Performing no-D NMR Experiments in TopSpin and IconNMR

updated: 15 Oct 2021 (cgf)

^{1}H NMR experiments can in many instances be obtained usefully in non-deuterated (proteo-) solvents: these experiments encompass the "no-D" label.[1] For some solvents — e.g., THF and DMF — no-D NMR may provide significant cost savings. The primary issue with no-D NMR is overlap of the huge ^{1}H solvent resonances: if the important regions of the solute spectrum can be avoided from having overlap from the solvent, no-D NMR may provide good quality data. The technique works best if solute concentrations are > 100mM; note however that this is not required, and useful data can be obtained with less solute.

The use of non-deuterated solvents prevents use of the field-stabilization lock, so long experiments will be degraded by magnet drift. Addition of 10% deuterated solvent should be done for long experiments (and strongly recommended if the deuterated solvent is inexpensive). Topshim does an excellent job with no-D NMR samples with proper changes in parameters, as discussed in sections B, D and E.

Spectra of other nuclei can be obtained in non-deuterated solvents. Decoupler issues do occur in ***^{13}C spectra*** *for samples in proteo-organic solvents*, but these can usually be resolved (see section F).

^{2}H experiments are now discussed in a separate document:

http://www.chem.wisc.edu/~cic/nmr/Guides/Ba3vug/AV3_D-NMR.pdf

A. ***Initial Setup:***

1. The value of the chemical shift, ν_{solv}, obtained in step 5 below will vary depending on the deutero-solvent last locked. If the sample prior to yours was in $CDCl_3$ and a few days later it is CD_3CN, ν_{solv} will differ.

   It is therefore recommended that a sample of known and identical solvent is locked just prior to performing the following steps. A simple way to do this is to run a 1 scan experiment in Icon – or simply lock on the sample in TopSpin – on the standard sucrose sample in D_2O kept on each spectrometer robot: location 96 on artemis and eos, and 24 on nyx and phoebe (these latter two may move around, so check).

   We are not yet certain that this procedure will yield identical ν_{solv} every time (our tests have been inconsistent with this), *but the above procedure will reduce variations.* Note also that many peaks move with changes in solvent composition with mixed solvents. In such cases, a scout scan should always be acquired to determine

2. Acquire a one-scan "scout" ^{1}H spectrum [**ns=1 ds=0 rg=1**].
3. Set: **ACQUPARS → LOCK → LOCNUC = off**
4. **ii↵ rga↵ zg↵**
5. Write down the chemical shift of the largest peak that is best resolved, ν_{solv}, by hovering the cursor over it. The value will be listed in the upper left corner.

B. ***Shimming:***

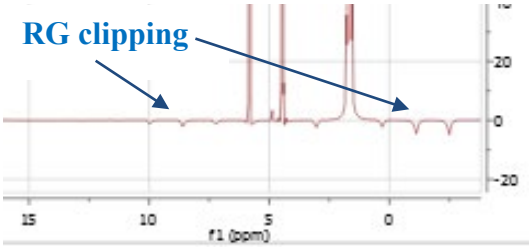
1. In TopShim, set options: **1h lockoff o1p=<value in ppm> selwid=0.5**

[1] *No-D NMR (no-Deuterium Proton NMR) Spectroscopy: A Simple Yet Powerful Method for Analyzing Reaction and Reagent Solutions.* T. R. Hoye et.al., Org. Lett. **6** (2004) 953-6.

2. If it topshim sends a message about reducing the echo time, add **convcomp** to the line above (always use convcomp with the Prodigy and DCH cryoprobes, and any time you are running non-ambient temperature experiments).
3. I (cgf) prefer the **selwid=0.5** as included above, which changes from the default 1 ppm selection width to 0.5 ppm. You can reduce selwid to 0.3 (so it ranges 0.3 to 1.0), but not less.

C. ***Resolving issues with RG clipping:***

The spectrometers often cannot get RG low enough to prevent FID clipping. The figure to the right shows typical appearance of negative artifacts present after Fourier transform, here for a sample in protonated isopropanol (vertically expanded 50×, **RG**=2.6, **PULPROG** = zg30).



A few techniques can remedy this situation:

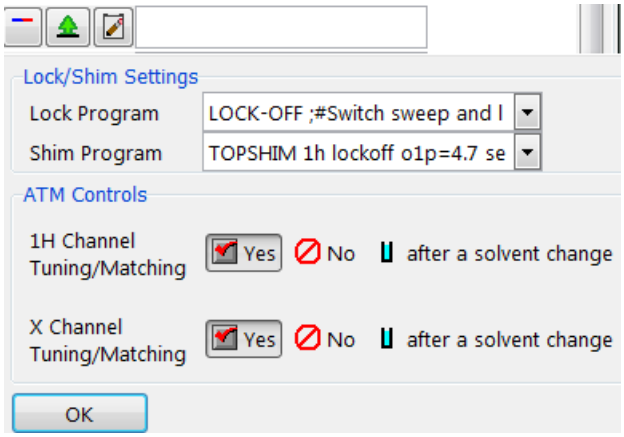
1. It can be helpful to prevent RGA from being done. In TopSpin, set **RG** = 1 and do not use **RGA**. In IconNMR, use **Parameters → Edit all Acquisition Parameters** and then click **AUTOMATION**. Change **AUNM = au_zgonly** and set **RG** = 1.

   This change is often insufficient to prevent clipping from still occurring. In these cases:

2. Reduce the flip or nutation angle used in the experiment. The standard sequence zg30 can be changed to zg10, zg05 and smaller (with the # indicating the flip angle). Note that the sensitivity will reduce as sin(θ). See *NMR staff* for more information.

   For information about ***Solvent Suppression:***
   http://www.chem.wisc.edu/~cic/nmr/Guides/Ba3vug/AV3_SolventSuppression.pdf

D. ***No-D NMR in IconNMR:***



1. Make sure a known sample, with the same deuterated solvent as used for your scout scan, is run just prior to your sample. Acquiring 1 scan for that sample is sufficient (see A.1).
2. You must know the value for ν_{solv} to set the topshim **o1p** for shimming (see section A, and 4 below).
3. You must have the change lock/shim/ATM button enabled. If it is grayed out in Icon, get staff to update your account.
4. Click on and select lockoff, and change topshim appropriately, similar to that shown below. The full shim program line is:

   TOPSHIM 1h lockoff o1p=4.7 selwid=0.5 change o1p=ν_{solv}

E. ***no-D setup for spreadsheet entry (only NMR staff can perform the following procedure):***

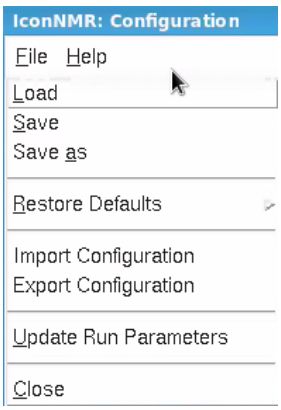
0. Do an **nmr_save** on the spectrometer you are modifying.
1. Follow the steps in section A to acquire a scout scan and determine ν_{solv}.
2. Decide on a proper value for **selwid**. When **selwid**=0.5, the selection is ±0.25ppm. If other peaks >10% of the main are encroaching this region, reduce **selwid**.
3. Icon has a few no-D solvents setup (created in edsolv):

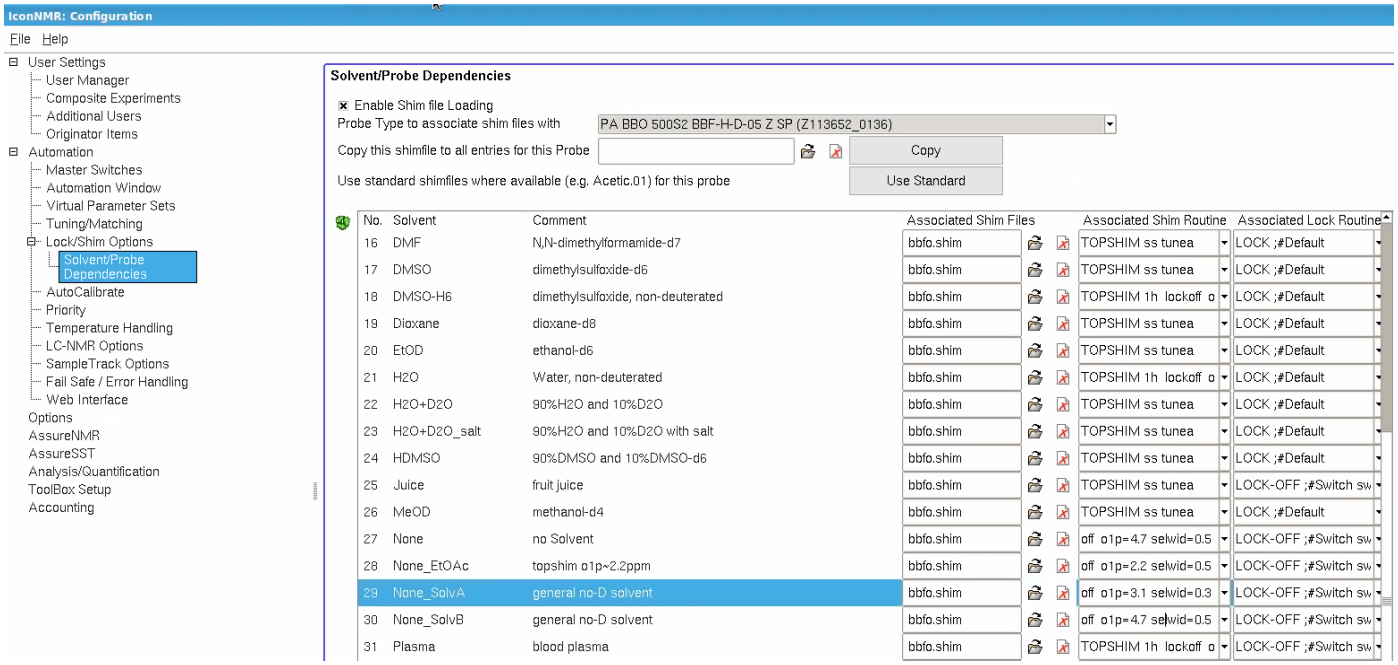
None	; **o1p**=4.7 **selwid**=0.5	for H_2O samples
None_EtOAc	; **o1p**=2.2 **selwid**=0.5	currently on spreadsheet
None_SolvA	; variable	will be added
None_SolvB	; variable	will be added

4. It is important to lock the spectrometer prior to the no-D experiments with the same solvent locked prior to doing the scout scan that determined ν_{solv}. The recommendation is to use D_2O using the standard sucrose sample on the spectrometers (loc 96 on artemis and eos).

   Setup a 1 scan acquisition for that sample to run just prior to the no-D experiments in the spreadsheet.
5. Use a solvent that seems appropriate in the spreadsheet. You will be changing the Icon default for the chosen solvent, so only use **None** (and likely **None_EtOAc**) if ν_{solv} matches exactly. Otherwise choose **None_SolvA** or **B**.
6. Make sure you are logged into the correct Unix account for spreadsheet import automation: **nmr** for artemis+callisto; **COVID1** for all others. Start topspin and icon. Choose Icon → **Configuration**

7. Select **Solv/Probe Dependencies** (see figure next page)
8. Change **o1p**= ν_{solv} **selwid=xxx** for the selected solvent (here None_SolvA) in the LOCK-OFF box 2nd from furthest right.
9. Now make sure you **File → Save** and **File → Update Run Parameters**, then **File → Close** to exit the Configuration editor.

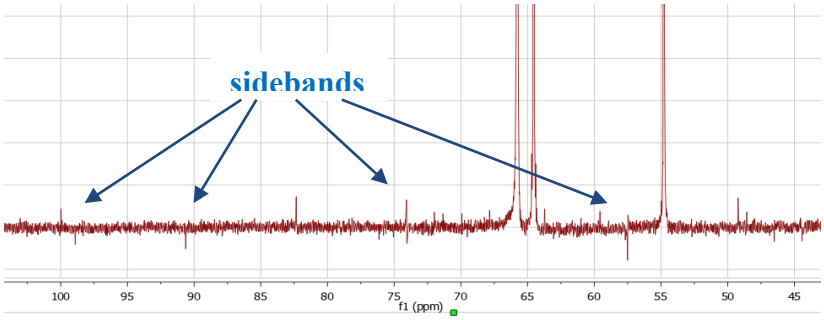




10. TopSpin and Icon are not consistent in their behavior in updating such paramaters. So I recommend exiting all the way out of Icon, and then TopSpin. You'll have to Pause and Stop the Icon run if it is going. Then re-enter both as normal and import the new no-D experiments from the spreadsheet. They will have the updated None_SolvA (or other solvent) parameters, and everything should be OK.

F. *^{13}C NMR – preventing ^{1}H decoupler sideband noise:*

In a protonated organic solvent, the ^{1}H decoupler will often produce decoupler sidebands large enough to interfere with other peaks n the spectrum. A simple change of the decoupler type will usually reduce these to the noise level.



a) Go to the ACQUPARS → panel. In Icon, use **Parameters → Edit all Acquisition Parameters** to get to the TopSpin ACQUPARS page. Then **ased** can be used rather than clicking through the panels/icons.

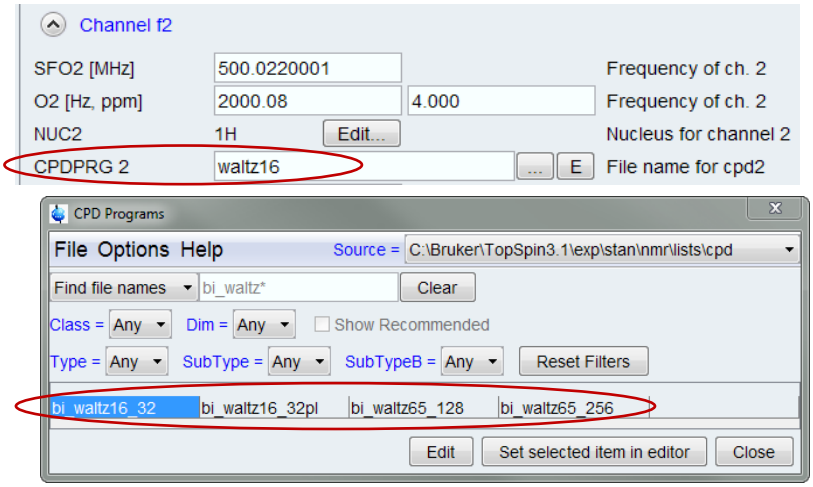
b) For the parameter **CPDPRG2** , the default is **waltz16**. Click [...] and choose one of bi-level waltz sequences. The limitation is that

NS = i × (ending #)

of the sequence.[2] Thus, for the sequence **bi_waltz65_128**

NS = 128, 256, 384 …

This suppresses sidebands better than **bi_waltz16_32**, but obviously takes longer to run (see footnote 2).



[2] This is the recommendation by Bruker. In the facility staff's experience, however, we find that bi_waltz65_128 seems to work fine with any setting of NS.