Chem 636, Fall 2008 **HW #9**

Due at the beginning of lab, the week of Oct 28 (cgf: updated 12 July 2010)

X-Nucleus NMR: ^{31}P and ^{19}F

Many nuclei in NMR can be detected in a manner similar to ^{13}C. ^{31}P and ^{19}F are two of the most common examples. These two nuclei are much more sensitive that ^{13}C: both are 100% naturally abundant isotopes, and both resonate at higher frequencies, $\nu_F = 272$ and $\nu_P = 121$ MHz when $\nu_C = 75$ MHz and $\nu_H = 300$ MHz. ^{19}F is very nearly as sensitive as ^{1}H. ^{31}P is 10× less sensitive than ^{1}H, but still 320× more sensitive than ^{13}C. One would suspect that ^{19}F and ^{31}P experiments are therefore easy to perform. But variations do exist that the researcher must be aware of. ^{19}F has a much larger chemical shift range than ^{1}H, but measurement of similar size couplings (both ^{19}F–^{19}F and ^{19}F–^{1}H) are often desired; being able to account for both typically requires optimization of the spectral window. A wide range of such variations exist for X-nuclei, and these dramatically affect the practical implementation of NMR experiments on different nuclei. Below are some general comments about all *X*-nuclei. After that, we'll address the issues specific to performing ^{31}P and ^{19}F NMR in our routine (300 MHz) laboratory.

I=1/2, +γ Nuclei

^{3}H, ^{13}C, ^{19}F, ^{31}P, ^{57}Fe, ^{77}Se, ^{171}Yb, ^{183}W, ^{187}Os, ^{195}Pt, ^{199}Hg, ^{205}Tl, ^{207}Pb

The major variations for this class of NMR-accessible nuclei are as follows:

I. If γ is too small, the resonance frequency will be small and sensitivity will suffer greatly, making direct detection difficult. ^{57}Fe, ^{187}Os, and ^{183}W fall into this category, with $\nu_{Fe} = 9.7$, $\nu_{Os} = 6.9$ and $\nu_W = 12.4$ MHz when $\nu_H = 300$ MHz.

II. All nuclei are only accessible if a probe is installed that is tuned to the nuclei's resonant frequency. In the routine portion of our facility, only ^{1}H and ^{13}C are available on *homer* and *hermes*, but ^{31}P and ^{19}F are also accessible on *athena*. This spectrometer has a special "quad" probe that switches between ^{31}P, ^{13}C and ^{19}F while staying tuned also to ^{1}H (as well as ^{2}H for the lock). The other nuclei listed above are all accessible on other spectrometers in the facility (on our AVANCE-360 and UNITY-500).

III. Various parameters—e.g., the resonance frequency (**SF0**), 90° pulse length (**PW**), spectral window (**SW** and **O1**), and relaxation delay (**RD**/**D1**)—must be set properly, typically by reading in a "jobfile". For some nuclei, the spectral window can be troublesome; e.g., ^{195}Pt has a chemical shift range of nearly 15,000 ppm. Normal liquids spectrometers can cover only a part of this range, so running multiple experiments covering different portions of the chemical shift range may be required in such cases. Fortunately, the more common nuclei of ^{13}C (220 ppm), ^{31}P (400 ppm) and ^{19}F (~400 ppm) can be accessed in a single experiment.

IV. For this class of nuclei, sensitivity is improved via NOE (by an amount $\cong 1+\frac{\gamma_H}{2\gamma_X}$), as done with routine $^{13}C\{^1H\}$, by turning the decoupler on throughout the experiment (**CPD**). DEPT and INEPT experiments can be used, with sensitivity improved by $\cong \frac{\gamma_H}{\gamma_X}$ (so these experiments are preferred as γ_X get smaller. Delays (**D2**, **D3**) based on coupling constants must be adjusted properly.

I=1/2, –γ Nuclei

^{3}He, ^{15}N, ^{29}Si, ^{89}Y, ^{103}Rh, ^{109}Ag, ^{113}Cd, ^{119}Sn, ^{125}Te, ^{129}Xe, ^{169}Tm

Negative γ prevents a simple implementation of NOEs to enhance sensitivity. DEPT and INEPT experiments, on the other hand, can still be used in a manner identical to use with positive γ nuclei (e.g., ^{13}C). Low natural abundance and low γ combine to prevent ^{15}N from being studied via direct detection on a regular basis. Labeled ^{15}N compounds are becoming more common, but even then detection is typically performed with "inverse experiments": ^{15}N is observed indirectly in ^1H-detected 2D experiments. Low γ makes direct observation of ^{89}Y, ^{103}Rh, ^{109}Ag uncommon. ^{29}Si and ^{119}Sn are most commonly observed in a similar to quantitative ^{13}C experiments, using INVGATE.AU. Relatively high sample concentrations are required (≥ 100 mM), and long experiment times may be required. Studies of these nuclei are regularly performed on our UNITY-500 spectrometer.

I ≠ 1/2 Nuclei

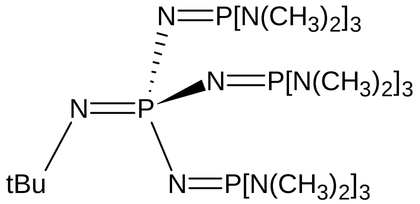
^{2}H, ^{6}Li, ^{7}Li, ^{11}B, ^{14}N, ^{17}O, ^{27}Al, ^{33}S, ^{55}Mn, ^{101}Ru, ^{187}Re ……

All non-spin-1/2 nuclei have a "quadrupole" moment, which can severely broaden the NMR resonances. ***^{2}H, ^{6}Li, ^{7}Li, ^{11}B*** are nuclei that give small to moderate broadening, so these nuclei are regularly studied by NMR. Very low natural abundance make some important nuclei hard to study irrespective of natural linewidths, ^{17}O and ^{33}S being the most prominent examples. Many metal nuclei have large quadrupole moments that severely broaden observed line shapes. NMR detection of such nuclei can be very difficult to impossible: ^{55}Mn, ^{101}Ru and ^{187}Re are three of many examples. Even so, significant numbers of publications with direct or indirect NMR detection of many I≠1/2 nuclei exist: see, for example, ^{17}O NMR Spectroscopy in Organic Chemistry, ed. D. W. Boykin (CRC Press, 1991, ISBN 0849348676)] and Transition Metal NMR, ed. P.S. Pregosin (Elsevier, 1991, ISBN 044488176X).

Access to the AVANCE-360 to enable research involving other nuclei can be provided upon request for students that have taken (or are taking) Chem 636. Access to the 500 and 600 MHz spectrometers is provided via Chem 637, offered each summer session.

^{31}P NMR Experiments on Athena

☞ Use the **P4-*t*Bu** sample in benzene-d_6 for ^{31}P experiments.



$^{31}P\{^1H\}$ experiments are relatively straightforward to acquire on Athena. If measurement of ^{31}P–^1H spin-spin couplings, J_{PH}, are wanted, the spectral window may need to be optimized. In these situations, setup similarly to the notes below for ^{19}F.

Setup and acquisition of $^{31}P\{^1H\}$ spectra:

1. Acquire a reasonable-quality ^1H spectrum. Make sure to save and TOPC this FID, since it will be used to reference the ^{31}P spectrum.
2. **FT** the ^1H spectrum on the spectrometer. Using **EP** mode, check the **O1** value that is centered on the protons that will require decoupling in the $^{31}P\{^1H\}$ spectrum.

   Warning: Check **O1** values by typing **O1** in EP-mode and noting the value listed. Enter ↵ afterwards (discarding the change). Do not *memorize* (save) the value by typing **O1** and then **M**; this would change the parameters, which would not match the current spectrum. Any further **O1** checks, without retaking the FID, would not be correct. This mismatch between parameters (changed with **^O**, or **O1** → **M**, without a following **ZG**) and a spectrum is a common source of confusion and mistakes on the AC spectrometers!

   The **O1** value must be within 5 ppm of all ^{31}P-coupled protons; otherwise the decoupler may leave residual couplings, i.e., broadening or splitting of the ^{31}P resonances. Write down this **O1** value. [If no single **O1** value covers all possible protons, then two values and two different ^{31}P experiments may be required. Such situations are unusual, but not unknown; asking for help in such cases is recommended.]
3. Read in parameters appropriate for $^{31}P\{^1H\}$ experiments: **RJ P31.1DJ↵**
4. Initialize the interface (make sure all hardware is properly setup) by entering **II↵**
5. Change **O2** to the value written down for **O1** in step 2 above.
6. Check that **DP** is set correctly, then turn on Waltz-16 (composite pulse) decoupling using: **CPD↵**
7. Acquire a $^{31}P\{^1H\}$ spectrum with **ZG** . Use **TR #↵** and check the signal-to-noise with **LB=2 EM FT↵** .
8. Acquire a 2nd FID—a ^1H-coupled ^{31}P spectrum—with the ^1H decoupler turned off: use **DO↵** . Use the same **NS** as above. [GATEDEC.AU would give better signal-to-noise, as it provides NOE. ^{31}P is often sensitive enough that the simple method above of just using **DO** and **ZG** is OK. Do not do this ^{13}C: always use GATEDEC.AU to acquire to obtain ^1H-coupled ^{13}C spectra.]
9. Workup both spectra in NUTS. Do not use a matched filter, but rather **LB=0.5** to **2**. A somewhat larger LB is typically used for processing X-nucleus spectra, sacrificing some resolution to obtain better signal-to-noise.

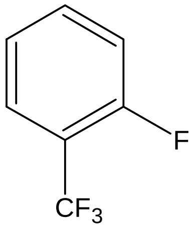
10. Reference the ^{31}P spectra using the ^{1}H spectrum. See section 6 of the NUTS Cheat Sheet for instructions on how to perform this "Unified Scale" referencing.

    Note: Use of the Unified Scale is the recommended method for referencing all NMR spectra, including ^{13}C spectra; see notes on the facility website at User Guides → Other for more details. Many chemists still reference ^{13}C spectra using solvent resonances (e.g., the 1:1:1 triplet of $CDCl_3$), ignoring the IUPAC recommendation. But for ^{13}C taken in D_2O, note that DSS or TSP need not be added; the spectrum should be referenced using the corresponding ^{1}H spectrum.

P1+P2 → Plot and turn-in the $^{31}P\{^{1}H\}$ and proton-coupled ^{31}P spectra on separate pages. Include proper annotations, and insets to better display the two major ^{31}P multiplets in each spectrum.

Q1 → Explain what is causing the quartet structure of the upfield (low frequency) multiplet in the ^{1}H–coupled multiplet.

Q2 → What was the obtainable resolution in these spectra?



^{19}F NMR Experiments on Athena

☞ Use the 2-fluorobenzo-trifluoride sample in $CDCl_3$ for ^{19}F experiments.

^{19}F NMR is unusual in a couple ways. First, its resonance frequency is close to ^{1}H: $\nu_F = 282$ MHz when $\nu_H = 300$ MHz. It is challenging to manufacture probes that can tune to both nuclei without incurring significant crosstalk. The most common solution for ^{19}F is "quad"-nucleus-style probes: Athena tunes to ^{1}H, ^{13}C, ^{19}F and ^{31}P. Broadband-style probes that tune to most X-nuclei—and are therefore common in NMR facilities—typically cannot ^{1}H-decouple while observing ^{19}F. $^{19}F\{^{1}H\}$ is only available on Athena and the INOVA-500, and $^{1}H\{^{19}F\}$ only on the INOVA-500 in our facility.

Important in practical terms for researchers is the large range of chemical shifts for ^{19}F. The range is 400 ppm, similar to ^{31}P, but the large γ_F makes 400 ppm = 113 kHz on Athena. This large spectral range, and the common need to measure ^{19}F–^{19}F and ^{19}F–^{1}H coupling constants will usually require optimization of the spectral window for each sample. Good resolution is needed to accurately measure coupling constants: acquisition times must be long enough to match the needed resolution (resolution ~ 1/AQ). Optimization of the spectral window will reduce the sweep width, which would otherwise limit the resolution due to too small an AQ.

Setup and acquisition of ^{19}F spectra:

1. Acquire a reasonable-quality ^{1}H spectrum. Make sure to save and TOPC this FID, since it will be used to reference the ^{19}F spectrum.
2. **FT** the ^{1}H spectrum on the spectrometer. Using **EP** mode, write down the **O1** value that is centered on the protons that will require decoupling in the $^{19}F\{^{1}H\}$ spectrum.

   Warning: Same as discussed above for ^{31}P.
3. Read in parameters appropriate for ^{19}F experiments: **RJ F19.1DJ↵**

[**F19ACET.1DJ, F19D2O.1DJ** or **F19C6D6.1DJ** will set O2 correctly in most cases.]

4. Initialize the interface (make sure all hardware is properly setup) by entering **II↵**
5. Change **O2** to the value written down for **O1** in step 2 above (or see step 3 [ ] above).
6. Check that **DP** is set correctly, then turn on Waltz-16 (composite pulse) decoupling using: **CPD↵**
7. Acquire a $^{19}F\{^{1}H\}$ spectrum with **ZG** . Use **TR #↵** and check the signal-to-noise with **LB=2 EM FT↵** . Make sure all ^{19}F in the compound are observed. Save and TOPC.
8. Note **AQ**, **TD** and **SW** for this standard setup. These parameters are related by $AQ = \frac{TD}{2SW}$

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   The *obtainable resolution* = 1/**AQ**. The standard setup will therefore not allow measurement of even moderately sized J_{FF} or J_{FH}.

Q3 → What is the obtainable resolution using the ^{19}F standard parameters (as read in from the F19.1DJ jobfile)?

Q4 → To resolve 1 Hz couplings, we need to set the obtainable resolution to ≤ 0.5 Hz. What must **AQ** equal or be greater than for this condition to be met?

9. Using EP-mode, optimize the spectral window by expanding the spectrum so all the ^{19}F resonances fit within the inner 8 horizontal squares on the AC display. At this point, enter **^O** [control-O]. The spectrometer will display the changes to **SW**, **O1** and **AQ**. Check that **AQ** ≥ 1 (**AQ** ≥ 3 is preferable; **SI** and **TD** can be set as large as 256K to assist with this).
10. Acquire a high-resolution $^{19}F\{^{1}H\}$ spectrum using **NS** from step 7.
11. Acquire and save a 2nd FID—a ^{1}H-coupled ^{19}F spectrum—with the ^{1}H decoupler turned off: use **DO↵** . Use the same **NS** as above.
12. Workup both spectra in NUTS. Use a matched filter, **LB=1/AQ**.
13. Reference the ^{19}F spectra using the ^{1}H spectrum, as described for ^{31}P (step 10 in that section).

P3+P4 → Plot and turn-in the $^{19}F\{^{1}H\}$ and the ^{1}H-coupled ^{19}F spectra on separate pages, with proper annotations, and insets to better display the two major ^{19}F multiplets in each spectrum.

15. The $^{19}F\{^{1}H\}$ spectrum should be straightforward to interpret, showing the aromatic fluorine as a quartet due to coupling to the 3 methyl fluorines; it should be clear why the CF_3 shows as a doublet.

    The ^{1}H-coupled ^{19}F spectrum is much more complex. The proton para to the aromatic fluorine is the only proton that does not have a resolved coupling to the aromatic fluorine. The other three protons form a doublet of doublet of doublets, all on top of the quartet arising from the CF_3 group: the pattern is a qddd.

Turn in 4 plots and answers to 4 questions.