**NMR Spectroscopy**

Nuclear magnetic resonance (NMR) spectroscopy is the most powerful and broadly applicable technique for structure determination available to organic chemists. It provides the most information about molecular structure and helps to identify the carbon–hydrogen framework of an organic compound, also lets us determine what the neighboring carbons look like.

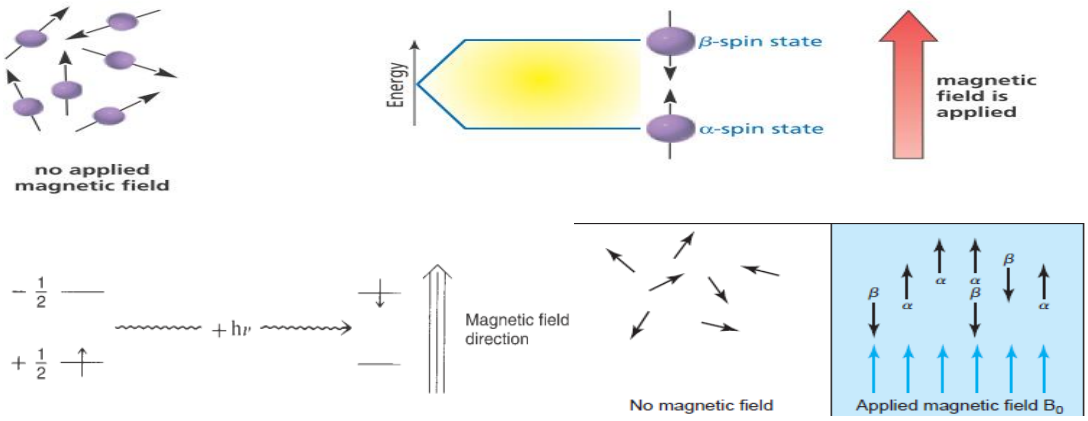
NMR Spectroscopy involves the absorption of radio frequency radiation by atomic nuclei in an applied magnetic field. Any atomic nucleus which possesses either odd mass, odd atomic number or both has spin angular momentum and a magnetic moment.

The NMR spectroscopy, use high wavelength and low energy between (1000-10000cm) (radio frequency waves ) which is not enough to transition or vibration or rotation only interact with atomic nuclei magnetically (exposing to magnetic field).

The more common nuclei that possess spin include $^{1}H_{1}$, $^{13}C_{6}$, $^{14}N_{7,}$ $^{17}O_{8}$, $^{19}F$ while $^{12}C_{6}$ and $^{16}O_{8}$ are not spin active.

Spinning charged nuclei generate a magnetic field, like the field of a small bar magnet. In the absence of an applied magnetic field, the nuclear spins are randomly oriented.

However, when a sample is placed in an applied magnetic field (Figure 1), the nuclei twist and turn to align themselves with or against the field of the larger magnet. More energy is needed for a proton to align against the field than with it. Protons that align with the field are in the lower energy **α-energy state**; protons that align against the field are in the higher-energy **β-energy state**. More nuclei are in the **α-spin state** than in the **β-spin state**. The difference in the populations is very small (about 20 out of a million protons), but is sufficient to form the basis of NMR spectroscopy. Because the nuclei are in resonance with the R.F radiation the term “nuclear magnetic resonance” came into being. In this context, “resonance” refers to the flipping back and forth of nuclei between the α- and β-spin states.




Fig(1): The orientation of the magnetic moments of protons in (a) the absence of an external magnetic field or (b) the presence of an external magnetic field.

The energy difference (ΔE) between the α- and β-spin states depends on the strength of the applied magnetic field ($B_o$) measured in tesla (T) (1T = $10^4$G).The greater the strength of the magnetic field to which we expose the nucleus, the greater is the difference in energy between the α- and β-spin states.

When the sample is subjected to a pulse of radiation whose energy corresponds to the difference in energy (ΔE) between the α- and β-spin states, nuclei in the α-spin states are promoted to β-spin states. This transition is called "flipping" the spin.

Because the energy difference between α- and β-spin states is so small for currently available magnets only a small amount of energy is needed to flip the spin Fig.(2).

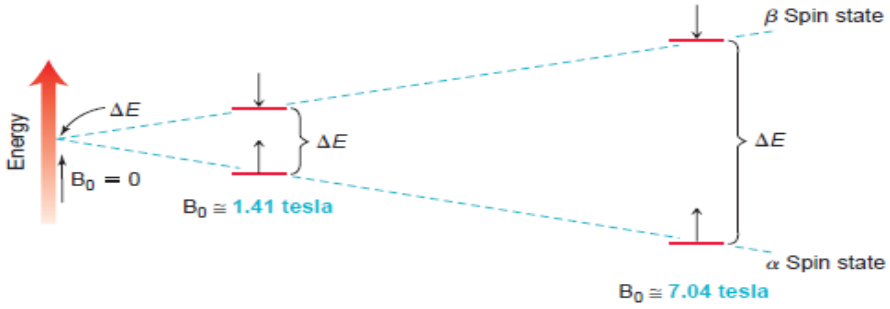



**Figure (2):** The relationship between the strength of the magnetic field and the energy gap between the alpha and beta spin states.

The radiation required is in the radiofrequency (R.F) region of the electromagnetic spectrum and is called ( R.F radiation). When the nuclei undergo relaxation (i.e., return to their original state), they emit electromagnetic signals whose

frequency depends on the difference in energy between the α- and β-spin states. The NMR spectrometer detects these signals and displays them as a plot of signal frequency versus intensity (an NMR spectrum) Fig.(3).

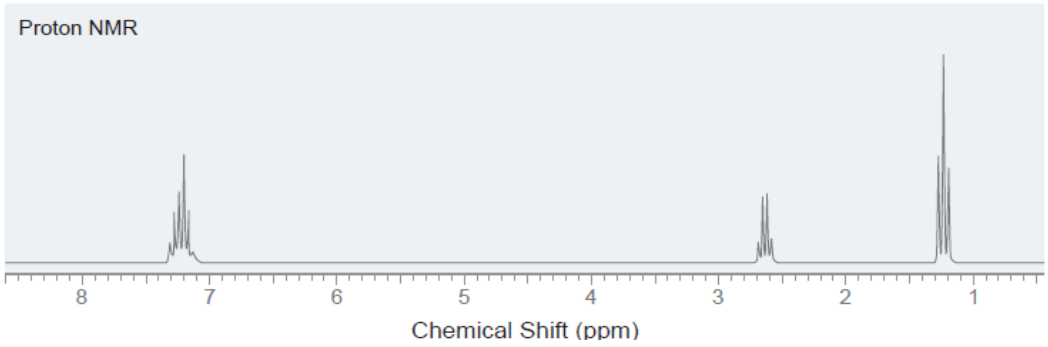



Figure (3): Example of NMR spectrum

The spectrum is generally rich with information that can be interpreted to determine a molecular structure. The first valuable information is the number of signals. This spectrum appears to have three different signals, means three different types of protons. In addition, each signal has three important characteristics:

**1.** The *location* of each signal indicates the electronic environment of the protons giving rise to the signal.

**2.** The *area* under each signal indicates the number of protons giving rise to the signal.

**3.** The *shape* of the signal indicates the number of neighboring protons.

**Instrumentation**

There are two main types of instruments (CW and FT-NMR). Generally the NMR spectroscopy makes use of a **magnet**, **radio frequency, detector and an amplifier**.

The CW- NMR spectrometer uses a constant-frequency RF signal and varies the magnetic field strength.

A typical spectrum is recorded from left to right, the magnetic field is increasing. As each chemically distinct type of proton comes into resonance, it is recorded as a peak on the chart. The peak at δ = 0 ppm is due to the internal reference compound TMS. Since highly shielded protons resonates more slowly than relatively unshielded protons, it is necessary to increase the field to induce them to resonate. Hence, highly shielded

protons appear to the right of NMR chart, and less shielded, or deshielded, protons appear to the left. The region of the chart to the left is sometimes said to be downfield (or at low field), and that to the right, upfield (or at high field).

## Fourier Transform NMR

In modern instruments called pulsed Fourier transform (FT) spectrometers, the magnetic field is kept constant and an R.F pulse of short duration excites all the protons simultaneously.

A mathematical operation known as a **Fourier transform**, producing a spectrum called a Fourier transform NMR (FT–NMR) spectrum.

The pulsed FT- NMR has several advantages over the CW method. It is **more sensitive**, and it can **measure weaker signals**. Five to 10 minutes are required to scan and record a CW spectrum; a pulsed experiment is much faster, and a measurement can be performed in a few seconds. With a computer and fast measurement, it is possible to repeat and average the measurement of the signal. This is a real advantage when the sample is small, in which case has weak intensity and great amount of noise associated with it. Noise is random electronic signals that are usually visible as fluctuations of the baseline in the signal.

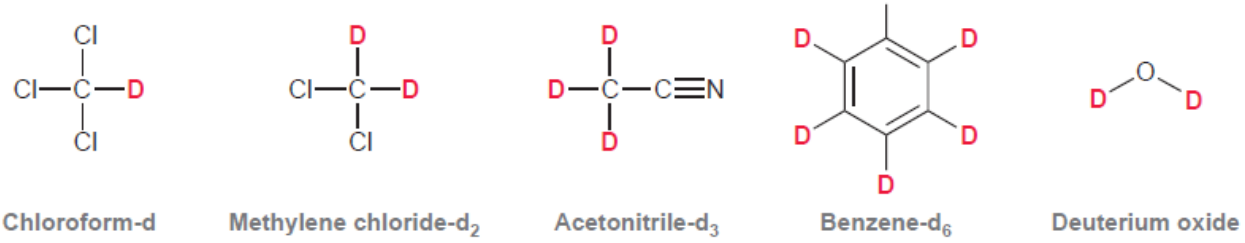
Since noise is random, its intensity does not increase as many iterations of the spectrum are added together. Using this procedure, one can show that the signal-to-noise ratio improves as a function of the square root of the number of scans n:

$\frac{S}{N} = f\sqrt{n}$ Pulsed FT-NMR is therefore especially suitable for the examination of nuclei that are not very abundant in nature like 13C-NMR, nuclei that are not strongly magnetic, or very dilute samples.

## Preparation of sample for NMR spectroscopy

The sample is dissolved in small amount (0.5ml) of a solvent (2-10%) containing no interfering protons (usually $CCl_4$ or $CDCl_3$), and a small amount of TMS is added to

serve as an internal reference. The sample cell is a small cylindrical glass tube that is suspended in the gap between the faces of the pole pieces of the magnet. The sample is spun around its axis to ensure that all parts of the solution experience a relatively uniform magnetic field. In practice, deuterated solvents are generally used.




## THE CHEMICAL SHIFT

It is very difficult to measure exact frequencies; hence, no attempt is made to measure the exact resonance frequency of any proton. Instead, a reference compound is placed in the solution of the substance to be measured, and the resonance frequency of each proton in the sample is measured relative to the resonance frequency of the protons of the reference substance. The standard reference substance that is used universally is tetramethylsilane, $(CH_3)_4Si$, also called TMS. This compound was chosen initially because the protons of its methyl groups are more shielded than those of most other known compounds, because silicon is less electronegative than carbon. There are no compounds that had better-shielded hydrogen's than TMS were known, and it was assumed that TMS would be a good reference substance since it would mark one end of the range. Thus when another compound is measured, the resonances of its protons are reported in terms of how far (in Hertz) they are shifted from those of TMS. The position at which a signal occurs in an NMR spectrum is called the chemical shift. The shift from TMS for a given proton depends on the strength of the applied magnetic field. In an applied field of 1.41 Tesla the resonance of a proton is approximately 60 MHz, whereas in an applied field of 2.35 Tesla (23,500 Gauss) the resonance appears at

approximately 100 MHz. The ratio of the resonance frequencies is the same as the ratio of the two field strengths:

$$\frac{100\ \text{MHz}}{60\ \text{MHz}} = \frac{2.35\ \text{Tesla}}{1.41\ \text{Tesla}} = \frac{23{,}500\ \text{Gauss}}{14{,}100\ \text{Gauss}} = \frac{5}{3}$$

Hence, for a given proton, the shift (in Hertz) from TMS is 5/3 larger in the 100-MHz range ($B_0$= 2.35 Tesla) than in the 60-MHz range ($B_0$ = 1.41 Tesla). This can be confusing for workers trying to compare data if they have spectrometers that differ in the strength of the applied magnetic field. The confusion is easily overcome if one defines a new parameter that is independent of field strength for instance, by dividing the shift in Hertz of a given proton by the frequency in megahertz of the spectrometer with which the shift value was obtained. In this manner, a field-independent measure called the chemical shift (δ) is obtained:

$$\delta = \frac{(\text{shift in Hz})}{(\text{spectrometer frequency in MHz})}$$ , example: $$\delta = \frac{162\ \text{Hz}}{60\ \text{MHz}} = \frac{270\ \text{Hz}}{100\ \text{MHz}} = 2.70\ \text{ppm}$$

Values of δ for a given proton are always the same irrespective of whether the measurement was made at 60 MHz or higher. By agreement, most workers report chemical shifts in delta (δ) units, or parts per million. (ppm), of the main spectrometer frequency. On this scale, the resonance of the protons in TMS comes at exactly 0.00 ppm.

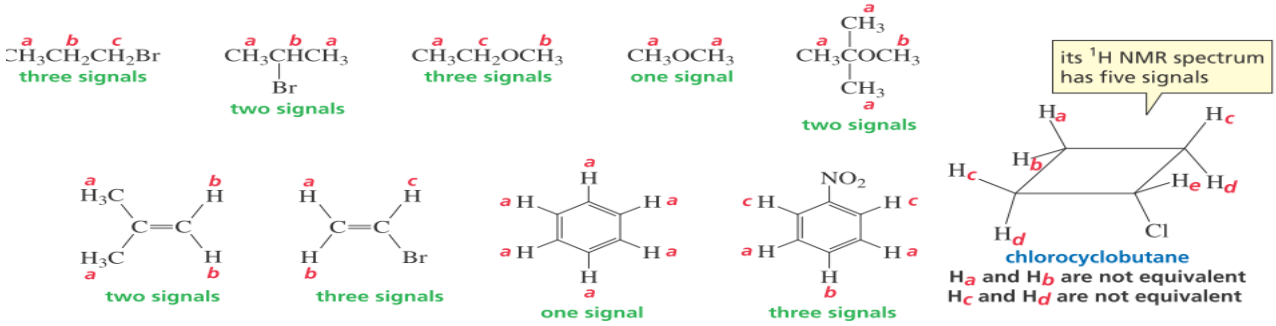

**Advantages of TMS**

1- It is chemically inert and miscible with a large rang of solvents.
2- It`s 12 protons are all magnetically equivalent.
3- Highly volatile and can be easily removed to get back the sample.
4- Resonance position is far away from other protons of organic compounds.

## The Number of Signals in the $^1$H-NMR Spectrum

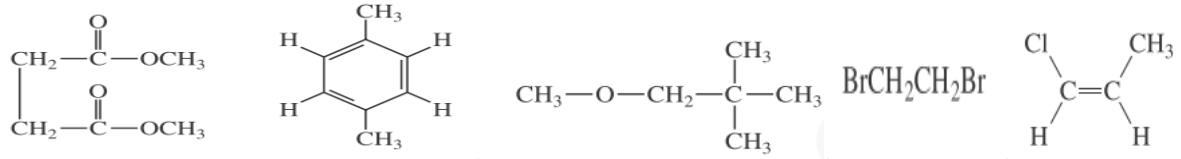
Protons in the same environment are called chemically equivalent protons, and they will produce only one signal.

**1-bromopropane** has three different sets of chemically equivalent protons. The chemically equivalent protons in the following compounds are designated by the same letter:

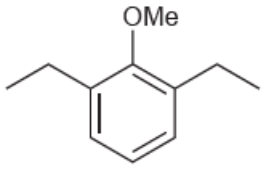



Sometimes, two protons on the same carbon are not equivalent. For example, the $^1$H-NMR spectrum of chlorocyclobutane has five signals. Even though they are bonded to the same carbon, the $H_a$ and $H_b$ protons are not equivalent because they are not in the same environment: $H_a$ is trans to Cl and $H_b$ is cis to Cl. Similarly, the $H_c$ and $H_d$ protons are not equivalent.

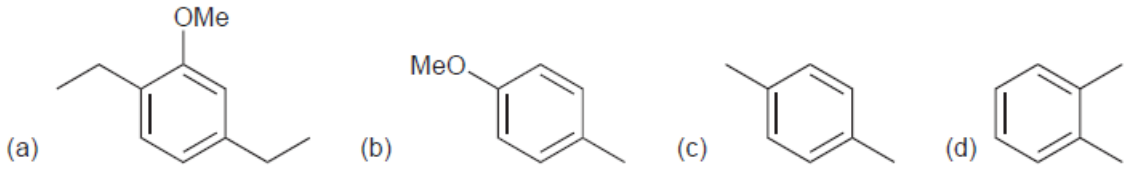
Q1/ determine the number of signals for each of the following:



Q2/ Identify the number of signals expected in the 1H NMR spectrum of the following compound.



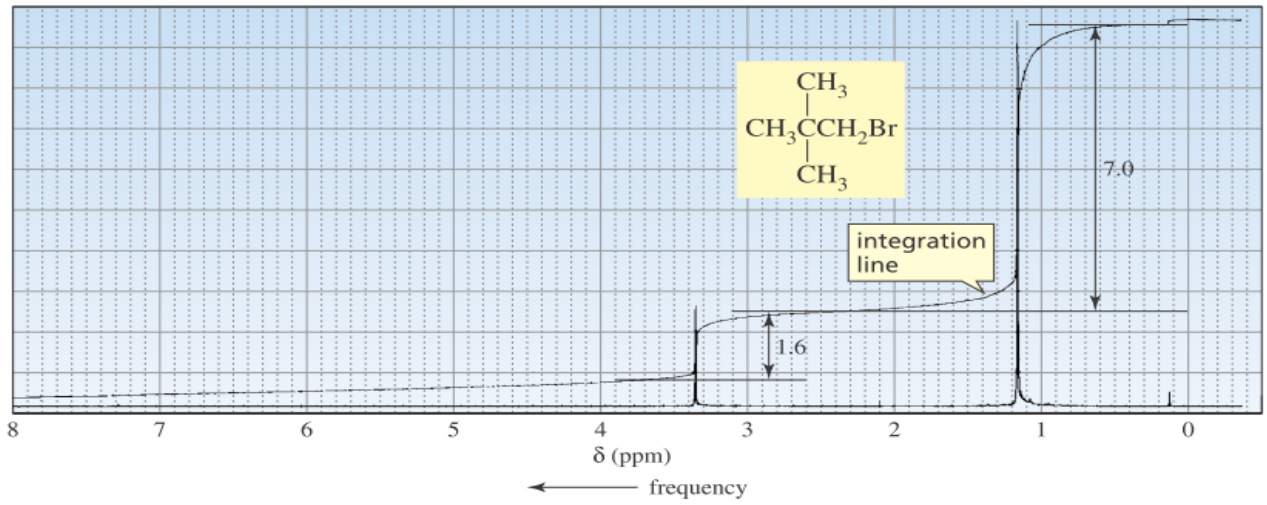

Q3/ Identify the number of signals expected in the 1H NMR spectrum of each of the following compounds.




Q4/ Identify the structure of a compound with molecular formula C9H20 that exhibits four CH2 groups, all of which are chemically equivalent. How many total signals would you expect in the 1H NMR spectrum of this compound?

**Integration of NMR Signals (The area under each signal indicates the number of protons giving rise to the signal).**

The NMR spectrum not only distinguishes how many different types of protons a molecule has, but also reveals how many of each type are contained within the molecule. In the NMR spectrum, the area under each peak is proportional to the number of hydrogens generating that peak. For example the two signals in the $^{1}$H-NMR spectrum of 1-bromo-2,2-dimethylpropane in Figure below are not the same size . The area under the signal occurring at the lower frequency is larger because the signal is caused by nine methyl protons, while the smaller, higher-frequency signal results from two methylene protons.

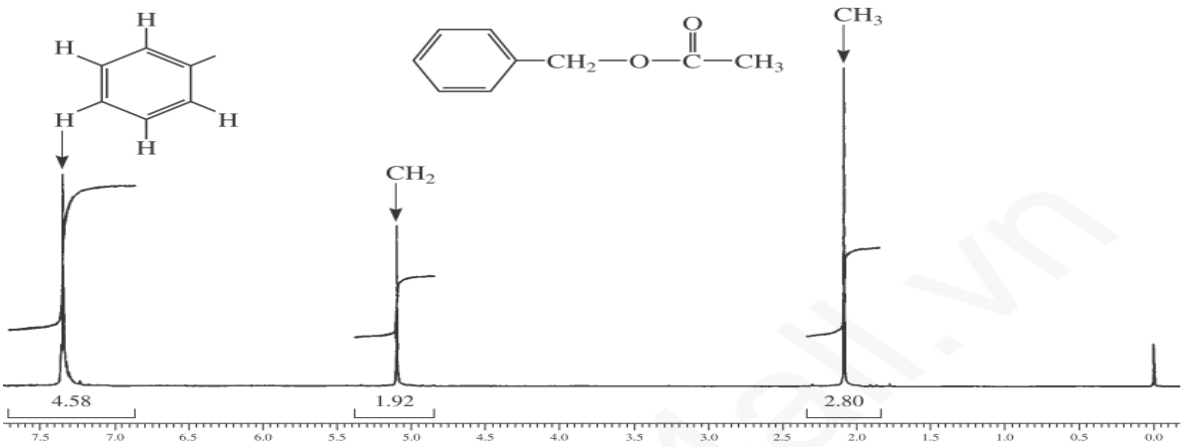



By measuring the heights of the integration steps, you can determine that the ratio of the integrals is approximately 1.6 : 7.0 dividing each by the smallest number = 1 : 4.4. and

multiply by 2 in order to cause all the numbers to be close to whole numbers . That means that the ratio of protons in the compound is 2: 8.8 which is rounded to 2:9.

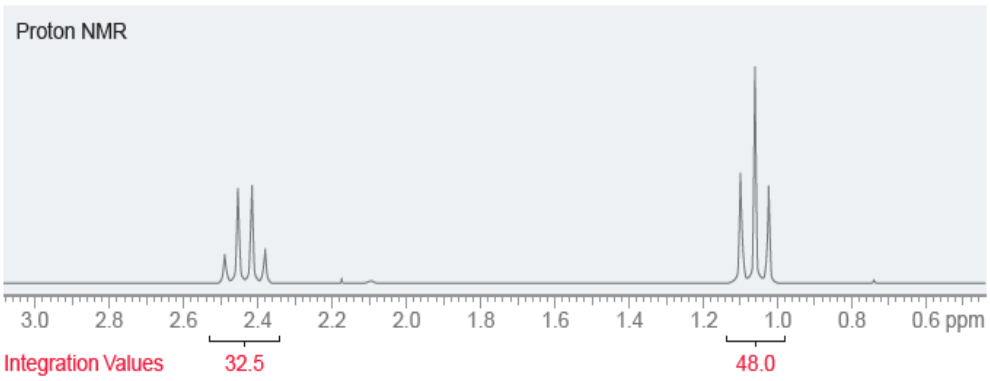
The **integration** tells us the relative number of protons that give rise to each signal, not the absolute number. For example, integration could not distinguish between 1,1-dichloroethane and 1,2-dichloro-2-methylpropane because both compounds would show an integral ratio of 1 : 3.

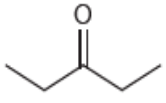
In modern spectrometers Integral lines are shown as before, but in addition, you will observe that digitized integral values for the integrals are printed below the peaks.




When analyzing an NMR spectrum of an unknown compound, we must also consider the impact of symmetry on integration values. For example, consider the structure of 3-pentanone.

This compound has only two kinds of protons, because the methylene groups are equivalent to each other, and the methyl groups are equivalent to each other. The $^{1}H$ NMR spectrum is therefore expected to exhibit only two signals.

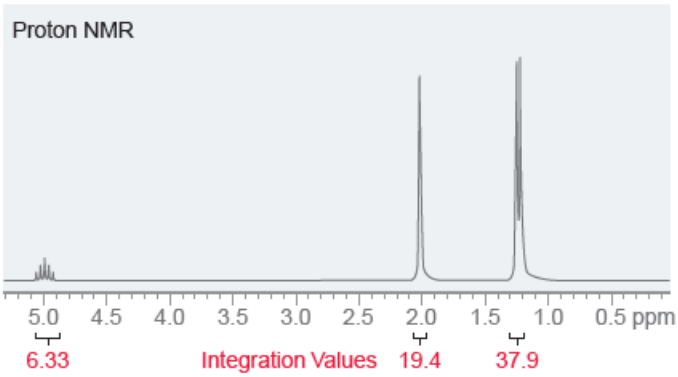


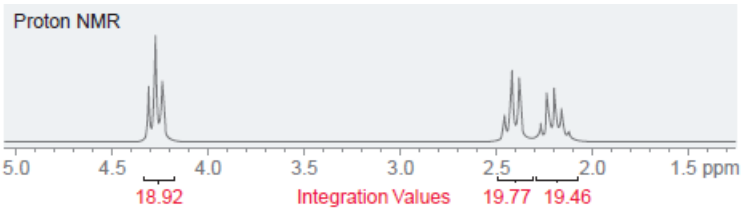

3-Pentanone

Compare the relative integration values: 32.5 and 48.0. These values give a ratio of 2: 3, but again the values 2 and 3 are just relative numbers. They actually represent 4 protons and 6 protons. This can be determined by inspecting the molecular formula ($C_5H_{10}O$), which indicates a total of 10 protons in the compound. Since the ratio of protons is 2: 3, this ratio must represent 4 and 6 protons, in order for the total number of protons to be 10. This analysis indicates that the molecule possesses symmetry.

Q5/ A compound with molecular formula $C_5H_{10}O_2$has the following $^1$H NMR spectrum. Determine the number of protons giving rise to each signal.

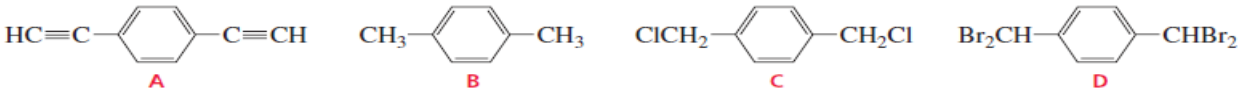


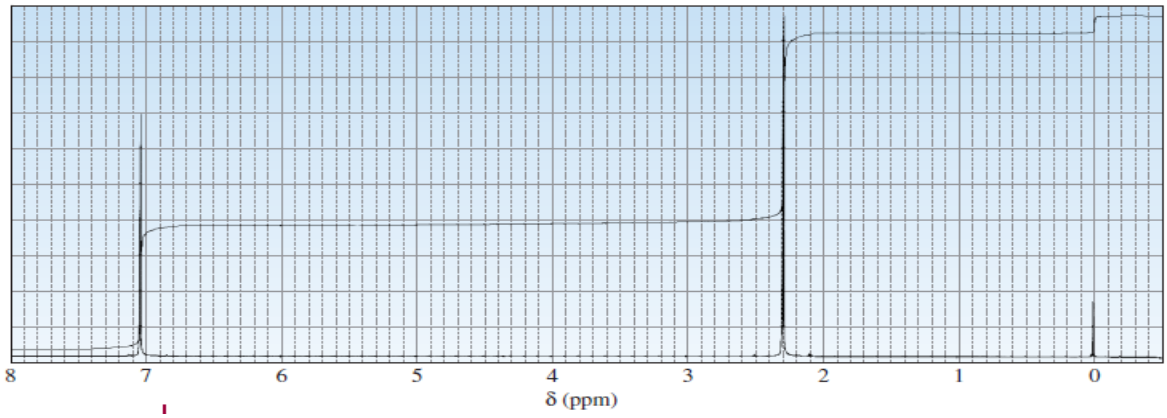

**Q6/** A compound with molecular formula C4H6O2 has the following NMR spectrum. Determine the number of protons giving rise to each signal.




Q7/ The $^1$H NMR spectrum of a compound with molecular formula $C_7H_{15}Cl$ exhibits two signals with relative integration 2 : 3. Propose a structure for this compound.

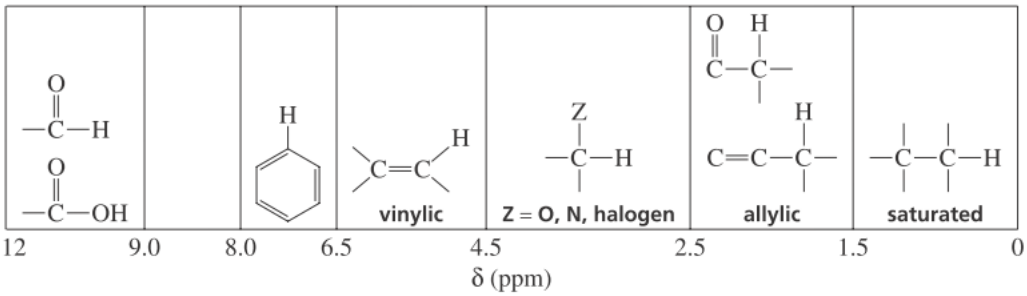
Q8/The $^1$H-NMR spectrum shown in Figure corresponds to one of the following compounds. Which compound is responsible for this spectrum?

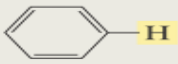
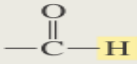
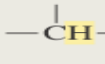
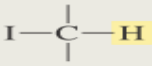
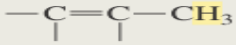
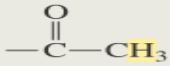
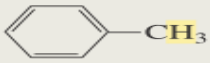
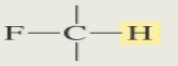
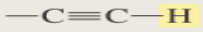
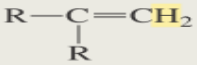
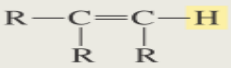
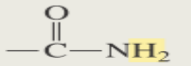



**Characteristic Values of Chemical Shifts: (The *location* of each signal indicates the electronic environment of the protons giving rise to the signal).**

Approximate values of chemical shifts for different kinds of protons are shown in Table below. $^{1}$H-NMR spectrum can be divided into six regions. Rather than memorizing chemical shift values, if you remember the kinds of protons that are in each region, you will be able to tell what kinds of protons a molecule has from a quick look at its $^{1}$H-NMR spectrum.



| Type of proton | Approximate chemical shift (ppm) | Type of proton | Approximate chemical shift (ppm) |
|---|---|---|---|
| $(CH_3)_4Si$ | 0 |  | 6.5–8 |
| $-CH_3$ | 0.9 | | |
| $-CH_2-$ | 1.3 |  | 9.0–10 |
|  | 1.4 |  | 2.5–4 |
|  | 1.7 | | |
| | |  | 2.5–4 |
|  | 2.1 | | |
| | |  | 3–4 |
|  | 2.3 | | |
| | |  | 4–4.5 |
|  | 2.4 | | |
| $R-O-CH_3$ | 3.3 | $RNH_2$ | Variable, 1.5–4 |
|  | 4.7 | ROH | Variable, 2–5 |
| | | ArOH | Variable, 4–7 |
|  | 5.3 |  | Variable, 10–12 |
| | |  | Variable, 5–8 |

[a]The values are approximate because they are affected by neighboring substituents.

**Factors influencing chemical shifts**

**1: Inductive effect (electronegativity effect)**

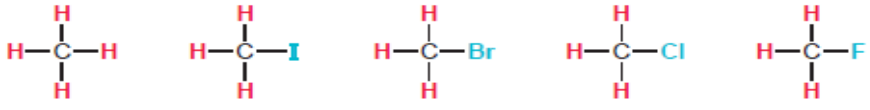
The chemical shift simply increases as the electronegativity of the attached element increases. Electronegative substituents attached to a carbon atom, because of their electron-withdrawing effects, reduce the valence electron density around the protons attached to that carbon. These electrons, shield the proton from the applied magnetic field (Called local diamagnetic shielding). Electronegative substituents on carbon reduce the local diamagnetic shielding in the vicinity of the attached protons because they reduce the electron density around those protons. Substituents that have this type of effect are said to be deshield the proton. The greater the electronegativity of the substituent, the more it deshields the protons and hence the greater is the chemical shift of those protons.

**DEPENDENCE OF THE CHEMICAL SHIFT OF $CH_3X$ ON THE ELEMENT X**

| **Compound $CH_3X$** | $CH_3F$ | $CH_3OH$ | $CH_3Cl$ | $CH_3Br$ | $CH_3I$ | $CH_4$ | $(CH_3)_4Si$ |
|---|---|---|---|---|---|---|---|
| **Element X** | F | O | Cl | Br | I | H | Si |
| **Electronegativity of X** | 4.0 | 3.5 | 3.1 | 2.8 | 2.5 | 2.1 | 1.8 |
| **Chemical shift δ** | 4.26 | 3.40 | 3.05 | 2.68 | 2.16 | 0.23 | 0 |

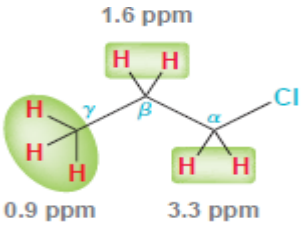
**SUBSTITUTION EFFECTS**

| $CHCl_3$ | $CH_2Cl_2$ | $CH_3Cl$ | $-CH_2Br$ | $-CH_2-CH_2Br$ | $-CH_2-CH_2CH_2Br$ |
|---|---|---|---|---|---|
| 7.27 | 5.30 | 3.05 | 3.30 | 1.69 | 1.25 |



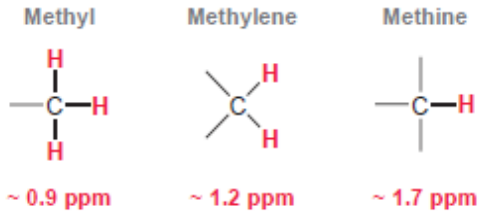


Each chlorine atom adds approximately 2 ppm to the chemical shift of the signal. The inductive effect tapers off drastically with distance, as can be seen by comparing the chemical shifts of the protons in 1-chloropropane.




The effect is most significant for the protons at the alpha position. The protons at the beta position are only slightly affected, and the protons at the gamma position are virtually unaffected by the presence of the chlorine atom.

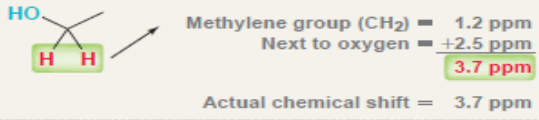
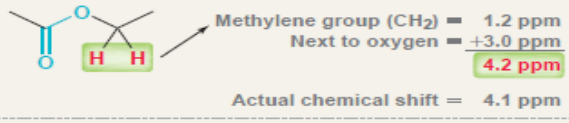
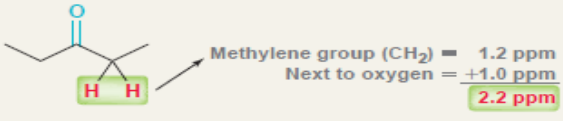
By committing a few numbers to memory, it is possible to predict the chemical shifts for the protons in a wide variety of compounds, including alcohols, ethers, ketones, esters, and carboxylic acids. The following numbers are used as benchmark values:



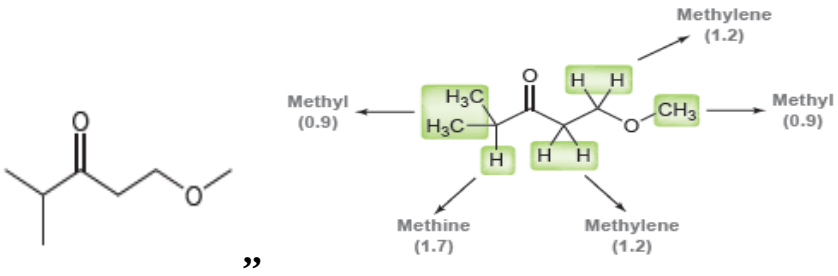

These are the expected chemical shifts for protons that lack neighboring electronegative atoms. In the absence of inductive effects, a methyl group ($CH_3$) will produce a signal near 0.9 ppm, a **methylene** group ($CH_2$) will produce a signal near 1.2 ppm, and a **methine** group (CH) will produce a signal near 1.7 ppm. These benchmark values are then modified by the presence of neighboring functional groups. Table below shows the effect of a few functional groups on the chemical shifts of alpha protons. The effect on beta protons is generally about **one-fifth** of the effect on the alpha protons.

For example, in an alcohol, the presence of an oxygen atom adds +2.5 ppm to the chemical shift of the alpha protons but adds only +0.5 ppm to the beta protons. Similarly, a carbonyl group adds +1 ppm to the chemical shift of the alpha protons but only +0.2 to the beta protons.

The three benchmark values, together with the three values shown in Table, enable us to predict the chemical shifts for the protons in a wide variety of compounds, as illustrated in the following exercise.

| FUNCTIONAL GROUP | EFFECT ON ALPHA PROTONS | EXAMPLE |
|---|---|---|
| **Oxygen** of an alcohol or ether | + 2.5 |  Methylene group ($CH_2$) = 1.2 ppm<br>Next to oxygen = +2.5 ppm<br>3.7 ppm<br>Actual chemical shift = 3.7 ppm |
| **Oxygen** of an ester | +3 |  Methylene group ($CH_2$) = 1.2 ppm<br>Next to oxygen = +3.0 ppm<br>4.2 ppm<br>Actual chemical shift = 4.1 ppm |
| **Carbonyl group** (C=O) All carbonyl groups, including ketones, aldehydes, esters, etc. | +1 |  Methylene group ($CH_2$) = 1.2 ppm<br>Next to oxygen = +1.0 ppm<br>2.2 ppm<br>Actual chemical shift = 2.4 ppm |

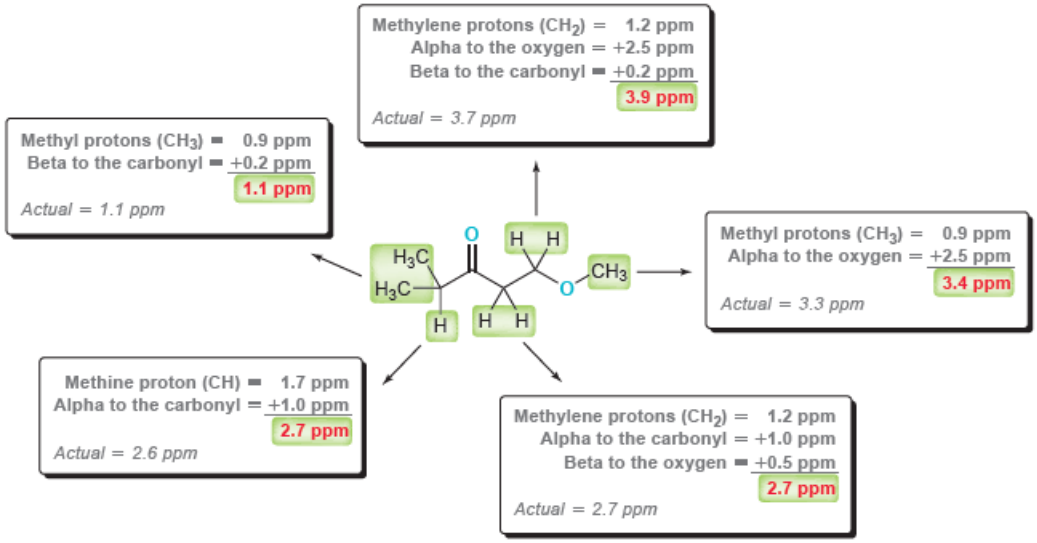
Q9/Predict the chemical shifts for the signals in the $^1$H NMR spectrum of the following compound.




„

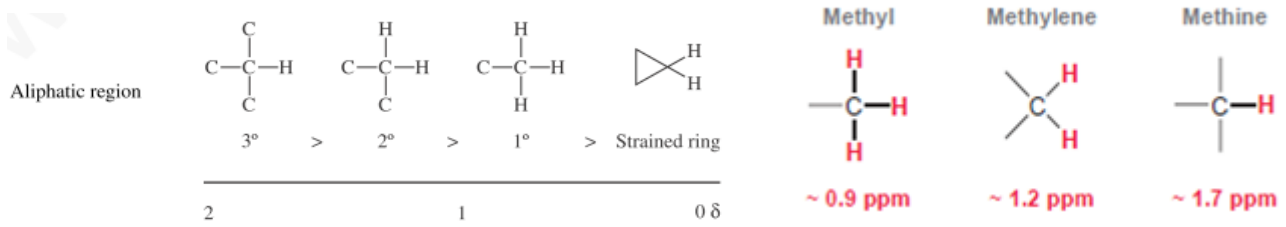
**Solution**

First determine the total number of expected signals. In this compound, there are five different kinds of protons, giving rise to five distinct signals. For each type of signal, identify whether it represents methyl (0.9 ppm), methylene (1.2 ppm), or methine (1.7 ppm) groups.




**2: Hybridization Effects (sp3, sp2, sp)**

All hydrogens attached to purely (**sp3**) carbon atoms (primary , secondary , tertiary and cycloalkanes) have resonance in the limited range from 0 to 2 ppm, provided that no electronegative elements or π-bonded groups are nearby. While the hydrogen's on an sp3carbon that is attached to a heteroatom ( -O-CH $_2$ - , and so on) or to an unsaturated carbon (-C=C- $CH_2$ - ) do not fall in this region but have greater chemical shifts.



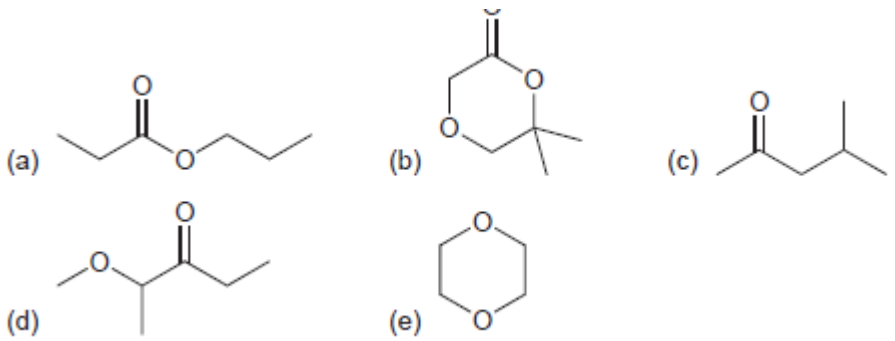

Q10/which underlined proton has the greater chemical shifts?

a. $CH_3CH_2\underline{C}H_2Cl$ or $CH_3CH_2\underline{C}H_2Br$

b. $CH_3CH_2\underline{C}H_2Cl$ or $CH_3CH_2\underline{C}HCH_3$ (Cl)

c. $CH_3CH_2\underline{C}(=O)H$ or $CH_3CH_2C(=O)\underline{C}H_3$

Q12/Predict the chemical shifts for the signals in the $^1H$ NMR spectrum of each of the following comp1unds:




**sp2 Hydrogens**

Simple vinyl hydrogen's (-C = C-H) have resonance in the range from 4.5 to 7 ppm. In an sp2-1s C-H bond, the carbon atom has more s character (33% s), which effectively renders it "more electronegative" than an sp3 carbon (25% s). Remember that (s) orbitals hold electrons closer to the nucleus than do the carbon p orbitals. If the sp2 carbon atom holds its electrons more tightly, this results in less shielding for the H nucleus than in an ( sp3-1s) bond. Thus, vinyl hydrogens have a greater chemical shift (5 to 6 ppm) than aliphatic hydrogens on sp3 carbons (1 to 4 ppm). Aromatic hydrogens appear in a range further downfield (7 to 8 pm). The downfield positions of vinyl and aromatic resonances are, however, greater than one would expect based on these hybridization differences.

Another effect, called anisotropy, is responsible for the largest part of these shifts Aldehyde protons (also attached to sp2 carbon) appear even further downfield (9 to 10 ppm) than aromatic protons since the inductive effect of the electronegative oxygen atom further decreases the electron density on the attached proton. Aldehyde protons, like aromatic and alkene protons, exhibit an anomalously large chemical shift due to anisotropy.

**sp Hydrogens**

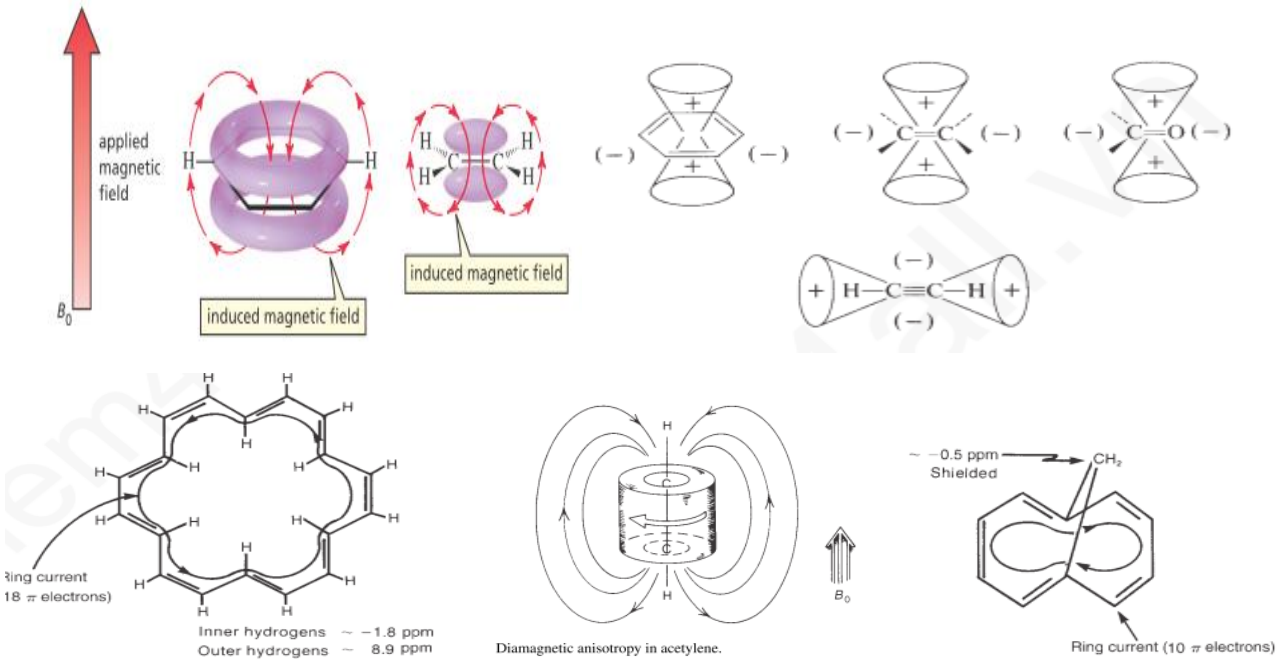
Acetylenic hydrogens (-C≡C-H, sp-1s) appear anomalously at 2 to 3 ppm owing to anisotropy. On the basis of hybridization alone, one would expect the acetylenic proton to have a chemical shift greater than that of the vinyl proton. An sp carbon should behave as if it were more electronegative than an sp2 carbon. This is the opposite of what is actually observed.

**3:Diamagnetic Anisotropy**

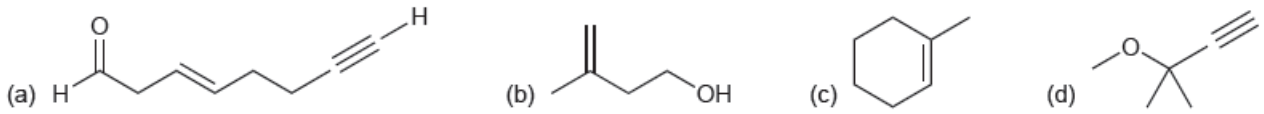
The unusual chemical shifts associated with hydrogens bonded to carbons that form π-bonds are due to diamagnetic anisotropy. Diamagnetic anisotropy describes an environment in which different magnetic fields are found at different points in space. Anisotropic is Greek for "different in different directions." Because π- electrons are less tightly held by nuclei than are σ- electrons, π- electrons are more free to move in response to a magnetic field. When a magnetic field is applied to a compound with π-electrons, the π- electrons move in a circular path. This electron motion causes an induced magnetic field. How this induced mag*n*etic field affects the chemical shift of a proton depends on the direction of the induced magnetic field in the region where the proton is located relative to the direction of the applied magnetic field.

Locations inside the ring are characterized by a local magnetic field that opposes the external field, while locations outside the ring are characterized by a local magnetic field that adds to the external field. The protons connected to the ring are permanently positioned outside of the ring, and as a result, they experience a stronger magnetic field.

These protons experience the external magnetic field plus the local magnetic field. The effect is similar to a deshielding effect, and therefore, the protons are shifted downfield. The magnetic field induced by the π- electrons of an alkene and other π-compounds are similar to benzene ring. Because frequency is proportional to the strength of the magnetic field experienced by the protons, the protons resonate at higher frequencies than they would have if the π- electrons had not induced a magnetic field.




Q12/ For each of the following compounds, identify the expected chemical shift for each type of proton:

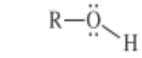



**4: Hydrogen bonding, Acidic and exchangeable protons**

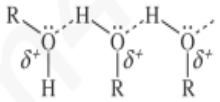
Protons that can exhibit hydrogen bonding (e.g., hydroxyl or amino protons) exhibit extremely variable absorption positions over a wide range. The more hydrogen bonding that takes place, the more deshielded a proton becomes. The amount of hydrogen bonding is often a function of concentration and temperature. In concentrated solution, their absorption is closer to 4–5 ppm.

**TYPICAL RANGES FOR PROTONS WITH VARIABLE CHEMICAL SHIFT**

| | | |
|---|---|---|
| Acids | RCOOH | 10.5–12.0 ppm |
| Phenols | ArOH | 4.0–7.0 |
| Alcohols | ROH | 0.5–5.0 |
| Amines | $RNH_2$ | 0.5–5.0 |
| Amides | $RCONH_2$ | 5.0–8.0 |
| Enols | CH=CH—OH | >15 |

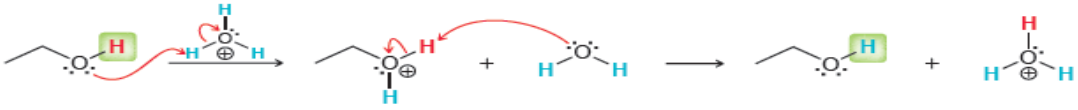


Free (dilute solution)



Hydrogen bonded (concentrated solution)

Hydrogens that can exchange either with the solvent medium or with one another also tend to be variable in their absorption positions.



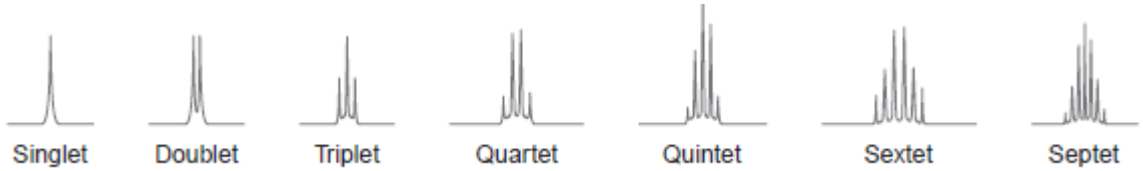
In this NMR spectrum notice that the hydroxyl proton is not split into a triplet from the neighboring methylene group. Generally, no splitting is observed across the oxygen of an alcohol, because proton exchange is a very rapid process that is catalyzed by trace amounts of acid or base.

Hydroxyl protons are said to be **labile**, because of the rapid rate at which they are exchanged. This proton transfer process occurs at a faster rate than the timescale of an NMR spectrometer. It is possible to slow down the rate of proton transfer by removing the trace amounts of acid and base dissolved in ethanol. Such purified ethanol does in fact exhibit splitting across the oxygen atom.

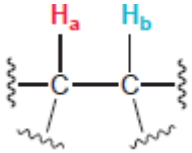
**Multiplicity**

**Coupling or spin-spin splitting**

The third, and final, characteristic of each signal is its **multiplicity**, which is defined by the number of peaks in the signal. A **singlet** has one peak, a **doublet** has two peaks, a **triplet** has three peaks, a **quartet** has four peaks, a **quintet** has five peaks, and so on.

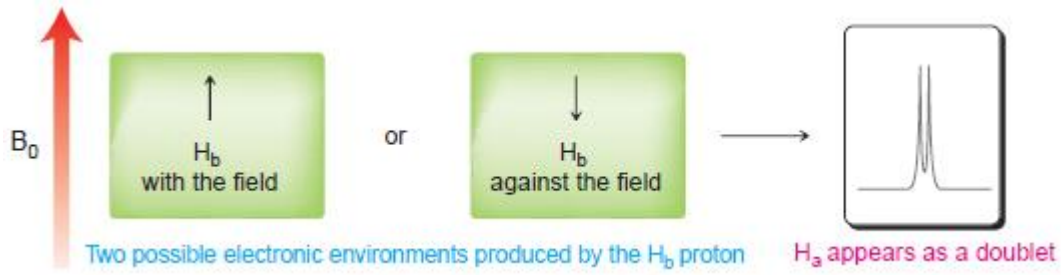


A signal's multiplicity is the result of the magnetic effects of neighboring protons and therefore indicates the number of neighboring protons. To illustrate this concept, consider the following example.



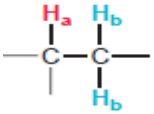

If (Ha) and (Hb) are not equivalent to each other, they will produce different signals. Let's focus on the signal produced by (Ha).

The chemical shift of (Ha) is impacted by the presence of (Hb), because (Hb) has a magnetic moment that can either be aligned with or against the external magnetic field. Hb is like a tiny magnet, and the chemical shift of Ha is dependent on the alignment of this tiny magnet. In some molecules, Hb will be aligned with the field, while in other molecules, Hb will be aligned against the field. As a result, the chemical shift of Ha in some molecules will be slightly different than the chemical shift of Ha in other molecules, resulting in the appearance of two peaks. In other words, the presence of Hb splits the signal for Ha into a doublet (Figure below).

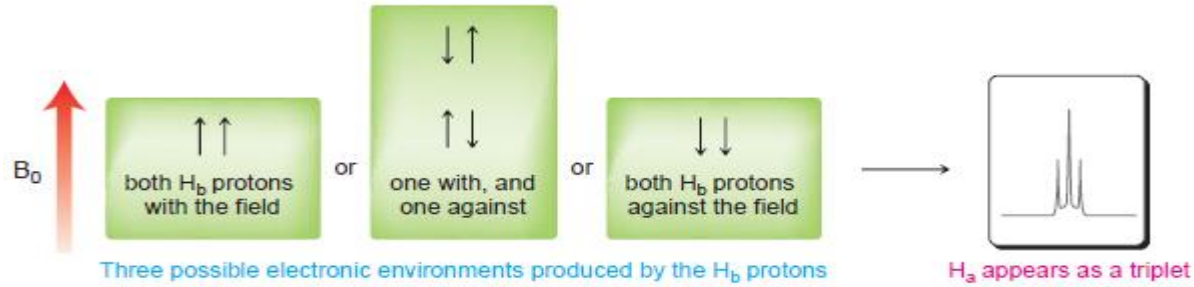



Ha has the same effect on the signal of Hb, splitting the signal for Hb into a doublet. This phenomenon is called **spin-spin splitting**, or **coupling**

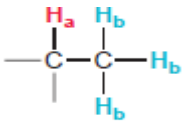
Now consider a scenario in which Ha has two neighboring protons.



The chemical shift of Ha is impacted by the presence of both Hb protons, each of which can be aligned either with or against the external field. Once again, each Hb is like a tiny magnet and has an impact on the chemical shift of Ha. In each molecule, Ha can find itself in one of three possible electronic environments, resulting in a triplet (Figure below). If each peak of the triplet is separately integrated, a ratio of 1: 2: 1 is observed, consistent with statistical expectations.




Now consider a scenario in which Ha has three neighbors




The chemical shift of Ha is impacted by the presence of all three Hb protons, each of which can be aligned either with the field or against the field. Once again, each Hb is like a tiny magnet and has an impact on the chemical shift of Ha. In each molecule, Ha can find itself in one of four possible electronic environments, resulting in a quartet (Figure below). If each peak of the quartet is integrated separately, a ratio of 1: 3: 3: 1 is observed, consistent with statistical expectations.

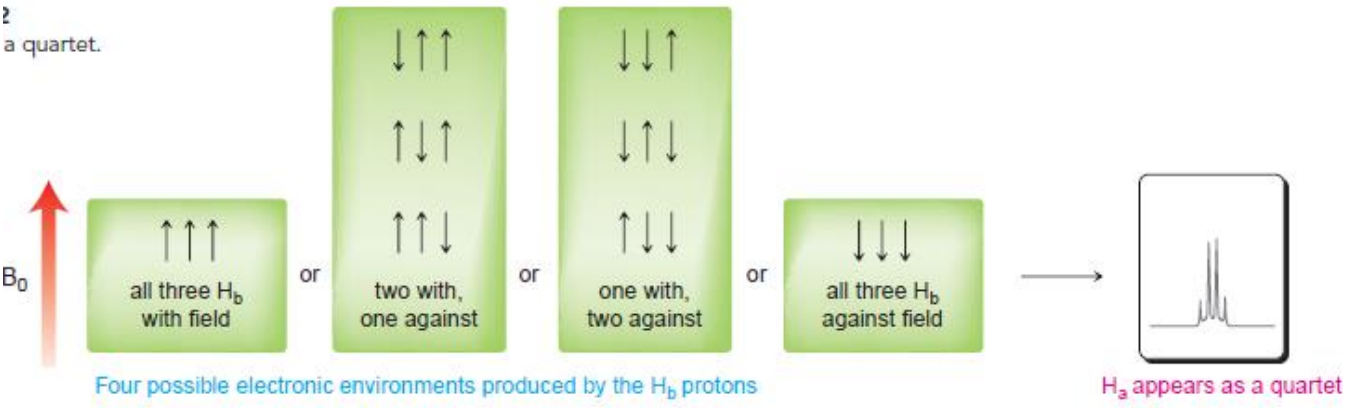
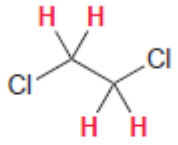


Table below summarizes the splitting patterns and peak intensities for signals that result from coupling with neighboring protons. If *n* is the number of neighboring protons, then the multiplicity will be *n* + *1*.Extending this rule, a proton with six neighbors (*n* = 6) will be split into a septet (7 peaks, or *n* + 1). This observation is called **the *n*+1 rule**.

| Peak area ratio | Signal |
|---|---|
| 1 | Singlet |
| 1 : 1 | Doublet |
| 1 : 2 : 1 | Triplet |
| 1 : 3 : 3 : 1 | Quartet |
| 1 : 4 : 6 : 4 : 1 | Quintet |
| 1 : 5 : 10 : 10 : 5 : 1 | Sextet |

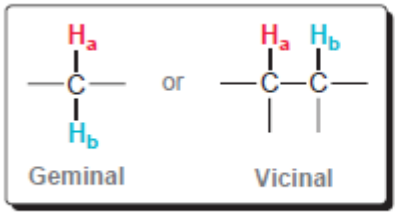



Four equivalent protons
No splitting

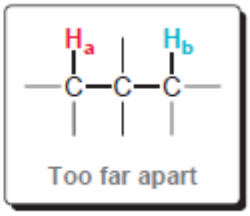
There are two major factors that determine whether or not splitting occurs:

1. Equivalent protons do not split each other. Consider the two methylene groups in 1, 2-dichloroethane. All four protons are chemically equivalent, and therefore, they do not split each other. In order for splitting to occur, the neighboring protons must be different than the protons producing the signal.

2. Splitting is most commonly observed when protons are separated by either two or three σ-bonds; that is, when the protons are either diastereotopic protons on the same carbon atom (geminal) or when they are connected to adjacent carbon atoms (vicinal).



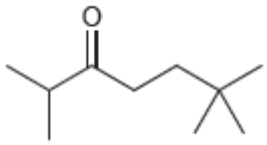

Splitting is observed




Splitting is generally not observed

When two protons are separated by more than three sigma bonds, splitting is generally not observed. Such long-range splitting is only observed in rigid molecules, such as bicyclic compounds, or in molecules that contain rigid structural moieties, such as allylic systems.

Q13/ Determine the multiplicity of each signal in the expected $^{1}$H NMR spectrum of the following compound.



The relative intensities of the individual lines of a multiplet correspond to the numerical coefficient of the lines in the binomial expression:

$(1 + x)^n = 1 + x$ if $n = 1$

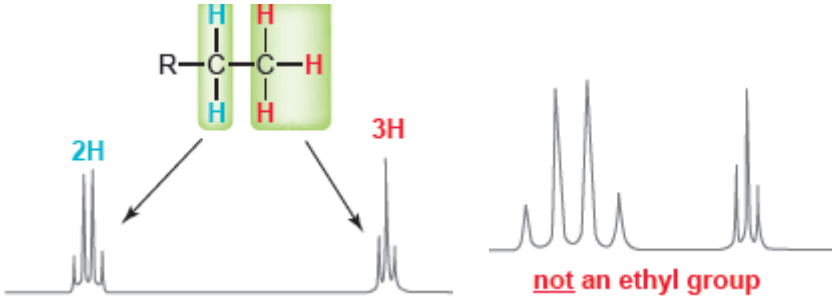
If $n = 2$, then $(1 + x)^2 = 1 + 2x + x^2$. Thus, the lines of the triplet have relative intensities 1: 2: 1

If $n = 3$, then $(1 + x)^3 = 1 + 3x^2 + 3x + x^3$. Thus, the lines of the quartet formed due to the influence of three equivalent protons will have relative intensities 1: 3: 3: 1. Similarly the lines of the pentet (quintet) formed will have relative intensities 1: 4: 6: 4:1.

Hence, **the splitting of a signal is due to the different environment of the absorbing proton not with respect to electrons but with respect to the nearby protons** (Protons attached to the adjacent carbon atom).

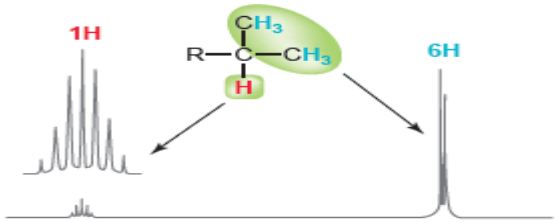
**Pattern Recognition**

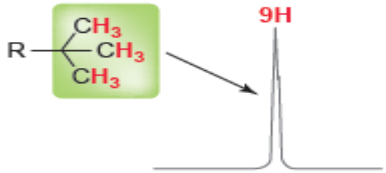
Specific splitting patterns are commonly seen in $^1$H NMR spectra, and recognizing these patterns allows for a more efficient analysis. For example, consider the splitting pattern produced by an ethyl group. A compound containing an ethyl group will display a triplet with an integration of (3), upfield from a quartet with an integration of (2) in its $^1$H NMR spectrum. The presence of these signals in a spectrum is strongly suggestive of the presence of an ethyl group in the structure of the compound.




Another commonly observed splitting pattern is produced by isopropyl groups. A compound containing an isopropyl group will display a doublet with an integration of 6,

upfield from a septet (seven peaks) with an integration of 1. The presence of these signals in a $^1$H NMR spectrum is strongly suggestive of the presence of an isopropyl group in the structure of the compound. A septet is usually hard to see, since it is so small (integration of 1), so an enlarged reproduction (inset) of the signal is often displayed above the original signal:

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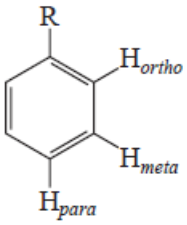
Another commonly observed pattern is produced by *tert*-butyl groups. A compound containing a *tert*-butyl group will display a singlet with a relative integration of 9.

The presence of this signal in a $^1$H NMR spectrum is strongly suggestive of the presence of a *tert*-butyl group in the structure of the compound.

**Aromatic compounds**

The hydrogens attached to aromatic rings are easily identified. They are found in a region of their own (6.5-8ppm). The largest chemical shifts are found for ring hydrogens when E.W. groups such as NO2 are attached to the ring. Conversely E.D. groups increase the shielding of these hydrogens causing them to move up field.

$^1$H CHEMICAL-SHIFT CALCULATIONS FOR SUBSTITUTED BENZENE RINGS



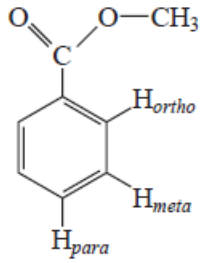

$$\delta_H \text{ ppm} = 7.27 + \Sigma\delta$$

| Substituents (−R) | $\delta_{ortho}$ | $\delta_{meta}$ | $\delta_{para}$ |
|---|---|---|---|
| Saturated carbon groups | | | |
| Alkyl | −0.14 | −0.06 | −0.17 |
| $-CH_2OH$ | −0.07 | −0.07 | −0.07 |
| Aldehydes and ketones | | | |
| −CHO | 0.61 | 0.25 | 0.35 |
| −COR | 0.62 | 0.14 | 0.21 |
| Carboxylic acids and derivatives | | | |
| −COOH | 0.85 | 0.18 | 0.34 |
| −COOR | 0.71 | 0.10 | 0.21 |
| −C≡N | 0.25 | 0.18 | 0.30 |
| Oxygen groups | | | |
| −OH | −0.53 | −0.17 | −0.45 |
| $-OCH_3$ | −0.48 | −0.09 | −0.44 |
| $-OCOCH_3$ | −0.19 | −0.03 | −0.19 |
| Nitrogen groups | | | |
| $-NH_2$ | −0.80 | −0.25 | −0.65 |
| $-NO_2$ | 0.95 | 0.26 | 0.38 |
| Halogen groups | | | |
| −F | −0.29 | −0.02 | −0.23 |
| −C1 | 0.03 | −0.02 | −0.09 |
| −Br | 0.18 | −0.08 | −0.04 |
| −I | 0.38 | −0.23 | −0.01 |

## Example Calculations

The formula allows you to calculate the *approximate* chemical-shift values for protons ($^1$H) on a benzene ring. Although the values given in the table are for *monosubstituted benzenes*, it is possible to estimate chemical shifts for disubstituted and trisubstituted compounds by adding values from the table. The calculations for *meta*- and *para*-disubstituted benzenes often agree closely with actual values. More significant deviations from the experimental values are expected with *ortho*disubstituted and trisubstituted benzenes. With these types of compounds, steric interactions cause groups such as carbonyl and nitro to turn out of the plane of the ring and thereby lose

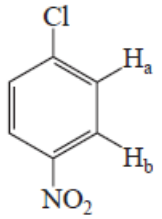
conjugation. Calculated values are often lower than the actual chemical shifts for *ortho*-disubstituted and trisubstituted benzenes.




$H_{ortho}$ = 7.27 + 0.71 = 7.98 ppm; actual = 8.03 ppm

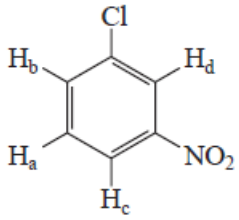
$H_{meta}$ = 7.27 + 0.10 = 7.37 ppm; actual = 7.42 ppm

$H_{para}$ = 7.27 + 0.21 = 7.48 ppm; actual = 7.53 ppm




$H_a$ { $\delta_{ortho}$ for −Cl = 0.03; $\delta_{meta}$ for $-NO_2$ = 0.26; $H_a$ = 7.27 + 0.03 + 0.26 = 7.56 ppm; actual = 7.50 ppm

$H_b$ { $\delta_{meta}$ for −Cl = –0.02; $\delta_{ortho}$ for $-NO_2$ = 0.95; $H_b$ = 7.27 – 0.02 + 0.95 = 8.20 ppm; actual = 8.20 ppm




$H_a$ { $\delta_{meta}$ for −Cl = –0.02; $\delta_{meta}$ for $-NO_2$ = 0.26; $H_a$ = 7.27 – 0.02 + 0.26 = 7.51 ppm; actual = 7.51 ppm

$H_b$ { $\delta_{ortho}$ for −Cl = 0.03; $\delta_{para}$ for $-NO_2$ = 0.38; $H_b$ = 7.27 + 0.03 + 0.38 = 7.68 ppm; actual = 7.69 ppm

$H_c$ { $\delta_{para}$ for −Cl = –0.09; $\delta_{ortho}$ for $-NO_2$ = 0.95; $H_c$ = 7.27 – 0.09 + 0.95 = 8.13 ppm; actual = 8.12 ppm

$H_d$ { $\delta_{ortho}$ for −Cl = 0.03; $\delta_{ortho}$ for $-NO_2$ = 0.95; $H_d$ = 7.27 + 0.03 + 0.95 = 8.25 ppm; actual = 8.21 ppm

Let's now summarize the kind of information that can be obtained from a spectrum:

1. The number of signals indicates the number of different kinds of protons that are in the compound.

2. The position of a signal indicates the kind of proton(s) responsible for the signal (methyl, methylene, methine, allylic, vinylic, aromatic, etc.), and the kinds of neighboring substituents.

3. The integration of the signal tells the relative number of protons responsible for the signal.

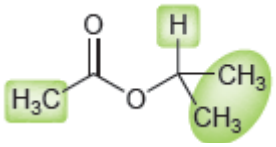
4. The multiplicity of the signal (N+1) tells the number of protons (N) bonded to adjacent carbons.

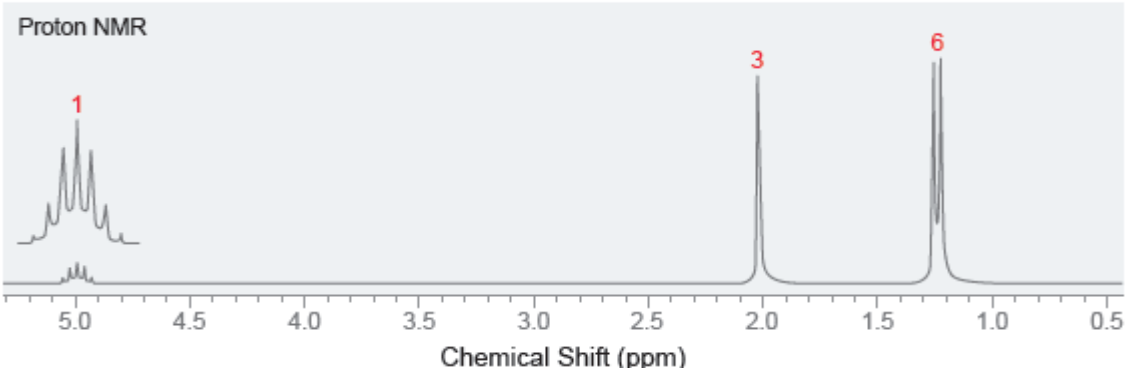
5. The coupling constants identify coupled protons.

**Drawing the Expected $^{1}$H NMR Spectrum of a Compound:**

The three characteristics of every signal are (chemical shift, multiplicity, and integration). Accordingly we will practice drawing the expected $^{1}$H NMR spectrum of a compound.

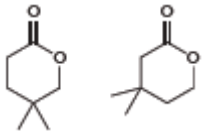
Q14/ Draw the expected $^{1}$H NMR spectrum of isopropyl acetate.




**Q15/ Using $^{1}$H NMR Spectroscopy to distinguish between Compounds**

1. Three constitutional isomers of xylene.

2. 

Interpretation of a $^{1}$H-NMR spectrum:

1. The number of signals.
2. The position of a signal (Chemical shifts).
3. The integration of the signal (Intensity).
4. The multiplicity of the signal (N+1), and the coupling constants (j-value).

Q16/ $C_8H_9BrO$

| Number of signals | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Chemical shifts | **2.4** | **3.4** | **6.6** | **7.4** |
| Multiplicity | t | q | d | d |
| Intensity | 6 | 4 | 4 | 4 |
| Ratio | 1.5 | 1 | 1 | 1 |

Q17/ $C_8H_8O_2$

| Number of signals | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Chemical shifts | **10** | **7.7** | **6.8** | **3.8** |
| Multiplicity | s | d | d | s |
| Intensity | 6 | 12 | 12 | 18 |
| Ratio | 1 | 2 | 2 | 3 |

Q18/ $C_3H_3Cl_5$

t(4.52ppm, 1H), d(6.1ppm, 2H)

Q19/ $C_3H_8O$

| Number of signals | 1 | 2 | 3 | 4 |
|---|---|---|---|---|
| Chemical shifts | **0.9** | **1.5** | **2.6** | **3.6** |
| Multiplicity | t | sextet | s | t |
| Intensity | 3 | 2 | 1 | 2 |

Q20/ $C_4H_7O_2Br$

| | | | | |
|---|---|---|---|---|
| Number of signals | 1 | 2 | 3 | 4 |
| Chemical shifts | **1.1** | **2.1** | **4.2** | **10.5** |
| Multiplicity | t | quintet | t | s |
| Intensity | 3 | 2 | 1 | 1 |

Q21/ a compound with $C_8H_8O$ give the following NMR data:

Multiplet (7.28ppm, 5H), d(2.8ppm,2H), t(9.7ppm,1H). Deduce the structure.

Q22/ a compound with $C_8H_{12}O$ give the following NMR data:

s(1.1ppm,6H), s(2.15ppm,3H), s(2.6ppm,2H), s(3.9ppm,1H). Deduce the structure

Q23/ Identify the structure of a compound with the molecular formula $C_9H_{10}O$ that exhibits the following $^1H$ NMR spectrum: