1. **Nuclear Magnetic Resonance by PAVIA**

Nuclear magnetic resonance (NMR) spectroscopy allows us not only to detect atomic nuclei but also tells us about their environment, i.e, which type of atoms they are attached with. For example the hydrogen of propanol’s hydroxyl group is different from the hydrogens of its carbon skeleton—it can be displaced by sodium metal, for example.

 NMR (actually 1H, or proton, NMR) can easily distinguish between these two sorts of hydrogens. Moreover, it can also distinguish between all the other different sorts of hydrogen atoms present. Likewise, carbon (or rather 13C) NMR can easily distinguish between the three different carbon atoms.

1.1 **NUCLEAR SPIN STATES**

Many atomic nuclei have a property called spin: the nuclei behave as if they were spinning. In fact, any atomic nucleus that possesses either odd mass, odd atomic number, or both has a quantized spin angular momentum and a magnetic moment. The more common nuclei that possess spin include 1 1H, 2 1H, 13 6C, 14 7N, 17 8O, and 19 9F. Notice that the nuclei of the ordinary (most abundant) isotopes of carbon and oxygen, 12 6C and 16 8O, are not included among those with the spin property. However, the nucleus of the ordinary hydrogen atom, the proton, does have spin. For each nucleus with spin, the number of allowed spin states it may adopt is quantized and is determined by its nuclear spin quantum number I. For each nucleus, the number I is a physical constant, and there are 2I+1 allowed spin states with integral differences ranging from +I to −I.

For instance, a proton (hydrogen nucleus) has the spin quantum number I= 1/2 and has two allowed spin states [2(1/2) + 1 =2] for its nucleus: −1/2 and +1/2 . For the chlorine nucleus, I= 3/2 and there are four allowed spin states [2(3/2 ) +1 =4]:− 3/2 ,− 1/ 2 ,+ 1/ 2 ,and + 3/ 2 . Table below gives the spin quantum numbers of several nuclei.

**TABLE SPIN QUANTUM NUMBERS OF SOME COMMON NUCLEI**

**Element 1 1H - 2 1H- 12 6C- 13 6C- 14 7N- 16 8O- 17 8O- 19 9F- 31 15P- 35 17Cl Nuclear spin quantum number-1/2- 1- 0 -1/2- 1- 0- 5/2 -1/2 -1/2- 2/3 ⎯ Number of spin states 2 - 3 - 0 - 2 - 3 - 0 - 6 - 2- 2 - 4**

In the absence of an applied magnetic field, all the spin states of a given nucleus are of equivalent energy (degenerate), and in a collection of atoms, all of the spin states should be almost equally populated, with the same number of atoms having each of the allowed spins.

**1.2 NUCLEAR MAGNETIC MOMENTS**

Spin states are not of equivalent energy in an applied magnetic field because the nucleus is a charged particle, and any moving charge generates a magnetic field of its own. Thus, the nucleus has a magnetic moment μ (meu) generated by its charge and spin. A hydrogen nucleus may have a clockwise (+1/ 2 ) or counterclockwise (⎯ 1/2 ) spin, and the nuclear magnetic moments (μ) in the two cases are pointed in opposite directions. In an applied magnetic field, all protons have their magnetic moments either aligned with the field or opposed to it. Figure 3.1 illustrates these two situations. Hydrogen nuclei can adopt only one or the other of these orientations with respect to the applied field. The spin state +1/2 is of lower energy since it is aligned with the field, while the spin state −1/2 is of higher energy since it is opposed to the applied field. We can consider these nuclei as the two magnets. The aligned configuration of magnets is stable (low energy). However, the opposed (not aligned) configuration is unstable (high energy). When an external magnetic field is applied, the degenerate spin states split into two states of unequal energy, as shown in Figure 3.3. In the case of a chlorine nucleus, there are four energy levels, as shown in Figure 3.4. The +3/2 and −3/2 spin states are aligned with the applied field and opposed to the applied field, respectively. The +1/2 and −1/2 spin states have intermediate orientations, as indicated by the vector diagram on the right in Figure 3.4.

**3.3 ABSORPTION OF ENERGY (Spin flipping)**

The nuclear magnetic resonance phenomenon occurs when nuclei aligned with an applied field are induced to absorb energy and change their spin orientation with respect to the applied field. It is called spin flipping. Figure 3.5 illustrates this process for a hydrogen nucleus. The energy absorption is a quantized process, and the energy absorbed must equal the energy difference between the two states involved.

Eabsorbed = (E⎯ 1/2 − E+ 1/2) = hυ

 In practice, this energy difference is a function of the strength of the applied magnetic field B0, as illustrated in Figure 3.6.

**FIGURE 3.3 The spin states of a proton in the absence and in the presence of an applied magnetic field.**

**FIGURE 3.4 The spin states of a chlorine atom both in the presence and in the absence of an applied magnetic field.**

The stronger the applied magnetic field, the greater the energy difference between the possible spin states:

E = f (B0)

The magnitude of the energy-level separation also depends on the particular nucleus involved. Each nucleus (hydrogen, chlorine, and so on) has a different ratio of magnetic moment to angular momentum since each has different charge and mass. This ratio, called the magneto gyric ratio γ, is a constant for each nucleus and determines the energy dependence on the magnetic field:

Delta E = f (γB0) = hυ

Since the angular momentum of the nucleus is quantized in units of h/2π, the final equation takes the form

Delta E =γ( h/2π)B0 = hυ

 Solving for the frequency of the absorbed energy, υ=(γ/2π)B0

 If the correct value of γ for the proton is substituted, one finds that an unshielded proton should absorb radiation of frequency 42.6 MHz in a field of strength 1 Tesla (10,000 Gauss) or radiation of frequency 60.0 MHz in a field of strength 1.41 Tesla (14,100 Gauss). Table 3.2 shows the field strengths and frequencies at which several nuclei have resonance (i.e., absorb energy and make spin transitions).

**1.4 The Mechanism of Absorption (Resonance)**

Although many nuclei are capable of exhibiting magnetic resonance, the organic chemist is mainly interested in hydrogen and carbon resonances. For a proton (the nucleus of a hydrogen atom), if the applied magnetic field has a strength of approximately 1.41 Tesla, the difference in energy between the two spin states of the proton is about 2.39 × 10−5 kJ/mole. Radiation with a frequency of about 60 MHz (60,000,000 Hz), which lies in the radiofrequency (RF) region of the electromagnetic spectrum, corresponds to this energy difference. Other nuclei have both larger and smaller energy differences between spin states than do hydrogen nuclei. The earliest nuclear magnetic resonance spectrometers applied a variable magnetic field with a range of strengths near 1.41 Tesla and supplied a constant radiofrequency radiation of 60 MHz. They effectively induced transitions only among proton (hydrogen) spin states in a molecule and were not useful for other nuclei. Separate instruments were required to observe transitions in the nuclei of other elements, such as carbon and phosphorus. Fourier transform instruments (Section 3.7B), which are in common use today, are equipped to observe the nuclei of several different elements in a single instrument. Instruments operating at frequencies of 300 and 400 MHz are now quite common, and instruments with frequencies above 600 MHz are found in the larger research universities.

**1.4 THE MECHANISM OF ABSORPTION (RESONANCE)**

Protons absorb energy due to their precessional frequency. Just like spinning top, spinning protons began to precess under the influence of magnetic field just as spinning top began to wobble under the influence of gravitational field.

When the magnetic field is applied, the nucleus begins to precess about its own axis of spin with angular frequency, which is sometimes called its Larmor frequency. This frequency at which a proton precesses is directly proportional to the strength of the applied magnetic field; the stronger the applied field, the higher the rate (angular frequency w) of precession. For a proton, if the applied field is 1.41 Tesla (14,100 Gauss), the frequency of precession is approximately 60 MHz. Since the nucleus has a charge, the precession generates an oscillating electric field of the same frequency. If radiofrequency waves of this frequency are supplied to the precessing proton, the energy can be absorbed. That is, when the frequency of the oscillating electric field component of the incoming radiation just matches the frequency of the electric field generated by the precessing nucleus, the two fields can couple, and energy can be transferred from the incoming radiation to the nucleus, thus causing a spin change. This condition is called resonance, and the nucleus is said to have resonance with the incoming electromagnetic wave. Figure 3.8 schematically illustrates the resonance process.

**1.5 POPULATION DENSITIES OF NUCLEAR SPIN STATES**

For a proton, if the applied magnetic field has a strength of approximately 1.41 Tesla, resonance occurs at about 60 MHz, and using E = hυ, we can calculate that the difference in energy between the two spin states of the proton is about 2.39 × 10−5 kJ/mole. Thermal energy resulting from room temperature is sufficient to populate both of these energy levels since the energy separation between the two levels is small. There is, however, a slight excess of nuclei in the lower-energy spin state. The magnitude of this difference can be calculated using the Boltzmann distribution equations.

Using Boltzmann Equation, one can calculate that at 298 K (25°C), for an instrument operating at 60 MHz there are 1,000,009 nuclei in the lower (favored) spin state for every 1,000,000 that occupy the upper spin state:

In other words, in approximately 2 million nuclei, there are only 9 more nuclei in the lower spin state. Let us call this number (9) the excess population (Fig. 3.9). The excess nuclei are the ones that allow us to observe resonance. When the 60-MHz radiation is applied, it not only induces transitions upward but also stimulates transitions downward. If the populations of the upper and lower states become exactly equal, we observe no net signal. This situation is called **saturation**. One must be careful to avoid saturation when performing an NMR experiment. Saturation is achieved quickly if the power of the radiofrequency signal is too high. Therefore, the very small excess of nuclei in the lower spin state is quite important to NMR spectroscopy, and we can see that very sensitive NMR instrumentation is required to detect the signal. If we increase the operating frequency of the NMR instrument, the energy difference between the two states increases (see Fig. 3.6), which causes an increase in this excess. Table 3.3 shows how the excess increases with operating frequency. It also clearly shows why modern instrumentation has been designed with increasingly higher operating frequencies. The sensitivity of the instrument is increased, and the resonance signals are stronger, because more nuclei can undergo transition at higher frequency. Before the advent of higher-field instruments, it was very difficult to observe less-sensitive nuclei such as carbon-13, which is not very abundant (1.1%) and has a detection frequency much lower than that of hydrogen (see Table 3.2).

**1.6 THE CHEMICAL SHIFT AND SHIELDING**

**Different protons resonate at different frequencies**:

Nuclear magnetic resonance has great utility because not all protons in a molecule have resonance at exactly the same frequency. This variability is due to the fact that the protons in a molecule are surrounded by electrons and exist in slightly different electronic (magnetic) environments from one another. The valence-shell electron densities vary from one proton to another.

**Local diamagnetic shielding or diamagnetic anisotropy:**

The protons are shielded by the electrons that surround them. In an applied magnetic field, the valence electrons of the protons are caused to circulate. This circulation, called a local diamagnetic current, generates a counter magnetic field that opposes the applied magnetic field. Figure 3.10 illustrates this effect, which is called diamagnetic shielding or diamagnetic anisotropy. Just like the flow of a current through a wire induces a magnetic field, circulation of electrons around a nucleus, in an atom, the local diamagnetic current generates a secondary, induced magnetic field that has a direction opposite that of the applied magnetic field.

This diamagnetic anisotropy shields the nearby proton from applied magnetic field. Strength of this shield is directly proportional to the electron density around the proton. The greater the electron density around a nucleus, the greater the induced counter field that opposes the applied field. As a result, the nucleus experiences a low applied field and resonates at low precessional frequency, so absorbs radiofrequency at low frequency. and the difference between the energy of the nucleus with lying with the applied field and against the applied field decreases and so it absorbs the radio frequency at low value and precesses at a lower frequency. This means that it also absorbs radiofrequency radiation at this lower frequency. Each proton in a molecule is in a slightly different chemical environment and consequently has a slightly different amount of electronic shielding, which results in a slightly different resonance frequency.

Internal reference compound

The differences in resonance frequency of different protons are very small. For instance, the difference between the resonance frequencies of the protons in chloromethane and those in fluoromethane is only 72 Hz when the applied field is 1.41 Tesla. Since the radiation used to induce proton spin transitions at that magnetic field strength is of a frequency near 60 MHz, the difference between chloromethane and fluoromethane represents a change in frequency of only slightly more than one part per million! It is very difficult to measure exact frequencies to that precision; 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. In other words, the frequency difference is measured directly. The standard reference substance that is used universally is tetramethylsilane, (CH3)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. At that time, no compounds that had better-shielded hydrogens 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 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:

Hence, for a given proton, the shift (in Hertz) from TMS is 5/3 larger in the 100-MHz range (B0 =2.35 Tesla) than in the 60-MHz range (B0 = 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 (d) is obtained

Delta (δ) = $\frac{shift in Hz}{spectrometer frequency in MHz}$

The chemical shift in δ units expresses the amount by which a proton resonance is shifted from TMS, in parts per million (ppm), of the spectrometer’s basic operating frequency. Values of **δ** for a given proton are always the same irrespective of whether the measurement was made at 60 MHz (B0 = 1.41 Tesla) or at 100 MHz (B0 = 2.35 Tesla). For instance, at 60 MHz the shift of the protons in CH3Br is 162 Hz from TMS, while at 100 MHz the shift is 270 Hz. However, both of these correspond to the same value of **δ** (2.70 ppm):

Delta (δ) = $\frac{162 Hz}{60 MHz}$z = $\frac{270 Hz}{100 MHz}$ = 2.70 ppm

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 (by definition). The NMR spectrometer actually scans from high values to low ones (as will be discussed in Section 3.7). Following is a typical chemical shift scale with the sequence of values that would be found on a typical NMR spectrum chart.

**THE NUCLEAR MAGNETIC RESONANCE SPECTROMETER**

**1.7 The Continuous-Wave (CW) Instrument**

Figure 3.11 schematically illustrates the basic elements of a classical 60-MHz NMR spectrometer. The sample is dissolved in a solvent containing no interfering protons (usually CCl4 or CDCl3), 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. Also in the magnet gap is a coil attached to a 60-MHz radiofrequency (RF) generator. This coil supplies the electromagnetic energy used to change the spin orientations of the protons. Perpendicular to the RF oscillator coil is a detector coil. When no absorption of energy is taking place, the detector coil picks up none of the energy given off by the RF oscillator coil. When the sample absorbs energy, however, the reorientation of the nuclear spins induces a RF signal in the plane of the detec- tor coil, and the instrument responds by recording this as a resonance signal, or peak.

At a constant field strength, the distinct types of protons in a molecule precess at slightly different frequencies.

 Rather than changing the frequency of the RF oscillator to allow each of the protons in a molecule to come into resonance, the CW NMR spectrometer uses a constant-frequency RF signal and varies the magnetic field strength. As the magnetic field strength is increased, the precessional frequencies of all the protons increase. When the precessional frequency of a given type of proton reaches 60 MHz, it has resonance. The magnet that is varied is actually a two-part device. There is a main magnet, with a strength of about 1.41 Tesla, which is capped by electromagnet pole pieces. By varying the current through the pole pieces, the worker can increase the main field strength by as much as 20 parts per million (ppm). Changing the field in this way systematically brings all of the different types of protons in the sample into resonance. As the field strength is increased linearly, a pen travels across a recording chart. A typical spectrum is recorded as in Figure 3.12. As the pen travels 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 d = 0 ppm is due to the internal reference compound TMS. Since highly shielded protons precess more slowly than relatively unshielded protons, it is necessary to increase the field to induce them to precess at 60 MHz. Hence, highly shielded protons appear to the right of this 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). Varying the magnetic field as is done in the usual spectrometer is exactly equivalent to varying the radio frequency, RF and a change of 1 ppm in the magnetic field strength (increase) has the same effect as a 1-ppm change (decrease) in the RF frequency (see Eq. 3.6). Hence, changing the field strength instead of the RF frequency is only a matter of instrumental design. Instruments that vary the magnetic field in a continuous fashion, scanning from the downfield end to the upfield end of the spectrum, are called continuous-wave (CW) instruments. Because the chemical shifts of the peaks in this spectrum are calculated from frequency differences from TMS, this type of spectrum (Fig. 3.12) is said to be a frequency-domain spectrum. A distinctive characteristic enables one to recognize a CW spectrum. Peaks generated by a CW instrument have ringing, a decreasing series of oscillations that occurs after the instrument has scanned through the peak (Fig. 3.13). Ringing occurs because the excited nuclei do not have time to relax back to their equilibrium state before the field, and pen, of the instrument have advanced to a new position. The excited nuclei have a relaxation rate that is slower than the rate of scan. As a result, they are still emitting an oscillating, rapidly decaying signal, which is recorded as ringing. Ringing is desirable in a CW instrument and is considered to indicate that the field homogeneity is well adjusted. Ringing is most noticeable when a peak is a sharp singlet (a single, isolated peak).

The Pulsed Fourier Transform (FT) Instrument:

The CW type of NMR spectrometer, which was described in Section 3.6A, operates by exciting the nuclei of the isotope under observation one type at a time. In the case of 1H nuclei, each distinct type of proton (phenyl, vinyl, methyl, and so on) is excited individually, and its resonance peak is observed and recorded independently of all the others. As we scan, we look at first one type of hydrogen and then another, scanning until all of the types have come into resonance.

An alternative approach, common to modern, sophisticated instruments, is to use a powerful but short burst of energy, called a pulse, that excites all of the magnetic nuclei in the molecule simultaneously. In an organic molecule, for instance, all of the 1H nuclei are induced to undergo resonance at the same time. An instrument with a 2.1-Tesla magnetic field uses a short (1- to 10-sec) burst of 90-MHz energy to accomplish this. The source is turned on and off very quickly, generating a pulse similar to that shown in Figure 3.14a. The pulse actually contains a range of frequencies centered about the fundamental, as shown in Figure 3.14b. This range of frequencies is great enough to excite all of the distinct types of hydrogens in the molecule at once with this single burst of energy. When the pulse is discontinued, the excited nuclei begin to lose their excitation energy and return to their original spin state, or relax. As each excited nucleus relaxes, it emits electromagnetic radiation.

Since the molecule contains many different nuclei, many different frequencies of electromagnetic radiation are emitted simultaneously. This emission is called a **free-induction decay (FID) signal** (Fig.3.15). Notice that the intensity of the FID decays with time as all of the nuclei eventually lose their excitation. The FID is a superimposed combination of all the frequencies emitted and can be quite complex. This is usually called a time domain signal. We usually extract the individual frequencies due to different nuclei by using a computer and a mathematical method called a Fourier transform (FT) analysis. In this way we can convert the time-domain signal to a frequency-domain signal, which is the standard format for a spectrum obtained by a CW instrument.

**Diffrences between two methods:**

1- CW spectrum; a pulsed experiment is much faster, and a measurement of an FID can be performed in a few seconds.

2- With a computer and fast measurement, it is possible to repeat and average the measurement of the FID signal. This is a real advantage when the sample is small, in which case the FID is weak in intensity and has a great amount of noise associated with it. Noise is random electronic signals that are usually visible as fluctuations of the baseline in the signal (Fig. 3.17). 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

3- Pulsed FT-NMR is therefore especially suitable for the examination of nuclei that are not very abundant in nature, nuclei that are not strongly magnetic, or very dilute samples. The most modern NMR spectrometers use superconducting magnets, which can have field strengths as high as 14 Tesla and operate at 600 MHz. A superconducting magnet is made of special alloys and must be cooled to liquid helium temperatures. The magnet is usually surrounded by a Dewar flask (an insulated chamber) containing liquid helium; in turn, this chamber is surrounded by another one containing liquid nitrogen. Instruments operating at frequencies above 100 MHz have superconducting magnets. NMR spectrometers with frequencies of 200 MHz, 300 MHz, and 400 MHz are now common in chemistry; instruments with frequencies of 900 MHz are used for special research projects.

CHEMICAL EQUIVALENCE—A BRIEF OVERVIEW

All of the protons found in chemically identical environments within a molecule are chemically equivalent, and they often exhibit the same chemical shift. Thus, all the protons in tetramethylsilane (TMS) or all the protons in benzene, cyclopentane, or acetone—which are molecules that have protons that are equivalent by symmetry considerations—have resonance at a single value of (but a different value from that of each of the other molecules in the same group). Each such compound gives rise to a single absorption peak in its NMR spectrum. The protons are said to be chemically equivalent.

On the other hand, a molecule that has sets of protons that are chemically distinct from one another may give rise to a different absorption peak from each set, in which case the sets of protons are chemically nonequivalent. The following examples should help to clarify these relationships:

You can see that an NMR spectrum furnishes a valuable type of information on the basis of the number of different peaks observed; that is, the number of peaks corresponds to the number of chemically distinct types of protons in the molecule. Often, protons that are chemically equivalent are also magnetically equivalent. Note, however, that in some instances, protons that are chemically equivalent are not magnetically equivalent. We will explore this circumstance in Chapter 5, which examines chemical and magnetic equivalence in more detail.

Molecules giving rise to two NMR absorption peaks—two different sets of chemically equivalent protons

Molecules giving rise to three NMR absorption peaks—three different sets of chemically equivalent protons

**3.9 Integrals and Integration**

The NMR spectrum not only distinguishes how many different types of protons are present in a molecule, but also reveals the number of each type of protons contained within the molecule. In the NMR spectrum, the area under each peak is proportional to the number of hydrogens generating that peak. Hence, in phenylacetone (see Fig. 3.12), the area ratio of the three peaks is 5:2:3, the same as the ratio of the numbers of the three types of hydrogens. The NMR spectrometer has the capability to electronically integrate the area under each peak. It does this by tracing over each peak a vertically rising line, called the integral, which rises in height by an amount proportional to the area under the peak. Figure 3.18 is a 60-MHz NMR spectrum of benzyl acetate, showing each of the peaks integrated in this way.

**Note that the height of the integral line does not give the absolute number of hydrogens. It gives the relative number of each type of hydrogen**. For a given integral to be of any use, there must be a second integral to which it may be referred. Benzyl acetate provides a good example of this. The first integral rises for 55.5 divisions on the chart paper; the second, 22.0 divisions; and the third, 32.5 divisions. These numbers are relative. One can find ratios of the types of protons by dividing each of the larger numbers by the smallest number:

55.5/22= 2.52 22/22= 1.0 32.5/22= 1.48

 Thus, the number ratio of the protons of all the types is 2.52:1.00:1.48. If we arrive at the true ratio by multiplying each figure by 2 and rounding off to 5:2:3. Clearly, the peak at 7.3 ppm, which integrates for five protons, arises from the resonance of the aromatic ring protons, whereas that at 2.0 ppm, which integrates for three protons, is due to the methyl protons. The two-proton resonance at 5.1 ppm arises from the benzyl protons. Notice that the integrals give the simplest ratio, but not necessarily the true ratio, of numbers of protons of each type.

**CHEMICAL ENVIRONMENT AND CHEMICAL SHIFT**

If the resonance frequencies of all protons in a molecule were the same, NMR would be of little use to the organic chemist. Advantage of this technique is that not only the different types of protons have different chemical shifts, but each also has a characteristic value of chemical shift. Every type of proton has only a limited range of delta values over which it gives resonance. Hence, the numerical value (in units or ppm) of the chemical shift for a proton gives a clue regarding the type of proton originating the signal, just as an infrared frequency gives a clue regarding the type of bond or functional group. For instance, notice that the aromatic protons of both phenylacetone (Fig. 3.12) and benzyl acetate (Fig. 3.18) have resonance near 7.3 ppm, and that both of the methyl groups attached directly to a carbonyl have resonance at about 2.1 ppm. Aromatic protons characteristically have resonance near 7 to 8 ppm, whereas acetyl groups (methyl groups of this type) have their resonance near 2 ppm. These values of chemical shift are diagnostic. Notice also how the resonance of the benzyl (-CH2-) protons comes at a higher value of chemical shift (5.1 ppm) in benzyl acetate than in phenylacetone (3.6 ppm). Being attached to the electronegative element oxygen, these protons are more deshielded (see Section 3.11) than those in phenylacetone. A trained chemist would readily recognize the probable presence of the oxygen from the value of chemical shift shown by these protons.

It is important to learn the ranges of chemical shifts over which the most common types of protons have resonance. Figure 3.20 is a correlation chart that contains the most essential and frequently encountered types of protons. Table 3.4 lists the chemical shift ranges for selected types of protons. For the beginner, it is often difficult to memorize a large body of numbers relating to chemical shifts and proton types. One actually need do this only crudely. It is more important to “get a feel” for the regions and the types of protons than to know a string of actual numbers. To do this, study Figure 3.20

3.11 LOCAL DIAMAGNETIC SHIELDING

The trend of chemical shifts that is easiest to explain is that involving electronegative elements substituted on the same carbon to which the protons of interest are attached. The chemical shift simply increases as the electronegativity of the attached element increases. Table 3.5 illustrates this relationship for several compounds of the type CH3X. Multiple substituents have a stronger effect than a single substituent. The influence of the substituent drops off rapidly with distance, an electronegative element having little effect on protons that are more than three carbons distant. Table 3.6 illustrates these effects for the underlined protons. Section 3.6 briefly discussed the origin of the electronegativity effect. 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, it will be recalled, shield the proton from the applied magnetic field. Figure 3.10 illustrates this effect, 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 deshield the proton. The greater the electronegativity of the substituent, the more it deshields protons and hence the greater is the chemical shift of those protons.

It is important to learn the ranges of chemical shifts over which the most common types of protons have resonance. Figure 3.20 is a correlation chart that contains the most essential and frequently encountered types of protons. Table 3.4 lists the chemical shift ranges for selected types of protons. For the beginner, it is often difficult to memorize a large body of numbers relating to chemical shifts and proton types. One actually need do this only crudely. It is more important to “get a feel” for the regions and the types of protons than to know a string of actual numbers. To do this,study Figure 3.20 carefully. Table 3.4 and Appendix 2 give more detailed listings of chemical shifts.

**Nuclear magnetic resonance**

Nuclear magnetic resonance (NMR) spectroscopy allows us not only to detect atomic nuclei but also tells us about their environment, i.e, which type of atoms they are attached with. For example the hydrogen of propanol’s hydroxyl group is different from the hydrogens of its carbon skeleton—it can be displaced by sodium metal, for example.

 NMR (actually 1H, or proton, NMR) can easily distinguish between these two sorts of hydrogens. Moreover, it can also distinguish between all the other different sorts of hydrogen atoms present. Likewise, carbon (or rather 13C) NMR can easily distinguish between the three different carbon atoms.

13C NMR spectroscopy

NMR is incredibly versatile: it can even scan living human brains but the principle is still the same: being able to detect nuclei (and hence atoms) in different environments. When NMR is used medically it is usually called Magnetic Resonance Imaging (MRI) for fear of frightening patients wary of all things nuclear .

Principle

NMR uses a strong magnetic ﬁeld. Imagine for a moment that we were able to ‘switch off’ the earth’s magnetic ﬁeld. One effect would be to make navigation much harder since all compasses would be useless. They would be free to point in whatever direction they wanted to and, if we turned the needle round, it would simply stay where we left it. However, as soon as we switched the magnetic ﬁeld back on, they would all point north—their lowest energy state. Now if we wanted to force a needle to point south we would have to use up energy and, of course, as soon as we let go, the needle would return to its lowest energy state, pointing north. In a similar way, some atomic nuclei act like tiny compass needles and have different energy levels when placed in a magnetic ﬁeld. The compass needle can rotate through 360°and have an essentially inﬁnite number of different energy levels, all higher in energy than the ‘ground state’ (pointing north). Fortunately, our atomic nucleus is more restricted—its energy levels are quantized, just like the energy levels of an electron, and there are only certain speciﬁc energy levels it can adopt. This is like allowing our compass needle to point, say, only north or south. Some nuclei (including ‘normal’ carbon-12) do not interact with a magnetic ﬁeld at all and cannot be observed in an NMR machine. The nuclei we shall be looking at, 1H and 13C, do interact and have just two different energy levels. When we apply a magnetic ﬁeld to these nuclei, they can either align themselves with it, which would be the lowest energy state, or they can align themselves against the ﬁeld, which is higher in energy.

**NUCLEAR SPIN STATES**

**Many atomic nuclei have a property called spin: the nuclei behave as if they were spinning. In fact, any atomic nucleus that possesses either odd mass, odd atomic number, or both has a quantized spin angular momentum and a magnetic moment. The more common nuclei that possess spin include 1 1H, 2 1H, 13 6C, 14 7N, 17 8O, and 19 9F. Notice that the nuclei of the ordinary (most abundant) isotopes of carbon and oxygen, 12 6C and 16 8O, are not included among those with the spin property. However, the nucleus of the ordinary hydrogen atom, the proton, does have spin.**

**In the absence of an applied magnetic field,all the spin states of a given nucleus are of equivalent. Nuclei that interact with magnetic ﬁelds are said to possess nuclear spin. The exact number of different energy levels a nucleus can adopt is determined by this nuclear spin, I , of the particular isotope. The nuclear spin I can have various values such as 0, 1 – 2, 1, 3 – 2 and the number of energy levels is given by 2 I + 1. Some examples are: 1H, I = 1/2; 2H (= D), I = 1; 11B, I = 5/2; 12C, I = 0.**

We have already seen that if we could switch off theearth’s magnetic ﬁeld it would be easy to turn the compass needle round. When it is back on we need to push the needle (do work) to displace it from north. If we turned up the earth’s magnetic ﬁeld still more, it would be even harder to displace the compass needle. It means that stronger the earth’s magnetic field, harder it will be to turn the compass needle as it is well magnetized.

Similar rule also applies on our nucleus in a magnetic ﬁeld, the difference in energy between the nuclear spin aligned with and against the applied ﬁeld depends on how strong the magnetic ﬁeld is, and also on the properties of the nucleus itself. The stronger the magnetic ﬁeld we put our nucleus in, the greater the energy difference between the two alignments. Now here is an unfortunate thing about NMR: the energy difference between the nuclear spin being aligned with the magnetic ﬁeld and against it is really very small—so small that we need a very, very strong magnetic ﬁeld to see any difference at all.

**NMR also uses radio waves**

A 1H or 13C nucleus in a strong magnetic ﬁeld can have two energy levels. We could do work to make our nucleus align against the ﬁeld rather than with it (just like turning the compass needle round). But since the energy difference between the two states is so small, we don’t need to do much work. In fact, the amount of energy needed to ﬂip the nucleus can be provided by electromagnetic radiation of radio-wave frequency. Radio waves ﬂip the nucleus from the lower energy state to the higher state. The nucleus now wants to return to the lower energy state and, when it does so, the energy comes out again and this (a tiny pulse of radiofrequency electromagnetic radiation) is what we detect. We can now sum up how an NMR machine works.

1 The sample of the unknown compound is dissolved in a suitable solvent and put in a very strong magnetic ﬁeld. Any atomic nuclei with a nuclear spin now have different energy levels, the exact number of different energy levels depending on the value of the nuclear spin. For 1H and 13C NMR there are two energy levels.

2 The sample is irradiated with a short pulse of radiofrequency energy. This disturbs the equilibrium balance between the two energy levels: some nuclei absorb the energy and are promoted to a higher energy level.

3 We then detect the energy given out when the nuclei fall back down to the lower energy level using what is basically a sophisticated radio receiver.

4 After lots of computation, the results are displayed in the form of intensity (i.e. number of absorptions) against frequency. Here is an example, which we shall return to in more detail later.



**Absorption of energy**

The nuclear magnetic resonance phenomenon occurs when nuclei aligned with an applied field are induced to absorb energy and change their spin orientation with respect to the applied field. Figure 3.5 illustrates this process for a hydrogen nucleus. The energy absorption is a quantized process, and the energy absorbed must equal the energy difference between the two states involved.

Eabsorbed = (E−⎯ 1/2 state − E+ 1/2 state) = hneu

In practice, this energy difference is a function of the strength of the applied magnetic field B0, as illustrated in Figure 3.6.

The stronger the applied magnetic field, greater will be the energy difference between two possible spin states.

Delta E = f(Bo)

magnet were placed on a pivot, it would spontaneously spin around the pivot into alignment (low energy). Hence, as an external magnetic field is applied, the degenerate spin states split into two states of unequal energy, as shown in Figure 3.3. In the case of a chlorine nucleus, there are four energy levels, as shown in Figure 3.4. The +⎯3 2 ⎯ and −⎯3 2 ⎯ spin states are aligned with the applied field and opposed to the applied field, respectively. The +⎯1 2 ⎯ and −⎯1 2 ⎯ spin states have intermediate orientations, as indicated by the vector diagram on the right in Figure 3.4.

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The stronger the applied magnetic field, the greater the energy difference between the possible spin states:

E = f (B0) Equation 3.3

The magnitude of the energy-level separation also depends on the particular nucleus involved. Each nucleus (hydrogen, chlorine, and so on) has a different ratio of magnetic moment to angular momentum since each has different charge and mass. This ratio, called the magnetogyric ratio g, is a constant for each nucleus and determines the energy dependence on the magnetic field:

E = f (gB0) = hn Equation 3.4

Since the angular momentum of the nucleus is quantized in units of h/2, the final equation takes the form E =g(⎯ 2 h p ⎯)B0 = hn Equation 3.5 Solving for the frequency of the absorbed energy, u=(⎯ 2 g p ⎯)B0 Equation 3.6 If the correct value of for the proton is substituted,one finds that an unshielded proton should absorb radiation of frequency 42.6 MHz in a field of strength 1 Tesla (10,000 Gauss) or radiation of frequency 60.0 MHz in a field of strength 1.41 Tesla (14,100 Gauss). Table 3.2 shows the field strengths and frequencies at which several nuclei have resonance (i.e., absorb energy and make spin transitions).

Although many nuclei are capable of exhibiting magnetic resonance,the organic chemist is mainly interested in hydrogen and carbon resonances. This chapter emphasizes hydrogen. Chapter 4 will discuss nuclei other than hydrogen—for example, carbon-13, fluorine-19, phosphorus-31, and deu- terium (hydrogen-2). For a proton (the nucleus of a hydrogen atom), if the applied magnetic field has a strength of approximately 1.41 Tesla, the difference in energy between the two spin states of the proton is about 2.39 × 10−5 kJ/mole. Radiation with a frequency of about 60 MHz (60,000,000 Hz), which lies in the radiofrequency (RF) region of the electromagnetic spectrum, corresponds to this energy difference. Other nuclei have both larger and smaller energy differences between spin states than do hydrogen nuclei. The earliest nuclear magnetic resonance spectrometers applied a variable magnetic field with a range of strengths near 1.41 Tesla and supplied a constant radiofrequency radiation of 60 MHz. They effectively induced transitions only among proton (hydrogen) spin states in a molecule and were not useful for other nuclei. Separate instruments were required to observe transitions in the nu- clei of other elements,such as carbon and phosphorus. Fourier transform instruments (Section 3.7B), which are in common use today, are equipped to observe the nuclei of several different elements in a single instrument. Instruments operating at frequencies of 300 and 400 MHz are now quite common, and instruments with frequencies above 600 MHz are found in the larger research universities.

**THE MECHANISM OF ABSORPTION (RESONANCE)**

To understand the nature of a nuclear spin transition, the analogy of a child’s spinning top is useful. Protons absorb energy because they begin to precess in an applied magnetic field. The phenomenon of precession is similar to that of a spinning top. Owing to the influence of the earth’s gravitational field, the top begins to “wobble,” or precess, about its axis (Fig. 3.7a). A spinning nucleus behaves in a similar fashion under the influence of an applied magnetic field (Fig. 3.7b).

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When the magnetic field is applied, the nucleus begins to precess about its own axis of spin with angular frequency , which is sometimes called its Larmor frequency. The frequency at which a proton precesses is directly proportional to the strength of the applied magnetic field; the stronger the applied field, the higher the rate (angular frequency w) of precession. For a proton, if the applied field is 1.41 Tesla (14,100 Gauss), the frequency of precession is approximately 60 MHz. Since the nucleus has a charge, the precession generates an oscillating electric field of the same frequency. If radiofrequency waves of this frequency are supplied to the precessing proton, the energy can be absorbed. That is,when the frequency of the oscillating electric field component of the incoming radiation just matches the frequency of the electric field generated by the precessing nu- cleus,the two fields can couple,and energy can be transferred from the incoming radiation to the nu- cleus, thus causing a spin change. This condition is called resonance, and the nucleus is said to have resonance with the incoming electromagnetic wave. Figure 3.8 schematically illustrates the reso- nance process.

**Why do chemically distinct nuclei absorb energy at different frequencies?**

 In the spectrum you see above, each line represents a different kind of carbon atom: each one absorbs energy (or resonates—hence the term nuclear magnetic resonance) at a different frequency. But why should carbon atoms be ‘different’? We have told you two factors that affect the energy difference (and therefore the frequency)—the magnetic ﬁeld strength and what sort of nucleus is being studied. So you might expect all carbon-13 nuclei to resonate at one particular frequency and all protons (1H) to resonate at one (different) frequency. But they don’t.

Actually the energy (or frequency) required to flip any nucleus from one (alpha) state to other (Beta) depends upon the difference in energy of the two states. This difference is due to the reason that different nuclei of different carbon atoms experience a magnetic ﬁeld that is not quite the same as the magnetic ﬁeld that we apply. Each nucleus is surrounded by electrons, and in a magnetic ﬁeld these will set up a tiny electric current. This current will set up its own magnetic ﬁeld (rather like the magnetic ﬁeld set up by the electrons of an electric current moving through a coil of wire or solenoid), which will oppose the magnetic ﬁeld that we apply. The electrons are said to shield the nucleus from the external magnetic ﬁeld. If the electron distribution varies from 13C atom to 13C atom, so does the local magnetic ﬁeld, and so does the resonating frequency of the 13C nuclei. This variation in frequency is known as the chemical shift. Its symbol is δ.



It means that NMR tells us about the chemistry of a molecule as well as about its structure.

As an example, consider ethanol, CH3CH2OH. The carbon attached to the OH group will have relatively fewer electrons around it compared to the other carbon since the oxygen atom is more electronegative and draws electrons towards it, away from the carbon atom. The magnetic ﬁeld that this (red) carbon nucleus feels will therefore be slightly greater than that felt by the (green) carbon with more electrons since the red carbon is less shielded from the applied external magnetic ﬁeld—in other words it is deshielded. Since the carbon attached to the oxygen feels a stronger magnetic ﬁeld, there will be a greater energy difference between the two alignments of its nucleus. The greater the energy difference, the higher the resonant frequency. So for ethanol we would expect the red carbon with the OH group attached to resonate at a higher frequency than the green carbon, and indeed this is exactly what the 13C NMR spectrum shows.

The chemical shift scale

When you look at an NMR spectrum you will see that the scale does not appear to be in magnetic ﬁeld units, nor in frequency units, but in ‘parts per million’ (p.p.m.). There is an excellent reason for this and we need to explain it. The exact frequency at which the nucleus resonates depends on the external applied magnetic ﬁeld. This means that, if the sample is run on a machine with a different magnetic ﬁeld, it will resonate at a different frequency. It would make life very difﬁcult if we couldn’t say exactly where our signal was, so we say how far it is from some reference sample, as a fraction of the operating frequency of the machine. We know that all protons resonate at approximately the same frequency in a given magnetic ﬁeld and that the exact frequency depends on what sort of chemical environment it is in, which in turn depends on its electrons. This approximate frequency is the operating frequency of the machine and simply depends on the strength of the magnet—the stronger the magnet, the larger the operating frequency. The precise value of the operating frequency is simply the frequency at which a standard reference sample resonates. In everyday use, rather than actually referring to the strength of the magnet in tesla, chemists usually just refer to its operating frequency. A 9.4 T NMR machine is referred to as a 400 MHz spectrometer since that is the frequency in this strength ﬁeld at which the protons in the reference sample resonate; other nuclei, for example 13C, would resonate at a different frequency, but the strength is arbitrarily quoted in terms of the proton operating frequency.

The reference sample—tetramethylsilane, TMS

The compound we use as a reference sample is usually tetramethylsilane, TMS. This is silane (SiH4) with each of the hydrogen atoms replaced by methyl groups to give Si(CH3)4. The four carbon atoms attached to silicon are all equivalent and, because silicon is more electropositive than carbon, are fairly electron-rich (or shielded), which means they resonate at a frequency a little less than that of most organic compounds. This is useful because it means our reference sample is not bang in the middle of our spectrum! The chemical shift, δ, in parts per million (p.p.m.) of a given nucleus in our sample is deﬁned in terms of the resonance frequency as:

δ= Frequency (Hertz) - frequency TMS (Hz)/frequency TMS (MHz)

No matter what the operating frequency (i.e. strength of the magnet) of the NMR machine, the signals in a given sample (e.g. ethanol) will always occur at the same chemical shifts. In ethanol the (red) carbon attached to the OH resonates at 57.8 p.p.m. whilst the (green) carbon of the methyl group resonates at 18.2 p.p.m. Notice that by deﬁnition TMS itself resonates at 0 p.p.m. The carbon nuclei in most organic compounds resonate at greater chemical shifts, normally between 0 and 200 p.p.m. Now, let’s return to the sample spectrum you saw on p. 000 and which is reproduced below, and you can see the features we have discussed. This is a 100 MHz spectrum; the horizontal axis is actually frequency but is usually quoted in p.p.m. of the ﬁeld of the magnet, so each unit is one p.p.m. of 100 MHz, that is, 100 Hz. We can tell immediately from the three peaks at 176.8, 66.0, and 19.9 p.p.m. that there are three different types of carbon atom in the molecule.

Regions of 13C Spectra

On the basis of chemical environment faced by the car- bon atoms, All 13C spectra can be divided into four major regions: saturated carbon atoms (0–50 p.p.m.), saturated carbon atoms next to oxygen (50–100 p.p.m.), unsaturated carbon atoms (100–150 p.p.m.), and unsaturated carbon atoms next to oxygen, i.e. C=O groups (150–200 p.p.m.).

The spectrum you just saw is in fact of lactic acid (2-hydroxypropanoic acid). When you turned the last page, you made some lactic acid from glucose in the muscles of your arm—it is the break- down product from glucose when you do anaerobic exercise. Each of lactic acid’s carbon atoms gives a peak in a different region of the spectrum.



Different ways of describing chemical shift

The chemical shift scale runs to the left from zero (where TMS resonates)—i.e. backwards from the usual style. Chemical shift values around zero are obviously small but are confusingly called ‘high ﬁeld’ because this is the high magnetic ﬁeld end of the scale. NMR spectra were originally recorded by varying the applied ﬁeld. They are now recorded by variation of the frequency of the radio waves and that is done by a pulse of radiation. The terms ‘high and low ﬁeld’ are memories from the days of scanning by ﬁeld variation. Alternatively, use ‘upﬁeld’ for high ﬁeld (small δ) and ‘downﬁeld’ for low ﬁeld (large δ). One helpful description we have already used is shielding. Each carbon nucleus is surrounded by electrons that shield the nucleus from the applied ﬁeld. Simple saturated carbon nuclei are the most shielded: they have small chemical shifts (0–50 p.p.m.) and resonate at high ﬁeld. One electro- negative oxygen atom moves the chemical shift downﬁeld into the 50–100 p.p.m. region. The nucleus has become deshielded. Unsaturated carbon atoms experience even less shielding (100–150 p.p.m.) because of the way in which electrons are distributed around the nucleus. If the π bond is to oxygen, then the nucleus is even more deshielded and moves to the largest chemical shifts around 200 p.p.m.

A guided tour of NMR spectra of simple molecules

We shall ﬁrst look at NMR spectra of a few simple compounds before looking at unknown structures. Our very ﬁrst compound, hexanedioic acid, has the simple NMR spectrum shown here. The ﬁrst question is: why only three peaks for six carbon atoms? Because of the symmetry of the molecule, the two carboxylic acids are identical and give one peak at 174.2 p.p.m. By the same token C2 and C5 are identical while C3 and C4 are identical. These are all in the saturated region 0–50 p.p.m. but it is likely that the carbons next to the electron-withdrawing CO2H group are more deshielded than the others. So we assign C2/C5 to the peak at 33.2 p.p.m. and C3/C4 to 24.0 p.p.m.

The bee alarm pheromone (heptan-2-one) has no symmetry so all its seven carbon atoms are differ- ent. The carbonyl group is easy to identify (208.8p.p.m., highlighted in red) but the rest are more difﬁ- cult. Probably the two carbon atoms next to the carbonyl group come at lowest ﬁeld, while C7 is certainly at highest ﬁeld (13.9p.p.m.). It is important that there are the right number of signals at about the right chemical shift. If that is so, we are not worried if we cannot assign each frequency to a precise carbon atom.

You met BHT on p. 000: its formula is C15H24O and the ﬁrst surprise in its NMR spectrum is that there are only seven signals for the 15 carbon atoms. There is obviously a lot of symmetry; in fact the molecule has a plane of symmetry vertically as it is drawn here. The very strong signal at δ = 30.4 p.p.m. belongs to the six identical methyl groups on the t-butyl groups and the other two signals in the 0–50 p.p.m. range are the methyl group at C4 and the central carbons of the t-butyl groups. In the aromatic region there are only four signals as the two halves of the molecule are the same. As with the last example, we are not concerned with exactly which is which; we just check that there are the right number of signals with the right chemical shifts.

Paracetamol is a familiar painkiller with a simple structure—it too is a phenol but in addition it has an amide on the benzene ring. Its NMR spectrum contains one saturated carbon atom at 24 p.p.m. (the methyl group of the amide side chain), one carbonyl group at 168 p.p.m., and four other peaks at 115, 122, 132, and 153 p.p.m. These are the carbons of the benzene ring. Why four peaks? The two sides of the benzene ring are the same because the NHCO·CH3 side chain can rotate rapidly so that C2 and C6 are the same and C3 and C5 are the same. Why is one of these aromatic peaks in the C=O region at 153 p.p.m.? This must be C4 as it is bonded to oxygen, and it just reminds us that carbonyl groups are not the only unsaturated carbon atoms bonded to oxygen (see the chart on p. 000), though it is not as deshielded as the true C=O group at 168 p.p.m.

The effects of deshielding within the saturated carbon region

We have mentioned deshielding several times. The reference compound TMS (Me4Si) has very shielded carbon atoms because silicon is more electropositive than carbon. Oxygen moves a saturat- ed carbon atom downﬁeld to larger chemical shifts (50–100 p.p.m.) because it is much more elec- tronegativethan carbon and so pulls electrons away from a carbon atom by polarizing the C–O bond. In between these extremes was a CO2H group that moved its adjacent carbon down to around 35 p.p.m. These variations in chemical shift within each of the 50 p.p.m. regions of the spectrum are a helpful guide to structure as the principle is simple.

Electronegativeatoms move adjacent carbon atoms downﬁeld (to largerδ)by deshielding.

For the carbon atom next to the carboxylic acid, the oxygen atoms are, of course, no longer adjacent but one atom further away, so their deshielding effect is not as great.

The reverse is true too: electropositive atoms move adjacent carbon atoms upﬁeld by shielding. This is not so important as there are few atoms found in organic molecules that are more electropositive than silicon and so few carbons are more shielded than those in Me4Si. About the only important elements like this are the metals. When a carbon atom is more shielded than those in TMS, it has a negative δ value. There is nothing odd about this—the zero on the NMR scale is an arbitrary point. Table 3.5 shows a selection of chemical shift changes caused to a methyl group by changes in electronegativity.

The last column in Table 3.5 shows the effect that each substituent has when compared to ethane. In ethane there is no electronic effect because the substituent is another methyl group so this column gives an idea of the true shift caused by a substituent. These shifts are roughly additive. Look back at the spectrum of lactic acid on p. 000: the saturated carbons occur at 19.9 and 66.0. The one at 66.0 is next both to an oxygen atom and a carbonyl group so that the combined effect would be about 42 + 22 = 64—not a bad estimate.

NMR is a powerful tool for solving unknown structures

Simple compounds can be quickly distinguished by NMR. These three alcohols of formula C4H10O have quite different NMR spectra.



Each alcohol has a saturated carbon atom next to oxygen, all close togetherin the range of 70 p.p.m. Then there are carbons next door but one to oxygen: they are back in the 0–50 p.p.m. region but at its low ﬁeld end— about 30–35 p.p.m.. In each case we have C–C–O and the effects are about the same. Two of the alcohols have carbon(s) one further away still at yet smaller chemical shift (further upﬁeld, more shielded) at about 20 p.p.m., but only the n-butanol has a more remote carbon still at 15.2. The numberand the chemical shiftof the signals identify the molecules very clearly.

A more realistic example would be an unknown molecule of formula C3H6O. There are seven reasonable structures, as shown. Simple symmetry can distinguish structures A, C, and E from the rest as these three have only two types of carbon atom. A more detailed inspection of the spectra makes identiﬁcation easy. The two carbonyl compounds, D and E, each have one peak in the 150–220 p.p.m. region but D has two different saturated carbon atoms while E has only one. The two alkenes, F and G, both have one saturated carbon atom next to oxygen, but F has two normal unsat- urated carbon atoms (100–150 p.p.m.) while the enol ether, G, has one normal alkene and one unsaturated carbon joined to oxygen. The three saturated compounds (A–C) present the greatest problem. The epoxide, B, has two different carbon atoms next to oxygen (50–100 p.p.m.) and one normal saturated carbon atom. The remaining two both have one signal in the 0–50 and one in the 50–100 p.p.m. regions. Only proton NMR (Chapter 11) and, to a certain extent, infrared spec- troscopy (which we will move on to shortly) will distinguish them reliably. Here are NMR spectra of three of these molecules. Before looking at the solutions, cover up the rest of the page and see if you can assign them to the structures above. Try also to suggest which sig- nals belong to which carbon atoms.

These shouldn’t give you too much trouble. The only carbonyl compound with two identical car- bons is acetone, Me2CO (E) so spectrum 3 must be that one. Notice the very low ﬁeld C=O signal (206.6 p.p.m.) typical of a simple ketone. Spectrum 1 has two unsaturated carbons and a saturated carbon next to oxygen so it must be F or G. In fact it has to be F as both unsaturated carbons are sim- ilar (137 and 116 p.p.m.) and neither is next to oxygen (>150 p.p.m., cf. 206.6 in spectrum 3). This leaves spectrum 2, which appears to have no carbon atoms next to oxygen as all chemical shifts are less than 50 p.p.m. No compound ﬁts that description (impossible for C3H6O anyway!) and the two signals at 48.0 and 48.2 p.p.m. are suspiciously close to the borderline. They are, of course, next to oxygen and this is compound B.

**1H NMR**

The differences between carbon and proton NMR

Although Proton (1H) NMR is more complicated than 13C NMR, still we have to confess that 1H NMR is the beautiful and powerful technique. Proton NMR differs from 13C NMR in a number of ways.

• 1H is the major isotope of hydrogen (99.985% natural abundance), while 13C is only a minor isotope (1.1%)

• 1H NMR is quantitative: the area under the peak tells us the number of hydrogen nuclei, while 13C NMR may give strong or weak peaks from the same number of 13C nuclei

• Protons interact magnetically (‘couple’) to reveal the connectivity of the structure, while 13C is too rare for coupling between 13C nuclei to be seen

• 1H NMR shifts give a more reliable indication of the local chemistry than that given by 13C spectra

We shall examine each of these points in detail and build up a full understanding of proton NMR spectra. The other spectra remain important, of course. Proton NMR spectra are recorded in the same way as 13C NMR spectra: radio waves are used to study the energy level differences of nuclei, but this time they are 1H and not 13C nuclei. Hydrogen nuclei have a nuclear spin of a half and so have two energy levels: they can be aligned either with or against the applied magnetic ﬁeld. The spectra look much the same: the scale runs from right to left and the zero point is given by the same reference compound though it is the proton resonance of Me4Si rather than the carbon resonance that deﬁnes the zero point. You will notice at once that the scale is much smaller, ranging over only about 10 p.p.m. instead of the 200 p.p.m. needed for carbon. This is because the variation in the chemical shift is a measure of the shielding of the nucleus by the electrons around it. There is inevitably less change possible in the distribution of two electrons around a hydrogen nucleus than in that of the eight valence electrons around a carbon nucleus. Here is a simple 1H NMR spectrum. This 10 p.p.m. scale is not the same as any part of the 13C NMR spectrum. It is at a different frequency altogether.

Integration tells us the number of hydrogen atoms in each peak

The chemical shift of the twelve hydrogen atoms of the four identical methyl groups in Me4Si is deﬁned as zero. The methyl group in the acid CH3COOH is next to the carbonyl group and so slightly de- shielded at about δ 2.0 p.p.m. and the acidic proton itself is very deshielded at δ 11.2 p.p.m. The same factor that makes this proton acidic—the O–H bond is polarized towards oxygen—also makes it resonate at low ﬁeld. So far things are much the same as in carbon NMR. Now for a difference. Notice that the ratio of the peak heights in this spectrum was about 3:1 and that that is also the ratio of the number of protons. In fact, it’s not the peak height but the area under the peaks that is exactly proportional to the number of protons. Proton spectra are normally integrated, that is, the area under the peaks is computed and recorded as a line with steps corresponding to the area, like this.

Simply measuring the height of the steps with a ruler gives you the ratio of the numbers of protons represented by each peak. Knowing the atomic composition from the mass spectrum, we also know the distribution of protons of various kinds. Here the heights are 0.75 and 2.25 cm, a ratio of about 1:3. The compound is C2H4O2SO, since there are 4 H atoms altogether, the peaks must contain 1 ×H and 3 × H, respectively. In the spectrum of 1,4-dimethoxybenzene, there are just two signals in the ratio of 3:2. This time the compound is C8H10O2 so the true ratio must be 6:4. Assigning the spectrum requires the same attention to symmetry as in the case of 13C spectra.

In this next example it is easy to assign the spectrum simply by measuring the steps in the integral. There are two identical methyl groups (CMe2) having 6 Hs, one methyl group by itself having 3 Hs, the OH proton (1 H), the CH2 group next to the OH (2 Hs), and ﬁnally the CH2CH2 group between the oxygen atoms in the ring (4 Hs).

Proton NMR spectra are generally recorded in solution in deuterochloroform (CDCl3)—that is, chloroform with the 1H replaced by 2H. The proportionality of the size of the peak to the number of protons tells you why: if you ran a spectrum in CHCl3, you would see a vast peak for all the solvent Hs because there would be much more solvent than the compound you wanted to look at. Using CDCl3 cuts out all extraneous protons.

Regions ofthe proton NMR spectrum

The integration gives useful—indeed essential—information, but it is much more important to understand the reasons for the exact chemical shift of the different types of proton. In the last example you can see one marked similarity to carbon spectra: protons on saturated carbon atoms next to oxygen are shifted downﬁeld to larger δvalues (here 3.3 and 3.9 p.p.m.). The other regions of the proton NMR spectrum are also quite similar in general outline to those of 13C spectra. Here they are.

protons on unsaturated carbons next to oxygen: aldehydes 8.5-10.5 p.p.m

protons on unsaturated carbons: benzene, aromatic hydrocarbons 6.5-8.5 p.p.m

protons on unsaturated carbons: alkenes 4.5-6.5 p.p.m

saturated CH3 CH2 CH next to Oxygen 3.0-4.5 p.p.m

CH2 CH3 saturated CH 0.0-3.0 p.p.m

These regions hold for protons attached to C:

protons attached to O or N can come almost any- where on the spectrum. Even for C–H signals, the regions are approximate and overlap quite a lot. You should use the chart as a basic guide, but you will need a more detailed understanding of proton chemical shifts than you did for 13C chemical shifts.

Protons on saturated carbon atoms Chemical shifts are related to the electronegativity of substituents We shall start with protons on saturated carbon atoms. If you study Table 11.1 you will see that the protons in a methyl group are shifted more and more as the atom attached to them gets more electro- negative. When we are dealing with simple atoms as substituents, these effects are straightfor- ward and more or less additive. If we go on adding electronegative chlorine atoms to a carbon atom, electron density is progres- sively removed from it and the carbon nucleus and the hydrogen atoms attached to it are progressively deshielded.

Protons on saturated carbon atoms

Chemical shifts are related to the electronegativity of substituents

Rule is same as with 13C NMR. The Protons in a methyl group are shifted more and more towards downfield as the atom attached to them gets more electro- negative. When we are dealing with simple atoms as substituents, these effects are straight for- ward and more or less additive. If we go on adding electronegative chlorine atoms to a carbon atom, electron density is progressively removed from it and the carbon nucleus and the hydrogen atoms attached to it are progressively deshielded, hence shifted downfield.

Proton chemical shifts tell us about chemistry

The truth is that shifts and electronegativity are not perfectly correlated. The key property is indeed electron withdrawal but it is the electron-withdrawing power of the whole substituent in comparison with the carbon and hydrogen atoms in the CH skeleton that matters. Methyl groups joined to the same element, say, nitrogen, may have very different shifts if the substituent is an amino group (CH3–NH2 has δH for the CH3 group = 2.41 p.p.m.) or a nitro group (CH3–NO2 has δH 4.33 p.p.m.). A nitro group is much more electron-withdrawing than an amino group. What we need is a quick guide rather than some detailed correlations, and the simplest is this: all functional groups except very electron-withdrawing ones shift methyl groups from 1 p.p.m. (where you ﬁnd them if they are not attached to a functional group) downﬁeld to about 2 p.p.m. Very electron-withdrawing groups shift methyl groups to about 3 p.p.m.

Methyl groups give us information about the structure of molecules

It sounds rather unlikely that the humble methyl group could tell us much that is important about molecular structure—but just you wait. We shall look at four simple compounds and their NMR spectra— just the methyl groups, that is. The ﬁrst two are the acid chlorides below.



 The ﬁrst compound shows just one methyl signal containing 9 Hs at δH 1.10 p.p.m.. This tells us two things. All the protons in each methyl group are the same; and all three methyl groups in the tertiary butyl (t-butyl, or Me3C–) group are the same. This is because rotation about C–C single bonds, both about the CH3–C bond and about the (CH3)3C–C bond, is fast. Though at any one instant the hydrogen atoms in one methyl group, or the methyl groups in the t-butyl group, may differ, on aver- age they are the same. The time-averaging process is fast rotation about a σ bond.

The second com- pound shows two 3H signals, one at 1.99 and one at 2.17 p.p.m. Now rotation is slow—indeed the C=C double bond does not rotate at all and so the two methyl groups are different. One is on the same side of the alkene as (or ‘cis to’) the –COCl group while the other is on the opposite side (or ‘trans’).

The second pair of compounds contain the CHO group. One is a simple aldehyde, the other an amide of formic acid: it is DMF, dimethylformamide. The ﬁrst has two sorts of methyl group: a 3H signal at δH 1.81 p.p.m. for the SMe group and a 6H signal for the CMe2 group. The two methyl groups in the 6H signal are the same, again because of fast rotation about a C–C σ bond.

 

The second compound also has two methyl signals, at 2.89 and 2.98 p.p.m., each 3H, and these are the two methyl groups on nitrogen. Restricted rotation about the N–CO bond must be making the two Me groups different. You will remember from Chapter 7 (p. 000) that the N–CO amide bond has considerable double bond character because of conjugation: the lone pair electrons on nitrogen are delocalized into the carbonyl group.