

Fall 2014 Chem 636 – HW #6

X-Nucleus NMR: ^{19}F , ^{31}P and ^{119}Sn

Assignment due at beginning of lab, week 7 (Oct 14 – Oct 17).

Use Persephone for this week's HW #6.

Although you may work in groups, each of you should setup and acquire your own data, and process and hand in that individual set of data.

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 than ^{13}C : both are 100% naturally abundant isotopes, and both resonate at higher frequencies, $\nu_{\text{F}} = 470.5$ MHz and $\nu_{\text{P}} = 202.4$ MHz when $\nu_{\text{H}} = 500$ MHz. ^{19}F is very nearly as sensitive as ^1H . ^{31}P is 10× less sensitive than ^1H , but still 320× more sensitive than ^{13}C . One might suspect that ^{19}F and ^{31}P experiments are therefore easy to perform. True in terms of relative sensitivity, but issues exist that the researcher must be aware of. ^{19}F has a much larger chemical shift range than ^1H , but measurement of similar size couplings (both $^{19}\text{F}-^{19}\text{F}$ and $^{19}\text{F}-^1\text{H}$) are often desired. Being able to manage a large chemical shift range and obtain high resolution requires optimization of the spectral window, while remembering to keep the acquisition time suitable large. Similar issues can be important for ^{31}P , although there more often the issue is one of resolving different species having small differences in chemical shift, while observing other species much farther away. Again, optimization of the spectral window and acquisition time is the key to obtain good quality ^{31}P data.

A wide range of such variations exist for X-nuclei, and these dramatically affect the practical implementation of NMR experiments for different nuclei. Below are some general comments about all X-nuclei. After that, we'll address the issues specific to performing ^{31}P , ^{19}F and ^{119}Sn NMR in our facility.

Note: Currently, only ^1H , ^{13}C , ^{19}F , ^{31}P , ^{11}B and ^{29}Si are available for direct observation on Artemis (Av-400). ^1H , ^{13}C , ^{19}F , ^{31}P can be studied using Athena. Only ^1H and ^{13}C can be observed on Hermes (Varian Mercury-300). ^1H , ^{13}C and ^2H can be observed on Callisto (do not attempt ^2H on Callisto without being specifically trained for this). All accessible NMR nuclei can be studied using Persephone (Av-500) and the Av-360.

$I=1/2$, $+\gamma$ Nuclei

^3H , ^{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. The experimental signal-to-noise, S , follows

$$S \propto \gamma_{\text{ext}} \times \gamma_{\text{obs}}^{5/2} \times \mathbf{B}_0^{3/2} \times \mathbf{c} \times \sqrt{t}$$

where γ = magnetogyric ratio (γ_{ext} = excitation nucleus; γ_{obs} = observe nucleus), \mathbf{B}_0 = magnetic field strength, c = concentration (of nuclei), t = time. ^{57}Fe , ^{187}Os , and ^{183}W have very small γ , with $\nu_{\text{Fe}} = 16.2$, $\nu_{\text{Os}} = 11.4$ and $\nu_{\text{W}} = 20.8$ MHz when $\nu_{\text{H}} = 500$ MHz. These nuclei are impossible to observe directly, unless the concentration is very high ($> 1\text{M}$).

II. All nuclei are only accessible if the NMR probe is tuned to the nuclei's resonant frequency. In the routine portion of our facility, only ^1H and ^{13}C are available on *hermes*, with ^{31}P and ^{19}F also accessible on *Athena*, and ^{11}B and ^{29}Si on *artemis*. *Artemis* has a broadband probe, so nuclei access is limited by time available on the spectrometer. *Athena* has a special "quad" probe that switches between ^{31}P , ^{13}C and ^{19}F while always staying tuned to ^1H (as well as ^2H for the lock). The other nuclei listed above are all accessible on the Avance-360 and Persephone-500 (low- γ only on the BBFO probe).

III. Various parameters—e.g., the resonance frequency (**SF0**), 90° pulse length (**P1 / PW**), spectral window (**SW** and **O1p**), and relaxation delay (**D1 / RD**)—must be set properly. Reading in a parameter set or "jobfile" will suggest a value, but a wide range often exists, so any one value of D1 cannot be correct in all cases; consulting the literature can be helpful. For some nuclei, setting 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 (limited by the probe; for $^{195}\text{Pt} \sim 2000\text{ppm}$), so running multiple experiments covering different portions of the chemical shift range may be required in such cases. Fortunately, the more common nuclei, ^{13}C (220 ppm), ^{31}P (400 ppm) and ^{19}F (~ 400 ppm), can be accessed in a single experiment.

IV. For spin = $+1/2$ nuclei, signal-to-noise is improved via NOE (by an amount $\cong 1 + \frac{\gamma_{\text{H}}}{2\gamma_{\text{X}}}$), as done with routine $^{13}\text{C}\{^1\text{H}\}$ by turning the decoupler on throughout the experiment (**CPD**). DEPT and INEPT experiments can also be used, with signal-to-noise improved by $\cong \frac{\gamma_{\text{H}}}{\gamma_{\text{X}}}$ (thus PT experiments are strongly preferred as γ_{X} gets smaller).

I=1/2, $-\gamma$ Nuclei

^3He , ^{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 are therefore used in a manner identical to that used with positive γ nuclei (e.g., ^{13}C). Note that these experiments require a coupling to be present (usually to ^1H , but to ^{31}P or ^{19}F might also work). Low natural abundance and low γ combine to prevent ^{15}N from being studied via direct detection unless concentrations are very high ($\geq 1\text{M}$). Labeled ^{15}N compounds are becoming more common, but even then detection is typically performed with "inverse experiments": ^{15}N observed indirectly via ^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 manner very similar to quantitative ^{13}C experiments using inverse-gate (IG) parameter sets. As with ^{13}C , relatively high sample concentrations ($\geq 50\text{mM}$), and relatively long experiment times are required. Studies of these nuclei are best performed using the Prodigy probe on Persephone.

I ≠ 1/2 Nuclei

^2H , ^6Li , ^7Li , ^{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 lines. ^2H , ^6Li , ^7Li , ^{11}B are nuclei that have small to moderate broadening, so these nuclei are regularly studied by NMR. Very low natural abundance make some nuclei hard to study irrespective of natural linewidths, ^{17}O and ^{33}S being the most prominent examples. [A lot of useful information has been obtained with ^{17}O experiments, but usually on labeled compounds.] Many metal nuclei have large quadrupole moments that severely broaden observed line shapes. NMR detection of such nuclei can be difficult to impossible: ^{55}Mn , ^{101}Ru , ^{105}Pd and ^{187}Re are four of many examples. Even so, significant numbers of publications with direct or indirect NMR detection of I≠1/2 nuclei exist: see, for example, [17O 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).

^{19}F experiments on Persephone (Bruker Avance 500)

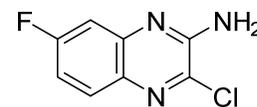
^{19}F NMR is unusual in a couple ways. First, its resonance frequency is close to ^1H : $\nu_{\text{F}} = 470$ when $\nu_{\text{H}} = 500$ MHz. It is challenging to manufacture probes that can tune to both nuclei without incurring significant crosstalk. The way probes achieve this ^{19}F tune can be important: the BBFO probe on the 500 tunes the X channel up to ^{19}F , leaving the ^1H channel available for decoupling. The Prodigy probe, on the other hand, tunes the ^1H channel down to ^{19}F . Thus, on that probe ^1H decoupling cannot be performed (but ^{31}P - ^{19}F or ^{13}C - ^{19}F double-resonance experiments are available). Athena uses a “quad”-style probe, tuning the X channel to ^{13}C , ^{19}F or ^{31}P , so $^{19}\text{F}\{^1\text{H}\}$ is available. The BBFO probes on the Av-400 and 500 also can do $^1\text{H}\{^{19}\text{F}\}$.

As important is the large range of chemical shifts for ^{19}F . The range is ~ 300 ppm, similar to ^{31}P , but the larger γ_{F} makes 300 ppm = 141 kHz on Persephone (whereas protons range ~ 5 kHz). The large ^{19}F spectral range, and the need to measure ^{19}F - ^{19}F and ^{19}F - ^1H coupling constants or resolve small differences in chemical shift typically requires optimization of the spectral window. Attention must also be paid to the acquisition time to enable sufficient resolution.

With a compound where the chemical shifts are unknown, usually one starts with the default parameter set, which should have a large spectral range (398 ppm on Persephone, which covers most fluorinated organic compounds). **For ^{19}F experiments, always use parameter sets from uwchem/par/ corresponding to the installed probe.** The standard Bruker parameter sets will not work!

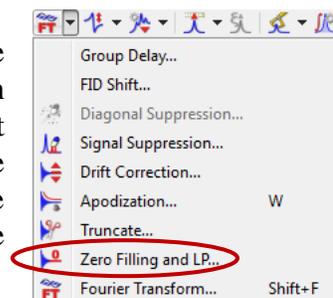
Use **3-amino-2-chloro-6-fluoroquinoxaline** in **DMSO** for ^{19}F experiments.

1. Acquire a standard $^{19}\text{F}\{^1\text{H}\}$ spectrum. ^1H decoupling helps by improving sensitivity. 8 scans is enough for this and following ^{19}F acquisitions. Use the standard ^{19}F parameter set from UWchem/par/. Make sure to check for the correct probe.



2. Acquire an optimized $^{19}\text{F}\{^1\text{H}\}$ spectrum. Here a command that copies the current spectrum into a new EXPNO is useful: **wra # ↵**. Then move into that new EXPNO using the command: **re # ↵**. Reprocess with **efp ↵**. Now you can optimize spectral window (**SW** and **O1p**) as follows:
 - a) Drag with the left mouse to expand about an appropriate spectral range, leaving about 10ppm of baseline on either side of the ^{19}F peaks. Then click the **.setsw** icon , which pops up a GUI with the new **SW** and **O1p** value. Record these values for future reference. Also record the chemical shifts of the two main ^{19}F peaks.
 - b) As learned earlier in the semester, when **SW** is changed in TopSpin, **AQ** is automatically modified. After changing **SW**, adjust **AQ** such that 0.5 Hz resolution can be achieved.
 - c) Additionally, by adjusting **AQ**, the number of points acquired, **TD**, is changed. In TopSpin, to retain the $1/\text{AQ}$ resolution, you must also change the number of points in the spectrum, i.e., that the FFT generates, **SI**, such that **SI** $\geq 2 \times \text{TD}$.
3. Acquire a standard ^1H spectrum. It is always recommended that you do this, and store the ^1H spectrum with the X-nucleus experiment (even when the ^1H spectrum is of no interest in and of itself). We've already seen how to use the ^1H spectrum as a check of the spectrometer shim. As importantly, the ^1H spectrum can be used to 'absolute reference' the X-nucleus spectrum (available in both MNova and TopSpin). This is an important check of the spectrometer referencing.
4. Acquire a ^{19}F experiment without ^1H decoupling. We've used two methods in the past for doing this:
 - i) *Not recommended:* Use **new ↵** and "Use Current Parameters" check box, then change the pulse sequence. Here the pulse sequence quandary is imposed: what sequence can we change to? ^{19}F is a *special* nucleus in terms of the spectrometer setup. Bruker standard setups don't work correctly for ^{19}F (at least, not in an easy-to-understand fashion). So the next method is recommended.
 - ii) *Recommended:* Use **new ↵** and read in a new Experiment. The problem here is that the optimized spectral window parameters will not be included in the new experiment. [This is possible, but manually making the change seems best.] After reading in the BBFO_F19 (or Prodigy_F19) parameter set, change **SW** and **O1p** to those recorded above in step 2b. Make the changes also to **AQ** and **SI** as done in 2c.

1. Plot the three ^{19}F spectra as a stack plot, expanded about the region at -105 ppm. Remember to setup matched filters in MNova. You should also check that MNova is zerofilling at least once: use the FT icon, and select Zero Filling and LP... Make sure the selected number (e.g., 64K) is twice the size of the Original Size (e.g., 32K). Note the improved resolution of the later spectra compared to the first (standard parameters) spectrum.

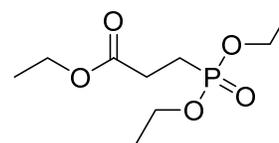


- Q1** The splitting in this $^{19}\text{F}\{^1\text{H}\}$ spectrum can be explained by looking at the molecular structure. What splitting would you expect and what do you see? Explain.

*It can be useful to identify heteronuclear couplings in proton spectra. The simplest method for doing so is to decouple the X nucleus, i.e., acquire an $^1\text{H}\{X\}$ 1D spectrum. It is important to realize, however, that a decoupler can cover only a portion of the spectral range for many nuclei, typically around 10-20kHz: the exact range depends on the probe used and the decoupler sequence selected. The limiting factor is power deposition in the probe and sample (it is possible to boil your sample with a decoupler; using high decoupler powers may damage the probe and other hardware on the spectrometer). It is imperative, therefore, that **O2p** — the center frequency of the decoupler — be within the decoupler bandwidth of the X nuclei of interest.*

Note: A 10 kHz decoupler bandwidth is sufficient to decouple most protons in $X\{^1\text{H}\}$ spectra. Some protons, such as boron hydrides, however, fall outside the decoupler range, and must be dealt with similar to as described below.

5. Acquire a $^1\text{H}\{^{19}\text{F}\}$ 1D acquisition (experiment probe_PROF19DEC in /UWchem/par/). Persephone can decouple a ~20 ppm range for ^{19}F . Use the standard parameters as is, including the setting for **O2p** (but note its value).
 6. Acquire up another $^1\text{H}\{^{19}\text{F}\}$ acquisition, but now change **O2p** to a value close to what you found for the ^{19}F peaks in step 2a.
 7. Acquire a last $^1\text{H}\{^{19}\text{F}\}$ acquisition, setting **O2p** to -170ppm.
- 2☞ Plot these three ^1H spectra with the original ^1H spectrum (from step 3; note that this spectrum is ^{19}F -coupled) as a stack plot. Expand the aromatic region for the plot.
- Q2** The splitting in the $^1\text{H}\{^{19}\text{F}\}$ spectra can also explained by looking at the molecular structure. Do the **O2p** values and observation of multiplet patterns of the aromatic protons make sense?
- Q3** Define an experimental procedure to test the usable decoupler bandwidth.
8. Now acquire a standard ^{13}C spectrum of this sample and process as usual. You will need at least 128 scans for this 50 mM sample on the BBFO probe.
- 3☞ Expand and plot the aromatic region.
- Q4** ^{13}C peaks in this spectrum show splitting. Why?
- Q5** Look more closely at the splittings. What information can you gain from them? How can this help with structure elucidation?

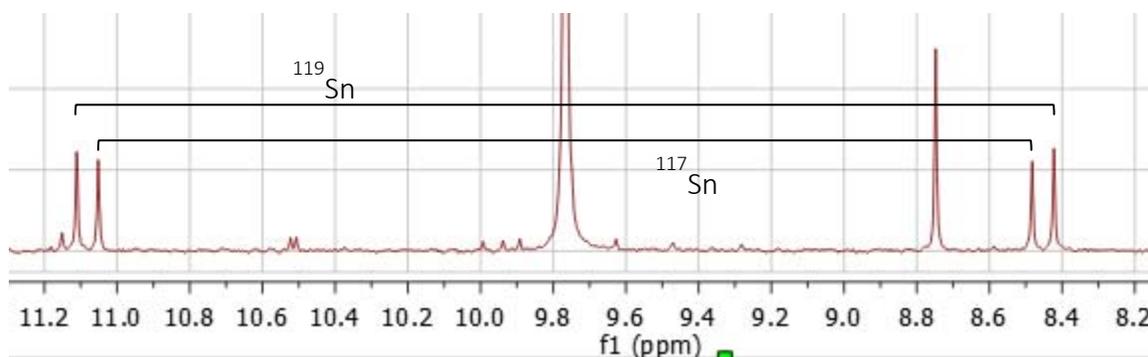
^{31}P experiments on Persephone

Use **triethylphosphono acetate** in CDCl_3 for ^{31}P experiments.

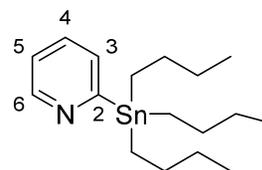
9. Always acquire a ^1H spectrum. This spectrum will be useful for checking shims and the referencing (via absolute referencing in MNova).
 10. Acquire a standard $^{31}\text{P}\{^1\text{H}\}$ experiment (P31CPD in /stan/nmr/par). The standard phase cycle (**NS**) will be sufficient for these experiments. Write down the default ^{31}P **SW** and **AQ** values.
 11. Acquire a spectral-window-optimized $^{31}\text{P}\{^1\text{H}\}$ spectrum by modifying the spectral region as described in section 2 above. As always, check that **AQ** is in a reasonable range (typically 1-2 s); then check that **SI** $\geq 2 \times \text{TD}$. Write down the chemical shift of the ^{31}P signal.
 12. Acquire a ^{31}P experiment with no decoupling. Adjust **SW**, **O1p**, **AQ**, and **SI** to match that in the spectra-window-optimized spectrum acquired in step 11.
- 4☞ Plot the three $^{31}\text{P}\{^1\text{H}\}$ spectra as a stack and submit. For ^{31}P , as with ^{13}C , the **lb** (or exponential value in MNova) is typically chosen to equal 1 to 2 Hz; this improves signal-to-noise at the expense of a slight loss in resolution. The optimized spectral window for this compound gives only marginal improvements in resolution.
13. Acquire a $^1\text{H}\{^{31}\text{P}\}$ (PROP31DEC). Adjust the **O2p** value to match the ^{31}P of interest.
- 5☞ Plot the two $^1\text{H}\{^{31}\text{P}\}$ spectra as a stack and submit.

For X-nuclei that are not 100% abundant, coupling satellites will be observed about the main peak in ^1H and ^{13}C (and ^{31}P and...) spectra. Some isotopes have more than one NMR active nucleus, so several pairs of satellites will be observed. The intensity of each set of satellites will be at the abundance of the isotope.

Sn has three NMR active $I=1/2$ isotopes: ^{115}Sn , ^{117}Sn and ^{119}Sn . ^{115}Sn only occurs with a natural abundance of 0.34% and is the least sensitive isotope. Natural abundance is 7.68% for ^{117}Sn compared to 8.59% for ^{119}Sn , so in ^1H and ^{13}C spectra, two sets of satellites with similar intensity will be observed; see the example for a ^{13}C methyl group below. ^{119}Sn is slightly more sensitive than ^{117}Sn and therefore is the preferred nucleus for direct detection.



^{119}Sn experiments on Persephone



Use the **tributylstannylpyridine** in CDCl_3 for ^{119}Sn experiments.

14. Always acquire a ^1H spectrum. This spectrum will be useful for checking shims and the reference (via absolute referencing in MNova).

15. Acquire a $^{119}\text{Sn}\{^1\text{H}\}$ spectrum (experiment SN119IG in /nmr/par). The chemical shift range of ^{119}Sn is about 2600ppm (from -1900 to 700 ppm).

Q6 Where approximately do you expect the peak here to show up? No idea? Google “NMR periodic table”. The Hebrew University of Jerusalem has a great website here where you can select the “nucleus of interest” from a periodic table.

17. Acquire a standard $^{13}\text{C}\{^1\text{H}\}$ experiment and process in MNova. Zoom into the aromatic region and save this plot too.

6. Plot the full and expanded ^{13}C spectra, and submit.

		$^1J(\text{Sn-C})$ (Hz)	$^2J(\text{Sn-C})$ (Hz)	$^3J(\text{Sn-C})$ (Hz)	$^4J(\text{Sn-C})$ (Hz)	$^5J(\text{Sn-C})$ (Hz)
aromatic	^{119}Sn	493.60	77.30	60.56	31.19	10.8
	^{117}Sn	471.87	74.03	57.94	30.22	
aliphatic	^{119}Sn	338.01	57.32	20.34	-	
	^{117}Sn	323.93	54.93			

Q7 Look more closely at the satellites on the peaks in the aromatic region. Using the information provided in the table above, you should be able to identify C-2 and C-3. Provide the chemical shift and size of $J(\text{Sn-C})$ for both carbons from the $^{13}\text{C}\{^1\text{H}\}$ spectrum.

Absolute Value Referencing in MNova: 

Absolute referencing using the Unified Scale is the recommended method for referencing all NMR spectra, including ^{13}C spectra; see

http://www.chem.wisc.edu/~cic/nmr/Guides/Other/Xi_chem_shift_scale.pdf

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 spectra acquired in D_2O , as important example, the spectrum can be referenced using the corresponding ^1H spectrum. This procedure has most value with Athena, as X referencing is not close on that spectrometer. It helps with Artemis, Callisto and Persephone: TopSpin usually gets the reference pretty close, but this procedure is a good check of accuracy.

- a) Process the proton spectrum as you normally would, including referencing it to TMS or similar.
- b) In the same document, process your X spectrum. Perform ‘absolute referencing’ by clicking on  and making sure that under ‘Spectra’ only the X spectrum is checked. Also make sure that at the top ‘Use as Reference’ is pointing at the ^1H 1D spectrum of this compound. Click OK.

Upload 6 plots as .pdf and .mnova files, and answer 7 questions.