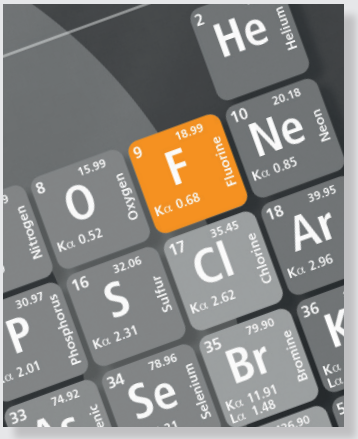
Application of a high performance benchtop NMR spectrometer for ^{19}F NMR spectroscopy

Application Note – Pulsar 004

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 organofluorine compounds. After ^{1}H and ^{13}C NMR, ^{19}F is the most common nucleus studied by this technique. ^{19}F nuclei are spin ½ nuclei and a have a high gyromagnetic ratio, which means that they have a high receptivity for NMR measurements. The ^{19}F isotope has 100% natural abundance, giving high NMR sensitivity. The ^{19}F resonance frequency on **Pulsar**™, a 1.45T magnet, is 56.76 MHz which is sufficiently close to the resonance frequency of ^{1}H such that ^{1}H and ^{19}F spectra can be measured using the same probe.



Measuring ^{19}F spectra on Pulsar

Pulsar is a high performance benchtop NMR spectrometer that does not require external services, such as liquid cryogens 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 5mm NMR tubes.

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

Trifluorotoluene is a useful reference material for ^{19}F NMR spectroscopy and can be used in a similar way to tetramethylsilane (TMS) for ^{1}H measurements.

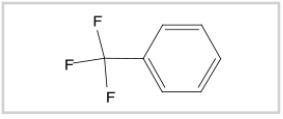
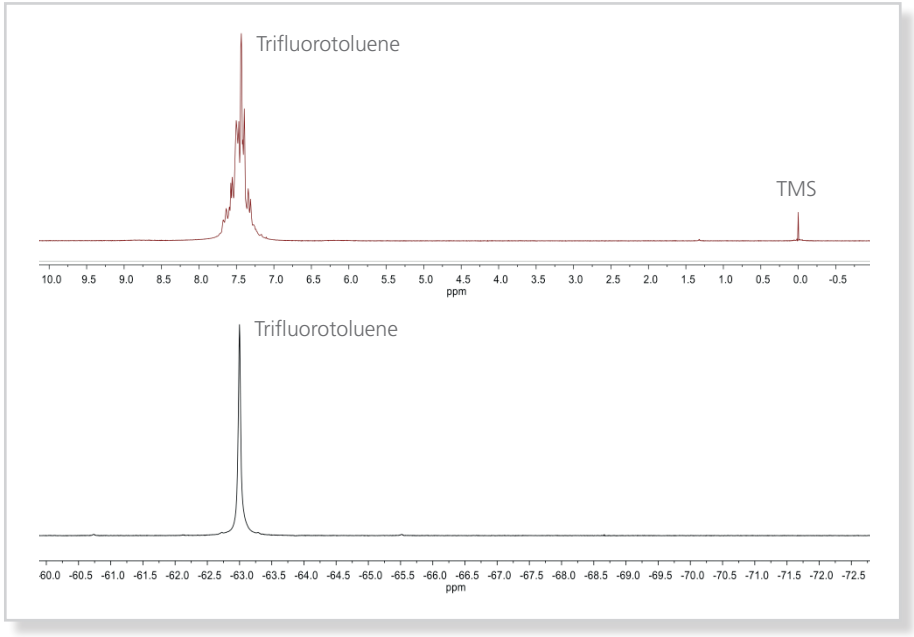


Figure 1 shows the ^{1}H and ^{19}F spectra of trifluorotoluene (TFT).



The ^{19}F spectrum consists of a single peak since the three F nuclei are in an equivalent chemical environment and are not in close proximity to any of the H nuclei in the molecule. The ^{1}H spectrum is more complex since the H nuclei on the aromatic ring are not equivalent and the homonuclear couplings give rise to splitting of the aromatic peak.

Figure 1. *^{1}H (top) and ^{19}F (bottom) spectra of trifluorotoluene*

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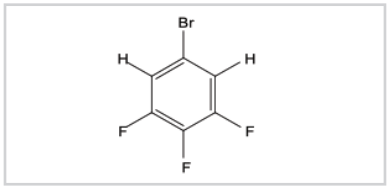
The spectrum shown in Figure 2 is a mixture of two fluorine-containing chemicals; Trifluorotoluene and trifluoroethanol.

Trifluorotoluene (TFT) is often used as a reference material for ^{19}F spectra. It appears as a strong, single peak with a chemical shift -63.72 ppm with $CFCl_3$ set at 0 ppm. It is a single peak as the structure consists of three equivalent F nuclei isolated from any other nuclei that would couple to it. By comparison the peak in the spectrum due to trifluoroethanol, at -77 ppm, is split into a triplet. This is due to the fact that the ^{19}F nuclei couples with the ^{1}H nuclei on neighbouring carbon atoms in the molecule, just as ^{1}H nuclei would couple with other neighbouring ^{1}H nuclei in the molecule.

Figure 3 shows the ^{1}H and ^{19}F spectra of the compound 5-Bromo-1,2,3-trifluorobenzene :



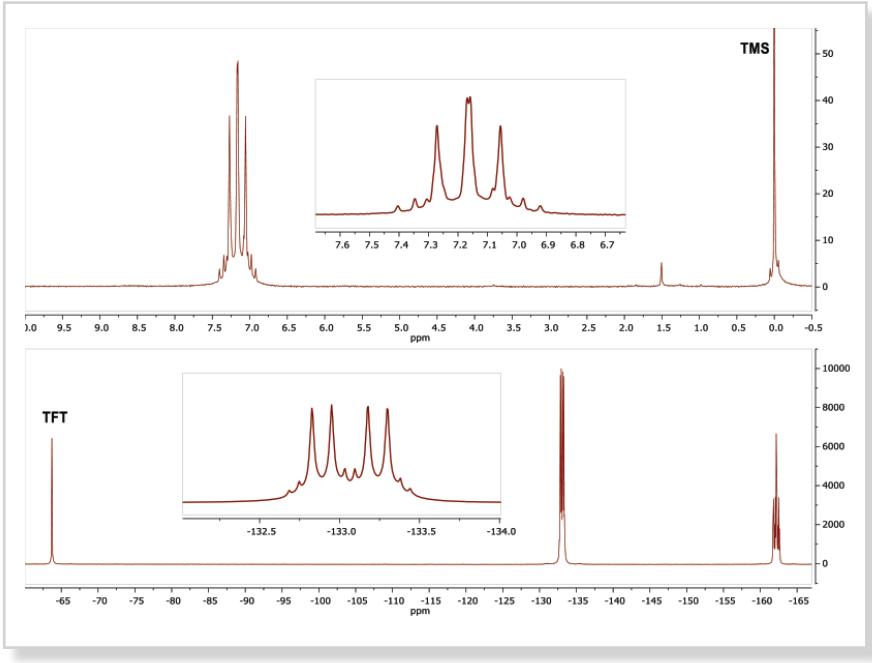


Figure 3. *^{1}H (top) and ^{19}F (bottom) spectra of 5-bromo-1,2,3-trifluorobenzene*

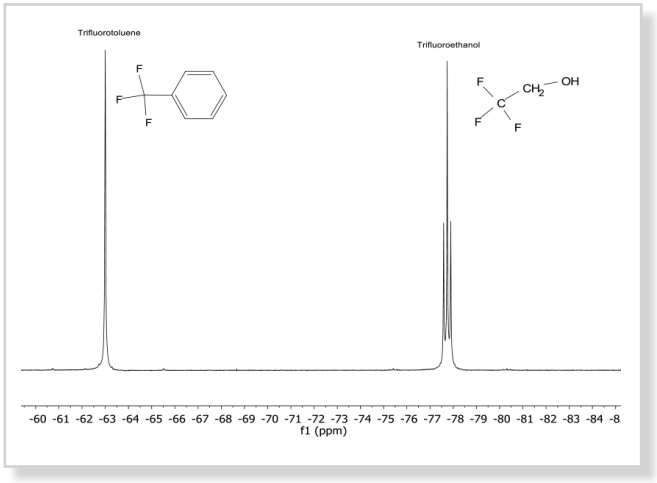


Figure 2. *^{19}F spectrum of a mixture of trifluorotoluene and trifluoroethanol*

The ^{1}H spectrum consists of a single multiplet of peaks resulting from the two equivalent ^{1}H nuclei and their couplings with ^{1}H, ^{19}F and ^{79}Br and ^{81}Br 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 ~ -133 ppm arises from the fluorines in positions 1 and 3 on the molecule while the resonance at -162 ppm arises from the fluorine in position 2. 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 at position 2 is coupled to two equivalent fluorines and two equivalent hydrogens. Any coupling between the fluorine and the bromine is too weak to be resolved in the spectrum.

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 show complex coupling patterns since each has two different fluorines and two different hydrogens and potentially a bromine as coupled neighbours.

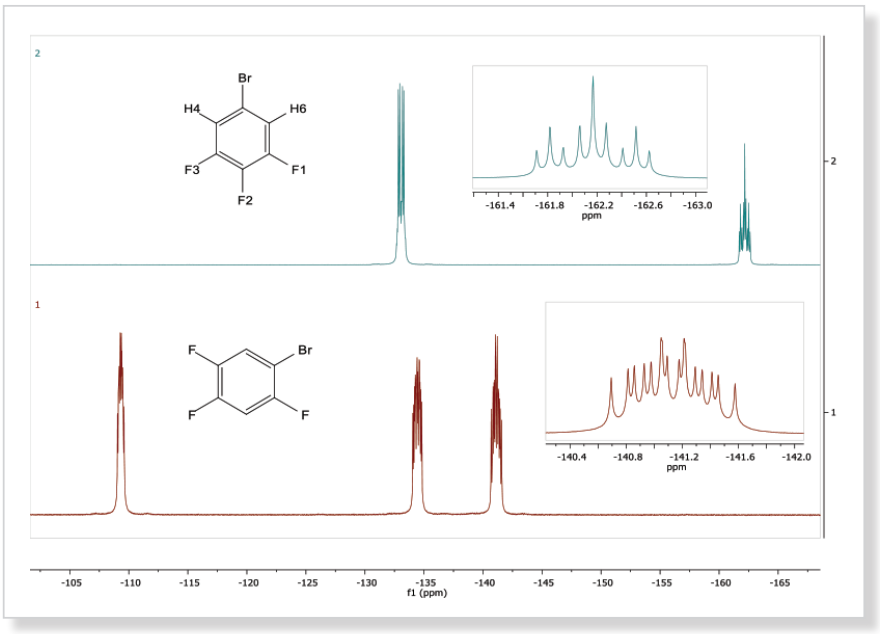


Figure 4. *^{19}F spectra of 5-bromo-1,2,3-trifluorobenzene (top) and 1-bromo-2,4,5-trifluorobenzene*

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 **Pulsar** it is possible to measure both ^{19}F and ^{1}H spectra of a sample within a couple of minutes using the same probe.

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