

Application Note 4

Application of a high performance benchtop NMR spectrometer for ^{19}F NMR spectroscopy

Background

Fluorine is an important element in industrial chemistry and has applications in a wide range of industries, such as pharmaceuticals, agrochemicals, polymers, surfactants and solvents. It is estimated that more than 20% of all pharmaceutical compounds contain fluorine. This includes some of the commercially important drugs such as Prozac (fluoxetine) and Paxil (paroxetine). Nuclear Magnetic Resonance (NMR) spectroscopy is a valuable technique for the measurement of compounds containing fluorine especially organo-fluorine compounds. After the proton (^1H) and carbon-13 (^{13}C) NMR, fluorine-19 (^{19}F) is the most common nucleus studied by this technique. ^{19}F nuclei have a nuclear spin of $\frac{1}{2}$, have a high gyromagnetic ratio, and have 100% natural abundance, ensuring they have a high receptivity for NMR measurements. The ^{19}F resonance frequency in a 1.4 T magnetic field, such as X-Pulse, is 56.2 MHz which is sufficiently close to the resonance frequency of ^1H , that proton and fluorine-19 spectra can be measured using the same probe.

Measuring ^{19}F spectra on X-Pulse

X-Pulse is a high performance broadband benchtop NMR spectrometer that does not require external services, such as liquid cryogenics or compressed air, and can be placed in the laboratory rather than in a specialised NMR facility. Spectra can be collected within a couple of minutes using standard 5 mm NMR tubes.



A series of spectra have been collected to demonstrate the ^{19}F and ^1H capability and performance of the instrument using the same probe.

a,a,a-Trifluorotoluene is a useful reference material for ^{19}F NMR spectroscopy and can be used as an internal standard in a similar way to tetramethylsilane (TMS) is for ^1H and ^{13}C measurements. The ^1H and ^{19}F spectra of *a,a,a*-trifluorotoluene are shown in figure 1.

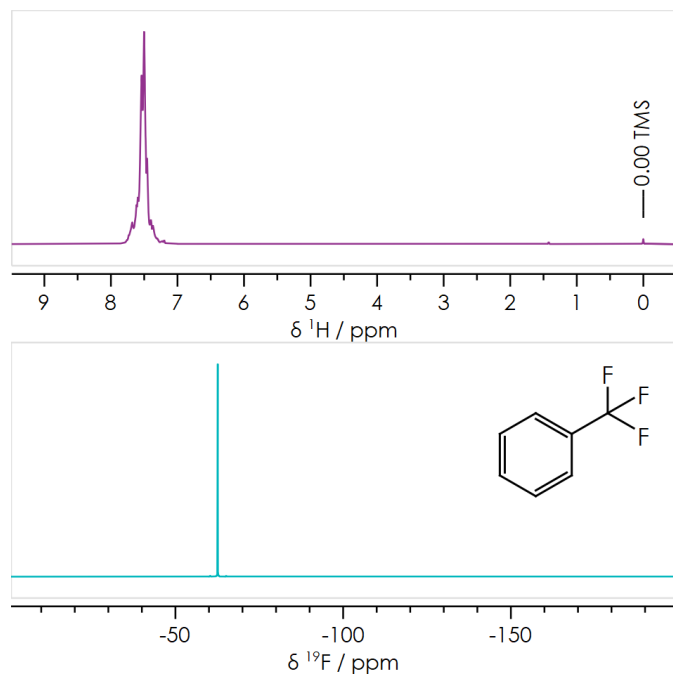


Figure 1: ^1H (top, purple) and ^{19}F (bottom, sea green) spectra of *a,a,a*-trifluorotoluene

The ^{19}F spectrum, shown in figure 1, consists of a single peak since the three fluorine nuclei are chemically and magnetically equivalent, and are not in close proximity to any of the protons in the molecule. The ^1H spectrum is more complex since the hydrogen nuclei on the aromatic ring are not equivalent and the resulting homonuclear couplings give rise multiple overlapping signals, appearing as a single multiplet.

The spectrum shown in figure 2 is a mixture of two fluorine containing chemicals; *a,a,a*-trifluorotoluene (TFT) and 2,2,2-trifluoroethanol. TFT is often used as a reference material for ^{19}F spectra; since it appears as a strong, single peak with a chemical shift of -62.6 ppm relative to the standard ^{19}F NMR chemical shift reference compound, CFCl_3 , at 0 ppm. (Angew. Chem. Int. Ed., 2018, 57, 9528-9533) It is a single peak as the structure consists of three equivalent fluorine nuclei isolated from any other nuclei that would couple to it. By comparison the peak in the spectrum due to trifluoroethanol, at -77.1 ppm, is split into a triplet. This is due to the fact that the ^{19}F nuclei couples with the two equivalent ^1H nuclei on the adjacent carbon atom in the molecule, just as ^1H nuclei would couple with other neighbouring ^1H nuclei in the molecule.

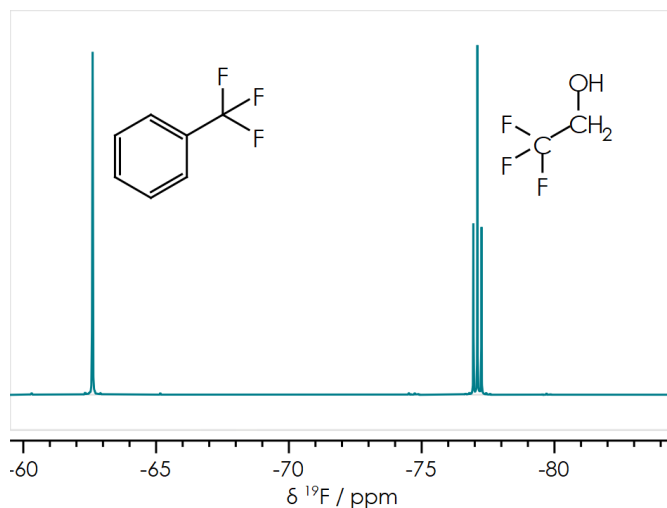


Figure 2: ^{19}F spectrum of a mixture of *a,a,a*-trifluorotoluene and 2,2,2-trifluoroethanol

Figure 3 shows the ^1H and ^{19}F spectra of the compound 5-bromo-1,2,3-trifluorobenzene. The ^1H spectrum consists of a single multiplet of peaks resulting from the two equivalent ^1H nuclei and their couplings with the chemically and magnetically inequivalent ^{19}F nuclei within the molecule. The ^{19}F spectrum consists of two resonances, each of which are multiplets due to the two different chemical environments of the ^{19}F nuclei. The resonance at -132 ppm arises from the fluorines in the *meta* positions of the molecule while the resonance at -161 ppm arises from the fluorine in the *para* position.

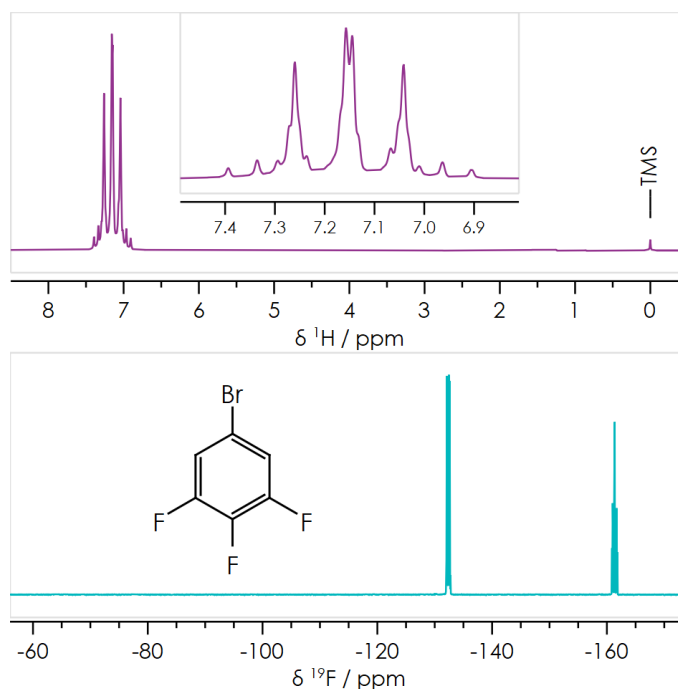


Figure 3: ^1H (top, purple) and ^{19}F (bottom, sea green) spectra of 5-bromo-1,2,3-trifluorobenzene

Each of these resonances shows a complex coupling pattern due to the other nuclei on the aromatic ring. Most easily recognisable is the triplet of triplet pattern at -162 ppm, arising because the fluorine in the *para* position is coupled to two equivalent fluorines in the *meta* positions and two equivalent hydrogens in the *ortho* positions.

Finally, a comparison has been made of the ^{19}F spectra of two different positional isomers of bromotrifluorobenzene. Figure 4 shows the ^{19}F spectra of 5-bromo-1,2,3-trifluorobenzene and 1-bromo-2,4,5-trifluorobenzene.

In contrast to the spectrum of 5-bromo-1,2,3-trifluorobenzene, the spectrum of 1-bromo-2,4,5-trifluorobenzene shows three ^{19}F resonances because each of the fluorines on the ring are in different chemical environments. They all appear as a doublet of doublets of doublets of doublets, since each is coupled to two inequivalent fluorines and two inequivalent hydrogens.

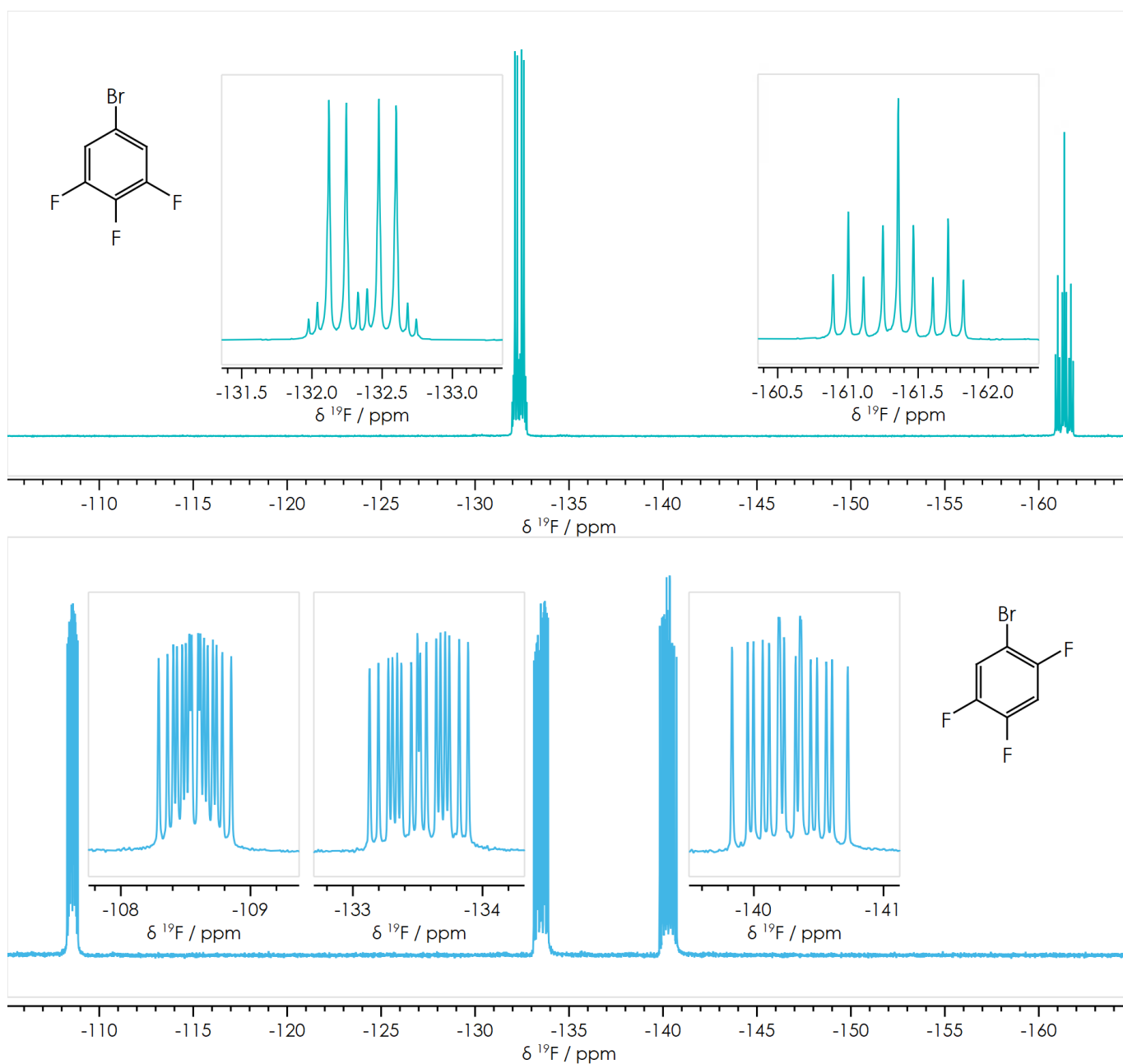


Figure 4: ^{19}F spectra of 5-bromo-1,2,3-trifluorobenzene (top, sea green) and 1-bromo-2,4,5-trifluorobenzene (bottom, deep sky)

Summary

The data presented here displays that benchtop NMR is a valuable analytical tool for measuring ^{19}F spectra and provides useful information for fluorine chemistry. With X-Pulse it is possible to measure both ^{19}F and ^1H spectra of a sample within a couple of minutes using the same probe.



If you have any questions about this application note, please contact our experts:
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