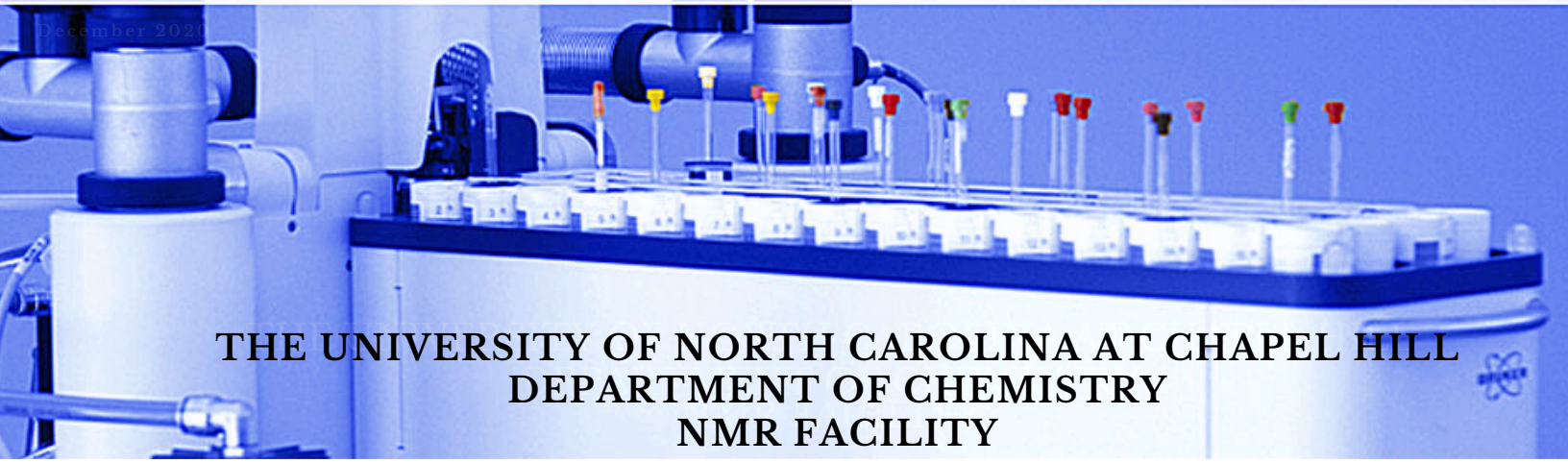
CHEMICAL RESEARCH INSTRUMENTATION TEACHING &CORE LABS

CRiTCL

December 2020



THE UNIVERSITY OF NORTH CAROLINA AT CHAPEL HILL
DEPARTMENT OF CHEMISTRY
NMR FACILITY

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QNMR

by Andrew Camp

Have you ever noticed that aryl protons tend to slightly under-integrate relative to other protons in the molecule? For routine acquisition, small differences in integration doesn't matter, but in other cases ...

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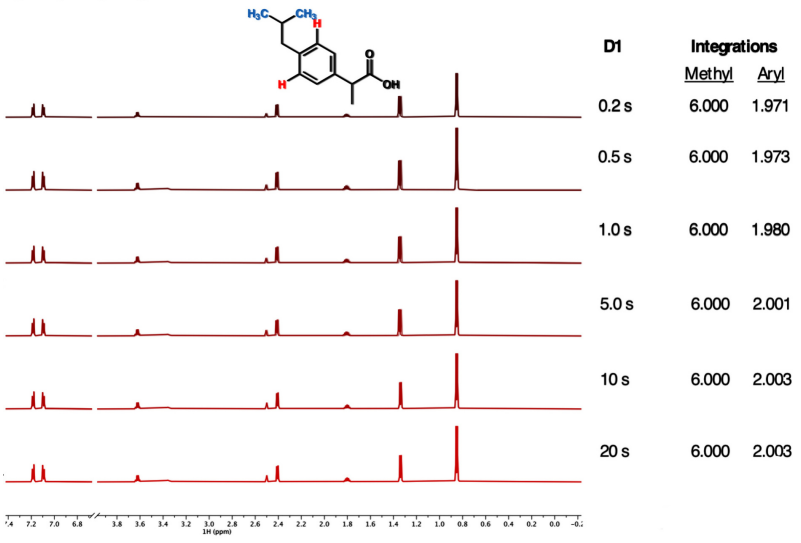


HELIUM RECOVERY

After many years of dreaming, we are finally recovering the helium gas from the magnets!

We collect helium gas from the regular boil off at the magnets and the extra gas expelled during a liquid helium fill. The gas is captured in a 5x10x5 bag and then compressed into standard cylinders. ARC3 delivers the full cylinders to the Biomolecular NMR Core where the gas is purified and reliquified. ARC3 will then transport the liquid helium back to the core for filling in magnets. And the cycle goes on and on and on and on! We hope to recycle more than 90% of the helium in 2021 and save more than $10 per liter of liquid helium. How much cash saved in total? We are aiming for more than $30,000 per year for the three NMR cores!!! This is a joint effort between the three NMR cores on campus: Chemistry, School of Pharmacy and the School of Medicine.

Special thanks to Gary Pielak who encouraged us to piggy back on his NIH grant to obtain the $250k supplement that paid for most of the project. Additional funds were received from CFAC, Chemistry, the School of Pharmacy, the Department of Biochemistry and Biophysics and the NMR Core.

HOLIDAY SCHEDULE

No Drop off or training December 21, 2020 through January 1, 2021.

Training requests must be submitted by Wednesday December 9.
Regular training will resume January 4, 2021

Support in the NMR Core will be limited **December 21, 2020 through January 1, 2021.**

Contact Marc ter Horst (terhorst@unc.edu) during this time.

NMR STAFF

The crew behind maintaining the NMR Spectrometers and making sure you all can obtain the spectra you need for research now includes a post-doctoral fellow.

We are fortune to have Dr. Andrew Camp, a recent graduate from the Miller group, joined the NMR Core in October. Andrew is splitting his time between core support and NMR research projects. Definitely let us know if you'd like to explore additional NMR applications! You'll hear more from Andrew at NMR memos, future workshop(s) and a department seminar in November.

Ling Xu joined the NMR Core early this summer. She has been balancing her time between the the NMR Core and taking classes. Ling was a tremendous help during the shutdown, setting up hundreds of samples each day, doing the N2 fills and shimming the magnets. She is working on applying 1D and 2D experiments for structure elucidation.

Jobel Barcoma continues as a workstudy student in the NMR Core. Those of you who submitted samples for drop off during the shutdown should thank Jobel for implementing the online forms we used to capture your information. She has also been the driving force behind the website. She also does N2 fills and shimming and is learning 2D NMR.

PUBLICATIONS OF WORK USING SPECTRA FROM THE NMR CORE

While working on the annual report for the NSF MRI grant used to purchase the NEO600 spectrometer, it became painfully obvious that we have done a poor job of keeping track of publications that were made possible, at least in part, by the spectrometers in the NMR Core.

Let's just say NSF strongly encouraged us to do much better! Please keep track of which spectrometers are used for your data so you can associate the appropriate spectrometer(s) with you published work. When you do publish, please submit the reference and which spectrometers were used here: https://tarheels.live/critclchem/nmr-core/submit-publication/

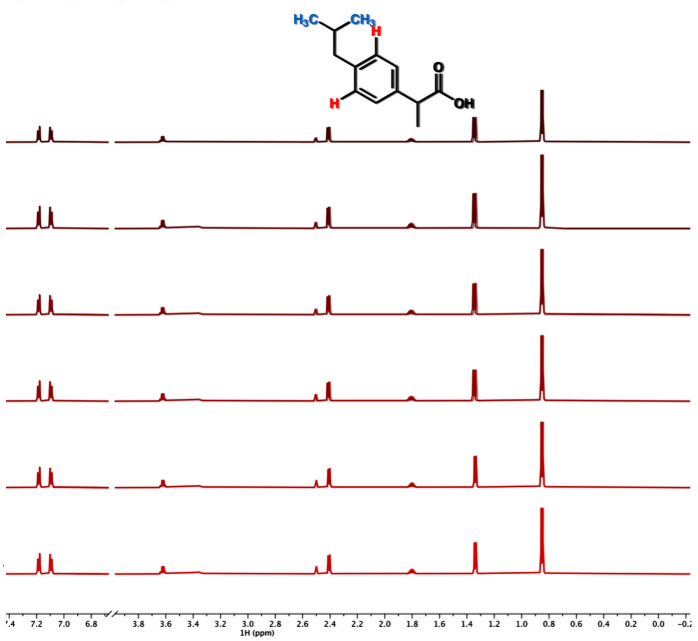
QUANTITATIVE NMR

cont. ... (catalysis, structural assignment, mass balance, NMR yields, etc.) knowing exact values is necessary. **Quantitative NMR** is a protocol of acquisition, experimental setup, and processing to produce the most accurate integrations possible.

The easiest way to determine if the relaxation time is adequate for quantitative work is to run a screen of different wait times before a scan to ensure that the molecule has sufficient time to relax completely. This parameter can be edited by typing "d1=X" into the topspin command tool bar, where X is the number of seconds before another scan occurs.

When the integrations between peaks in solution stop changing, you are at a long enough d1 to ensure complete relaxation of the molecule (Figure 1).

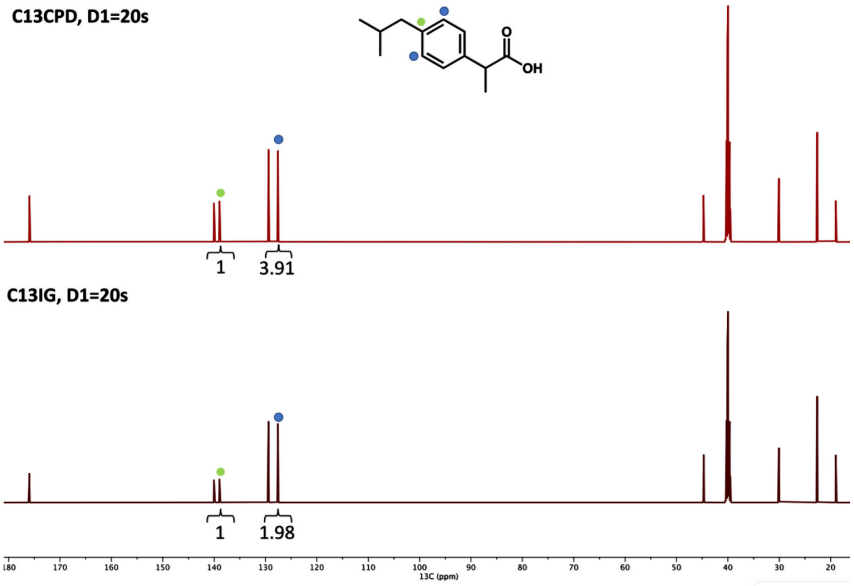
Bene Nota: Use more than 1 scan; insufficient relaxation times are most evident in experiments with large numbers of scans (like 13C); when comparing d1 values use at least 8 scans (ns=8) or preferably the same number you will be using in your quantitative experiments.



D1	Integrations	
	Methyl	Aryl
0.2 s	6.000	1.971
0.5 s	6.000	1.973
1.0 s	6.000	1.980
5.0 s	6.000	2.001
10 s	6.000	2.003
20 s	6.000	2.003

Figure 1

Use that d1 in future experiments, though note that changes to the system (deoxygenation, addition of other molecules) can influence relaxation times. An example of the role of d1 in influencing accurate integrations between isopropyl methyl and aryl protons is shown below; as d1 increases the relative integration approaches the expected 3:1 ratio of protons.



In addition to relaxation delay, additional considerations need to be taken into account to ensure the most quantitative spectra. Many heteronuclear experiments are run proton decoupled to simplify spectral interpretation. As a consequence, some of the magnetization from the decoupled protons can be transferred to the heteronuclear signal, increasing the signal to noise – a phenomenon known as Nuclear Overhauser Effect (NOE) enhancement.

While this is great for increasing signal in qualitative spectra, this means that carbons with more neighboring protons can substantially differ from expected integrations (Figure 2, top). Instead of a different pulse sequence is used for quantitative work, known as the inverse gated (IG) sequence, where the decoupler is only on during acquisition.

Using this experiment, NOE enhancement does not occur, yielding the expected 1:2 ratio (Figure 2, bottom). Both types of experiments are available for routine use on the spectrometers and on dropoff; the parameter sets for each are listed to the left.

Parameter Sets and Descriptions

C13CPD – broad band decoupling (not quantitative)
C13IG – decoupling is only ON during acquisition minimizing NOE (**quantitative**)
P31CPD – broad band decoupling (not quantitative)
P31IG – decoupling is only ON during acquisition minimizing NOE (**quantitative**)
F19CPD – not decoupled during acquisition (**quantitative**)*
*Bruker changed the labeling scheme in 19F for some reason

SPECTROMETER DETAILS

SPECTROMETER SELECTION

	^{1}H	^{31}P	^{13}C	^{19}F	^{11}B, ^{29}Si and other nuclei	Variable Temp	COSY, HSQC, HMBC, NOESY	5mm tubes with the following exceptions
400NB	Yes	Yes	Yes (conc.)	Yes	some are possible	N.A.	Yes	greater than 6 inches
NEO400 ("Prodigy")	Yes (low conc.)	Yes (low conc.)	Yes	Yes, no 1H decoupling	Yes	~ -40 to +120	Yes (low conc.)	special spinners for variable temperature
NEO600 (cryoQNP)	Yes (low conc.)	Yes (low conc.)	Yes (low conc.)	No	No	0 to 60 Celsius	Yes (low conc.)	short J-Young tubes
B600 (cryoQCI)	Yes (low conc.)	No	Yes (low conc.)	Yes (low conc.)	No	0 to 60 Celsius	Yes (low conc.)	
500 (bbo or bbi probe)	Yes	Yes (best on bbo)	Yes (conc., bbo)	No	Yes (bbo)	**-120 to +120**	Yes	special spinners for variable temperature

Yes (conc.): requires concentrated samples
Yes (low conc.): good for dilute samples

NEO 400

Our newest spectrometer is a Bruker NEO 400 MHz spectrometer equipped with a 60 position sample changer and a nitrogen cooled cryoprobe. The broad band cryoprobe, call a Prodigy, offers about an 2x improvement in signal to noise for most nuclei over standard probes at 400 MHz. People routinely use the spectrometer to acquire data on 1H, 13C, 19F (no proton decoupling), 31P, and 29Si. We have also acquired data on 11B, 15N, 113Cd, and 195Pt. The NEO400 can be reserved in an iLab calendar to submit samples to run in automation and is available for experiments not feasible on other spectrometers.

400NB

The Bruker AVANCE III Nanobay 400 MHz spectrometer is equipped with an older BACS 60 position sample changer and a standard broadband probe. The sample changer is in need of service but is available to run batch samples. Data is routinely acquired on 1H, 13C, 19F (with and without 1H decoupling), and 31P. Other nuclei are possible. The 400NB is available through reserving time in an iLab calendar.

500

The Bruker AVANCE III 500 MHz spectrometer is equipped with a broad band probe and an inverse probe (optimized for 1H experiments). A wide range of nuclei have been observed on this spectrometer. It's claim to fame is a wide range of temperatures available for experiments. The 500 can be reserved up to a week in advance for long runs and the same day for short runs.

NEO 600

The Bruker NEO 600 MHz spectrometer is equipped with a 24 position sample changer and a helium cooled cryoprobe. While all sample changers can encounter difficulties handling long NMR tubes, this sample changer can only run shorter tubes. The fixed frequency probe, the cryoQNP, is configured to acquire high sensitivity 13C, 31P and 15N as well as 1H spectra.
People routinely run spectra on 1H, 13C and 31P and in much shorter time than the previously mentioned spectrometers! This spectrometer should only be used for lower concentration samples.

B600

The Bruker AVANCE III 600 MHz spectrometer is equipped with a 60 position sample changer and a helium cooled cryoprobe. The fixed frequency probe, the cryoQCI, is configured to acquire high sensitivity 1H, 19F, 13C, and 15N. People routinely run spectra on 1H, 13C and 19F (with and without 1H decoupling) and in much shorter time than the lower field spectrometers! This spectrometer should only be used for lower concentration samples.

360

The Bruker DMX 360 MHz spectrometer is equipped with 4mm and 7mm CP/MAS probes for the detection NMR signals in solids. Routine 13C and 29Si 1D spectra have been acquired as well as select other nuclei.

EPR

The JEOLJES-FA100 EPR spectrometer is an X band electron paramagnetic resonance spectrometer.