CARBON-13 NMR SPECTROSCOPY

In a 1.9 T field the precession frequency of ^{13}C is 20 MHz, that for ^{1}H being 80 MHz and ^{12}C being nonmagnetic. In principle, therefore, it is not difficult to observe ^{13}C NMR. The magnetic moment of ^{13}C is about one-quarter that of ^{1}H, so that signals are inherently weaker, but the overwhelming problem is that the natural abundance of ^{13}C is only 1.1 per cent. The problem in simple molecules can be overcome by synthesizing ^{13}C-enriched samples, but this is of little value in complex molecules.

3.13 NATURAL ABUNDANCE ^{13}C NMR SPECTRA

In practice, routine 'natural abundance' ^{13}C NMR spectra are recorded by the pulsed FT method discussed in section 3.3.2, with the sensitivity enhanced by summation of several spectra (commonly a few hundreds to several thousands, depending on the solubility of the compound, the amount available and the number of carbon atoms in the molecule).

An example is shown in figure 3.33 of the ^{13}C spectrum of menthol, and for comparison the ^{1}H spectrum of menthol is also shown.

3.13.1 Resolution

Each of the ten lines in the carbon-13 NMR spectrum in figure 3.33 represents one carbon atom of menthol, and two immediate differences from the ^{1}H spectrum are apparent; the ^{13}C spectrum is much simpler, and much more highly resolved.

The chemical shift range in the ^{1}H spectrum is only $\approx$ 4 ppm (320 Hz in this 80 MHz spectrum), while the range in the ^{13}C spectrum is $\approx$ 80 ppm (1600 Hz in this 20 MHz spectrum). Expressed otherwise, the chemical shift differences in the ^{13}C spectrum are about 20 times those shown in the ^{1}H spectrum, and this is typical in all other molecules.

3.13.2 Multiplicity

Both ^{13}C and ^{1}H have $I = \frac{1}{2}$, so that we should expect to see coupling in the spectrum between (a) $^{13}C—^{13}C$ and (b) $^{13}C—^{1}H$. The probability of two ^{13}C atoms being together in the same molecule is so low that $^{13}C—^{13}C$ couplings are not usually observed. Couplings from $^{13}C — ^{1}H$ interaction have already been discussed (page 156) and these couplings should be observed in the ^{13}C spectra. However, these couplings make the ^{13}C spectra extremely complex, and they have been eliminated by decoupling. The proton-coupled (or non-decoupled) spectrum is shown in figure 3.33.

3.13.3 ^{1}H Decoupling—Noise Decoupling—Broad Band Decoupling

To eliminate the complicating effects of the proton couplings in the ^{13}C spectra, we must decouple the ^{1}H nuclei by double irradiation at *their* resonant frequencies (80 MHz at 1.9 T, etc.). This is an example of

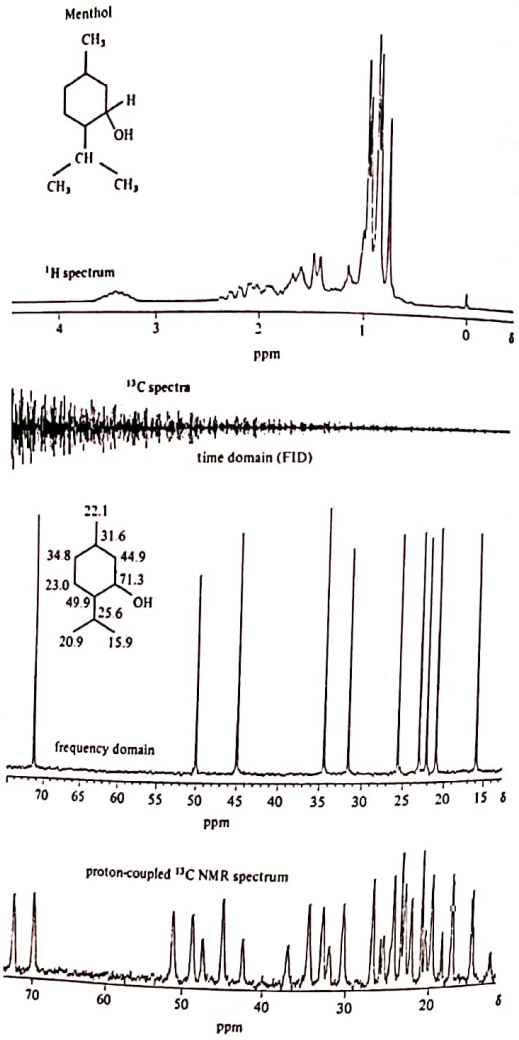


Figure 3.33 *Comparison of the proton and ^{13}C NMR spectra of menthol, recorded at the same field strength, 1.9 T (80 MHz and 20 MHz, respectively, in $CDCl_3$). The proton-coupled (i.e. non-decoupled) ^{13}C NMR spectrum is shown at the bottom.*

heteronuclear decoupling (see page 155), but we do not wish merely to decouple specific protons; rather, we wish to double irradiate *all* protons simultaneously while recording the ^{13}C spectrum. A decoupling signal is used that has all the ^{1}H frequencies spread around 80 MHz, and is therefore a form of radiofrequency noise; spectra derived thus are ^{1}H-*decoupled*, or *noise-decoupled*. Most ^{13}C spectra are recorded in this way; see the menthol spectrum in figure 3.33.

The alternative name *broad band decoupled* spectra simply takes cognizance of the fact that a wide spread of decoupling radiofrequency can be produced by several electronic techniques, other than by simple noise modulation.

The convenient notation ^{13}C-{^{1}H] can be used to identify proton-decoupled carbon-13 NMR spectra; in the same way ^{31}P-{^{1}H} spectra are phosphorus-31 NMR spectra with all proton coupling to phosphorus removed by broad band (or noise) decoupling, and ^{15}N-{^{1}H} corresponds for nitrogen-15, etc.

3.13.4 Deuterium Coupling

Deuteriated solvents (such as deuteriochloroform ($CDCl_3$), deuteriobenzene (C_6D_6), deuterioacetone (CD_3COCD_3) or hexadeuteriodimethylsulfoxide (CD_3SOCD_3)) give rise to carbon-13 signals which are split by coupling to deuterium. The multiplicity is calculable from the general formula $2nI + 1$ and deuterium has $I = 1$, so that in molecules with one deuteron attached to each carbon (as in $CDCl_3$ and C_6D_6) the carbon-13 signal from the solvent is a 1 : 1 : 1 triplet; this is seen in figures 3.1(b) and 3.34. For CD_3 groups (as in CD_3COCD_3 and CD_3SOCD_3), the solvent gives rise to a septet with line intensities 1 : 3 : 6 : 7 : 6 : 3 : 1; see the insert in figure 3.34. See also section 3.9.4.

3.13.5 NOE Signal Enhancement

Since decoupling can interfere with (and thereby shorten) relaxation times, the nuclear Overhauser effect (see section 3S.1.3) may operate and lead to signal enhancement of certain ^{13}C peaks. The line intensities in the ^{13}C spectrum of menthol are not all equal, because of these relaxation effects.

It turns out that the major relaxation route for a ^{13}C nucleus involves dipolar transfer of its excitation energy to the proton(s) directly attached to it; there is a corollary that maximum nuclear Overhauser effect operates on CH_3, CH_2 and CH carbons, whereas no enhancement arises for quaternary carbons (and this includes those carbons on aromatic rings with substituents attached). It happens also that these non-proton-bearing carbons have long relaxation times and also tend to give low-intensity signals for this reason (unless special steps are taken to ensure otherwise).

These dual influences ensure easy identification of such carbons: in figure 3.1(b), for example, there are three signals of lower intensity,

assigned, respectively, to the two substituted ring carbons and to the carbonyl carbon.

3.13.6 Quantitative Measurement of Line Intensities

The number of nuclei in any environment (measured by integration of peak areas) in proton NMR is routine and quite accurately quantitative, but this is not so in routine carbon-13 NMR spectra. As we have seen above, there are two main reasons for this.

The nuclear Overhauser effect tends to *increase* the line intensities for those carbons bearing protons, and to leave the quaternary carbons unaltered. To eliminate the nuclear Overhasuer effect requires a special pulse sequence, which is described in section 3S.3, but it is not usually routinely applied.

In the pulsed FT mode used for normal ^{13}C work, the pulses are applied with only short delays between each successive pair; carbon nuclei with long relaxation times will not have fully relaxed after one pulse before the next pulse is applied. The signals are therefore slightly saturated (see section 3.2) and of lower intensity. It is the quaternary carbons which tend to have long relaxation times, so that they show lowered intensities; in contrast to this, proton-bearing carbons not only have shorter relaxation times, *but also experience the enhanced line intensities caused by the nuclear Overhauser effect*.

To avoid this saturation effect would involve longer delays between pulses; because T_1 is a measure of an exponential process, it would be necessary to wait for approximately $5T_1$ before relaxation is complete. Since this would counteract the main asset of the FT method—speed—it is not done unless quantitative information is essential.

Interestingly, small symmetrical molecules (such as the solvents used in NMR, $CDCl_3$, C_6D_6, etc.) also tend to have carbons with long relaxation times; this is one of the reasons for the observation that the solvent peaks in ^{13}C NMR spectra are of low intensity.

Paramagnetic ions may be added to the sample to supply the fluctuating electromagnetic vectors which catalyze the relaxation processes for the excited carbon nuclei; this leads to improvement in the quantitative line heights. Typical paramagnetic species are chromium acetylacetonate ($Cr(ACAC)_3$), or the shift reagents discussed in section 3.11.3 (which, of course, cause shifts in the δ values except for the Gd complexes).

3.13.7 Off-Resonance Proton Decoupling

Fully proton-decoupled carbon-13 NMR spectra offer two main advantages over fully coupled spectra (sometimes called *non-decoupled* spectra): removal of coupling multiplicity makes the spectrum simpler in appearance and ensures almost no confusing overlap in adjacent signals, but there is a sensitivity bonus in addition. As an example, the methyl carbon in

p-hydroxyacetophenone (figure 3.1(b)) would appear in a non-decoupled spectrum as a quartet (intensity ratio 1 : 3 : 3 : 1) because of the three attached and coupling protons and, when this is decoupled, the whole of the signal intensity appears as a single line (of intensity 8 relative to the outside lines of the quartet). The fact that the signal is a quartet proves that it arises from a methyl group, and unfortunately this valuable piece of information is lost in the fully decoupled ^{13}C-{^1H} NMR spectrum. There are several techniques which allow this information to be retained; the simplest (but not the best) consists of carrying out the proton decoupling by irradiation of the sample with radiofrequency which is not quite exactly that of the protons but is a few hundred hertz displaced. The consequence of this *off-resonance decoupling* is an incomplete collapse of the multiplicity, and vestigial quartets remain from methyl carbons, with triplets from CH_2, doublets from CH and singlets from fully substituted carbons. More elaborate procedures (which allow the separate plotting of subspectra, respectively, from CH_3, CH_2 and CH carbons) are discussed in section 3S.3 and these are used in preference to off-resonance decoupling.

It is convenient to annotate signals in ^{13}C-{^1H} spectra to indicate multiplicity, with the abbreviations q, t, d and s for quartet, triplet, doublet and singlet, respectively, as in figure 3.34.

3.14 STRUCTURAL APPLICATIONS OF ^{13}C NMR

Differentiation among alternative organic structures has a long history in ^1H NMR and it is substantially extended by ^{13}C NMR. Increased shift resolution (compared with ^1H spectra) is often sufficient in itself to lead to correct structural assignment, but the use of correlation data for chemical shift positions and the calculation of multiplicity in non-decoupled spectra both have their contributions to make. Figure 3.35 shows the approximate chemical shift positions for common organic functional groups; the shifts are measured in ppm from TMS as standard.

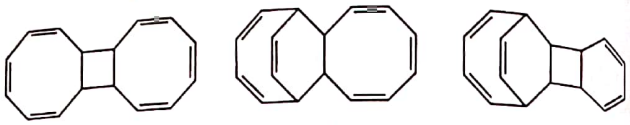
Example 3.9

Question. There are three isomeric ethers with the molecular formula $C_4H_{10}O$: name them, and state how many signals will arise in the carbon-13 NMR spectrum of each.

Model answer. The three ethers are diethyl ether (I), methyl propyl ether (II) and methyl isopropyl ether (III). Only in methyl propyl ether are all four carbons in different environments, so this ether shows four signals in its spectrum. In diethyl ether each ethyl group is equivalent, so that only two different environments (and, hence, signals) are present. The two methyl groups of the isopropyl group are equivalent, so methyl isopropyl ether gives rise to three signals in the spectrum.

$CH_3CH_2OCH_2CH_3$ $CH_3OCH_2CH_2CH_3$ $CH_3OCH(CH_3)_2$

I II III



IV V VI

Figure 3.1(b) shows the ^{13}C-{^1H} NMR spectrum of *p*-hydroxyacetophenone, *p*-$CH_3COC_6H_4OH$; the fact that it is the *para* isomer is easily confirmed from the spectrum, since only six nonequivalent carbons are present in the molecule (C-2 and C-6 are equivalent, as are C-3 and C-5). Both the *ortho* and *meta* isomers would have given spectra with eight signals, from the eight nonequivalent sites in each molecule.

(In section 3.15.1 we shall predict the chemical shifts for the carbons in these isomers, thus definitively identifying each isomer.)

Exercise 3.16 State the number of nonequivalent carbon environments (a) in *o*-dinitrobenzene and in its *m*- and *p*-isomers; (b) in *o*-dimethoxybenzene and its *m*- and *p*-isomers; and (c) in the three possible structures, IV, V and VI, for the dimer of cyclooctatetraene. (The actual dimer showed four signals in its ^{13}C NMR spectrum, so which is the correct structure?)

Exercise 3.17 State the number of nonequivalent carbon environments in (a) the three isomeric methyl esters of chlorobenzoic acid (*o*-, *m*- and *p*-) and (b) the three isomers of hydroxybiphenyl, PhC_6H_4OH, (2-hydroxy-, 3-hydroxy- and 4-hydroxybiphenyl).

3.15 CORRELATION DATA FOR ^{13}C NMR SPECTRA

While it is possible to offer reasonable rationales for proton NMR chemical shifts (section 3.4), the explanation of carbon-13 NMR chemical shifts is much less self-consistent, despite extensive studies; happily, predictions based on the tables of empirical data which follow are very reliable.

It is usually very difficult to deduce *a priori* the structure of an organic molecule from its ^{13}C NMR spectrum; indeed, this would be at variance with experimental experience, where much other information is often simultaneously available—both chemical and spectroscopic (IR, UV, MS and proton NMR spectra). Proof of structure usually involves hypothesizing what the likely structures for the compound are, and then using the

tables to predict *for each of these possibles* the appearance of the ^{13}C NMR spectrum, and that structure which gives the best fit with observed values is likely to be correct.

Some general features should be given consideration.

sp^3 hybridized carbons

Figure 3.35 shows that sp^3 carbons come to resonance in the range δ 0–80; within this overall range, it is worth noting that the carbons of C—O bonds, C—N bonds and C—S bonds appear in the narrower ranges indicated. Exceptions abound, usually as a consequence of influential electronic or steric effects. An extreme and interesting exception is the signal for the carbon atom in tetraiodomethane, CI_4, at δ −300 (that is, at 300 ppm *lower* frequency than TMS).

sp^2 hybridized carbons

Alkene and aromatic carbon atoms give signals in overlapped areas of the spectrum (δ 80–150 and δ 110–140, respectively)—a fact which can make their distinction less clear than in the proton NMR spectrum. The great diversity of C=O groups is mirrored in their significantly differing shift positions (see table 3.17). A less common sp^2 class (not shown in figure 3.35) is in the C=N group of aromatic imines, often called *Schiff's bases*; the range is δ 130–150. (Aliphatic imines are unstable and tend to decompose or polymerize.)

sp hybridized carbons

For the sp carbons of alkynes, nitriles and isonitriles, the shift ranges are usefully narrow (see figure 3.35).

Each main class of carbon environment (sp^3, sp^2 and sp) will be discussed, showing how the effects of further substitutions can be predicted.

The first steps in deducing the structure of an organic compound, using the ^{13}C NMR spectrum, are:

1. Count the number of signals in the spectrum; this is the number of nonequivalent carbon environments in the molecule. (Identify and discount the signal(s) from solvent; see table 3.19.)
2. Use figure 3.35 to assign signals approximately to the regions δ 0–80, δ 80–150 and δ 160–220 (carbonyl carbons).
3. Note the intensities of the peaks: non-proton-bearing carbons give lower intensity signals, and groups of two or more equivalent carbons give higher intensity signals.
4. Take account of any multiplicity information (q, t, d or s).
5. Use the Correlation Tables (section 3.16.1) to predict the chemical shifts of all carbons in each putative structure.

3.15.1 Use of the Correlation Tables

There are two principal predictable influences which we can quantify in determining the chemical shift positions of any carbon atom:

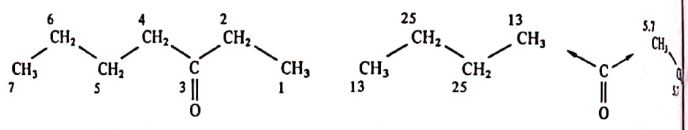
1. The number of other carbon atoms attached to it (and whether these are CH_3, CH_2, CH or C groups).
2. The nature of all other substituents attached (or nearby along a chain of other carbon atoms).

It is imperative to compute 1 before 2.

Example 3.10

Question. Predict the chemical shift positions for the carbons in 3-heptanone (butyl ethyl ketone), I.

Model answer. To do this we must first know the δ values for butane, II, and ethane, III: these are listed in table 3.11 and are shown in the formulae. *Only thereafter* can we predict the influence of the carbonyl substituent on each of these moieties; the influence of C=O on alkane carbons is given in table 3.15.



3-heptanone, I butane, II ethane, III

For C-1 we take the base value for ethane (δ 5.7) and note from table 3.15 that a carbonyl group, COR, β to it increases the value of the chemical shift by 2 ppm. The predicted value is therefore δ 7.7 (*ca* δ 8).

For C-2 we again take the base value for ethane (δ 5.7) but the carbonyl group is α to this carbon in 3-heptanone, so the increment is 30 ppm. The predicted value is therefore δ 35.7 (*ca* δ 36).

For C-4 we take the base value for the terminal carbon in butane and add to this (still table 3.15) 30 ppm, giving a predicted shift position of δ 43.

For C-5 the base value of δ 25 is increased by a β-carbonyl group to δ 27.

For C-6 the carbonyl group is in the γ position; for reasons that are not totally clear, but may correlate with molecular geometry, γ shifts are commonly negative—as here, where the base value of δ 25 is decreased (by −3) to δ 22.

For C-7 the effect of the carbonyl group is vanishingly small.

Note that the point of attachment of C=O on butane and ethane (C-2 and C-4) is CH_2CO; hence, the increment in each case is 30. This is notwithstanding the fact that the terminal carbon in each parent hydrocarbon is CH_3. (See also example 3.11.)

Thus, the predicted δ values (to the nearest integer) for the sp^3 carbons in 3-heptanone are, from C-1 on, as follows: 8, 36, 43, 27, 22 and 13; the observed values are 8, 36, 42, 26, 23 and 14.

Table 3.17 lists the chemical shift for the C=O carbon of a dialkyl ketone at δ 205–218; it is observed at δ 211.

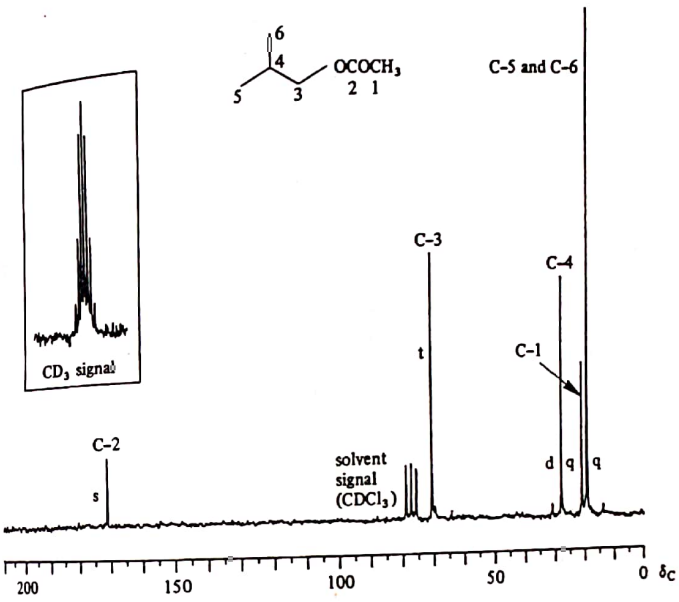


Figure 3.34 ^{13}C *NMR spectrum of isobutyl acetate. (*20 MHz *in* $CDCl_3$*, broad band proton decoupled.) Multiplicities (s,d,t,q) come from off-resonance data.* Insert*: Appearance of the septet signal from solvents containing the* CD_3 *group, such as acetone-*d_6 *or* DMSO-d_6 ($(CD_3)_2SOCD_3$).

Example 3.11

Question. Predict the chemical shift positions for the carbons in (a) *sec*-butyl acetate, IV, and (b) isobutyl acetate, V.

Model answer. (a) The starting point again is butane, whose δ values are given in table 3.11. On this occasion the functional group is attached to the C-2 of butane; although this is a CH_2 group in butane itself, it is CH in *sec*-butyl acetate, so we therefore use the increment 50 (not 52) in table 3.15.