5.7: 13C-NMR Spectroscopy

The ^{12}C isotope of carbon - which accounts for up about 99% of the carbons in organic molecules - does not have a nuclear magnetic moment, and thus is NMR-inactive. Fortunately for organic chemists, however, the ^{13}C isotope, which accounts for most of the remaining 1% of carbon atoms in nature, has a magnetic dipole moment just like protons. Most of what we have learned about ^{1}H-NMR spectroscopy also applies to ^{13}C-NMR, although there are several important differences.

The magnetic moment of a ^{13}C nucleus is much weaker than that of a proton, meaning that NMR signals from ^{13}C nuclei are inherently much weaker than proton signals. This, combined with the low natural abundance of ^{13}C, means that it is much more difficult to observe carbon signals: more sample is required, and often the data from hundreds of scans must be averaged in order to bring the signal-to-noise ratio down to acceptable levels. Unlike ^{1}H-NMR signals, the area under a ^{13}C-NMR signal cannot easily be used to determine the number of carbons to which it corresponds. The signals for some types of carbons are inherently weaker than for other types – peaks corresponding to carbonyl carbons, for example, are much smaller than those for methyl or methylene (CH_2) peaks. For this reason, peak integration is generally not useful in ^{13}C-NMR spectroscopy.

The resonance frequencies of ^{13}C nuclei are lower than those of protons in the same applied field - in an instrument with a 7.05 Tesla magnet, protons resonate at about 300 MHz, while carbons resonate at about 75 MHz. This is fortunate, as it allows us to look at ^{13}C signals using a completely separate 'window' of radio frequencies. Just like in ^{1}H-NMR, the standard used in ^{13}C-NMR experiments to define the 0 ppm point is tetramethylsilane (TMS),

although of course in ^{13}C-NMR it is the signal from the four equivalent *carbons* in TMS that serves as the standard. Chemical shifts for ^{13}C nuclei in organic molecules are spread out over a much wider range than for protons – up to 200 ppm for ^{13}C compared to 10-12 ppm for protons (see Table 3 for a list of typical ^{13}C-NMR chemical shifts).

The chemical shift of a ^{13}C nucleus is influenced by essentially the same factors that influence a proton's chemical shift: bonds to electronegative atoms and diamagnetic anisotropy effects tend to shift signals downfield (higher resonance frequency). In addition, sp^2 hybridization results in a large downfield shift. The ^{13}C-NMR signals for carbonyl carbons are generally the furthest downfield (170-220 ppm), due to both sp^2 hybridization and to the double bond to oxygen.

Exercise 5.15

How many sets of non-equivalent carbons are there in each of the molecules shown in exercise 5.2?

Exercise 5.16

How many sets of non-equivalent carbons are there in:

a) methylbenzene

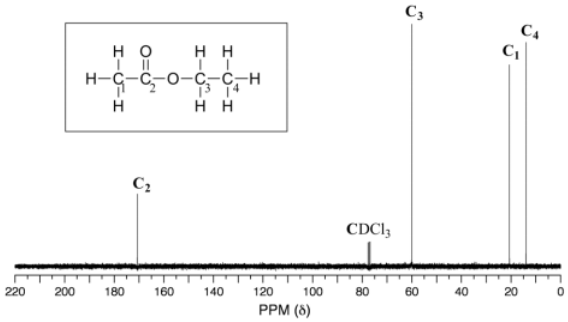
b) 2-pentanone

c) 1,4-dimethylbenzene

d) triclosan

(all structures are shown earlier in this chapter)

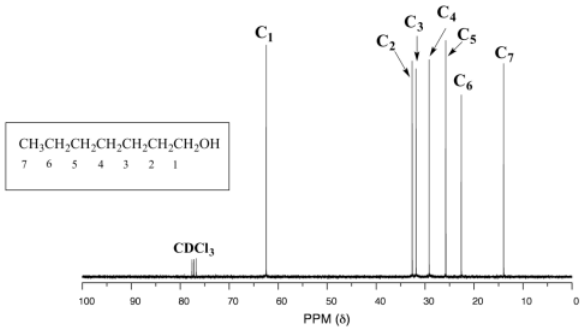
Because of the low natural abundance of ^{13}C nuclei, it is very unlikely to find two ^{13}C atoms near each other in the same molecule, and thus *we do not see spin-spin coupling between neighboring carbons in a ^{13}C-NMR spectrum*. ^{13}C nuclei are coupled to nearby protons, however, which results in complicated spectra. For clarity, chemists generally use a technique called **broadband decoupling**, which essentially 'turns off' C-H coupling, resulting in a spectrum in which all carbon signals are singlets. Below is the proton-decoupled ^{13}C-NMR sectrum of ethyl acetate, showing the expected four signals, one for each of the carbons. We can also see a signal for the carbon atom in the deuterated chloroform ($CDCl_3$) solvent (although a detailed discussion is beyond our scope here, it is interesting to note that this signal is split into a triplet by deuterium, which is NMR active and has *three* possible spin states rather than two). We can ignore the solvent signal when interpreting ^{13}C-NMR spectra.



While broadband decoupling results in a much simpler spectrum, useful information about the presence of neighboring protons is lost. However, another NMR technique called DEPT (Distortionless Enhancement by Polarization Transfer) allows us to determine how many hydrogens are bound to each carbon. This information is usually provided in problems in which you are asked to interpret the ^{13}C-NMR spectrum of an unknown compound. (Details of how the DEPT technique works is beyond the scope of this book, but will be covered if you take a more advanced course in spectroscopy.)

One of the greatest advantages of ^{13}C-NMR compared to ^{1}H-NMR is the breadth of the spectrum - recall that carbons resonate from 0-220 ppm relative to the TMS standard, as opposed to only 0-12 ppm for protons. Because of this, ^{13}C signals rarely overlap, and

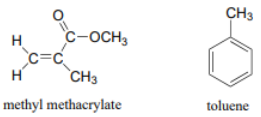
we can almost always distinguish separate peaks for each carbon, even in a relatively large compound containing carbons in very similar environments. In the proton spectrum of 1-heptanol we saw earlier only the broad singlet of the alcohol proton (H_a) and the triplet for (H_b) are easily analyzed. The other proton signals overlap, making analysis difficult. In the ^{13}C spectrum of the same molecule, however, we can easily distinguish each carbon signal, and we know from this data that our sample has seven nonequivalent carbons. (Notice also that, as we would expect, the chemical shifts of the carbons get progressively lower as they get farther away from the deshielding oxygen.)



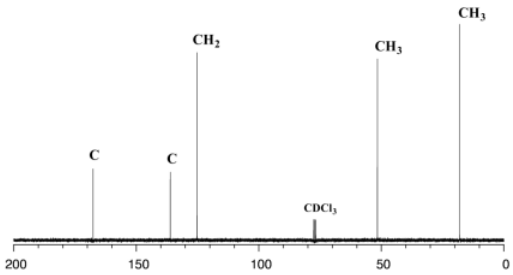
This property of ^{13}C-NMR makes it very helpful in the elucidation of larger, more complex structures.

Exercise 5.17

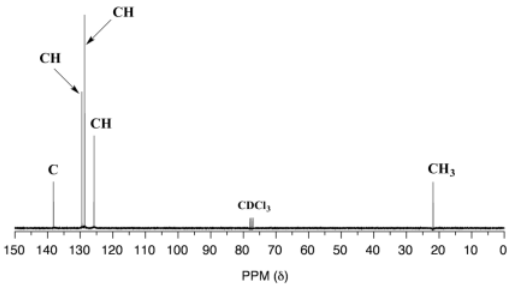
Below are ^{13}C-NMR spectra for methylbenzene (common name toluene) and methyl methacrylate. Match the spectra to the correct structure, and make peak assignments.



Spectrum A:



Spetrum B:



Exercise 5.18

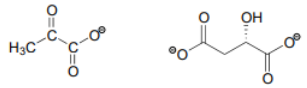
^{13}C-NMR data for some common biomolecules are shown below (data is from the Aldrich Library of ^{1}H and ^{13}C NMR). Match the NMR data to the correct structure, and make complete peak assignments.

spectrum a: 168.10 ppm (C), 159.91 ppm (C), 144.05 ppm (CH), 95.79 ppm (CH)

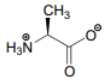
spectrum b: 207.85 ppm (C), 172.69 ppm (C), 29.29 ppm (CH_3)

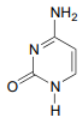
spectrum c: 178.54 ppm (C), 53.25 ppm (CH), 18.95 ppm (CH_3)

spectrum d: 183.81 ppm (C), 182. 63 ppm (C), 73.06 ppm (CH), 45.35 ppm (CH_2)


pyruvate

(S)-malate


alanine


cytosine

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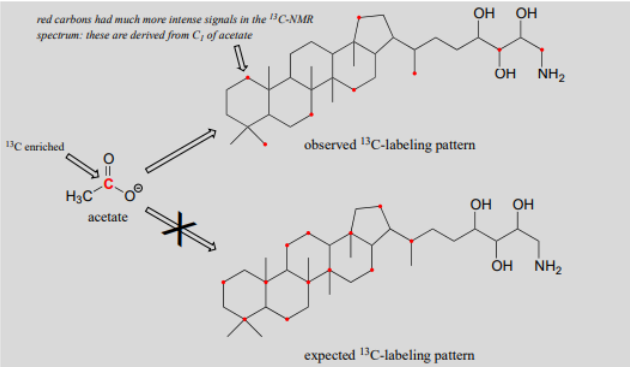
^{13}C-NMR in Isotopic Labeling Studies

Although only about 1 out of 100 carbon atoms in a naturally occurring organic molecule is a 13C isotope, chemists are often able to synthesize molecules that are artificially enriched in 13C at specific carbon positions. This can be very useful in biochemical studies, because it allows us to 'label' one or more carbons in a small precursor molecule and then trace the presence of the 13C label through a biosynthetic pathway all the way to the final product, providing insight into how the biosynthesis occurs. For example, scientists were able to grow bacteria in a medium in which the only source of carbon was acetate enriched in 13C at the C1 (carbonyl) position. When they isolated an isoprenoid compound called amino-bacterio-hopanetriol synthesized by the bacteria and looked at its 13C-NMR spectrum, they observed that the 13C label from acetate had been incorporated at eight specific positions. They knew this because the 13C-NMR signals for these carbons were much stronger compared to the same signals in a control (unlabeled) compound.



This result was very surprising - the scientists had expected a completely different pattern of 13C incorporation based on what they believed to be the isoprenoid biosynthesis pathway involved. This unexpected result led eventually to the discovery that bacteria synthesize isoprenoid compounds by a completely different pathway then yeasts, plants, and animals. The newly discovered bacterial metabolic pathway is currently a key target for the development of new antibiotic and antimalaria drugs. (Eur. J. Biochem. 1988, 175, 405).
