Ibuprofen

Ibuprofen (C\textsubscript{13}H\textsubscript{18}O\textsubscript{2}) is a non-steroidal anti-inflammatory drug (NSAID) commonly used for pain relief, fever reduction and to reduce inflammation. The \textsuperscript{1}H NMR spectrum of 250 mM ibuprofen in CDCl\textsubscript{3} measured in a single scan taking 15 seconds to acquire is shown in Figure 1. All peaks and \textsuperscript{1}H-\textsuperscript{1}H couplings are well resolved and the integrals of the peaks correspond to the number of protons in the groups with very high accuracy.

![Figure 1: \textsuperscript{1}H NMR spectrum of 250 mM ibuprofen in CDCl\textsubscript{3} measured on a Spinsolve 60 MHz in a single scan.](image)

\textsuperscript{13}C Spectra

Figure 2 shows the \textsuperscript{13}C NMR spectra of 1 M ibuprofen in CDCl\textsubscript{3} acquired using NOE and DEPT polarization transfer from \textsuperscript{1}H to \textsuperscript{13}C and \textsuperscript{1}H decoupling. The 1D Carbon experiment using NOE (top spectrum) is sensitive to all \textsuperscript{13}C nuclei in the sample. It clearly resolves the 9 expected resonances. The DEPT experiments show only \textsuperscript{13}C nuclei directly attached to \textsuperscript{1}H and can be used for spectral editing. Since the peaks at 181, 140 and 137 ppm do not show in the DEPT spectra they must belong to quaternary carbons. The DEPT-90 experiment gives only signal from CH groups, whilst the DEPT-45 and DEPT-135 give signals of CH, CH\textsubscript{2} and CH\textsubscript{3} groups, but the CH\textsubscript{3} groups appear as negative peaks in the DEPT-135.

![Figure 2: Carbon NMR spectra of 1 M ibuprofen in CDCl\textsubscript{3} measured on a Spinsolve 60 MHz using NOE (top) and DEPT 45, 90 and 135 sequences. An interesting feature evident in these sub-spectra is that the peak at 45 ppm is made up of a CH and a CH\textsubscript{3} resonance with identical chemical shifts.](image)
2D COSY

The 2D COSY experiment allows one to identify coupled \(^1\)H nuclei as they generate cross peaks out of the diagonal of the 2D data set. For example, the methyl group at position 3 couples to the CH group at position 2 (red), whilst the methyl groups at positions 12 and 13 couple to CH and CH\(_2\) groups at positions 11 (violet) and 10 (blue), respectively. Furthermore, the coupling between groups 11 and 10 is marked in green.

![2D COSY spectrum of ibuprofen](image)

Figure 3: COSY experiment of a 250 mM Ibuprofen sample acquired in 10 minutes on a Spinsolve 60.

2D J-Resolved

This experiment is useful to identify the chemical groups generating a single line for each group by collapsing the J-coupling along the direct direction. The multiplets are generated along the vertical direction.

![2D J-Resolved spectrum of ibuprofen](image)

Figure 4: Homonuclear J-resolved spectrum of 250 mM ibuprofen in CDCl\(_3\).
HSQC-me

The HSQC is a powerful sequence widely used to correlate the $^1$H with the one-bond coupled $^{13}$C nuclei. The Spinsolve is equipped with a multiple-edited version (HSQC-me) of this method. It provides the editing power of the DEPT-135 sequence, which is useful to identify the signal of the CH$_2$ groups (blue) from the CH and CH$_2$ (red). Figure 5 shows the HSQC-me spectrum of 1 M ibuprofen in CDCl$_3$ acquired in 35 minutes.

To obtain long-range $^1$H-$^{13}$C correlations through two or three bond couplings, the Heteronuclear Multiple Bond Correlation (HMBC) experiment can be used. Figure 6 shows, as an example, the long range correlation of protons 2 with carbons 3, 5 and 9 in the benzene ring, and carbon 1 (the sequence shows the correlation with quaternary carbons too). At the same time it can be notice that there is no correlation peak at the position of carbon 2.

The same exercise can be repeated for each proton signal along the horizontal scale to identify which carbon are long-range coupled. It is interesting to note that there is correlation between protons 12 and 13 with carbons 13 and 12. This is due to the three bond coupling between protons 12 with carbon 13 and vice versa.

Figure 5: HSQC-me spectrum of 1 M Ibuprofen showing the correlation between the $^1$H (horizontal) and $^{13}$C (vertical) signals.

Figure 6: HMBC spectrum of 1 M Ibuprofen showing the long range couplings between $^1$H and $^{13}$C nuclei.
$T_1$ proton relaxation

This experiment is useful to measure the $T_1$ relaxation time of each chemical group. Figure 7 shows the $T_1$ build up curves for the different protons (color coded) in Ibuprofen. The $T_1$ values obtained by fitting the build up curves with single exponential functions are shown next to the build up curves. The remarkable quality of the fits demonstrate the high signal-to-noise and reproducibility of the Spinsolve spectrometer.

![Figure 7: Proton $T_1$ relaxation measurement done on 250 mM Ibuprofen dissolved in CDCl$_3$.](image)

$T_2$ proton relaxation

This experiment uses a CPMG sequence to allow the protons to relax with the transverse relaxation time, $T_2$, and acquires only the signals during the last echo. To acquire the full data set it is necessary to repeat the experiment incrementing the duration of the CPMG module by increasing the number of echoes generated during this period. The $T_2$ values are obtained by fitting the peak integrals of each group as a function of the CPMG evolution time. Figure 8 shows the $T_2$ decay curves for the different protons in Ibuprofen (color coded).

![Figure 8: Proton $T_2$ relaxation curves measured for 250 mM Ibuprofen dissolved in CDCl$_3$.](image)