CHEM 403: SpectroscopyII L2 P1 T0 (2 Credits)

This is an advanced course of physical methods of measuring physical phenomenon in chemistry that helps to identify the structure of the compound. Application of UV, IR, NMR spectroscopy and mass spectroscopy to the determination of structures of organic compounds. Prerequisite: CHEM 307

Chapter 1

1.0 Nuclear Magnetic Resonance (NMR)

Pauli provided the basis for the theoretical explanations of NMR spectroscopy. He suggested that certain atomic nuclei have the properties of spin and magnetic moments and therefore, exposure to magnetic field would lead to splitting of their energy levels. Bloch and Purcell demonstrated that nuclei absorb electromagnetic radiation in a strong magnetic field as a result of energy level splitting that is induced by the magnetic field.

Certain nuclei behave like tiny spinning magnetic bar magnets e.g. ^{1}H, ^{13}C, ^{19}F, and ^{31}P. All of the nuclei all have a spin of ½. There are other nuclei that have a spin of zero and therefore give no nuclear resonance signals, e.g., ^{12}C and ^{16}O. When a proton is placed in a uniform magnetic field, it can only take up two positions with respect to the field: (i) a low energy orientation in which the nuclear magnet is aligned with the field (ii) a high energy orientation in which the nuclear magnet is aligned against the field. The transition between the two states can only occur by the absorption of a quantum of suitable electromagnetic radiation of energy *hv* or field strength of the order 10,000 gauss. The energy to flip the nuclear magnet is supplied by the radiofrequency range of the electromagnetic spectrum (in the range 10- 100MHz). A molecular environment influences the absorption of radio frequency radiation by a nucleus in a magnetic field which can be correlated with the molecular structure.

For us to obtain an NMR signal we need to have (i) a radiofrequency transmitter (ii) a homogeneous magnetic field (iii) a radio frequency receiver and a (iv) a unit to sweep the magnetic or frequency field over a small range. Two general types of NMR spectrometers are in use viz; (a) a continuous-wave and pulsed spectrometer and (b) an FT- NMR spectrometer. It is of note that different hydrogen atom in a molecule is in a different environment hence it will resonate when placed in a constant magnetic field at different frequencies. Therefore a field sweeper is needed to sweep the magnetic field to detect these resonances. A schematic diagram of the position of the sample to the basic component of an NMR instrument is shown below. In practice, the field to be monitored in order to bring different proton in different chemical environment to resonance is only ten parts in a million. This implies that the homogeneity of the magnetic field is highly essential. This may be achieved by designing a magnet with a small air gap between the poles and by spinning the sample solution about the vertical axis of the sample tube making field inhomogeneity's perpendicular to the direction of spinning can be averaged out. Once a homogenous magnetic field is obtained in an NMR experiment, a good NMR

spectrum can be obtained. About 1.0 sample size is required dissolved in about 0.5-1.0 ml of solvent ($CDCl_3$) and a tube of about 4 mm filled to 3-7 cm. A standard (few percent, tetramethylsilane) is added to the sample and the spectrum acquired. If the sample size is little (few micrograms), the sample needs to be scanned several times to average out instrumental noise and sample signal added up. The procedure described so far is that of a continuous sweeping of a small range (a small range of the spectrum is excited at a given time) of the magnetic spectrum at constant frequency (continuous wave spectrum). The S/N ratio obtainable with technique will be poor especially when the sample size is small, when dealing with a nucleus with natural low sensitivity ^{13}C (natural abundance is 1.1%) 2and the magnetogyric ratio makes the sensitivity about 10^{-4} of that of ^{1}H signal. To overcome this problem we use FT techniques where a radio frequency is applied at one end of the spectrum as a short powerful pulse that behave like s spread of frequencies. If ΔH is the range of frequency of chemical shift to be monitored in the spectrum, then the pulse length ($t_{p\ sec}$) must be such that $t_p << 1/4\ \Delta$. With 13C tp is of the order of μsec. That is all nuclei will be excited by a single pulse and their magnetization is monitored as they decay back to their equilibrium state. The decay is like complex sine waves which can be interpreted by an FT program on the computer. Several pulse may be obtained and the spectrum added together to obtain good S/N ratio.

1.1 Chemical Shift

Protons in an NMR spectrum resonate at frequency given by equation (1)

$$p = \gamma H/2\pi \quad (1)$$

H is the local field experienced by the proton which will be different from the applied magnetic field H_0 since it will its nucleus will be surround by its electrons. The extent of shielding is given the parameter, σ, and

$$H = H_0(1- \sigma) \quad (2) \text{ therefore}$$

$$p = \gamma H_0(1- \sigma)/2\pi \qquad (3)$$

Equation 3 shows that different proton with different σ values (different chemical environment) can become resonant either by doing a frequency sweep or a constant field sweep. Looking at an NMR spectrum, one cannot tell between a frequency or magnetic sweep spectrum. A complete proton NMR will have been obtained a given compound when equation 3 has been satisfied for every proton in the molecule.

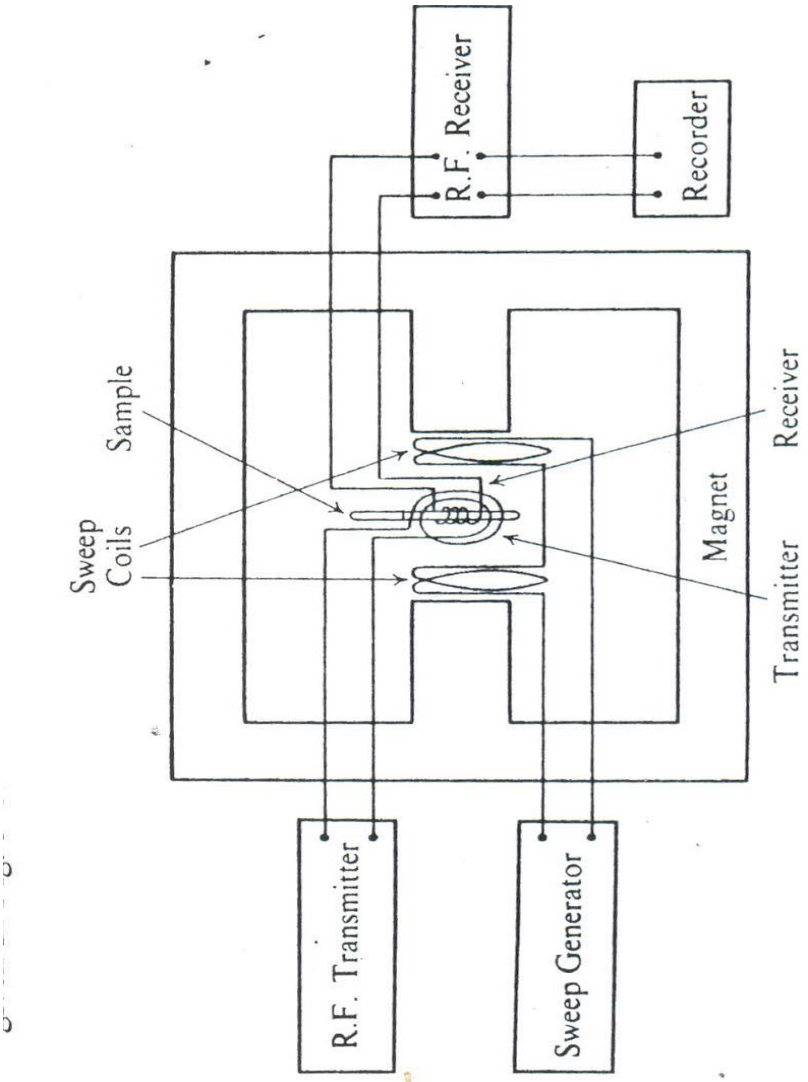


Fig 1.1 Schematic Diagram of an NMR instrument with sample in position

The positions of proton resonances in an NMR spectrum are measured relative to the resonance position of the twelve equivalent protons of an arbitrary reference substance, tetramethylsilane (TMS). The twelve protons of TMS are chemically equivalent and all resonate at the same value of the applied field and therefore give rise to a single line (fig. 1). TMS is a convenient reference substance because: (1) it is a volatile liquid which can be added in trace amount to a sample solution in carbon tetrachloride (CCl_4) or deuterochloroform ($CDCl_3$). Sample can then be easily recovered (2) Protons in the vast majority of organic compounds resonate at lower field than the protons of TMS. Therefore, by arbitrarily assigning $\nu_{TMS}= 0$, we can define a scale such that most proton resonances will be of same sign (positive for convenience) (3) TMS does not interact with the sample. Such interaction will be undesirable since it will modify the electronic environment of the TMS protons and hence change the absolute resonance position of the protons

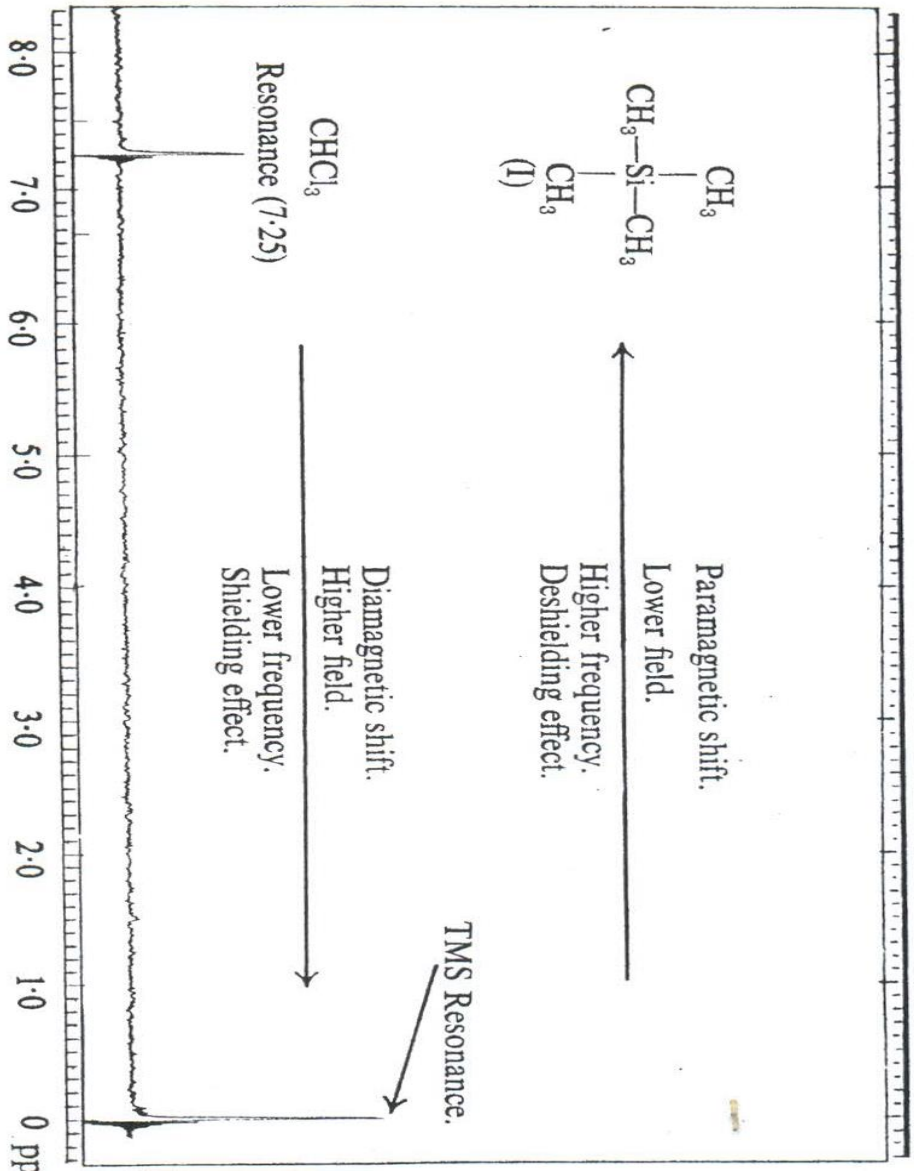


Fig 1.2 TMS NMR Spectrum

The NMR spectrum could be reported in principle as cycles per second (Hz-frequency unit) or milligauss (Field units). In practice, we measure ν_s-ν_{TMS} where ν_s *and* ν_{TMS} are resonances of the sample and the TMS respectively; therefore it is not convenient to express our results in Hz because it is show from eqn. 3 that the frequency of any resonance will be proportional to the applied magnetic field. Since several models of the instrument are available with different field strength, it is good to have a scale that is field-independent unit. A parameter δ (chemical shift parameter) has been derived which is field dependent because the operating frequency of an instrument is directly proportional to the strength of the magnetic field as shown in equation 4.

$$\delta = \nu_s - \nu_{TMS} / \text{operating freq. in MHz}$$

ν_s-ν_{TMS} is in Hz and the denominator is in MHz therefore δ will be in parts per million (ppm). For a field strength of 60 MHz δ = ν_s-ν_{TMS}/60 and ν_{TMS} =0 therefore δ = ν_s/60. Some common terms used in describing the position of the resonance of a proton relative to another or the movement of a peak in a spectrum are shown if Fig7.2.

The following two important points are good to know: (1) The frequency of a particular resonance increases in direct proportion to the increase in the field strength. Therefore we can compare spectrum from different instruments with different field strength (2) In any spectrum which must be determined at either constant frequency or constant field, the frequency increases in the direction of decreasing field strength as shown in Fig.7.2. Deuterated chloroform is good NMR solvent because it does not contain any hydrogen which might obscure regions of the spectrum.

We also use another parameter ζ to describe chemical shift of a proton. ζ = 10- δ ppm.

1.2 Intramolecular Factors Affecting Chemical Shifts

In dilute solutions factors that affect chemical shifts are mostly intramolecular which are divided into three categories: (1) **Inductive Effect**: when an atom is placed in a uniform magnetic field, the electrons surrounding the nucleus are caused to circulate in way that produces a secondary field which is opposed to the applied field in the region of the nucleus. (Fig. 7.3)

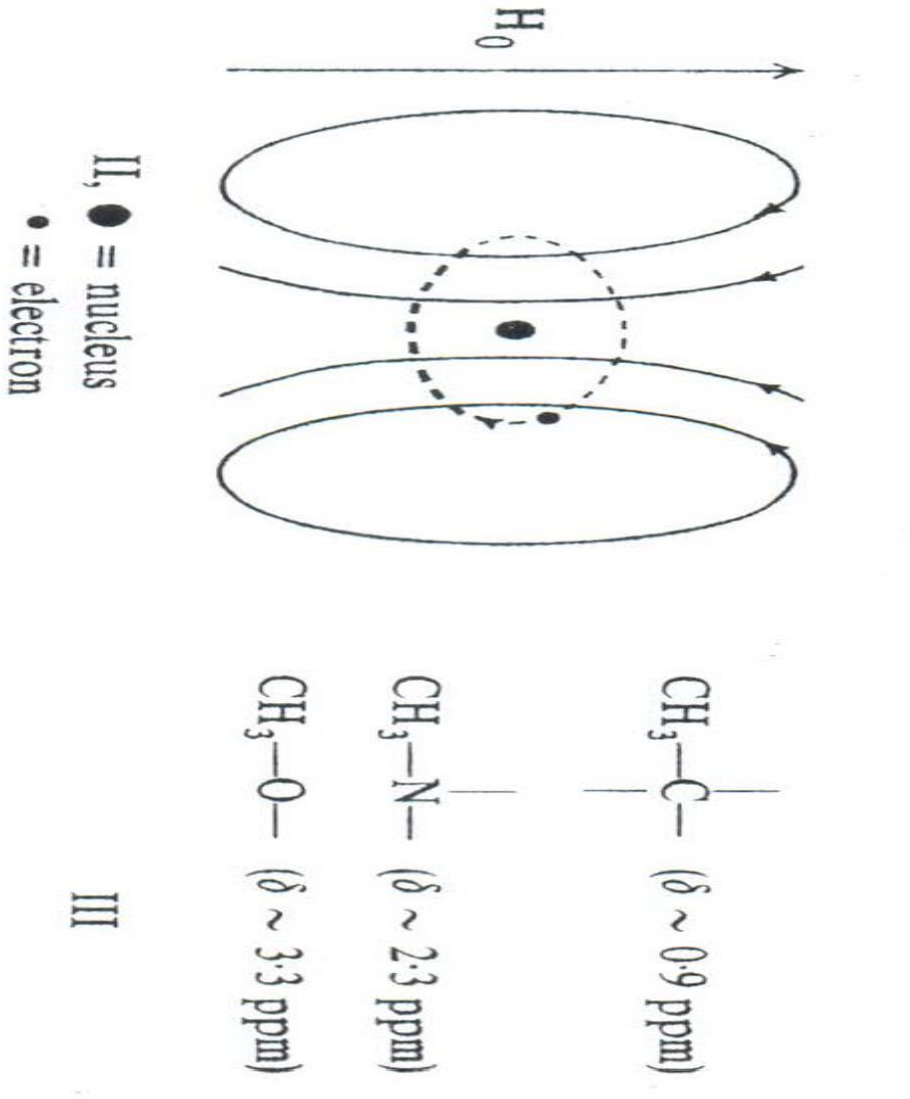


Fig 1.3 Circulation of electrons of an atom placed in an external Magnetic Field

If the electron density around an atom is reduced due to the inductive effect of a nearby electronegative atom, the secondary field will also be reduced with the result that resonance can now occur at lower value of the applied field. Therefore electron withdrawing group will cause the deshielding of a proton. For example the proton of a methyl group attached to O (CH_3-O, δ= 3.3 ppm) resonates at a lower field that one attached to N (CH_3-N, δ = 2.3 ppm) and a (CH_3-C, δ = 0.99 ppm) (2) **Anisotropy of a chemical bond:** The modification of an applied magnetic field in the region of a give structural unit (e.g. a carbonyl group) are both distance (r) and angle (ϕ) dependent. This is so because the applied field will cause circulations of the electrons within a functional group to be more facile in one plane than the other. That is, the circulations are angle dependent and so are the secondary magnetic fields. Thus, chemical bonds are magnetically

anisotropic. The anisotropy of a carbonyl group will cause deshielding of protons lying in a cone extending from the carbonyl oxygen atom or the plane of the trigonal hybrid bonds and shielding of protons lying outside the cone. The deshielding will be the greatest with an aldehyde proton directly bonded to the hybridized carbon atom. Aldehyde proton resonates at extremely lower field, usually in the $\delta = 9.3- 10$ ppm region. Olefinic protons (CH=CH) usually resonate in the $\delta = 4.5- 6.5$ ppm region. The large deshielding is due to the anisotropy of the π- system. Protons lying in the X and Z axes of the π- bond are deshielded by about 1.0 ppm relative to a methylene proton in a saturated aliphatic chain. Protons attached to a ring system that can sustain a ring current suffer paramagnetic shift relative to Olefinic protons of isolated double bonds. O example, benzene protons resonate at $\delta = 6.5- 8.0$ ppm region. This is caused by additional deshielding of the benzene protons because when a benzene nucleus is placed in a uniform magnetic field (Ho), the π- electrons are made to circulate in opposite direction to the applied field and perpendicular to the plane of the ring. The induced secondary reinforces the applied field around the aromatic protons which makes nit to resonate at lower field of the applied field. The protons of benzene are chemically equivalent and therefore appear as a six proton singlet ($\delta = 7.3$ ppm). The electron withdrawing substituents like NO_2 will cause deshielding in the order o>p>m because their withdrawing effect is felt more at the o and p- positions then the m-positions while electron donating substituents like NH_2 will cause shielding of the ring protons again in the order o>p>m. This order of deshielding is caused by the a combination of steric, anisotropy and inductive effects. (iii) Van der Walls deshielding Effect: When protons attached to different carbon atoms are brought so close together for van der walls force to have an effect mutual deshielding will occur. The mutual deshielding is in the order of 1.0 ppm or less. Steric hindrance only causes deshielding which often ≤ 1.0 ppm. In conclusion, inductive effects usually lead to paramagnetic shifts. The methyl, methylene and methane protons in many environments cause shifts that are largely due to inductive effects of the electronegative atoms. For any functional group, δ(methyl)< δ(methylene< δ(methane) δ

1.3 Effect of Concentration, Solvent and Temperature.

There is no effect of concentration on chemical shifts of protons attached to carbon between 0.05 -0.5 M range of $ClCD_3$ or CCl_4 the effect of temperature. But there are significant effect of both concentration and temperature on protons attached directly to an electronegative atom (OH, SH, NH). The same is true for solvent effects. For example, The NMR spectrum of acetic acid (CH_3COOH) and H_2O, the hydrogen of the carboxyl group occurs at a lower field than that of water. However, the spectrum of a mixture of both contains only one resonance due to both kinds of protons (the pure COOH and OH in their pure forms). The shift is a linear function of the mole fraction of acetic acid in water and is due to the fact that the OH protons are exchanging very rapidly so that the system only see the proton in a time averaged environment. In some cases, the exchange times may be slow when compared to the transition times between magnetic states, then separate resonances will be observed. Addition of acid to the solution or increase in temperature or a change in solvent may increase the rate of exchange and time averaged

environment will be observed by the system to give single line resonances. In some situations, the mean life times before exchange is comparable with the transition times, a broad line is observed. This is common with NH protons because ^{14}N nucleus has nuclear spins and electric dipole. A proton attached to ^{14}N nucleus has the opportunity of seeing an average of several possible magnetic quantum states. This type of N-H broadening is said to be due to ***quadrupole relaxation***. When a sample is suspected to have OH, SH or NH proton, the sample solution may be shaken with deuterium oxide and the spectrum reacquired. The active hydrogen will be replaced and the resonance will disappear from the NMR spectrum.

1.4 Hydrogen Bonding

When a proton is hydrogen bonded, the effect is to cause a downfield shift relative to the unbonded state. The paramagnetic shift associated with H—bonding sometimes is large and it is common to see the H-bonded of phenols and carboxylic acids to appear at $\delta > 10$ ppm. It is noticed that when ethanol is heated or diluted with CCl_4 its δ will shift upfield because its H-bonding is broken.

1.5 Spin-Spin Coupling

The NMR spectrum of 1, 1, 2-trichloroethane ($Cl\text{-}CH_2CHCl_2$) is shown in Fig7.4 below. The H_b adjacent to two chlorine atoms will resonate at a lower frequency than the H_a attached to carbon with one chlorine attachment because of inductive effect. There is a doublet peak at 3.95 ppm and a triplet at 5.77 ppm.

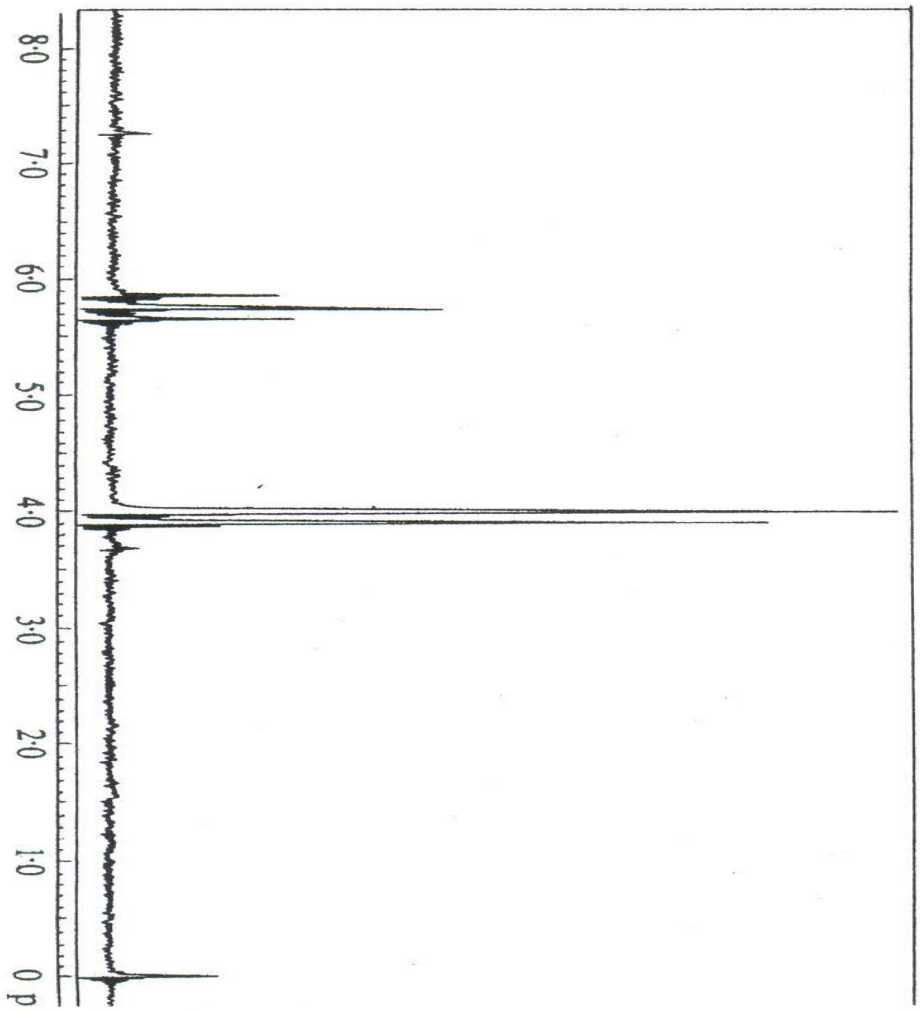


Fig. 1.4 NMR Spectrum of 1,1,2-trichloroethane

The appearance of the triplet and doublet peaks is due to spin-spin coupling of the H on adjacent carbon atoms. If we consider the local field experienced by H_b, the precise value of the field will depend on the orientations the two protons H_a whose nuclear can either be (1) both parallel (2) One parallel and the other antiparallel (3) One antiparallel and the other parallel (4) Both antiparallel. Options 2 and 3 are the same since both hydrogens are equivalent and indistinguishable. Hence, the possible combinations of the nuclear of the two H_a atoms require that proton H_b will experience three slightly different local fields and therefore appear as a triplet with its intensities the same as the ratio of the combinations of H_a atoms (1:2:1). The H_a atoms are chemically equivalent and will not show spin –spin coupling due to interactions among themselves. Hence, their interaction does not result in observable spin-spin splitting. The protons H_a only experience 2 possible orientations of the nuclear magnet of H_b and therefore H_a appears as a doublet. The separation of the lines in the triplet or doublet gives the coupling constant (J) between the H_a and H_b protons. We can then come to a general rule that says (1) if a proton has neighbors, set n_a, n_b, n_c…of chemically equivalent protons, the multiplicity of its

resonance will be $(n_a +1)(n_b +1)(n_c+1)$ (2) For one neighboring group of n equivalent protons, the relative intensities of the n +1 multiplet components are given by the coefficient of the terms in the expansion $(x + 1)^n$. This is the basis of interpreting spin-spin coupling patterns in NMR spectra by the ***first-order approximation***. The first approximation rules holds if the value of δ between interacting protons is large compared with the coupling constant (J). First, large coupling only occurs between germinal (H-C-H) or vicinal (-CH-CH-) protons and secondly J is independent of the applied field whereas the δ (in Hz) is proportional to the applied field. Thirdly, proton- proton coupling occurs through the electrons of the bonds between them. The proximity between them is no reason for spin-spin coupling to occur.

The NMR spectrum of ethanol (CH_3CH_2OH) shows a triplet due to CH_3 protons near the methylene (CH_2) protons with the intensities ratio 1:2:1 $(x+1)^2$, a quartet peak of the CH_2 proton near a CH_3 proton with intensity ratio 1:3:32 $(x+1)^3$ and a singlet due to H of the OH proton. It is evident the OH proton did not couple with the CH_2 proton. The chemical shift of the OH depends on H bonding, chemical exchange and spin-spin coupling between the protons of a CH-OH he bases in the alcohol or using dimethyl sulfoxide as solvent for spectral determination.

In the spectrum of 1-nitropropane ($CH_3CH_2CH_2$-NO_2) in Fig.1.5, the CH_3 and the CH_2 attached to the No_2 group shows a triplet at 1.03 ppm and 4.38 ppm respectively. The CH_2 in the middle is expected to be coupled with the nitro CH_2 to give a triplet which will each be splitted to a quartet by the CH_3 protons resulting into a 12 lines, (3+ 1)(2+1) lines. But in practice J_{ab} and J_{bc} are equivalent hence there will be great overlapping of the lines so what is observed is that the middle CH_2 protons to the first approximation have 5 equivalent neighboring protons which gives a sextet line with a relative intensities corresponding to $(x+1)^5$ i.e. 1:5:10:10:5:1 at 2.07 ppm. The spectrum shows a little perturbation of the sextet line because J_{ab} and J_{bc} are exactly not equivalent, hence, the intensity ratios are not exactly what it should be.

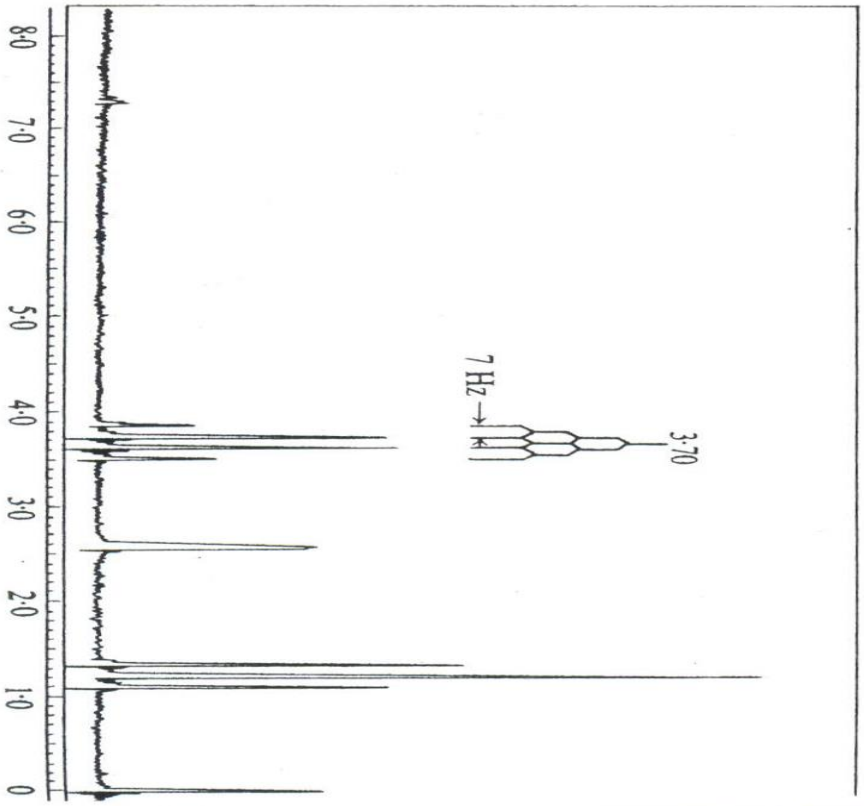


Fig. 1.5 NMR Spectrum of 1-nitropropane.

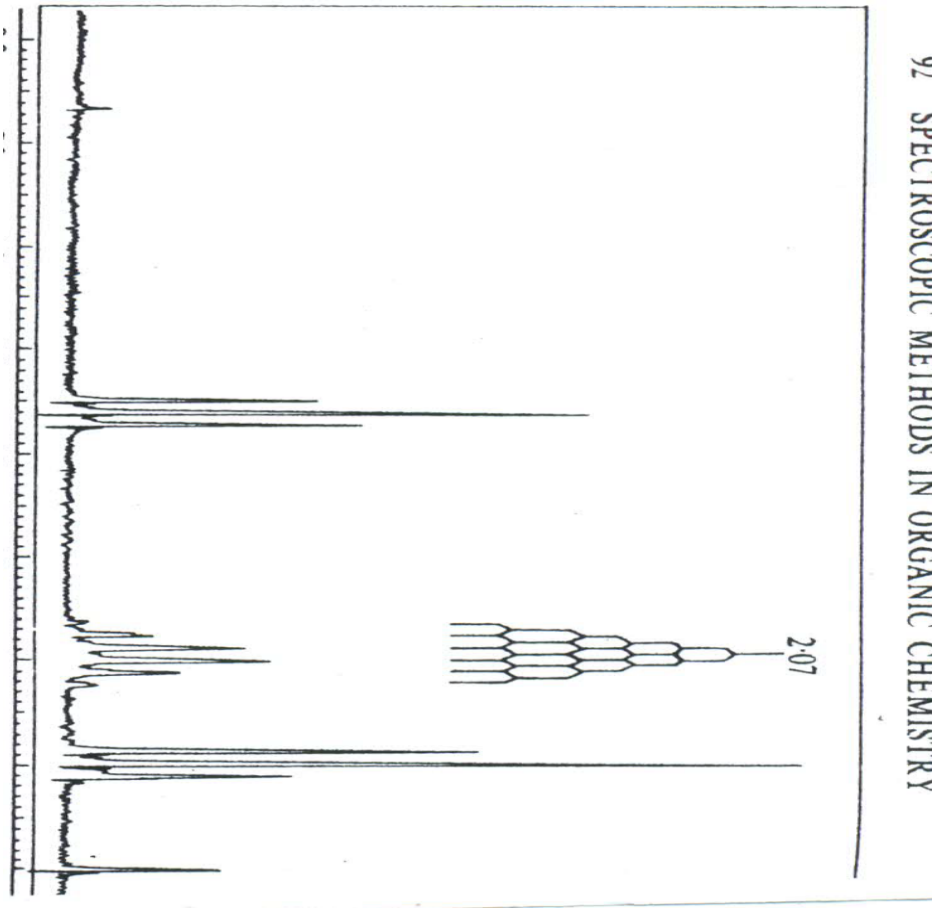


Fig. 1.6 NMR Spectrum of 1-nitropropane.

1.6 Integration

For complicated molecules, it is not possible to manually and accurately estimate the number of protons in the molecule. The spectrum usually is instrumentally integrated. For a given sample run under a given set of conditions, the total area under all peaks assignable to the protons in a particular environment depends on the number of such protons and their relaxation times. The relaxation times dependency can be eliminated by operating the instrument at very low radio frequency power level and hence the various regions of the spectrum will be proportional to the number of protons in the corresponding various chemical environments. The area associated with one proton can be determined by integrating the whole spectrum and dividing the whole area by the number of protons in the molecule under investigation.

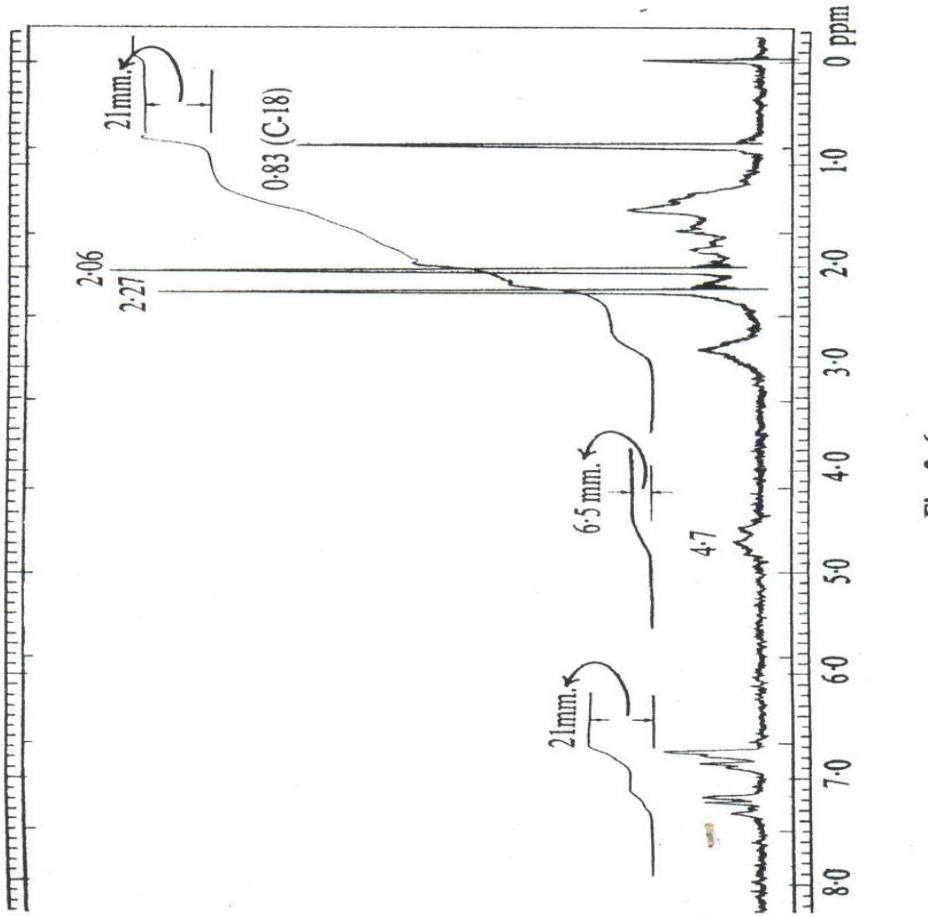
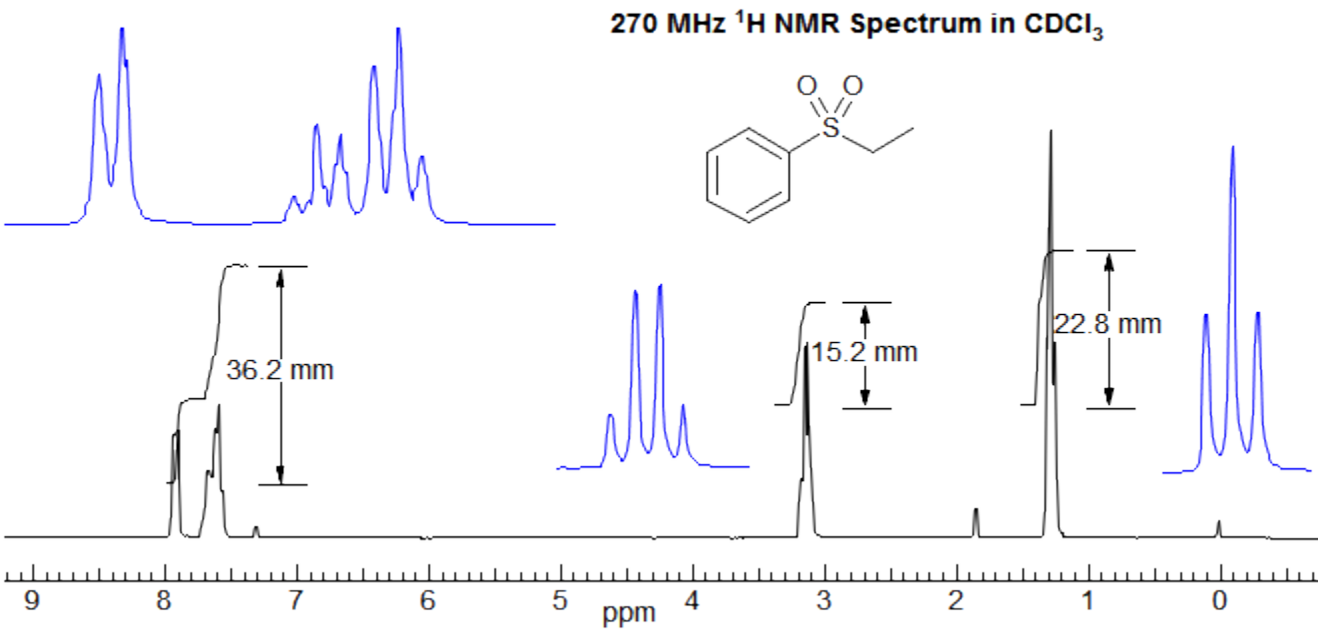


Fig. 1.7 NMR Spectrum of.

NMR is unique among common spectroscopic methods in that signal intensities are directly proportional to the number of nuclei causing the signal (provided certain conditions are met). In other words, all absorption coefficients for a given nucleus are identical. This is why proton NMR spectra are routinely integrated, whereas IR and UV spectra are not. A typical integrated spectrum is shown below, together with an analysis.



The vertical displacement of the integral gives the relative number of protons It is not possible to determine the absolute numbers without additional information (such as a molecular formula). In the example above, if we add up all of the integrals, we get 74.3. Dividing each integral by the smallest one (15.2) gives a ratio of 2.38/1.0/1.50 for the three signals. Multiplying by two gives 4.76/2.0/3.03, which is close to the integral numbers (5/2/3) expected for a pure compound. However, there is nothing in the spectrum that rules out 10/4/6 or higher multiples. If we have a molecular formula (in this case $C_8H_{10}O_2S$), dividing by the number of hydrogens gives 7.4 mm per H. We can then determine the number of protons corresponding to each multiplet by rounding to the nearest integer. It is generally possible to reliably distinguish signals with intensities of 1 to 10 or so, but it becomes progressively harder to make a correct assignment as the number of protons in a multiplet increases beyond 10, because of the inherent inaccuracies in the method.

The two parts of aromatic proton integral at δ 7.6 and 7.9 can be separately measured as a 2:3 ratio of ortho to meta+para protons.

If given the molecular formula ($C_8H_{10}O_2S$), we know there are 10H in molecule

Total area: 36.2 + 15.2 + 22.8 = 74.2 mm

Thus 7.4 mm per H

36.2 / 7.4 = 4.89 i.e. 5H
15.2 / 7.4 = 2.05 i.e. 2H
22.8 / 7.4 = 3.08 i.e. 3H

Carbon-13 nuclear magnetic resonance

From Wikipedia, the free encyclopedia

Carbon-13 nuclear magnetic resonance (most commonly known as **carbon-13 NMR** or **^{13}C NMR** or sometimes simply referred to as **carbon NMR**) is the application of nuclear magnetic resonance (NMR) spectroscopy to carbon. It is analogous to proton NMR (^{1}H NMR) and allows the identification of carbon atoms in an organic molecule just as proton NMR identifies hydrogen atoms. As such ^{13}C NMR is an important tool in chemical structure elucidation in organic chemistry. ^{13}C NMR detects only the ^{13}C isotope of carbon, whose natural abundance is only 1.1%, because the main carbon isotope, ^{12}C, is not detectable by NMR since it has zero net spin.

Contents

Implementation

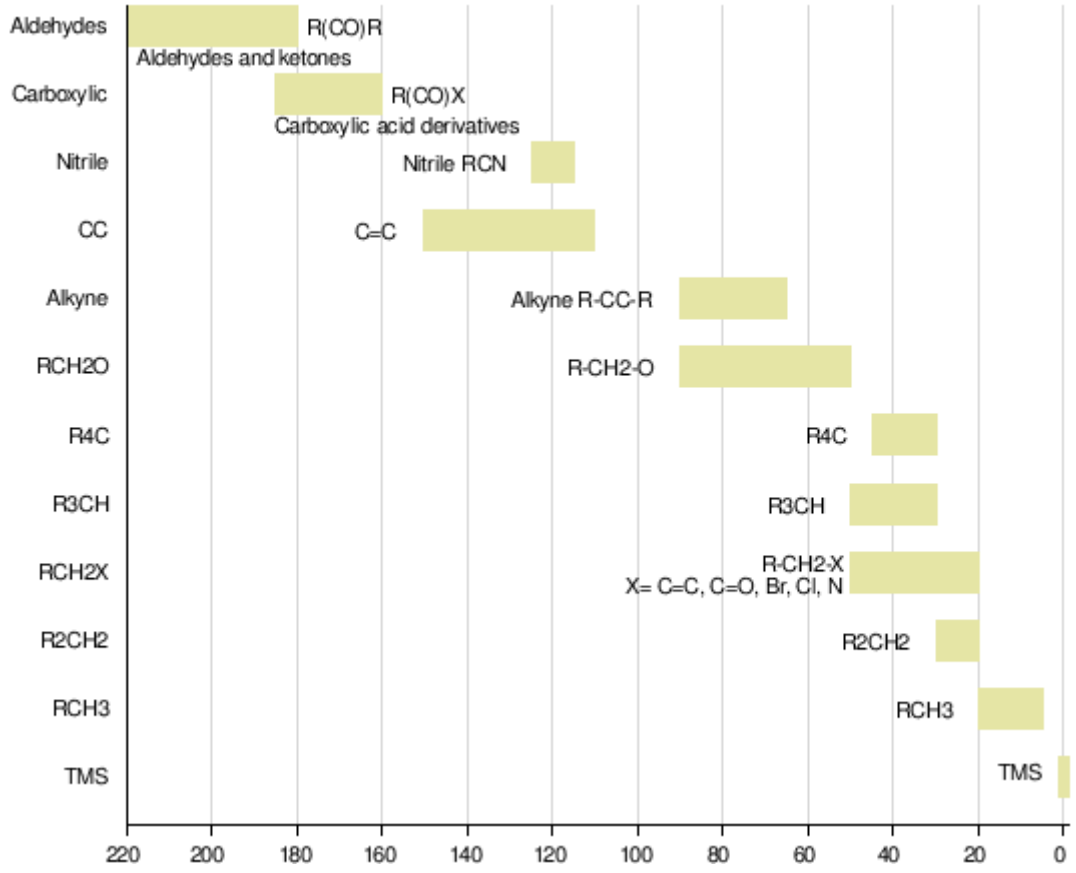
^{13}C NMR has a number of complications that are not encountered in proton NMR. ^{13}C NMR is much less sensitive to carbon than ^{1}H NMR is to hydrogen since the major isotope of carbon, the ^{12}C isotope, has a spin quantum number of zero and so is not magnetically active and therefore not detectable by NMR. Only the much less common ^{13}C isotope, present naturally at 1.1% natural abundance, is magnetically active with a spin quantum number of 1/2 (like ^{1}H) and therefore detectable by NMR. Therefore, only the few ^{13}C nuclei present resonate in the magnetic field, although this can be overcome by isotopic enrichment of e.g. protein samples. In addition, the gyromagnetic ratio (6.728284 10^{7} rad T^{-1} s^{-1}) is only 1/4 that of ^{1}H, further reducing the sensitivity. The overall *receptivity* of ^{13}C is about 4 orders of magnitude lower than ^{1}H.[1]

Another potential complication results from the presence of large one bond J-coupling constants between carbon and hydrogen (typically from 100 to 250 Hz). In order to suppress these couplings, which would otherwise complicate the spectra and further reduce sensitivity, carbon NMR spectra are proton decoupled to remove the signal splitting. Couplings between carbons can be ignored due to the low natural abundance of ^{13}C. Hence in contrast to typical proton NMR spectra which show multiplets for each proton position, carbon NMR spectra show a single peak for each chemically non-equivalent carbon atom.

In further contrast to ^{1}H NMR, the intensities of the signals are not normally proportional to the number of equivalent ^{13}C atoms and are instead strongly dependent on the number of surrounding spins (typically ^{1}H). Spectra can be made more quantitative if necessary by allowing sufficient time for the nuclei to relax between repeat scans.

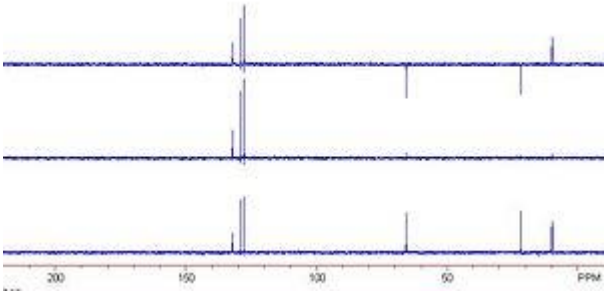
High field magnets with internal bores capable of accepting larger sample tubes (typically 10 mm in diameter for ^{13}C NMR versus 5 mm for ^{1}H NMR), the use of relaxation reagents,[2] for example $Cr(acac)_3$ (chromium (III) acetylacetonate, CAS number 21679-31-2), and appropriate pulse sequences have reduced the time needed to acquire quantitative spectra and have made quantitative carbon-13 NMR a commonly used technique in many industrial labs. Applications range from quantification of drug purity to determination of the composition of high molecular weight synthetic polymers.

^{13}C chemical shifts follow the same principles as those of ^{1}H, although the typical range of chemical shifts is much larger than for ^{1}H (by a factor of about 20). The chemical shift reference standard for ^{13}C is the carbons in tetramethylsilane (TMS), [3] whose chemical shift is considered to be 0.0 ppm.



Typical chemical shifts in ^{13}C-NMR

Distortionless enhancement by polarization transfer spectra



Various DEPT spectra of propyl benzoate
From top to bottom: 135°, 90° and 45°

Distortionless enhancement by polarization transfer (DEPT).[4] is a NMR method used for determining the presence of primary, secondary and tertiary carbon atoms. The DEPT experiment differentiates between CH, CH_2 and CH_3 groups by variation of the selection angle parameter (the tip angle of the final ^1H pulse): 135° angle gives all CH and CH_3 in a phase opposite to CH_2; 90° angle gives only CH groups, the others being suppressed; 45° angle gives all carbons with attached protons (regardless of number) in phase.

Signals from quaternary carbons and other carbons with no attached protons are always absent (due to the lack of attached protons).

The polarization transfer from ^1H to ^{13}C has the secondary advantage of increasing the sensitivity over the normal ^{13}C spectrum (which has a modest enhancement from the nuclear overhauser effect (NOE) due to the ^1H decoupling).

Attached proton test spectra

Another useful way of determining how many protons a carbon in a molecule is bonded to is to use an **attached proton test** (APT), which distinguishes between carbon atoms with even or odd number of attached hydrogens. A proper spin-echo sequence is able to distinguish between S, I_2S and I_1S, I_3S spin systems: the first will appear as positive peaks in the spectrum, while the latter as negative peaks (pointing downwards), while retaining relative simplicity in the spectrum since it is still broadband proton decoupled.

Even though this technique does not distinguish fully between CH_n groups, it is so easy and reliable that it is frequently employed as a first attempt to assign peaks in the spectrum and elucidate the structure.[5] It is sometimes possible that a CH and CH_2 signal have coincidentally equivalent chemical shifts resulting in annulment in the APT spectrum due to the opposite phases. For this reason the conventional $^{13}C\{^1H\}$ spectrum or HSQC are usually also acquired.

References

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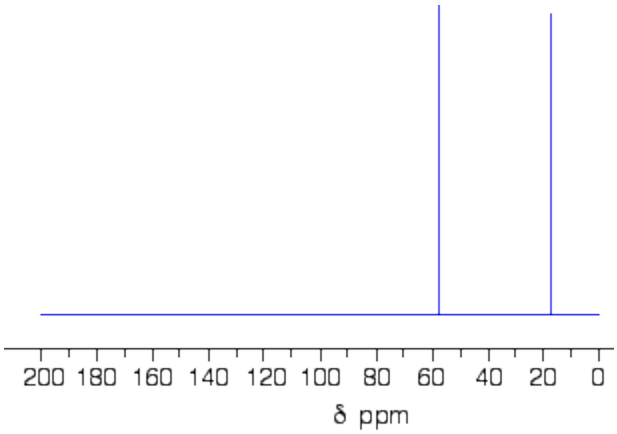
INTERPRETING C-13 NMR SPECTRA?

This page takes an introductory look at how you can get useful information from a C-13 NMR spectrum.

Important: If you have come straight to this page via a search engine, you should be aware that this is the second of two pages about C-13 NMR. Unless you are familiar with C-13 NMR, you should read the introduction to C-13 NMR first by following this link.

Taking a close look at three C-13 NMR spectra

The C-13 NMR spectrum for ethanol



Note: The nmr spectra on this page have been produced from graphs taken from the Spectral Data Base System for Organic Compounds (SDBS) at the National Institute of Materials and Chemical Research in Japan.

It is possible that small errors may have been introduced during the process of converting them for use on this site, but these won't affect the argument in any way.

Remember that each peak identifies a carbon atom in a different environment within the molecule. In this case there are two peaks because there are two different environments for the carbons.

The carbon in the CH_3 group is attached to 3 hydrogens and a carbon. The carbon in the CH_2 group is attached to 2 hydrogens, a carbon and an oxygen.

So which peak is which?

You might remember from the introductory page that the external magnetic field experienced by the carbon nuclei is affected by the electronegativity of the atoms attached to them. The effect of this is that the chemical shift of the carbon increases if you attach an atom like oxygen to it. That means that the peak at about 60 (the larger chemical shift) is due to the CH_2 group because it has a more electronegative atom attached.

Note: In principle, you should be able to work out the fact that the carbon attached to the oxygen will have the larger chemical shift. In practice, given the level I am aiming at (16 - 18 year old chemistry students), you always work from tables of chemical shift values for different groups (see below).

What if you needed to work it out? The electronegative oxygen pulls electrons away from the carbon nucleus leaving it more exposed to any external magnetic field. That means that you will need a smaller external magnetic field to bring the nucleus into the resonance condition than if it was attached to less electronegative things. The smaller the magnetic field needed, the higher the chemical shift.

All this is covered in more detail on the introduction to C-13 NMR page mentioned above.

A table of typical chemical shifts in C-13 NMR spectra

carbon environment	*chemical shift (ppm)*
C=O (in ketones)	*205 - 220*
C=O (in aldehydes)	*190 - 200*
C=O (in acids and esters)	*160 - 185*
C in aromatic rings	*125 - 150*
C=C (in alkenes)	*115 - 140*
RCH_2O-	*50 - 90*
RCH_2Cl	*30 - 60*
RCH_2NH_2	*30 - 65*
R_3CH	*25 - 35*
CH_3CO-	*20 - 50*
R_2CH_2	*16 - 25*
RCH_3	*10 - 15*

Note: I have no confidence in the exact values above. The table is a composite of three separate tables, with values which I have selected in order to make sense of the spectra I am talking about.

The values vary depending on the exact environment of the carbon, and these values should just be taken as an approximation. In an exam, your examiner should give you values which are consistent with the spectra they are asking you about.

In the table, the "R" groups won't necessarily be simple alkyl groups. In each case there will be a carbon atom attached to the one shown in red, but there may well be other things substituted into the "R" group.

If a substituent is very close to the carbon in question, and very electronegative, that might affect the values given in the table

slightly.

For example, ethanol has a peak at about 60 because of the CH_2OH group. No problem!

It also has a peak due to the RCH_3 group. The "R" group this time is CH_2OH. The electron pulling effect of the oxygen atom increases the chemical shift slightly from the one shown in the table to a value of about 18.

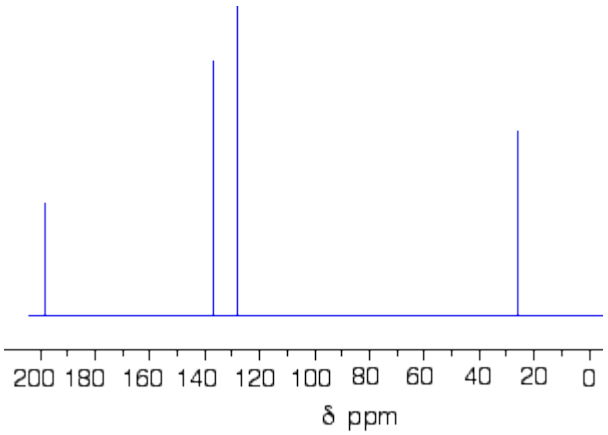
A simplification of the table

You may come across a simplification of the above table which is useful in easy cases just to pick out the main types of carbon environments in a compound:

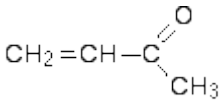
carbon environment	*chemical shift (ppm)*
C-C	*0 - 50*
C-O	*50 - 100*
C=C	*100 - 150*
C=O	*150 - 200*

The C-13 NMR spectrum for but-3-en-2-one

This is also known as 3-buten-2-one (amongst many other things!)



Here is the structure for the compound:



You can pick out all the peaks in this compound using the simplified table above.

The peak at just under 200 is due to a carbon-oxygen double bond. The two peaks at 137 and 129 are due to the carbons at either end of the carbon-carbon double bond. And the peak at 26 is the methyl group which, of course, is joined to the rest of the molecule by a carbon-carbon single bond.

If you want to use the more accurate table, you have to put a bit more thought into it - and, in particular, worry about the values which don't always exactly match those in the table!

The carbon-oxygen double bond in the peak for the ketone group has a slightly lower value than the table suggests for a ketone. There is an interaction between the carbon-oxygen and carbon-carbon double bonds in the molecule which affects the value slightly. This isn't something which we need to look at in detail for the purposes of this topic.

You must be prepared to find small discrepancies of this sort in more complicated molecules - but don't worry about this for exam purposes at this level. Your examiners should give you shift values which exactly match the compound you are given.

The two peaks for the carbons in the carbon-carbon double bond are exactly where they would be expected to be. Notice

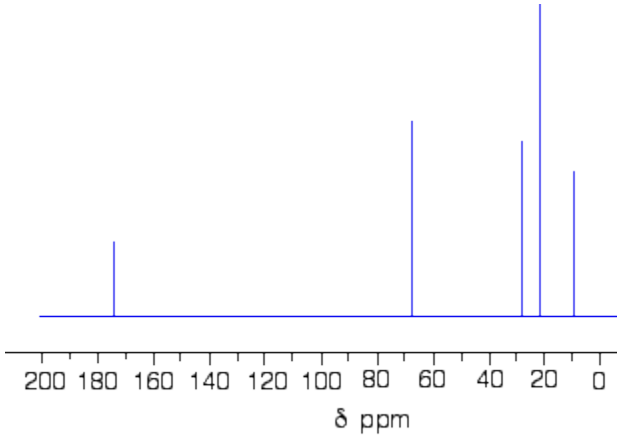
that they aren't in exactly the same environment, and so don't have the same shift values. The one closer to the carbon-oxygen double bond has the larger value.

And the methyl group on the end has exactly the sort of value you would expect for one attached to C=O. The table gives a range of 20 - 50, and that's where it is.

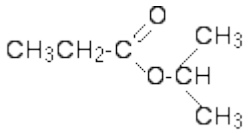
One final important thing to notice. There are four carbons in the molecule and four peaks because they are all in different environments. But they aren't all the same height. In C-13 NMR, you can't draw any simple conclusions from the heights of the various peaks.

The C-13 NMR spectrum for 1-methylethyl propanoate

1-methylethyl propanoate is also known as isopropyl propanoate or isopropyl propionate.



Here is the structure for 1-methylethyl propanoate:

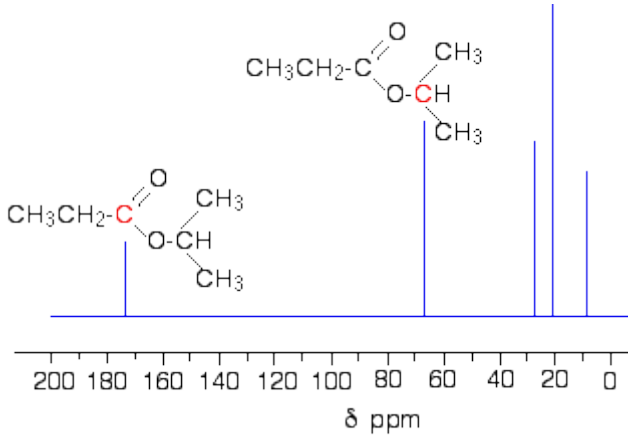


Two simple peaks

There are two very simple peaks in the spectrum which could be identified easily from the second table above.

The peak at 174 is due to a carbon in a carbon-oxygen double bond. (Looking at the more detailed table, this peak is due to the carbon in a carbon-oxygen double bond in an acid or ester.)

The peak at 67 is due to a different carbon singly bonded to an oxygen. Those two peaks are therefore due to:



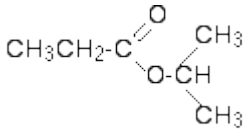
Before we go on to look at the other peaks, notice the heights of these two peaks we've been talking about. They are both due to a single carbon atom in the molecule, and yet they have different heights. Again, you can't read any reliable information directly from peak heights in these spectra.

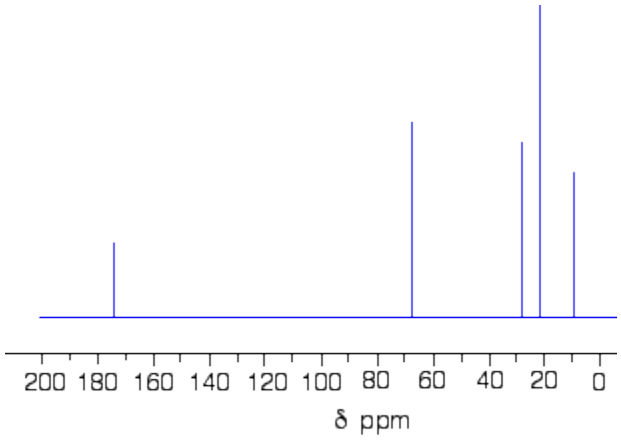
The three right-hand peaks

From the simplified table, all you can say is that these are due to carbons attached to other carbon atoms by single bonds. But because there are three peaks, the carbons must be in three different environments.

The more detailed table is more helpful.

Here are the structure and the spectrum again:





The easiest peak to sort out is the one at 28. If you look back at the table, that could well be a carbon attached to a carbon-oxygen double bond. The table quotes the group as CH_3CO-, *but replacing one of the hydrogens by a simple* CH_3 *group won't make much difference to the shift value.*

The right-hand peak is also fairly easy. This is the left-hand methyl group in the molecule. It is attached to an admittedly complicated R group (the rest of the molecule). It is the bottom value given in the detailed table.

The tall peak at 22 must be due to the two methyl groups at the right-hand end of the molecule - because that's all that's left. These combine to give a single peak because they are both in exactly *the same environment.*

If you are looking at the detailed table, you need to think very carefully which of the environments you should be looking at. Without thinking, it is tempting to go for the R_2CH_2 *with peaks in the 16 - 25 region. But you would be wrong!*

The carbons we are interested in are the ones in the methyl group, not in the R groups. These carbons are again in the environment: RCH_3. *The R is the rest of the molecule.*

The table says that these should have peaks in the range 10 - 15, but our peak is a bit higher. This is because of the presence of the nearby oxygen atom. Its electronegativity is pulling electrons away from the methyl groups - and this tends to increase the chemical shift slightly.

Once again, don't worry about the discrepancies. In an exam, your examiners should give you values which match the peaks

in the spectra.

Remember that you are only doing an introduction to C-13 NMR at this level. It isn't going to be that hard in an exam!

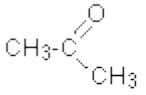
Working out structures from C-13 NMR spectra

So far, we've just been trying to see the relationship between carbons in particular environments in a molecule and the spectrum produced. We've had all the information necessary. Now let's make it a little more difficult - but we'll work from much easier examples!

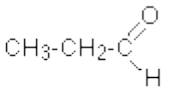
In each example, try to work it out for yourself before you read the explanation.

Example 1

How could you tell from just a quick look at a C-13 NMR spectrum (and without worrying about chemical shifts) whether you had propanone or propanal (assuming those were the only options)?



propanone



propanal

Because these are isomers, each has the same number of carbon atoms, but there is a difference between the environments of the carbons which will make a big impact on the spectra.

In propanone, the two carbons in the methyl groups are in exactly the same environment, and so will produce only a single peak. That means that the propanone spectrum will have only 2 peaks - one for the methyl groups and one for the carbon in the C=O group.

However, in propanal, all the carbons are in completely different environments, and the spectrum will have three peaks.

Example 2

Thare are four alcohols with the molecular formula $C_4H_{10}O$.

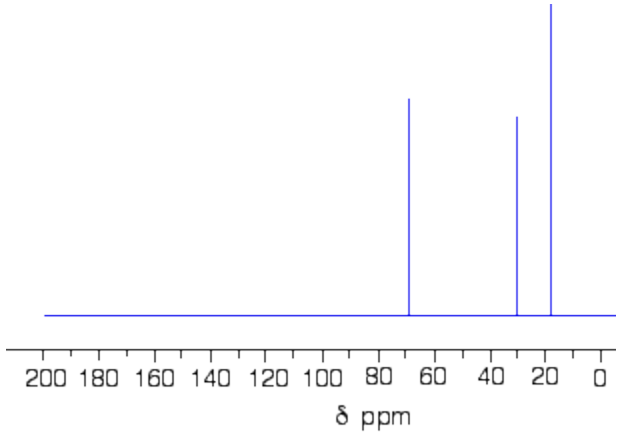
A $CH_3CH_2CH_2CH_2OH$

B $CH_3CH_2CH(OH)CH_3$

C $CH_3CH(CH_3)CH_2OH$

D $CH_3C(CH_3)(OH)CH_3$

Which one produced the C-13 NMR spectrum below?



You can do this perfectly well without referring to chemical shift tables at all.

In the spectrum there are a total of three peaks - that means that there are only three different environments for the carbons, despite there being four carbon atoms.

In A and B, there are four totally different environments. Both of these would produce four peaks.

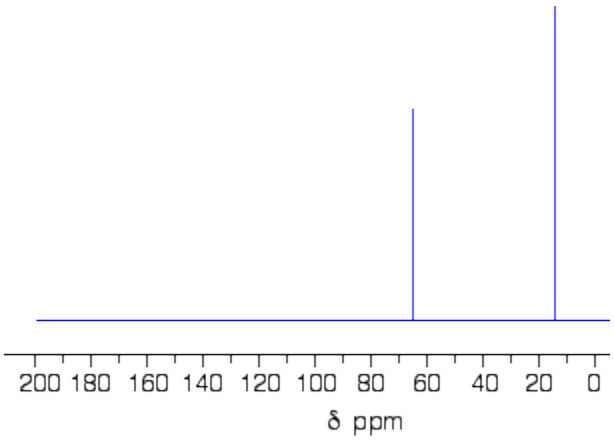
In D, there are only two different environments - all the methyl groups are exactly equivalent. D would only produce two peaks.

That leaves C. Two of the methyl groups are in exactly the same environment - attached to the rest of the molecule in exactly the same way. They would only produce one peak. With the other two carbon atoms, that would make a total of three. The alcohol

is C.

Example 3

This follows on from Example 2, and also involves an isomer of $C_4H_{10}O$ but which isn't an alcohol. Its C-13 NMR spectrum is below. Work out what its structure is.



Because we don't know what sort of structure we are looking at, this time it would be a good idea to look at the shift values. The approximations are perfectly good, and we will work from this table:

carbon environment	*chemical shift (ppm)*
C-C	*0 - 50*
C-O	*50 - 100*
C=C	*100 - 150*
C=O	*150 - 200*

There is a peak for carbon(s) in a carbon-oxygen single bond and one for carbon(s) in a carbon-carbon single bond. That would be consistent with C-C-O in the structure.

It isn't an alcohol (you are told that in the question), and so there must be another carbon on the right-hand side of the oxygen in

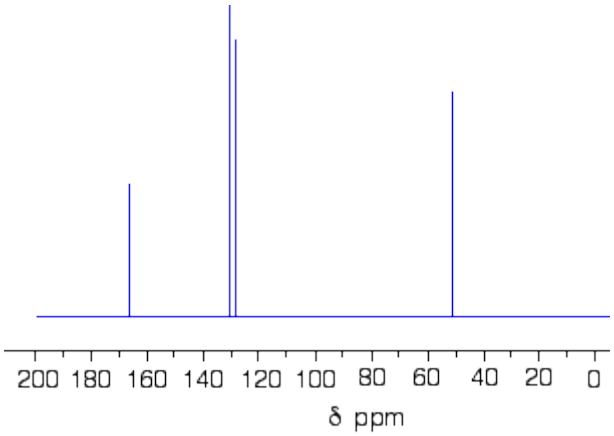
the structure in the last paragraph.

The molecular formula is $C_4H_{10}O$, and there are only two peaks. The only solution to that is to have two identical ethyl groups either side of the oxygen.

The compound is ethoxyethane (diethyl ether), $CH_3CH_2OCH_2CH_3$.

Example 4

Using the simplified table of chemical shifts above, work out the structure of the compound with the following C-13 NMR spectrum. Its molecular formula is $C_4H_6O_2$.

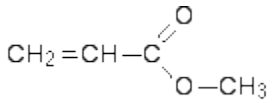


Let's sort out what we've got.

- *There are four peaks and four carbons. No two carbons are in exactly the same environment.*
- *The peak at just over 50 must be a carbon attached to an oxygen by a single bond.*
- *The two peaks around 130 must be the two carbons at either end of a carbon-carbon double bond.*
- *The peak at just less than 170 is the carbon in a carbon-oxygen double bond.*

Putting this together is a matter of playing around with the structures until you have come up with something reasonable. But you can't be sure that you have got the right structure using this simplified table.

In this particular case, the spectrum was for the compound:



If you refer back to the more accurate table of chemical shifts towards the top of the page, you will get some better confirmation of this. The relatively low value of the carbon-oxygen double bond peak suggests an ester or acid rather than an aldehyde or ketone.

It can't be an acid because there has to be a carbon attached to an oxygen by a single bond somewhere - apart from the one in the -COOH group. We've already accounted for that carbon atom from the peak at about 170. If it was *an acid, you would already have used up both oxygens in the structure in the -COOH group.*

Without this information, though, you could probably come up with reasonable alternative structures. If you were working from the simplified table in an exam, your examiners would have to allow any valid alternatives.

2.1 Principles of Mass Spectrometry

Mass spectrometer is an instrument that determines the molecular weight and structure of a compound.

It does so by fragmenting a compound and measuring the mass/charge ratio (m/z) of the fragments ions of the compound. If the molecule is stable, the molecular ion also appears as a fragment ion whose m/z ratio is also measured. There are many types of mass spectrometers using different methods of ionization of the compound, analyzing, collecting and detecting of the fragment ions. The versatility of mass spectrometry is such that it has reached an outstanding position among analytical methods: unequalled sensitivity, detection limits, speed and diversity of applications. It has been applied to various fields that include proteome, metabolome, drug discovery, pollution control, food control, forensic science, natural products, atomic physics, reaction kinetics, inorganic analysis etc.

2.2 Types and Schematics of Mass Spectrometers

There are many types of mass spectrometers that includes: (1) Magnetic sector only- single-focusing (unit resolution) (2) electrostatic field only(3) Magnetic-Electrostatic field- double focusing (high resolution) (4) Quadrupole (5) Ion Cyclotron Resonance (6) Ion Trap and (7)

Orbitrap. All of them based their method of ionization on (i) hard ionization- electron ionization method (i) soft ionization method e.g. chemical ionization. The word electron impact is a misnomer because it is not the impact of the electron on the molecule that causes ionization but the transfer of energy from the electron to the molecule. Typically a mass spectrometer has (1) inlet (2) ionization cell or ion source (3) analyzer (4) detector and (5) read out

2.2.1. Inlets: The inlet is heated and only allows the sample to be introduced into the source of the mass spectrometer. Mass spectrometer has two types of inlet that include (i) a direct infusion (ii) a gas inlet with a hypodermic needle (iii) a direct inlet probe with a matrix

2.2.2 Ion Sources: This is where the sample is vaporized and ionized. Ion sources include the following: (a) Electron Ionization (b) Chemical Ionization (c) Field Ionization and Desorption (d) Fast atom bombardment (e) Laser desorption (f) Plasma desorption (g) Matrix Assisted Laser Desorption Ionization (h) Thermospray (i) electrospray (j) Atmospheric Pressure Chemical Ionization (k) Atmospheric Pressure Photoionization etc.

2.2.3. Analyzers: The analyzer transfer the ions based on their m/z ratio to the collector. It operates under vacuum ($10^{-7} – 10^{-8}$)The mass analyzers include (a) Quadrupole (b) Ion trap (c) Magnetic and electromagnetic (d) Orbitrap or Electrostatic Trap (e) Ion Cyclotron Resonance and Fourier Transform (f) Hybrid e.g. electromagnetic coupled with quadrupole or ion trap

2.2.4. Detectors. The ions from the analyzer are detected and amplified by the electron multiplier. Detectors include (1) Photographic plate (2) Faraday cup (3) Electron multipliers (4) Electro-optical detectors

2.2.5. Readout or Data Processor: The read out integrates it, reduce it, search the library, plot the abundances vs m/z ratio (mass spectrum) and then print the result out. Read out includes (i) plotters and (2) computers and printers

Figure 2.1 Schematics of a Mass Spectrometer

Some mass spectrometers combine the inlet and the ionization source together and others combine the mass analyzer and the detector together.

The initial step in mass spectrometry analysis of compounds is the making of gas phase ions of the compound by bombarding it with electrons of about 70 eV energy at pressures of ~ 10^{-5} torr. The initial electron /molecule interaction produces series of molecular ions with internal energies ranging from 0- 10 eV

$$M + e^- \longrightarrow M^{\cdot +} + 2e^- \quad (1)$$

The energized molecular ions fragment into fragment ions that are seen in the Electron impact (EI) spectrum. The molecular ion fragments because it is a radical cation with an odd number of electrons. It can fragment to give an ion with even number of electrons and a radical or a neutral molecule with a new odd number radical cation. The two ions in equation's 2 and 3 are different and they have different chemical properties. The primary fragment ions can further fragment into smaller ions

$$M^{\cdot +} \longrightarrow EE^+ + \text{radical} \quad (2)$$

$$M^{\cdot +} \longrightarrow OE^{+\cdot} + N \quad (3)$$

The critical energy to fragment some molecular ions of some compounds is very low (zero) which result into no molecular ions seen in their mass spectrum. All these ions are separated by their m/z ratio, detected and recorded as the mass spectrum of the molecule by the mass spectrometer.

The mass spectrum can be recorded as a table or a bar graph of the relative abundance versus the m/z ratio as shown in figure 1.1 and table 1.1 below. The most abundant ion is called the base peak and arbitrarily assigned 100% abundance. The abundance of other peaks in the spectrum are calculated relative to the base peak. Most positive ions have a charge due to loss of an electron but large molecules can lose more than one electron to become multiply charged. The total charge on an ion is represented as q = ze, where z = the number of charges, e = the electron charge (e = 1.6 x 10^{-19} C), m = relative mass, M and z have no unit so m/z is dimensionless

Table 1 The mass spectrum of Methanol

m/z	**Rel. Abundance**	**m/z**	**Rel. Abundance**
12	0.33	28	6.3
13	0.72	29	6.4
14	2.4	30	3.8

15	13	31	100
16	0.21	32	66
17	1.0	33	0.73
18	0.9	34	-0.1

Figure 2.2 Mass spectrum of Methanol

quantity. The highest peak in the mass spectrum of a compound if present is the molecular ion. Isotopic masses always accompany the molecular ion and in the same spectrum of methanol are m/z 15 corresponding to a methyl group due to loss of m/z 17 which is loss of a hydroxyl group. m/z 16 may be due to $CH_4^{\cdot+}$, O^+ or CH_3OH^{2+}. O^+ is on likely to occur and CH_3OH^{2+} will most likely not occur for a small molecule.

The atomic mass units, u or Da (Dalton) = $1.9927 \times 10^{-23}/12 = 1.6606 \times 10^{-27}$ kg

There are different ways to define or calculate the mass of an atom, molecule or ion. For stoichiometric calculations chemist use the **average mass** calculated using atomic weight (weighted average of the atomic masses of all the isotopes of the molecule). In mass spectrometry, the nominal or monoisotonic mass is used. The **nominal mass** is calculated with the integer mass of the most abundance isotope of the molecule rounded up to the nearest integer that corresponds to the mass number. Masses of isotope are not exact whole number due to mass defects of the constituent particles that made up the molecule (e, p, n). The mass defect is equivalent to the binding energy that hold these particles together. **The monoisotonic** mass takes account of the mass defects to calculate the **exact mass** of the most abundant isotope. The type of mass determined by the mass spectrometer depends on the resolution and accuracy of the analyzer. For example, considering CH_3Cl, chlorine has two isotopes with exact masses at 34.968852u and 36.96590u with relative abundances of 75.77% and 24.23% respectively. The average mass of chlorine is (34.968852x0.7577 + 36.96590x0.2423= 35.453 Da). The average mass of CH_3Cl is (12.011 + (3x 1.00794) + +35.453 =50.4878) whereas the monoisotonic mass is (12.000000 + (3 x 1.007825) + 34.968852 =49.992327 Da). When the mass spectrometer is used to measure the mass of CH_3Cl, two isotopic masses at m/z (34.968852 +12.000000 + (3x 1.007825) = 49.992327 Da rounded up to 50) and (36.96590 +12.000000 + (3 x 1.007825) = 51.989365 rounded up to 52 Da) appear in the spectrum with their relative abundances

(24.23/75.77 = 31.98% and 75.77/75.77% respectively). The isotopic contribution of hydrogen is small compared to that of chlorine, so it is neglected in the calculation. For larger molecules, the differences in the type of mass calculated for the molecule may be significantly different. For example the insulin molecule has a molecular formula of $C_{257}H_{383}N_{65}O_{77}S_{6}$. The nominal mass is 5801 Da using the integer mass of its elemental composition (C= 12, H=1, N=14, O=16, S= 32 Da).Its monoisotonic mass is 5803.6375 Da using the exact mass using the predominant isotope of its elements (C = 12, H= 1.0079, N= 14.0031, O = 15.9949, S= 31.9721 Da). The Average mass of 5807.6559 Da using the atomic weight for each element (C= 12.011, H= 1.0078, N= 14.0067, O= 15.9994, S= 32.066 Da)

2.1 Ion Free Path

Because a mass spectrometer operates under high vacuum (low pressure) the fragment ions are free to with no collisions to reach the detector,. Collision will make the ions lose their trajectory and their charge against the wall of the instrument. Also the collision can produce unwanted reaction which will make the mass spectrum more complex. Typical vacuum pressure in a mass spectrometer is 10^{-3} – 10^{-6} Torr. Sample is introduce at atmospheric pressure into a vacuum. Mechanical or turbo pump is used to maintain the vacuum in the spectrometer

In summary, a mass spectrometer should do the following:

1. Produce ions from the sample under high vacuum (low pressure)
1. Separate ions according to their m/z ratio in the first analyzer
2. Fragment the selected ions and analyze the fragmented ions in the second analyzer
3. Detect the ions coming from the analyzers, measure their relative abundances and convert the ions into electric signals
4. Process the electric signals and transmit it to the data processor to produce a mass spectrum
5. Control the instrument through feedback mechanism

2.3 Ionization Techniques

There are two major ionization techniques employed in mass spectrometry: (a) energetic or hard ionization method which fragments sample extensively like electron impact technique and (b) soft ionization which produces only molecular ion like chemical ionization and field desorption technique which are suitable for volatile and thermally stable compounds. Others that are not thermally labile and have sufficient vapor pressure are introduced into the spectrometer by direct insertion (samples in solution or in solid phase (probe or a matrix)). The most important consideration both processes is the amount of internal energy transfer during ionization and the physico-chemical properties of the analyte that can be ionized.

2.3.1 Electron Ionization

Electron ionization or electron impact bombards molecules in the vapor phase with a high energy electron beam (70 eV) and record the result of the electron impact as a spectrum of positive ions separated based on their m/z ratio. A heated filament in the source generates electron which are accelerated towards the anode at 70 eV and collides with the sample molecules injected into the source. The sample absorbs the energy from the electrons and forms the molecular ion which subsequently fragments into smaller ions. Most of these ions are singly charged but some are multiply charged. The highest m/z ion often serves as the molecular ion in samples that are not totally fragmented and is represented as $M^{\cdot+}$. The molecular ion in turn produces fragment ions. The technique works well for gas phase molecules but produce extensive fragmentation so that the molecular ions are not always observed. Resolution of fragment peaks is very important. Resolution can be determined by selection adjacent peaks with less than 10% valley between them. This degree of resolution is called 'unit resolution' and can be obtained for massed approximately 500-2000 Da. The resolution R can be represented as $R= M_n/M_n-M_m$ where M_n is the peak of higher mass and M_m the peak that is one unit less than M_n. Low resolution instruments that separates unit masses up to 2000 and high resolution instruments separates two ions to one tenth of fifteen thousand (R =10000-150000). A typical EI mass spectrum of Benzamide ($C_6H_5CONH_2$) is shown if Figure 2.3 below.

.

Figure 2.3 EI Mass Spectrum of Benzamide

2.3.2 Chemical Ionization Method (C.I)

EI method of ionization produces extensive fragmentation to the extent that the molecular ion might not be observed in its mass spectrum. The chemical ionization technique is a less energetic process that yields spectrum with less fragmentation in which the molecular species are observed. Chemical ionization is complementary to EI method and it produces sample ions by the collision of sample molecules with ions present in the source. The collision ions may be from the reagent gas or the sample itself. This is an example of an ion-molecule reaction process which is obtainable at very low pressures of $10^{-5} – 10^{-6}$ Torr

A typical CI reaction occurs by the equation shown below:

$$R + e \rightarrow R^{\pm} \quad (4)$$

$R^{\pm} + M \rightarrow M^{\pm} + R$ (5)

R = reagent gas, M= Neutral sample molecule

Equation 4 shows the reagent ion being ionized first before reacting with the neutral sample molecules to form the molecular peak in equation 5. The reagent ions are in a larger concentration than the neutral sample concentration in the source of the spectrometer. Chemical reaction can occur by variety of possible ionization reactions. Among them are proton transfers, hydride abstraction, charge transfer, adduct ion formation. These ions are termed ions of molecular species or psuedomolecular ions formed by ion-molecule reactions. The most common of these reactions is the proton transfer as shown below:

$CH_4 + e \rightarrow CH_5^+$

$\searrow C_2H_5^+$ (6)

$M + CH_5^+ \rightarrow MH^+ + CH_4$ (7)

$M + C_2H_5^+ \rightarrow MH^+ C_2H_4$ (8)

$M + C_2H_5^+ \rightarrow [M+ C_2H]^+$ (9)

(M= sample molecule, R= the reagent gas).

This reaction can be described as a Bronstead acid- Bronstead base reaction. Proton transfer could be from the reagent ion or form the sample ion

$M^+ + M \rightarrow MH^+ + [M-H]$ (10)

Common reagent gases used in CI are methane, butane, isobutane, ammonia. Equations 7 and 8 are proton transfer reaction while equation 9 is an adduct formation reaction. Example of a CI spectrum is shown in Figure 2. 4 below

Figure 2.4 CI Mass Spectrum of Butyl Methacrylate

The choice of reagent ions can be tailored towards the problem to be solved. The problems that suits CI techniques include (1) molecular mass determination: Initial ion molecule reaction between electrons and the sample molecule produces array of molecular ions with internal energy ranging from 0-10 eV. The energy to fragment the molecular ion in some compounds is

so low that the molecular ion fragments extensively to the extent that no molecular ion survives the 10^{-5} seconds required before the mass analysis is done under EI condition. The CI method in this case is used to produce characteristic fragment ions and molecular ion for the sample. Proton transfer is the commonly used method in this case (2) structural elucidation: Majority of CI reactions use proton transfer methods to elucidate the structural information of an unknown molecule. Major fragmentation reactions in such cases involve elimination of stable neutral molecules HY where Y is a functional group such as OR, NR_2, halogen etc. present in the molecule (3) identification and quantitation: Chromatography has been coupled with CIMS and it has allowed proper identification and quantitation to be done with CI.

2.4 Other Forms of Chemical Ionization

Proton transfer is not the only CI ion-molecule reaction procedure available. Other types of CI reactions include:

(a) Charge Exchange or Transfer Reaction: $X^{+\cdot} + M \rightarrow M^{+\cdot} + X$
(b) Hydride or Negative ion Transfer reaction: $X^+ + M \rightarrow [M\text{-}H]^+ + XH$
(c) Condensation Reaction: $A^+ B \rightarrow [AB]^* \xrightarrow{M} AB^+ \longrightarrow C^+ + D$
(d) Electron attachment: $e + M \rightarrow M^{\cdot -}$
(e) Adduct, association or cluster formation: $X^{\pm} + M \rightarrow XM^{\pm}$
(f) Associative detachment Reaction: $X^- + N \rightarrow XN + e$

2.5 Uses of Chemical Ionization Mass Spectrometry

Uses of CIMS include: (a) molecular information (2) identification (3) quantitation (4) structural elucidation (5) determination of thermochemical properties like proton affinity, hydride ion affinity, reaction rates and constants, electron affinity, ethalpy