^{13}C One- and Two-Dimensional Benchtop NMR Spectroscopy

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The benchtop NMR system

^{13}C NMR spectroscopy is an important tool in chemical structure elucidation, as it detects the carbon backbone of organic molecules. While ^{13}C NMR is routinely used at high field, it has until now not been utilised in benchtop NMR. One of the main reasons for this is the low sensitivity of the ^{13}C nucleus. Overall, the receptivity is reduced by about 4 orders of magnitude compared to ^{1}H NMR. The acquisition of meaningful ^{13}C NMR spectra of dilute samples is only possible if the spectrometer provides high stability to enable signal averaging and sufficient sensitivity.

In this work we demonstrate the performance of ^{13}C NMR on a 1 Tesla permanent magnet system using a dilute, non-enriched organic molecule. The results presented here show that benchtop ^{13}C NMR methods can reveal information which is not available with ^{1}H NMR and that the findings are consistent with high field NMR.

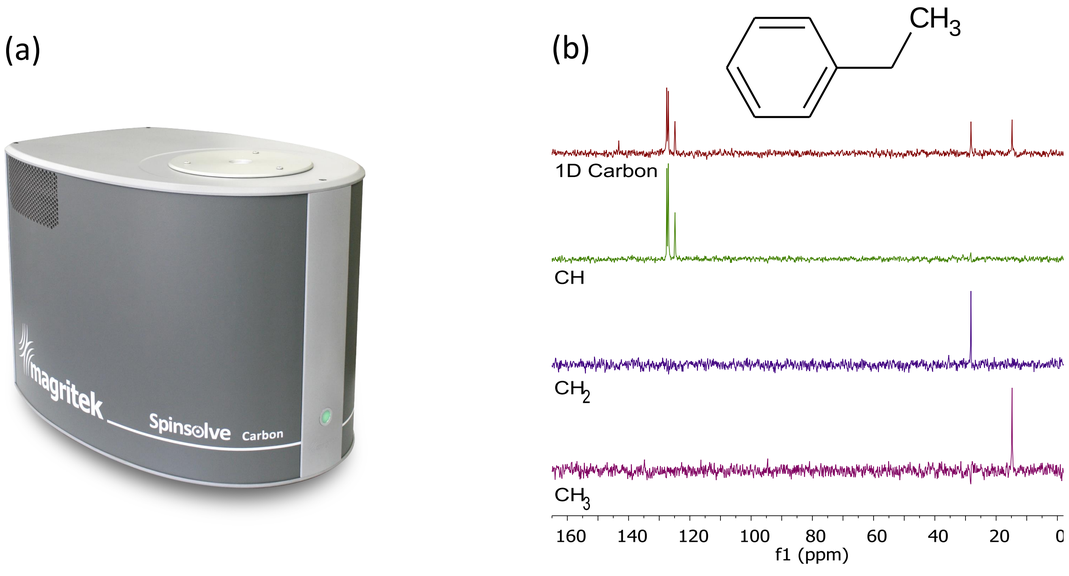

Figure 1: (a) The SpinsolveCarbon benchtop NMR system, (b) carbon-13 spectra of neat ethylbenzene. The spectrum at the top is the full 1D spectrum showing all carbons in the molecule. Spectral editing such as DEPT enable the measurement of subspectra originating from CH, CH_2 and CH_3 groups.

Comparing high and low field 1D NMR spectroscopy

One of the difficulties encountered when dealing with low field proton NMR spectra is that there is often a strong peak overlap due to the homonuclear spin couplings being similar in size as the chemical shift separation between inequivalent spins. These strong coupling effects decrease as the frequency difference between multiplets increases, so that high-field (i.e. high-frequency) NMR spectra display less distortion than lower frequency spectra. Figure 3 (a) shows ^{1}H spectra of the quinine sample at 43 and 500 MHz. At low field, the spectrum shows severe peak overlap due to strong coupling effects, whilst at high field all peaks are well separated.

Due to the low natural abundance of the ^{13}C nucleus, there is no significant homonuclear spin coupling in ^{13}C spectra. As a consequence, the peak structure of ^{13}C spectra at low field is identical to high field, as shown in Figure 3 (b).

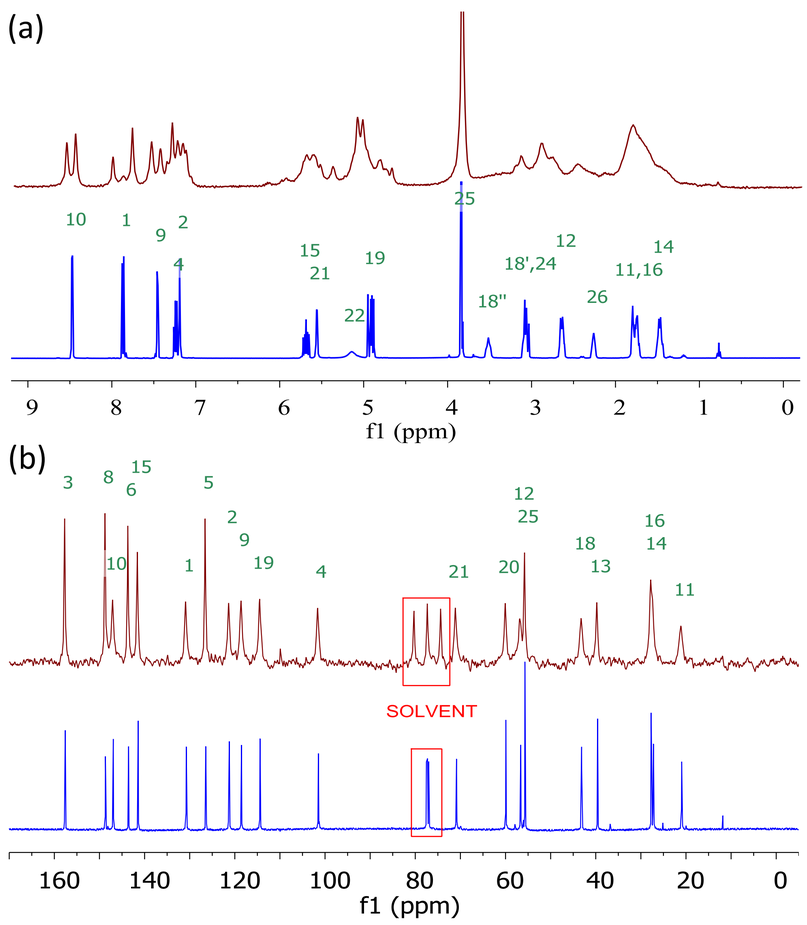

Figure 3: Proton (a) and carbon (b) spectra of the quinine sample measured at 11.7 T (blue) and 1 T (brown). Note that the benchtop proton spectrum shows significant peak overlap due to strong coupling, whilst the benchtop carbon spectrum is essentially identical to the one at high field allowing unambiguous peak assignment [2].

Quinine

Quinine ((8α,9R)-6'-methoxycinchonan-9-ol) is a natural white crystalline alkaloid having antipyretic (fever-reducing), antimalarial, analgesic (painkilling), and anti-inflammatory properties and a bitter taste. The molecular formula is $C_{20}H_{24}N_2O_2$, with a mass of 324.4 Da. The sample for the experiments reported here was a solution of non-enriched quinine in $CDCl_3$ with a concentration of 2 M in a 5 mm NMR tube. Figure 2 shows the molecular structure.

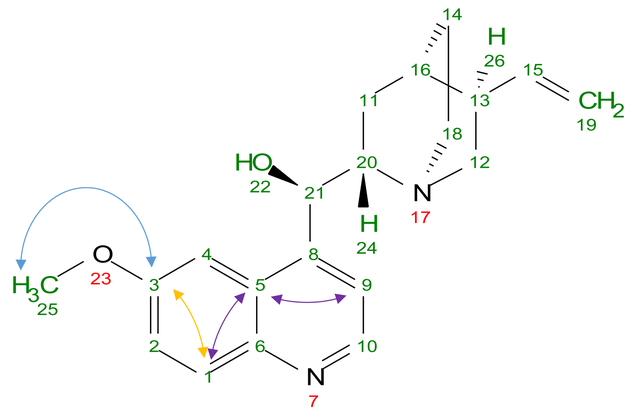

Figure 2: Chemical structure of quinine [1].

2D proton-carbon correlation spectroscopy

Heteronuclear 2D correlation spectroscopy experiments are particularly useful in helping assign crowded spectra with overlapping peaks, as they detect coupling partners of different nuclei. The introduction of the second (f1) dimension in these experiments provides valuable structural information to organic chemists.

The HSQC (Heteronuclear Single Quantum Correlation) type experiments correlate the chemical shift of protons with the chemical shift of the directly bonded carbon. Cross-peaks in these spectra are between carbons and directly attached protons.

The HMBC (Heteronuclear Multiple Bond Correlation) experiment differs from the HSQC in that multiple-bond couplings over two or three bonds (J = 2-15 Hz) are utilised. Direct one-bond correlations are suppressed, and cross-peaks in HMBC spectra are between protons and carbons that are two or three bonds away.

Figures 4 and 5 show the HSQC (a) and HMBC spectra (b) of quinine at 1 T and 11.7 T, respectively. While it is possible to observe all available correlations in the HSQC experiment at high-field (500 MHz), some of the more diagnostic correlations do stand out at low-field (43 MHz). For example, the oxymethyl CH_3-25 can be observed, as well as oxymethine CH-21 and protonated alkene carbon CH_2-19. Likewise in the HMBC experiment, the characteristic one-bond leakthrough from CH_3-25 is observed, along with its correlation to C-3. The lower left quadrant of the 2D spectrum shows correlations that are consistent with three-bond connectivity in the heteroaromatic region of quinine.

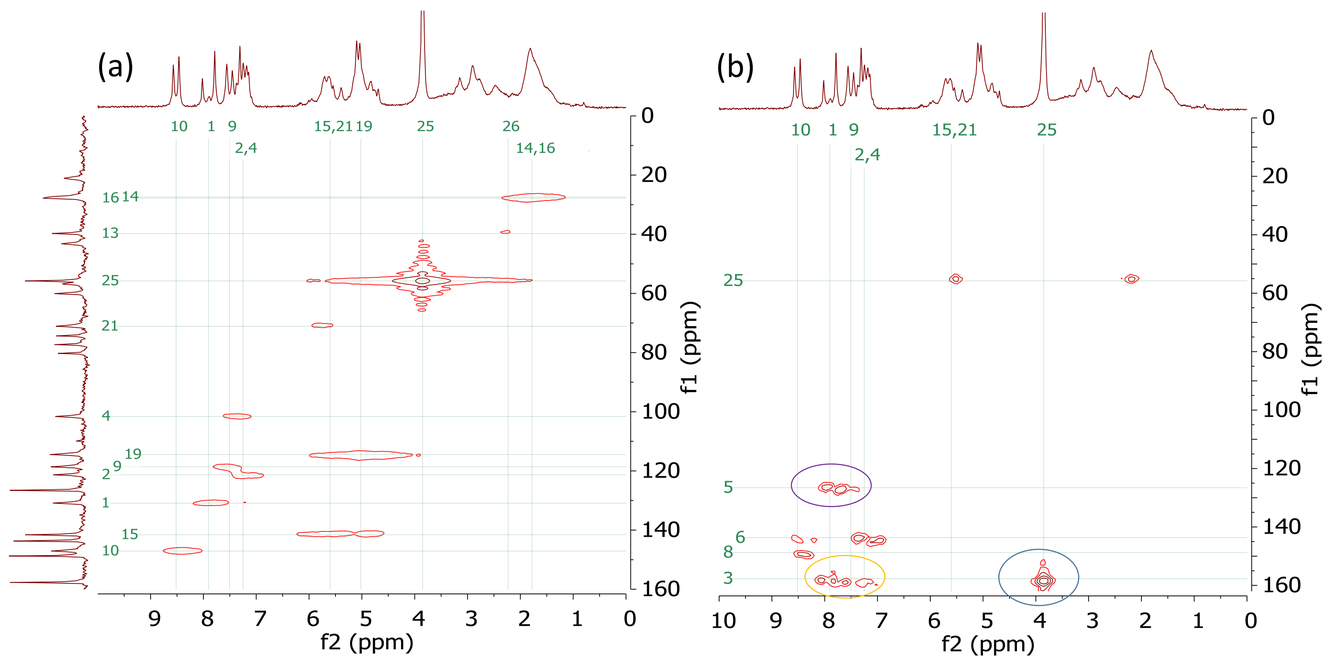

Figure 4: HSQC (a) and HMBC (b) spectrum of quinine at 1 T.

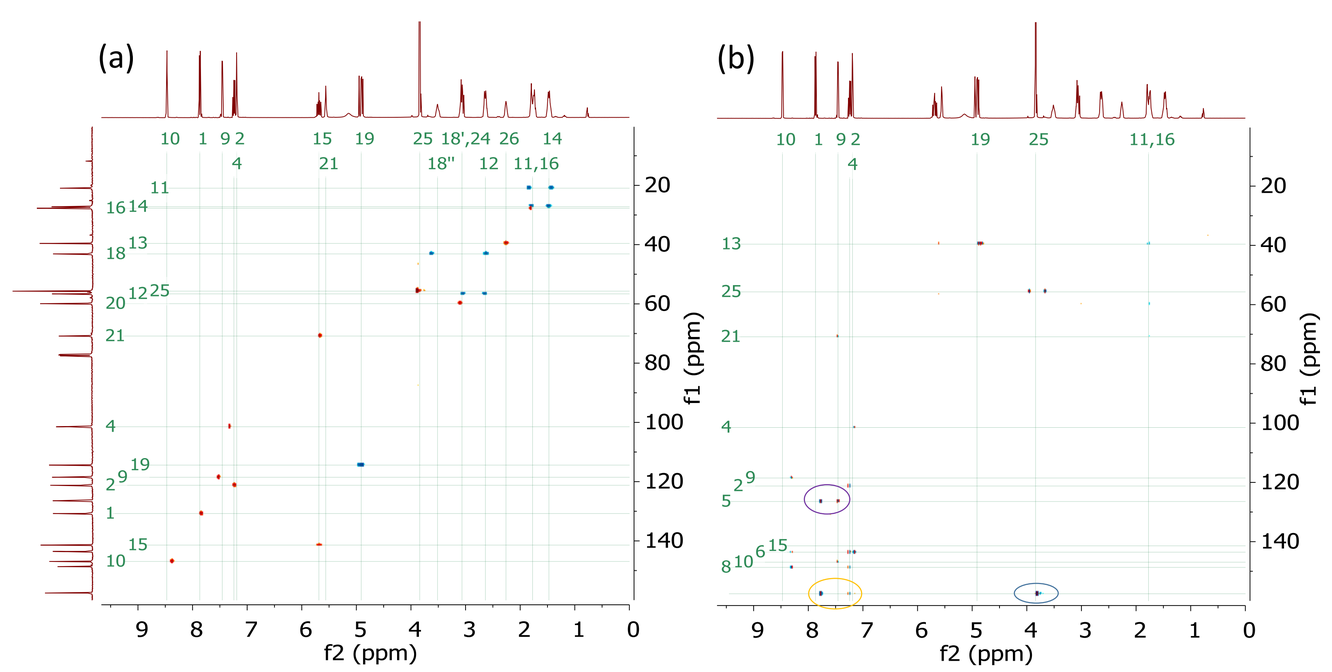

Figure 5: HSQC (a) and HMBC (b) spectrum of quinine at 11.7 T.

References

[1] http://www.chemspider.com/Chemical-Structure.84989.html

[2] http://www.chem.wisc.edu/~cic/nmr/NMRdatab/res_cmpd/pdfs/quin_assignment_example-for-pdf.pdf