THE NMR NEWSLETTER

No. 446

November 1995

THE NMR NEWSLETTER

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## Thoughts/Comments/Wishes

- The lack of an advertisement for this prime location in the Newsletter has prompted me to provide a rare page of miscellany. More occurrences of this can be avoided if a suitable one-page ad materializes. The general decline in the number of ads and sponsors is beginning to concern me, for without these sources of revenue, the fiscal viability of the Newsletter could be compromised. Please do whatever you can to help cheer on both past and present advertisers. Also, note those super-loyal advertisers who are so instrumental in keeping the Newsletter afloat on these financial uncertain seas. Kindly let them know that their commitment is appreciated.

- Richard Ernst's contribution on pages 5 and 6 is, of course, worth reading for its own content. Its appearance also reminds me invite others to write Newsletter pages which could be broadly categorized as commentary, editorializing, or whatever. For Newsletter participant/subscribers who have trouble getting organizational clearance to provide more purely technical contributions, this route would satisfy the periodic contribution requirement. Book reviews are also fair game, but please check with Bill Smith (TCU Chem. Dept.) or me first.

- Why doesn't Ray F. (aka Grandpa, aka Dominique's father) send in one of his splendid cartoon pages more than once every decade?

- The cartoon below does *not* emanate from Cambridge, but from Uwe Oehler in Canada. It is one of my favorites, and first appeared in the Newsletter in December 1987.

BLS 10/27/95

***A la Recherche du Lunch Perdu***

## *THE NMR NEWSLETTER* NO. 446, NOVEMBER 1995 AUTHOR INDEX



## *THE NMR NEWSLETTER* NO. 446, NOVEMBER 1995 ADVERTISER INDEX



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## FORTHCOMING NMR MEETINGS

37th ENC (Experimental NMR Conference), Asilomar Conference Center, Pacific Grove, California, **March 17 - 22, 1996**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4573; Fax: (505) 989-1073.

NMR Symposium at the 38th Rocky Mountain Conference on Analytical Chemistry, Denver, Colorado, **July 22-25, 1996**; Contact: Dr. Joel R. Garbow, Monsanto Company, 700 Chesterfield Parkway North, St. Louis, MO 63198; (314) 537-6004; Fax: (314) 537-6806; e-mail: jrgarb@snc.monsanto.com; See Newsletter 445, 48.

XVIIth International Conference on Magnetic Resonance in Biological Systems, Keystone, Colorado, **August 18 - 23, 1996**; Contact: ICMRBS, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4735; Fax: (505) 989-1073.

38th ENC (Experimental NMR Conference), Orlando, FL, **March 23 - 27, 1997***[sic]*; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4573; Fax: (505) 989-1073.

Additional listings of meetings, etc., are invited.

Molecular Sciences Department
Central Research Division
Pfizer Inc
Eastern Point Road
Groton, CT 06340

**Central Research**
*NMR Spectroscopy*

October 25, 1995

(received 10/26/95)

Dr. Barry Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303

Resolution vs. Escalation

Dear Dr. Shapiro,

One of the issues that every NMR spectroscopist must face is spectrometer maintenance and repair. It is generally true that for all but the extremely wealthy spectrometer down-time is measured in minutes and hours, not days and weeks. Most spectrometers at pharmaceutical companies are run in one of two ways: either an NMR spectroscopist (or group) run an instrument, taking in samples and providing data and maybe interpretation, or an instrument is run by a large group of users and the spectroscopist intervenes only to calibrate, tune, and fix the instrument. At Pfizer in Groton we have both types of installations, have instruments from two major vendors, and have many years experience troubleshooting instrument problems.

Troubleshooting is usually accomplished by first evaluating the spectrometer in simple ways (are all the appropriate lights flashing, are there RF pulses, do you smell smoke, etc.), then doing simple spectroscopic tests (can you see a proton signal, a heteronuclear signal, what is the signal sensitivity, are the gradients recovering, does the lineshape look okay), and then calling the vendor for advice (applications), parts (service), or help (engineers). Finally you pray for a rapid response.

Then you wait. And hope for rapid **resolution**.

Sooner or later you consider calling someone you know at the vendor company with enough pull to make your request the most important one in the queue. Sometimes this process is known as **escalation** of the request. Unfortunately, days and weeks are required to elapse before escalation is either warranted or necessary.

We have had and extremely good experience with service administered through the new Bruker Center response line in resolving problems with our DMX-500, and I would like to use them to illustrate the power of this approach (which fosters shared responsibility for success). We are **not** a preferred customer, either.

On the day that the lights went out on our third channel power amplifier we called the Bruker Center, and Mr. Tom Kelly did triage: is the amplifier plugged in, do serial cable changes affect things, is the fuse blown. Fifteen minutes later he concluded that an internal component went bad (we were under warranty), and we were running with a new unit the next morning. We had **resolution** of a major component failure in 16 hours.

On the day that our preamplifier got scrambled (house power failure, and no warranty this time) we did the same thing. This time Tom diagnosed the problem as scrambled preamp software, found the fix in Billerica, called us back and talked us through rebuilding the software module. We had **resolution** in 45 minutes!

I've never seen a problem resolved through **escalation** in under two weeks, regardless of vendor.

Sincerely, Walt

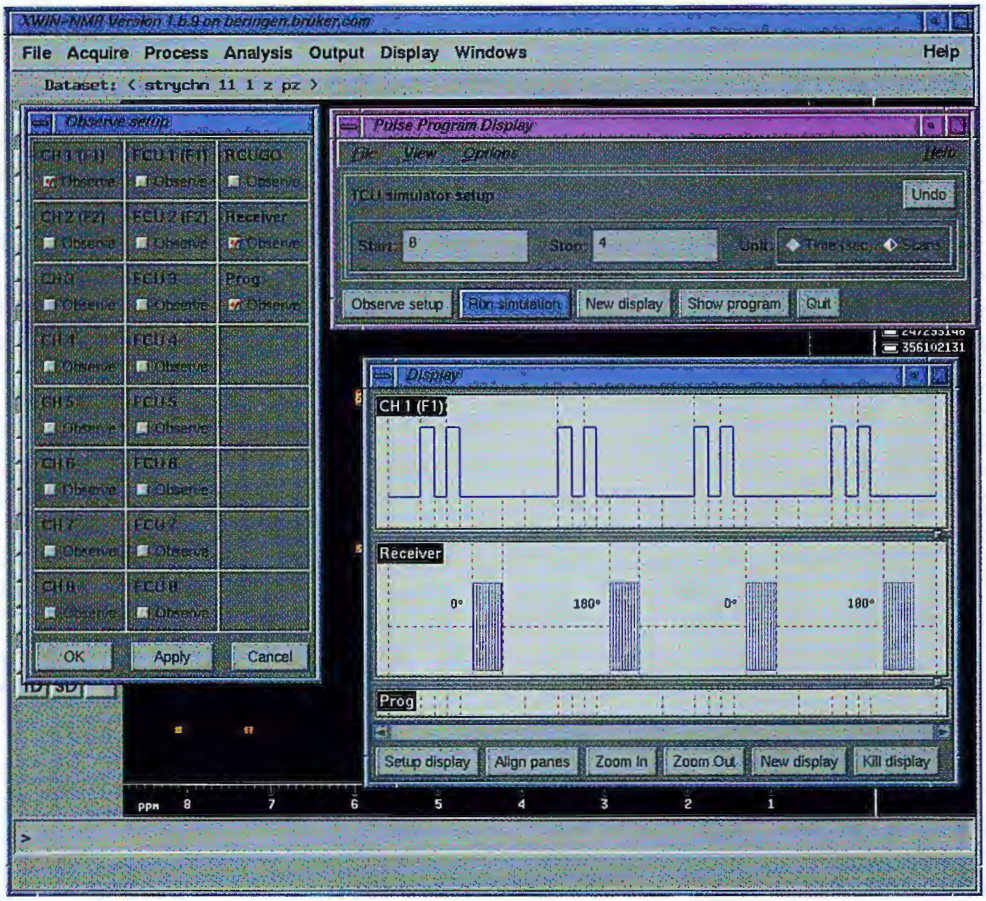
Walter Massefski, Jr.
203-441-5962
203-441-4734 (FAX)
email: wwm@pfizer.com

The NMR Revolution advances...

BRUKER

# XWIN-NMR™ Software:

# Pulse Program Display




The *Pulse Program Display* module in XWIN-NMR, Bruker's new NMR software package, provides **exact** graphical visualization of a pulse sequence on the *AVANCE* spectrometers. This includes illustration of the amplitude, timing and phase for all RF and gradient channels. All this to make even the most complicated experiment look easy!

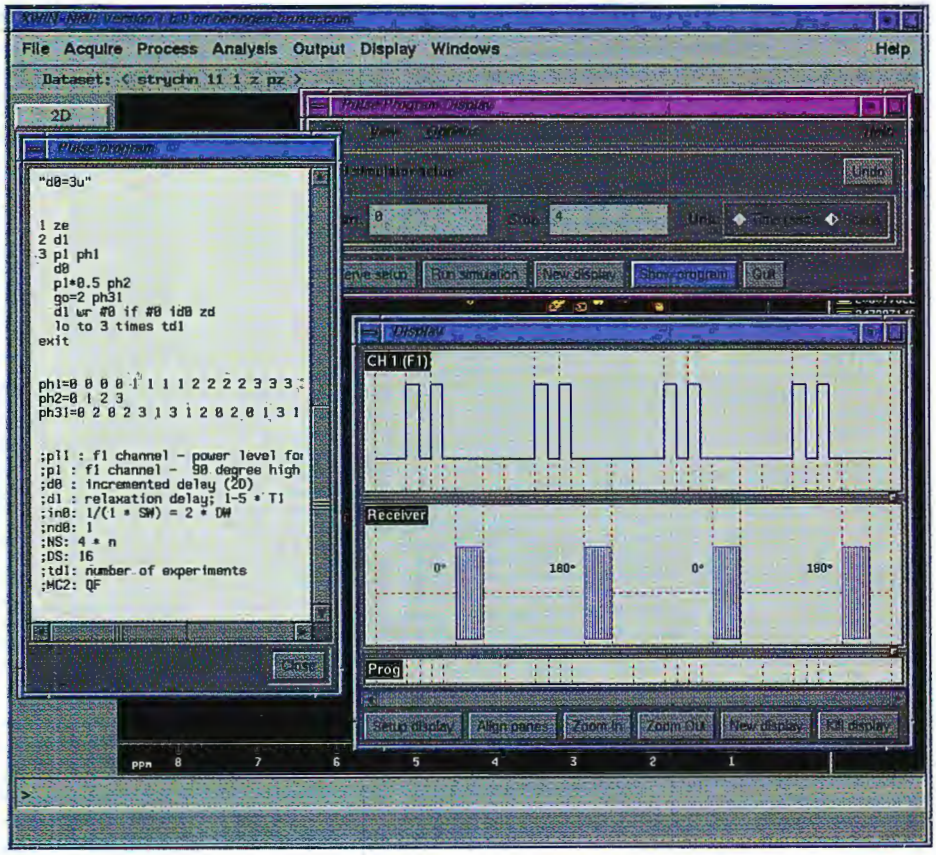
The *Pulse Program Display* uses the *same* XWIN-NMR pulse program compiler to create the graphical display *and* to control the hardware. Other graphical display programs use a separate interpreter to create the sequence display. This latter approach introduces possibilities for error, leading to frustration in debugging the pusle sequences.

BRUKER

...The NMR Revolution advances

## Features of the *Pulse Program Display*:

- easy-to-use graphical X11/Motif user interface,
- simple scrolling through the displayed sequence,
- easy set-up and navigation,
- zoom from 12.5 nsec to entire experiment,
- multiple displays in independent windows,
- number of channels, pulse-gating, phase and amplitudes individually selectable,
- simulation in units of time or scans,
- simulation of multidimensional sequences including evolution.




For more information on *Pulse Program Display* as well as XWIN-NMR, contact your local sales representative.

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*Laboratorium für Physikalische Chemie*
*Prof. Dr. R. R. Ernst*

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E-mail: rier@nmr.lpc.ethz.ch

Zürich, October 11, 1995
(received 10/16/95)
2515

Dr. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303

**The Responsibility of NMR Spectroscopists in Science Policy**

Dear Barry,

The current political trends in many countries around the world tend to manoeuvre science into a position of secondary importance. The financial support is reduced and the recognition of scientific work is often missing. Even excellent scientists have difficulties to find adequate jobs, and the standard of living of them has fallen below the average of equally qualified people in other professions. No wonder that many of the most gifted students no longer select science for majoring. Much has to do with the financial bottleneck in most of the states. But it is also connected to the all too often negative assessment of science in the public opinion. Frequently, science is considered to be responsible for the problems of our rapidly changing and, in many places, deteriorating world.

We scientists, we know that without science and technology our civilization would not survive for long and the environment would deteriorate even faster. We are convinced that science and technology are of fundamental importance for the future of menkind and of our globe. We are convinced that it is not only necessary to maintain the present level of science support but that additional investments into our future are required.

Why do I spoil precious space of the NMR Newsletter with all these truisms ? Because I think that it is part of the responsibility of every single scientist to act against these deplorable tendencies, not so much to defend his own job nor the employment of scientists in general, but to provide a healthy basis for the future development of our civilization and culture.

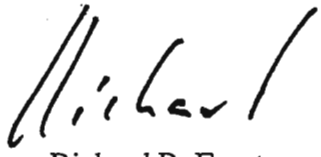
I am convinced that we NMR spectroscopists are in a particularly privileged position to exemplify the importance of basic and applied research. NMR is such an universal technique, with

its wide spread indispensability from solid state physics to clinical medicine, that it is a predestinate example for demonstrating the importance of applying basic principles of natural science by means of sophisticated instrumentation to questions of everybody's relevance. I do not have to give examples at this place.

NMR spectroscopists can be excellent missionaries for convincing politicians and the general public of the importance of science. I would like to encourage you to take advantage of our assets and actively contribute towards a better public understanding of science. There are many possible ways, such as public lectures, radio broadcasts, tv shows, popular articles in wide-spread magazines and newspapers, and personal contacts to influential politicians, educators, writers, philosophers, and business persons. NMR makes excellent stories by telling its history, showing its present astounding activity, or projecting its importance into the future. I hope more for long-term effects, but of course there are also immediate particular needs which are worth fighting for.

Such efforts take time, and each scientist can invest only a limited part of his energy into public relation work. But nevertheless, the integral effect of all personal activities could become appreciable. The privilege to work in one of the most exciting and rewarding fields of science imposes also obligations upon us, and I hope that we will fulfil them as well as we do our science. It will be for the sake of a prosperous future for everybody.

Sincerely yours,



Richard R. Ernst

CENTRAL RESEARCH & DEVELOPMENT
Experimental Station
P.O. Box 80328
Wilmington, Delaware 19880-0328

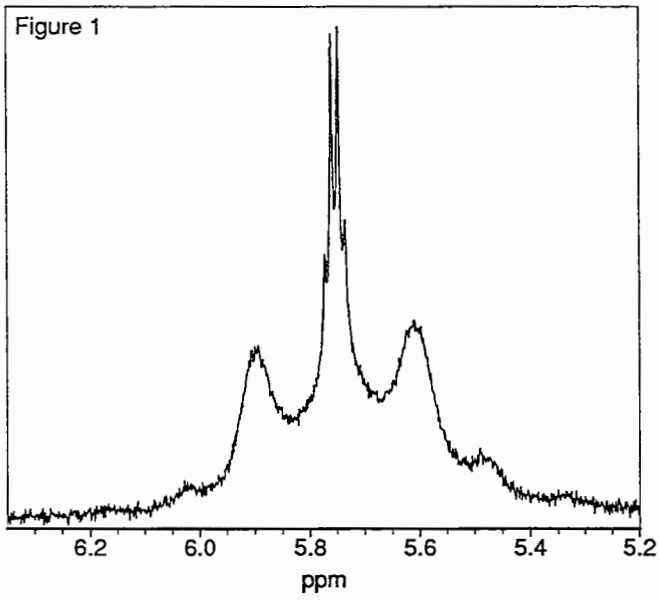
Dr. Bernard L. Shapiro
The NMR Newsletter
966 Elsinore Court,
Palo Alto, CA. 94303

Oct. 22, 1995
(received 10/25/95)

**$^{19}$F spin rotation relaxation affects $^{1}$H nmr lineshape**

Dear Barry,

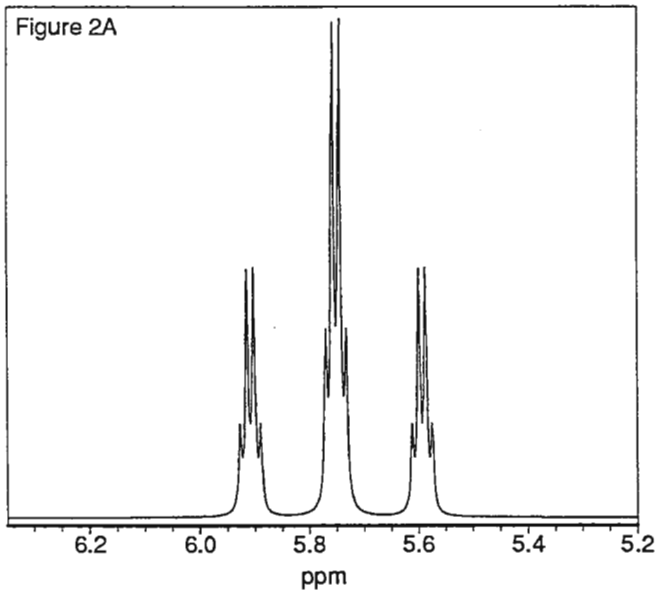
We were recently puzzled to witness the $^{1}$H NMR spectrum of $CH_3CHF_2$, the methine portion of which is shown in Figure 1. The most striking thing about the spectrum is the breadth of the outer wings of the triplet ($^{2}J_{FH}$ = 52 Hz) compared to the central transition which is sharp enough to reveal the quartet splitting from the methyl group ($^{3}J_{HH}$ = 4.5 Hz). The methyl region is similar in that it has broad outer wings ($^{3}J_{FH}$ = 13 Hz) and a sharp central doublet (coupling to the methine proton). Since the sample for this spectrum was in the gas phase, we anticipated that spin rotation would be the dominant relaxation mechanism and that this relaxation would be more efficient for fluorine than for protons ($^{19}$F $T_1$ = 15 ms, $^{1}$H $T_1$ = 4 s). Nevertheless, these expectations did not at first seem to offer an explanation for the difference in the proton linewidths.

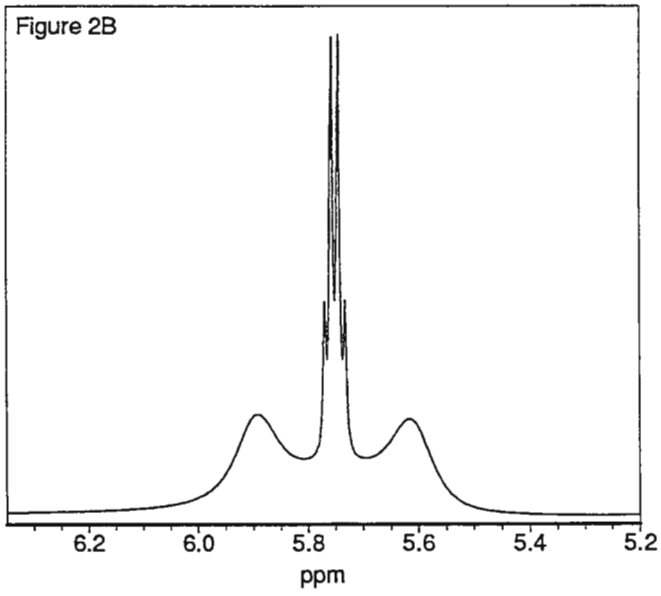


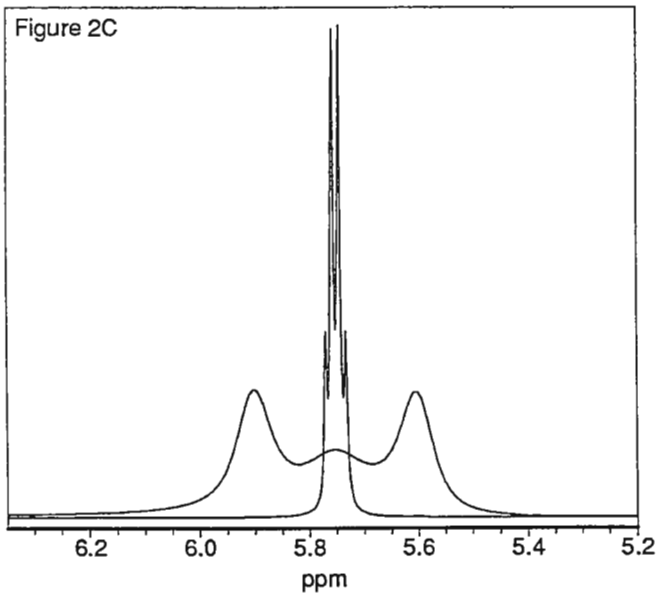

It turns out that the key to this little puzzle is that the two fluorines are equivalent, and must therefore be described by the wavefunctions $|\alpha\alpha\rangle$, $|\beta\beta\rangle$, $|(\alpha\beta + \beta\alpha)/\sqrt{2}\rangle$ and $|(\alpha\beta - \beta\alpha)/\sqrt{2}\rangle$. The first three of these wavefunctions are symmetric, and the spin rotation mechanism gives rise to fast relaxation (akin to exchange) between these states. The last wavefunction is anti-symmetric, and the spin rotation mechanism is apparently inefficient in bringing about transitions between this state and the others.

Somewhat more subtle features are obscured by the spectrum in Figure 1. The first is that the large triplet splitting is only an apparent coupling constant. The "true" value of $^{2}J_{FH}$ is 56.9 Hz as measured in dilute C6D6 solution, and the apparent splitting in the gas phase decreases to 38 Hz as the pressure is lowered from 4.5 atm to 0.5 atm. There is a concommitant decrease in the $^{19}$F $T_1$ which may be viewed as an increase in the rate of exchange among the symmetric (or triplet) states. A simulation of the above parameters with a linewidth appropriate for the gas phase is shown in Figure 2A in the absence and (2B) in the presence of this relaxation phenomenon. The deconvolution of the lineshape in Figure 2C reveals that the central line of the triplet state is twice as broad as

the wings (a feature common to 3-site exchange problems). The simulations seem to give a reasonable accounting of the observed lineshape, and it is presumed that the small differences arise from the rather poor shimming conditions under which the spectrum was obtained (from a decoupler coil on an old 12mm $^{19}F$ probe).



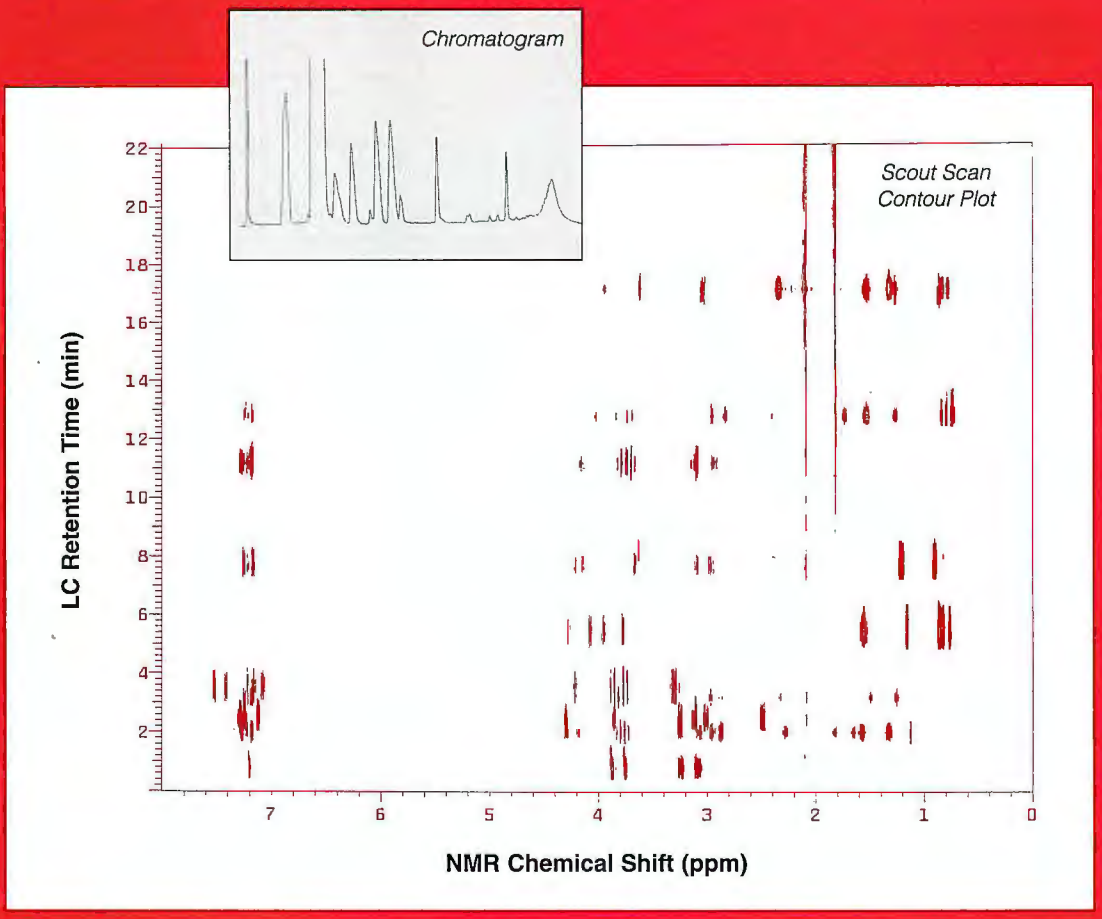

It should be noted that these phenomena cannot be said to be new! It turns out that this same system was the object of an early study (G.W. Flynn and J.D. Baldeschwieler, *J. Chem. Phys.* **37**, 2907 (1962)) involving proton-fluorine double resonance. Increasing levels of $^{19}F$ decoupling left the central sharp multiplet unchanged while the broad outer features of the triplet shifted toward the center and ultimately narrowed to produce the simple multiplet expected from solution work. These double resonance experiments prove that the outer lines in the proton spectrum arise from the $^{19}F$ triplet states, and that the width of these peaks is determined by the fluorine relaxation time. What is new here is the calculation of the dynamic lineshape and presentation of the methine proton spectrum; for the original article, only the methyl group gave sufficient signal-to-noise to be presented.

With sincere best wishes,

Chris

D. Christopher Roe

# LC-NMR: Separations and Structures




*On-flow 500 MHz $^1H$ LC-NMR data of a peptide mixture using Scout Scan and WET solvent suppression during an LC gradient. The sample was a 100 µl injection of ~1 mg/mL peptides separated using a $CH_3CN:D_2O$ solvent gradient (5% $CH_3CN$ to 50% in 22 min).*

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September 19, 1995

Bernard L. Shapiro, Editor
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

**Gradient-Enhanced HMQC-TOCSY with Direct Response Editing**

Dear Barry,

Gradient-enhanced 2D NMR experiments represent an obvious means of saving time when acquiring 3D NMR data sets on uniformly labeled molecules such as proteins and peptides. We also have an interest in using these experiments to characterize small molecules. To this end, although an absolute value gradient-enhanced HMQC-TOCSY experiment was described by Boban John and colleagues[1], their experiment could not be extended to allow direct response editing.[2,3] As an alternative, we recently described[4] a pure absorption phase gradient-enhanced HMQC-TOCSY experiment with direct response editing capabilities. The pulse sequence for our experiment is shown in Figure 1.

Our gradient-enhanced sequence circumvents the necessity of an absolute value presentation by virtue of the 180° $^{13}C$ pulses employed in conjunction with gradients gt1 and gt2 and the fixed delays, $\tau$. Dephasing which normally occurs during the gradient pulse is reversed by the 180° pulse and refocused during $\tau$ by the beginning of the evolution period. The process is repeated in reverse following the end of the evolution. This approach to the experiment also allows a pure absorption phase HMQC spectrum to be recorded if data acquisition and decoupling are initiated following the refocusing delay, $\Delta$, which follows the second 90° $^{13}C$ pulse. For purposes of creating a pure absorption phase HMQC-TOCSY experiment, however, a mixing period is initiated following the refoucing delay, $\Delta$. After the MLEV mixing period, magnetization is again refocused. At this point in the experiment, the investigator has a choice of recording a conventional HMQC-TOCSY spectrum in which all responses are positively phased. Alternatively, the pulse sandwich shown in Figure 1 may be invoked. In the case where the pulse sandwich applies 180° pulses to both $^{1}H/^{13}C$ direct responses are selectively inverted to take full advantage of the

pure absorption phase character of the experiment. Direct responses may also be selectively nulled by applying a 90° pulse to $^{1}H$ at the same time the 180° pulse is applied to $^{13}C$.[3]

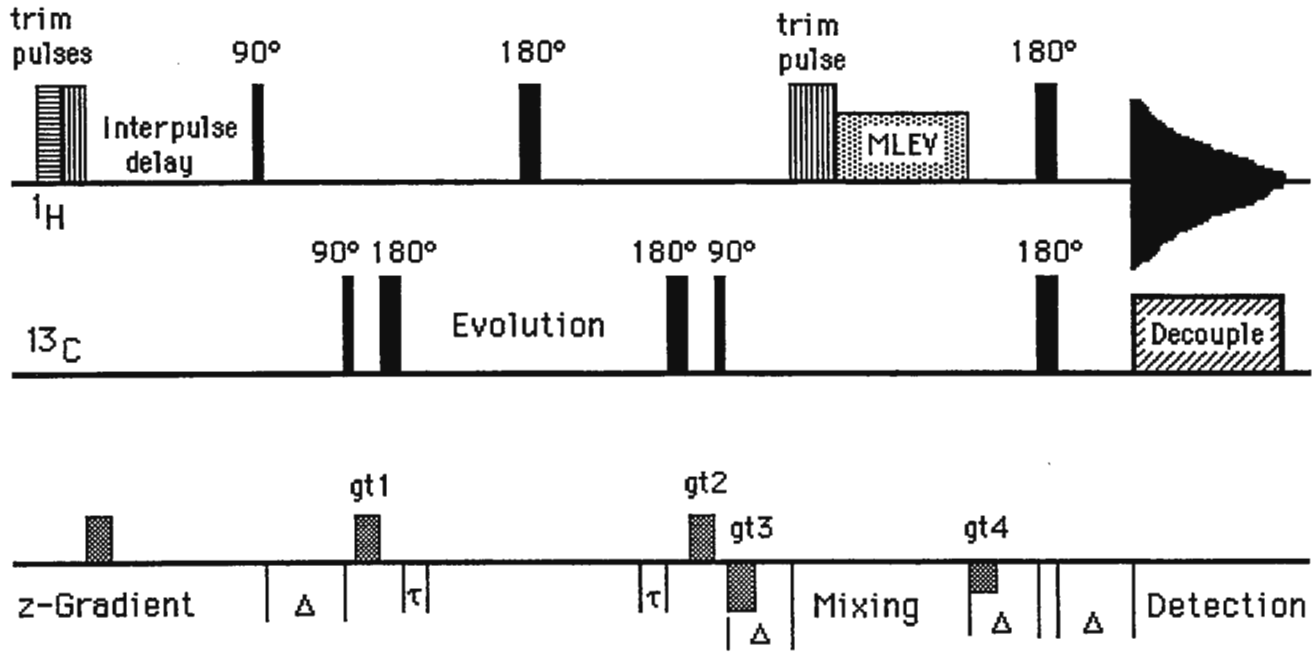
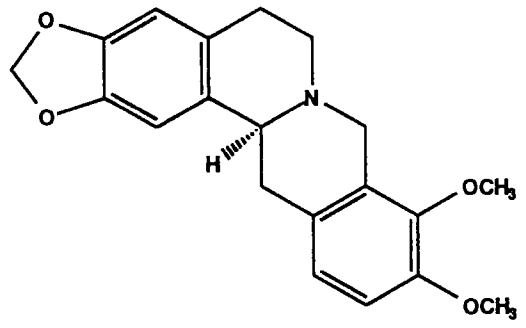



Figure 1. Pulse sequence used for IDR-(Inverted Direct Response)-GHMQC-TOCSY.[4] The fixed delays, Δ, were optimized as a function of $1/2(^{1}J_{CH})$ giving 3.6 msec where J=140 Hz; the fixed delays, τ, were set equal to the duration of the gradient times which were uniformly 1.5 msec. In the case of delays containing a gradient (gt3 and gt4) the total duration of the delay was held constant at 3.6 msec with the gradient applied during the first 1.5 msec. The experiment was performed with gradient ratio pairs of 2:2:2:1 and 2:2:-2:-1; DAC values of 6000:6004:6035:3020 for gt1-gt4, where 6000 = 0.008T, were employed. The gradient following the proton trim pulses was utilized as a homospoil with the power and duration set equivalent to gt1. The 180° $^{1}H/^{13}C$ pulse sandwich following the MLEV isotropic mixing interval was used to selectively invert direct responses. Elimination of this pulse sequence element would give a conventional phase-sensitive GHMQC-TOCSY spectrum with direct and relayed responses of identical phase. Employing a 90° $^{13}C$ pulse in lieu of the final $^{13}C$ 180° pulse would afford a spectrum in which direct responses are suppressed obviating the need for broadband decoupling during acquisition and allowing, if necessary, higher levels of digital resolution to be employed in $F_2$ than would otherwise be possible.

To illustrate the performance of our GHMQC-TOCSY experiment, we used a 10 mg sample of the simple alkaloid tetrahydroberberine (1) dissolved in 600 μl $d_6$-DMSO in a 5 mm Wilmad tube. All data were acquired using the same Nalorac Z•SPEC® IDTG-500-5 probe to negate any possible performance differences that might be attributable to a probe. Two spectra were acquired (Figure 2). A conventional IDR-(Inverted Direct Response)-HMQC-TOCSY spectrum was

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spectrum also with a 12 msec mixing period. Both spectra were acquired using 1536 x (80 x 2) hypercomplex files. The conventional experiment was acquired using 8 transients/$t_1$ increment with a total acquisition time of 41 min. The data are shown plotted with a vertical scale of 8000. The gradient-enhanced data were acquired using 4 transients/$t_1$ increment giving an acquisition time of 25 min. The data for the gradient experiment are plotted at twice the vertical scale (16,000) of the conventional data to highlight any noise. Processing of the two data sets was identical.

Clearly, the gradient data are superior to the conventional data despite the fact that they were acquired with half the number of transients/$t_1$ increment. Tracking due to $t_1$ noise in $F_1$ is nearly eliminated and responses are much more clearly visible in the gradient experiment. Overall resopnse intensity is, however, inherently weaker in the gradient data as is the case whenever gradient experiments are employed. Despite the weaker response intensity in the gradient experiment, the eradication of $t_1$ noise provided by using the gradients more than amply compensates the investigator who choses to use this approach to acquiring the data. HMQC-TOCSY is lower in sensitivity by a factor ranging from two to about four relative to HMQC. Hence, by eliminating $t_1$ noise, relayed responses can be observed more quickly and more reliably than would be possible in the conventional experiment making it more practical to consider using this technique to solve complex sturctural problems.

Sincerely,

Ronald C. Crouch  Ann O. Davis  Gary E. Martin

1. B. K. John, D. Plant, S. L. Heald, and R. E. Hurd, *J. Magn. Reson.*, **94**, 664 (1991).
2. T. Domke, *J. Magn. Reson.*, **95**, 174 (1991).
3. R. C. Crouch, T. D. Spitzer, and G. E. Martin, *Magn. Reson. Chem.*, **30**, S71 (1992).
4. R. C. Crouch, A. O. Davis, and G. E. Martin, *Magn. Reson . Chem.*, in press (1995).

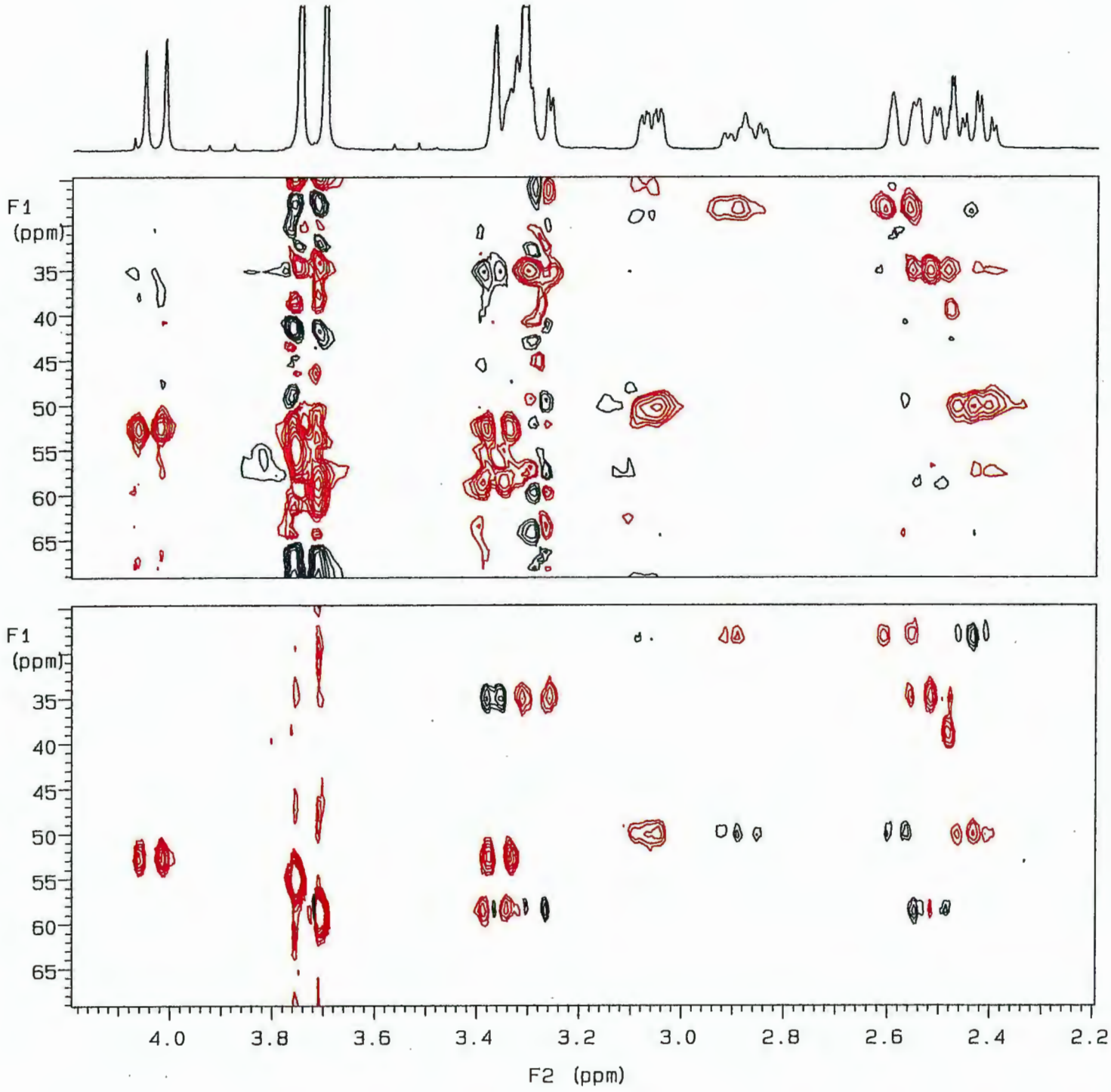


Figure 2. Comparison plots of IDR-(Inverted Direct Response)-HMQC-TOCSY (TOP) and IDR-GHMQC-TOCSY (BOTTOM) spectra acquired under identical conditions with a 12 msec mixing period. Both spectra were acquired using a Nalorac Z•SPEC® IDTG-500-5 probe. The gradient amplifier was not powered up for the conventional HMQC-TOCSY experiment. Both spectra were acquired as 1536 x (80 x 2 ) hypercomplex files. The IDR-HMQC-TOCSY spectrum was acquired in 8 transients/$t_1$ increment; the IDR-GHMQC-TOCSY spectrum was acquired in 4 transients per $t_1$ increment. Acquisition times were 41 and 25 min., respectively. The data were processed identically. The conventional spectrum (TOP) is presented with a vertical scale of 8000; the gradient spectrum (BOTTOM) is presented at a vertical scale of 16000 to highlight what little $t_1$ noise was present. Direct responses are inverted and shown in RED; relayed responses have positive phase and are shown in BLACK.

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| Pulse power (min.) into 50 ohms | 2000 W | 1000 W |
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| Linearity (±1 dB to 30 dB down from rated power) | 1,500 W | 800 W |
| Pulse width | 20 ms | 20 ms |
| Duty cycle | Up to 10% | Up to 10% |
| Amplitude droop | 5% to 20 ms typ. | 5% to 20 ms typ. |
| Harmonics | Second: -25 dBc max.<br>Third: -24 dBc max. | |
| Phase change/output power | 10° to rated power, typ. | |
| Phase error overpulse | 4° to 20 ms duration, typ. | |
| Output noise (blanked) | < 10 dB over thermal | |
| Blanking delay | < 1 µ s on/off, TTL signal | |
| Blanking duty cycle | Up to 100% | |
| Protection | 1. Infinite VSWR at rated power<br>2. Input overdrive<br>3. Over duty cycle/pulse width<br>4. Over temperature | |

### Supplemental Characteristics:

| | | | |
|---|---|---|---|
| Indicators, front panel | 1. AC power on<br>2. CW mode | 4. Overdrive<br>5. Over pulse width | 6. Over duty cycle<br>7. LCD peak power meter |
| System monitors | 1. Forward/Reflected RF power<br>2. Over pulse width/duty cycle | 3. DC power supply fault | 4. Thermal fault |
| Front panel controls | 1. AC power | 2. Forward/Reflected power | |
| AC line voltage | 208/230 VAC, 10%, 1Ø, 47-63 Hz | | |

| | 3445 | 3446 |
|---|---|---|
| AC power requirements | 1400 VA | 700 VA |
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Institut für Makromolekulare Chemie
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**Prof. Dr. Bernhard Blümich**

Tel.: 0241/80 6420
Fax: 0241/8888 185
e-mail: bluemich@rwth-aachen.de
Datum: 09.10.95

RWTH, Makromolekulare Chemie, SB Chemie
Worringer Weg 1, D-52056 Aachen

(received 10/16/95)

Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, Ca 94303, USA

Re.: Spin-Diffusion Imaging of Electrical Aging of High-Power Cable Insulation Material

Dear Barry,

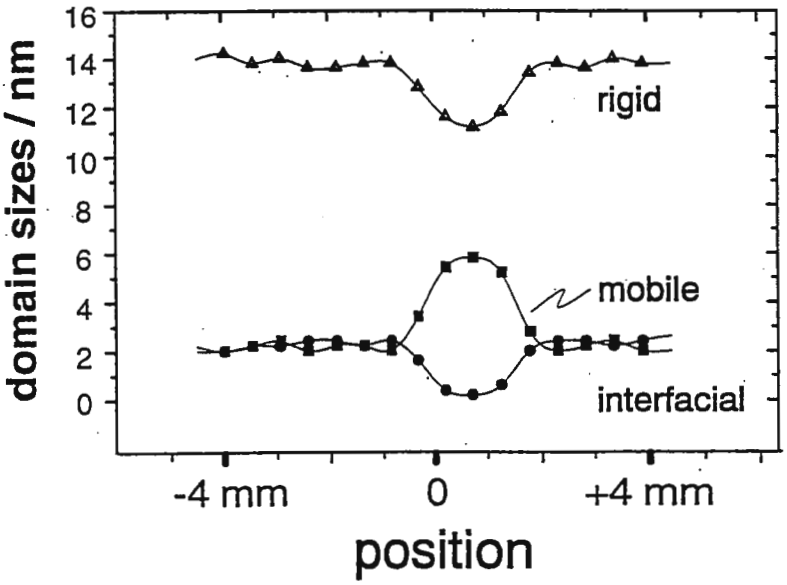
spin diffusion is a phenomenon of incoherent magnetization transfer, which is widely exploited for mapping polymer morphology on the 0.1 to 100 nm distance scale. We have been considering for quite a while how to use spin diffusion as a contrast for NMR imaging of materials. It turns out, that such a scheme actually is not too difficult to devise: The experiment begins with the creation of a magnetization gradient by some type of magnetization filter. This establishes islands of longitudinal magnetization, from which the magnetization spreads in a subsequent spin diffusion time to establish a spatial magnetization equilibrium across the sample. Following the spin diffusion time, space is phase encoded by a magic-echo sandwich with pulsed gradients and the spectroscopic response is detected for further analysis.

After testing the method on polymer phantoms of known morphology, we have performed one-dimensional imaging experiments on a section of LDPE cable insulation material. RWTH in Aachen is a University of Technology, well known for its engineering schools. Work at one of the engineering departments focusses on testing and improving high power cable insulation material. Typically this is low-density polyethylene synthesized, and processed under different conditions and with different additives. Electrical testing is performed on $(1.5\ cm)^3$ large samples with the electrodes arranged in a needle-plate geometry. The AC voltage is increased to about 40 kV and about 200,000 electrical discharges are observed until arcing occurs. The latter may be familiar to some of us who were a bit to rough on their high-power solid-state NMR probes. At each electrical discharge a small cavity with a few μm in diameter is formed, and the cavities together form a so-called electrical tree. We have obtained such an electrically aged LDPE sample from the Department of High Voltage Engineering for mapping the morphological changes across the treeing region.

Polyethylene consists of rigid crystalline lamellae separated by mobile amorphous layers. The interface between both domains shows intermediate mobility and has been

characterized previously by NMR spin diffusion experiments. In the spin-diffusion imaging experiment we applied a mobility filter to localize the nonequilibrium magnetization in the amorphous domains for subsequent equilibration across the interface and the crystalline lamellae. The signal amplitude from the mobile amorphous regions was extracted from decomposition of the spectroscopic proton response for each position in 1D space. The signal decrease as a function of the spin-diffusion time was corrected for $T_1$ relaxation and numerically analyzed by fitting a three-phase model of the polymer morphology to the spin-diffusion curves. In this way, the fit variables being the diameters of the crystalline, interfacial and amorphous domains were determined.

The resultant domain sizes are plotted in the Figure as a function of space across the treeing region. We note, that the thickness of the crystalline lamellae has decreased on the expense of the amorphous domains. This can be explained by rapid deposition of heat energy during each electrical discharge followed by rapid dissipation afterwards, which partly quenches recristallization. Suppressed crystallization of lamellae may explain the lack of the interface in the three-layer model: Instead of crystalline lamellae with more or less well defined surfaces, rough surfaces consisting of regions of high and low molecular mobilities could be formed with efficient magnetization transfer from mobile domains to rigid peaks of incomplete lamellae. It can be concluded, that spin-diffusion-NMR imaging has revealed an interesting new feature, which can be explored for optimization of material properties.




Spatially resolved domain sizes of cristalline, interfacial, and amorphous domains of LDPE across a region of treeing from electrical discharges.

Frank Weigand Dan Demco Bernhard Blümich

Frank Weigand Dan Demco
MPI für Polymerforschung, Mainz

Bernhard Blümich
RWTH Aachen

# *Chemagnetics Technology for Broadband Solid-State Triple Resonance Experiments*

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Triple resonance applications in solid-state NMR have increased in number and sophistication in the last few years. Chemagnetics triple resonance probes and instruments provide the necessary state-of-the-art technology to keep pace with these new experiments.

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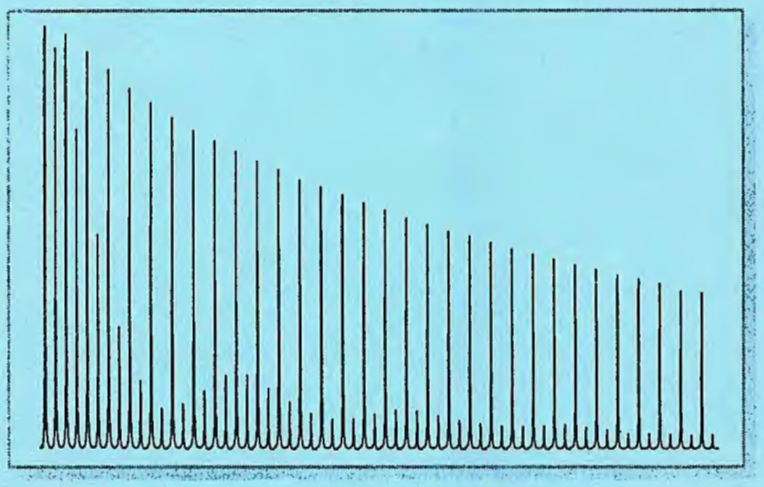


**$^{13}C/^{15}N$ REDOR with $^{1}H$ decoupling,** obtained on [2-$^{13}C$,$^{15}N$]-glycine.

$^{1}H$ decoupling field, stable RF and stable spinning speed are all critical for REDOR experiments.

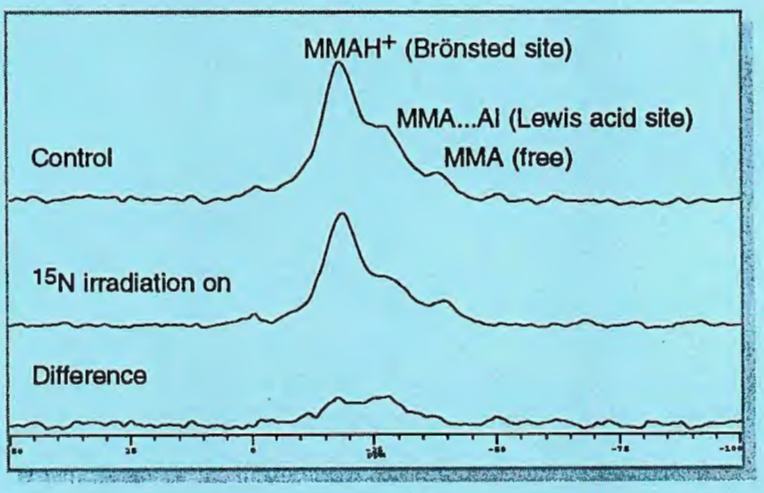
Control experiments (1st, 3rd, etc. peaks) demonstrate high decoupling powers. Significant signal remains after 64 rotor periods, as seen in the next to last peak.

**$^{27}Al/^{15}N$ TRAPDOR with $^{1}H$ decoupling,** of monomethyl amine (MMA) on a zeolite surface, obtained at -140°C to freeze amine motion on the zeolite surface.

Stability in probe tuning and spinning speed must be maintained at -140°C in order to obtain TRAPDOR data.

The TRAPDOR technique is similar to REDOR in that distance information is obtained through dipolar couplings.

data courtesy of C. Grey, SUNY, Stony Brook.

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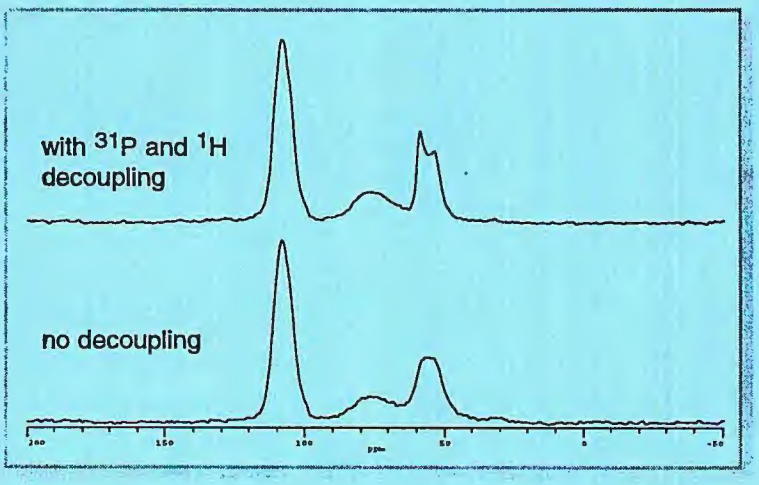
## *Chemagnetics Triple Resonance Technology*




**$^{27}Al$ Observation with X/H decoupling,** of $AlPO_4$-H2.

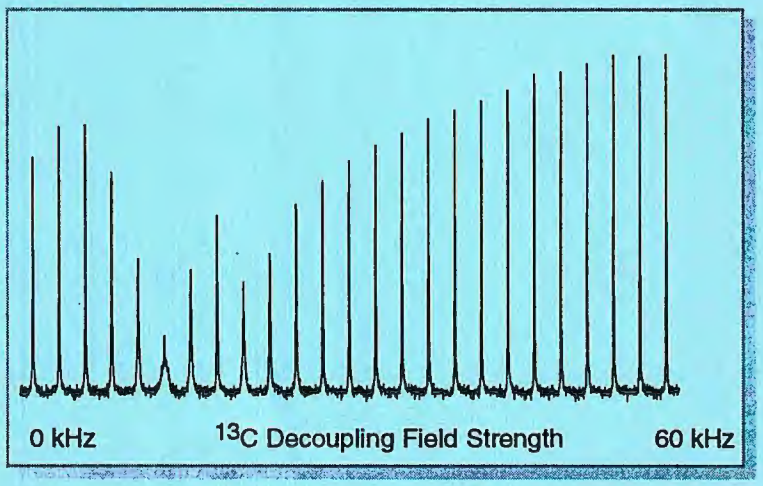
Decoupling of the $^{31}P$ and $^{1}H$ nuclei provides enhanced resolution in the $^{27}Al$ spectrum.

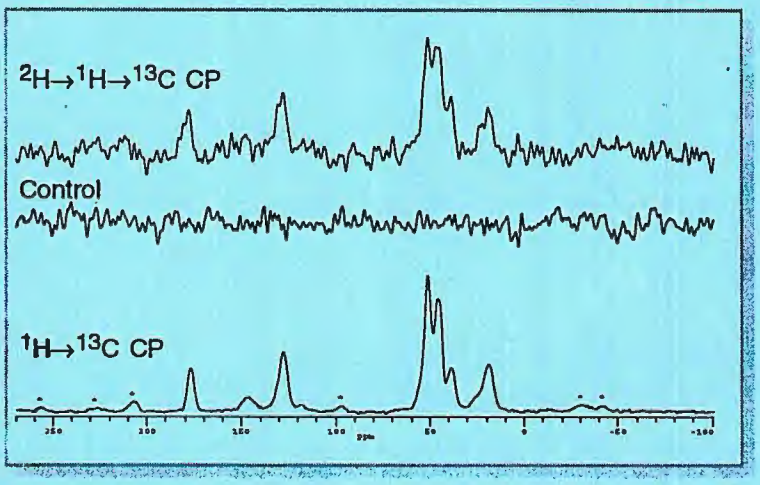
The signal-to-noise does not degrade with addition of $^{1}H$ and $^{31}P$ decoupling. This is the result of good X/Y channel isolation in the probe and filtering between the probe and receiver.

**$^{15}N$ Double-Cross Spectra** of [2-$^{13}C$,$^{15}N$]-glycine. Cross polarization is performed in the direction $^{1}H \rightarrow {}^{13}C \rightarrow {}^{15}N$.

As the $^{13}C$ decoupling field increases from left to right, the noise level remains the same. Signal-to-noise is best with a sufficient level of $^{13}C$ decoupling.

Minima in peak intensities correspond to $^{13}C$ decoupling fields equal to and at twice the spinning frequency.




**$^{13}C$ CP and Double-Cross Spectra** of $d_8$-PS/PMMA copolymer.

$^{1}H \rightarrow {}^{13}C$ CP shows peaks from both PS and PMMA components of the copolymer, indicating intimate mixing of the two materials. The $^{2}H \rightarrow {}^{1}H \rightarrow {}^{13}C$ double-cross spectrum demonstrates $^{2}H$ polarization transfer to $^{13}C$ via $^{1}H$'s. The Control Experiment, with $^{2}H$ CP power off, shows that all double-cross signal originated from $^{2}H$.

*spinning sidebands. Sample/idea courtesy of N. Zumbulyadis, Eastman Kodak.

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c:\msoffice\winword\dokument\pek\dnmr\tamu.doc
Institutionen för oorganisk kemi
**Docent Julius Glaser**

Stockholm, 20 September 1995
(received 9/25/95)

## Magnetization transfer without visible transfer...

*Dear prof. Shapiro,*

In the case of slow exchange on the time scale defined by the chemical shift difference the inversion transfer is often a method of choice. A few pre-experiments may serve to decide if it is feasible to study the system. Usually, one inverts one peak (with the longest relaxation time $T_1$) and records the intensity of the other(s). No variation of the latter means that the magnetization transfer technique doesn't work and one has to use some of the classical kinetic methods. The only information that can be extracted is $T_1$ for the inverted peak. This ungracious situation has occurred to us and is illustrated in Figure 1 below.

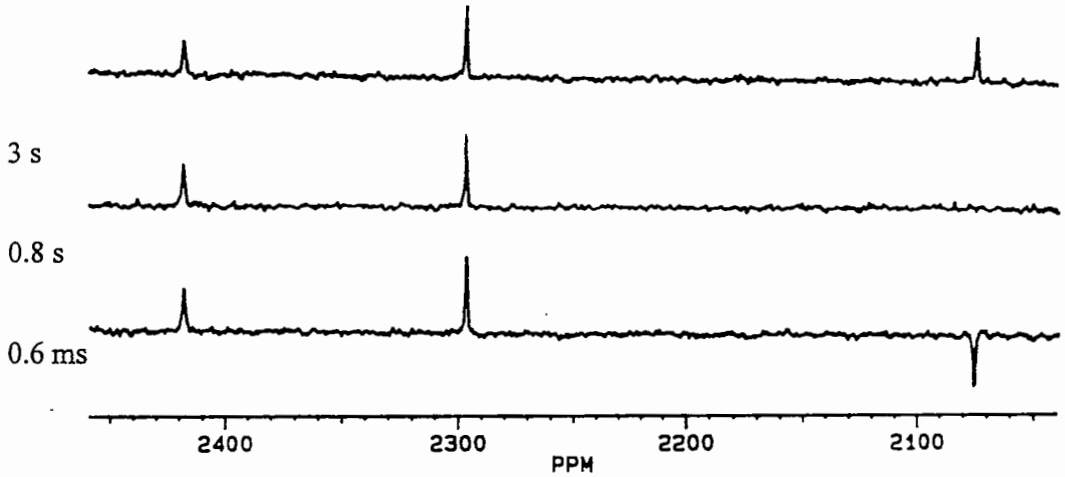


***Figure 1.*** *$^{205}Tl$ -NMR of a solution of $Tl_{aq}^{3+}$, $Tl(CN)^{2+}$ and $Tl(CN)_2^{+}$ (right to left) after inversion of the $Tl_{aq}^{3+}$ signal. Delay after the 180°pulse is given.*

However, changing the amount of the free cyanide in this solution revealed that $^{205}Tl$ NMR relaxation time $T_1$ for the $Tl_{aq}^{3+}$ ion is varying, which made us more happy. ***Figure 2***

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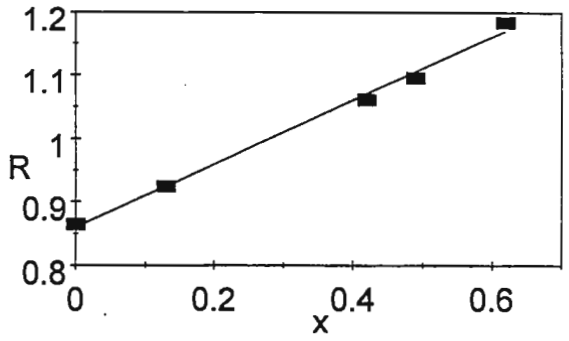
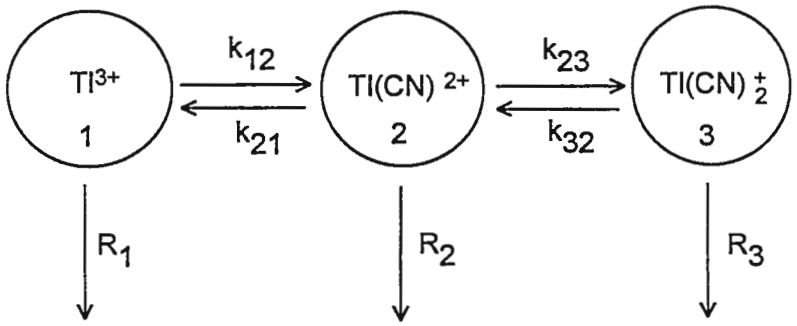
shows this situation in the absence and in the presence of different concentrations of $CN^-$




The following scheme offers the possible explanation:




The magnetization produced by the $\pi$ pulse at site (1) has two possibilities:

- relaxation via $R_1$ or
- transfer to site (2) and (3) and relaxation there.

Since $R_1 << k_{12}$ , the magnetization transfers quantitatively to site (2). Since $R_2 >> k_{23}$ the magnetization leaks out from the system at site (2). Since $R_2 >> k_{12}$ , the value of the apparent spin - lattice relaxation time of species (1):

$$1/T_1(app) = 1/T_1(1) + k_{12}$$

Knowing $T_1(1)$ from an independent experiment, $k_{12}$ may be determined.

Sincerely,

István Bányai

Julius Glaser

The NMR Revolution advances...

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# Combinatorial Chemistry:

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## BACKGROUND

Until now, the search for new medicinal chemicals has been an exercise in tedium. Working with solutions in test tubes, chemists could only conveniently assemble new molecules one at a time, typically at the rate of one or two per week. Now a new approach, "Combinatorial Chemistry," is allowing properly equipped laboratories to produce new compounds at the rate of 100 to 200 per week.

Based on techniques developed in the 1960's, and re-discovered in the early 1980's by Leznoff,[1] Frechet[2] and others, combinatorial chemistry is a technique by which molecular fragments are assembled in multiple combinations on a polymer bead substrate to produce thousands of new molecules almost overnight.

The traditional method of analyzing compounds directly attached to polymer supports requires that the compound be removed from the resin, which is time consuming and may also structurally alter the reaction product. On the other hand, NMR assignment of compounds "on resin" using typical high resolution techniques is difficult or impossible because the polymer beads restrict molecular motion and cause the resonances to be broadened by direct dipolar coupling.

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**Features include:**

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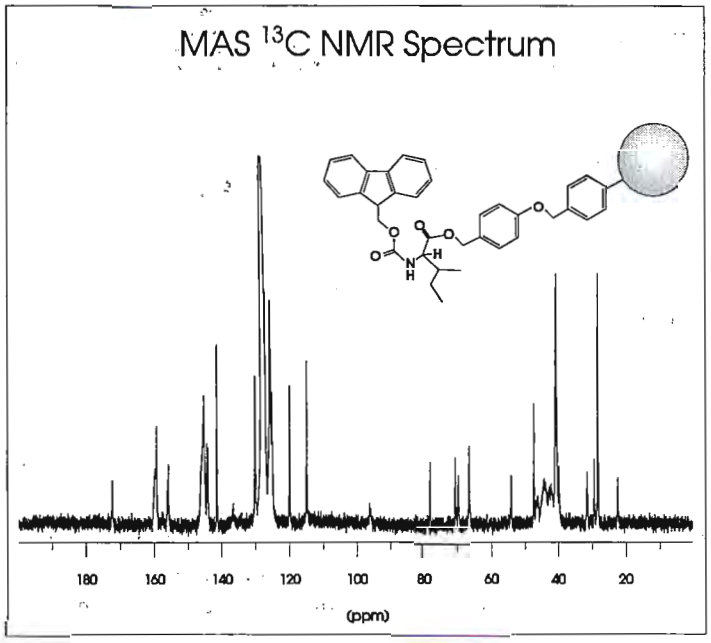


The Bruker CCA accessory is available for all *AVANCE* 400 and 500 MHz standard bore NMR systems. On special request, it can also be offered at other frequencies and bore sizes. Also available is the new Bruker HFX accessory, which enables the probe to be used for X observation with simultaneous decoupling of $^{1}$H and $^{19}$F.

Please contact your local Bruker representative for more information.

*Figure 1: $^{13}$C MAS spectrum of a typical compound [3].*

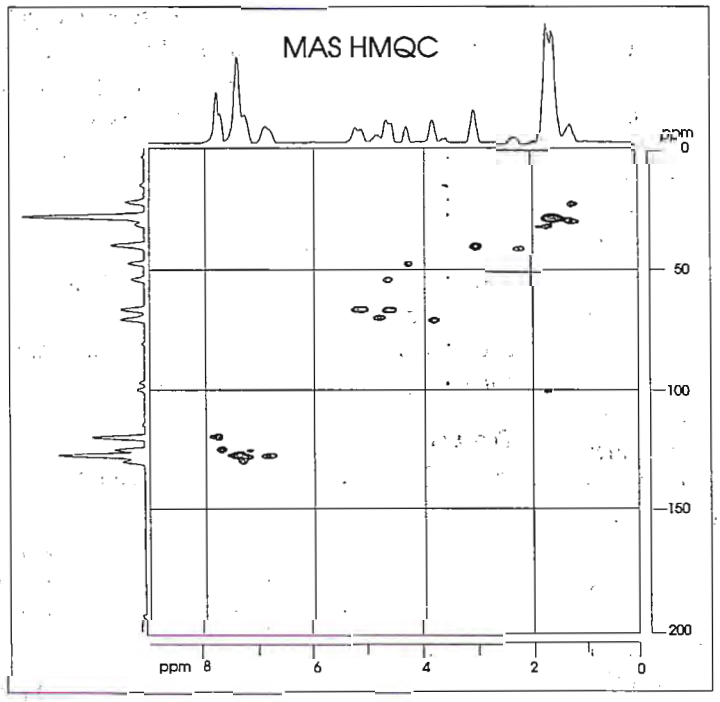


*Figure 2: A two dimensional HMQC spectrum of the compound shown in Figure 1.*

[1] C.C. Leznoff, Acc. Chem. Res. **11**, 327 (1978)
[2] J.M.J. Frechet, Tetrahedron **37**, 663 (1981)
[3] R.C. Anderson, M.A. Jarema, M.J. Shapiro, J.P. Stokes and M. Ziliox, Bruker Report **142/96**

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*The Procter & Gamble Company*
*Miami Valley Laboratories*
*P.O. Box 538707, Cincinnati, Ohio 45253-8707*

October 5, 1995
received 10/10/95

**Diffusion and NOESY Studies of a Surfactant-Polymer Complex**

Dear Barry,

We've been spending some time in recent months learning and applying some of the NMR techniques for studying surfactant solutions and for studying interactions between surfactants and other solution components. Our access to pulsed field gradients allows us to measure self-diffusion coefficients, which are quite useful for studying molecular aggregates like micelles. We've also used NOESY to study interatomic contacts in complex molecular aggregates.

We started with a system consisting of potassium oleate (18 carbons, KOA) and polyethylene glycol (MW=8000, PEG). KOA alone forms a viscoelastic solution which becomes a Newtonian liquid upon addition of PEG. We set out to use NMR to find a molecular-level explanation for the rheological changes.

The diffusion coefficient of water in KOA is close to that for neat water, indicating that the high viscosity is caused by the presence of large structures which don't interfere much with the microenvironment of water. Diffusion of KOA alone was quite slow, corresponding to an effective hydrodynamic radius of more than 3,000 Å. We can't claim that this is the true size of the KOA aggregates, and we don't know their shape from the NMR data alone, but it is clear that the aggregates are quite large.

When PEG is added to the KOA, water diffusion is again relatively unaffected, KOA diffusion speeds up dramatically, and PEG diffusion slows down. The two components have identical diffusion coefficients in the mixture. The effective hydrodynamic radius of the complex has a strong temperature dependence, but lies in the range of 850 Å to 150 Å between 5° C and 50° C. This sharp reduction in aggregate size can explain the rheological changes.

Cryo transmission electron microscopy was also used to study this system, and the results are consistent with the NMR study. In the absence of PEG, the KOA forms a network of long, worm-like micelles which give the system its viscoelastic character. When PEG is added, these are replaced with smaller, spherical micelles which produce the Newtonian liquid.

We were curious about the microscopic structure of the KOA-PEG complex, so we acquired a series of NOESY spectra with variable mixing times. The system is in the spin-diffusion motional limit, giving cross peaks with the same sign as the diagonal. PEG exhibited cross peaks with all resolvable oleate resonances.

The relative, normalized build-up rates for resolvable cross peaks with PEG were 74% (position 2), 95% (position 3), 100% (positions 4-7 and 12-17), 66% (positions 8 and 11), 48% (positions 9-10), and 28% (position 18). Obviously, the isolated spin pair approximation isn't a very useful way to get structural information from these data, since it would imply a 23% difference in the distances of the closest and furthest atoms from the PEG. More importantly, we know that surfactant aggregates are dynamic and structurally heterogeneous. It is probably better to use a diffusion model, in which case the NOE build-up rates for two resolvable atoms in different molecules would depend in part on the probability of being nearest neighbors. Spin-diffusion and differences in dynamics will affect cross-relaxation as well. It would be interesting and informative to try a relaxation matrix analysis of this and other models to explore the effects of spin-diffusion and dynamics and to see what kind of information can be extracted. Based only on the relative intensities, which are generally higher near the polar head group and lowest at the end of the tail, it appears that PEG is more likely to interact with the polar end of the surfactant. This supports a model in which the polymer interacts with the surfactant head groups, stabilizing smaller structures with higher surface area.

Charles Eads  Zuchen Lin

**Department of Pure and Applied Chemistry**
**The University of Strathclyde**
**Glasgow G1 1XL Scotland**

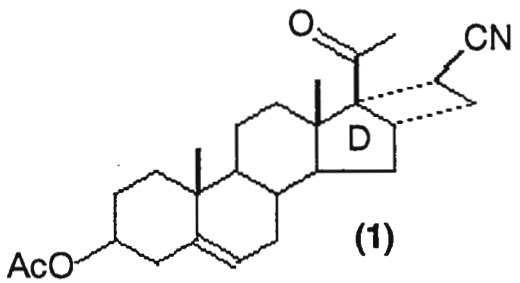
11th October 1995
(received 10/16/95)

Dr B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto CA 94303
U. S. A.

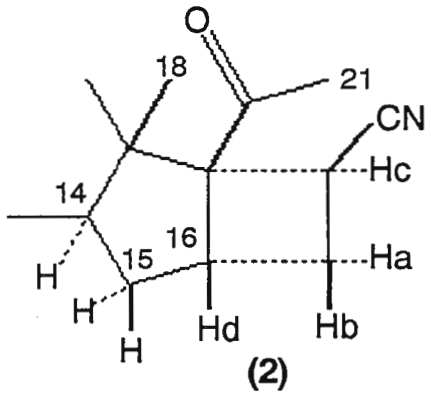
Ancient Chemistry Revisited Part 3.
Photochemical Addition of Acrylonitrile to $\Delta^{16}$–Pregnene–20–ones

Dear Barry,

In the 1960's an investigation into the ultraviolet irradiation of a solution of 3β–acetoxy–pregn–5,16–dien–20–one and acrylonitrile in benzene led to the isolation of two isomeric photo–adducts.. The structures of these compounds have hitherto not been certain. A recent study of the NMR spectra of the major isomer allows its structure to fixed as (1). The presence of ketone carbonyl and nitrile groups was known from infrared spectral evidence and was confirmed by the 13–C nmr spectrum. The proton spectrum and noesy experiments were however crucial in fixing the structure. The four protons (a, b, c, and d) formed an easily recognized subspectrum ( structure 2); the strong Noe between Hd and the protons of the 18 methyl group means that cyclobutane ring is joined to ring D by alpha links. Noe's are also observed between the 21 methyl protons and Hb and Hd (but not Hc) showing that the cyano group is above the plane of the cyclobutane ring. The placing of the cyano group on C17a as shown in (2), and not on C16a , follows from the Noe's observed between Ha and the alpha protons on carbons 14 and 15.




(1)




(2)

Yours sincerely

Peter Bladon.

Peter Bladon

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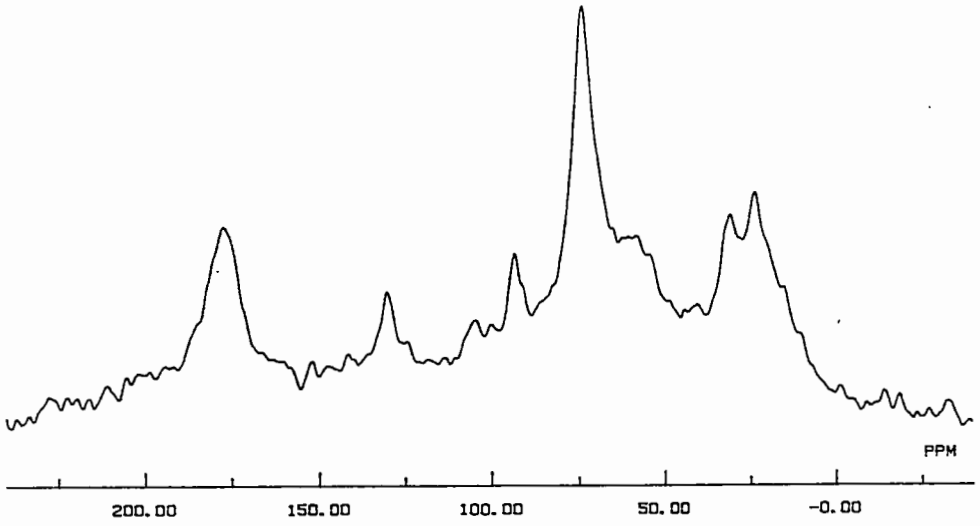
Dr. Barry Shapiro
The NMR Newsletter
966 elsinore Court
Palo Alto, CA 94303

September 29, 1995
(received 10/5/95)

Mushroom Nuclear Magnetic Resonance

Dear Barry,

You and your readers may not know this fact, but a staple of the economy of northern Delaware and nearby Pennsylvania is mushrooms, as anyone not having a cold can detect as he/she drives the 15 miles from Newark to Kennett Square, Pennsylvania. Like many food products, they are complex systems, which one might expect to show broad, unresolved spectra. We have begun to investigate what solid-state $^{13}C$ MAS NMR spectroscopy can tell one about dried mushrooms. In the figure we show the spectrum of dried whole Porcini mushrooms, taken without any cleanup other than grinding to make a uniform powder. The spectrum is complex and there is overlap, but regions are relatively easily resolved. One can identify resonance intensity in the region between 70 and 100 ppm, most likely arising from cellulosic carbons, but one can also distinguish several other kinds of carbon from the spectrum.




One can imagine a series of experiments to analyze such a complex system with NMR from analysis of various fractions after separation (analogous to the use of mass spectrometry of volatile materials from such systems after varous treatments) to multi-dimensional analysis to separate spectra of independent components spectroscopically. Here I wanted to point out that NMR analysis of mushrooms may prove interesting and useful, and that even at this stage, resolution into categories is possible. An important advantage of these materials is that one may eat the sample after analyzing them!!

Yours truly,

Cecil

Cecil Dybowski

446-30

DEPARTMENT OF HEALTH & HUMAN SERVICES — Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

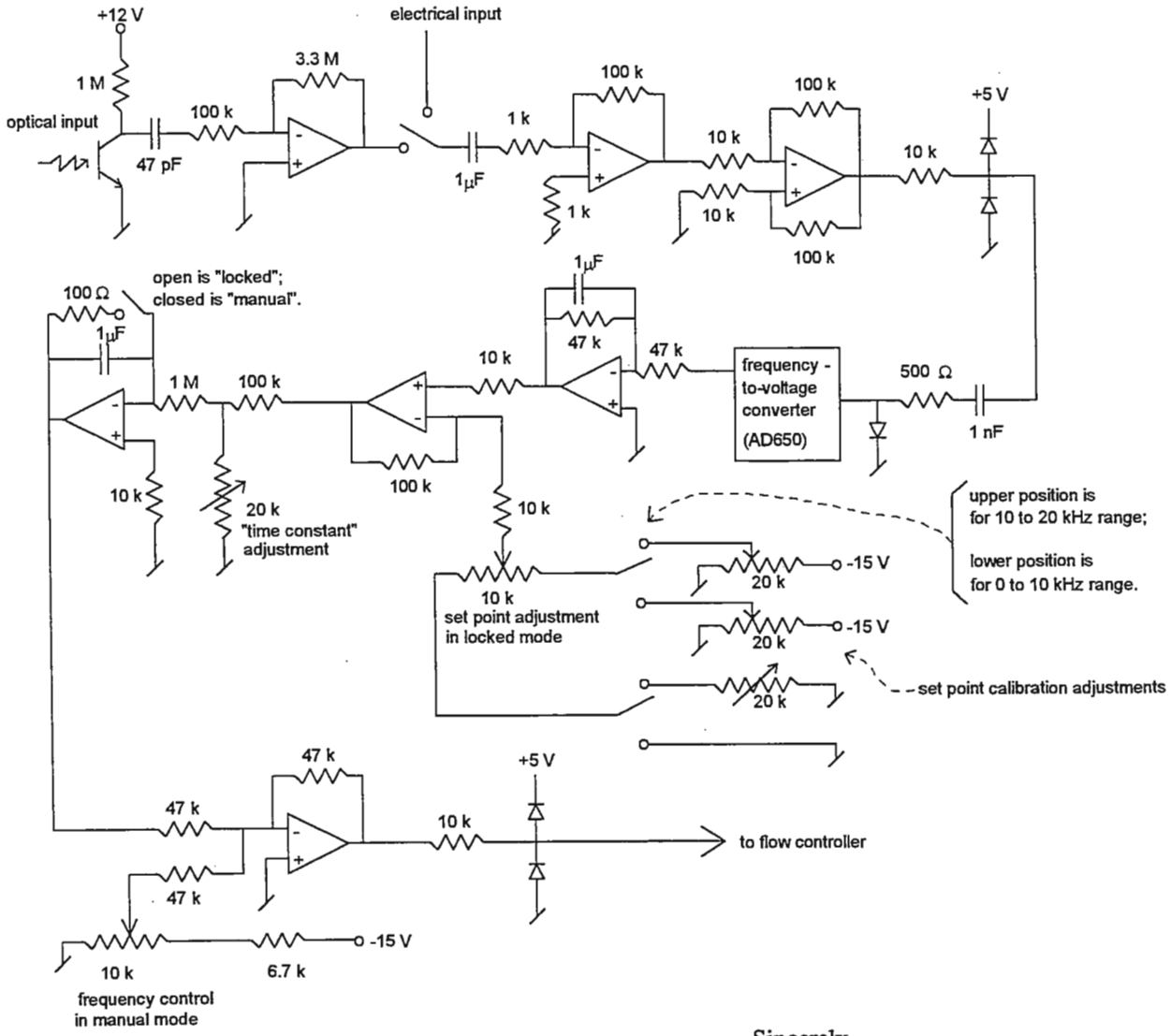
B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Building 5, Room 112
October 2, 1995
(received 10/6/95)

**Spinning Speed Controller Circuit**

Dear Barry:

Rolf Tschudin, Nghia Tang, and I have recently built a new circuit for controlling the sample spinning frequency in magic angle spinning experiments. A schematic is given below. The circuit runs in either "manual" or "locked" mode. In locked mode, either an optical or an electrical signal from the spinner assembly may be used. Two ranges for the frequency set point are possible. Typically, we use the manual mode to set the spinning frequency close to the desired set point, then switch to the locked mode. We currently use this circuit to drive an MKS 1159B flow controller, but we plan to replace this with something that can provide more flow. The circuit works quite well, and is simple and inexpensive to build.




Sincerely,

Robert Tycko

KARL-FRANZENS-UNIVERSITÄT GRAZ
**Institut für Organische Chemie**

Dr.Heinz Sterk

A-8010 Graz, .....26.9.95.....
Heinrichstraße 28
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Unser Zeichen:

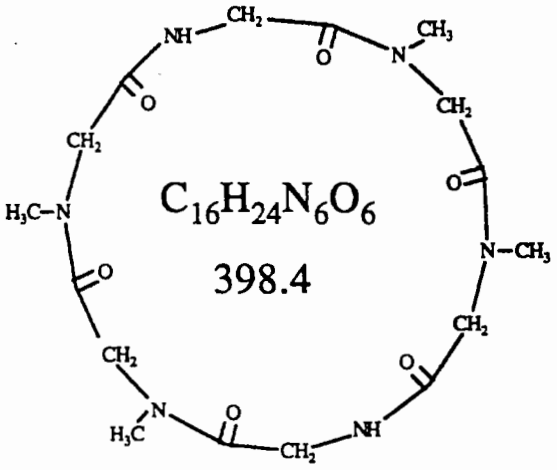
(received 10/11/95)

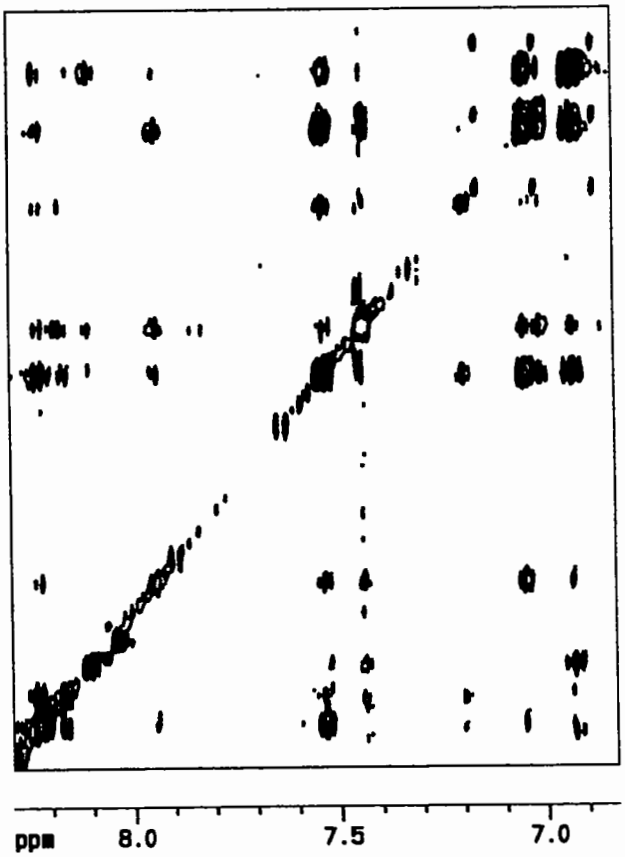
Dr. Bernhard Shapiro
NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

A sample for a "textbook case" exchange experiment.

Dear Dr. Shapiro :

Sometimes, as we all know, things turn out to be much more complicated than expected at the first glance. As a matter of fact in our peptide group a cyclic $(Gly\text{-}Sar\text{-}Sar)_2$ peptide was synthesized. The two NH protons give reason to the following exchange spectrum, which shows that 9 different isomeric NH positions are in exchange which each other. The conformers thereby are formed by cis trans isomerization of the peptide bonds in sarcosine, the rotational barrier of which is largely reduced due to the methyl substitution at the nitrogen, compared to an unsubstituted amide. One conformer, the all cis one, does not exist, due to the enormous steric strain, whereas all other possible 6 conformers give reason to one or two amide proton signals depending on the symmetry and thus are the reason for our 2D-exchange spectrum.




Yours sincerely

H.Sterk A.Artl

**Schering-Plough Research Institute**

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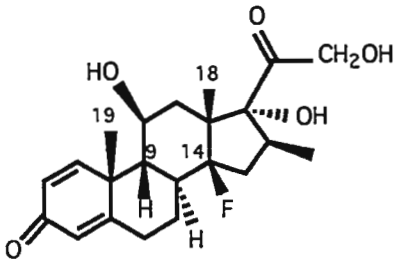
Dr. B. L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

October 11, 1995 (received 10/16/95)

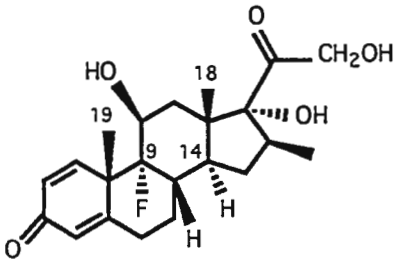
**Proton-Fluorine Coupling - Through Space or Through Bond?**

Dear Barry,

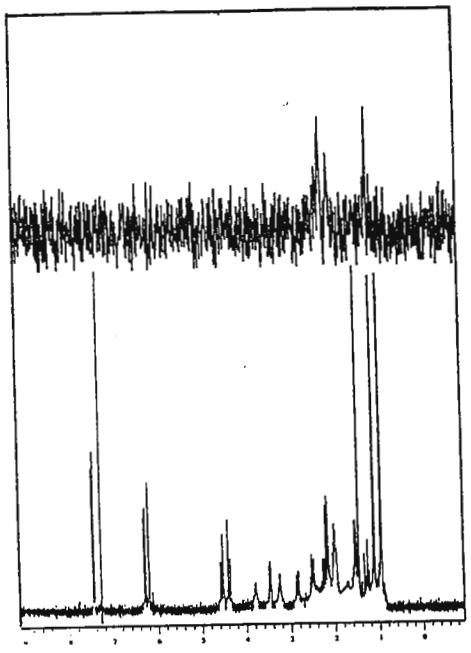
We recently undertook to determine the structure of an isomer (**1**) of betamethasone (**2**). A variety of homonuclear $^1H$ experiments (COSY, NOESY, HMQC-TOCSY and HMBC) suggested the indicated structure for the isomer:




**1**




**2**



This structure was confirmed by an H-F heteronuclear NOE experiment which was carried out on our Omega 400 spectrometer by tuning the probe to the vicinity of fluorine. The Figure shows the 1D $^1H$-NMR spectrum of **1**, along with a (somewhat detuned) 1D NOE difference spectrum ($^1H$ observe) obtained by steady-state irradiation of F-14. The NOE spectrum shows cross-relaxation between F and $CH_3$-18, H-9 and possibly H-7 and H-15, as would be expected if F occupied the β face of the molecule.

Inspection of the $^1H$ signal for $CH_3$-18 shows a $J_{HF}$ of 4 Hz. This four bond coupling between F and $CH_3$ in a *cis* relationship has been well-documented in fluorosteroids. The corresponding *trans* orientation does not always give rise to observable splitting (e.g., in **2**). The always present long range *cis* HF coupling has been attributed to a through space coupling component (**J. Am. Chem. Soc.** (1964) **86**, 4005, 4110) according to the "converging vector" rule. Perhaps this rule is a manifestation of forced orbital overlap which has been invoked to explain some "through space" proton-metal couplings observed by Mike Summers' group in rubredoxin {e.g., *New J. Chem.*, **18**, 387 (1994)}.

Sincerely,

T. M. Chan H. Eaton A. Evans D. Tsai K. Belsky

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(received 10/20/95)

Dr. Bernard L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

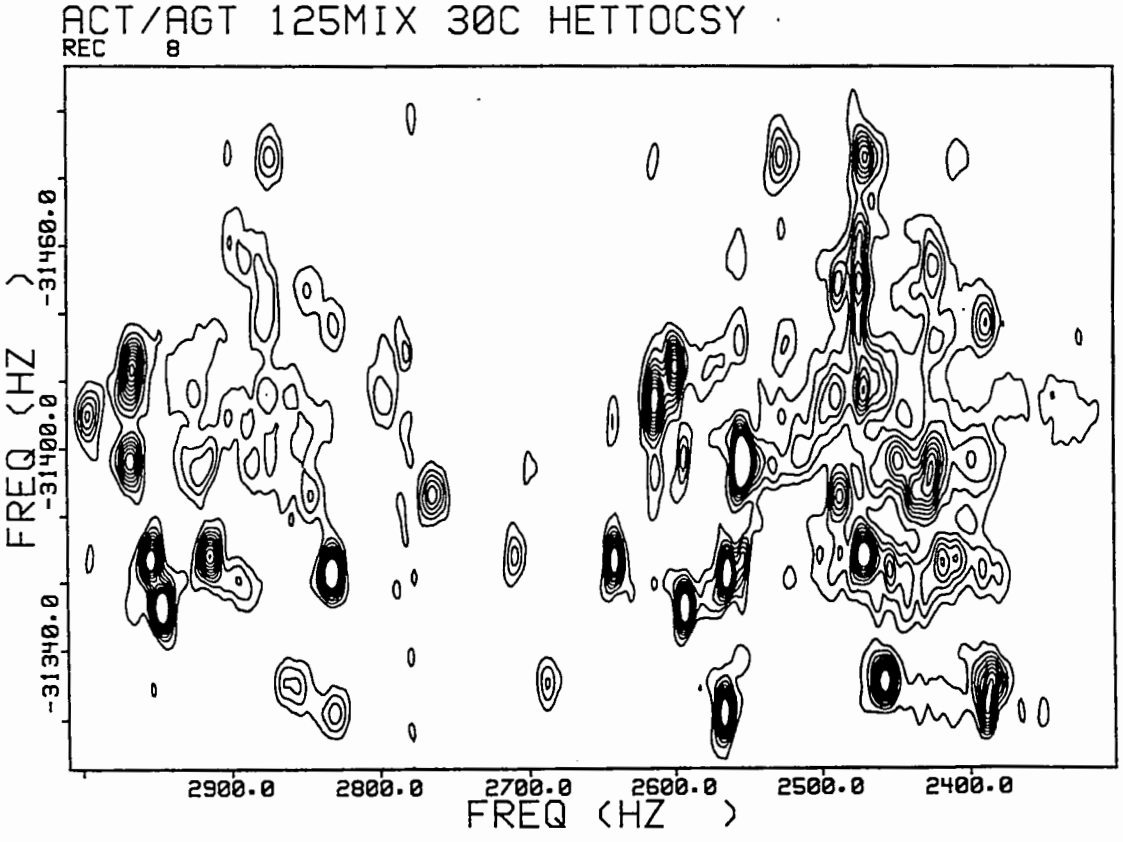
***31-P Hetero-TOCSY***

Dear Barry,

We have been measuring some $^{31}P$ / $^{1}H$ hetero-TOCSY spectra. The interesting thing about these experiments is that, at least in our hands, they seem rather probe dependent. We have two probes available for this experiment, an ancient double resonance broad-band indirect detection probe, and an up-to-date HCP triple resonance indirect detection probe. Perversely, we find we get much better $^{31}P$ hetero-TOCSYspectra with our old double resonance probe than we do with the new triple resonance one, despite the fact the new probe has a much better proton sensitivity. Presumably, the difference between the probes lies elsewhere.

When experiments are very probe dependent, it is common to assume that this is due to RF inhomogeneity. So we decided to investigate and it does seem that the RF homogeneity of decoupler coil on our double-resonance indirect detection probe is much better than that of the triple resonance HCP probe. So, despite the common belief that cross-polarization experiments quite tolerant of RF-inhomogeneity, does seem possible that hetero-TOCSY experiments are quite demanding in harware terms.

An example of the kind of hetero-TOCSY spectra we get from an assymetric 11-mer DNA sample is shown below:-



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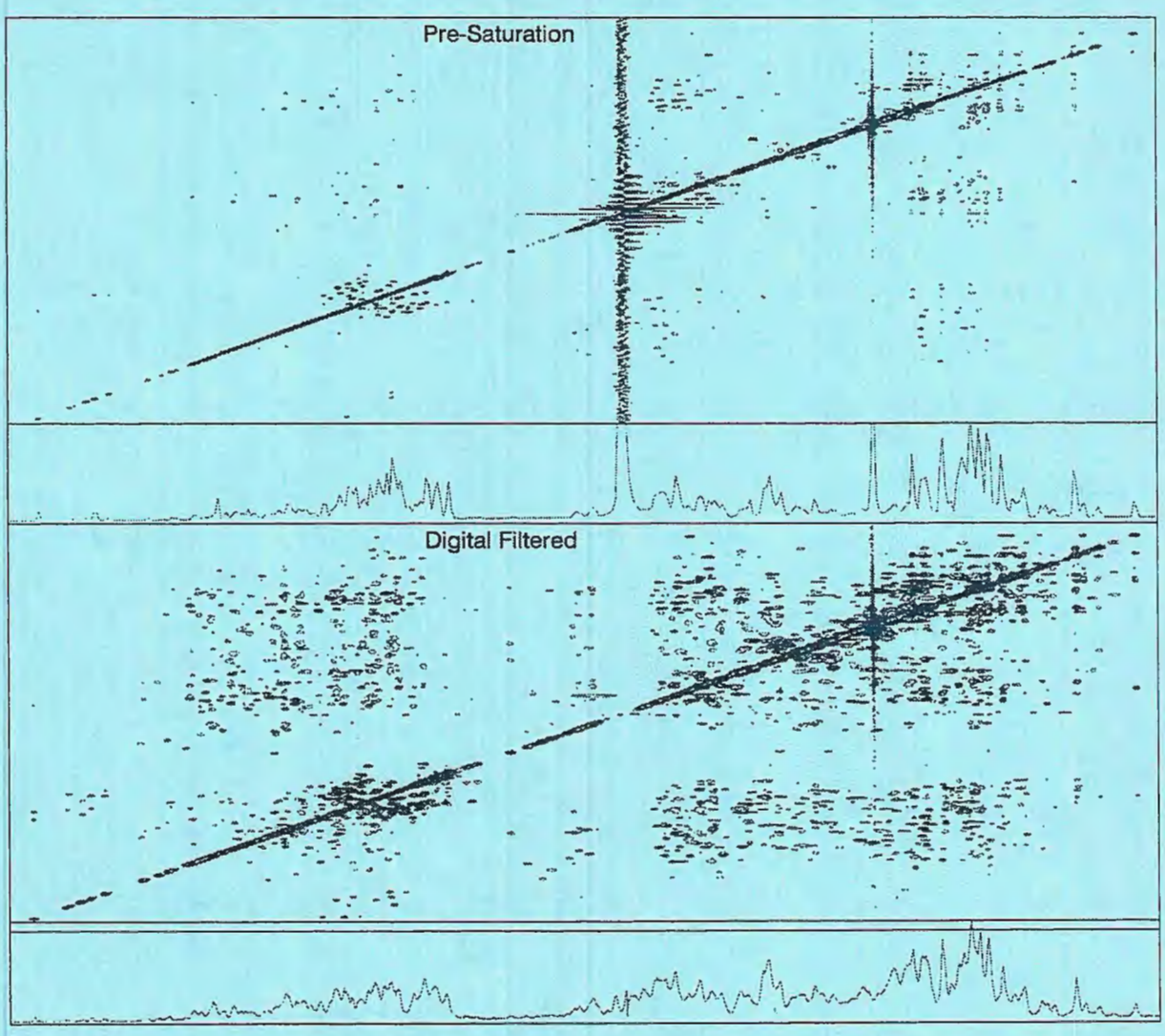


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