THE NMR NEWSLETTER

No. 443

August 1995

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PTS 500	1-500 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$8,720.00 (1 Hz resol., OCXO freq. std.)
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PTS x10	user specified 10 MHz decade	1 Hz	1-5μs	standard	3½"H×19"W	BCD (std) or GPIB (opt)	$3,000.00 (1 Hz resol., OCXO freq. std.)
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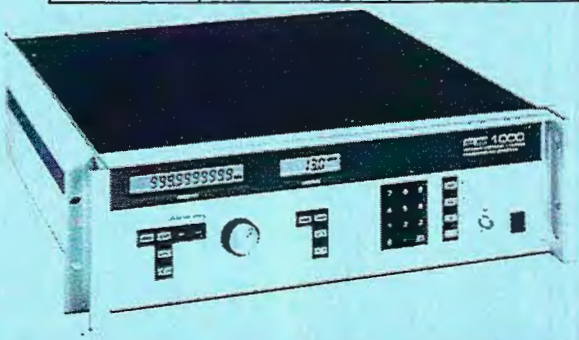

1 Switching Time is dependent on digit (decade) switched; see detailed instrument specifications.

2 For applicable digits, see detailed instrument specifications.

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FORTHCOMING NMR MEETINGS

3rd Scientific Meeting, Society of Magnetic Resonance, and 12th Meeting European Society for Magnetic Resonance in Medicine and Biology, Nice, France, **August 19 - 25, 1995**; Contact: Society of Magnetic Resonance, 2118 Milvia St., Suite 201, Berkeley, CA 94704; Tel. (510) 841-1899; Fax: (510) 841-2340.

Western Biotech Conference, San Diego, CA, **October 18 - 21, 1995**; Contact: Western Biotech Conf. Registr'n., c/o Tom Lobl, Tanabe Research, 4540 Towne Centre Court, San Diego, CA 92121; Tel. (619) 622-7035; Fax: (619) 622-7080; E-mail: tjlobl@cerf.net.

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.

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.

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BLS & LWS

UNIVERSITY OF CAMBRIDGE
DEPARTMENT OF CHEMISTRY
Lensfield Road
Cambridge CB2 1EW

Ray Freeman *Telephone:* **(01223) 336450**

Professor Bernard Shapiro,
966 Helsingførs Court,
Palo Alto,
California, 94303
USA.

14 July 95

(received 7/20/95)

Dear Barry,

"Graf von Liverwurst"

Back in the early 1980's, Malcolm Levitt once asked me *"Is the decoupling saga nearly over ?"* and I told him, *"Sagas are forever."* Many a true word spoken in jest. It seems that, 15 years later, there are still improvements to be made in the achievable decoupling bandwidth for a given radiofrequency power dissipation. The latest innovations have tended to employ adiabatic fast passage to invert the spins over a wide frequency range.[1-3] Hyperbolic secant pulses,[4,5] tangential sweep, and constant adiabaticity pulses all have their champions.

But elegant algebra is not the only consideration, and we have found that all these methods can be improved by "stretching." This term is used in the sense of a stretch limousine or stretch jetliner — leave the nose and tail the same, but insert a ridiculously long centre section. Better still, design a new vehicle with a long body and short extremities. So we use a linear sweep, adiabatic passage with an amplitude function given by:

$$A = \pm A_0\{1 - |\sin\theta|^n\}$$

where n is a hefty number like 20 or 40. This has a shape much like a sausage or a WW1 zeppelin, so we call these WURST pulses (wideband, uniform rate, smooth truncation).

If we define a figure of merit (the *Wang*) $\Xi = 2\Delta B(\text{max})/B_2(\text{rms})$

where $2\Delta B(\text{max})$ is the effective decoupling bandwidth, and $B_2(\text{rms})$ is the constant radiofrequency level that would have the same power dissipation as the actual amplitude-modulated B_2 field; then we can compare different schemes on an equal footing. For example, GARP[6] has $\Xi = 4.8$, whereas WURST can have Ξ greater than 50, at the expense of rather bad cycling sidebands. No room to give more details here . . .
A full paper has just been submitted to J. Magn. Reson.

Kindest regards,

Ray Eriks

Ray Freeman, Ēriks Kupče

[1] S. L. McCall and E. L. Hahn, *Phys. Rev.* **183**, 457 (1969).
[2] M. S. Silver, R. J. Joseph, and D. I. Hoult, *Phys. Rev. A.* **31**, 2753 (1985).
[3] J. Baum. R. Tycko, and A. Pines, *Phys. Rev. A.* **32**, 3435 (1985).
[4] T. Fujiwara, T. Anai, N. Kurihara and K. Kakayama, *J. Magn. Reson.A.* **104** , 5103 (1993).
[5] M. R. Bendall, *J. Magn. Reson.A* **112**, 126 (1995).
[6] A. J. Shaka, P. B. Barker, and R. Freeman, *J. Magn. Reson.* **64** , 547 (1985).

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ROCHE RESEARCH CENTRE

05 July 1995 (received 7/11/95)

Dr G Williams
Physical Methods Department
Direct Line: +44 1707-366548
E-mail : glyn.williams@roche.com

Dr Bernard L Shapiro
Editor/Publisher *The NMR Newsletter*
Palo Alto, California 94303

Dear Barry,

Re : PROTEIN NMR USING AN LC-PROBE

The recent acquisition of a dedicated ^1H lc-nmr probe in our laboratory provided opportunities not just for the chromatographer, but also for the protein nmr spectroscopist. Since both applications depend on having good proton signal-to-noise, we decided to investigate the possibility of using our Bruker lc-nmr probe as a high sensitivity, small volume probe for protein applications. The cell volume of our 4 mm lc-nmr probe measures at 270 µl, or about half of a conventional high resolution probe.

In a series of preliminary experiments, aliquots of H_2O were injected into a flowing hplc pump connected to the lc-probe (flow rate 0.8mls/min), which had been pre-equilibrated with 10% D_2O / 90% H_2O. By monitoring the decrease and recovery of the lock signal, it is possible to determine the concentration profile of the sample (in this case 100% H_2O) as it passes through the active volume of the probe. Schematic representations of the H_2O concentration in the active volume after injections of 250 µl (a) and 500 µl (b) of H_2O are shown in Figure 1.

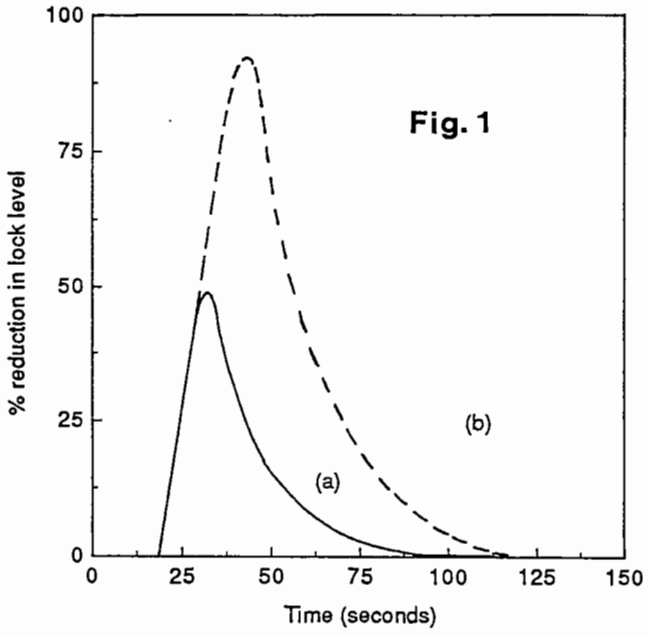

Fig. 1

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Signal-to-noise determinations were performed using a solution of lysozyme (2 mgs/ml) in 90% H_2O / 10% D_2O. The following measurements were made:

i. after injecting a single 250 µl aliquot (0.5 mgs of protein) and stopping the flow at the maximum in the concentration profile (32 secs).

ii. after flushing the entire probe volume with 2 mls of protein solution to ensure the cell volume (0.27 mls) was completely filled.

iii. measurements were also performed with a comparable amount of protein (2 mgs/ml x 0.27 ml = 0.54 mgs) in a 500 µl sample using a Bruker 5 mm BB-inverse probe. The results are given in Table 1 and have been normalised.

Given a limited amount of sample, optimum signal-to-noise is obtained from the 5 mm probe. In our laboratory, there is over 40% difference between this and the lc-nmr probe and this difference could be increased by using a Shigemi tube in conjunction with the conventional probe. In addition, our lc probe appears to contain significant amounts of protonated materials and thus requires the use of relaxation-weighted pulse sequences to avoid poor baselines. An added disadvantage of the lc-nmr probe is the difficulty of efficiently introducing the sample into the active volume. Despite the small cell volume, over 500 µl of sample is required to uniformly fill the cell at the concentration of the starting solution, C; 250 µl of sample gave a maximum concentration of about C/2 (Figure 1 and Table 1). A better approach is to introduce the sample in as small a volume as possible (<50 µl) and allow it to diffuse throughout the cell.

In principle, the coil/sample design of the lc-nmr probe provides a potential improvement in signal-to-noise which is of interest to all nmr spectroscopists. When experiment times are measured in days, the added difficulty of inserting and removing the sample is relatively unimportant. At present, however, the measurements indicate that no sensitivity improvement is obtained. Realising this potential will require further development work.

Probe/Sample	Relative S/N
1. lc-nmr probe/250 µl injection of 2 mgs/ml lysozyme	31
2. lc-nmr probe/flushed with 2 mls of 2 mgs/ml lysozyme	56
3. 5 mm BB-inv. probe/0.54mgs lysozyme in 500 µl solvent	100

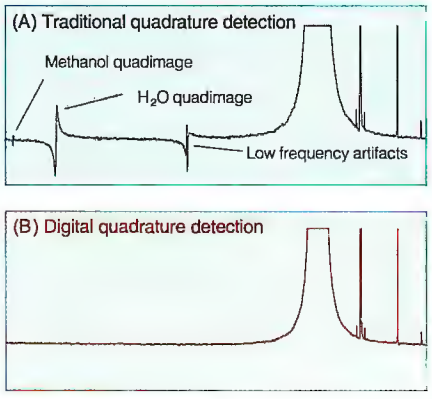
TABLE 1

B D Scott I W A Whitcombe G Williams

Digital NMR
Digital Lock
Digital Filtering
Digital Oversampling
Digital Signal Processing
Digital Signal Routing
Digital Gradient Shaping

The NMR Revolution advances...

Digital Quadrature Detection



Bruker standard dynamic range sample, obtained with (B) and without (A) DQD

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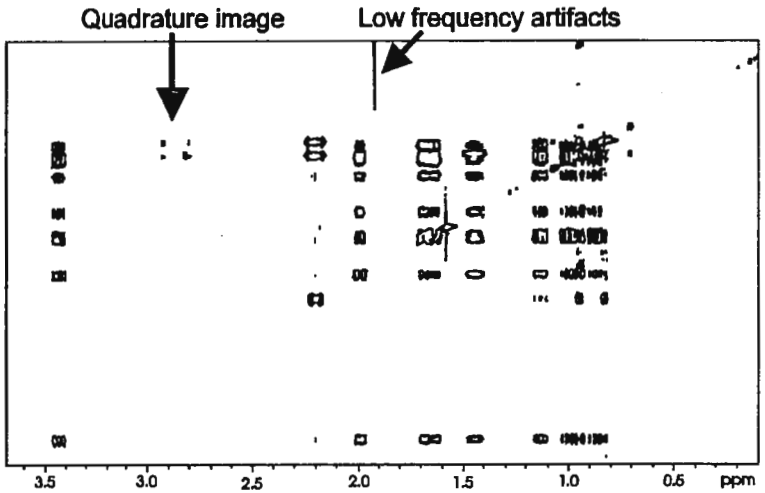

Figure 1: Traditional quadrature detection
1 scan per t_1 increment, **15 minutes**

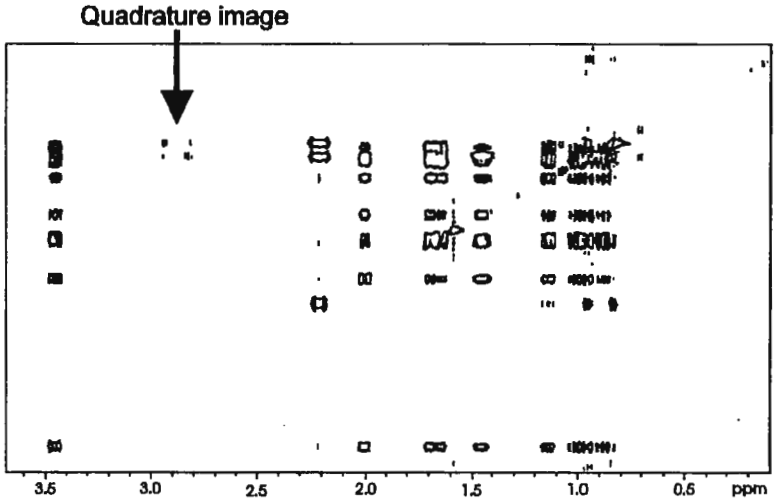

Figure 2: Traditional quadrature detection
2 scan per t_1 increment, **30 minutes**

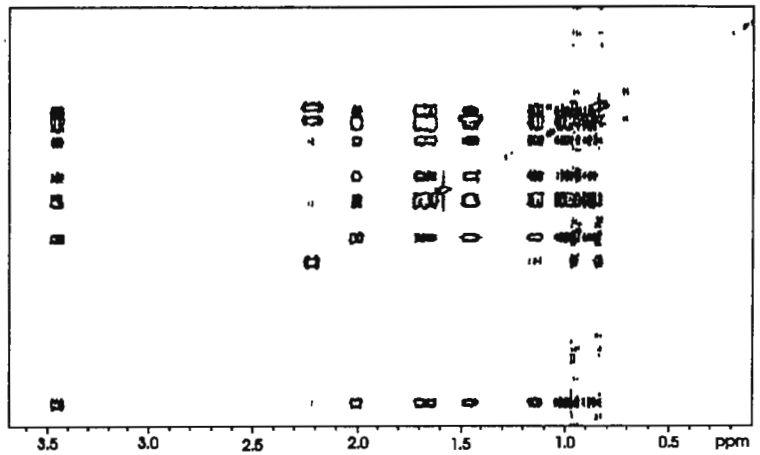

Figure 4: Digital quadrature detection
1 scan per t_1 increment, **15 minutes**

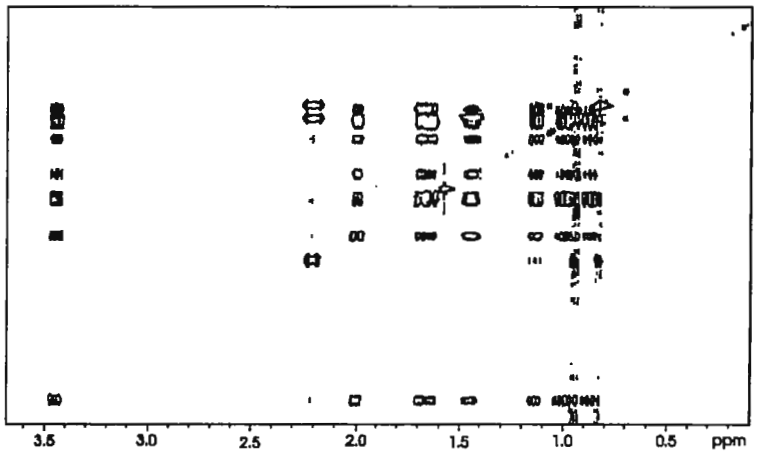

Figure 3: Traditional quadrature detection
4 scan per t_1 increment, **60 minutes**

NORTHWESTERN UNIVERSITY

Joseph B. Lambert
Clare Hamilton Hall Professor of Chemistry

Department of Chemistry
2145 Sheridan Road
Evanston, Illinois 60208-3113
Telephone (708) 491-5437
Internet lambert@casbah.acns.nwu.edu
Facsimile (708) 491-7713

July 13, 1995

(received 7/20/95)

Title: Before Jurassic

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

Dear Barry:

Many trees exude a sticky, resinous material when damaged. These resins are composed of terpenes that begin to polymerize and crosslink on exposure to air. The resulting fossilized resin is insoluble in almost all solvents and is extremely hard and stable. As a class they have been called resinites, or, if from northern European sources, amber. Most fossil resins come from the Tertiary period (2-65 million years ago). Anything younger tends to be less stable, more soluble, and much softer, and makes poor jewelry. We have been studying Tertiary resins by solid state NMR in order to draw geographical distinctions and to determine the paleobotanical sources. We wrote you about these studies previously.

Now we have obtained some really old stuff (65 million years is youthful) from George O. Poinar, Jr. of Berkeley, the man who suggested to Michael Crichton that dinosaurs might have left a DNA trace in the remains of mosquitoes trapped in amber. So far, we have found two basic families of Cretaceous amber (65 to 140 million years ago). One set with representatives from Alaska, the U.S., Greenland, France, and Lebanon gives spectra that have resemblances to the genus Agathis. Figure 1 shows spectra of a sample from France with normal and interrupted decoupling. A very different pattern comes from a few samples from Australia and Arkansas (Figure 2 shows an Australian example), and we conclude that a different botanical source gave rise to these resins.

We were able to obtain a small sample of Triassic amber from Bavaria (that's earlier than Jurassic), with an age of 220-230 million years, possibly the oldest fossil resin known. The spectrum of Figure 3 looks like a broadened version of Figure 1 (normal decoupling), so we suspect that the botanical source is similar. By the way, the best opportunities for obtaining dinosaur DNA would be from Cretaceous samples, such as those in this study, not Jurassic. More amber, more dinosaurs. I guess that Cretaceous Park or even Kamp Kretaceous isn't sufficiently commercial or menacing. NMR, at any rate, is successfully characterizing all these fossil resins, so that both geographical and paleobotanical conclusions may be drawn.

Sincerely,

Joseph B. Lambert

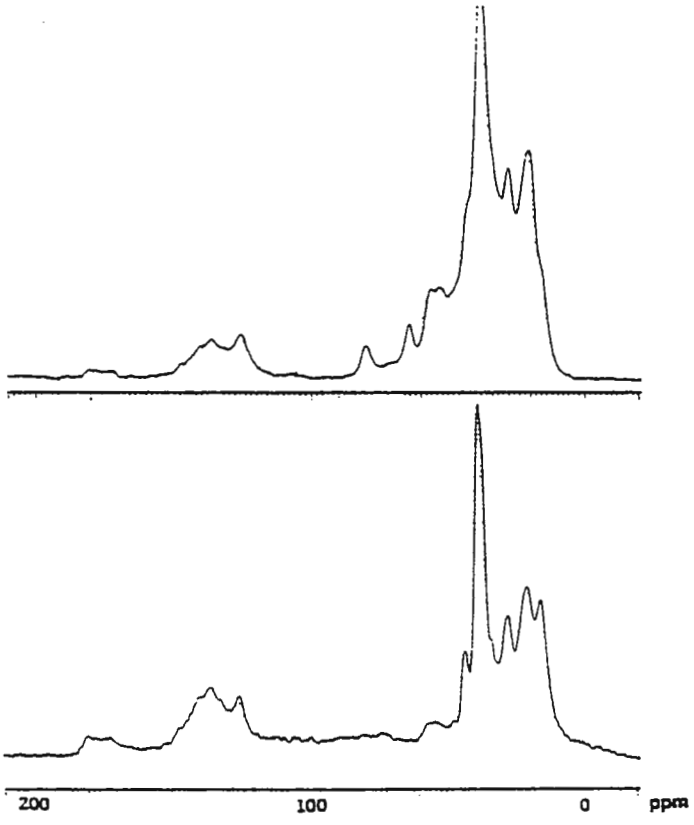

Figure 1

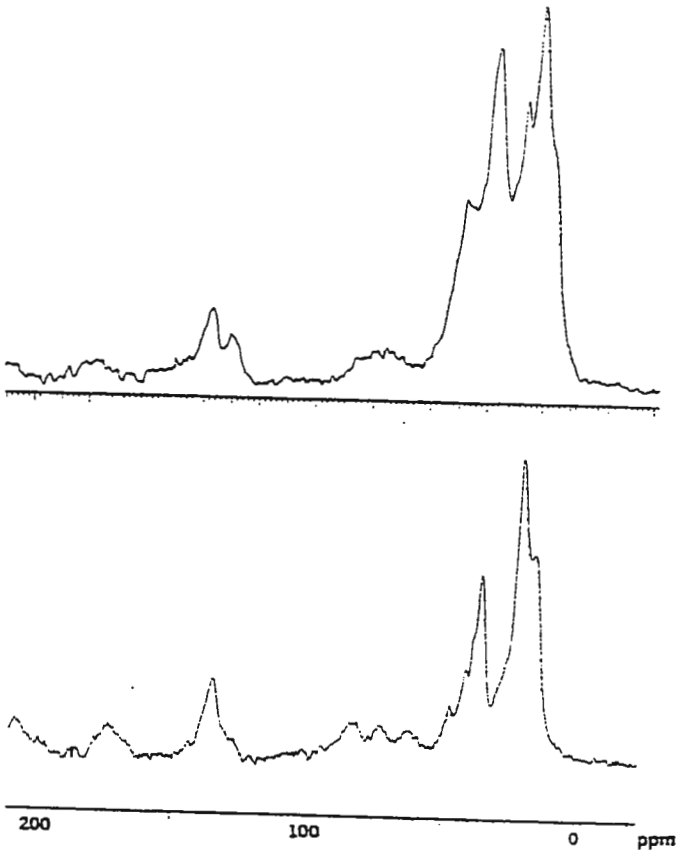

Figure 2

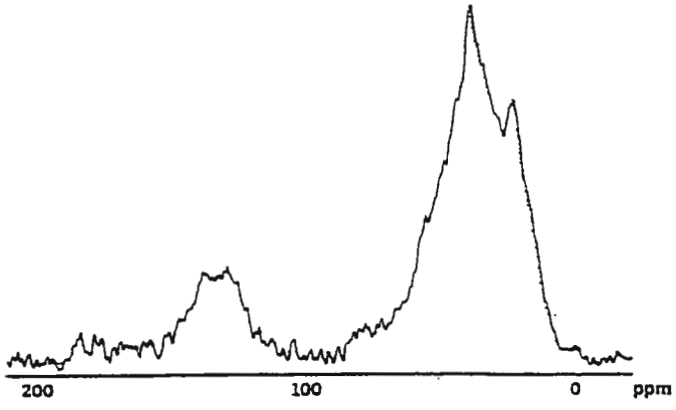

Figure 3

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June 13, 1995. (received 6/22/95)

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

ADEQUATE INADEQUATES

Dear Dr. Shapiro,

The NMR group at Massey University, under the direction of Prof. Paul Callaghan, is interested is taking out a subscription to The NMR Newsletter. Please accept this letter as our first contribution. Please put the account in Paul Callaghan's name.

I have recently joined the group as a postdoctoral researcher, having fled Swinburne University in Melbourne, Australia, an institution that saw fit to dispose of its only superconducting NMR. In the dying days of the Swinburne NMR centre , having been deserted by the two able spectroscopists, I was left in control of the instrument as I wrote my thesis. With the resulting abundant spectrometer time, I pursued that popular, but often impossible, experiment, the ^{13}C-^{13}C INADEQUATE.

The spectrometer was a Varian 200 MHz $^{1}H/^{13}C$ Gemini, equipped only with a 5mm probe. Despite having produced able-looking pulse-sequence code for such a spectrometer, the Gemini applications folks at Palo Alto had assured me that such an experiment would not be possible on our instrument. A combination sensitivity, feasible experiment times, and long pulse width/excitation problems would see to that.

Undeterred, I continued, making an approximately 90% pentanol in d_6-DMSO solution, heavily doped with $Cr(acac)_3$, to aid relaxation delays. The result is shown in Fig. 1. The excellent spectrum shown was acquired in 3 days, however an FT half way through the experiment yielded a spectrum as good as that shown here. Next, I reached for the standard 30% menthol in $CDCl_3$ solution, supplied with the spectrometer. This sample was undoped. The result is shown in Fig. 2. Whilst some doublets are not complete, especially in the methyl region where longer T_1's are predominant, a full assignment can still be made. This spectrum was acquired in 4.5 days.

Whilst obviously not becoming a standard overnight procedure, it was most pleasing to see such results obtained from moderately concentrated solutions over a long weekend.

However, both the spectrometer and I left Swinburne, and I'm now at Massey University, where the focus is very much on novel applications of micro-imaging. We shall bring you news of some developments in this area in later letters.

Yours Sincerely

RWMair

Ross W. Mair
Research Officer

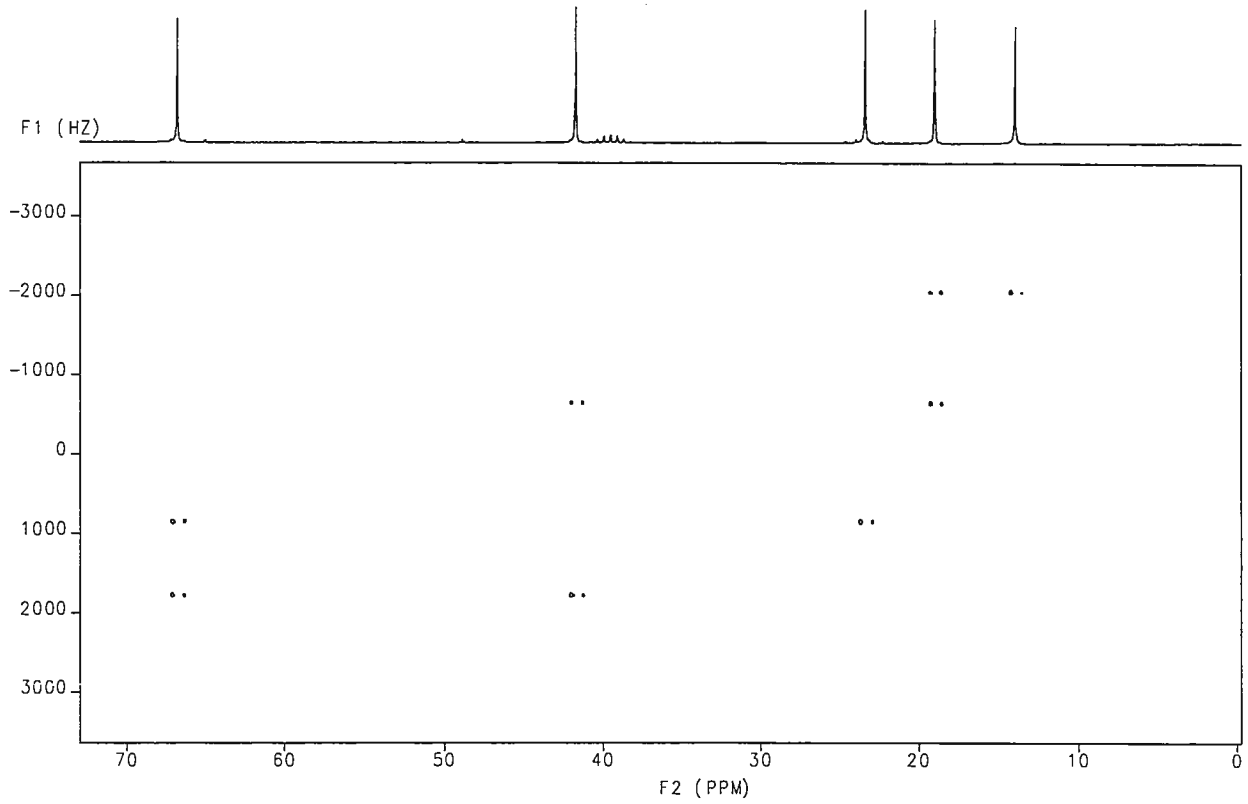

Fig. 1: ^{13}C-^{13}C INADEQUATE spectrum of 90% pentanol in DMSO acquired on a 5mm 200 MHz spectrometer.

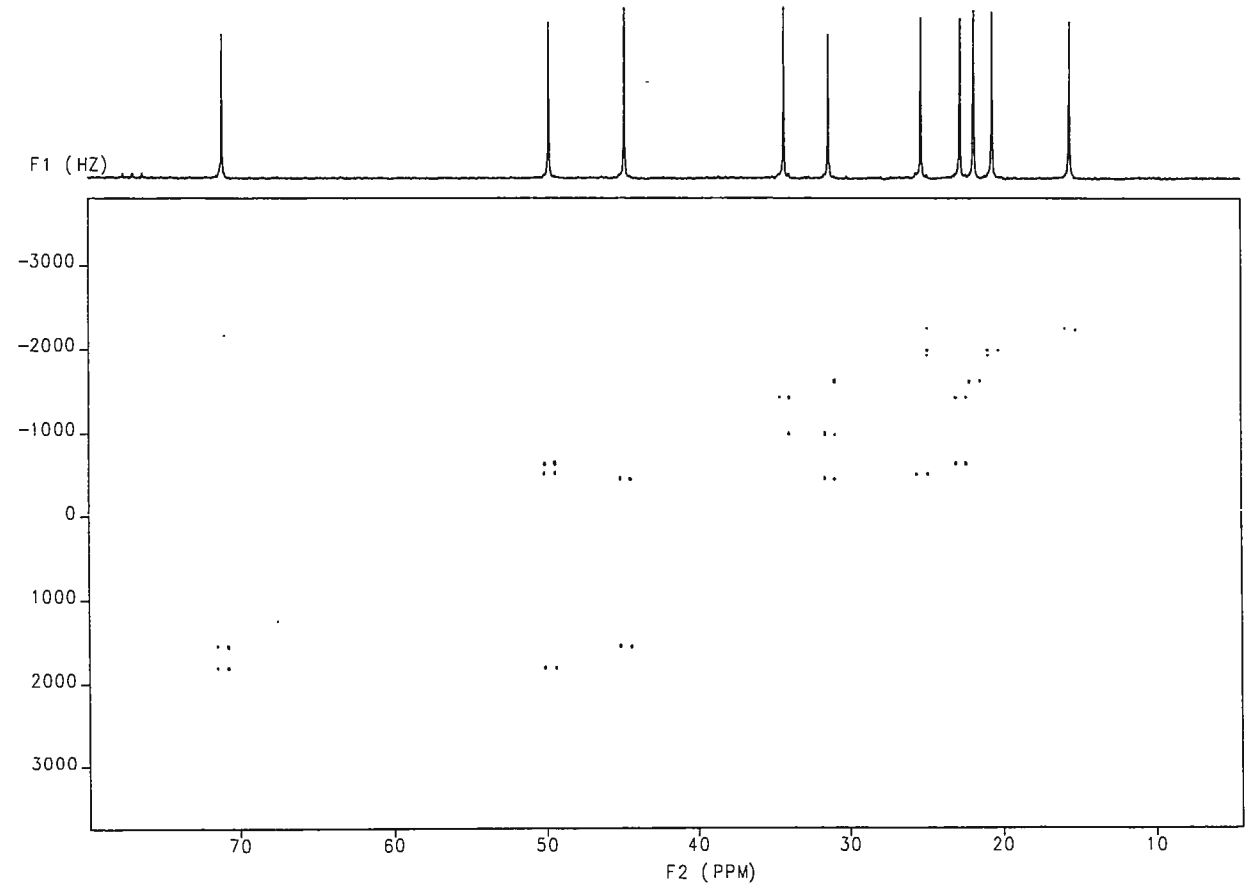

Fig. 2: ^{13}C-^{13}C INADEQUATE spectrum of 30% menthol in $CDCl_3$ acquired on a 5mm 200 MHz spectrometer.

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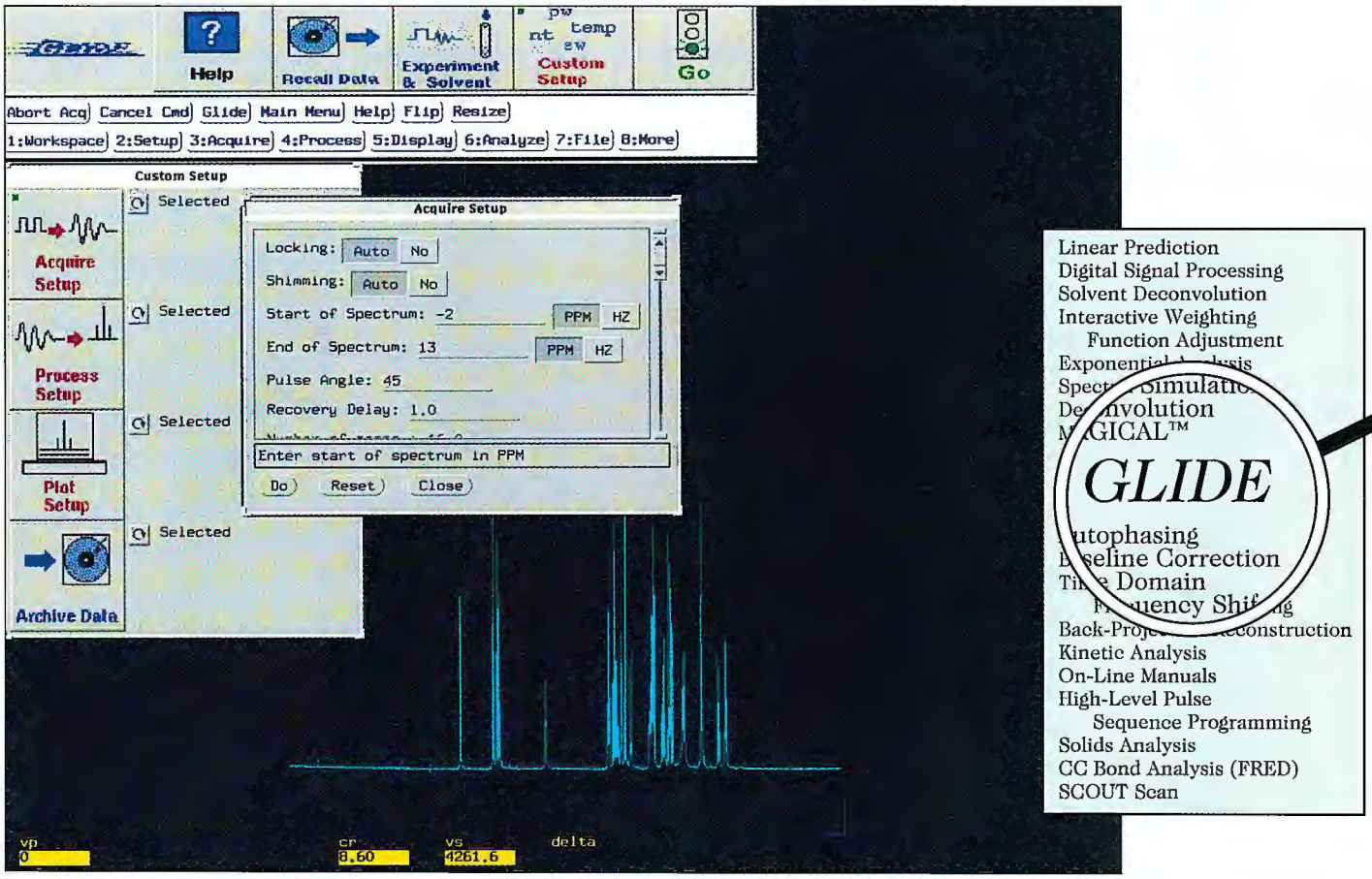

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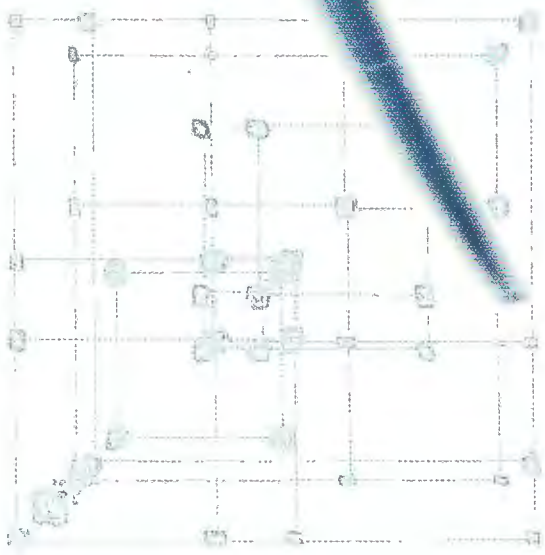

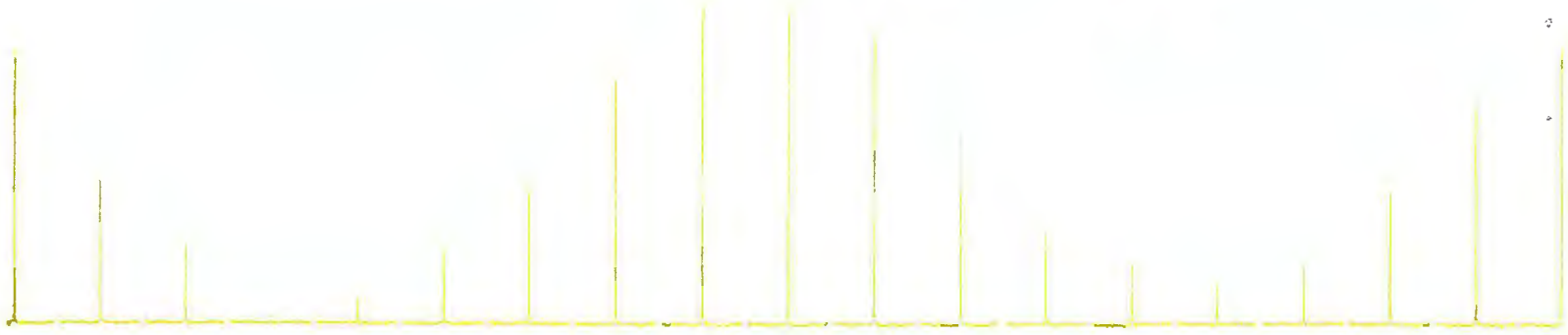

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BHP Research
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(received 7/19/95)

Dr. Bernard Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303 USA

Improved NMR Spectroscopy

Dear Dr. Shapiro,

We recently took delivery of a Unity plus 300 NMR. Since last November we have taken a "double" quantum leap forward in our NMR studies compared to what we were able to achieve with our old WP 200 Bruker spectrometer which had served us well for fifteen years. By the way of example, the improvement in performance was evident in a study of 1,4-cyclohexanedimethanol.

The use of more concentrated samples with the old spectrometer resulted in a carbon spectrum for this compound which exhibited additional splitting of the CH_2-OH and CH carbon resonances. Such splitting was not observed in more dilute solution as routinely used with the new spectrometer (see Figure). Intermolecular H-bonding is believed to be the cause of the resonance splitting observed in the more concentrated solution. With the help of our colleague, Irene Yarovsky, the charge distribution for one conformation has been calculated for two cases: one with, and one without H-bonding. The calculated variations in the charge distribution around the carbons correlate well with the observed chemical shift variations.

Your Sincerely

Dr. M. Iko Burgar, Dr. David Cookson, Dr. Brian Smith

BHP Research Melbourne Laboratories 245-273 Wellington Road Mulgrave Victoria 3170 Australia
PO Box 264 Rosebank MDC Clayton Victoria 3169 Australia Telephone 03 560 7066 Facsimile 03 561 6709

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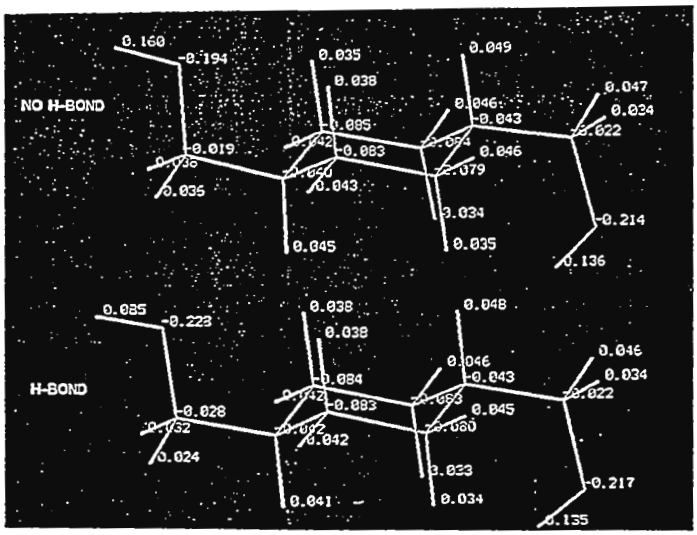
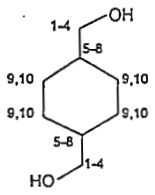
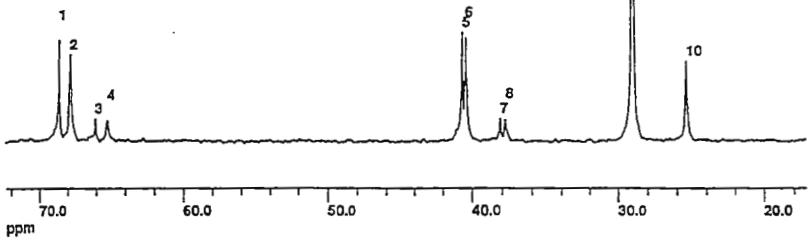


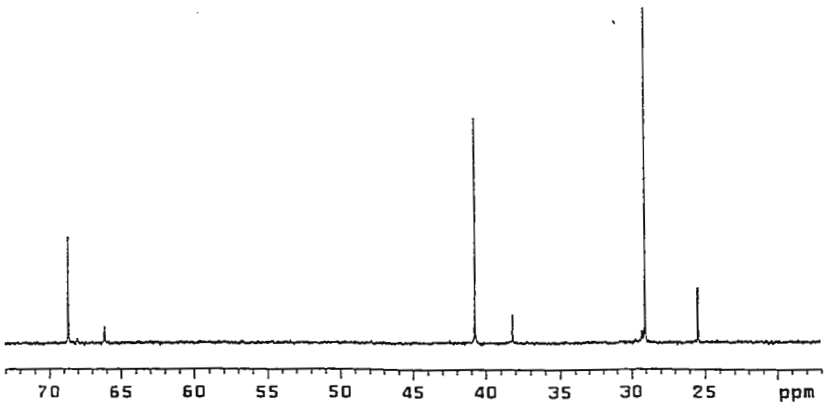
1,4-CHDM in CDCl3

Peak	Integral	ppm	ppm(calc.)
1	0.72	68.52	71.4
2	0.71	67.72	71.4
3	0.27	66.03	71.7
4	0.27	65.22	71.4
5	0.85	40.64	35.5
6	0.84	40.42	35.5
7	0.25	38.10	35.5
8	0.25	37.73	35.5
9	3.18	28.99	27.6
10	0.91	25.35	27.6

1,4-CHDM







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Acorn NMR Inc.

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July 20, 1995

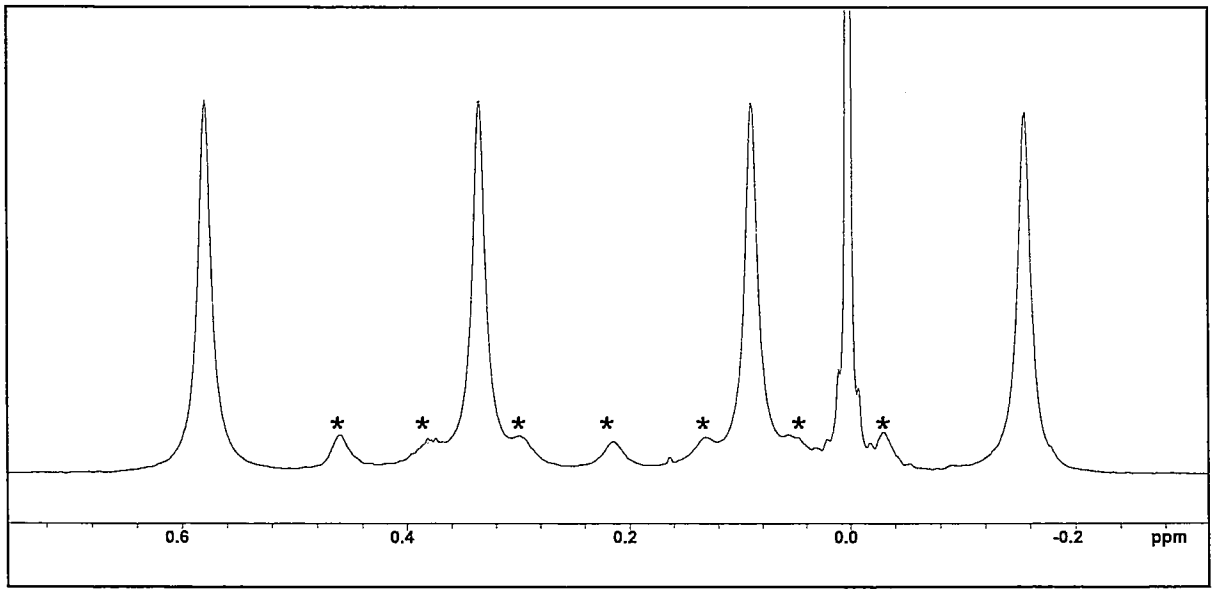
(received 7/21/95)

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

Fun with Spins

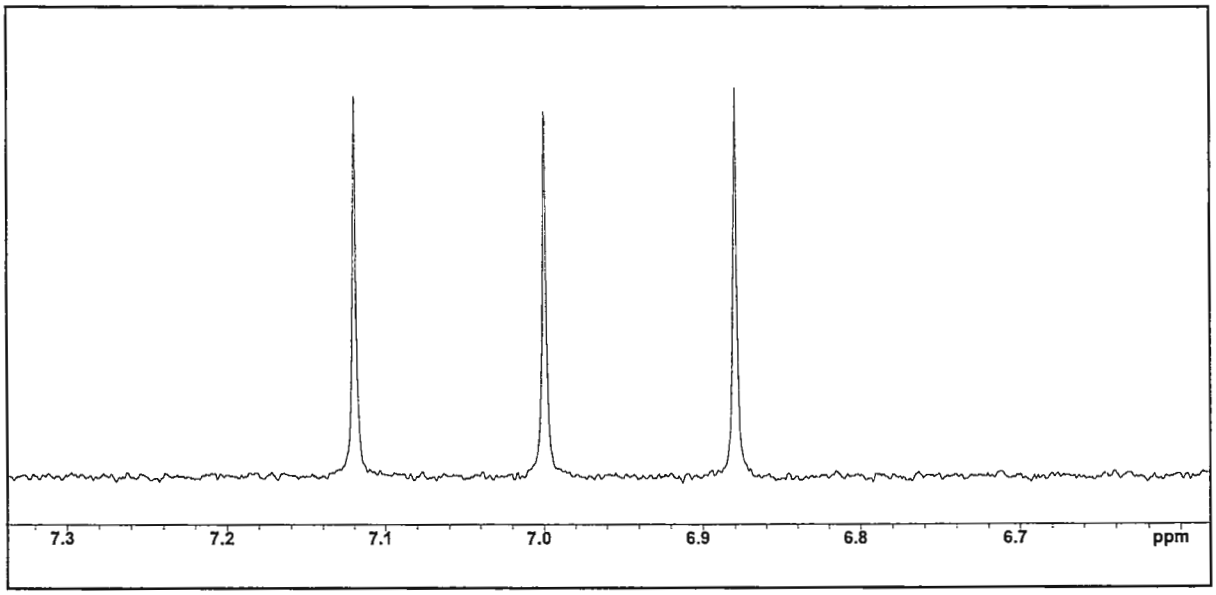
Dear Barry,

We had a fun puzzle recently, and thought it might be worth sharing. The figure below is from an actual proton spectrum of a customer's sample. (The peak at 0 ppm is TMS.) Not only were the shifts unusual, but the regularity of the line spacing seemed suspicious. Consultation with the customer confirmed that this sample was the result of a reduction reaction.
What we are seeing is BH_4^+. Boron exists as 80% ^{11}B (I=3/2) and 20% ^{10}B (I=3). The four larger lines are from ^{11}B (2nI+1 = 4; J = 88 Hz) and the 7 smaller peaks (marked with *) are from ^{10}B (2nI+1 =7; J = 30 Hz). The symmetry of BH_4^+ results in sufficiently narrow lines to make the splittings observable.



It is fairly uncommon to observe this sort of pattern with NMR, but being able to recognize it can be important. Take for example the chemist (true story) who followed a multi-step synthesis of an aromatic heterocycle by ^1H NMR, assuming the 3 equal-intensity peaks he was seeing at 7.25, 7.00, and 6.75 ppm (on an XL-200) were his desired material. However, upon acquisition of a spectrum at 400 MHz, the chemical shifts became 7.12, 7.00, and 6.88 ppm. That is, he had a 1:1:1 triplet at 7.0 ppm with J = 50

Hz, resembling the simulated spectrum shown below. What he had was not an aromatic compound at all, but NH_4^+!



The NH_4^+ spectrum was generated from the NMR "flight simulator" accessory (in development) to our NUTS NMR data processing software. The flight simulator, or virtual spectrometer, is a teaching tool which generates realistic spectra based on "acquisition" parameters set by the user.

Best Regards,

V. W. Miner
Virginia W. Miner

Joyce
Joyce James

Woody
Woodrow W. Conover

Sam Le Chien

Specially designed

Thin Wall NMR Sample Tube

Shigemi's high precision thin wall NMR sample tube has a unique construction. The wall thickness of this particular tube is reduced only around the position of the detection coil. The result of this new invention allows an increase in the sample volume and higher sensitivity without sacrificing its mechanical strength. Therefore, there is no need for special handling during routine usage of our Shigemi NMR tubes.

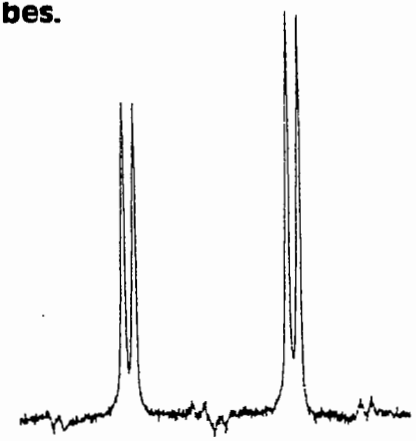
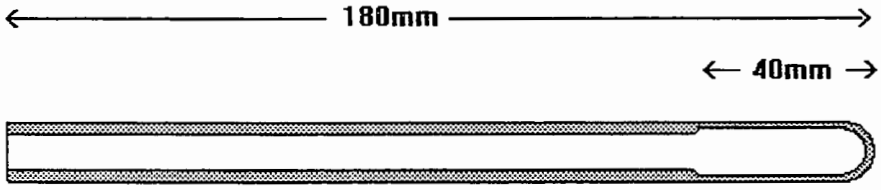
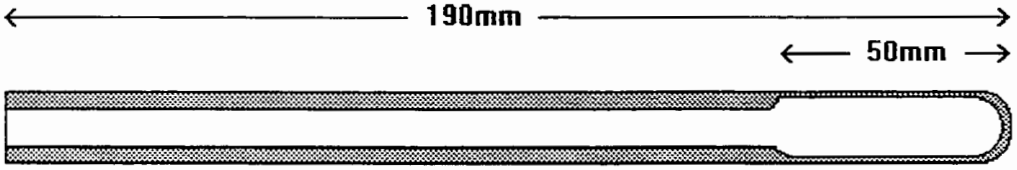


Fig.1a Fig.1b

The spectra of 20mm sucrose in D_2O were obtained with a single scan without apodization prior to Fourier transformation on a Bruker AMX-600 spectrometer at 298 K. By using Shigemi high quality 5mm standard tube (Fig.1a) and the Shigemi highly sensitive thin wall 5mm tube (Fig.1b), the spectra confirms a sensitivity enhancement of about 10%.



PST-001 and PST-002



ST8-001,ST8-002, ST10-001, and ST10-002

O.D. (mm)	Product Number	Wall (mm)	Concentricity/Camber (μ)	OD (mm)	ID (mm)	Price Each 1-99	Price Each 100+
5	PST-001	0.21	20/ 8	4.96 + 0.00 - 0.01	4.54 ± 0.01	$15.00	$13.50
	PST-002	0.21	40/15	4.96 + 0.00 - 0.01	4.54 ± 0.01	$13.00	$12.00
8	ST8-001	0.25	40/ 8	8.00 + 0.00 - 0.01	7.52 ± 0.01	$31.00	$28.00
	ST8-002	0.25	50/15	8.00 + 0.00 - 0.01	7.52 ± 0.01	$27.00	$25.00
10	ST10-001	0.25	40/ 8	9.98 + 0.00 - 0.01	9.52 ± 0.01	$36.00	$32.00
	ST10-002	0.25	50/15	9.98 + 0.00 - 0.01	9.52 ± 0.01	$32.00	$28.00

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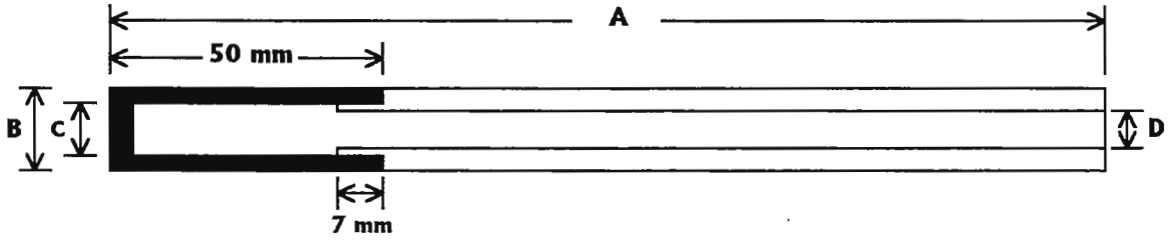

	A Length (mm)	B OD (mm)	C ID (mm)	D OD (mm)	Camber (μ)
Si-005	180	4.965 + 0 − 0.005	4.0 ± 0.1	2.5	± 0.02
Si-010	190	10.0 + 0 − 0.01	9.0 ± 0.1	6.5	± 0.02

Type	Diameter	Price for 5 tubes
Si-005	5 mm	$300.00
Si-010	10 mm	$400.00

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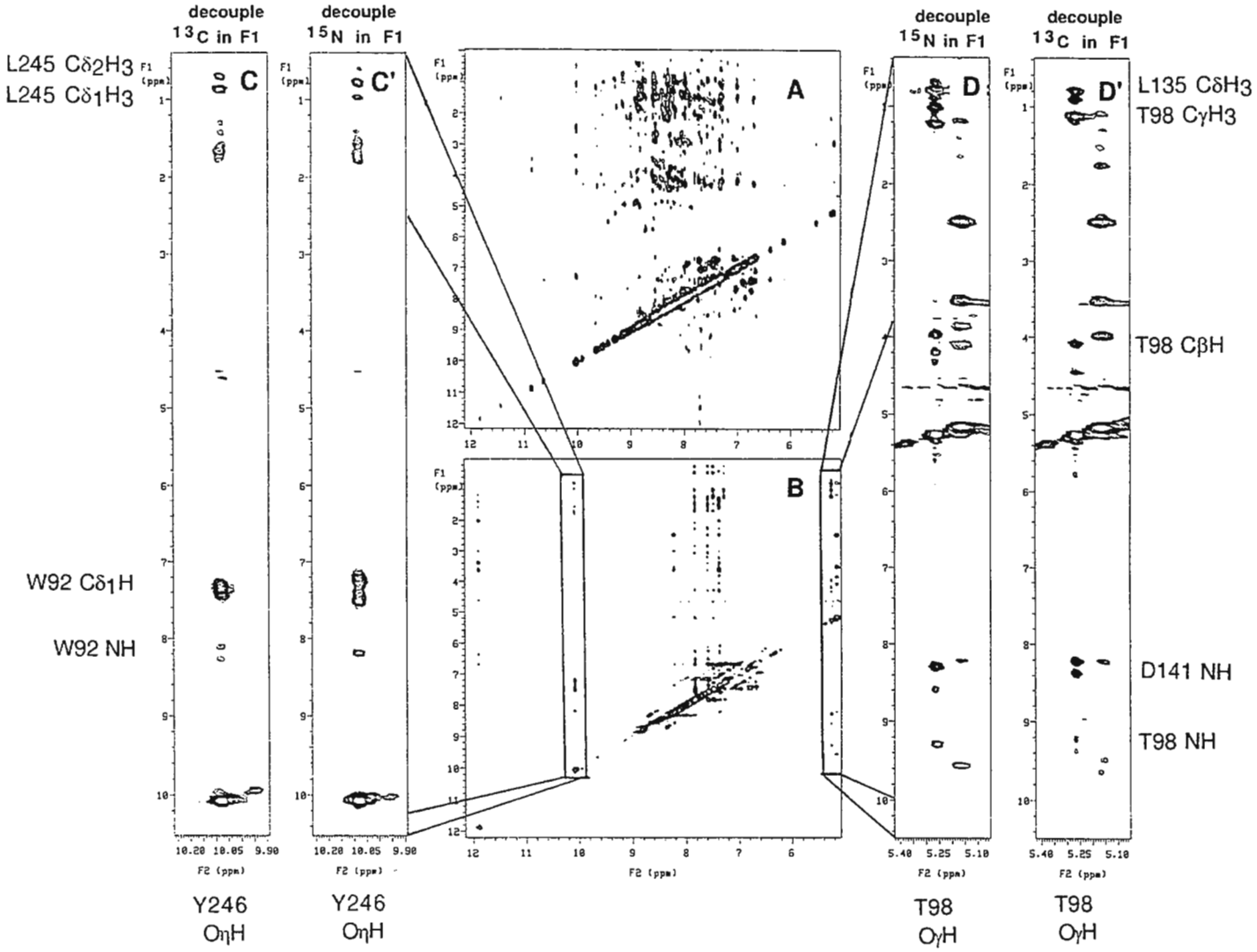
July 21, 1995
(received 7/24/95)

Hoffmann-La Roche

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

Identification of Slowly-Exchanging Hydroxyl Protons in X-Filtered-NOESY Spectra of $^{15}N/^{13}C$-Enriched Proteins

In structural studies of non-enriched molecules in complex with a $^{13}C/^{15}N$-enriched protein, it is convenient to use X-filtered methods[1] to eliminate the ^{13}C- and ^{15}N-attached proton resonances. Removal of the ^{13}C- and ^{15}N-attached protons from a NOESY spectrum will facilitate not only the characterization of ^{14}N- and ^{12}C-attached protons, but also the identification of hydroxyl protons. Here we demonstrate the observation of two slowly-exchanging hydroxyl protons using X-filtered NOESY on a sample of $^{13}C/^{15}N$-enriched stromelysin (173 amino acids) in complex with an unlabeled inhibitor. The experiments presented employ standard presaturation at 40°C and are, therefore, not optimal for observation of hydroxyl protons in intermediate to fast exchange. Figure A shows the ^{15}N-selected NOESY spectrum of the stromelysin-inhibitor complex at 40°C, pH=5.1. In Fig. A all of the resonances along F2 involve ^{15}NHs of stromelysin. Figure B shows the $^{13}C/^{15}N$-filtered NOESY spectrum for the same complex. While the majority of signals in Fig. B involve NOEs to the ^{14}N- and ^{12}C-attached protons of the inhibitor, the expansions shown in Fig. C, C', D, and D' involve slowly-exchanging hydroxyl protons of stromelysin. Figures C and C' involve NOEs between Tyr 246 OηH (10.1 ppm) and other stromelysin protons. Decoupling during F1 was permuted between ^{13}C and ^{15}N, in order to differentiate between signals which originate from ^{13}CHs and those from ^{15}NHs.[2] Figures D and D' involve NOEs between Thr 98 OγH (5.3 ppm) and other stromelysin protons. Clearly the $^{13}C/^{15}N$-filtered NOESY allows great simplification of the spectrum. The utility of these X-filtered experiments extends from the traditional role of characterizing complexes with unlableled partners to that of observing NOEs to slowly exchanging hydroxyl protons, with no pulse-sequence modifications. The side-chain hydroxyl proton resonances of serine, threonine, and tyrosine are typically not observable in spectra acquired with water presaturation. The reduction of hydroxyl-proton signal intensity is due to rapid exchange of the OH proton with solvent. Fast exchange leads to both saturation transfer, and to chemical shift averaging with H_2O protons. Elegant solvent-suppression methods have been devised for observation of ROESY and NOESY correlations involving more rapidly-exchanging hydroxyl protons by eliminating saturation transfer before the t_1 frequency labeling period.[3] Extension of X-filtered methods to include solvent suppression after t1 frequency labeling, should enhance observability for more rapidly-exchanging hydroxyl protons in $^{13}C/^{15}N$-enriched proteins.



1. M. Ikura and A. Bax; *J Am Chem Soc*, **1992**, *114*, 2433-2440.
2. S.D. Emerson; *TAMU News*, **1993**, *422*, 21-22.
3. G. Otting, E.L. Liepinsh, B.T. Farmer II, and K. Wuthrich; *J. Biomol. NMR*, **1991**, *1*, 209-215.

Please credit this contribution to the account of David C. Fry.

Sincerely,

Steven Donald Emerson David C. Fry Joseph H. Pease

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July 6, 1995
(received 7/11/95)

Dr. Bernard Shapiro
The NMR Newsletter
966 Elsinor Ct.
Palo Alto, CA 94303

Noise Figure

Dear Barry:

Following Dr. Dykstra's letter on measuring receiver sensitivity in the July 1995 issue, I thought it worth reminding people of an analogous test using a calibrated noise source. We use this regularly to monitor our spectrometers. It requires a less expensive calibrated noise source which does not need to be pre-equilibrated as apparently the signal generator does. There is a good write-up on this approach to measuring system noise figure in recent editions of the Amateur Radio Handbook, and at least Varian spectrometers have a routine for analyzing the data. We purchased a 6 db noise source from Noise/Com in Paramus, NJ, for about $700 for this purpose, though there are other suppliers of such devices. One note about using the Varian command "noise" to calculate the noise figure. For the calculation of the noise figure, the base mean square noise determined with no excess noise injected is used as a parameter. The value is obtained by the Varian "noise" command applied to data collected with the noise source off. The value displayed is an integer while the rms noise is given as a decimal number. For the proton channel, particularly at 600 MHz, the base noise is a small number, and therefore the mean square noise suffers some roundoff error in being limited to an integer value. More accurate results may be obtained by squaring the rms value manually rather than taking the integer value as given from the output of the noise routine. A sweep width setting of 10000 Hz and an acquisition time of 1 s is used with no RF pulse and the desired receiver gain. Since the noise source covers a broad spectrum, ours goes from 100 MHz to greater than 700 MHz, one can quickly measure noise figures at different frequencies with a minimum of effort.

Sincerely yours,

David Live

Universität Bern
Institut für organische Chemie

CH - 3012 Bern, Freiestrasse 3
Tel. 031 / 631 43 11 Fax 031 / 631 80 57

Dr. Bernard Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 943030, USA

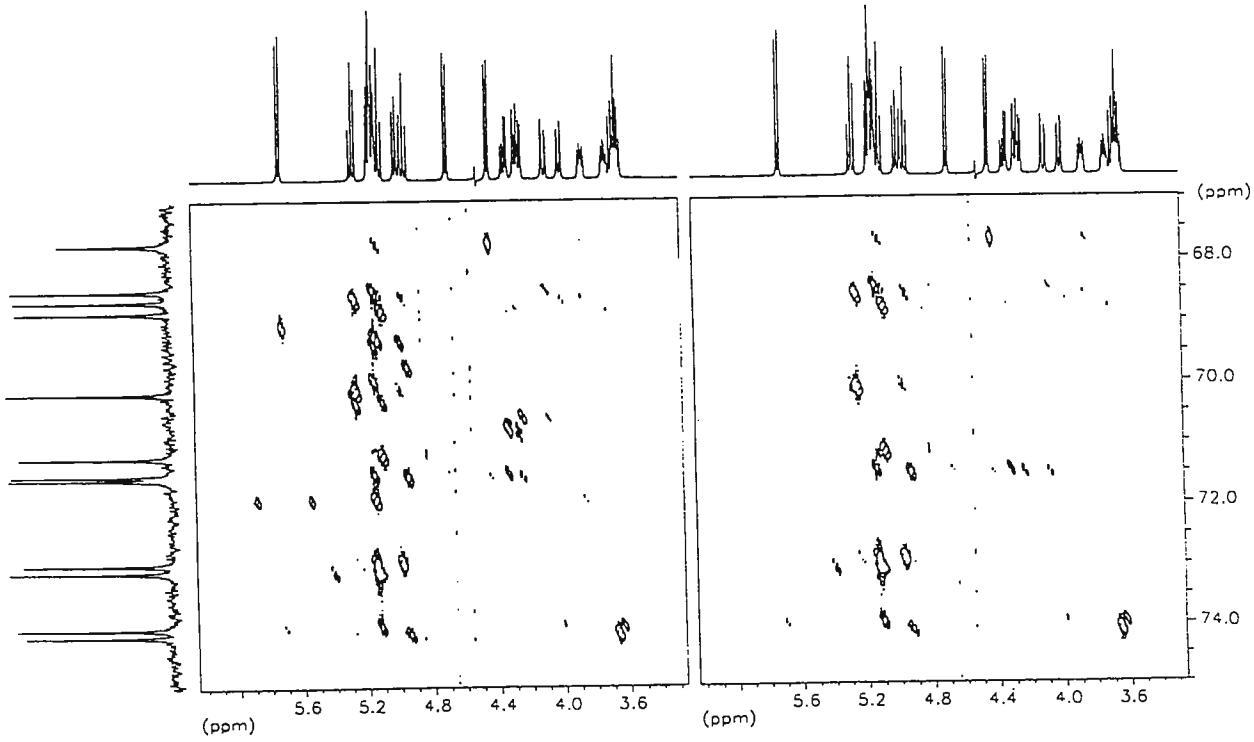
June 21st 1995
(received 6/26/95)

SPECTRAL FILTERS FOR THE $^{13}C/^{1}H$ LONG-RANGE SHIFT CORRELATION EXPERIMENT

Dear Dr. Shapiro

heteronuclear long-range spin-spin interactions are most popular to establish molecular structures of organic compounds. We have applied the standard BRUKER 2D pulseprogram INV4GSLRLP on our new DRX 500 spectrometer using the Gradient unit BGPA10.

Whereas the recently introduced digital filtering technique allows to select a spectral window in F2 properly rejecting any signal from outside the chosen window, no spectral filtering is possible with the standard experiment in the second frequency domain F1. To circumvent folding-over problems in this domain we slightly modified the basic pulseprogram by replacing the second and third 90 degree 13C hard pulse in the pulse sequence by there selective analogues (90 degree soft tophat pulse). Their length, offset frequency and shape determine the profile of the selected F1 window. The two spectra of a peracetylated trisaccharide were acquired with the basic (A) and the modified (B) sequence. A F1 spectral window with part of the ring carbon resonances was selected. F1 folding-over artifacts as observed in spectrum A are completly absent in spectrum B thereby fascilitating spectral analysis. The same S/N ratios were detected for both spectra.



Yours sincerely

Dr. P. Bigler
e-mail: bigler@ioc.unibe.ch

Q-SWITCHING™

Bruker has developed a series of probes with switchable quality factor, called Q-Switch™ probes. These probes enable rapid switching (<2 μs) between a high and low Q factor of the proton channel.

The Q-switch probe offers a solution to the mutual coupling between a strong NMR signal and the radio frequency coil of the probe known as radiation damping. Radiation damping adversely affects samples with intense resonance lines. Since it increases for probes with higher quality factor "Q", reducing the Q minimizes this effect.

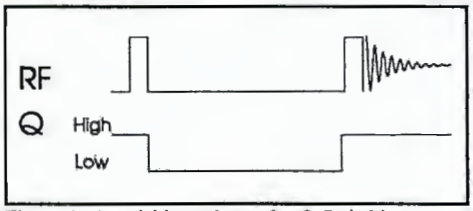


Figure 1: Acquisition scheme for Q-Switching during free-precession

A traditional approach to reduce radiation damping has been to lower the Q of the probe by detuning the probe circuit. However, this results in a loss of sensitivity since the induced voltage in the coil is also proportional to Q. Other approaches to reducing radiation damping have included the use of spin lock pulses or magnetic field gradients. *Now with the Bruker Q-Switch probe a high Q factor can be used during rf pulses and data acquisition for maximum efficiency and sensitivity, while a low Q mode can be used for suppression of radiation damping during free precession delays in the NMR sequence.*

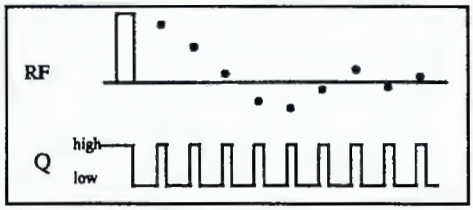


Figure 2: Acquisition scheme for data sampling with Q-Switching

With the Q-Switch probes, rapid switching of the Q (<2 μsec) allows suppression of radiation damping without sacrificing sensitivity. Typically, Q-Switching occurs *between* the excitation pulse and data acquisition (Figure 1). But its benefits can also be realized by applying Q-switching *during* the actual data acquisition (Figure 2), which is now possible due to the rapid switching ability of this accessory.

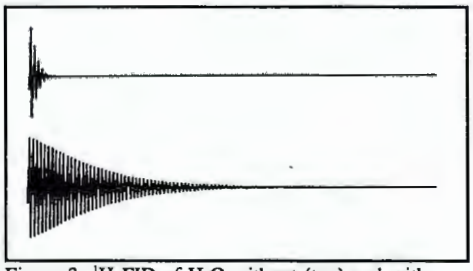


Figure 3: ^1H FID of H_2O without (top) and with (bottom) Q-Switching during acquisition

The benefits of Q-switching are evident in the observation of H_2O (Figure 3). The proton free induction decay for water is significantly increased by reducing the Q during the acquisition. The resultant spectra (Figure 4) clearly shows a narrower linewidth for the water resonance by the reduction of radiation damping.

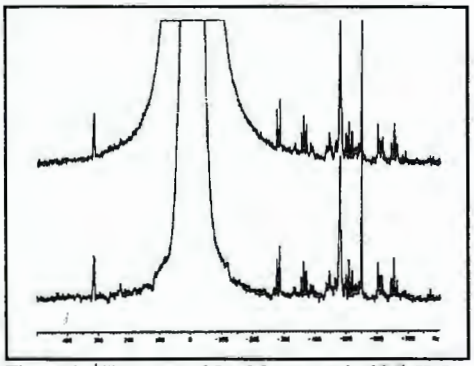
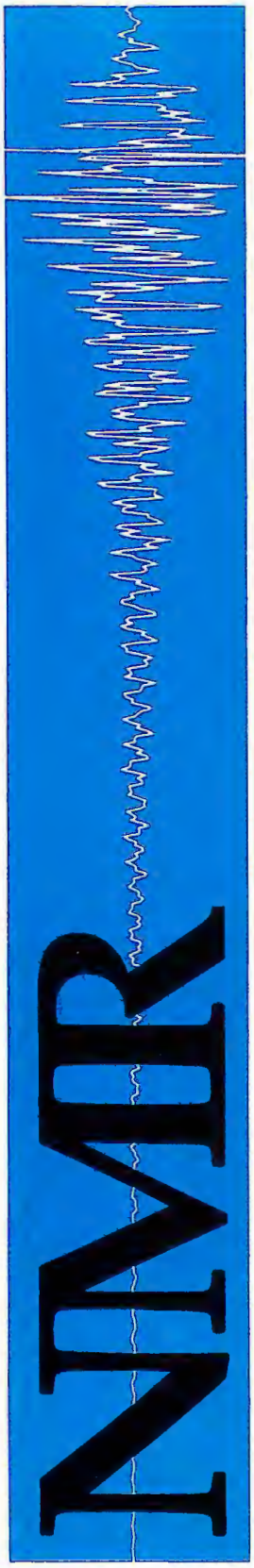


Figure 4: ^1H spectra of 2 mM sucrose in 90% H_2O without (top) and with (bottom) Q-Switching during acquisition



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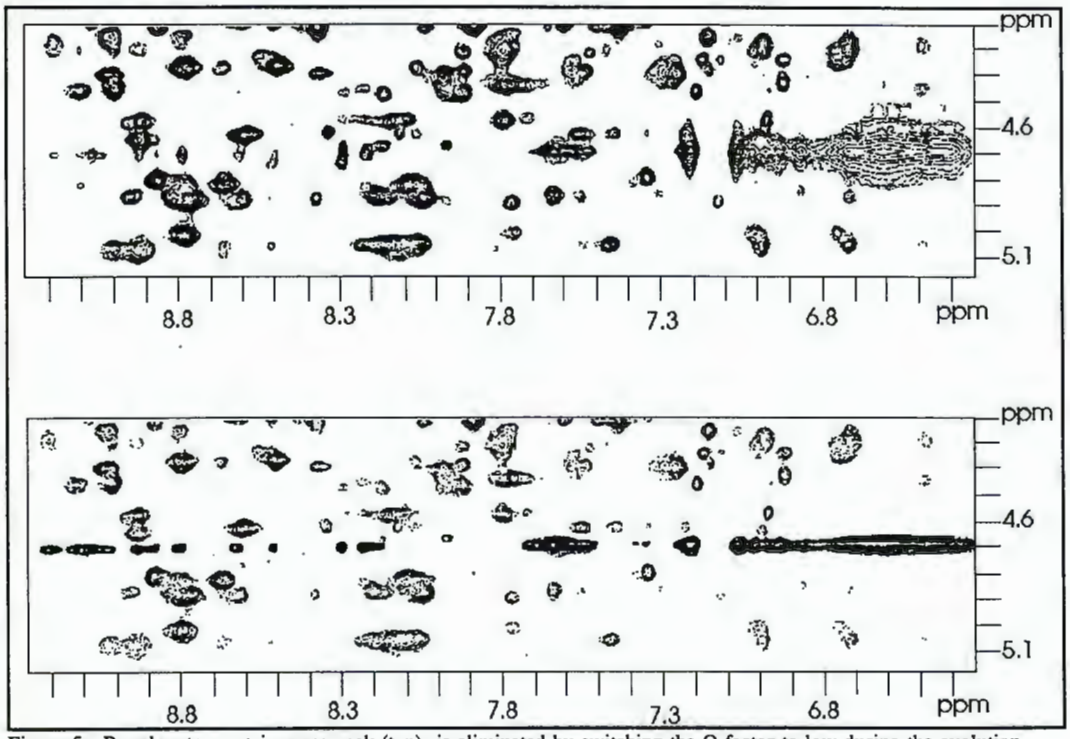

Figure 5: Broad water-protein cross peak (top), is eliminated by switching the Q factor to low during the evolution time t_1 (bottom)

The use of a Q-Switch is particularly attractive for the observation of intermolecular cross peaks between proteins and water, where experiments recorded at high Q result in substantial line-broadening of the water-protein cross peaks. The extent of line-broadening caused by radiation damping is illustrated by a NOESY experiment on an aqueous solution of lysozyme (Figure 5). Switching the Q factor low during the evolution time efficiently eliminates radiation damping. The resulting narrowed resonances in f_1 allows the observation of cross peaks between the water signal (4.7 ppm) and the lysozyme NH and aromatic CH protons.

Q-Switch™ probes (5 mm inverse with or without gradients) are available for 500, 600 and 750 MHz UNIX based Bruker spectrometers. Contact your local Bruker representative for more information.

references:
1. C.G. Anklin, M. Rindlisbacher, G. Otting, F.H. Laukien, *J.Magn.Reson. B* **106**, 199 (1995)
2. W.E. Maas, F.H. Laukien, D.G. Cory, *J.Magn.Reson. A* **113**, 274 (1995)
G. Otting, E. Liepinsh, *J.Magn.Reson. B* **107**, 192 (1995)

UNIVERSITY OF VIRGINIA
DEPARTMENT OF CHEMISTRY
McCORMICK ROAD
CHARLOTTESVILLE, VIRGINIA 22901

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

July 19, 1995
(received 7/20/95)

Upgrade of NT-360 and GN-300 with Tecmag Acquisition Systems

Dear Dr. Shapiro:

One and a half years ago we replaced the computer and pulse programmer in our Nicolet NT-360 with a Tecmag Libra Acquisition system and Macintosh Quadra 800 computer. The installation took two days and we encountered no problems; the only problem we have had since the installation was a Quadra disk crash. Two months ago we did a similar upgrade of our General Electric GN-300; we added a Tecmag Scorpio Acquisition system and a Power Macintosh 8100/80. Again the initial installation time was short but unfortunately the deuterium lock and the tune routine did not function properly. After phone communication failed to provide solutions, Tom Egan of Tecmag visited us and quickly solved our problems. There are timing loops in the MacNMR software which are dependent on the Mac CPU clock rate and the software had to be modified to function properly with our Mac.

Our GN-300 is often used over 20 hours a day by about 100 synthetic chemists. Since the upgrade we have successfully performed all the experiments commonly used in the past including homonuclear proton decoupling, proton 1D NOE, DEPT, COSY, and both single and multiple bond heteronuclear chemical shift correlation. Most users had little trouble learning the MacNMR software. Several labs now have MacNMR installed on their lab Macs and use it routinely to process and analyze their data. Data transfer via ethernet between Macs is quick and easy. We have set up a World Wide Web home page for our NMR lab that currently contains instructions for using our NT/Tecmag 360 and GN/Tecmag 300 to acquire and process 1D spectra. Instructions for other procedures and experiments will be added in the future. The home page URL is http://ernst.chem.virginia.edu.

Immediately following the installation of the Tecmag Scorpio unit we were a bit disappointed with the problems mentioned above but we found Tecmag to be extremely helpful. Our experience indicates that the Scorpio really is an upgrade for the following reasons: replacement of old, expensive-to-fix hardware with faster inexpensive-to-fix hardware, ease of data transfer between computers and remote processing of data with the same software used to acquire the data, MacNMR and AppleScript replace and expand previous software capabilities, and finally, Tecmag provides excellent support.

Jeff Ellena

Jeff Ellena jfe@virginia.edu 804-924-3163

Lehigh University

Department of Chemistry
telephone (610) 758-3470
fax (610) 758-3461

Seeley G. Mudd Building
Lehigh University
6 East Packer Avenue
Bethlehem, Pennsylvania 18015-3172

July 20, 1995

(received 7/24/95)

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

PROBE PROTECTION CIRCUIT; INTRODUCTION

Dear Barry,

The solid-state NMR spectrometer at Lehigh University is based on a GN-300, with high power amplifiers from Amplifier Research and ENI and Doty Scientific probes. The GN-300 software was designed to accomodate both solution and solid-state measurements, so data acquisition times in excess of several seconds are possible. Unfortunately, some NMR users (including recalcitrant faculty members!) sometimes neglect to check ALL data acquisition parameters, leading to long pulses at very high power. For example, proton decoupling in solid-state NMR is usually performed by CW high power (i.e. 100-400 Watts) CW irradiation. If the acquisition time is accidently set to 4 seconds instead of a more normal 50 milliseconds, all sorts of bad things start happening in the probe.

Dr. Tom Neiss (now at Hercules) helped design and implement a simple timed protection circuit to limit high power pulse lengths. The proton and observe channels each contain a separate circuit, consisting of a retriggerable monostable multivibrator (74LS122J) which supplies a logic pulse to a low power single pole single throw radiofrequency switch (Daico 100C1041F). The output of the multivibrator is routed through a double input NAND gate (LS7400) to supply a clean signal. The rf switch is placed BEFORE each amplifier on the low power input (rf levels approximately 1 mW). The switch isolation of > 70 dB assures quite low power levels at the probe if the switch is closed.

The monostable multivibrator is configured with a time constant determined by selecting one of two resistors (270 kOhm and 1 MOhm, in series with a 1 microfarad capacitor), corresponding to 108 and 400 milliseconds, respectively. The rising edge of a logic pulse from the pulse programmer is used to trigger each circuit, which then allows pulses of 108 (or 400) milliseconds to reach the probe. Each pulse program has an interval specifically for setting this logic line. Because the circuits are retriggerable, it is possible to repeat this trigger step later in the program if a long delay between rf pulses is required, as in some T_1 measurements. This circuit works quite reliably and has saved probe damage on a minimum of four occasions so far. Extensive details are available on request.

Some changes have recently occurred at Lehigh. Bill officially retired on June 30, but has been appointed Adjunct Professor of Chemistry. We are glad that he is remaining with us. Dr. Dah-Jyuu Wang has been hired as Director of Chemical Instrumentation. D. J. spent several years with Professor Jack Leigh at the University of Pennsylvania following his doctoral work with Professor Springer at SUNY Stony Brook. In addition to the four NMR spectrometers (AM-500, AMX-360 with microimaging, GN-300, and FX-90Q), D. J. has responsibility for three mass specs, two FT-IRs, and many smaller instruments. Jim is still here.

With kindest regards,

James E. Roberts

William Anderson

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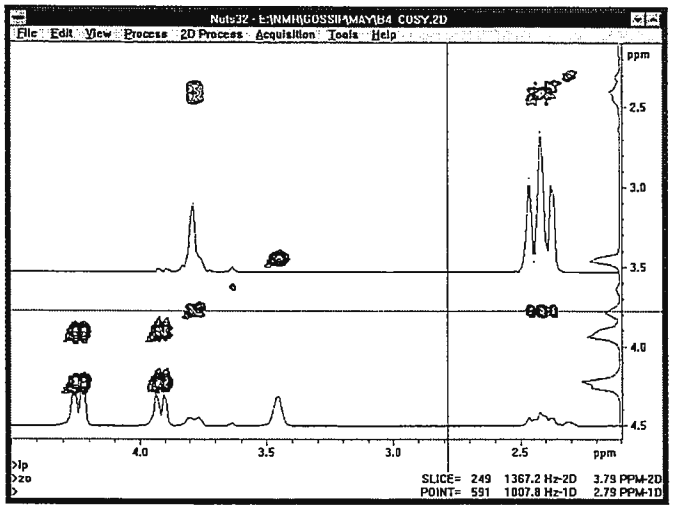

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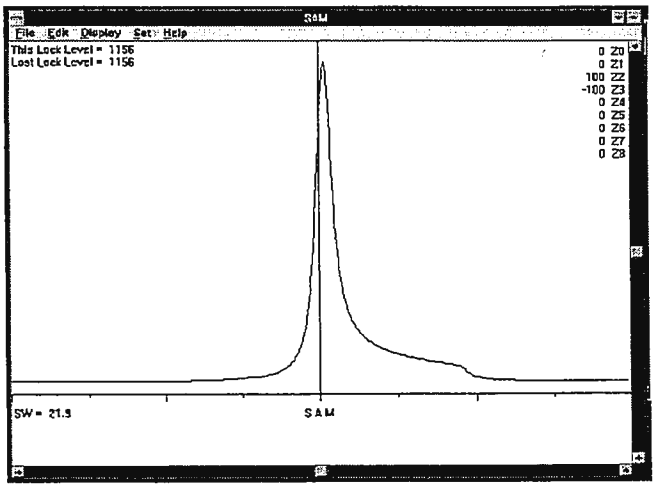

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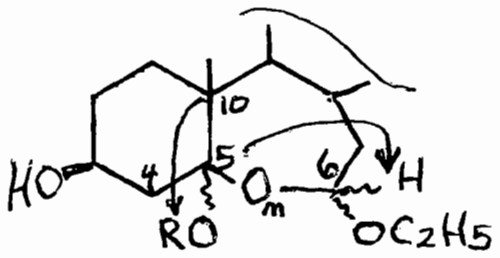
13 July 1995
(received 7/17/95)

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

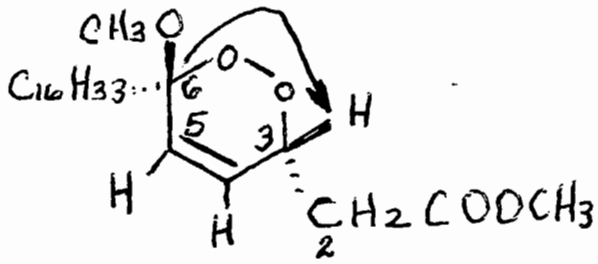
HMBC $^4J_{CH}$ Through Peroxide Bonds?

Dear Barry:

In response to your green ultimatum we have the following curious result to report. In attempting to select between epidioxide-alcohol structure **1** and ether-hydroperoxide structure **2** of a cholesterol ozonide formed in ethanol we considered that heteronuclear correlation spectra should include readily distinguished $^3J_{CH}$ correlations C-10/O<u>H</u> and/or C-4/O<u>H</u> for **1** or $^3J_{CH}$ C-5/H-6 for **2**. An anticipated correlation of C-5/δ_H 10 (of O<u>H</u> or OO<u>H</u>) would be ambiguous, being $^2J_{CH}$ for **1** but $^3J_{CH}$ for **2**.



1 R = H, n = 2
2 R = OH, n = 1



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Recorded ^1H, ^{13}C, COSY, and HETCOR spectra at 6.35 T were uninstructive in this matter, but HMBC data at 14.1 T (preparation time τ = 125 ms) revealed two perplexing correlations: a stronger C-5/ H-6 (thus $^4J_{CH}$ for **1** or $^3J_{CH}$ for **2**) but also a weaker C-10/δ_H 10 (O<u>H</u> or OO<u>H</u>) (thus $^3J_{CH}$ for **1** or $^4J_{CH}$ for **2**). Clearly a four-bond correlation is indicated in either case.

As either formulation **1** or **2** has the requisite four-bond connectivity through the peroxide bond, to our dismay a choice of structure was not possible. Moreover, we have not discovered a precedent for four-bond heteronuclear correlations involving the peroxide bond in such systems. In order to test the matter with the cyclic peroxide chondrillin (**3**) we repeated the HMBC experiment at 14.1 T and τ = 125 ms initially used.

Both ^{13}C (at 9.4 T) and ^1H (at 20.0 T) data as well as COSY (at 9.4 T) and HMQC/HMBC data (at 14.1 T) support in detail the previously assigned structure of chondrillin (analysis of the $C_{16}H_{33}$ moiety not attempted). As seen in the HMBC slice (Fig.1) there is a weak correlation of C-6 (δ_C 100.48) with H-3 (δ_H 4.793), a four-

bond correlation. Also observed in chondrillin HMBC spectra were $^4J_{CH}$ correlations for C-2/H-5 and ester OCH_3/H-2. Such correlations are known in sp^3 and sp^2 systems, but our present observations in spectra of the sterol ozonide and of chondrillin demonstrate that $^4J_{CH}$ correlations may also involve the peroxide bond.

As a lark, we note that our present study has been conducted at four fields with instruments now at our University: 6.35 T (270 MHz) for initial HETCOR data, 9.4 T (400/100 MHz) for COSY, ^{13}C, and HMBC data, 14.1 T (600/150 MHz) for HMQC and HMBC data, and 20.0 T (750 MHz) for ^1H spectra. The increased sensitivity available with the 14.1 T spectrometer permits signal observations at the long τ = 125 ms despite considerable signal loss to T_2 relaxation (Fig.2).

Yours truly,

Edward L. Ezell Elliott Gozansky Leland L. Smith

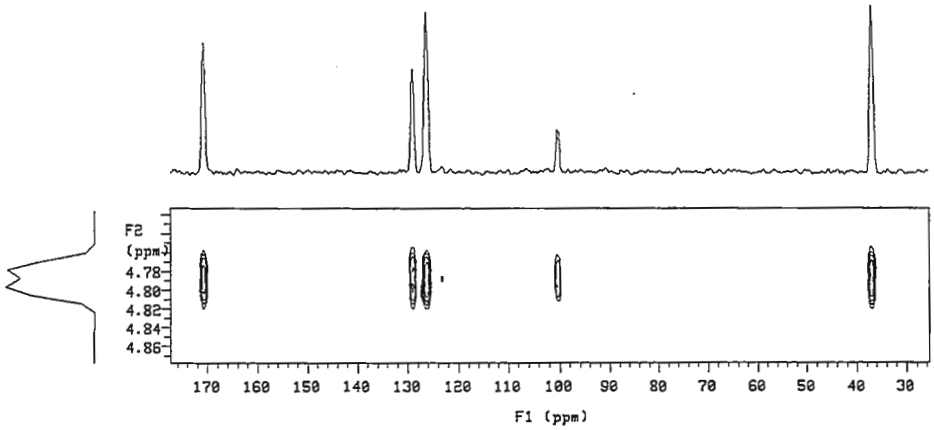

Fig.1. Four-bond HMBC correlation of C-6/H-3 (δ_C 100.48, δ_H 4.793) of chondrillin (3).

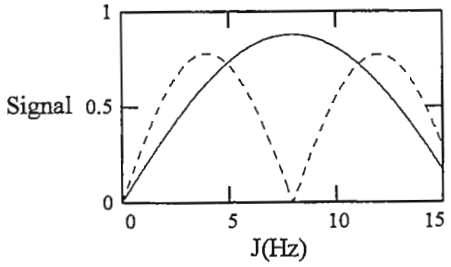

Fig.2. Signal response for $^nJ_{CH}$ calculated from the equation:

$$\text{Signal} = | \cos(\pi\tau_1)\cdot\sin(\pi\tau_2)\cdot\exp(-\tau_2/T_2) |$$

where τ_1 = 3.6 ms ($^1J_{CH}$ optimized for 139 Hz coupling), with two τ_2 values 62.5 ms (——) and 125 ms (- - -) and assumed T_2 = 500 ms.

THE UPJOHN COMPANY
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UPJOHN LABORATORIES
Brian J. Stockman Ph.D.
Research Scientist
Structural, Analytical &
Medicinal Chemistry
7255-209-007
Tel (616) 385-7582
Fax (616) 385-7522
E-mail bjstockm@upj.com

July 21, 1995

(received 7/21/95)

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

NMR relaxation studies on an increasingly paramagnetic protein sample

Dear Dr. Shapiro:

We have recently begun NMR relaxation studies on a variety of proteins in order to obtain direct information about molecular dynamics in solution. We have carried out the typical ^{15}N NOE, T_1 and T_2 measurements to probe protein backbone motions of individual residues. One of the proteins that we have characterized is ^{15}N-enriched *Desulfovibrio vulgaris* flavodoxin (supplied by Dr. Richard P. Swenson at Ohio State University). This electron transfer protein contains 147 amino acid residues and one non-covalently bound flavin mononucleotide cofactor. The flavin cofactor has three oxidation states: oxidized, semiquinone (one-electron reduced) and hydroquinone (two-electron reduced). Our studies have involved the oxidized protein--or so we thought!

The ^{1}H-^{15}N HSQC spectrum of flavodoxin is quite impressive (1). Resonance dispersion is excellent and the linewidths, even at room temperature, are sharp for a protein of this size. Consequently, ^{15}N NOE, T_1 and T_2 values can be extracted for almost all residues with excellent precision. However, T_1 and T_2 values determined for several of the residues gave particularly poor fits for exponential decays. For example, T_1 values for 11 residues (E16, I22, T59, E66, Q68, G94, D95, S96, L112, G123 and G128) and for the flavin $^{1}H^{N3}$ group had errors more than one standard deviation greater than the mean error (the average standard error in T_1 for 127 backbone amide resonances was 3.34%). Most of the residues that give poor fits to the data are among those that comprise the flavin binding site. This is shown in Figure 1, where the positions of these 11 amide groups with respect to the flavin cofactor are indicated in the Molscript (2) rendition of flavodoxin (the amide groups of I22 and L112 are behind the secondary structure representations). The amide group of T59, located extremely close to the flavin isoalloxazine ring, had the poorest fit (22.6% error).

Acquisition of the series of T_1 experiments was ordered by increasing relaxation delay time, starting with 20 ms and ending with 801 ms. During the time required to collect the entire series (roughly 3 days), the sample turned from its normal bright yellow color to a gray-yellow color. This is something that we have observed with numerous flavodoxin samples, and is caused by reduction of the flavin cofactor to the semiquinone state in a portion of the protein present (we estimate 5% of the total protein after 3 days). Since the semiquinone state is paramagnetic, peak intensities are reduced for backbone amide groups in the vicinity of the cofactor. Since the formation of semiquinone happens concomitantly with increasing relaxation delay, two factors contribute to the decreasing resonance intensity for a subset of the correlations, and the result is a poor fit to the exponential decay for these residues.

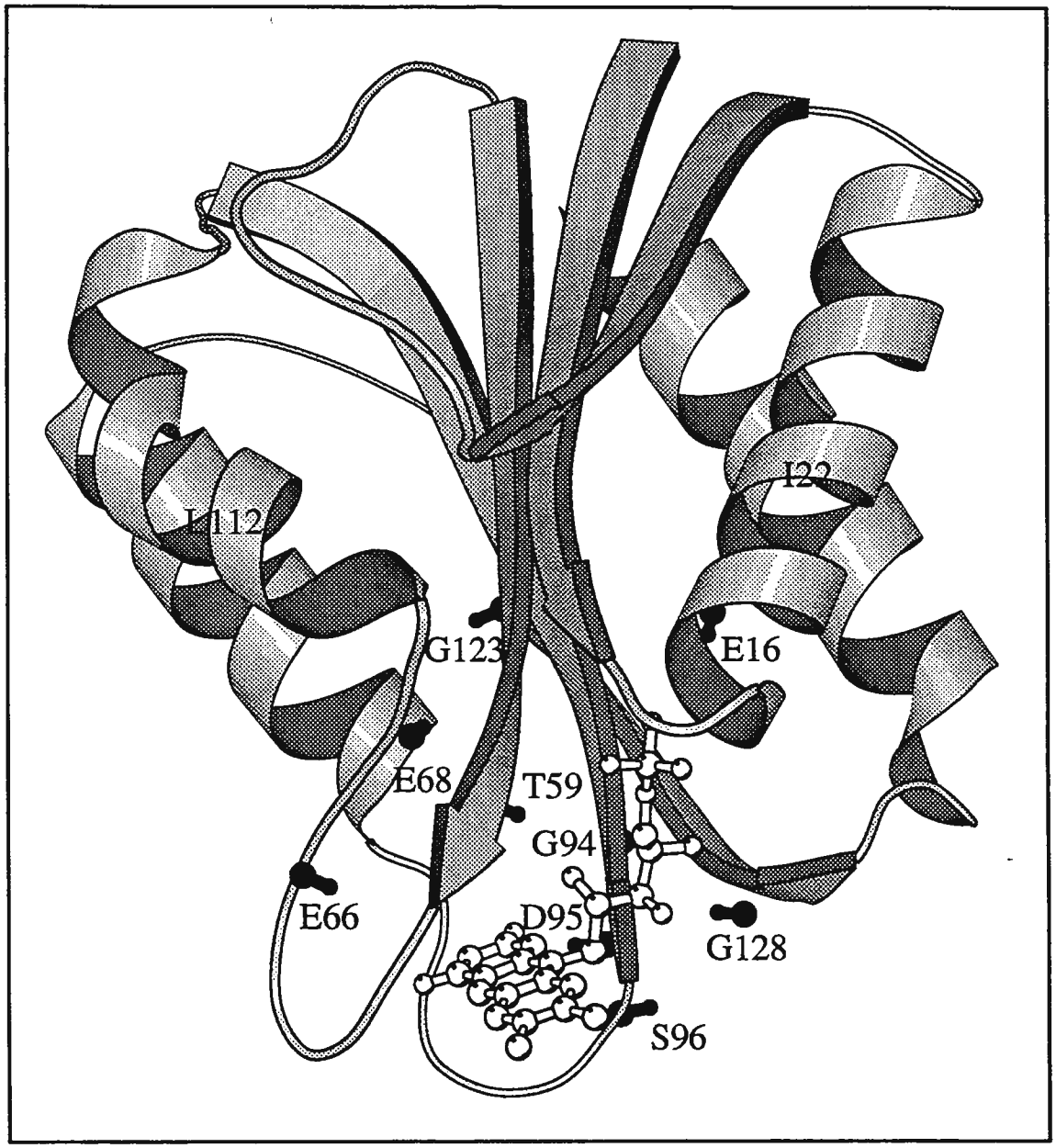

Figure 1. Molscript (2) rendition of flavodoxin. The flavin cofactor and the NH groups of the residues with poor fits are shown in open and filled ball-and-stick format, respectively.

It is apparent from Figure 1 that not all residues near the cofactor are affected, while some residues distal from the cofactor are affected. Attempts to rationalize this data with delocalization of the unpaired electron in the flavin ring system, and/or with protein-protein interactions, are in progress.

1. Stockman, B. J. et al., *J. Biomol. NMR 3*, 133-149 (1993).
2. Kraulis, P., *J. Appl. Crystallogr. 24*, 946-950 (1991).

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The **NMR Newsletter**
Bernard L. Shapiro
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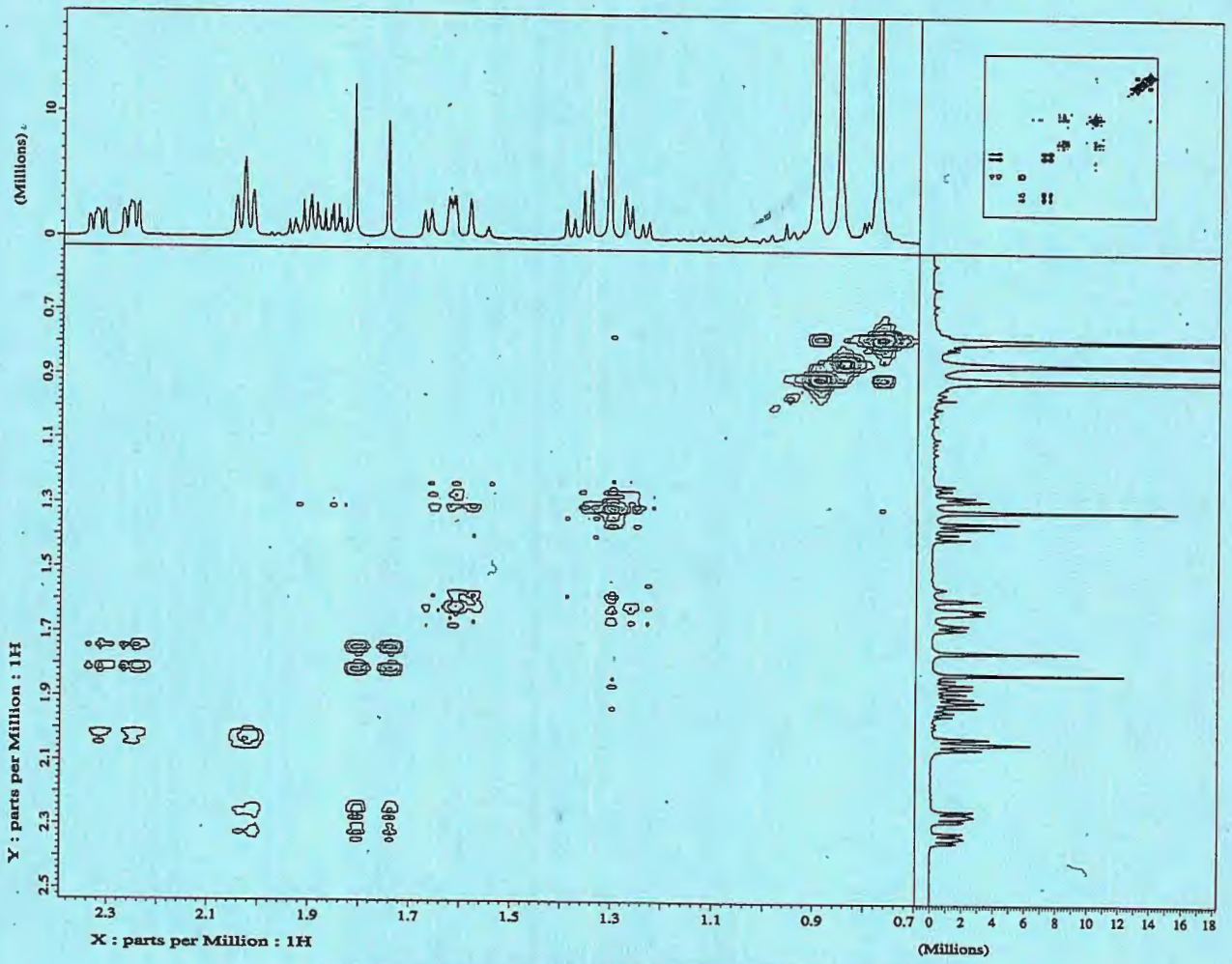

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