Structure Elucidation of Fluorinated Compounds by NMR

INTRODUCTION

- Fluorine is increasingly being used in many new drugs
  - As of 2011 there were approximately 200 fluorine containing drugs. [ref 1]
  - Fluoro-organic compounds account for 40% of the new chemical entities entering phase III trials in 2012 and 2013. [ref 2]
  - Fluorine is use in a wide range of drug applications including: Anesthetics, Antacids, Anti-anxiety, Antibiotics, Antidepressants, Anti-fungal antibiotics, Antihistamines, Antilipemics, Anti-malarial, Antimetabolites, Appetite suppressants, Arthritis/ anti-inflammatory agents, Psychotropic, Steroids/ anti-inflammatory agents. [ref 3]
- Fluorine is now appearing in illicit and illegal synthetic drugs:
  - These include: Cannabinoids [ref 4], and psychedelic phenethylamines [ref 5]
- Fluoro Polymers are important to everyday life, for example PTFE (Teflon™)

CHALLENGES

- The potential Fluorine chemical shift range is 500 ppm, 188 kHz at 9.4T (^{1}H 400 MHz) to 282 kHz at 14.1T (^{1}H 600 MHz).
- ^{19}F-^{1}H j coupling constants up to 60 Hz
- ^{19}F-^{13}C j coupling constants up to 280 Hz
- ^{19}F long range J coupling interactions complicate NMR spectra making interpretation difficult
- These spectral features combine to make ^{19}F difficult to excite and to decouple from other nuclei.

SOLUTIONS

- What is needed is a robust easy to use HFX NMR Probe and NMR console that can do every routine or sophisticated HFX experiment well!
- Including all HFX experiments, ^{1}H{^{19}F}, ^{19}F{^{1}H}, ^{13}C{^{1}H,^{19}F} & X{^{1}H,^{19}F}

By utilizing new published and patented probe technologies the powerful general-purpose ROYAL Probe now provides coupled with ECZ consoles unparalleled flexibility as the new JEOL ROYAL-HFX Probe.

How does the Technology Work?

- The Royal HFX probe uses for the first time in any commercial NMR probe magnetic coupling as an efficient purely “on” or “off” switch for the associated coil to be dual-tuned to ^{1}H and ^{19}F or single tuned to each. These improvements are related to the use of magnetic coupling in NMR circuits to improve the performance and function of NMR probes. [ref 6 - 8].
- Magnetic tuning allows the probe to retain the exact same highest performance for either ^{1}H or ^{19}F in single tune mode. In dual tune mode the switch can be tuned to easily balance the relative efficiencies of ^{19}F and ^{1}H. Because of the huge ^{19}F spectral window.
- JEOL ECZ NMR Spectrometer
- ECZS routine NMR spectrometers can generate simultaneous ^{1}H and ^{19}F frequencies with no additional hardware
- ECZR research NMR spectrometers with an optional 3rd channel can collect ^{1}H and ^{19}F data over wide ^{19}F frequency ranges in all dimensions.
- JEOL Royal HFX NMR Probe
- Spec’s Royal Probe = Spec’s Royal HFX Probe
- No Loss in RF or S/N performance relative to the standard ROYAL probe for ^{1}H, ^{19}F, ^{13}C, or X
- Includes Auto-Tune compatibility to allow easy switching between modes.

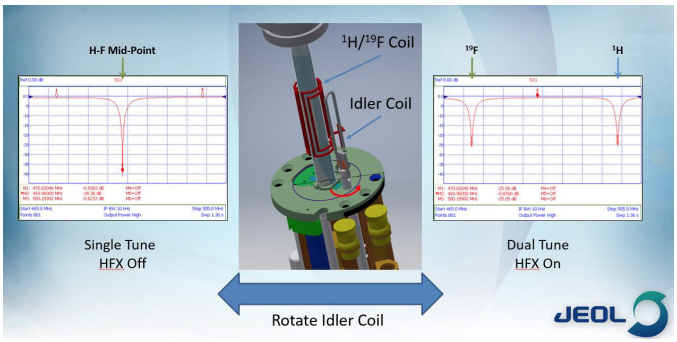

Figure 1. *Illustration of magnetic coupling technology as a perfect switch between single tune and dual tune modes in the ROYAL-HFX Probe.*