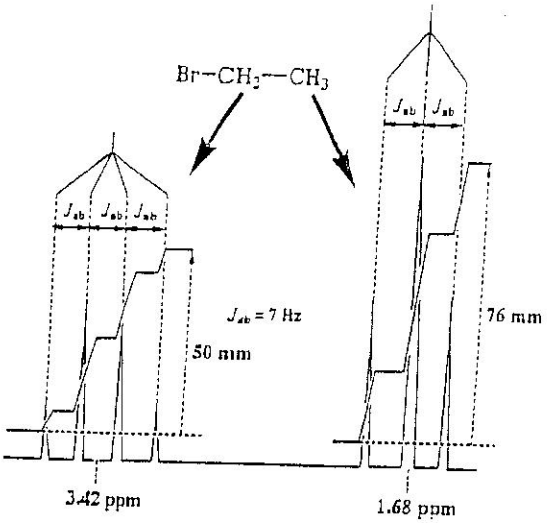
ii) Two protons H_a are deshielding H_b and one proton H_a is shielding H_b ↓↑↑ ↑↓↑ ↑↑↓

iii) Two protons H_a are shielding H_b and one proton H_a is deshielding H_b ↑↓↓ ↓↑↓ ↓↓↑

iv) All three protons H_a are shielding H_b ↓↓↓

The distribution of shielding/deshielding states represents a simple probability analogous to flipping three coins. Out of 800 flips, all three coins would be predicted to come up heads 100 times, two heads and one tails 300 times, one heads and three tails 300 times, and all three tails 100 times.

If a proton H_b is split by coupling with 3 protons on the adjacent carbon, then the signal for H_b will be split into a pattern of 4 lines that are equally spaces and with a ratio of intensities of the four lines of 1:3:3:1. That is, it will be a quartet.



It is possible to predict the extent of splitting of the signal for a given proton by counting the number of protons on adjacent carbons that would be responsible for splitting. A useful rule is the "$N + 1$" rule. If the signal for a proton H_X is split by a set of "N" protons on adjacent carbons, then the signal for H_X will be split into a multiplet having "$N + 1$" lines. If a proton H_X is in a position where there are two or three adjacent carbons that bear hydrogen atoms that can couple with H_X, for example CH_n-CH_X-CH_m, then, in the simplest case, the multiplicity of the signal for H_X will be a multiplet having $(n + m + 1)$ lines. For example, in an isopropyl group, as in isopropyl iodide, $(CH_3)_2CHI$, the signal for the proton on the middle carbon is split by a total of 6 hydrogens on the two neighboring carbons, giving a seven line pattern, a septet.

Another important feature of simple multiplets is the relative line intensities of the lines. This can be predicted by considering Pascal's triangle:

```
                1
              1   1
            1   2   1
          1   3   3   1
        1   4   6   4   1
      1   5  10  10   5   1
    1   6  15  20  15   6   1
  etc.
```

Thus, if the signal for a proton is split by coupling with a set of 5 protons on adjacent carbons, it will be seen as a sextet (6 lines) that will be in relative line intensities of 1:5:10:10:5:1.

Magnitude of coupling constants:

For conformationally mobile alkyl groups, which will be the most common examples encountered in this course, the magnitude of the coupling constant J for coupling between protons on adjacent carbons is about 6-8 Hz.

Coupling between two nonequivalent hydrogen atoms attached to the same carbon (*geminal coupling*) is larger, typically in the range of 12-30 H.

If two protons are farther removed from each other than adjacent carbons the magnitude of coupling is very small, and for sp^3 hybridized carbons is rarely large enough to be seen. We may encounter some long-range coupling in aromatic systems and will address them at that point.

It is important to recognize that a true simple multiplet, doublet, triplet, quartet, pentet, sextet, septet, *etc*. is not just any collection containing a certain number of lines. A true simple multiplet has uniform spacing between lines and a symmetrical pattern in terms of line intensities in the multiplet.