THE
NMR
NEWSLETTER

No. 449

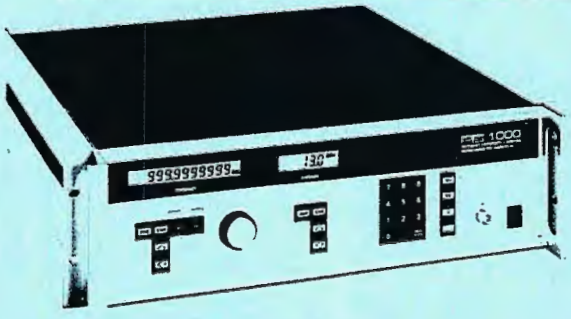
February 1996

PTS
FREQUENCY SYNTHESIZERS

AGILE FREQUENCY GENERATORS-DIRECT SYNTHESIZERS

Accurate, stable frequencies on command, fast switching. For NMR, SATCOM, Surveillance, ATE, Laser, Fluorescence, Clock Sources. Low noise/jitter. Sources adapting to your needs with options. High demonstrated reliability. 20,000+ delivered in 20 years.

	Frequency Range	Resolution	Switching Time[1]	Phase-Continuous Switching[2]	Rack-Mount Cabinet Dim.[3]	Remote-Control Interface	Price Example[4]
PTS 040	.1-40 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$5,330.00 (1 Hz resol., OCXO freq. std.)
PTS 120	90-120 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$5,330.00 (1 Hz resol., OCXO freq. std.)
PTS 160	.1-160 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$6,495.00 (1 Hz resol., OCXO freq. std.)
PTS 250	1-250 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$7,440.00 (1 Hz resol., OCXO freq. std.)
Type 1 **PTS 310** Type 2	.1-310 MHz	1 Hz	1-20μs	standard	3½"H×19"W	BCD (std) or GPIB (opt)	1 Hz resol., OCXO: $6,425.00 1 Hz resol., OCXO: $5,850.00
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.)
PTS 620	1-620 MHz	optional .1 Hz to 100 KHz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$9,625.00 (1 Hz resol., OCXO freq. std.)
PTS 1000	0.1-1000 MHz	optional .1 Hz to 100 KHz	5-10μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$11,830.00 (1 Hz resol., OCXO freq. std.)
PTS 3200	1-3200 MHz	1 Hz	1-20μs	optional	5¼"H×19"W	BCD (std) or GPIB (opt)	$14,850.00 (1 Hz resol., OCXO freq. std.)
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.)
PTS D310	two channels .1-310 MHz	.1 Hz	1-20μs	standard	5¼"H×19"W	BCD (std) or GPIB (opt)	$8,560.00 (.1 Hz resol., OCXO freq. std.)
PTS D620	two channels 1-620 MHz	.1 Hz/.2 Hz	1-20 μs	standard	5¼"H×19"W	BCD (std) or GPIB (opt)	$13,240.00 (.1 Hz/.2 Hz resol., OCXO freq. std.)



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

2 For applicable digits, see detailed instrument specifications.

3 Bench cabinets are 17" wide.

4 Prices are U.S. only and include Manual and Remote (BCD) Control; PTS 3200 Digital Front Panel.

PROGRAMMED TEST SOURCES, INC.

P.O. Box 517, 9 Beaver Brook Rd., Littleton, MA 01460 Tel: 508-486-3400 FAX: 508-486-4495

THE NMR NEWSLETTER **NO. 449, FEBRUARY 1996** **AUTHOR INDEX**

THE NMR NEWSLETTER **NO. 449, FEBRUARY 1996** **ADVERTISER INDEX**

SPONSORS OF *THE NMR NEWSLETTER*

Abbott Laboratories
Aldrich Chemical Company, Inc.
American Microwave Technology
Amgen, Inc.
Anasazi Instruments, Inc.
Bruker Instruments, Inc.
Cryomag Services, Inc.
The Dow Chemical Company
Eastman Kodak Company
E. I. du Pont de Nemours & Company
Glaxo Wellcome
Hewlett-Packard Company
Isotec, Inc.
JEOL (U.S.A.) Inc., Analytical Instruments Division
The Lilly Research Laboratories, Eli Lilly & Company
Nalorac Cryogenics Corporation
Otsuka Electronics USA Inc.
Oxford Instruments
Programmed Test Sources, Inc.
SINTEF Unimed MR Center, Trondhiem, Norway
Tecmag
The Upjohn Company
Unilever Research
Varian, Analytical Instrument Division

FORTHCOMING NMR MEETINGS

Advances in NMR Applications, Symposium at Pebble Beach, CA, **March 17, 1996**; Contact: Nalorac's ENC Coordinator, 841-A Arnold Drive, Martinez, CA 94553; (510) 229-3501; Fax: (510) 229-1651; e-mail: sales@nalorac.com; See Newsletter 449, 38.

37th ENC (Experimental NMR Conference) "Farewell to Asilomar", Asilomar Conference Center, Pacific Grove, CA, **March 17 - 22, 1996**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87501; (505) 989-4573; Fax: (505) 989-1073. See Newsletter 448, 23.

Society of Magnetic Resonance, Fourth Scientific Meeting and Exhibition, New York, NY, **April 27 - May 3, 1996**; Contact: SMR Office, 2118 Milvia St., Suite 201, Berkeley, CA 94704; (510) 841-1899; Fax: (541) 841-2340. E-mail: info@smr.org . Future meetings: 1997, April 12-18, Vancouver, BC, Canada; 1998, April 18-24, Sydney, Australia; 1999, Philadelphia, PA; 2000, Denver, CO.

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.

42nd International Conference on Analytical Sciences, London, Ontario, Canada, **August 10-13, 1996**; Contact: Martin Stillman, Chemistry Dept.,Univ. of Western Ontario, London, Ont., Canada N6A 5B7; (519) 661-3821; Fax (519) 661-3022; e-mail 42info@uwo.ca

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. See Newsletter 448, 36

28th Congress Ampere on Magnetic Resonance & Related Phenomena, Canterbury, England, **September 1-7, 1996**; Contact: The Secretary, 28th Congress Ampere on Magnetic Resonance, Physics Laboratory, The University of Kent at Canterbury, Canterbury, Kent, CT2 7NR, England; +44-(0)1227-823767; Fax +44-(0)1227-827558; Email ampere@ukc.ac.uk; url http://wwwnmr.ukc.ac.uk/nmr/index.html.

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

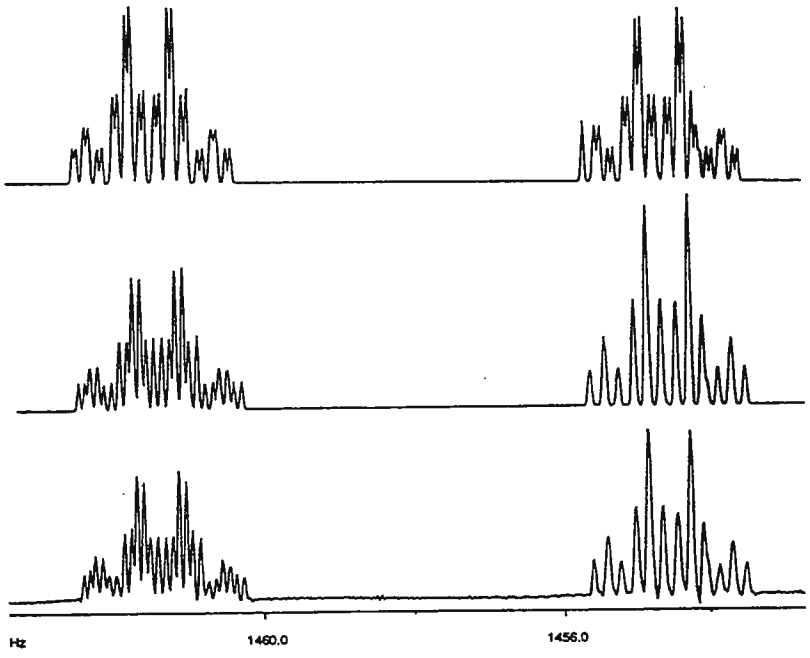
THE UNIVERSITY OF MANITOBA
DEPARTMENT OF CHEMISTRY
Winnipeg, Manitoba
Canada R3T 2N2

Tel: (204) 474-9321
Fax: (204) 275-0905
Telex: 07-587721

January 9, 1996
(received 1/18/96)
Dr. B.L. Shapiro
The NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Dear Barry,

Because of the anisotropy in its magnetic susceptibility, $\Delta\chi$, benzene is partially aligned (order parameter) by B_o. In consequence, the quadrupole splitting in C_6H_5D, for example, does not quite disappear from the high resolution ^2H nmr spectrum (Ann. Repts. NMR Spectrosc. 19, 35 (1987)). Again, another traceless tensor interaction, the dipolar, is not quite averaged to zero: for benzene itself small dipolar couplings, D, have been measured for ortho protons (J. Magn. Resn. Series, A, 104, 238 (1993)) at 400 MHz. In principle, therefore, high resolution spectra of benzene derivatives are affected by D (Magn. Reson. Chem. 24, 723 (1986)) and failure to include D in an analysis causes an error of some millihertz in J, certainly in ^3J, even though we have found that, with an rms error of, say, 5 mHz, we can reproduce all the peaks in the ^1H nmr spectrum at 300 MHz and 300K when ignoring D.



Spectrum by Scott Kroeker

The figure gives an example where this level of precision in analysis does demand the inclusion of at least one D, that for the magnetically equivalent CH_2 protons in phenylallene (allene itself is D_{2d}). The bottom is the experimental spectrum of the CH_2 protons for a benzene solution at 300 MHz and 300K. The spectrum at the top shows the best fit obtained in the absence of D, using J values which give a very good fit to the peaks of the methine and aromatic protons. The middle has $D(CH_2)$ = +0.0150(4) Hz; a negative value fails to yield a fit.

In the planar form, the internuclear vector of the CH_2 protons is perpendicular to the molecular plane; in the orthogonal conformation it is parallel to the molecular plane. Clearly, the sign and magnitude of D depends on $\Delta\chi$ and on the potential hindering the motion about the C_6H_5-allenyl linkage. Hey, a neat problem for a student of physical chemistry, a somewhat sparse species these days, it seems.

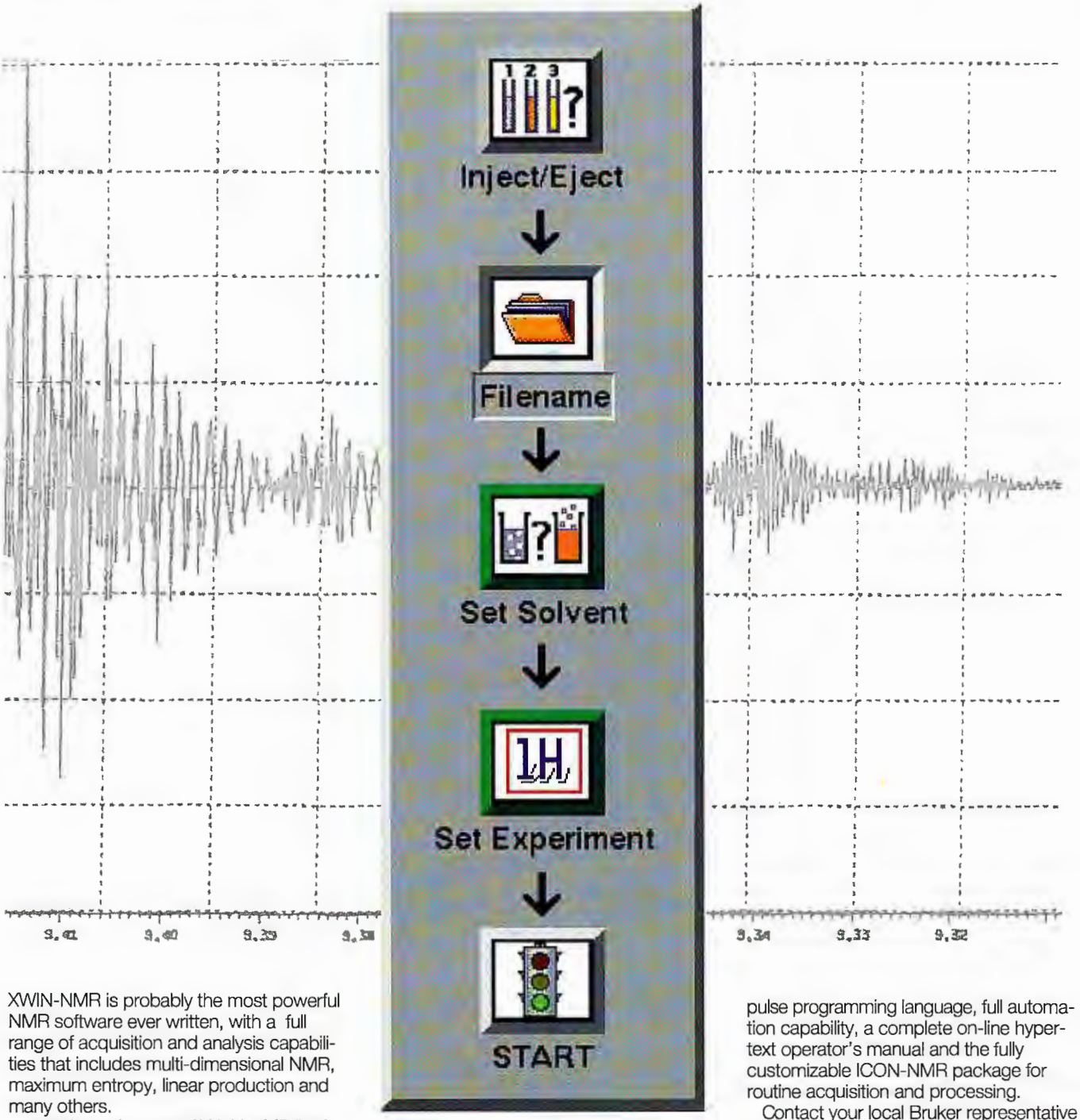
Best wishes from

Ted

Ted Schaefer

/ca

It doesn't get any easier than this:



XWIN-NMR is probably the most powerful NMR software ever written, with a full range of acquisition and analysis capabilities that includes multi-dimensional NMR, maximum entropy, linear production and many others.

But the real power of XWIN-NMR lies in the ease with which all of these advanced features can be accessed and put to use.

Not only does it provide a fully menu-driven user interface with an industry standard layout, it also includes an intuitive pulse programming language, full automation capability, a complete on-line hypertext operator's manual and the fully customizable ICON-NMR package for routine acquisition and processing.

Contact your local Bruker representative and find out how easy NMR can be.

ICON-NMR

We're pushing NMR way past easy!

Bruker Instruments, Inc., Manning Park, Billerica, MA 01821, www.bruker.com

In Europe: Bruker Analytische Messtechnik GmbH Silberstreifen, D-76287 Rheinstetten 4, Germany www.bruker.de

BRUKER

Comprehensive Support for Innovative Systems

AVANCE™ – The easy to use Digital NMR Spectrometer

- Digital Lock
- Digital Filtering with Oversampling
- Digital Signal Processing
- Digital Signal Routing
- Surface Mounted Devices
- UNIX Workstation Computer
- X-11 Windows and MOTIF
- Quick-NMR™ Interface
- Broadest Choice of Probes
- Extensive Pre-tested Experiment Library
- Comprehensive Applications Support

Digital, modular and flexible.

Now, the fundamentally superior precision and stability of digital signal processing is available from a precedent-setting series of NMR spectrometers. With its digital advantage, the Bruker AVANCE™ series sets revolutionary standards for performance, long-term reliability and ease of use, whether for routine applications or the most demanding research. The modular architecture of the Bruker AVANCE design makes extensive use of digital signal processing technology, incorporating high performance RISC-based processors into the lock, filters, timing control unit, gradient generation, and many other key areas of the system. The result is increased sensitivity, higher dynamic range, cleaner spectra, flat baselines and unprecedented stability.

The AVANCE Series of high performance spectrometers.

The comprehensive AVANCE family of NMR spectrometers was developed in direct response to the increasing demands of the NMR community for greater performance and stability in a highly automated, easy to use instrument. Within the AVANCE series of DPX, DRX, DMX and DSX systems there is a virtual continuum of configuration options from 200 to 750 MHz, including solids, liquids and imaging. Whatever the environment or application, there is an appropriate AVANCE model to choose from. Your Bruker representative will be happy to recommend a configuration that is optimum for your needs - today and tomorrow.

For complete details or to arrange a demonstration please contact your nearest Bruker representative.

BRUKER

Comprehensive Support for Innovative Systems

Australia: BRUKER (Australia) PTY. LTD., Alexandria, New South Wales, Tel. (02) 550 64 22
Belgium: N.V. BRUKER SPECTROSPIN S.A, Brussels, Tel. (02) 6 48 53 99
Canada: BRUKER SPECTROSPIN LTD., Milton, Ontario, Tel. (604) 656-1622
P.R. China: BRUKER INSTRUMENTS, LTD., Beijing, P.R. China, Tel. (00861) 255 75 30
England: BRUKER SPECTROSPIN, LTD., Coventry, Tel. (0 12 03) 85 52 00
France: BRUKER SPECTROSPIN SA, Wissembourg/Cedex, Tel. (88) 73 68 00
Germany: BRUKER ANALYTISCHE MESSTECHNIK GMBH, Rheinstetten/Karlsruhe, Tel. (07 21) 51 61-0
BRUKER ANALYTISCHE MESSTECHNIK GMBH, Karlsruhe, Tel. (07 21) 95 28 0
BRUKER-FRANZEN ANALYTIK GMBH, Bremen, Tel. (04 21) 22 05 0
BRUKER-SAXONIA, ANALYTIK GMBH, Leipzig, Tel. (03 41) 2 35 36 05
India: BRUKER INDIA, SCIENTIFIC PVT. LTD., Bombay, Tel. (22) 626 2232
Israel: BRUKER SCIENTIFIC ISRAEL LTD., Rehovot, Tel. (972) 8 409660
Italy: BRUKER SPECTROSPIN SRL, Milano, Tel. (02) 70 63 63 70
Japan: BRUKER JAPAN CO. LTD., Ibaraki, Tel. (0298) 52 12 34
Netherlands: BRUKER SPECTROSPIN NV, AB Wormer, Tel. (75) 28 52 51
Scandinavia: BRUKER SPECTROSPIN AB, TNby, Sweden, Tel. (08) 7 58 03 35
Spain: BRUKER ESPAÑOLA S.A., Madrid, Tel. (1) 504 62 54
Switzerland: SPECTROSPIN AG, Fällanden, Tel. (01) 8 25 91 11
USA: BRUKER INSTRUMENTS, INC., Billerica, MA, (508) 667-9580,
Regional Offices in Lisle, IL, (708) 971-4300/Wilmington, DE, (302) 478 8110
The Woodlands, TX (713) 292-2447/Fremont, CA (510) 683-4300

Technische Universität München
Garching bei München

Garching, 12. January 1996

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

(received 1/22/96)

Dr. Gerd Gemmecker
Org. Chemie and Biochemie II, TU München
Lichtenbergstraße 4
D-85747 Garching (Germany)

email: gg@joshua.org.chemie.tu-muenchen.de
Tel./Fax: ++49 (89) 3209-3308/-3210

Dear Dr. Shapiro,

recently we celebrated the official opening of our new NMR building in Prof. Kessler's group, housing two new spectrometers DMX600 and DMX750 (the latter one shared with several other NMR groups in Germany). After a smooth installation, both machines are now fully operational.

The newest feature on both spectrometers (just installed a month ago) is the *gradient shimming* procedure. It uses the shielded gradient coils inside our high-resolution probes (we have xyz-triple gradient quadruple resonance probes for both machines) to get a 3D image of the homogeneity in the sample volume. Bases on the field maps for all 27 shims (that have to be acquired once in the same way) the program then calculates the corrections necessary to compensate for the observed deviations from perfect homogeneity. The procedure can be run iteratively, remaining deviations from homogeneity are displayed after each step.

To check out the algorithm's capabilities, I've run several iterations on a sample containing ca. 0.45 mL of a 1 mM aqueous solution of a 20 kDa protein. I started with a severely mis-shimmed probe (all shims Z1-5, X, Y, XZ, YZ, XZ2, YZ2, X3, Y3 set to zero!, cf. first trace in Fig.1). After one iteration (ca. 2 min.) the result bore some resemblance to an NMR spectrum, and after the second one the water lineshape already looked pretty good (no humps, symmetric, $b_{1/2} \approx 30$ Hz). However, the graphic display of the gradient shimming program (Fig.2) indicated still considerable inhomogeneity, and two more iterations indeed led to a significant improvement, which is only visible with sharper resonance lines, such as the EDTA peak shown on the right of Fig.1. After four iterations it reaches a linewidth of ca. 2.5 Hz at half-height (the water line staying at 30 Hz). This last improvement would have been very difficult to obtain by manual shimming, since the intensity of the lock signal (D_2O) increased only marginally between the 2^{nd} and the 4^{th} iteration.

Gradient shimming was especially useful for checking out various sample paramenters (temperature, pH, ionic strength, detergents) to optimize protein lineshape, since it delivers an excellent shim with high reproducibility, so that any effects of field homogeneity on the protein linewidths in the different runs can be safely neglected. Starting from a standard shim file for the probe (other than the worst-case scenario from Fig.1), two iterations (of ca. 2 min. duration each)

proved sufficient to achieve an excellent shim even with difficult samples (e.g., small sample volumes), which is much faster than manual shimming - at least with me!

Please credit this contribution to the account of Prof. F. Köhler, TU Munich.

Yours sincerely

Gerd (Ruth)

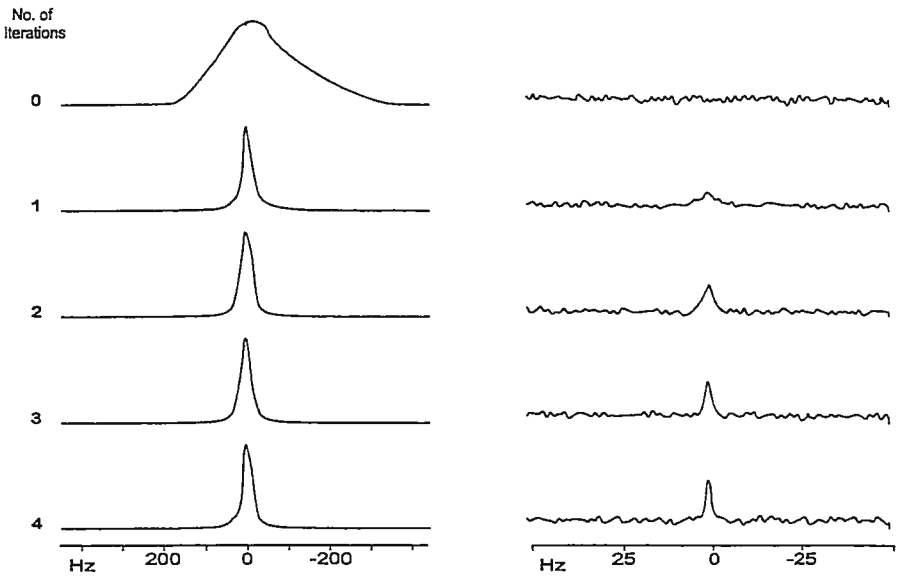


Fig.1

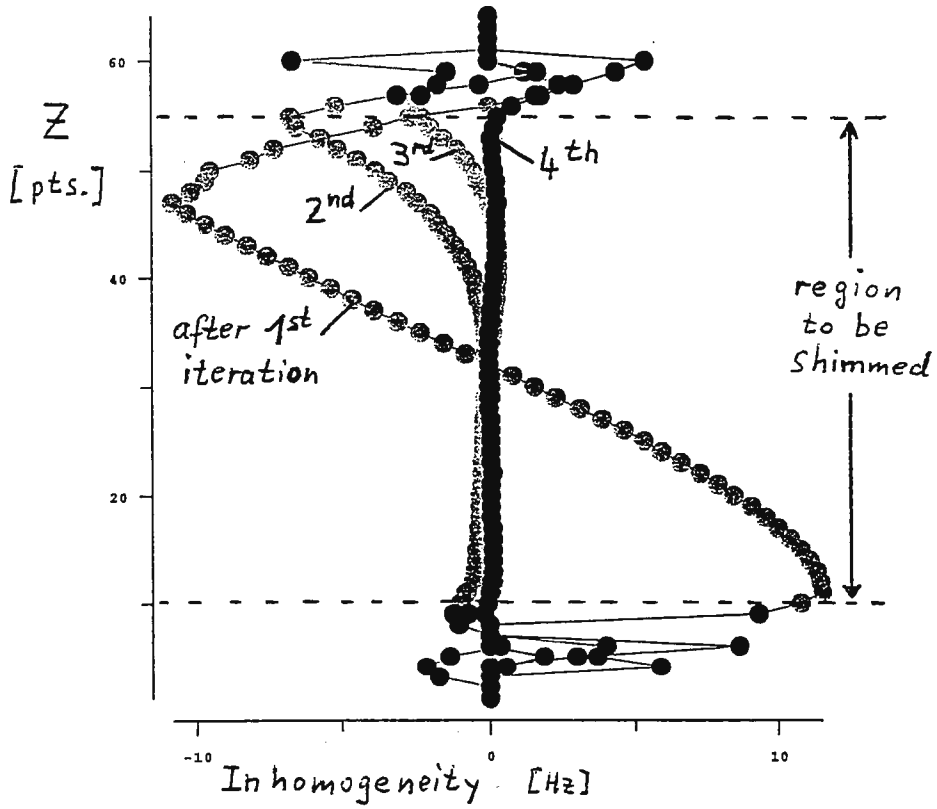


Fig.2

TLI THE LOVELACE INSTITUTES
Improving Human Health through Research and Technology

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

January 5, 1996
(received 1/8/96)

Efficacy of Blood Substitutes Determined by ^{31}P-NMR Spectroscopy.

Dear Barry,

Artificial blood substitutes are being developed for their promise as non-infectious, universally accepted, low-storage-cost alternatives to human blood. Previous attempts to replace blood have utilized perfluorocarbon emulsions or stroma-free, cross-linked or encapsulated hemoglobin solutions (***1***). An alternative to these approaches is to manufacture recombinant human hemoglobin (***2-4***). The efficacy of such a product with respect to oxygen transport and delivery would need to be established *in vivo*. We have utilized ^{31}P-NMR spectroscopy to determine the efficacy of recombinant human hemoglobin (Somatogen Inc., Boulder, Colorado), as an oxygen carrier *in vivo* by monitoring the high-energy phosphorus metabolism of the rat abdomen during and after complete replacement of the blood by a solution of recombinant human hemoglobin.

Methods: Anesthetized cannulated rats were placed into the bore of a 1.9 Tesla horizontal magnet. Metabolite ^{31}P-NMR signals were detected with a 30 mm diameter surface coil placed over the abdomen. Time-dependent spectral data were collected in 5 min. blocks from control animals, animals whose blood was replaced with human serum albumin (HSA), containing no oxygen carrier, and from animals whose blood was replaced by a solution of recombinant human hemoglobin (rHb). Animal's hematocrits were reduced to less than 3% by isovolemic exchange transfusion. The stability of the metabolite signals over the course of the experiments was determined from the ^{31}P signal integrals after curve-fitting.

Results: The data obtained from control animals showed no significant changes in the metabolite levels during several hours in the magnet. The results from hour-long, albumin-exchange experiments in 5 rats are summarized in Fig. 1, where we have plotted a 15 min moving average of the concentration, normalized to its value before the exchange, of high energy phosphates (HEP), the sum of PCr and β-ATP concentration, vs. the $[Hb]_{rbc}$, the hemoglobin concentration in the red blood cells. A fit of the data to a Michaelis-Menten type equation, $[HEP] = V_{max}\,[Hb]_{rbc} / ([Hb]_{rbc} + K_m)$, gave a value of K_m of 0.87 g/dl, indicating that the $[Hb]_{rbc}$ has to fall by more than a factor of 15 before a 50% drop in high-energy phosphates can be seen. For $[Hb]_{rbc} > 10.0$, the mean value of [HEP] was 97.5 (±2.2, n=10)%, while for $2.5 < [Hb]_{rbc} < 3.5$ the mean value of [HEP] was 78.5 (±4.6, n=5)%, a value which is significantly smaller (α=0.0025) than that found at normal $[Hb]_{rbc}$. At the end of the HSA exchange, for $[Hb]_{rbc}$ less than 1%, the animals were unstable and eventually died. Prior to death a 4-fold increase in orthophosphate and a 50 % drop in phosphocreatine and ATP was observed. The tissue pH dropped from 7.35 at the start of the experiment to 6.8 at the end.

In contrast to the albumin-exchange, exchange transfusion with recombinant human hemoglobin (5 g/dl [Hb], which is 1/3 the [Hb] of normal blood) resulted in no significant drop in high-energy phosphates no rise in low-energy phosphates, and no change in tissue pH from 7.35 ± 0.15 over a period of 5 hours (data not shown). The animals given recombinant hemoglobin lived for 5-6 hours after the exchange.

Because there are sound physiological reasons to expect that free hemoglobin solutions might deliver oxygen better than whole blood (1), and because we observed no compromise in [HEP] metabolism with 5 g/dl [Hb] concentration rHb, we diluted the rHb to a concentration of only 3 g/dl [Hb], and repeated the exchange experiments. Note that we found above that there was a greater than 20% drop in [HEP] at [Hb] = 3 g/dl during HSA exchange.

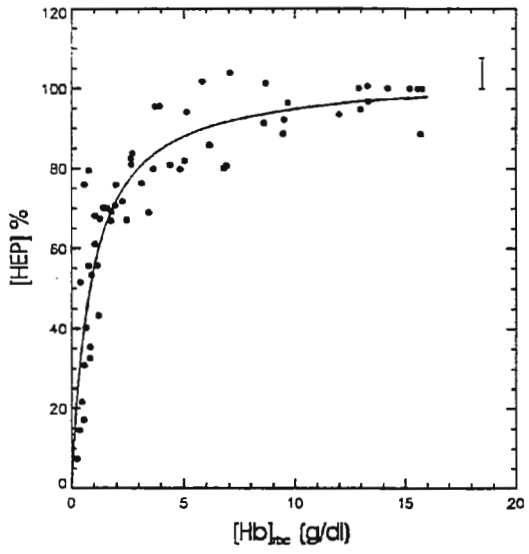


Fig 1. Exchange with albumin

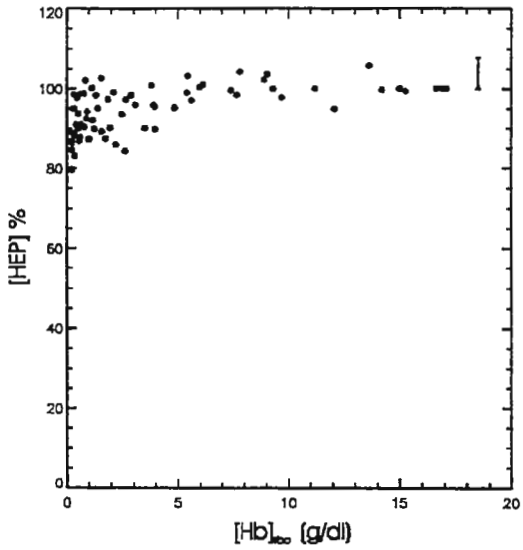


Fig 2. Exchange with artificial blood substitute

Fig. 2 shows the combined results from 6 rats for an exchange transfusion with a 3 g/dl solution of rHb. For $[Hb]_{rbc} > 10.0$, the mean value of [HEP] was 100.0 (±1.6, n=9)%, while for $[Hb]_{rbc} < 1.0$ the mean value of [HEP] was 91.0 (±3.8, n=6)%, which is significantly smaller than previous value (α=0.025). All the animals continued to live at [Hb] < 1 g/dl for one-hour after the exchange was terminated, during which data was collected. At the end of this period the animals were sacrificed. Thus at a total [Hb] of 3 g/dl in the blood, the phosphorus metabolism is slightly affected but the animal remained alive.

Conclusions: Our results appear to indicate that free, extra-cellular hemoglobin performs better at sustaining high energy phophorus metabolism than the same hemoglobin content in blood within the erythrocytes. We base this conclusion on our finding that [HEP] determined at a total [Hb] of 3 g/dl with rHb (91.0 (±3.8, n=6)%) was found to be significantly higher (α=0.05) than that found at the same [Hb] with erythrocytes during HSA exchange (78.5 (±4.6, n=5)%). Recombinant human hemoglobin, even at only 1/3 the normal concentration of 15 g/dl sustains vital energy-producing functions of tissues at levels which are indistinguishable from those found when whole blood is present. ^{31}P-NMR spectroscopy was found to be a useful method for studying the efficacy of blood substitutes in this setting.

References:

(*1*) Winslow, R.M., Vandegriff, K.D., and Intaglietta, M. Eds. "Blood Substitutes: Physiological Basis of Efficacy" Birkhauser (Boston: 1995).
(*2*) S. J. Hoffman, D. L. Looker, J. M. Roerich, P. E. Cozart, S. L. Durfee, J. L. Tedesco and G. L. Stetler "Expression of fully functional tetrameric human hemoglobin in Escherichia Coli" Proceedings of the National Academy of Sciences (USA) **87**(1990)8521-8525.
(*3*) D. L. Looker, D. Abbott-Brown, P. Cozart, S. Durfee, S. Hoffman, A. J. Mathews, J. Miller-Roerich, S. Shoemaker, S. Trimble, G. Fermi, N. H. Komiyama, K. Nagai, and G. L. Stetler "A human recombinant haemoglobin designed for use as a blood substitute" Nature **356**(1992)258-260.
(*4*) T. Shen, N. T. Ho, V. Simplaceanu, M. Zou, B. N. Green, M. F. Tam and C. Ho "Production of unmodified human adult hemoglobin in Escherichia Coli." Proceedings of the National Academy of Sciences (USA) **90**(1993)8108-8112.

Yours sincerely,

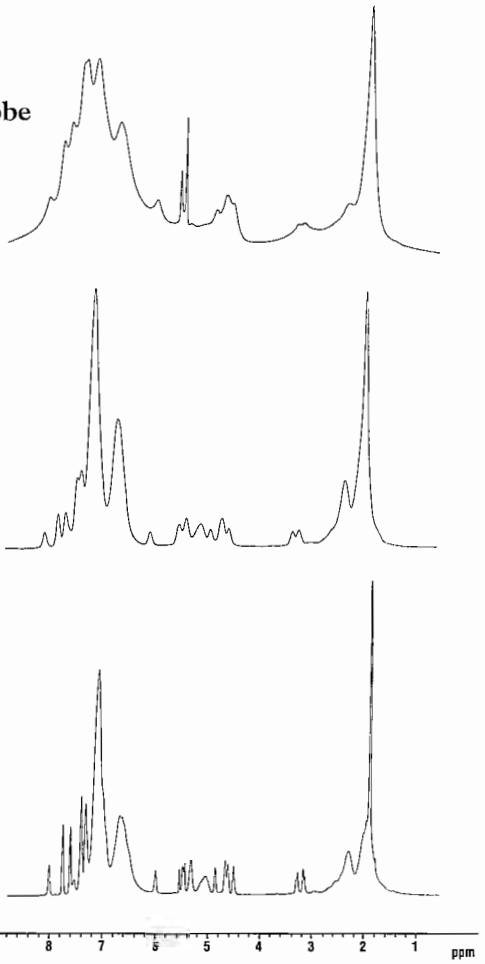
Laurel O. Sillerud Arvind Caprihan

Highest Resolution for Solid-Phase Synthesis

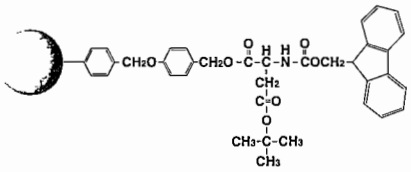
A. Vertical spinning probe

B. CP/MAS probe

C. ^{1}H Nano•nmr probe



^{1}H spectra of Fmoc-L-aspartic-ß(t-butyl) ester Wang resin in CD_2Cl_2 obtained utilizing a vertical spinning probe (A), a CP/MAS probe (B), and a ^{1}H Nano•nmr probe (C). J. Magn. Reson. (1996), in press.



Varian's ^{1}H and ^{13}C{^{1}H} Nano•nmr probes for combinatorial chemistry

Obtain the highest resolution for your solid-phase synthetic products with Varian's Nano•nmr probe, a truly unique probe combining magic-angle spinning with high-resolution probe technology.

The ultimate resolution for solid-phase synthesis products such as produced in combinatorial chemistry is dependent on probe design and materials.

Only Varian's ^{1}H and ^{13}C{^{1}H} Nano•nmr probes deliver maximum spectral resolution for these heterogeneous samples by eliminating line-broadening caused by magnetic susceptibility discontinuities *around and within* the sample.

Don't settle for the lower resolution of a CP/MAS probe. Profit from the additional structural information provided with the higher resolution of Varian's Nano•nmr probe–the probe with the highest demonstrated resolution for both ^{1}H and ^{13}C samples.

Nano•nmr probes are compatible with both *GEMINI* and UNITY NMR spectrometers. For more information, contact the Varian office nearest you.

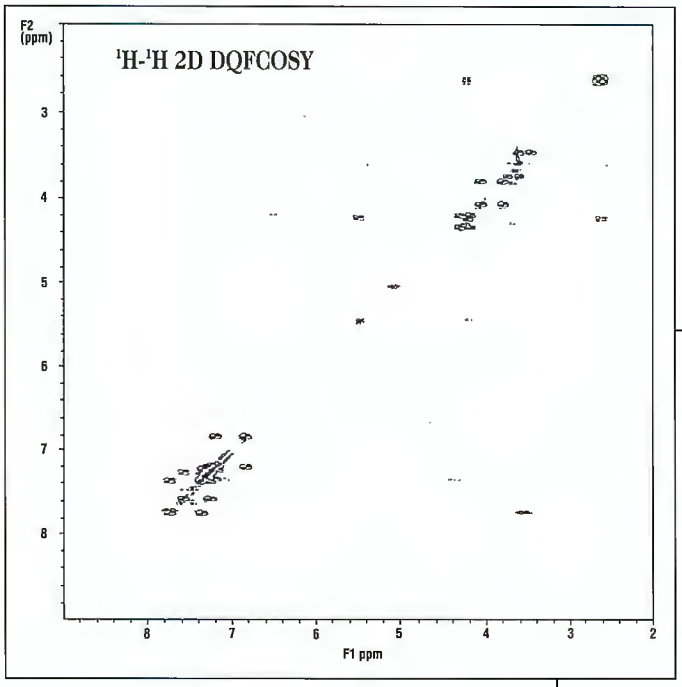
Send for your Solid-Phase Synthesis ^{1}H and ^{13}C NMR Spectral Catalog, attention:
Bee Sehrt at Varian NMR Instruments
3120 Hansen Way M/S D-298
Palo Alto, CA 94304-1030

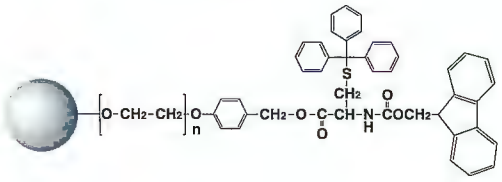
varian

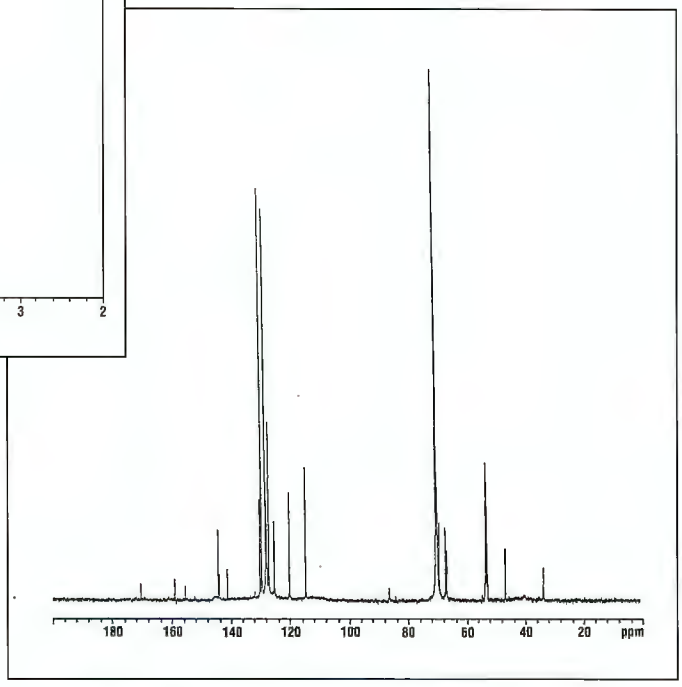
For the full story, our 129-page Solid-Phase Synthesis ^{1}H and ^{13}C NMR Spectral Catalog features an extensive collection of NMR spectra of samples still bound to a variety of solid-phase synthesis resins. Send your spectral catalog request to:

Bee Sehrt
Varian NMR Instruments
3120 Hansen Way M/S D-298
Palo Alto, CA 94304-1030

High Resolution ^{1}H 2D Spectra from Solid-Phase Synthesis Gels







High Resolution ^{13}C Spectra from Solid-Phase Synthesis Gels

Manufacturing Facilities Varian NMR Instruments, Building 4, 3120 Hansen Way, Palo Alto, California 94304-1030, Tel 415.493-4000 • **Australia** Mulgrave, Victoria, Tel 3.9.560.7133 • **Austria** Vösendorf, Tel 1.69.5445 • **Belgium** Brussels, Tel 2.721.4850 • **Brazil** São Paulo, Tel 11.820.0444 • **Canada** Mississauga, Ontario, Tel 1.800.387.2216 • **China** Beijing, Tel 1.256.4360 • **France** Les Ulis, Tel 1.6986.3838 • **Germany** Darmstadt, Tel 06151.7030 • **Italy** Milan, Tel 2.921351 • **Japan** Tokyo, Tel 3.5232.1211 • **Korea** Seoul, Tel 2.3452.2452 • **Mexico** Mexico City, Tel 5.514.9882 • **Netherlands** Houten, Tel 3063.50909 • **Russian Federation** Moscow, Tel 095.203.7925 • **Spain** Madrid, Tel 91.472.7612 • **Sweden** Solna, Tel 8.82.00.30 • **Switzerland** Zug, Tel 42.448.844 • **Taiwan** Taipei, Tel 2.705.3300 • **United Kingdom** Walton-on-Thames, Tel 01932.898.000 • **United States** California, Tel 800.356.4437 • **Other sales offices and dealers throughout the world**

MAG-8501/591

varian

The University of Texas Medical Branch at Galveston

School of Medicine
Graduate School of Biomedical Sciences
School of Allied Health Sciences
School of Nursing

Marine Biomedical Institute
Institute for the Medical Humanities
UTMB Hospitals and Clinics

Department of Human Biological Chemistry & Genetics
Sealy Center for Structural Biology

January 3, 1996 (received 1/10/96)

Re: 3D NOESY NOESY at 750 MHz

Dear Barry,

We have been enjoying our recent move to Galveston and the new equipment (Varian 400, 600 and 750 Unity Plus spectrometers) and the opportunities it has afforded. Last winter most days were delightfully balmy and warm. Far different from the cold in our recent past. Of course then summer came and then the hurricanes...

We've been particularly interested in developing 3D NOESY NOESY in conjunction with our complete relaxation matrix program MORASS for high resolution structural studies of biomolecular systems. While heteronuclear 3D NMR spectroscopy has been used more often to make the sequential assignment and obtain distance estimates, 3D homonuclear NOE-NOE methods have been found to contain more information for quantitatively determining the structure once the assignments have been made.

While it is true that many good quality structures have been obtained from NMR, especially with the development of heteronuclear 3D and 4D NMR, it is obvious that using more and tighter constraints will achieve greater precision (and hopefully accuracy) in the refined structures. Indeed as shown in Figure 1, the number of 3D volumes that can be integrated increases dramatically as the threshold level of cutoff of peak volume decreases. At high field and larger sample volumes, thousands of 3D volumes are available for refinement constraints.

One decided disadvantage of 3D NOESY NOESY is the problem of S/N for the 3D crosspeaks. The intensity of the crosspeak is effectively the product of the intensity of two 2D crosspeaks and good spectrometer sensitivity (or lots of sample!) is essential. We have found that our new 750 MHz spectrometer has been especially helpful for these difficult 3D NOE NOE experiments. Our newest Varian 5 mm ^{1}H probe has a S/N of >1400:1 and this has provided us with excellent quality 3D NOE NOE spectra.

So far, most quantitative 3D NOE-NOE studies are based upon the two-spin approximation. However, as we have recently demonstrated[1], at realistic mixing times that allow reasonably accurate measurement of 3D NOE NOE volumes, both the two-spin and the Taylor series expansion approximation methods can lead to considerable systematic errors and complete relaxation methods are essential.

Both 2D and 3D NOE spectra are a function of the 2D relaxation matrix, which depends on the distances between pairs of spins. 3D NOE-NOE spectra can be described by,

$$\mathbf{A}_{ijk} = [\exp(-\tau_{m1}\mathbf{R})]_{ij}[\exp(-\tau_{m2}\mathbf{R})]_{jk}M_0 \tag{1}$$

where $\mathbf{R}$ is the relaxation rate matrix, τ_{m1} and τ_{m2} are the two mixing times and M_0 is the equilibrium magnetization. In terms of 2D and 3D volumes,

$$A^{3D}_{ijk} \propto A^{(1)}_{ij} A^{(2)}_{jk} \tag{2}$$

where A^{3D}_{ijk} is a single 3D volume and $A^{(1)}_{ij}$ and $A^{(2)}_{ij}$ are the 2D volumes during the two mixing times.

We have recently introduced a new algorithm that allows us to deconvolute the 3D volume matrix into a hybrid-hybrid NOE volume matrix[2]. Basically an initial model structure and the measured r_{ij} values are used to calculate the rate matrix. We then simulate 2D NOESY and 3D NOE-NOE spectra. The experimental and simulated 3D NOE-NOE data are scaled and then merged to create a hybrid 3D data set. The 3D hybrid data are then deconvoluted into a 2D matrix, with elements

$$< A_{ij} >= \frac{1}{n}\sum_{k=1}^{n} \frac{A^{exp}_{ijk}}{A^{*}_{jk}} \tag{3}$$

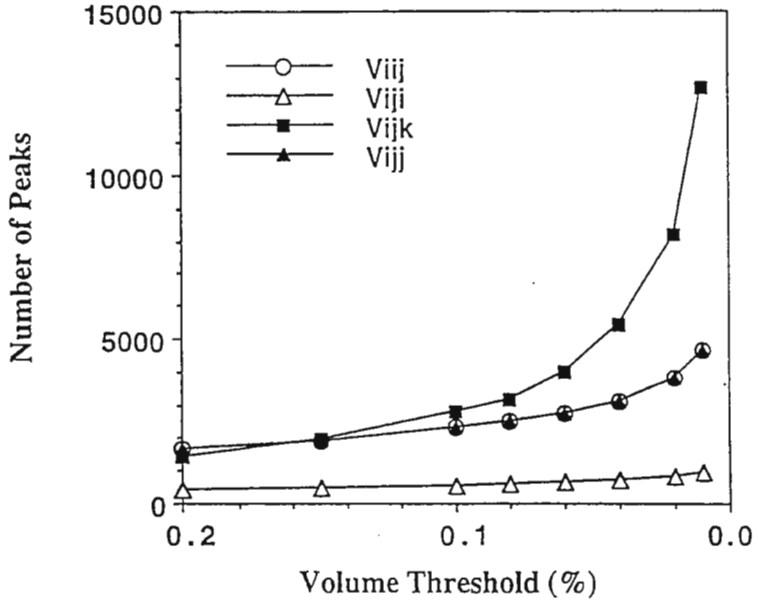


Figure 1. Number of integratable 3D volumes as a function of the percentage intensity relative to the largest diagonal peak in a simulated 3D NOE-NOE spectrum for d(CGCGAATTCGCG)$_2$ with τ_c = 3.2 ns and $\tau_{m1} = \tau_{m2}$ = 100 ms.

where non-zero A^*_{jk} values may be obtained from * = exp (experimental) or * = simul (simulated) 3D spectra. Additional experimental or simulated 2D NOESY volumes can then be merged into the deconvoluted matrix to give a complete 2D hybrid-hybrid volume matrix. Importantly 2D NOEs from 3D or 4D HMQC-NOESY experiments can also be merged into the hybrid-hybrid volume matrix. The rate matrix can then be calculated from the hybrid-hybrid volume matrix, using our MORASS (or other) relaxation matrix approach. The resulting distances are taken from the cross-relaxation rates and then utilized in a distance geometry or restrained molecular dynamics refinement of the structure. The entire process is repeated until a satisfactory agreement between the calculated and observed 3D crosspeak volumes is obtained.

3D NOE-NOE spectra hold the promise of giving more accurate structures given the vastly increased number of resolvable 3D NOE-NOE volumes. Approximation methods may not yield accurate distances for the mixing times required to achieve adequate magnetization transfer and signal-to-noise[1]. Competing with the hybrid-hybrid matrix method described here, are various direct gradient NOE refinement methods which scale as n^3 whereas the hybrid-hybrid matrix method is still basically an n^2 problem (diagonalization of the n×n volume matrix).

Sincerely yours,

David G. Donne, Elliott K. Gozansky, Frank Q. Zhu, Shanmin Zhang, Bruce A. Luxon and David G. Gorenstein

1. Donne, D.G., Gozansky, E.K., & Gorenstein, D.G., "Exact vs. Approximate Methods in the imulation of 3D NOE-NOE Spectra," *J. Magn. Reson. Series B*, **106**, 156-163 (1995).

2. Zhang, Q., Chen, J., Gozansky, E.K., Zhu, F., Jackson, P.L., & Gorenstein, D.G., "A hybrid-hybrid Matrix Method for 3D NOE-NOE data Analysis," *J. Magn. Reson. Series B*, **106**, 164-169 (1995).

p.s.: In celebration of the new Sealy Center for Structural Biology at UTMB, we will be holding a structural biology symposium March 1-3, 1996 in Galveston. NMR, X-ray, computational and macromolecular interactions talks and posters will be presented. Further information will be made available on the WEB (http://www.nmr.utmb.edu/). Come on down and help us celebrate.

University of Nebraska Medical Center
Nebraska's Health Science Center

Department of Radiology
600 South 42nd Street
P.O. Box 981045
Omaha, NE 68198-1045
Fax (402) 559-4675

Chairman
(402) 559-6396
Thomas J. Imray, M.D.
Genitourinary Radiology

Diagnostic Radiology
(402) 559-4477/4478
Joseph C. Anderson, M.D.
Ultrasound
Charles A. Dobry, M.D.
Chest Radiology
Jeff L. Fidler, M.D.
Abdominal Imaging
Timothy C. Goertzen, M.D.
Angiography and Interventional Radiology
Jud Gurney, M.D.
Chest Radiology
Francis J. Hahn, M.D.
Neuroradiology
Roger K. Harned, M.D.
Gastrointestinal Radiology
Robert F. LeVeen, M.D.
Angiography and Interventional Radiology
Robert P. Lieberman, M.D.
Angiography and Interventional Radiology
Aurelio Matamoros, M.D.
Ultrasound
James R. McConnell, M.D.
Pediatric Radiology and Neuroradiology
Timothy C. McCowan, M.D.
Angiography and Interventional Radiology
Timothy E. Moore, M.B., Ch.B., F.R.A.C.R.
Musculoskeletal Radiology
Donald F. Orton, M .D.
General Radiology
Ralph Read, M.D.
General Radiology
Jean A. Saigh, M.D.
General Radiology
Craig W. Walker, M.D.
Musculoskeletal Radiology
Cheryl A. Williams, M.D.
Mammography
Robert J. Witte, M.D.
Neuroradiology

Nuclear Medicine
(402) 559-5280
Glenn V. Dalrymple, M.D.
Katherine A. Harrison, M.D.
Karen P. Holdeman, M.D.

Radiation Biology
(402) 559-7811
David A. Crouse, Ph.D.
Martin H. Schneiderman, Ph.D.
John G. Sharp, Ph.D.

Radiation Physics
(402) 559-5275
Gamal Akabani, Ph.D.
Wei-Kom Chu, Ph.D.
William G. Hawkins, Ph.D.
Peter Leichner, Ph.D.

Radiochemistry
(402) 559-8906
Janina Baranowska-Kortylewicz, Ph.D.

Radiology Research
(402) 559-5937
Randall W. Jones, D.E.

December 22, 1995
(received 12/26/95)

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

RE: In Vivo Detection of Brain Propylene Glycol by Proton MR Spectroscopy

Dear Dr. Shapiro:

We have been using brain proton MR spectroscopy (^{1}H MRS) to assess *in vivo* pathologic metabolism in children and infants.

Recently, we found four patients in our study group to have an unexpected *doublet* signal at 1.1 ppm. Case 1 had encephalitis, seizures and lactic acidosis. (Fig. a) Case 2 hand severe hypoxic encephalopathy, seizures and liver/kidney failure. The decreased N-AcetylAspartate (NAA) in this patient is likely due to neuronal loss. (Fig. b) Case 3 had mild encephalopathy after recovery from bone marrow transplant. (Fig. c) Case 4 had mild birth asphyxia and seizures. These cases were being treated with various drugs containing propylene glycol (PG). The *doublet* at 1.1 ppm on the *in vivo* brain spectra indicates the putative signal of the PG methyl protons. The *in vitro* sample contained 5 mM of propylene glycol (PG) and 5 mM of lactate (Lac) as a chemical shift reference at 1.3 ppm. (Fig. d) All spectra were done on a 1.5 Tesla clinical scanner using single voxel PRESS sequence.

Comparison of the *in vivo* brain and *in vitro* PG/Lac spectra revealed identical coupling, phase modulation and chemical shift at 1.1 ppm. Moreover, the *in vivo* brain spectra are consistent with reports of *ex vivo* ^{1}H MRS of tissues containing PG.(1,2)

PG is a solvent vehicle for many drugs. It's usually considered non-toxic, but there are reports that it can cause hyperosmolality, lactic acidosis, hemolysis and renal failure.(3,4,5) We suggest that *in vivo* ^{1}H MRS can be used to assess brain PG and may be clinically useful in the investigation of its toxicity.

University of Nebraska Medical Center
Nebraska's Health Science Center

Department of Radiology
600 South 42nd Street
P.O. Box 981045
Omaha, NE 68198-1045
· Fax (402) 559-4675

Chairman
(402) 559-6396
Thomas J. Imray, M.D.
Genitourinary Radiology

Diagnostic Radiology
(402) 559-4477/4478
Joseph C. Anderson, M.D.
Ultrasound
Charles A. Dobry, M.D.
Chest Radiology
Jeff L. Fidler, M.D.
Abdominal Imaging
Timothy C. Goertzen, M.D.
Angiography and Interventional Radiology
Jud Gurney, M.D.
Chest Radiology
Francis J. Hahn, M.D.
Neuroradiology
Roger K. Harned, M.D.
Gastrointestinal Radiology
Robert F. LeVeen, M.D.
Angiography and Interventional Radiology
Robert P. Lieberman, M.D.
Angiography and Interventional Radiology
Aurelio Matamoros, M.D.
Ultrasound
James R. McConnell, M.D.
Pediatric Radiology and Neuroradiology
Timothy C. McCowan, M.D.
Angiography and Interventional Radiology
Timothy E. Moore, M.B., Ch.B., F.R.A.C.R.
Musculoskeletal Radiology
Donald F. Orton, M .D.
General Radiology
Ralph Read, M.D.
General Radiology
Jean A. Saigh, M.D.
General Radiology
Craig W. Walker, M.D.
Musculoskeletal Radiology
Cheryl A. Williams, M.D.
Mammography
Robert J. Witte, M.D.
Neuroradiology

Nuclear Medicine
(402) 559-5280
Glenn V. Dalrymple, M.D.
Katherine A. Harrison, M.D.
Karen P. Holdeman, M.D.

Radiation Biology
(402) 559-7811
David A. Crouse, Ph.D.
Martin H. Schneiderman, Ph.D.
John G. Sharp, Ph.D.

Radiation Physics
(402) 559-5275
Gamal Akabani, Ph.D.
Wei-Kom Chu, Ph.D.
William G. Hawkins, Ph.D.
Peter Leichner, Ph.D.

Radiochemistry
(402) 559-8906
Janina Baranowska-Kortylewicz, Ph.D.

Radiology Research
(402) 559-5937
Randall W. Jones, D.E.

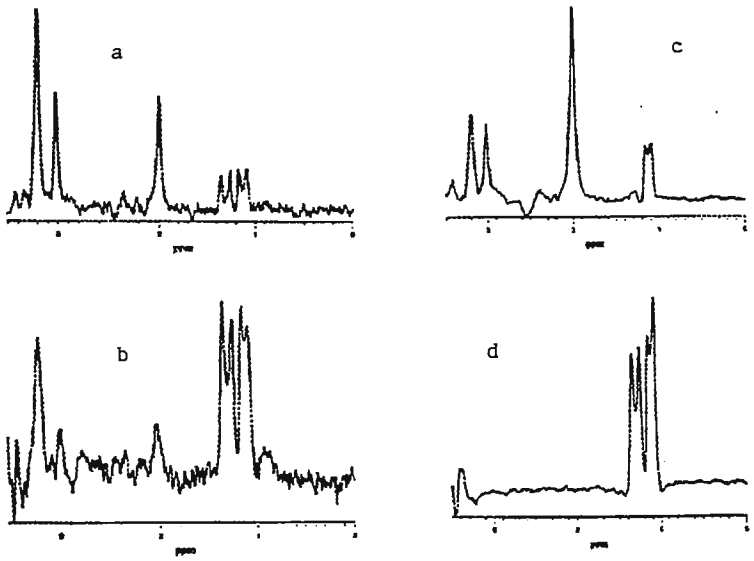
1. Petroff, OAC; Spencer, DD; Alger JR; and Prichard, JW. High-field proton magnetic resonance spectroscopy of human cerebrum obtained during surgery for epilepsy. Neurology 1989; 39:1197-1202.
2. Petroff, OAC; Yu, RK; and Ogiono T. High-resolution proton magnetic resonance analysis of human cerebrospinal fluid. Journal of Neurochemistry 1986; 47:1270-1276.
3. Bedichek, E; Krischbaum, B. A case of propylene glycol toxic reaction associated with etomidate infusion. Arch Intern Med 1991; 151:2297-2298.
4. Demey, HE; Daelemans, RA; Verpooten, GA; De Bre, ME; Van Campenhout, Ch M; Lakiere, FV; Schepens, PJ; and Bossaert, LL. Propylene glycol-induced side effects during intravenous nitroglycerin therapy. Intensive Care Medicine 1988; 14:221-236.
5. Levy, ML; Aranda, M; Zelman, V; Giannotta, SL. Propylene glycol toxicity following continuous etomidate infusion for control of refractory cerebral edema. Neurosurgery 1995; 327 No.2:363-371.

Sincerely,

James R. McConnell, M.D.

Chin Sing Ong, M.S.

JRM/kjm



There's a part of each one in every Oxford Instruments magnet

With over 4000 successful installations worldwide, Oxford Instruments continues to lead the field with innovative technology - the benchmark of NMR magnet excellence!

Such distinct and advanced engineering requires the best possible resources. Oxford Instruments has full design, manufacturing and test capability for its products, including state of the art CNC machine tools, precision winding machines and a wide range of specialised processing and test equipment.

But creating world-beating products relies on more than just technology, behind our success there is a highly trained workforce with extensive skills and talent. Their combined expertise is an invaluable resource, enabling us to deliver design, engineering, service and support around the world.

At Oxford Instruments we pride ourselves on being a world-class company of excellence, whose customers demand and get the best service. That's why we are dedicated to a programme of investment in people and technology focused on delivering customer satisfaction at all times.

Oxford Instruments remains the preferred choice for NMR specialists worldwide. Whether you need a custom approach or a specific application, ask the experts first, talk to...

Oxford Instruments

Certificate No. FM30231

ISO 9001 CERTIFIED

OXFORD

Oxford Instruments
NMR Instruments

The Oxford Instruments Heritage

Oxford Instruments are the pioneers of NMR magnet systems and associated cryogenic technology. After more than 30 years, we are still leading the way maintaining our worldwide reputation for transforming scientific ideas into usable, practical technology:

- Oxford Instruments were the first company to introduce NMR quality super-conducting magnets at 400, 500, 600 and 750 MHz.
- We designed and built the world's first compact superconducting storage ring for X-ray lithography.
- 20 Tesla magnets are routinely produced for physics research.

Making this happen are the people of Oxford Instruments, their expertise and dedication makes them our greatest asset and a unique resource for our customers.

Our accumulated knowledge and experience is unparalleled and some of the best minds in research technology are consistently working in partnership with our customers, exploring new techniques and setting new standards in the design and manufacture of specialist research products.

But it does not stop there; supporting our customers day to day, and around the world, is a team of engineers and technical specialists. Always on hand, to keep our products fully functional and equipped with the latest refinements.

New products such as the Oxford NMR^{750} are practical examples of our innovation so you can be sure of Oxford Instruments commitment to providing the very best in people and products for many years to come.

Standard specifications

Magnetic field Strength (^{1}H-MHz)	Room Temperature Bore Diameter (mm)	Field Stability (^{1}H-Hz/Hour)	Maximum Helium Refill Interval (Days)	Minimum Operational Ceiling Height (m)
750	51	15	60	3.8
600	51	10	120	3.4
500	51	10	150	3.2
400	54	8	365	2.8
360	54	8	365	2.8
300	54	3	365	2.8
270	54	2.7	365	2.8
200	54	2	365	2.8
100	54	1	365	2.8
500	89	15	120	3.4
400	89	10	180	2.8
360	89	10	365	2.8
300	89	3	365	2.8
270	89	2.7	365	2.8
200	89	2	365	2.8
100	110	1	119	2.8

We would be delighted to discuss your custom specification requirements for any specialist systems. For more information please contact your local Oxford Instruments sales and service organisation.

UK
Oxford Instruments
NMR Instruments,
Osney Mead, Oxford OX2 0DX,
England
Tel: +44 (0) 1865 269500
Fax: +44 (0) 1865 269501

Germany
Oxford Instruments GmbH
Kreuzberger Ring 38,
Postfach 4509, D-6200 Wiesbaden,
Germany
Tel: (611) 76471
Fax: (611) 764100

USA
Oxford Instruments Inc.
130A Baker Avenue, Concord,
MA 01742, USA
Tel: (508) 369 9933
Fax: (508) 369 6616

France
Oxford Instruments SA
Parc Club-Orsay Universite,
27, rue Jean Rostand,
91893 - Orsay Cedex,
France
Tel: (1) 6941 8990
Fax: (1) 6941 8680

Japan
Oxford Instruments K.K.
8F, Second Funato Building,
1-11-11, Kudankita,
Chiyoda-ku, Tokyo 102
Japan
Tel: (3) 3264-0551
Fax: (3) 3264-0393 · 0626

Oxford Instruments Inc.
West Regional Office,
331c Lakeside Drive,
Foster City, California 94404
USA
Tel: (415) 578 0202
Fax: (415) 578 9018

OXFORD

Oxford Instruments, NMR Instruments
Osney Mead
Oxford OX2 0DX, England
Telephone +44 (0) 1865 269500 Fax +44 (0) 1865 269501

UNIVERSITY OF CALIFORNIA, DAVIS

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO SANTA BARBARA • SANTA CRUZ

UCD NMR FACILITY DAVIS, CALIFORNIA 95616

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

1/5/96
(received 1/12/96)

E-coupler Thermal Problems

Dear Barry,

We recently have had problems with the proton RF amplifier (A.K.A. the e-coupler) on our Bruker AMX-400. The symptoms were that when running a 1-3-3-1 sequence with a recycle time of 0.25 sec, we experienced a significant power drop. This was evident from the power meter on the console and a lengthening of 90° pulse. The power drop would occur gradually over time. After helpful consultation with Bruker and replacing the e-coupler twice we decided the problem was a thermal problem and installed Bruker's fan upgrade on the e-coupler. This seemed to help a bit but did not cure the problem.

At that point we sent a message to AMMRL asking for suggestions. The responses indicated two common problems with the e-coupler. One was a thermal problem and the other was that the capacitors on the power supply would not fully recharge before the next pulse when run at high duty cycles. We checked the droop on the 28 volt power supply and it was negligible. This was not too surprising since we run at only a 0.1% duty cycle. To test the thermal aspect, we pulled the e-coupler out of the cabinet, hooked it up with extension cables, and mounted 3 fans on it. This has taken care of the problem -- albeit barely. Concerned about dust, we mounted standard AC filter material above the fans. This apparently cut the air flow just enough for the problem to reappear. This is definitely a heat problem and we suspect the power transistors are not adequately heat sunk.

Our solution for the time being is to leave the e-coupler out on the floor. This is not entirely satisfactory -- not only for aesthetic reasons -- but also because even in this configuration, it is just barely thermally stable. Moreover, one of the extension cables is the wiring harness with the in line break-out box. Thus, the next time there's a problem, it is unavailable for diagnostics without a great deal of rearrangement. Alternatives include 1) going to great lengths to properly heat sink the transistors, 2) replace the transistors with others that have better thermal characteristics (i.e. mil-spec.), or 3) replace the e-coupler with another RF amplifier. The first and third have been successfully done by other people. We may try one of these eventually but 1) is time intensive and 3) will cost about $1500.00.

In conclusion, the problem was a thermal one as Bruker suggested. We suspect that the power transistors on the e-coupler are not adequately heat sunk. The symptoms include a reading of less than 50 watts of power on the panel meter even when full power is selected. We have had enough problems with this that we thought others might benefit from our experience. Please credit this contribution to Gerd La Mar's account.

Sincerely,

Jeffrey H. Walton

Jeffrey S. de Ropp

OKLAHOMA STATE UNIVERSITY

OSU

College of Arts and Sciences
Department of Chemistry
107 Physical Sciences
Stillwater, Oklahoma 74078-3071
405-744-5920
FAX 405-744-6007

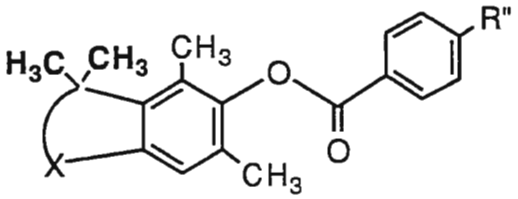
12/18/95
(received 12/26/95)

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

SHORT TITLE: Rotational barrier to a Ar'OC(O)Ar group in hindered esters

Dear Dr. Shapiro:

Your note arrived recently regarding a need for a contribution from us to the NMR Newsletter. Our XL-400 was down for repairs for a fair amount of time during this year, and more people are now using this single instrument which we currently have operational in the Department. Thus, our time on the spectrometer has been reduced. However, we have been examining the energy barrier for rotation around the Ar'-OC(O)Ar bond in hindered esters of the type as shown below in the general formula. The equation utilized for the calculation of the energy barrier was $\Delta G^* = 4.58\ T_c\ [9.97 + \log (T_c/\Delta\nu)]$ (J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill Company, New York, 1959).



ΔG^* = 15.9-16.1 kcal/mole

This system is especially easy to follow since the individual signals for the methyl protons in boldface are clearly visible at 26 °C but merge suddenly between 26 °C and 27 °C. Thus, the ΔG^* ranged from 15.7 and 16.1 kcal/mole. Alternatively, the signals for the methyl groups on the ring attached to the oxygen atom remain unchanged at this temperature. Indeed, the environment around the ArC(O)O- group appears to of such a nature that these methyl groups "ortho" to the Ar'-O bond remain nonequivalent up to 50 °C. However, these methyl groups may influence the Ar'-O energy barrier considerably. We have not as yet examined spectra at higher temperatures since we anticipate that chemical degradation may occur. The size of the ring holding the boldface methyl groups, as well as the nature of X, may also influence the barrier and remains to be assessed.

We have treated the system above as a simple two-site exchange, but this may not be valid and may give a ΔG^* which could be low. Thus, a full NMR temperature analysis may be required. Work is continuing in this area.

We trust that this will serve as our contribution to the NMR Newsletter. Best regards.

Sincerely yours,

Darrell

K. Darrell Berlin
Regents Professor

Model 3445/3446 Amplifiers from AMT

10-130 MHz Bandwidth

1000 and 2000 watt Models available

For High Performance NMR/NMRI Applications

Your NMR/NMRI requirements are pushing the leading edge of science and you need AMT RF power technology! The 3446 and 3445 operate from 10-130 MHz and are rated at 1000 watts for low field NMR and up to 2000 watts for NMRI applications up to 3 Tesla. AMT has brought together the highest possible RF performance at a most cost effective price. Nobody builds a better NMR/NMRI amplifier than AMT...

Additional Features Include:

- 10-130 MHz bandwidth for use in systems up to 3T
- Up to 2000 watts of power for imaging
- CW power capability for decoupling
- Blanking delay time >1 µs for multi-pulse

AMT

3080 Enterprise Street ■ Brea, CA 925621 ■ (714) 993-0802 ■ Fax (714) 993-1619

Models 3445/3446

10-130 MHz, pulsed, solid-state, RF power amplifier systems

Key Specifications:

Models:	3445	3446
Frequency range	10-130 MHz	10-130 MHz
Pulse power (min.) into 50 ohms	2000 W	1000 W
CW power (max.) into 50 ohms	200 W	100 W
Linearity (±1 dB to 30 dB down from rated power)	1500 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. 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 2. Input overdrive 3. Over duty cycle/pulse width 4. Over temperature	

Supplemental Characteristics:

Indicators, front panel	1. AC power on 2. CW mode	4. Overdrive 5. Over pulse width	6. Over duty cycle 7. LCD peak power meter
System monitors	1. Forward/Reflected RF power 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
Size (HWL, inches)	8.75 x 19 x 24	8.75 x 19 x 24
Net weight	110 lbs.	75 lbs.

Other members of AMT's NMR/NMRI Family:

3205/3200
6-220 MHz, 300/1000 W

3304/3303
30-310 MHz, 400/700 W

PowerMaxx™ series
25-175 MHz, 4kW/7 kW

3137/3135/3134
200-500 MHz, 50/150/300 W

AMT

FOR ADDITIONAL INFORMATION , PLEASE CALL:

AMT United States	Gigatron Associates Canada	Dressler Germany, Switzerland	JEOL Trading Co. Japan	Goss Scientific Instruments United Kingdom, France, Benelux
Ph: (714) 993-0802 Fx: (714) 993-1619	Ph: (613) 225-4090 Fx: (613) 225-4592	Ph: 49 2402 71091 Fx: 49 2402 71095	Ph: 81 3 3342 1921 Fx: 81 3 3342 1944	Ph: 44 1245 478441 Fx: 44 1245 473272

3080 Enterprise Street ■ Brea, CA 925621 ■ (714) 993-0802 ■ Fax (714) 993-1619

TEXAS A&M UNIVERSITY
Department of Chemistry
College Station, Texas 77843-3255
(409) 845-2011
FAX (409) 845-4719

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

January 2, 1996
(received 1/20/96)

VnmrX Plotter/Printer Definitions under Solaris 2.4

Dear Barry:

I have just finished installing Solaris 2.4 and VnmrX 5.1 as the operating environment for all of our UNIX-based spectrometer systems and workstations. In the process, I came to realize that the standard Varian procedure for defining printer and plotter devices is rather cumbersome, redundant, and rather unwieldly to manage and modify. This is especially true for laser jet type devices, which may be defined with as many as 8 different aliases for the same device, what with different resolutions, rotatations, and formats. Defining multiple names for the same device under SunOs was simply a matter of listing the various names in the /etc/printcap table. This is no longer true under Solaris 2.x, which does not use printcap, but requires that each device be explicitly defined, with its own spool and protocol.

My solution to this was to define a single, generic plotter entry for the device and then to modify the Varian-supplied vnmrplot script to translate the names defined in the devicenames table to the generic plotter name. In this way, VnmrX has its full complement of logical device names, but Solaris only sees the one generic name. Specifically, I have defined under Solaris a plotter named LaserJet4_plt that is physically connected to a LaserJet 4M printer. I have created a plotter.equiv file which contains the line (all one long line):

```
LaserJet4_plt laserjet4_150 laserjet4_150R laserjet4_300 laserjet4_300R laserjet4_600
laserjet4_600R laserjet4_PS laserjet4_PS_R
```

The first entry is the Solaris plotter name, which may also be a logical name, and all of the remaining entries are logical plotter names defined in the /vnmr/devicenames file. The /vnmr/bin/vnmrplot script is modified to include a line:

```
printer=`grep $1 /vnmr/plotter.equiv | awk "{print $1}" `
```

All subsequent references to $1 are replaced with $printer, and additionally a test is made to verify that $printer is not null. If it is, it is defined to be $1, supplying no translation of plotter names.

This same technique can also be applied to printer devices, making the same changes in vnmrprint script and creating a printer.equiv file. I have defined LaserJet4_prn as a printer device and aliased all of the plotter names to it so that any of the valid names can be used for either plotting or printing, even though the different resolutions and orientations will not affect the output.

Complete, modified copies of vnmrprint and vnmrplot (as plot_equiv.tar.Z), along with sample plotter.equiv and printer.equiv files, have been submitted to the user library at Varian. Those versed in writing and modifying bourne shell scripts can implement this technique immediately. Those loading the scripts from the userlib need only edit the plotter.equiv and printer.equiv files to have a functioning system.

Administering a number of different plotter devices, especially networked devices on different machines, is tremendously simplified by having an aliasing mechanism such as this. Even for plotters such as the HP7550, that may not have multiple names, it is possible to map the logical name of HP7550 to one of several physical devices, as long as they are all defined under Solaris. I can define output to go to a different plotter device when the normal device is down for repair or being 'borrowed' elsewhere.

Sincerely,

Steve Silber

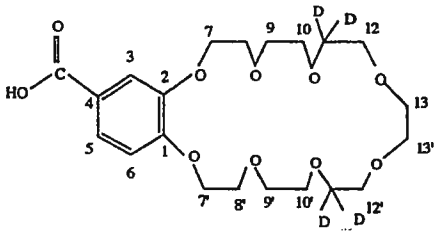
Carleton University
Ottawa, Canada K1S 5B6

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

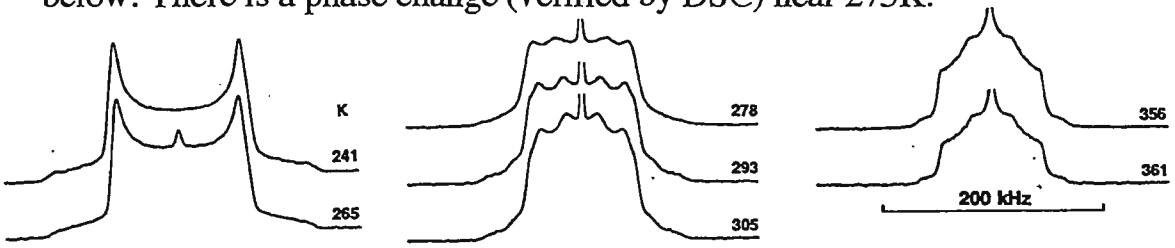
Dec. 12,1995
(received 1/4/96)

Title: Large Amplitude Molecular Motion in Solid 4-Carboxy- Benzo-24-Crown-8

The first hint of the title phenomenon was observed in the dipolar dephased ^{13}C CPMAS spectrum which showed considerable residual intensity in the CH_2-O region. Subsequently we prepared two selectively deuterated d4 derivatives,one of whose structure is shown below.



Some of the ^{2}H solid state spectra as a function of temperature are presented below. There is a phase change (verified by DSC) near 273K.



Despite the lack of symmetry of these molecules, the spectra can be nicely simulated using a simple 2 site model with 2-fold flips of the CD_2 groups.

Unfortunately no X-ray crystal data are available as yet. If our model is correct, however, it would suggest in the crystal that the molecule may possess a mirror plane, perhaps that defined by the aromatic ring.

The motional type here is similar to that which we have previously reported for solid 18-crown-6 and 12-crown-4 complexes [1,2].

1. C.I. Ratcliffe, J.A. Ripmeester, G. W. Buchanan and J.K. Denike. J.Am. Chem. Soc. 114, 3294 (1992).
2. C.I. Ratcliffe, G.W. Buchanan and J.K. Denike. J.A.C.S. 117, 2900 (1995).

G.W. Buchanan, Professor of Chemistry

Department of Chemistry ☐ Steacie Building ☐ (613) 788-3841
Department FAX (613) 788-3749

Otsuka Electronics

GOOD CONVERSATION, GREAT PRODUCTS

CRAB GRAB

WINE

NMR SPECTRA

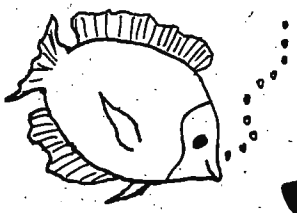
SPINSIGHT™ SOFTWARE

CMX INFINITY

SOLUTION STATE NMR

BEACH

ENC 1996



Asilomar

See us in Scripps

SOLID STATE NMR

BEER

FAREWELL TO ASILOMAR

HARDWARE

SAND AND SEA

GIFTS

PROBES

CHEMAGNETICS™

UNIVERSITY OF LEICESTER

P O BOX 138 · MEDICAL SCIENCES BUILDING
UNIVERSITY ROAD · LEICESTER LE1 9HN

BIOLOGICAL
N M R CENTRE

DIRECTOR

Professor G C K ROBERTS
0116 252 5533
(Direct Line)

FACSIMILE
0116 252 3995

MANAGER

Dr L Y LIAN
0116 252 3055
(Direct Line)

0116 252 2522
(Switchboard)

TELEX
347250 LEICUN G

8/1/96

(received 1/16/96)

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

Dear Dr. Shapiro,

8mm Triple Resonance Gradient Probehead

Many proteins are unstable at concentrations greater than 0.5mM and temperatures above about 10°C, these temperature being chosen as a compromise between the linewidths and the stability limits of the protein. In order that these unstable proteins could be studied, we explored the possibility increasing the sensitivity of the NMR spectrum of dilute samples; one solution was to use an 8mM probehead. With about a three fold increase in volume, one would expect the sensitivity increase in the order of nearly two. We tested the probehead for water suppression, particularly by gradients, for sensitivity improvements and other qualities such as ease of shimming. We used samples of protein at 0.5mM concentrations, up to 200mM NaCl, 50mM phosphate, and at 20-25°C.

While the probehead was relatively easy to shim, with lineshapes comparable to the 5mm probehead, the gain in sensitivity and the lengths of pulsewidths were disappointing. Compared with the 5mm triple resonance (^{1}H, ^{13}C, ^{15}N) gradient probehead, the 90 degree proton pulsewidth was 15us at approximately 30 watts (compared with 6us at approx. 16 watts for a 5mm probehead); for the ^{15}N pulsewidth, we obtained 53us at full power (compared with 35us at approx. 180 watts for a 5mm probehead). The power levels were chosen to avoid putting excessive amount of power into the probehead. There was also no apparent gain in sensitivity in the spectrum obtained using the 8mm probehead when compared with the 5mm one. Furthemore, there was an increase in the amount of radiation damping in the spectrum obtained with gradient water suppression.

In summary we have yet to find convincing arguments for using an 8mm proton-detection probehead in preference to a 5mm one. As far as studying unstable large proteins are concerned, other methods will have to be found to improve the spectral quality in order to make these studies feasible.

Please credit this contribution to the subsription of Gordon Roberts.

Yours sincerely,

Lu-Yun Lian.

SINTEF
UNIMED

SINTEF UNIMED

Address:
N-7034 Trondheim, NORWAY
Location:
Olav Kyrresgt. 3

Telephone:
+47 73 59 70 62
Fax:
+47 73 59 10 05
Telex:
55 620 sintf n

Enterprise No.: 948007029

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

Your ref.:	Our ref.:	Direct line:	Trondheim,
Title :		(47) 7359 8763	1996-01-17
NMR in Norway			(received 1/24/96)

Dear Barry,

For my first contribution to, yet another, subscription, a few words about the state of NMR in Norway and SINTEF might be in order. While SINTEF is Scandinavia's largest independent contract research organization (with about 2000 employees) and now comprising about nine sections or research institutes, we have significant interactions with both the industrial and academic communities, including having a large number of students working on advanced degrees. The MR Centre itself is a subset of the SINTEF UNIMED research institute and is involved with everything from whole body imaging services at the Regional Hospital in Trondheim to sophisticated ultrasound and CT studies.

As part of a government decision (about two years ago) to specifically fund / upgrade virtually all NMR equipment and facilities in the country (eventually involving the purchase and upgrading of more than a dozen instruments), we have now found ourselves in possession of a serious number of new toys. At the moment, these include: Bruker : DRX600, DRX500, DMX200 (solids, liquids, microimaging, diffusion - equipped), and DBX100 imaging system; Resonance Instruments : 10-30 MHz imaging system (40 cm bore superconducting magnet), and 2 MHz benchtop system; and a Picker 1.5T whole body imaging system to be delivered next month. In addition we currently have two Phillips whole body imaging systems already in place, although one is about to be retired (to a museum in Oslo I think).

The low field instruments are used mainly for petrophysical related projects (in conjunction with the CT and in situations where relaxation properties can, of course, be used to advantage in comparison to high field instrumentation). The low and intermediate fields are also used for a diverse number of projects including: imaging of food, salmon, cattle feed, clothing, shoes, time release drugs / pharmaceuticals, plastics - and solid state NMR measurements of many of the same materials. Metabolism studies, cardiac, stroke / drug, and epilepsy research projects combine both whole body imaging and high field spectroscopic capabilities. The high field instrumentation is primarily used for protein and molecular modeling studies. Now that things are starting to settle down we can begin to contribute regularly to the scientific content of the Newsletter! (Although the weather here, even in winter, is surprisingly mild, at least for a transplanted Canadian, there is only one 9 hole golf course within several hundred km of us...)

Sincerely,

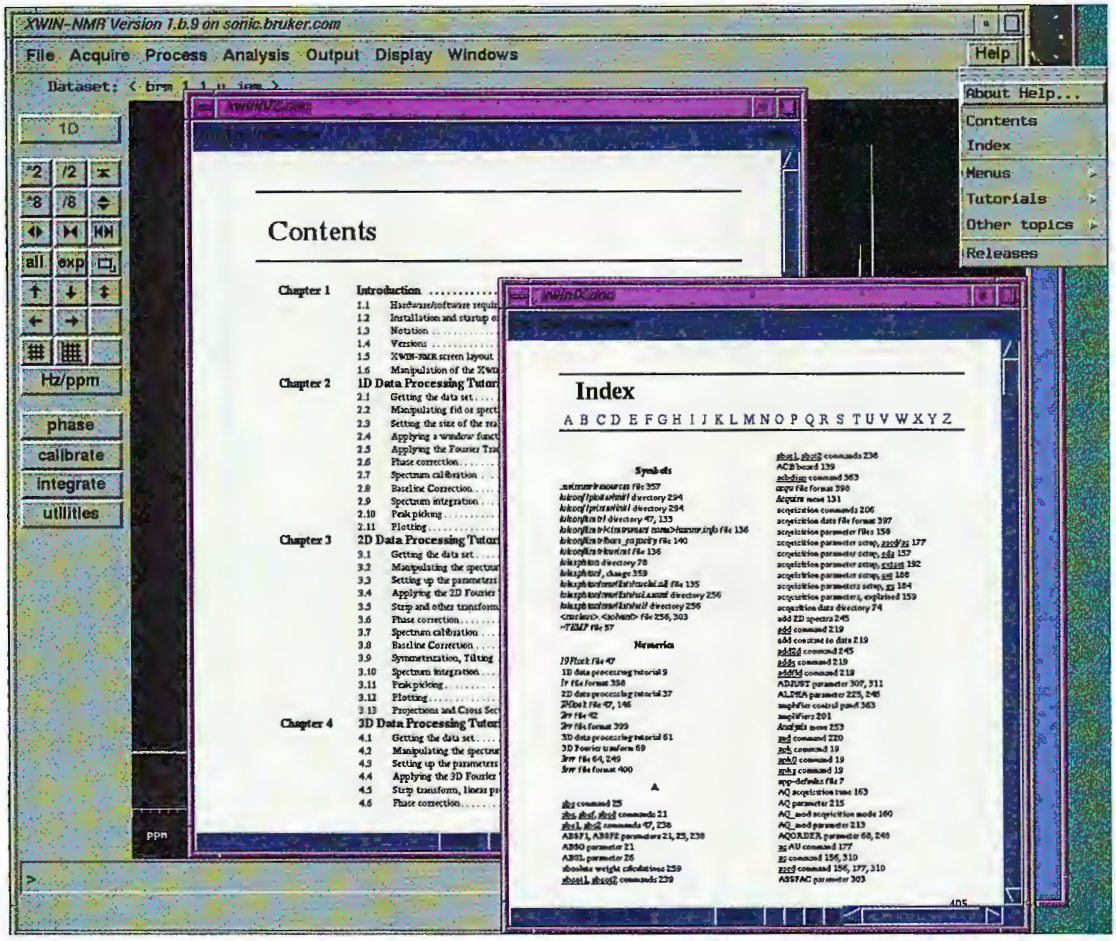
Dave Axelson

The NMR ~~Re~~evolution advances...

BRUKER

XWIN-NMR™ Software:

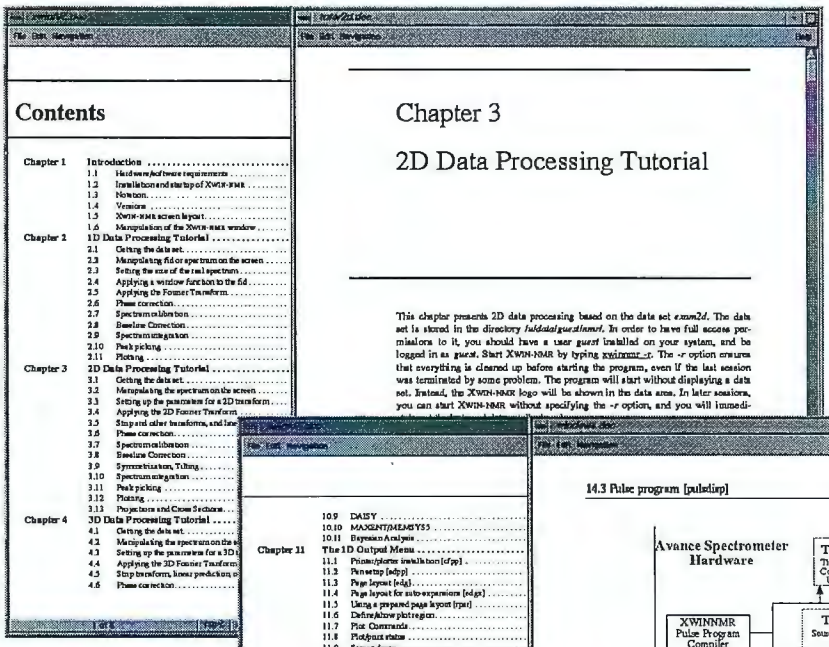
On-line help is just a click away!



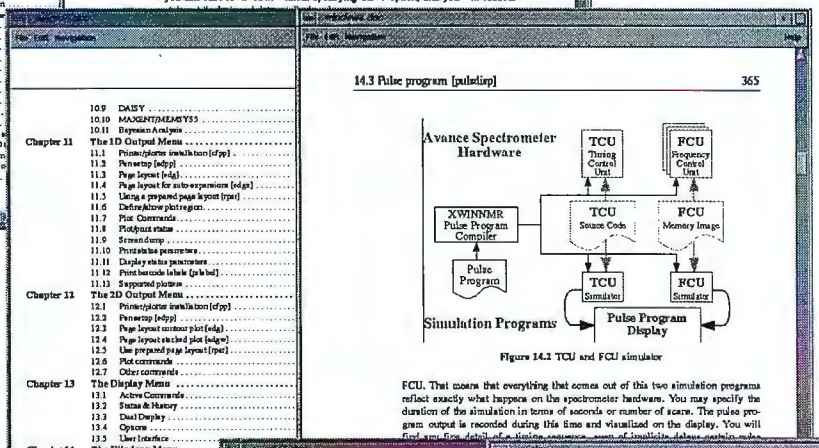
Bruker's new NMR software package, *XWIN-NMR™*, comes complete with an **on-line** manual. *XWIN-NMR™* uses the Frame-Viewer utility to display the manual. Additionally, the table of contents and a keyword index for the manual are organized as hypertext for fast display of a desired item. Now "help" is just a click away!

BRUKER

...The NMR ~~Re~~evolution advances

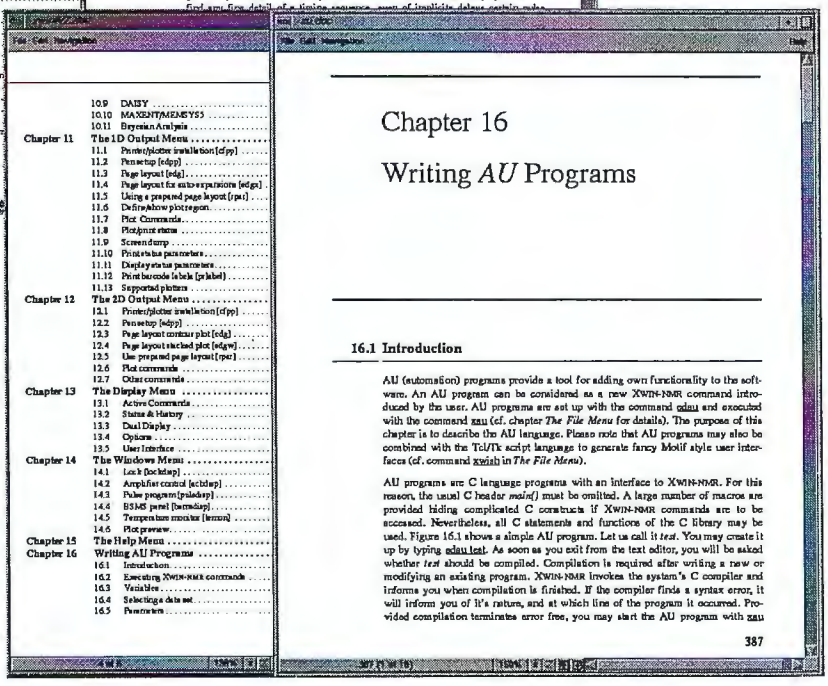


Here are some pages from the on-line manual, showing the Table of Contents that was used to find the page.



Top: Shows the tutorial help available with *XWIN-NMR*™ for 2D processing.

Middle: Explains functionality of the pulse program display software.



Bottom: Explains the fundamentals of writing and using AU programs.

For more information on *XWIN-NMR*™ software and our other new products, contact your local sales representative.

See us on the WEB at http://www.bruker.com

CENTRO DE INVESTIGACION Y DE ESTUDIOS AVANZADOS DEL I.P.N.

Departamento de Química
Apartado 14-740
México, D.F. 07000

Tel: (525) 747-7112
Fax: (525) 747-7002
(525) 747-7113

January 10, 1996

(received 1/22/96)

Dr. Bernard L. Shapiro
Editor/Publisher
The NMR Newsletter
900 Elsinore Ct.
Palo Alto, CA 94303 USA

Additivity of long-range isotope effects in N-methylindole

Dear Professor Shapiro:

We are currently studying isotope effects on the carbon-13 shielding in indoles[1]. In this letter, we describe the deuterium isotope effects on the ^{13}C shielding $^{n}\Delta^{13}C(^{2}H)$ in N-methyl-d_1, d_2 and d_3-indoles (**1-3**).

The deuterium isotope effects measured from isotopomeric mixtures (ratio $^{2}H/^{1}H$ 4:1) in DMSO-d_6 solutions are collected in the Table. Negative sign denotes upfield deuterium induced ^{13}C chemical shift. All $^{n}\Delta^{13}C(^{2}H)$ are given in ppb (10^{-9}).

Within the limits of accuracy of the measurements, the values of the $^{1}\Delta$ and $^{3}\Delta$ to $^{6}\Delta$ deuterium isotope effects are proportional to the number of replaced isotopes, and led to the following averages $^{1}\Delta$ = -231.8, $^{3}\Delta$ = -12.5 and $^{4}\Delta$, $^{5}\Delta$ and $^{6}\Delta$ = -4.8 ppb per deuterium atom. An example of the measurement is given in the Figure in which, for effects through one bond, the appearance of the CD_3 carbon signal is a 1:3:6:7:6:3:1 septet, shifted 52.5 Hz (at 75.5 MHz) upfield of the unlabeled carbon, which in turn appears as a 1:3:3:1 quartet (J = 138.5 Hz), whereas, the CHD_2 and CH_2D carbons are shifted upfield 34.9 and 17.5 Hz, and appear as a clear double quintet and as a triple triplet, respectively.

Table. Isotope effects on $^{n}\Delta^{13}C(^{2}H)$ in **1-3**.

	$^{1}\Delta$	$^{3}\Delta$		$^{4}\Delta$			$^{5}\Delta$		$^{6}\Delta$
	Me	C2	C7a	C3	C3a	C7	C4	C6	C5
1	-231.8	-12.5	a	-5.0	b	-	b	-4.8	-4.7
2	-462.3	-25.2	a	-9.8	b	-	b	-10.3	-9.3
3	-695.4	-37.7	a	-14.4	b	-	4.8	-15.3	-13.9

a: broad
b: below the magnet resolution (0.2 Hz)

The measured carbon-deuterium coupling constants $^{1}J^{13}C(^{2}H)$ = 21.3 Hz and $^{3}J^{13}C2(^{2}H)$ = 0.51 Hz, based on the equation $J(XH) = (\gamma_H/\gamma_D)\, J(XD)$ with γ_H/γ_D = 6.5144, are in general agreement with the literature data for benzene-d_1[2].

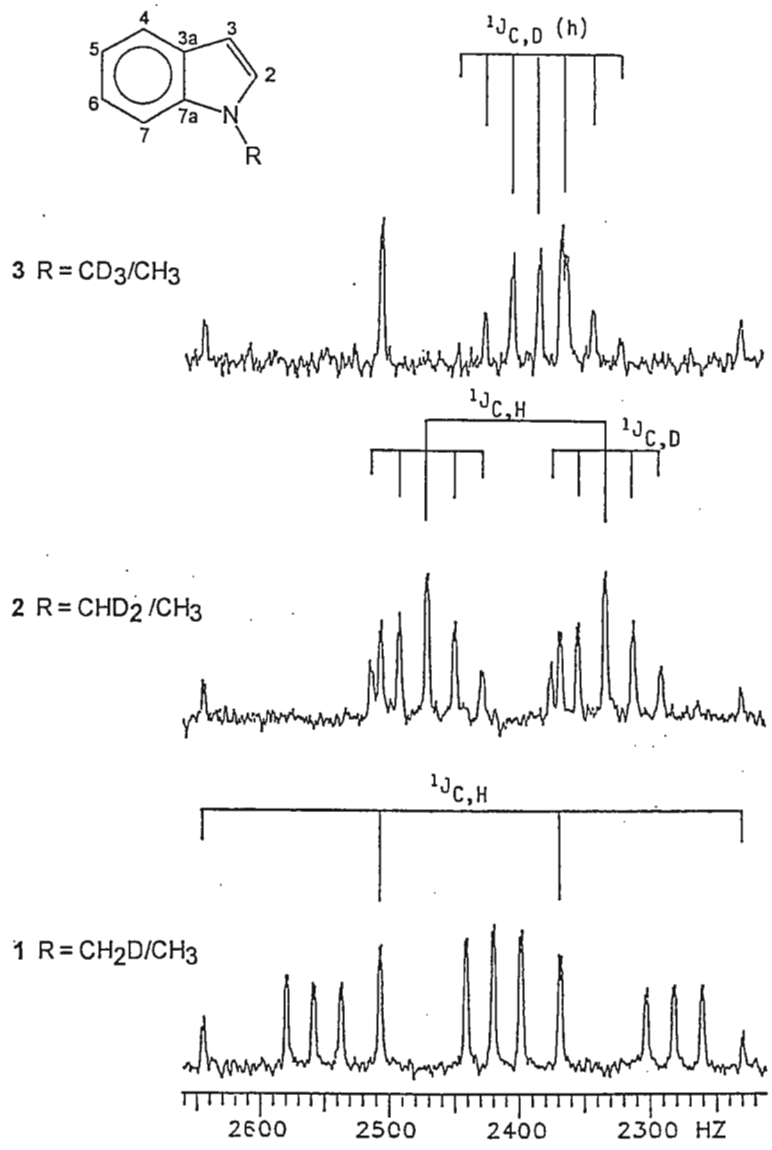


Figure. The 75.5 MHz proton coupled ^{13}C NMR signals of the N-methyl group in a mixture of isotopomeric N-methylindoles.

(1).P. Joseph-Nathan, R.E. del Río and M.S. Morales-Ríos, Heterocycles **27**, 377 (1988); M.S. Morales-Ríos, R.E. del Río and P. Joseph-Nathan, Magn. Reson. Chem. **26**, 552 (1988); M.S. Morales-Ríos and P. Joseph-Nathan, Magn. Reson. Chem. **29**, 893 (1991).

(2) H. Günther, H. Seel and M.E. Günther, Org. Magn. Reson. **11**, 97 (1978).

Sincerely yours,

Martha S. Morales-Ríos

Pedro Joseph-Nathan

NEW FOR 1996

1996 Stable Isotopes

Whether you are involved in the multistep synthesis of labelled compounds or simply in need of deuterated solvents for NMR studies, we are sure that this catalog will fulfill your research needs. Contact an Aldrich Representative for a FREE copy.

We are pleased to provide you with the 1996 Stable Isotopes catalog which features:

- **Nearly 600 products** including ^{2}H, ^{12}C, ^{13}C, ^{15}N, ^{10}B, and ^{6}Li products
- Nearly **100 new listings** used in important areas such as:
  - NMR spectroscopy
  - Polymer research
  - Environmental studies
  - Agrochemical research
  - Labelled protein and nucleic acid synthesis
  - ^{13}C breath tests
  - ^{10}B-NCT (Neutron Capture Therapy)
- Custom synthesis
- Individualized pages for deuterated NMR solvents
- Separate sections for deuterated products and other isotope products

chemists helping chemists in research and industry

Aldrich Chemical Company, Inc.

P.O. Box 355, Milwaukee, WI 53201 USA

Telephone (414) 273-3850 • 800-558-9160 FAX (414) 273-4979 • 800-962-9591

Products for LC-NMR

Techniques employed for the detection of compounds separated by HPLC have traditionally included refractive index, UV, fluorescence, IR, and mass spectroscopy. Despite the non-invasive nature and wealth of information obtainable from NMR spectroscopy, this technique was not utilized as a detection method until recently.[1] Advances in NMR instrumentation (i.e., improved sensitivity, increased solvent peak suppression, and increased lock stability) have resulted in the increased use of this technique.[2] It has found utility in the characterization of drug metabolites,[3] of impurities in drug substances,[4] in studies of reaction pathways,[5] and in other applications.[6]

As researchers discover the usefulness of this technique, they are sure to find many more applications for the detection of minute quantities of components contained in natural or synthetic mixtures such as body fluids, plant extracts, or molecular weight distributions in polymers.

Aldrich offers deuterated and protonated HPLC grade solvents, buffers, and related products for research in this area. Additionally, use of modern manufacturing methods allows us to economically manufacture large quantities of deuterated solvents. Talk to us about your product needs. You'll be glad you did!

References: (1) Dorn, H.C. *Anal. Chem.* **1984**, *56*, 747A. (2) For recent reviews, see: (a) Hofmann, M. et al. *LaborPraxis Med.* **1993**, *17*, 36. (b) Braumann, U. et al. *GIT Fachz. Lab.* **1994**, *38*, 77. (c) Spraul, M. et al. *Anal. Proc.* **1993**, *30*, 390. (d) Spraul, M. et al. *Bruker Rep.* **1990**, 12. (3)(a) Seddon, M.J. et al. *J. Pharm. Biomed. Anal.* **1994**, *12*, 419. (b) Spraul, M. et al. *Methodol. Surv. Bioanal. Drugs* **1994**, *23*, 21. (c) Spraul, M. et al. *Anal. Chem.* **1993**, *65*, 327. (d) Spraul, M. et al. *J. Pharm. Biomed. Anal.* **1993**, *11*, 1009. (e) Wilson, I.D. et al. *J. Chromat.* **1993**, *617*, 324. (f) Spraul, M. et al. *J. Pharm. Biomed. Anal.* **1992**, *10*, 601. (4) Roberts, J.K.; Smith, R.J. *J. Chromat. A* **1994**, *677*, 385. (5) Johnson, S. et al. *J. Chem. Soc., Perkin Trans. 1* **1994**, 1499. (6) Albert, K. et al. *Anal. Chem.* **1989**, *61*, 772. Also see references 2-12 from reference 1d.

chemists helping chemists in research & industry

Aldrich Chemical Co., Inc.

P.O. Box 355, Milwaukee, WI 53201 USA
Phone (414) 273-3850 • 800-558-9160
FAX (414) 273-4979 • 800-962-9591

Deuterated NMR Solvents

15,180-7 Acetonitrile-d_3, 99.6 atom % D
5g $16.15; 10g $30.70; 25g $72.80; 50g $126.10; 10 x 10g $273.00

15,194-7 Methyl-d_3 alcohol-*d*, 99.8 atom % D
1g $10.25; 5g $35.00; 10g $57.95; 50g $248.85

15,188-2 Deuterium oxide, 99.9 atom % D
25g $18.90; 100g $51.80; 250g $115.00; 10 x 100g $450.00; 1kg $406.00

18,641-4 Ethyl-d_5 alcohol-*d*, anhydrous, 99+ atom % D
1g $27.40; 5g $90.45

HPLC Grade Deuterated NMR Solvents

Note: Chemical purity of these products is equal to or better than the HPLC grade, protonated solvents. The percent purity assigned represents deuterium content.

44,947-4 Acetonitrile-d_3, 95+ atom % D
100mL $185.00; 1L $1350.00

43,577-5 Deuterium oxide, 90 atom % D
25g $17.50; 100g $49.00

43,578-3 Deuterium oxide, 10 atom % D **100g $7.50**

44,946-6 Methyl-d_3 alcohol-*d*, 95+ atom % D
100mL $300.00; 1L $2150.00

HPLC Grade Protonated Solvents

27,071-7 Acetonitrile, 99.9+% **100mL $18.10; 1L $34.55; 2L $51.90; 6 x 1L $159.00; 4 x 2L $156.00; 4 x 4L $283.40; 18L $262.50**

27,037-7 Toluene, 99.8%, HPLC Grade **100mL $14.10; 1L $18.40; 2L $27.65; 6 x 1L $84.60; 4 x 2L $82.80; 4 x 4L $134.40**

27,047-4 Methyl alcohol, 99.9+%, ACS HPLC grade
100mL $14.20; 1L $18.70; 2L $28.05; 6 x 1L $85.80; 4 x 2L $84.00; 4 x 4L $128.20; 18L $110.25

27,074-1 Ethyl alcohol, reagent, denatured, HPLC grade **100mL $15.05; 1L $22.30; 2L $33.40; 6 x 1L $102.90; 4 x 2L $100.40; 4 x 4L $158.40**

Buffers

32,991-6 Potassium dideuteriumphosphate, 98 atom % D **1g $28.00; 10g $199.00**

22,980-6 Potassium dihydrogenphosphate, 99.99% **25g $50.35; 250g $385.85**

22,131-7 Potassium hydrogenphosphate trihydrate, 99+% **25g $11.90; 500g $36.50; 12 x 500g $253.20**

34,044-8 Potassium deuteriumphosphate, 98 atom % D **1g $22.70; 10g $164.00**

THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
AT DALLAS

Department of Radiology
The Mary Nell and Ralph B. Rogers
Magnetic Resonance Center

Southwestern Medical School
Southwestern Graduate School
of Biomedical Sciences
Southwestern Allied Health Sciences School

December 18, 1995
(received 12/21/95)

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

Early Days of NMR at Mobil in Dallas

Dear Barry,

In the early 1950's, farsighted individuals in Mobil Corporation had keen interests in applications of NMR to industrial research. This interest started in the Field Research Laboratory (FRL) of Magnolia Petroleum Company, a Mobil subsidiary in Dallas, Texas. Apparently, there were independent efforts in FRL to apply NMR to petroleum exploration and to production problems. In production research, Mr. Sidney M. Foulks became interested in NMR and promoted it strongly. The idea was to look inside a porous rock and measure the fluid flow paths under dynamic conditions. Sidney M. Foulks and Dr. Sam R. Faris visited Varian in late 1951 or early 1952 to look at their NMR equipment and inquire about purchasing it. Varian was surprised at this interest because they thought that only academic institutions would be interested in NMR, and they were trying to figure out how to market their products to academia. Unexpectedly, here were industrial people who wanted to buy it, with no marketing problem! Jim Shoolery was very helpful in demonstrating the equipment to them. As a result of this visit, the Laboratory manager, Dr. Dayton Clewell, signed an order for Varian NMR equipment totaling 50 to 75 thousand dollars (a huge sum in those days, especially for new technology without proven applicability). Mr. Foulks left for graduate school in late 1952, before the equipment arrived. He returned to Mobil in late 1955, with his Ph.D., and went on to other research.

The first machine to arrive was a Varian continuous wave, broad line (low resolution) spectrometer. It was the *first* commercial NMR machine. The magnet had 12-inch diameter pole faces and Serial No. 4, made in San Carlos, CA. Dr. Ted Burdine, a physicist, used the machine to study fluid flow/displacement in porous rocks. This was done by detecting proton NMR and displacing the fluid with D_2O. Apparently, the results were less than spectacular, because of the inhomogeneity of the magnet and of the difficulties in making quantitative measurements with continuous wave spectrometers. Research with this machine was discontinued and Burdine became excited about the prospect of using spin echoes to circumvent the magnetic field inhomogeneity. The second machine from Varian was a pulse spin-echo machine (Serial No. 1, made in San Carlos, CA) with a Varian 6-inch electromagnet that operated at approximately 25 MHz. According to a Varian engineer in the early 1960's, the pulse programmer was probably built by Irwin Hahn in his garage. It was the *first* commercial pulse NMR machine made in the U.S., and also the *last* that Varian built for many years. (Varian visited Herb Gutowsky in the middle 1950's to seek his advice on marketing pulse machines, but evidently they did not foresee sufficient demand to continue with pulse machines at that time. This was long before the development of Fourier Transform NMR.) The third NMR machine from Varian was a 40 MHz high resolution, continuous wave spectrometer. Parenthetically, Varian's first high resolution spectrometer (30 MHz) went to Nugent Chamberlain at Exxon in Baytown, TX. The one that Mobil got was either the second or third that Varian sold. The third, or second high resolution spectrometer, probably went to Dr. C. A. Reilly at Shell Development Company in Emeryville, CA.

The other early NMR effort at FRL was in petroleum exploration research. In the late 1940's, Russell Varian had demonstrated proton free precession in the earth's magnetic field (2 kHz Larmor frequency) and suggested the possibility of using it for well logging (NML). The idea was that, because oil is more viscous than water, oil would have shorter NMR relaxation times than water. This difference would allow measurements of the amounts of each in a rock formation and, also, the total porosity. (I do not know whether FRL people were aware of his idea.) As I mention later in this history, in the early 1950's people at several different places in the U.S. started to develop NMR well logging. The basic approach in well logging is to determine what physical measurements that can be made in the laboratory can also be made in the bore hole of an oil well. Then, after constructing the logging "tool" that makes the measurement, carry out research to determine how to extract useful information from the measurement.

At FRL, soon after Erwin L. Hahn published his 1950 paper (1) on spin echoes, Robert A. Broding, manager of the well logging group, read his article. Broding was interested in finding ways to get response from the different chemical elements in rocks to differentiate between different rocks and NMR looked like a good way to obtain response from hydrogen, using relaxation times in the analysis. He interested a young man with a Master's degree, named John O. Ely, in this work. Ely built (about 1951 or early 1952) a "breadboard" pulse NMR machine for making laboratory experiments to get proton NMR signals from liquids in rocks. This took him only about six months. With this instrument he proved that he could observe, in the laboratory, such signals from liquids in rocks at high magnetic fields and also measure the T_1 and T_2 of these protons. This was demonstrated to Dr. Clewell, manager of the Laboratory. The work was not published, for proprietary reasons. The results were encouraging and Ely and co-workers filed a patent application (2) on NMR well logging (January 19, 1952) and Mobil ordered from Varian the pulse NMR instrument mentioned above. It was delivered to Mobil in 1952 or 1953, after Ely had gone to MIT graduate school to get a Ph.D. to better carry out this NMR research (Ely died before getting his degree). John R. Zimmerman was hired by Mobil for the summer of 1953; he also had the idea of using relaxation in NMR well logging.

After summer 1953, Zimmerman returned to the University of Colorado for about six months. During this time, he considered an attractive offer from Schlumberger in Ridgefield, CT, but accepted an offer from Mobil. He assumed leadership of all the NMR research at FRL when he returned in the first half of 1954. The Varian high resolution instrument then arrived and one of his major efforts was to develop high resolution NMR for analyzing petroleum and other liquids. (Among the liquors, a certain cheap cognac had the purest form of ethanol.) Because the highest possible resolution was needed, Zimmerman worked on sample spinners and sample tubes soon after the machine arrived. With W. F. Mueller, an excellent mechanical instrument maker at Mobil, he designed several prototype spinners. They ran into materials problems because sample spinning requires a high degree of dimensional uniformity for the glass sample tubes. Also, some batches of glass gave magnetic susceptibility artifacts because of variations in glass purity. To solve these problems, he invited representatives from a glass products company in Landisville, NJ to Dallas to discuss his needs. This visit was the start of Wilmad in the NMR sample tube business. Spectral referencing was another problem, and Zimmerman worked with Wilmad in developing the coaxial tube external referencing system (3), with the reference in the thin cylindrical shell between the two tubes. (This was before the time that TMS was universally adopted as an internal sample reference.) Initially, there was much concern that intermolecular interactions between the dissolved reference and the sample might cause a shift in the Larmor frequency of an internal reference so as to render it unreliable.

In research aimed at interpreting NMR well logs, around 1953-1954 Zimmerman found from high field pulse NMR experiments that contact with a solid surface such as silica gel will greatly shorten the proton relaxation times of water and that two-component relaxation curves can be observed (because of proprietary considerations, Mobil delayed publication of this research (4) for several years). Zimmerman and Ely filed a well logging patent application (5) on May 20, 1954. Apparently, as Mobil found out later, the California group (mentioned later in this account) had also filed a patent application. The Mobil patent was granted on January 17, 1961. Litigation ensued and Mobil sold its rights to the California group for $100,000 and also agreed to help the California group fight a suit filed by Texaco that it based on a "paper" patent application. It turned out that

Mobil had filed two days before the California group. A later patent, filed by G. L. Hoehn, D. E. Woessner, and J. R. Zimmerman of Mobil on March 1, 1960, described the use of a pulse to refocus the protons and form a spin-echo to overcome the inhomogeneity in the earth's field and the deadtime of the electronics. The patent (6) was granted on August 23, 1966 and, apparently, was also bargained away to Chevron by Mobil's lawyers.

The effect of internal pore surfaces on relaxation was discovered at several other places at about the same time as at Mobil. Up until that time, it was not generally recognized that contact with a solid surface decreases the proton NMR relaxation times of water. Because the water relaxation times were spread over a wide range of values, Varian's idea to distinguish water from oil would not work. In addition, some of the relaxation times were so short that the NMR signals would be undetectable by earth's field NML, precluding even a measurement of total porosity.

In that general time frame, Bloembergen, not realizing that a surface shortens the water relaxation times, published a curve that he interpreted as showing long range forces of surfaces in liquids that affected molecular diffusion (at that time, many thought that surfaces could exert forces in liquids that extend many hundreds of angstroms). Schlumberger hired Bloembergen as a consultant because it had some general idea that NMR might be used for well logging. However, the problem of the surface relaxation effects caused Schlumberger to postpone the project.

Elsewhere, in the early 1950's Byron Jackson Tools, Inc. sponsored experiments by Varian on the feasibility of using NMR in well logging. again encountering the surface effects on relaxation. Chevron began an independent NML development even though the original objectives of measuring total rock porosity and distinguishing between oil and water could not be achieved. The idea was to exploit the effects of the rock surface on NMR relaxation. Because the surface effects cause the relaxation times to be sensitive to the local surface-to-volume ratio, information related to pore size, permeability, producible fluid, etc., would be available. The term "free fluid" was adopted for the fluid that could be observed with the earth's field NML. Because the low frequency, 2 kHz, caused the electronics to respond slowly after NMR excitation, the first 35 msec of the free induction decay was lost. Then, Chevron, Byron Jackson, and Borg Warner (which had acquired Byron Jackson) carried out cooperative tool development and made field tests in the late 1950's. D. O. Seevers did NMR research at high fields on fluids in rocks, and R. J. S. Brown did research in the earth's field and developed the earth's field NML. The Chevron work was aided by several consultants who spent extended periods at Chevron: H. C. Torrey, Jean Uebersfeld (from France), and Jan Korringa. At Shell Oil, J. D. Robinson and others did early NMR work on rocks and participated in early tests of the experimental NML tool described above.

The California logging tool had important early success in locating oil in California in wells where the oil was extremely viscous and had a T_2 that was shorter than the 35 msec dead time of the tool. Consequently, it did not give an NMR signal from the oil, but it gave a good signal from zones that would have given unwanted water production. At zones where other logging tools showed significant rock porosity, the tool indicated the oil formations by the absence of an NMR signal.

In 1958, I joined Zimmerman's group to carry out new research to understand the NMR relaxation phenomena of liquids on surfaces to support the interpretation of NMR well logs in terms of quantities useful to the log analyst. This was shortly after publication of the famous NMR exchange paper (7) by Zimmerman and Brittin in 1957 that quantitatively explained the two-component observations on silica gel in terms of exchange between sites with different relaxation times. I continued the previous research on silica gel surfaces and prepared to extend the research to clay surfaces because most of the pore surface area in sandstones is provided by extremely high surface area clays such as montmorillonite, illite, and kaolinite.

The basic philosophy was to carry out fundamental research to understand NMR relaxation phenomena in liquid water and hydrocarbons and in water at surfaces to best interpret the NMR signals from logging tools. To do this, I needed to understand relaxation phenomena of water in electrolyte solutions, of nonspherical liquid hydrocarbon molecules, and nonspherical molecules at silica and clay surfaces. This entailed much theoretical

work on anisotropically reorienting molecules in the bulk liquid and in surface layers. Experimental data were needed. To obtain data on clays, the performance of the spin echo equipment was upgraded. G. L. Hoehn did early work on improving the response of the NMR receivers. Robert A. McKay extended the work on receivers and also developed successful Q-switching NMR probes (8) to greatly decrease the deadtime. Also, I developed the idea that spin echo measurements can be used to measure restricted diffusion and that such measurements could be used to measure the average pore size in rocks; I filed a patent application on April 6, 1962 (9). During all this time, I was looking for new commercial equipment so that we could minimize our efforts in equipment development. In the early 1960's a new company (Bruker) sent us a brochure on their pulse NMR equipment. In 1963 Bruker had a booth at the Pittsburgh Conference and I asked Dr. G. Laukien about details of pulse response. Although he assured me that their equipment was the best available, it was clear that the equipment we had at Mobil was superior for our research. We continued with our in-house development and gradually replaced all of the original Varian components except the high voltage power supply for the pulse transmitter. McKay then developed the first automated pulse programmer and data acquisition system (10). Previously, the pulse intervals had to be set manually and the pulse NMR signals had to be collected by visually observing them on an oscilloscope and manually recording them. Now, the pulsing procedure was automated and the signals were automatically integrated and recorded on paper tape to be read by computer key punch operators (in those days, data and computer programs were entered on punched cards).

At the same time, John Zimmerman continued to improve NMR methods of hydrocarbon analysis. To this end, he wanted to obtain the highest magnetic field possible. He received information about a Swiss comapny, Traub-Tueber, that had a new 90 MHz high resolution spectrometer. He obtained information from them, but they would not sell their instrument in the U. S. (Traub-Tueber later became the high resolution component of Bruker). Then, Varian proposed to upgrade the 40 MHz spectrometer to 100 MHz with new electronics and new pole faces for the magnet. Mobil purchased this conversion for about $8,000. It was delivered in 1964, but Varian supplied a whole new magnet because they had found that the magnet conversion was too difficult. This was an early Varian HR-100 NMR spectrometer. Later, Varian introduced an NMR lock and marketed the HA-100 spectrometer.

Also, we realized that the NMR relaxation times of liquids in rocks at 2 kHz could be different from those obtained from high field spin echo measurements and that measurements on rocks in the earth's field were needed to calibrate them for well log interpretation. For this, in 1963-64 McKay constructed an earth's field machine for measurements on fluids in 3.5 inch diameter rock samples. He made such measurements over the next few years. In the meantime, the lackadaisical performance of the commercial NML tool and operators during field tests that I attended caused Mobil to gradually lose interest even though NMR was still deemed to be the potentially most useful tool to detect permeable zones. Also, Mobil was de-emphasizing logging tool development.

Zimmerman left Mobil for a leave of absence in 1968 and I continued high field relaxation research in preparation for an eventual successful commercial logging tool. During this period and in later years, I carried out much research on NMR relaxation phenomena in solutions and aqueous heterogeneous media. My special interest was on the effects of structure on relaxation in clays, biopolymers, and solutions. This led to occasional collaboration with biomedical researchers. All of this research was to become very useful in my biomedical research after leaving Mobil in 1992. Mobil discontinued well logging research in 1992, just when real spin-echo NMR well logging at "high" fields (1 to 2 MHz) became commercially available.

ACKNOWLEDGMENT: I wish to thank R. A. Broding, S. R. Faris, S. M. Foulks, R. A. McKay, L. E. Nelson, and J. R. Zimmerman for invaluable conversations concerning NMR at Mobil and R. J. S. Brown for his perspective of NML developments relating to Chevron.

1. E. L. Hahn, *Phys. Rev.* **80**, 580 (1950).
2. W. B. Huckabay, J. K. Godbey, and J. O. Ely, U. S. Patent No. 3,597,681.
3. J. R. Zimmerman and M. R. Foster, *J. Phys. Chem.* **61**, 282 (1957).
4. J. R. Zimmerman, B. G. Holmes, and J. A. Lasater, *J. Phys. Chem.* **60**, 1157 (1956).

5. J. R. Zimmerman and J. O. Ely, U. S. Patent No. 2,968,761.
6. G. L. Hoehn, Jr., D. E. Woessner, and J. R. Zimmerman, U. S. Patent No. 3,268,800.
7. J. R. Zimmerman and W. E. Brittin, *J. Phys. Chem.* **61**, 1328 (1957).
8. R. A. McKay and D. E. Woessner, *J. Sci. Instrum.* **43**, 838 (1966).
9. D. E. Woessner, U. S. Patent No. 3,213,355.
10. D. E. Woessner, B. S. Snowden., Jr., R. A. McKay, and E. Thomas Strom, *J. Magn. Reson.* **1**, 105 (1969).

I think that this personal historical account illustrates a different mind set than is current in America. The early days of NMR were exciting and I am glad to have been practicing NMR in those days.

Sincerely,

Don Woessner

TLI THE LOVELACE INSTITUTES

Improving Human Health through Research and Technology

4th International Conference on Magnetic Resonance Microscopy
"Heidelberg Conference in Albuquerque"
September 21-25, 1997
Preliminary Announcement

The 4th International Conference on Magnetic Resonance Microscopy will be held from September 21 to September 25, 1997, in Albuquerque, New Mexico, USA. This is a continuation of the series started in Heidelberg in 1991, with subsequent meetings in Heidelberg, again, in 1993 and Würzburg in 1995. The scientific program consists mainly of plenary lectures by experts in the field and submitted poster contributions. Attendance will be limited to 300 and there will be no parallel sessions. In addition, there will be an educational program to take place on the 20th and 21st summarizing the subjects to be covered in the conference, namely, present techniques and applications of NMR/EPR microscopy and imaging. This will be a greatly expanded session compared to the past sessions and will cover the applications of spatially resolved magnetic resonance to the study of materials, polymers, plants, biomedicine, etc. Industrial participants are especially welcome. Commercial vendors of NMR/EPR-related equipment are invited to take part in an exhibition of their products.

This is a preliminary announcement. Please see the first announcement scheduled for March, 1996 for further and final details. We plan to have a World Wide Web site with a possibility of abstract submission by internet. Inquiries about commercial displays and possible financial assistance may be directed to Eiichi Fukushima at the letterhead address.

2425 Ridgecrest Drive SE • Albuquerque, New Mexico 87108-5127 • Phone 505-262-7155 • Fax 505-262-7043

Merck Frosst Canada Inc.
C.P. 1005
Pointe-Claire – Dorval
(Québec) H9R 4P8
Téléphone: (514) 428-7920
Télécopieur: (514) 695-0693

(received 1/17/96)

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

MERCK FROSST
Centre de recherche thérapeutique

Magnetic Shielding

Dear Barry,

In the last NMR Newsletter (#447, p. 32), Kip Shaffer illustrated in a funny way the problems of having NMR magnets in environments not suited for them. Two of the most commonly occuring problems with high static magnetic field are 1) distortions of computer screens (loss of focus and altered colors) and 2) potential disturbance of the field homogenity by moving metallic objects close to or within the 5 gauss line. The most obvious solution for both problems is to keep any object, including the computer controlling the spectrometer outside of the 5 gauss line but this is often impossible to do due to space constraints. One way to circumvent this problem is to try shielding. I use the word try because there are no standard shielding receipes and trial and error must be used.

As a post-doctoral fellow with Dr. Lewis E. Kay, I encountered the first type of problem. We had a fuzzy monitor screen that could not be moved away from the 500 and 600 MHz magnets. Therefore, there was no solution other than building a shield that would channel the field around the monitor as opposed to it going through the yoke and thus altering the focus and screen colors.

The shield was simply a five faced cube (dimension of 2' x 2' x 2') made of quarter inch thick plywood covered with shielding material. Nu-metal was considered but rejected due to its very high price (about 500 CDN$) so we used M6 material (available from Siemens-BCL magnetics, Burlington, ON, Canada, phone 905-335-2530). The M6 material has a very high magnetic permeability, about 30 000X greater than air. Also, it possesses an anisotropic structure, meaning that its ability to channel magnetic field is higher in one direction than the other. The material must therefore be positioned on the box with the direction of high magnetic permeability parallel with the magnetic field (see the double arrows on Figure 1). A 2 x 3 inch (5cm x 8cm) notch was made to allow the cables to go to the computer. The dimensions were chosen to allow good ventilation but small fans can be installed if overheating inside the box is a problem. Finally, the bottom of the shield is fixed with metal screws in order to allow easy removal of the the shield for servicing purposes. The end result was perfect: an unperturbed computer screen at low cost (>200 CDN$).

At the end of last October, I started as an NMR spectroscopist at Merck Frosst Canada Inc. and one of the first projects I was involved in was another shielding problem. The research center housing the NMR facility was expanding with the addition of a third floor. The floor plan was unfortunately designed such that a corridor would be directly above a 300 MHz instrument . Before the construction of the new floor started, my supervisor and I undertook the task of shielding the area above the magnet. The 5 gauss line extended about 12 in. (30 cm) above the concrete floor over top of the instrument. Again here, we used M6 as shielding material and installed 2 layers of M6 separated by a layer of stainless steel (type 316, ~1/32" (~1mm) thick) so as to cover an area of about 9' x 9' (3m x 3 m). The idea of using two layers, according to the people at BCL-magnetics, is to pick-up whatever field the first layer could not channel with the second layer. If insufficient shielding is obtained, additional layers can be added where each layer is separated by a non-magnetic spacer (low magnetic permeability such as wood, aluminium, stainless steel, etc...). It's like putting a gutter under an overflowing gutter! The higher the "magnetic flow" the more "gutters" are needed. Trial and error is the golden rule. Ideally, one would like to encase the magnet in a barrel shaped room but this is not often possible! The type of separator depends on where the shield

will be positioned. If it's against a wall, wood is an inexpensive option, but if it's on a floor, as is the case in our situation, non-magnetic metal is more appropriate. Moreover, the shield above the 300 MHz spectrometer was to be placed within a newly poured concrete floor. In this situation, aluminium is a bad choice because it would react with the concrete causing the metal to oxidize which would lift and crack the newly poured concrete slab. For this reason, we used stainless steel that has a very low magnetic permeability of about 1. Now that the shield above the 300 magnet is installed, the field above the shield is less than the 1 gauss detection limit of our measuring device.

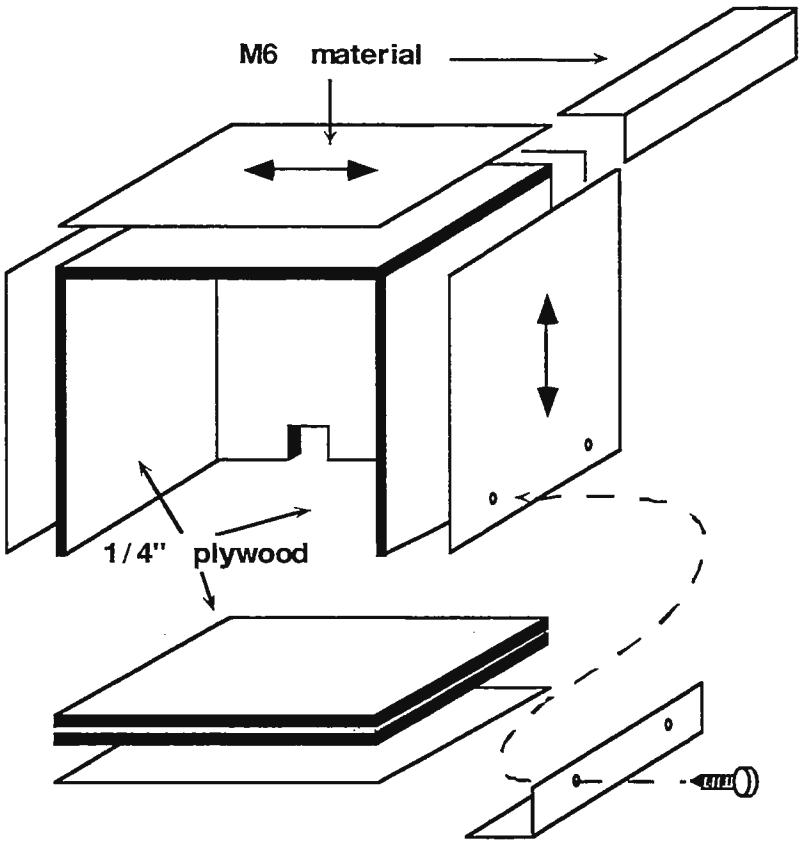


Figure 1: Exploded view of the monitor shield. The shield is made of an inner cube of plywood covered with M6 material. The dimensions for the five 1/4'' (6 mm) thick plywood parts: top is 2' x 2' (60 cm x 60 cm); left and right sides are 2' x 1'-11 3/4" (60 cm x 59.4 cm); back is 1'-11 1/2" x 1'-11 3/4" (58.8 cm x 59.4 cm) and the bottom is made of two sections of 2' x 2' (60 cm x 60 cm) glued together for better support. The top, sides and back are glued and screwed together with small blocks of wood (not shown) and then covered with M6. The M6 sheets (2' x 2' (60 cm x 60 cm)) can be epoxied to the wood but I used "pop" rivets instead. To allow a good contact between M6 sheets at the edges, 2" x 2' (5 cm x 60 cm) strips were bent to a 90° angle and riveted. This is important in order to avoid any gap between two adjacent sheets which would diminish the shielding efficiency. Finally, the bottom is covered with a sheet of M6 and 3 90° angle strips. The TOP and BOTTOM are fixed together with metal screws as shown and can be removed so as to allow servicing of the monitor.

Yours sincerely,

Yves Aubin
yves_aubin@merck.com

Laird A. Trimble
laird_trimble@merck.com

Address all Newsletter correspondence to:

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

(415) 493-5971* - *Please call only between 8:00 am and 10:00 pm, Pacific Coast time.*

Deadline Dates

No. 451 (April)	22 Mar. 1996
No. 452 (May)	26 April 1996
No. 453 (June)	24 May 1996
No. 454 (July)	28 June 1996
No. 455 (August)	26 July 1996

*Fax: (415) 493-1348, at any hour. Do not use fax for technical contributions to the Newsletter, for the received fax quality is very inadequate.

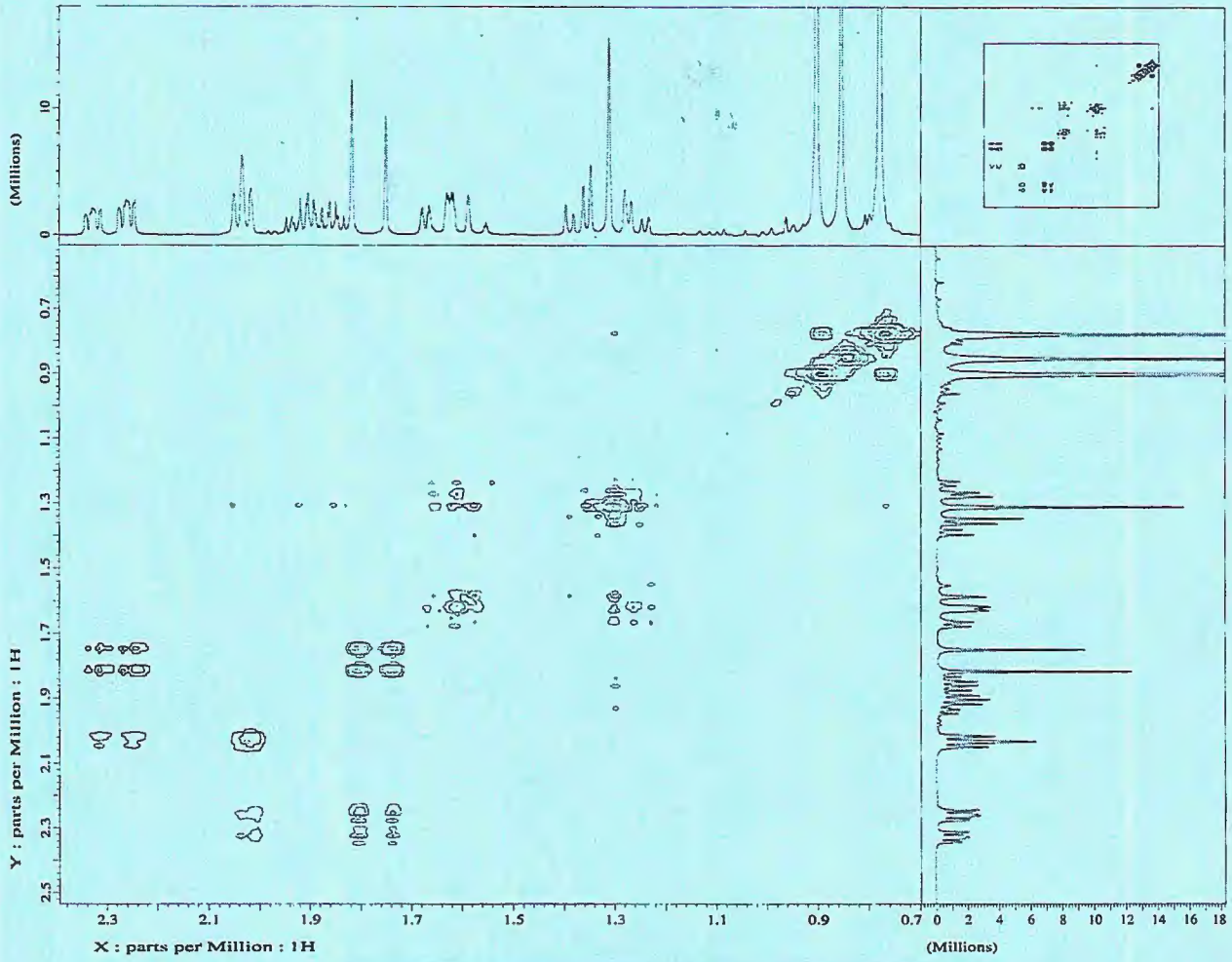
E-mail: 71441.600@compuserve.com or barry@nmrnewsletter.com.

☆ **The Newsletter's fiscal viability depends very heavily on the funds provided by our Advertisers and Sponsors. Please do whatever you can to let them know that their support is noted and appreciated.**

Mailing Label Adornment: Is Your Dot Red ?

If the mailing label on your envelope is adorned with a large **red dot**: this decoration means that you will not be mailed any more issues until a technical contribution has been received.

ECLIPSE NMR Advantage: Gradient Enhanced 2D NMR Spectroscopy



Eclipse NMR *The Better Way!*

The ECLIPSE NMR Spectrometer from JEOL USA just increased your productivity. In less than one half of the 40 minutes usually required to complete the COSY, you can be back in your laboratory with proton, carbon and the COSY data. With JEOL's new low cost Matrix Gradients, this Double Quantum Filtered COSY data was completed in less than 3 minutes. The ECLIPSE now expands the usual routine beyond the normal one dimensional proton survey spectrum to include the power of two dimensional NMR.

Now you can use the ECLIPSE NMR Advantage to your advantage.

JEOL USA, Inc.
11 Dearborn Road
Peabody, MA 01960
Tel: 508/535-5900
FAX: 508/536-2205
EMAIL: NMR@JEOL.COM

JEOL
Analytical Instruments Division
MS · NMR · ESR