A true multinuclear spectroscopy case study Spinsolve 80

¹H, ¹⁹F, and ¹³C spectra acquired with simultaneous decoupling of multiple nuclei

5-Bromo-1,2,3-trifluorobenzene ($BrC_6H_2F_3$) is a structurally simple molecule commonly used as a building block in a variety of synthetic organic reactions. As this molecule contains ¹H, ¹⁹F, and ¹³C (in natural abundance), it is a beautiful example to demonstrate the unique advantage offered by the Spinsolve of accessing all three nuclei simultaneously without requiring retuning or user intervention. Figure 1 shows the ¹H NMR spectrum of neat 5-Bromo-1,2,3-trifluorobenzene measured in a single scan taking 10 seconds to acquire (top) and the respective 1D proton ¹⁹F decoupled spectrum (bottom). As no retuning of the probe is required to switch from ¹H and ¹⁹F, the ¹H signal can be acquired while the ¹⁹F nuclei are being decoupled.



Figure 1: ¹H NMR spectrum of neat 5-Bromo-1,2,3-trifluorobenzene measured on a Spinsolve 80 MHz system in a single scan.

¹⁹F Spectra

5-Bromo-1,2,3-trifluorobenzene is a good example to highlight the advantage of ¹⁹F protocols with ¹H decoupling possibilities. The usual ¹⁹F NMR spectrum (top spectrum) allows one to identify the two expected ¹⁹F resonances for the fluorine atoms at positions 8, 9, and 10. The bottom spectrum shows the ¹H decoupled ¹⁹F NMR spectrum. The multiplet structure of each peak is defined only by the fluorine couplings, so as expected we can observe a triplet at position 9 and a doublet at positions 8 and 10.



Figure 2: ¹⁹F NMR spectrum of neat 5-Bromo-1,2,3-trifluorobenzene measured on a Spinsolve 80 MHz system in a single scan. With (bottom) and without (top) ¹H decoupling.

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¹³C Spectra

Figure 3 shows the ¹³C NMR spectra of neat 5-Bromo-1,2,3-trifluorobenzene acquired using NOE polarization transfer. The top spectrum was measured without any decoupling. It clearly resolves the expected resonances but shows a crowded multiplicity structure for each carbon. The 1D carbon acquired with ¹H decoupling (middle spectrum) eliminates some couplings and slightly simplifies some of the peaks, but only the 1D carbon acquired with simultaneous ¹H, ¹⁹F decoupling (bottom spectrum) shows a singlet for each carbon atom to clearly resolve the four expected resonances.



Figure 3: Carbon NMR spectra of neat 5-Bromo-1,2,3-trifluorobenzene measured on a Spinsolve 80 MHz system using NOE (top), ¹H decoupling (middle) and ¹H,¹⁹F decoupling sequences (bottom).

¹³C DEPT Spectra

Figure 4 shows the ¹³C NMR spectra of neat 5-Bromo-1,2,3-trifluorobenzene acquired using NOE and DEPT polarization transfer from ¹H to ¹³C and ¹H decoupling. The 1D Carbon experiment using NOE (top spectrum) is sensitive to all ¹³C nuclei in the sample. It clearly resolves the expected resonances. The DEPT experiments show only ¹³C nuclei directly attached to ¹H and can be used for spectral editing. Since the peaks in the range of 160-130 ppm do not appear in the DEPT spectra they must correspond to the quaternary carbons.



Figure 4: Carbon NMR spectra of neat 5-Bromo-1,2,3-trifluorobenzene measured on a Spinsolve 80 MHz using NOE (top) and DEPT-45, -90 and -135 sequences.



2D ¹H-COSY and ¹⁹F-COSY

The 2D ¹⁹F COSY experiment (right) allows one to identify coupled ¹⁹F nuclei as they generate cross peaks out of the diagonal of the 2D data set. The fluorine atom at position 9 couples to the fluorine atoms at positions 8 and 10 (light blue). The respective ¹H COSY (left) in the same manner allows one to identify coupled ¹H nuclei. In Figure 5 this is not very useful as no coupling between protons is expected for the corresponding molecule.



Figure 5: ¹H COSY (left) and ¹⁹F COSY (right) experiment of a neat 5-Bromo-1,2,3-trifluorobenzene sample acquired in 10 minutes on a Spinsolve 80 MHz system.

2D HF-COSY

The HF COSY experiment allows one to identify ¹H and ¹⁹F nuclei that couple with each other. Here, the benzene protons at positions 4 and 5 couple to the fluorine atoms at position 8 and 10 (green). On the other hand, the same benzene protons couple to the fluorine atom at position 9 (orange).



Figure 6: HF-COSY experiment of a neat 5-Bromo-1,2,3-trifluorobenzene sample acquired in 17 minutes on a Spinsolve 80 MHz system.



2D HSQC-ME

The HSQC is a powerful sequence widely used to correlate the ¹H with the one-bond coupled ¹³C nuclei. The Spinsolve is equipped with a multiplicity 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 CH₂ groups (blue) from the CH and CH₃ (red). Figure 8 shows the HSQC-ME spectrum of neat 5-Bromo-1,2,3-trifluorobenzene acquired in 34 minutes.



Figure 8: HSQC-ME spectrum of neat 5-Bromo-1,2,3-trifluorobenzene showing the correlation between the ¹H (horizontal) and ¹³C (vertical) signals.

2D HMBC

To obtain long-range ¹H-¹³C correlations through two or three bond couplings, the Heteronuclear Multiple Bond Correlation (HMBC) experiment can be used. Figure 9 shows the long-range correlation of protons 4 and 5 with carbons 6, 1, 2 and 3 (the sequence shows the correlation with quaternary carbons, too).



Figure 9: HMBC spectrum of neat 5-Bromo-1,2,3-trifluorobenzene showing the long-range couplings between ¹H and ¹³C nuclei.



T₁ proton relaxation

This experiment is used to measure the T_1 relaxation time of each chemical group. Figure 10 shows the T_1 build up curves for the protons 4 and 5 in 5-Bromo-1,2,3-trifluorobenzene. The T_1 value obtained by fitting the build up curve with a single exponential function is shown next to the build up curve. The remarkable quality of the fits demonstrate the high signal-to-noise ratio and reproducibility of the Spinsolve spectrometer.



Figure 10: Proton T, relaxation measurement done employing neat 5-Bromo-1,2,3-trifluorobenzene on a Spinsolve 80 MHz system.

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 11 shows the T_2 decay curve for the protons 4 and 5 in 5-Bromo-1,2,3-trifluorobenzene.



Figure 11: Proton T₂ relaxation curves measured for neat 5-Bromo-1,2,3-trifluorobenzene on a Spinsolve 80 MHz system.

