TEXAS A&M UNIVERSITY

NMR NEWSLETTER

No. 350

November 1987

continued on page 54

Announcing... **AN OUTSTANDING ADDITION TO THE WILMAD NMR LINE...**

our COMPLETELY NEW 5mm "THRIFT" TUBE

at 95¢ each!

- ***INEXPENSIVE***
- ***PRACTICAL***
- ***RELIABLE***
- ***GUARANTEED***

...THE BEST POSSIBLE ANSWER FOR LOWER-END NMR SPECTROSCOPY NEEDS.

COMPARE THESE OUTSTANDING FEATURES OF OUR NEW WG-5mm-THRIFT-7 TUBE:

- **100% Wilmad inspection of structural parameters.**
- **Spinning Reliability. Passes our stringent Spinner Bearing Test which determines straightness and spinning stability using a Precision Bore Bearing just 0.002″ larger than the tube O.D. No halted data accumulations or scratched tubes. Send for your free 5mm Spinner Bearing today.**
- **Round bottom is standard. Flat bottom . . . no extra charge.**
- **Non-Pyrex compatible borosilicate glass.**
- **Packaged individually for maximum protection.**
- **Standard length is 7″. Available in 8″ and 9″ lengths. (Add 15¢ per inch.)**
- **Immediate shipment from available stock.**

The Wilmad 5mm THRIFT tube is one of the most important recent developments in NMR tube manufacture. It is not recommended for use in high resolution spectrometers, but it provides exceptional performance in lower-end spectroscopic investigations and, at the same time, retains its low cost. It is manufactured from Non-Pyrex compatible borosilicate drawn tubing and is carefully selected for size and structure. At 95¢ each, this tube is really a bargain.

In fact, it is an infinitely better bargain **in both price and quality** than the following Norell tubes: 508-UP ($4.50 each); 507-HP ($3.50 each); 506-P ($2.50 each); 505-P ($1.80 each); XR-55 ($2.00 each); and 502 (80¢ each). Our examination of numerous Norell tubes has shown that the only significant difference between them is price. They consistently fail to meet even the most liberal structural standards used to define them.

Even with our less expensive 5mm THRIFT tubes, you'll soon learn why IT PAYS TO STANDARDIZE ON WILMAD!

WILMAD GLASS COMPANY, INC.

Serving the Spectroscopic Aftermarket

Route 40 and Oak Road, Buena, NJ 08310, U.S.A.

Phone: (609) 697-3000 • TWX 510-687-8911

TEXAS A&M NMR NEWSLETTER NO. 350, NOVEMBER 1987

AUTHOR INDEX

TEXAS A&M NMR NEWSLETTER NO. 350, NOVEMBER 1987

ADVERTISER INDEX

SPONSORS OF THE TAMU NMR NEWSLETTER

Abbott Laboratories
The British Petroleum Co., Ltd. (England)
Bruker Instruments, Inc.
Cryomagnet Systems, Inc.
Eastman Kodak Company
E. I. du Pont de Nemours & Company
General Electric Company, Medical Systems Group, NMR Instruments
Intermagnetics General Corporation
JEOL (U.S.A.) Inc., Analytical Instruments Division
The Lilly Research Laboratories, Eli Lilly & Company
Millipore Corporation, Waters Chromatography Division
The Monsanto Company
The Procter & Gamble Company, Miami Valley Labs
Programmed Test Sources, Inc.
Shell Development Company
Spectroscopy Imaging Systems Corporation
Spectral Data Services, Inc.
Unilever Research
Union Carbide Corporation
Varian, Analytical Instrument Division

FORTHCOMING NMR MEETINGS

Fritz Haber International Workshop on Modern Techniques in Magnetic Resonance - Dec. 13-17, 1987; Weizman Institute of Science, Rehovot, Israel; See page 7 of Newsletter #341, February 1987, for additional information.

NMR-88 - Feb. 14-18, 1988; Thredbo Alpine Hotel, Thredbo, N.S.W. Australia. Chairman: Dr. L.R. Brown, The Australian National University. For further information, contact: Leslie Harland, Research School of Chemistry, The Australia National University, Canberra, A.C.T. 2601, Australia. Telex: AA62172. Facsimile: (61-62)-49-7817. Telephone: (61-62)-49-2863. See Newsletter 349, 20.

29th ENC (Experimental NMR Conference) - Apr. 17-21, 1988; Rochester, New York; Chairman: Professor Stanley J. Opella, Dept. of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania 19104, (215) 898-6459. For information, contact Professor Edward O. Stejskal, ENC Secretary, Dept. of Chemistry - Box 8204, North Carolina State University, Raleigh, North Carolina 27695-8204; telephone (919) 737-2998.

9th EENC (European Experimental NMR Conference) - May 16-20, 1988; Bad Aussee, Austria; For further information, write Professor H. Sterk, Karl-Franzens-Universitaet Graz, Institut fuer Organische Chemie, Heinrichstrasse 28, A-8010 Graz, Austria. See Newsletter 348, 15.

XIII Intl. Conference on Magnetic Resonance in Biological Systems - Aug. 14-19, 1988; Madison, Wisconsin. See Newsletter 349, 60.

Additional listings of meetings, etc., are invited.

All Newsletter Correspondence Should be Addressed to:

Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303 U.S.A.

(415) 493-5971

DEADLINE DATES

No. 352 (January) ---- 18 December 1987
No. 353 (February) ----- 22 January 1988
No. 354 (March) ------ 19 February 1988
No. 355 (April) --------- 18 March 1988

Advertising in the TAMU NMR Newsletter

During the past year, the companies listed below have advertised in the Newsletter.

Bishop Instruments, Inc.

Bruker Instruments, Inc.

Chemagnetics, Inc.

General Electric Company, Medical Systems Group, NMR Instruments

IBM Instruments, Inc.

JEOL (U.S.A.) Inc., Analytical Instruments Division

M-R Resources, Inc.

New Era Enterprises

New Methods Research, Inc.

NMR Concepts

Norell, Inc.

Oxford University Press

Polyflon Company

Programmed Test Sources, Inc.

Technical Computer Services

Varian Associates, Analytical Instruments Division

VCH Publishers, Inc.

Wilmad Glass Company, Inc.

The existence of the Newsletter continues to depend to a significant extent on support by our Advertisers, many of whom have been loyal, continuous supporters of the Newsletter for many years. All Newsletter subscriber/participants are, then, respectfully urged to take whatever opportunities they can find to let our Advertisers know that their efforts are appreciated. From our position, we also thank our Advertisers, and note the exceptional cooperation we have received from each and every one.

Additional advertising is solicited. Can you help?

Bernard L. Shapiro
Editor/Publisher, TAMU NMR Newsletter

TAMU NMR Newsletter

Policies and Practical Considerations

(Revised October 1987)

The TAMU NMR Newsletter (formerly the IIT NMR Newsletter, and originally the Mellon Institute NMR Newsletter) continues with the same name, under the aegis of Texas A&M University, although the undersigned Editor/Publisher has moved to California. The Newsletter, now in its thirtieth year of consecutive monthly publication, continues under the same general policies as in the past. All communication with the Newsletter must be directed to the address overleaf.

1. Policy:

The **TAMU NMR Newsletter** is a means for the rapid exchange of information among active workers in the field of nuclear magnetic resonance. As such, it will serve its purpose best if the subscriber/participants impart whatever they feel will be of interest to their colleagues, and inquire about whatever matters concern them.

Since the subscriber/participant clearly is the best judge of what he or she considers interesting, our first statement of policy is "We print anything." (This usually is followed by the mental reservation, "that won't land us in jail.") Virtually no editorial functions are performed, although on rare occasions I feel the need to classify a contribution as 'not for credit' (*v.i.*). I trust that the need for this policy is obvious.

The **TAMU NMR Newsletter** is not, and will not become, a journal. We merely reproduce and disseminate exactly what is sent in. Foreign participants should not feel obliged to render their contributions in English.

2. Public Quotation and Referencing:

Public quotation of Newsletter contents in print or in a formal talk at a meeting, etc., is expressly forbidden (except as follows), and reference to the TAMU NMR Newsletter by name in the scientific literature is never permissible. *In order to quote results or use material from the Newsletter, it is necessary, in each individual case, to obtain the prior permission of the author in question and then to refer to the material quoted as a "Private Communication".* If your copy of the Newsletter is shared with other readers, it is your obligation as the actual recipient of the Newsletter to see that these other readers of your copy are acquainted with, and abide by, these statements of policy.

3. Participation is the prime requisite for receiving the TAMU NMR Newsletter:

In order to receive the Newsletter, you must make at least occasional technical contributions to its contents.

We feel that we have to be quite rigorous in this regard, and the following schedule is in effect: Eight months after your last contribution you will receive a "Reminder" notice. If no technical contribution is then forthcoming ten months after your last contribution, you will receive an "Ultimatum" notice, and then the next issue will be your last, absent a technical contribution. Subscription fees are not refunded in such cases. If you are dropped from the mailing list, you can be reinstated by submitting a contribution, and you will receive back issues (as available) and forthcoming issues at the rate of nine per contribution.

Frequent contributions are encouraged, but no "advance credit" can be obtained for them. In cases of joint authorship, either contributor, but not both, may be credited. Please indicate to whose account credit should be given. Please note that meeting announcements, as well as "Position Available," "Equipment Wanted" (or "For Sale"), etc., notices are very welcome, but only on a not-for-credit basis, i.e., such items do not substitute for a *bona fide* technical contribution. Similar considerations must occasionally be applied to a few (quasi-)technical items as mentioned above.

continued

4. **Finances**:

The Newsletter is wholly self-supporting, and depends for its funds on advertising, donations, and individual subscriptions.

The annual fee for **Subscriptions** is currently $90.00 per year, with a 50% academic or personal discount being available. Subscriptions are available only for the twelve monthly issues which begin with the October issue and run through that of the following September. However, a subscription can be initiated at any time, and the issues back to the previous October will be provided.

Companies and other organizations are also invited to consider joining the list of **Sponsors** of the Newsletter. Sponsors' names appear in each month's Newsletter, and copies of the Newsletter are provided to all Sponsors. The continuation of this non-commerical Newsletter depends significantly on the interest and generosity of our Sponsors, most of whom have been loyal supporters of this publication for many years. We will be happy to provide further details to anyone interested.

Another major, indeed quite essential, source of funds for the Newsletter is **Advertising**. We earnestly encourage present and potential participants of the Newsletter to seek advertising from their company or institution. Our rates are very modest - please inquire for further details.

5. **Practical Considerations**:

a) All contributions to the TAMU NMR Newsletter will always be included in the next issue if received before the published deadline dates.

b) Contributions should be on the *minimum* (NOTE!!) number of 8-1/2 x 11" (21 x 27.5 cm) pages, printed on one side only. Margins should be between 2 and 3 cm on all sides. Please observe these limits. Black ink for typing, drawings, etc., is essential. We are not equipped to deal with pieces of paper larger than 8-1/2 x 11" (21 x 27.5 cm).

Please conserve space by avoiding double spacing (except where necessary), ultra-wide margins, half-filled pages, etc. In general, please plan and construct your contribution so as to fill the minimum number of pages needed. On the other hand, drawings and spectra lose both eye-appeal and utility when they are too small. Only in very rare and absolutely necessary circumstances will a contribution in excess of three pages - including drawings, figures and references - be accepted, and only with prior approval. Economic necessity requires this policy.

Since reproductions of various kinds often do not reproduce too well, contributors are urged to submit their photographic originals to us (if the size does not exceed 8 1/2 x 11"), and we will be happy to return these if requested. Such originals should be mounted in place on the 8 1/2 x 11" pages.

c) Please provide short titles of all topics of your contributions, as they will ensure accuracy in preparing the table of contents.

d) Each "Position Available," "Equipment Wanted (or Available)," or similar notice should not exceed a total size of one-half page, including addresses, etc.

e) Please do not send in manuscripts, theses, books, etc., and ask us to be your conscience in selecting what should and shouldn't go into the Newsletter.

6. **Suggestions**: They are always welcome.

B L Shapiro 10/23/87

B. L. Shapiro

Address for all correspondence: Dr. Bernard L. Shapiro
Editor/Publisher
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303
U.S.A.

Telephone: (415) 493-5971.

SCRIPPS CLINIC
AND RESEARCH FOUNDATION

10666 NORTH TORREY PINES ROAD
LA JOLLA, CALIFORNIA 92037
619455-9100

Mark Rance, Ph.D.
Assistant Member
Department of Molecular Biology
Research Institute of Scripps Clinic
10666 North Torrey Pines Road
La Jolla, California 92037

October 2, 1987 (recd 10/5/87)

Dr. Bernard L. Shapiro, Editor/Publisher
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Intramolecular Exchange Effects in Multiple Quantum Spectroscopy

Dear Dr. Shapiro:

Multiple quantum spectroscopy has become a very important tool for the assignment of proton NMR spectra of biological macromolecules. There are many advantages in using multiple quantum techniques. For example, in a 2D multiple quantum spectrum there are no diagonal peaks present (in the absence of multi-exponential relaxation effects), which facilitates the identification of nearly degenerate coupling partners. Also, the presence of so-called "remote" peaks (1) in 2D MQ spectra can be used to confirm assignments derived from the observation of "direct" peaks and to identify spins which have a common coupling partner but which are not necessarily mutually coupled.

We would like to point out some advantages of using multiple quantum techniques to study systems exhibiting exchange broadening due to chemical reorganization processes. One advantage stems from the fact that most peaks in a 2D multiple quantum spectrum have a predominantly in-phase multiplet structure in the ω_1 dimension, unlike COSY or relayed-COSY experiments which give rise to cross peaks with anti-phase multiplet structure in both dimensions. This allows some peaks to be observed in MQ spectra and not in COSY in cases where the linewidth is large compared to the relevant J coupling (2).

A more interesting advantage of multiple quantum spectroscopy applied to exchanging systems can be illustrated by an example from the protein basic pancreatic trypsin inhibitor (BPTI). At intermediate temperatures the 2,6-CH and 3,5-CH resonances of the phenylalanine-45 aromatic ring suffer significant exchange broadening due to 180° ring flips which cause the 2-CH and 6-CH and the 3-CH and 5-CH protons to mutually exchange sites (3). However, a double quantum coherence can be generated between the 3-CH and 5-CH protons due to their scalar coupling to the 4-CH, and this 2Q coherence will not be exchange broadened since its frequency is the sum of the shifts of the 3-

CH and 5-CH protons and is therefore insensitive to their mutual exchange. This 2Q coherence can be transferred to single quantum coherence of the 4-CH proton, generating an easily observed "remote" peak in the 2Q spectrum. Slices from a 500 MHz 2Q spectrum of BPTI (in D_2O at 32°C and pH 4.6, MQ excitation period of 30 ms), taken parallel to the ω_1 axis at the ω_2 shift of the 4-CH of Phe 45, are shown in the accompanying figure. Due to the in-phase character of the peaks in the ω_1 dimension a very broad resonance can be observed which arises from the 2Q coherence between the 3,5-CH and 4-CH protons. The strong, relatively sharp peak represents the remote connectivity of the 3-CH and 5-CH protons. Two adjacent slices, A and B, are shown because in the ω_2 dimension the direct and remote peaks have opposite phase characteristics (absorption/dispersion) and different multiplet component intensities so that their maxima occur at slightly different ω_2 frequencies. (Note that while a MQ excitation period of 30 ms is about optimum for the 4-CH + 3,5-CH direct peaks, it results in the remote peak having approximately half of its maximum intensity.) In COSY or double quantum-filtered COSY spectra under the same conditions no cross-peaks are observed for the Phe 45 aromatic ring spin system; Fig. C is a ω_1 slice through a DQF-COSY spectrum at the ω_2 shift of the 4-CH proton, and shows only a diagonal peak. This example demonstrates a unique and potentially very valuable advantage of MQ spectroscopy in studies of exchanging systems.

Please credit this contribution to the account of Dr. Peter Wright.

Sincerely,

Mark Rance

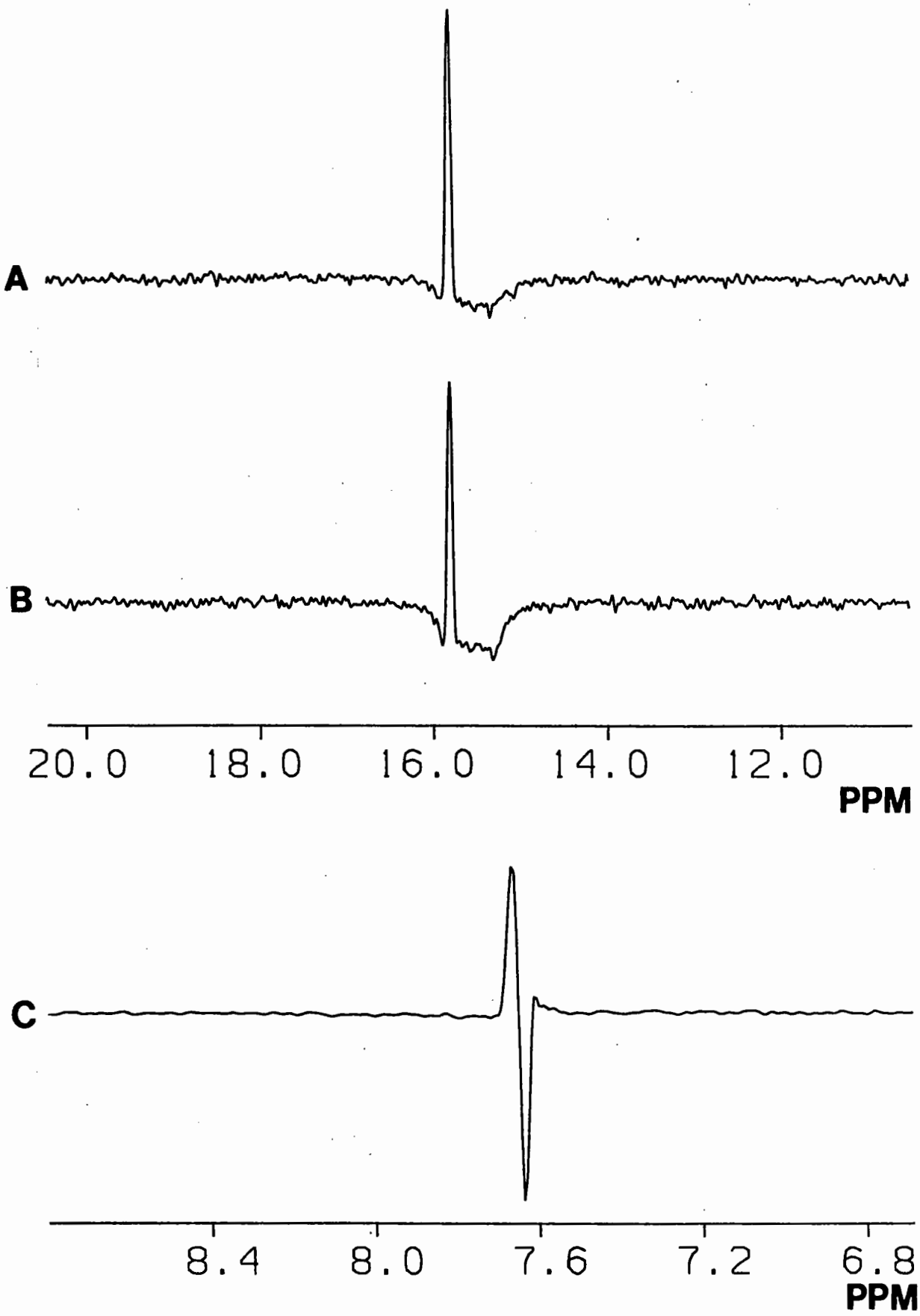
Mark Rance

MR/mlh

(1) L. Braunschweiler, G. Bodenhausen and R.R. Ernst, Mol. Phys. 48, 535 (1983).

(2) C. Dalvit, P.E. Wright and M. Rance, J. Magn. Reson. 71, 539 (1987).

(3) G. Wagner, D. Brühwiler and K. Wüthrich, J. Mol. Biol. 196, 227 (1987) and references sited therein.


A
B
20.0
18.0
16.0
14.0
12.0
PPM
C
8.4
8.0
7.6
7.2
6.8
PPM

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

October 2, 1987

(received 10/13/87)

Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Ct.
Palo Alto, CA 94303

Dear Dr. Shapiro:

Processing Phase Sensitive 2D Data on NT Spectrometers with the NMR Program

At least two programs are currently in use for obtaining and processing data on Nicolet NT spectrometers with 1180E or 1280 computers. The NMC program is used with the Dexter/2 operating system. The NMR program, which is currently supported by General Electric NMR, is very similar to NMC but is used with the TMON operating system. TMON is the current operating system for General Electric GN and QE spectrometers. Some NT users, including us, have upgraded our hard disk storage capacity and switched from NMC to NMR. This switch was made because Dexter/2 is not compatible with the new disk.

When using the States et al. (1) method for obtaining phase sensitive 2D data, two sets of quadrature FIDs are collected, the second set is 90° out of phase with respect to the first. In the NMC program, the DT command handles the t2 processing and replacement of the imaginary part of the first set of data with the real part of the second set. Unfortunately the DT command or an equivalent is not part of the NMR program.

In order to perform the functions of the DT command when using the NMR program, we have used the following procedure. The two sets of FIDs must be collected with AL on; the first step in processing is to separate them. This may be done by first changing the block size to one-half that of the block containing the two sets of FIDs and then using the links GCCBSD for the first set and BØGCCBB1SD for the second set. The two sets of data are now separately processed in the usual way with a link containing: baseline correction*, apodization function*, zero fill*, FT, phase adjustment, scaling factor, baseline adjustment*, and immediately before the save command the block size should be changed to one-half its current value (* indicates an optional operation). It would be convenient at this point to reorganize the locations of the t1, f2 data in the appropriate way with the link BØGCB1 GDCBSC however this does not work. One must use the link GCSA to convert the t1, f2 files from the 2D to the 1D format, change the block size to twice that of the t1, f2 files, and use the following link: BØGAB1GBCBSC to obtain a data set containing the "real" parts of the initial and out of phase t1, f2 data sets. The final link also converts the data from 1D to 2D format. One can then proceed with the processing as usual.

Sincerely,

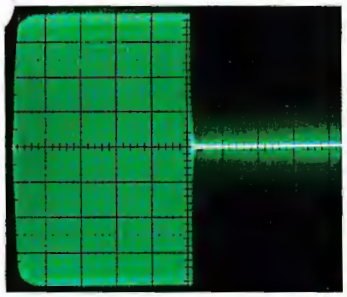
Jeff Ellena

Jeff Ellena

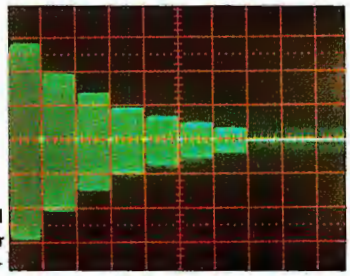
1. States, D.J., Haberkorn, R.A., and Ruben, D.J. (1982) J. Mag. Res. 48, 286.

Now, with the new GN Series high resolution NMR spectrometers, GE brings you the greatest versatility in multinuclear liquids and solids research . . . and backs it up with GE's unequalled quality, reliability, and continuous support.

A 5μsec ^{1}H observe pulse. ▼



15° phase shift through 360°. ►



Shaped decoupler pulse. ►

GE is committed to providing you with the highest performing NMR systems today and in the future. With the GN Series, available at various field strengths and bore sizes, you can perform simple one-pulse analysis, or complex state of the art experiments like triple quantum correlation and various selective excitation experiments through the system's automated hardware features which include:

- ☐ A comprehensive observe and decoupling phase shifter for < 90° phase shifts.
- ☐ Complete computer gain control of lock observe and proton/x-nucleus decoupler channels.
- ☐ A new, super-sensitive deuterium lock.

The Spectrometer Control Processor is easily controlled by GEM, the latest generation of NMR software. GEM-users can direct the GN system to perform a complete series of predetermined experiments for total sample analysis — or take control of individual components and develop their own custom NMR analysis.

With a variety of accessories including array processor, x-nucleus decoupler, liquids probes and six different solids probes with unique capabilities, and a choice of data storage devices, your GN spectrometer can give you an ultimate advantage!

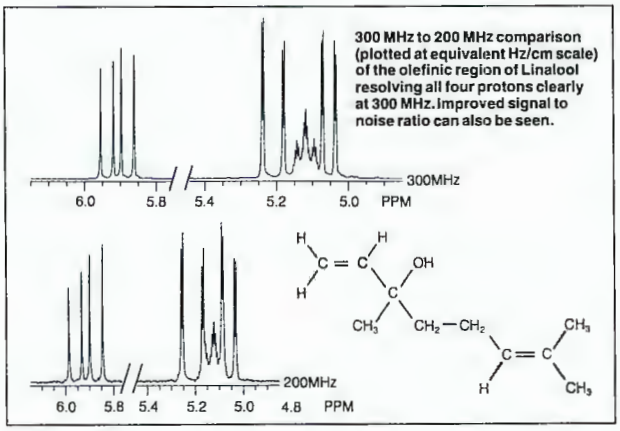
Step into the future with GE. We're ready to assist you with expanding support through our toll-free 800 customer service number. To receive a comprehensive new GN Series brochure or arrange for a demonstration, call (415) 490-8310, or write General Electric Company, NMR Instruments, 255 Fourier Ave., Fremont, CA 94539.

Ultimate Advantage

GENERAL ELECTRIC

More and more labs are looking into the automated QE-300 NMR system for superior results at a price of just $160,000.

For powerful analytical insight . . . you need fast, accurate NMR results that you can interpret at a glance. With the General Electric QE-300 system you will not have to accept a compromise system that almost does the job. For the lab, a 300 MHz system can now be your minimum acceptable field strength with the best price/performance ratio.



300 MHz to 200 MHz comparison (plotted at equivalent Hz/cm scale) of the olefinic region of Linalool resolving all four protons clearly at 300 MHz. Improved signal to noise ratio can also be seen.

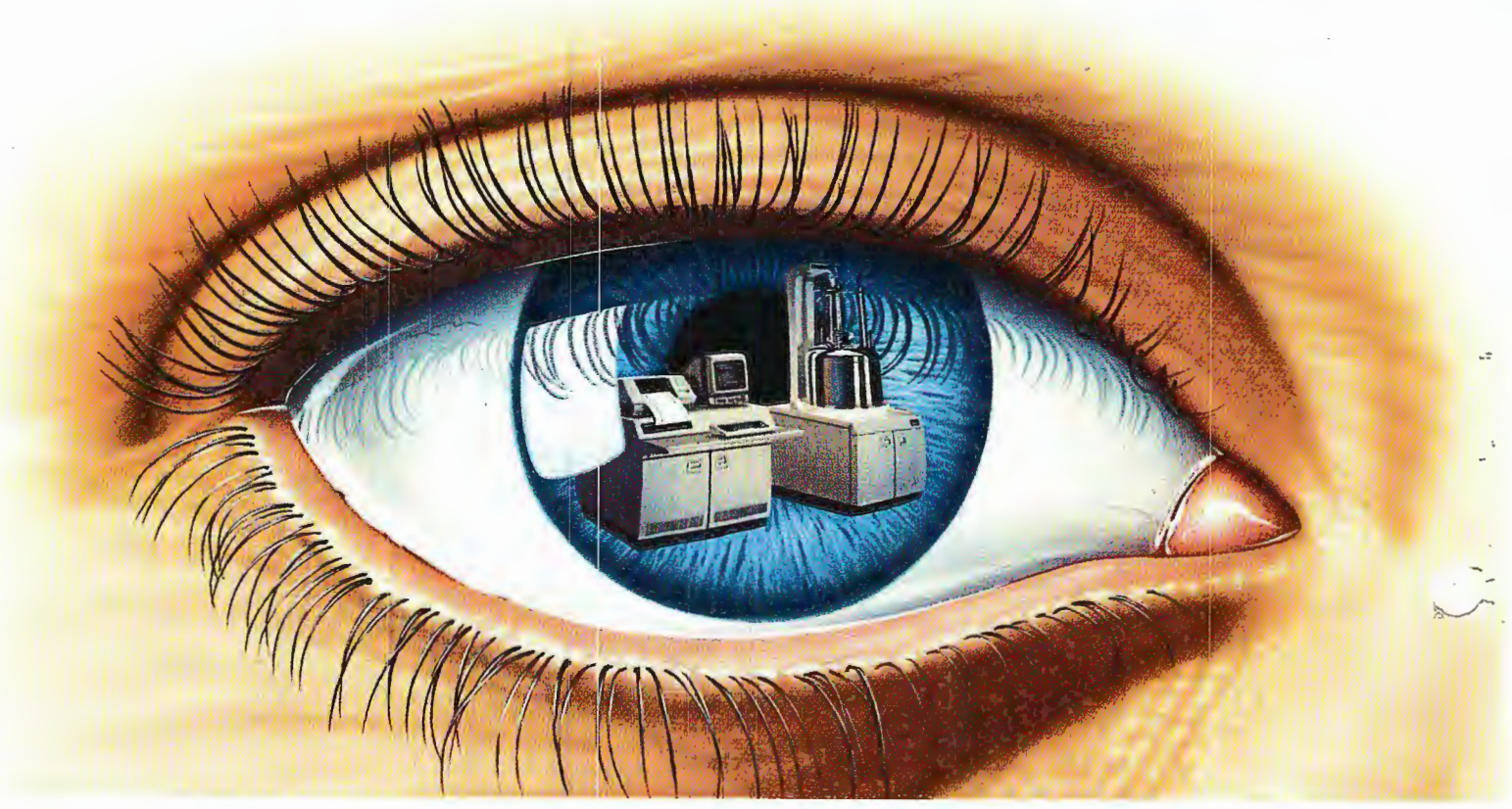
Better dispersion, faster analysis, and easier interpretation result directly from a 300 MHz superconducting magnet under the control of our custom analysis software . . . software that adapts with a few keystrokes to fit your specific analytical needs.

With the QE-300 you obtain exceptional high-resolution proton and carbon spectra from the same sample in just minutes. Plus, you have the option to observe a wide variety of other nuclei ranging from phosphorus through nitrogen. Our hardware/software options allow you to customize the system to fit your lab.

To find out what more there is to see in the QE-300 system, call (415) 490-8310 or write General Electric, NMR Instruments, 255 Fourier Avenue, Fremont, CA 94539.

See what you've been missing.

GENERAL ELECTRIC



Thomas L. James, Ph.D.
UCSF Magnetic Resonance Laboratory
Department of Pharmaceutical Chemistry
The University of California
926 Medical Science
San Francisco, CA 94143-0446
(415) 476-1569

University of California, San Francisco ... A Health Science Campus UCSF

September 23, 1987
(received 9/28/87)

Professor Bernard L. Shapiro
~~Department of Chemistry~~
~~Texas A&M University~~
~~College Station, TX 77843-3255~~

Re: Program for Complete Relaxation Matrix Analysis of 2D NOE Spectra (CORMA) as an Aid to Molecular Structure Determination in Solution

Dear Barry:

The initial basis for determining a high-resolution molecular structure in solution is the generation of a large number of structural constraints in the form of internuclear distances and torsion angles. Of all possible techniques, two-dimensional NMR has the greatest capability for structural characterization of moderate size molecules (≤15000 daltons) in non-crystalline environments. The two-dimensional nuclear Overhauser effect (2D NOE) experiment, in particular, has the potential for yielding a large number of internuclear distances which may be used with other structural constraints to give a detailed molecular structure in solution. Following the lead of Wuthrich's lab, several labs are now using 2D NOE to provide qualitative or semi-quantitative internuclear distance information. We have been developing the methodology for *accurately* determining a large number of internuclear distances from the phase-sensitive two-dimensional nuclear Overhauser effect (2D NOE) experiment[1,2].

There have been papers in the recent literature which report estimated internuclear distances from NOE measurements using the assumption that a given pair of protons is isolated from all others when the mixing time is kept short. Use of short mixing times definitely limits the signal-to-noise ratio obtainable with cross-peaks in the 2D NOE spectrum. In addition, the isolated spin pair approximation (ISPA) is very often not valid in practical cases.

To avoid the assumption of isolated spin pairs commonly used for analysis of NOEs, and consequent errors in distance determinations, we have been developing a (nearly) complete relaxation matrix analysis program (CORMA) for 2D NOE spectra[1]. (Since they are rather small, we ignore scalar coupling and cross-correlation effects.) In contrast to the approximate approach, exact intensities in the 2D NOE spectrum are calculated for a given three-dimensional array of protons after diagonalizing the relaxation matrix. The approach we have been developing is (a) accurate, (b) can accommodate any size spin system (computer time and memory limitations only), (c) is not limited to any range of mixing times, (d) incorporates spin diffusion naturally, and (e) can utilize any molecular motion model. We have carried out a number of theoretical calculations as well as experimental studies. In summary: (a) Distances up to 5-6A with an accuracy of 10% should be attainable with knowledge of individual relaxation times. (b) Detailed knowledge of the molecular motions is not required for this distance accuracy; it is generally sufficient for a single *effective* isotropic correlation time to be used in the spectral density expression for any nucleus. There is, however, work remaining to improve the methods of refinement for obtaining the distances from the experimental 2D NMR data,

as well as improved methods of data analysis.

We have used CORMA to determine interproton distances quantitatively in small molecules[2], but our primary interest is in biopolymers[3]. With the increasing availability of more powerful computers, it will soon be possible to refine the structures of modest-sized biopolymers (i.e., those yielding *ca.* 500×500 2D NOE matrices) using their 2D NOE spectra. Consequently, we are investigating the effects of experimental errors in peak intensities on the refinement process for nucleic acid and protein structure. We have begun developing a program for the refinement of molecular structure based on 2D NOE intensities. The goal is to optimize a trial structure while minimizing the error between calculated and observed intensities. We have incorporated CORMA into a program with a Marquardt-Levenberg least-squares optimizer, and have had some success in refinement. However, this aspect of our studies is incomplete.

We have, though, developed a "user-friendly" version of CORMA, which is available for both UNIX and VMS operating systems. Based on an input set of coordimates (e.g., from an x-ray structure or other model), this version calculates all peak intensities in a 2D NOE spectrum taking into account all proton dipole-dipole interactions (with or without random noise added), compares the root mean square deviation (rmsd) of intensities between experimental and theoretical spectra (for as much or as little of the spectrum as desired), and compares the rmsd between and within amino acyl or nucleotide residues. The results are available in tabular form or can be plotted either as an intensity rank or as an approximately gray-scale figure. An example of the latter is included with this letter. Contact us if you have use for such a program.

Sincerely yours,

Thomas L. James, Ph.D.
Professor of Chemistry, Pharmaceutical
Chemistry and Radiology

Brandan Borgias

TLJ:vax

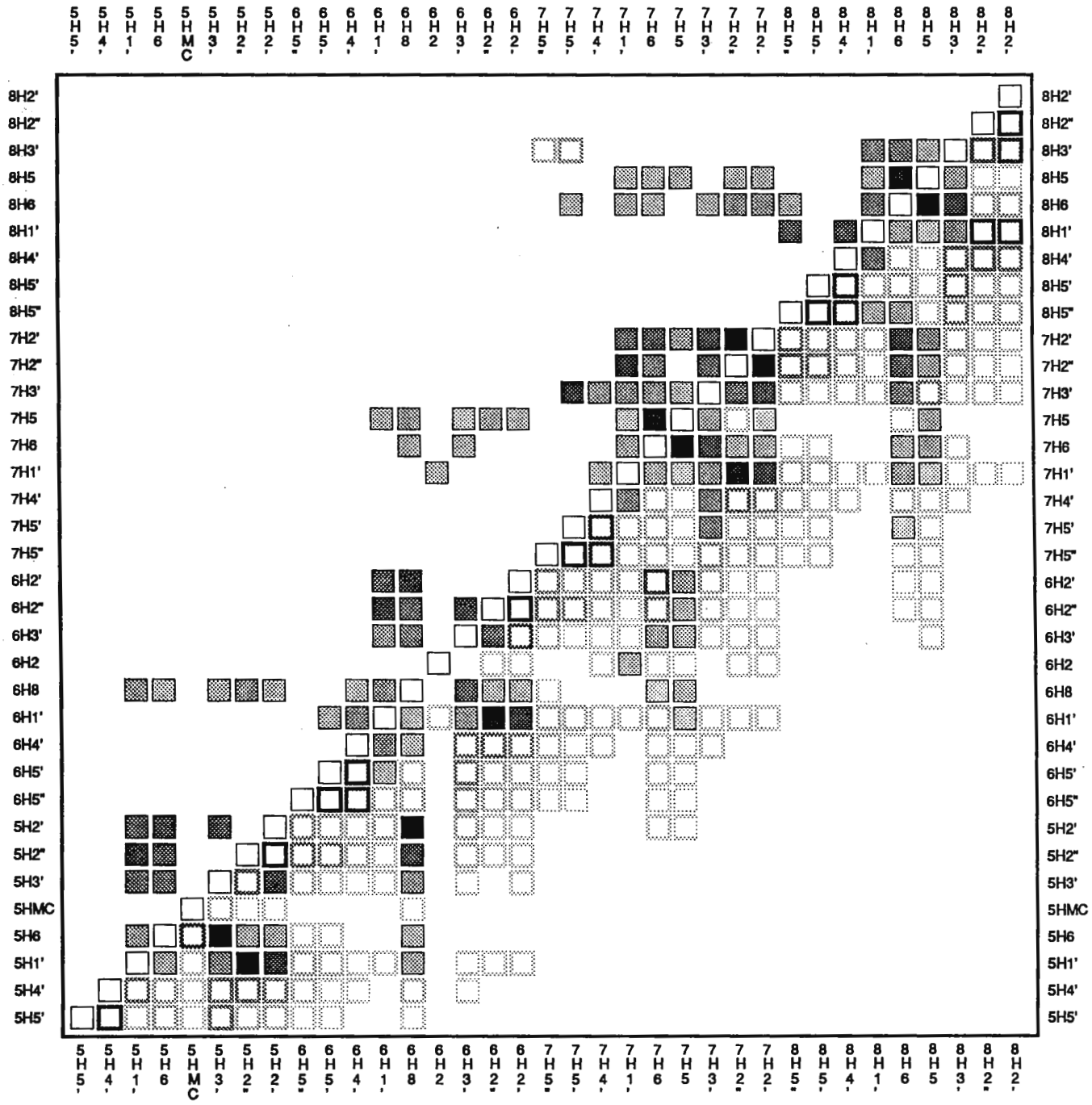
---

1. J.W. Keepers and T.L. James, *J. Magn. Reson.* **57**, 404 (1984).
2. G.B. Young and T.L. James, *J. Am. Chem. Soc.* **106**, 7986 (1984).
3. E.I. Suzuki, N. Pattabiraman, G. Zon and T.L. James, *Biochemistry* **25**, 6854 (1986).

BITNET ADDRESS: James@nmr.ucsf.edu.bitnet

SCHEMATIC PLOT OF 2DNOE INTENSITIES
EXP250.INT.1 vs cab31.INT.1
ISOTROPIC B form with C3' endo sugar (as in A form) TAUc 4ns TAUm 0.250

Intensity Scale:



*Positive intensities are drawn with a border. Negative peaks have no border.
Intensities for EXP250.INT.1 are plotted in upper triangle.
Intensities are normalized by the ratio between the sum of cross-peaks.
Intensities with no corresponding observed or calculated intensities are shown as open squares.

Carnegie Mellon

Department of Chemistry
Carnegie Mellon University
4400 Fifth Avenue
Pittsburgh, Pennsylvania 15213-3890
412-268-3149

October 1, 1987
(received 10/5/87)

Dr. Bernard L. Shapiro
TAMUNMR
966 Elsinore Court
Palo Alto, CA 94303

$R(AA'BB') = 0$ *

Dear Barry:

Loved Robin Harris's letter--I can't resist commenting on a few aspects of the problems. The use of "multinuclear" to describe NMR or spectrometers has always struck me as implying the existence of techniques or instruments to observe NMR on a single nucleus. I've had a hard time thinking of a better term--Heteronuclear? Varinuclear? Multinuclidal? Polyisotopal? Worse and worse.

Sweep width or spectral width. Actually neither is quite correct, because of possible aliasing. "Nyquist frequency" or Nyquist spectral range" is closer, if longer.

"Number of transients" and "Number of fids" look about equally attractive to me.

"High/low field" and "low/high frequency" are inextricably bound up with the historical presentation of spectra with "high-field" on the right (when people really did sweep field), not to mention the historic τ-δ schism. Nowadays, with the use of field-frequency locked spectrometers, it is not clear what is varying and how much during an experiment, but the concept of signals observed at higher or lower frequency is clear and unambiguous enough to me. I suppose a purist might argue that the sign should be reversed for nuclei with negative gyromagnetic ratios, but who would pay any attention to that? Incidentally, I think we have lost the opportunity to honor one of our distinguished pioneers in this area by not naming a unit of chemical shift ($10^{-6}\nu_0$) after him--it would give me much pleasure to describe a signal as being located 3 Blochs up from TMS (in frequency units, of course).

Anisotropy and asymmetry have distinct meanings, as usually used for second rank tensors such as field gradient or susceptibility. Anisotropy

could be renamed axiality ($T_{ii}-\frac{1}{3}(T_{jj} + T_{kk})$), but I don't see any special advantage to it. With the same tensor, the asymmetry is ($T_{jj}-T_{kk}$). MacLean, and others use ΔT for the anisotropy (or axiality) of T, and δT for the asymmetry. This is neat and easy. Standardizing symbols is tougher than standardizing nomenclatures, however, and probably inherently impossible because the combinations of parameters one wishes to discuss in new publications keeps changing, and the parameters themselves outnumber the letters of the latin, greek, hebrew and cyrillic alphabets put together. Everybody has trouble with this (T for temperature, time k for Boltzman constant, rate constant, etc.).

We would immediately get in trouble with χ as a symbol for quadrupole coupling constant, since we (and many others) use it for magnetic susceptibility, and the quadrupole splitting in a magnetically anisotropic molecule oriented by a strong field would then be governed by the equation

$$\upsilon_s = \chi\Delta\chi B^2/10kT$$

with the first χ being the qcc and $\Delta\chi$ being the anisotropy of the molecular magnetic susceptibility. How about ν_q for the quadrupole coupling constant (or ω_q if you are a physicist and like things in radians)?

One set of symbols that's used for several different things:

ρ, σ: density matrix, density, shielding, auto- and cross-relaxation rates.

Suggestions: density matrix = C (not used for much else in NMR; the spin-rotation tensor, sometimes)
Auto and cross-relaxation = R_{ii}, R_{ij} (becoming more common practice)

S: orientation parameter, second spin in an IS system.

Suggestion: Stick to I_1, I_2, I_3 etc. for spins
S for $(3/2\ \cos^2\theta-1/2)$.

Please do *not* count this as a contribution. (Aha and so there, Robin!) *

Sincerely,

Aksel

Aksel A. Bothner-By

AAB/rs

*Courtesy of the Ed.

Surely the word needed in the top line of this page is aksiality, mon vieux? (You knew I'd do that, didn't you?)

BLS

MASSACHUSETTS INSTITUTE OF TECHNOLOGY
CAMBRIDGE, MASSACHUSETTS 02139

Postdoctoral Position Available

Dear Barry:

An opening for a postdoctoral associate seems to have appeared somewhat unexpectedly, and I invite inquiries from interested parties. The project is connected with NMR at very low (.01-1K) temperatures, with emphasis on high sensitivity study of surface species. A candidate should have some NMR experience (preferably in solids), and most importantly a "feel" for experiments and sometimes cranky apparatus. He or she would work with 1 (or maybe 2) others in this general area. This type of appointment is made for 1 year, but is normally renewable for a second year by mutual agreement. The position will be available about January, 1988 or later.

Yours,

John S. Waugh

POST-DOCTORAL POSITION AVAILABLE

The Huntington Medical Research Institutes (HMRI) has a post-doctoral position available in its division of magnetic resonance spectroscopy. Applicants should have experience in NMR spectroscopy and a PhD in one of the following areas; biochemistry, physiology, pharmacology or chemistry. The research group has interests in cancer, kidney and heart research as studied by NMR spectroscopy and high-field (NMR) imaging; equipment available includes a 4.7T, 33 cm bore General Electric "CSI" spectrometer/imager, an 180 MHz Nicolet spectrometer, access to other high field (360, 500 MHz) spectrometers and a Diasonics 0.35T whole-body imager. Extensive surgical, physiological and workshop facilities are also available.

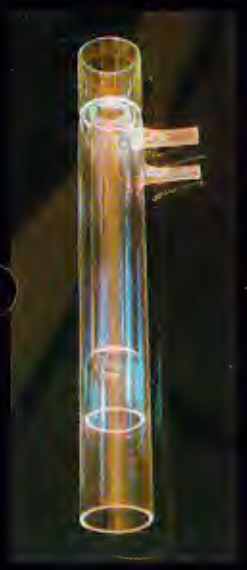
The appointment is for two years, $21,000 per annum plus benefits, starting as soon as possible. Please send a *curriculum vitae* and the names and addresses of three referees to

Dr Peter B. Barker,
Huntington Medical Research Institutes,
10 Pico Street,
Pasadena, CA 91105.

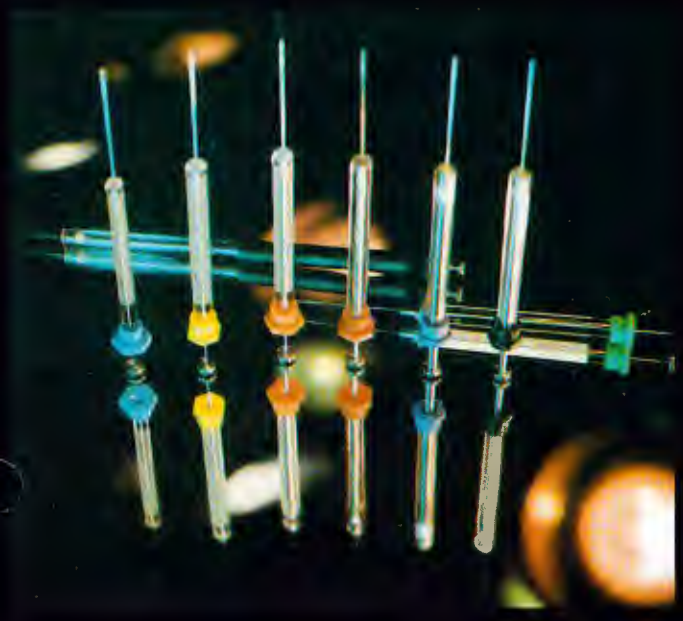
Presented Graphically, inside are our Products and Services.

Via our unique
Graphic Arts Department,
which includes in-house
color photography studio and lab,
computerized typesetting,
color photo-offset printing,
word processing,
plus direct mailing,
we reach over 50,000 scientists
in USA alone.

If you have a unique product,
write to us inquiring
as to how
we can promote
it for you.



NORELL, INC.
314 Arbor Ave.
Landisville, NJ 08326 USA
Tel. (609) 697-0020



DEUTERATED SOLVENTS
for use in
NMR Spectroscopy
are manufactured by
Norell Chemical Co.,
Division of Norell, Inc.
Request catg. No. DC-1000.

NMR LAB.
We provide
proton
NMR Analysis
at low cost

Quality Control
of our
Deuterated
Solvents
is maintained
by NMR
and other
instrumentation.

Upgrading
of Heavy Water.

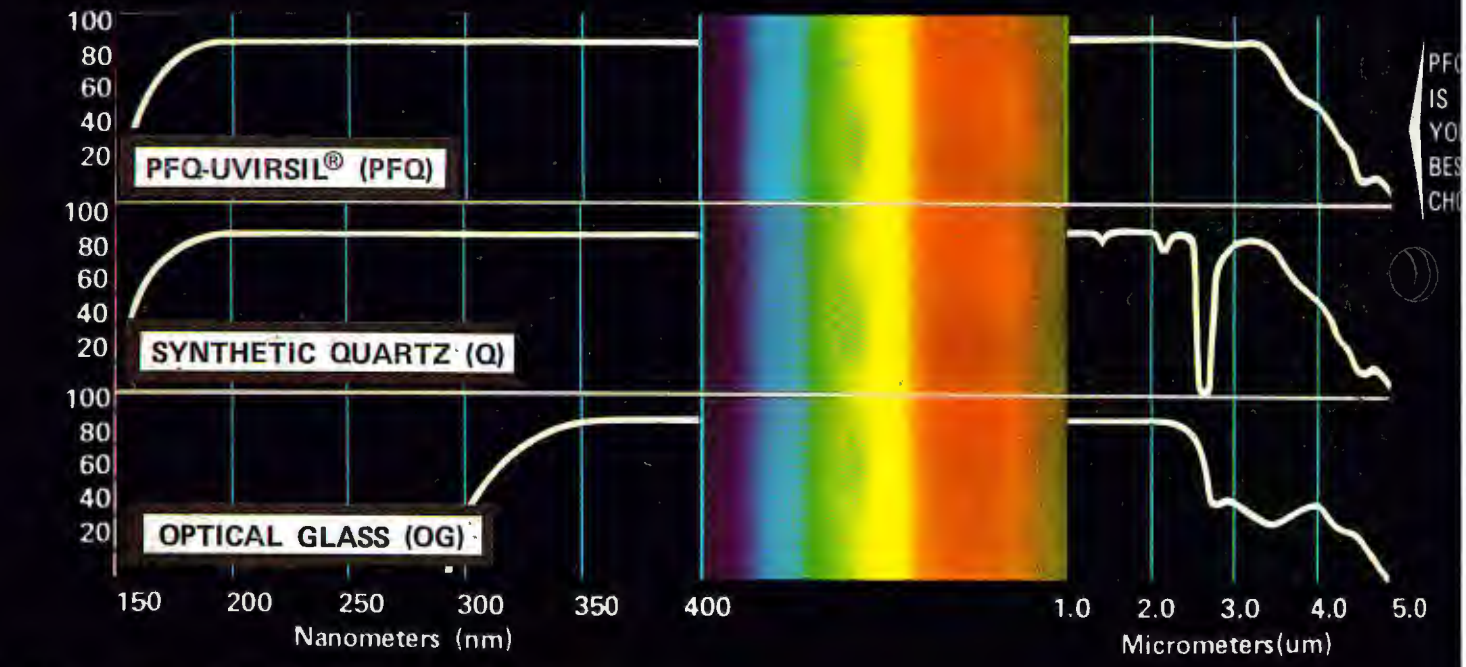
Production
of Deuterated
Solvents.

Organic
Synthesis
Lab.

Spectrophotometric Cells. Request Brochure No. SC-500.

Top Quality Spectrophotometer Cells

GRAPHS SHOWING APPROXIMATE PERCENTAGE TRANSMISSION OF CELLS FILLED WITH A NON-ABSORBING LIQUID OF THE SAME REFRACTIVE INDEX AS WINDOW MATERIAL.



Wide range of color-coded microsyringes. Request Catg. No. MS-317.

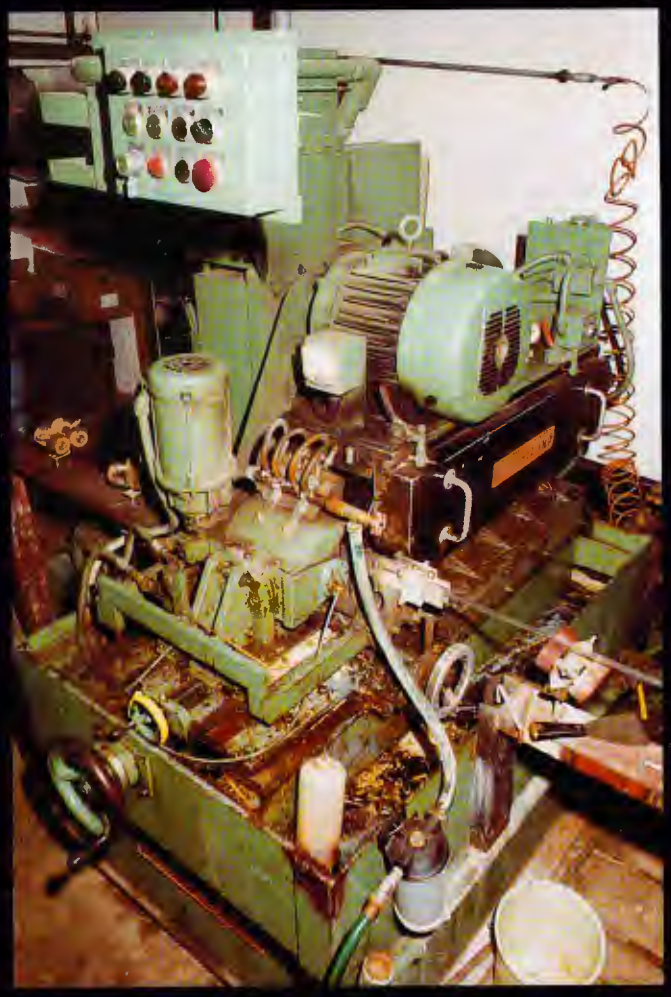
Coulometric Moisture Determination Apparatus. Request Brochure No. KF-700.

TECHNICAL DATA

...Coulometric generation of iodine by pulsed servo controlled DC, intensity 500 mA. ...End point detection AC polarization. ...Automatic compensation of reagent background. ...Alphanumeric fluorescent gas display, 16 digits, 16 segments. Results with four digits, floating point and unit. ...Possibility of subtracting the water blank value. ...Operation compatible with most coulometric reagents, with or without pyridine. ...Measurement range 5 micrograms to 100 milligrams of water. ...Sensitivity 0.1 microgram. ...Accuracy 1 microgram for 5 to 350 micrograms of determined water. Error less than 0.3% for more than 350 micrograms. ...Maximum determination speed 2.8 mg/min.

Electrothermal Heating Mantles, Melting Point Apparatus, plus other related equipment. Request Brochure No. ET-250.

Precision Bore
Glass Tubing
and Rods.
Request Brochure
No. PB-600.



Centerless Grinder
used in precision
grinding
and polishing
of glass tubing
and rod.

ICP
Torch &
Accessories.
Request
Brochure
No. PT-325.

Via computerized data and word processing, we stay in touch with our customers.

Our computerized photo-typesetting equipment is used to prepare high quality copy for advertising.

With our in-house printing facility, together with our color photo studio and color processing lab, we have the ability to print and distribute brochures and other literature in a very short time period.

NORELL, INC. is basic producer and supplier of NMR Sample Tubes, Deuterated Solvents, Chart Paper, Precision Bore Glass Tubing and Rod, Spectrophotometric Cells, Microsyringes, Coulometric Moisture Determination Apparatus, Electrothermal Heating Mantles, Witeg Laboratory Apparatus, plus other laboratory equipment and supplies.

We invite you to visit us at the Pittsburgh Conference and Exposition, held in Atlantic City, NJ, March 9-12, 1987 (Booths 28000/28002) and in New Orleans, LA, February 22-26, 1988.

NORELL, INC., 314 Arbor Ave., Landisville, NJ 08326 USA Tel: (609) 697-0020

MONTEDIPE

13rd October, 1987
(received 10/21/87)

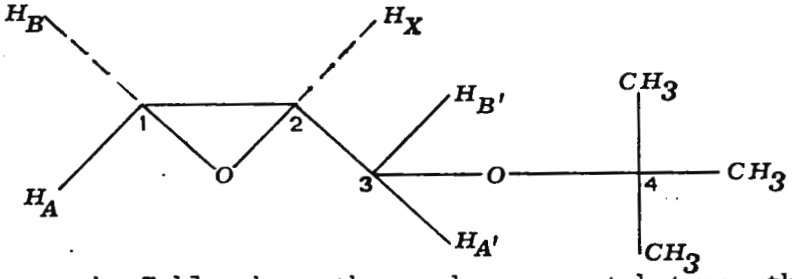
Professor BERNARD L. SHAPIRO
Editor Publisher
TAMU NMR NEWSLETTER
966 Elsinore Court
PALO ALTO, California 94303
U.S.A.

MONTEDIPE/PM/CER
Stab.to Petrolchimico
Via della Chimica, 5
30175 PORTO MARGHERA VE
ITALY

Dear Professor Shapiro,

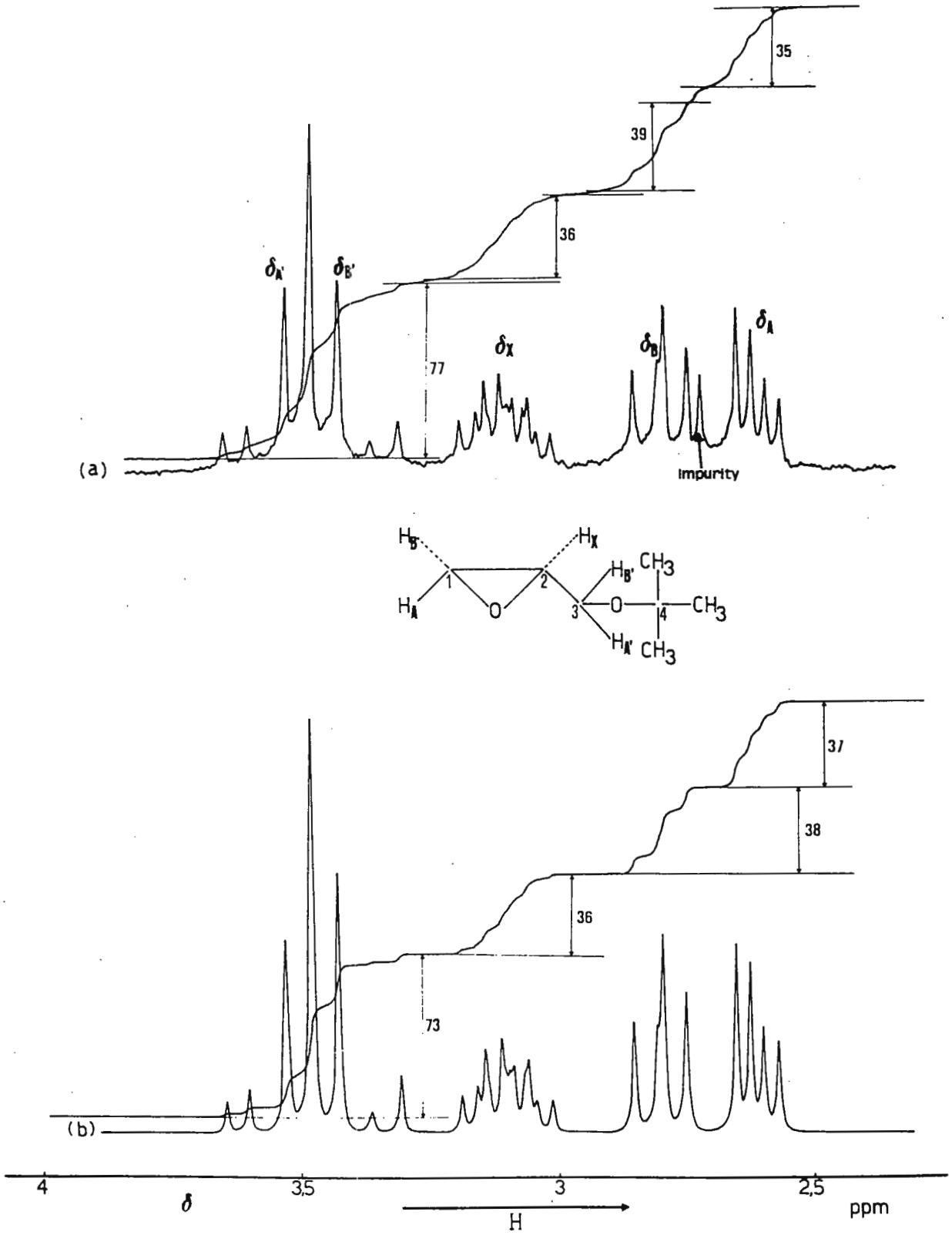
Title: ^{13}C and ^{1}H analysis of ter-butoxymethyl-oxirane

We have analyzed a sample of ter-butoxymethyl-oxirane of unknown purity grade by ^{13}C and ^{1}H NMR spectroscopy with Bruker WH90 operating in FT mode. The synthesis of the compound is described in (1). The ^{13}C spectrum of a 6% (w/v) $CDCl_3$ solution was recorded at 306 K. The chemical shifts, relative to internal TMS, are reported in the Table 1. The gated spectrum allowed us to assign the different c.s. according to the formula:



A glance at the Table shows the good agreement between the ^{1}J CH coupling constants observed in this oxirane derivative and similar systems (2,3,4,5). The long range ^{3}JCCCH of CH_3- groups was measured and its value (4.0 $\pm$ 0,7 Hz) was found to fit those reported in the literature for the ter-butyl compounds (5). A 6% (w/v) $CDCl_3$ solution was used for the ^{1}H spectrum.
An inspection of the experimental spectrum shows that the eight line pattern (2.5 - 2.9 ppm) is the AB part of an ABX system (see nuclei: A, B and X of the formula) and that the apparent seven line pattern (3.3 and 3,7 ppm) is the AB part of another ABX system (see nuclei: A', B', X). The ^{1}H NMR parameters of Table 2 were obtained from a computer simulation of the five spin system (see simulated spectrum in the Figure). The comparison of the calculated data with those of similar systems (3, 6, 7) are reported in Table 2.

Observed (a) and simulated (b) spectra



MONTEDIPE
Montedison Petrolchimica

FOGLIO N

The ^1H c.s. of the oxirane derivative are compared with those of 2.3-epoxy-1-propanol (7) and of ethylene oxide (3) and the coupling constants with those of the ethylene oxide and of methyloxirane. Because of the free rotation around the C_2-C_3 bond we are not able to assign univocally the $H_{A'}$ and $H_{B'}$ c.s.

Sincerely yours

Giorgio Gurato Giorgio Gurato Flaviano Coletta* Flaviano Coletta
Alessandro Gambaro* A. Gambaro Giancarlo Agostini* Giancarlo Agostini
* Dipartimento di Chimica Fisica of the University, via Loredan 2 - PADOVA

References

(1) Beilstein, Band 17/2-S.988
(2) Stothers, Carbon-13 NMR Spectroscopy, Academic Press, p.326,333 (1972)
(3) Brügel, Handbook of NMR Spectral Parameters - Heyden, vol. 2, p.386 (1979)
(4) Stothers, Carbon-13 NMR Spectroscopy, Academic Press, p. 342 (1972)
(5) Ibidem, p. 351
(6) Sadtler Standard Spectra 18790M (2,3 epoxy-1-propanol)
(7) Booth, Progress in NMR Spectroscopy, vol. 5, Pergamon Press, Oxford p. 184 (1965).

Table 1

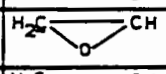
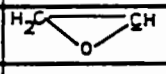
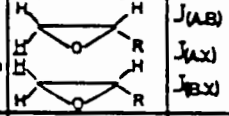
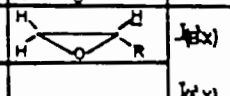
^{13}C c.s. (ppm) (TMS=0)	Carbon atoms	Multiplicity ^{13}C-^1H couplings	Assignments	Chemical groups	$^1J_{^{13}C-^1H}$ (Hz)	Literature data $^1J_{^{13}C-^1H}$ (Hz)
δ_{CH_3} = 27.47	3	Quartet	$\underline{C}H_3$	$OC(\underline{C}H_3)_3$	125.4 ± 1.0	125 (2)
δ_1 = 45.03	1	Triplet	$\underline{C}H_2$		176.0 ± 1.0	175.8 (3) 176 (4)
δ_2 = 51.41	1	Doublet	$\underline{C}H$		177.0 ± 1.0	
δ_3 = 63.07	1	Triplet	$\underline{C}H_2$	$\underline{C}H_2OC(CH_3)_3$	140.4 ± 1.0	
δ_4 = 73.31	1	Singlet	$-\underline{C}-$	$O\underline{C}(CH_3)_3$	—	

Table 2

^1H c.s. (ppm) (TMS=0)	Literature data c.s.	Hydrogen atoms	Fine structure ^1H-^1H couplings	Assignments	$J_{^1H-^1H}$ (Hz)	Literature data $J_{^1H-^1H}$ (Hz)
δ_{CH_3} = 1.21		9	Singlet	$(C\underline{H}_3)_3C$		
$\delta_{(A)}$ = 2.62	2.79 (6) 2.54 (3)	1	Part AB of a		$J_{(A,B)}$ = 5.05 $J_{(A,X)}$ = 2.74	$J_{(gem)}$ = 5.6 (3) $J_{(gem)}$ = 5.37 (7) $J_{(trans)}$ = 2.9 (3) $J_{(trans)}$ = 2.57 (7)
$\delta_{(B)}$ = 2.80	2.91 (6)	1	ABX spectrum (8 lines)		$J_{(B,X)}$ = 4.10	$J_{(cis)}$ = 3.88 (7)
$\delta_{(X)}$ = 3.10	3.27 (6)	1	Multiplet		$J_{(B,X)}$ = 5.29	
$\delta_{(B')}$ = 3.41 $\delta_{(A')}$ = 3.54	3.49 (6) 3.92	2	Part AB of a ABX spectrum (7 lines)	$-C\underline{H}_2O$	$J_{(A',X)}$ = 3.77 $J_{(A',B')}$ = -10.77	

Brandeis University

Graduate Department of Biochemistry

Waltham, Massachusetts 02254-9110

September 21, 1987
(received 10/1/87)

Professor Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Convenient Method for Small Sample Volumes

Dear Prof. Shapiro:

We think that we have found a convenient method to use thin- and medium-walled 5 mm NMR tubes for small sample volumes. This is a concern especially to the biochemists, who are frequently sampled-limited and must use small volumes to keep sample concentrations high enough to obtain reasonable S/N in reasonable times. The microcells we have been using are often difficult to shim and give rolling baselines, in part due to the large amount of glass and the solution/glass interface. A more critical concern for the protein biochemist is the possibility of denaturing the sample as it is drawn up and down the long narrow neck of the microcell.

Our technique is to put telfon beads in the NMR tube. These 1/8" diameter spheres, from Cole-Parmer, displace 12 µL/bead. In our 500 MHz spectrometer, 350 µL is required to effectively fill the coil volume using a thin-walled 5 mm tube; 200 µL is necessary in a medium-walled tube. Four beads plus 300 µL or 4 beads plus 150 µL, provide the requisite volume to obtain good spectra. In our Varian 300, 300 µL in a medium-walled 5 mm tube is required. The examples shown here are proton spectra of a solution of 20 mM L-alanine in D_2O run on the Varian XL300 using 300 µL or 264 µL plus 3 beads in Wilmad 524-PP 5 mm tubes. The spectra were obtained with spinning at 20 rps. This produces some spinning side-bands around the residual water peak in the sample with beads, but the linewidths and line-shapes of the sample resonances in the two spectra are identical. Without spinning, all lines are broadened on both samples to the same values. In other experiments on our 500 MHz instrument, using 5'-uridine-monophosphate in 90% H_2O/10% D_2O (not shown) identical spectra were obtained with and without beads. Significantly, the 2-1-4 pulse parameters for water non-excitation were unchanged by the addition of beads (4 beads plus 150 µL solution). The use of 8 beads with 100 µL was not successful, however, presumably because the field homogeneity in the sample is severely distorted by the presence of so many bead/solution interfaces.

The beads were then used in a 21 kD MW protein sample in both our 500 MHz instrument for ^{15}N decouple/^{1}H observe experiments using a J_xR_y pulse for water non-excitation, and in the Varian 300 for ^{31}P experiments. Proton and phosphorus lineshapes and linewidths again were not affected by the beads.

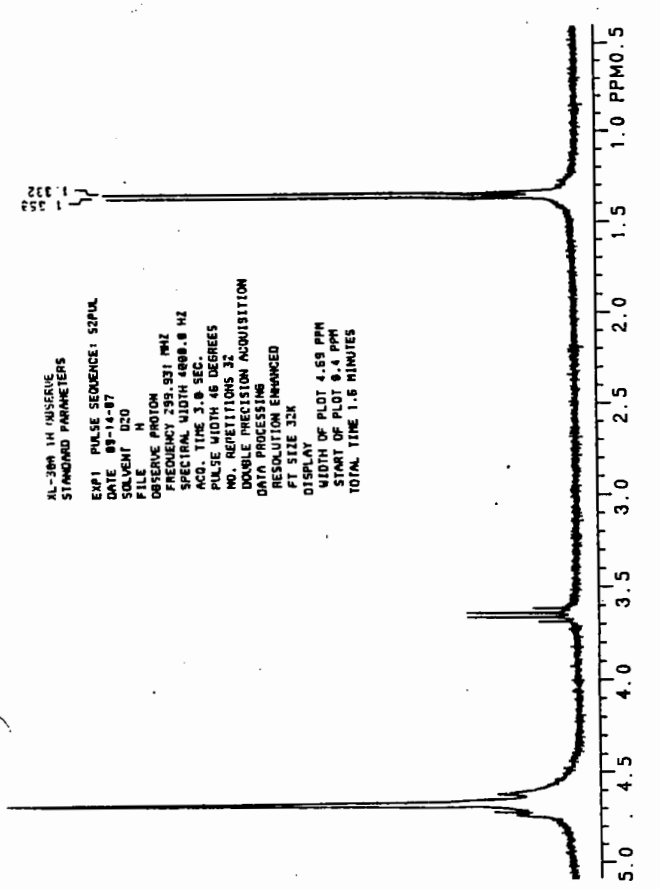
Although the beads will expand slightly with increasing temperature, they fit so loosely that this is not likely to be a problem. Because Teflon is inert in biological systems and can be acid-washed and autoclaved, it is useful for both proteins and nucleic acids (which won't adhere to it, either). Samples can be removed easily, and the beads washed in situ for complete sample recovery. One limitation: they are not recommended for ^{19}F NMR experiments.

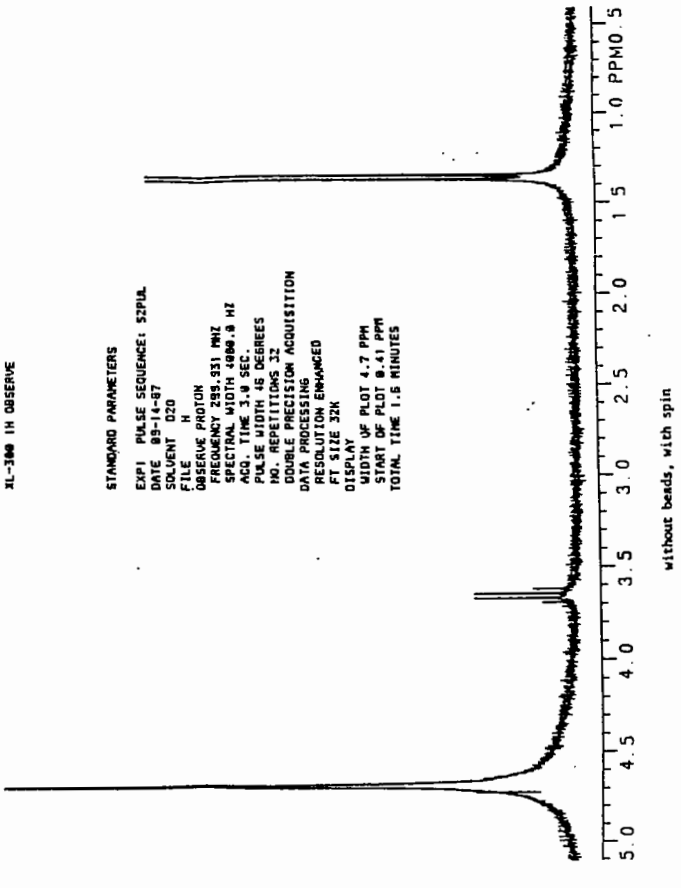
Please credit this to the account of Al Redfield.

Sincerely,

Kathleen Hall

Sharon Burk





McMASTER UNIVERSITY
Department of Chemistry
1280 Main Street West, Hamilton, Ontario, L8S 4M1
Telephone: 525-9140

September 18th, 1987
(received 9/29/87)

Dr. B.L. Shapiro,
Tamu NMR Newsletter,
966 Elsinor Court,
Palo Alto, California,
94303
U.S.A.

New address and
New Simulations

Dear Barry:

I'm writing to your new address from my new address. I will miss my former colleagues at Bruker, and I will have to get used to buying equipment, but McMaster is already well equipped. (AM500, MSL100, WM250). I'm also taking over McMaster's subscription from Ian Thompson, so I hope that the renewal form with the name change has reached you.

To start things in my name, I enclose some recent results from my SIMPLTN program. The new version will simulate almost any experiment on a homonuclear or heteronuclear AB or ABX spin system. To test the program, I've duplicated Gareth Morris and Kari Smith's results on virtual coupling in heteronuclear shift correlations (Mol.Phys, 61 467 (1987)).

The bottom spectrum is a simulation of carbon 5 in 2,3-dibromothiophene, with parameters from the paper, and the top spectrum shows the same experiment, but with proton 5 moved 10 Hz to higher frequency. As we can see, the virtual coupling effects can be large, but they are sensitive to exact values of parameters.

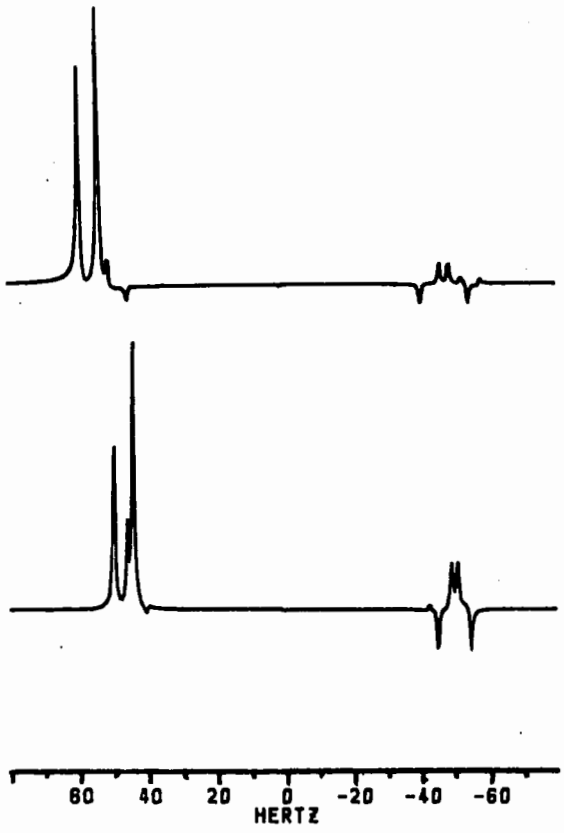
The new version of SIMPLTN has been sent to ABACUS, the Bruker users' society, so people with Aspect computers can play with the program themselves.

All the best to you in sunny California.

Yours truly,

Alex D. Bain
Associate Professor
of Chemistry.

ADB/jp
encls.



RESEARCH & DEVELOPMENT
Mailing Address: P.O. Box 1539, King of Prussia, PA 19406-0939 • (215) 270-4800
cable SMITHKLINE PHILADELPHIAPA telex 83-4487

Smith Kline &French Laboratories
A SMITHKLINE BECKMAN COMPANY

October 12, 1987

(received 10/16/87)

Professor B.L. Shapiro
966 Elsinore Court
Palo ALto, CA 94303

Dear Dr. Shapiro:

Our department has a postdoctoral position available for an interested individual to develop and apply NMR methods for the characterization of proteins and protein-drug interactions.

Our facility has excellent instrumentation and resources, including a 500 MHz spectrometer, off line data processing, expertise in molecular modeling and molecular biology. Persons interested in further details should contact me at (215) 270-6658 or at the above address.

Sincerely yours,

Luciano Mueller

Luciano Mueller, Ph.D.
Physical & Structural Chemistry
Department, L-940

NORTHWESTERN UNIVERSITY COLLEGE OF ARTS AND SCIENCES

Department of Chemistry

2145 Sheridan Road
Evanston, Illinois 60201

September 25, 1987
(received 9/28/87)

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

Dear Barry:

We have found chlorine-35 and chlorine-37 NMR spectroscopies to be extremely useful in clarifying the structure of silyl perchlorates. In the ionic form on the left side of eq. 1, the chlorine atom is in a tetrahedral environment and quadrupolar interactions are ineffective. Linewidths therefore should be narrow (10s of Hz). Association through ion pairing (middle of eq. 1) or covalent bond formation (right side) should increase the

$$R_3Si^+ \ ClO_4^- \rightleftarrows R_3Si^+ClO_4^- \rightleftarrows R_3Si\text{-}OClO_3 \qquad (1)$$

electric field gradient and cause considerable line broadening. Although no one has been brave enough yet to measure the linewidth of an alkyl perchlorate, other covalent bonds to chlorine bring about kHz linewidths.

We have examined the ^{35}Cl and ^{37}Cl spectra for various silyl perchlorates. Typically, at very low concentrations (<0.01 M) the linewidth is less than 30 Hz. The peak broadens as the concentration increases, reaching more than a kHz by 0.1 M. At the same time the ^{35}Cl chemical shift also is changing. For Me_3Si^+ and Ph_3Si^+ these changes take the typical S shape indicative of a two site, rapid exchange. For Me_3Si^+, nonlinear least-squares analysis of a dozen concentrations indicates that the ^{35}Cl linewidths and chemical shift for the free ion respectively are <20 Hz and δ 5; for the associated form (ion paired or covalent) they are 2600 Hz and δ -33. Exact percentages of free ion were calculated from the equilibrium constant. Thus at 0.0047 M, the mixture contained 98% free ion, and at 0.584 M there was 14% free ion. Similar experiments have been carried out with other silyl perchlorates to give percentages of the free ion.

These experiments were also carried out with ^{37}Cl NMR, which gave similar results. The $^{35}Cl/^{37}Cl$ ratio of linewidths was about 1.7, except at very low concentrations, 0.005 M, when it reached the expected ratio of 1.2 (the ratio of quadrupolar moments). The value of 1.7 is puzzling and makes us wonder if the free $\rightleftarrows$ associated equilibrium is not entirely fast, so that chemical exchange is contributing to linewidths. Does anyone know about the mutual effects of chemical exchange and electric field gradient on ^{35}Cl and ^{37}Cl linewidths?

Sincerely,

Wojciech Schilf

Joseph B. Lambert

Title: Chlorine NMR of Free Silyl Cations in Solution

How to bring true computer power to your NMR research

Introducing: the new VXR 5000 Series computers which integrate Varian's NMR processing and control software with computer workstations from one of the world's leading manufacturers—Sun Microsystems.*

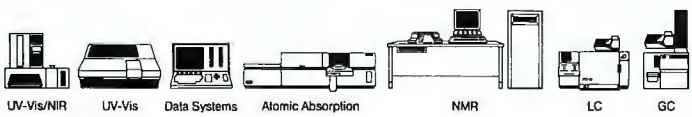
Now, for the first time, you can add a broad range of true computer capabilities to your NMR research. These features make that possible:

- **Industry-standard computers and advanced version of the UNIX* operating system**—provide high reliability and peak performance
- **Advanced windowing system**—fast and extremely easy to use
- **Flexible data processing**—from routine 1-D spectra to automatic 2-D analysis
- **Image processing**—quickly processes large, multidimensional images
- **Multipurpose and multiuser**—expands laboratory capabilities and increases productivity

The VXR 5000 series computers, standard on all our VXR and imaging spectrometers, feature a choice of monochrome or color/grayscale displays and a variety of options for enhancing performance.

Call now for all the facts
In the United States, call 800-231-5775.
In Canada, call 416-457-4130.
In Europe, call Zug, Switzerland, at (042) 44 88 44; Darmstadt, Germany, at (06151) 70 30. In Japan, call (3) 204 12 11.

*Sun Microsystems is a trademark of Sun Microsystems, Inc.
UNIX is a trademark of AT&T Bell Laboratories.



INTELLIGENT SOLUTIONS FOR YOU

varian

MAG-4615/338

UNIVERSITÀ DI MILANO
ISTITUTO DI BIOCHIMICA E DI CHIMICA

VIA CELORIA, 2
20133 MILANO
TEL. (02) 2663662

Milano, September 25th, 1987
(received 10/13/87)

Prof. BERNARD L. SHAPIRO
TAMU NMR NEWSLETTER
966 Elsinore Court
PALO ALTO, CALIFORNIA 94303
U.S.A.

Dear Barry,

CONFORMATIONAL ANALYSIS OF 9-DEOXYDAUNOMYCIN BY MOLECULAR MECHANICS AND TRANSIENT NOE STUDIES

We have just finished a conformational analysis of 9-deoxydaunomycin in solution, and we will report here the results of this study performed by extensive use of quantitative transient NOE. We have recently adopted this method with success to study an anticancer agent of this family (1). The interproton distance ratios obtained through the cross-relaxation rates have shown an accuracy comparable to X-ray method.

In recent years many efforts have been devoted to elucidate the mechanism of action of the antitumor anthracyclines; however, questions concerning the chemical attributes responsible for the antitumor efficacy still await a satisfactory answer. The main target of these antibiotics in responsive biological systems is considered to be the cell DNA, whose conformation and function are thought to be impaired as a result of drug intercalation. The X-ray study of the crystalline complex daunorubicin-hexanucleotide d(CpGpTpApCpG), carried out by Quingley et al. (*), revealed that the intercalation of the chromophore is stabilized by a possible hydrogen bonding between N3 and N2 of the second guanine and the hydroxyl group at C-9. In order to confirm the importance of the 9-OH, as concerns the shape of ring A and the geometry of the chromophore-sugar bonds, the DNA-complex stability and the biological activity, we have studied 9-deoxydaunomycin. We have at first used the N-trifluoroacetyl derivative in order to operate in $CDCl_3$.

The internal motions which are of importance to define the molecular shape are the inversion of the sugar ring, the inversion of ring A and the rotation around C(7)-O(7) and O(7)-C(1') bonds. All these processes are fast with respect to the n.m.r. time scale. The conformation of the sugar ring and of the aglycone ring A was easily defined as a chair $^{1}C_{4'}$(L) and a half-chair $^{9}H_{8}$ respectively, through the values of proton coupling constants and on the basis of a preceding study of daunomycin derivatives (2). The orientation of the sugar with respect to the chromophore moiety has been obtained by transient NOE experiments. We have also performed phase-sensitive NOESY experiments, in order to have a view of the principal NOE interactions, but the monodimensional technique gave a better accuracy. The interproton distances have been deduced from the cross-relaxation rates, determined by measuring the time development of NOEs, after selective inversion of single resonances. The experimental points were fitted through a non-linear least-squares procedure to the equation given in Figure 1.

UNIVERSITÀ DI MILANO
ISTITUTO DI BIOCHIMICA E DI CHIMICA

Table 1. Cross-relaxation rates (s^{-1}), interproton distances (Å) and J(H,H) for 9-deoxy-N-trifluoroacetyldaunomycin

i-j	σ(i-j)			r(i-j)		
H(1')-H(7)	0.2019	±	0.0070[a]	2.18	±	0.04[b]
H(1')-OH(6)	0.0171	±	0.0024	3.28	±	0.12
H(7)-H(8ax)	0.1070	±	0.0108	2.43	±	0.07
H(7)-H(8eq)	0.1027	±	0.0201	2.43	±	0.11
H(5')-H(8eq)	0.0852	±	0.0100	2.51	±	0.08
H(5')-H(4')	0.1091	±	0.0080	2.42[d]		
H(5')-H(9)	0.0355	±	0.0039	2.91	±	0.09
H(9)-H(8eq)	0.0605	±	0.0129	2.67	±	0.13
H(3')-H(4')	0.0856	±	0.033	2.51	±	0.19

coupling constants[e]			
7,8eq	2.6	1',2'eq	1.1[f]
7,8ax	3.3	1',2'ax	4.1
8eq,8ax	14.1	2'eq,2'ax	13.3
8eq,9	2.6	2'eq,3'	5.0
8ax,9	13.1	2'ax,3'	12.7
9,10eq	5.2	3',4'	2.8
9,10ax	11.8	4',5'	1.3
10eq,10ax	18.7	2'eq,4'	1.0[f]
8eq,10eq	1.7	1',4'	1.0[f]
7,10ax	0.6	3',NH	8.9
		4',OH	8.7

[a] Standard deviation

[b] Uncertainties calculated from the standard deviations of σ value through the error propagation law.

[d] Reference value, obtained from the average of T_1 experiments, molecular mechanics calculations and X-ray analyses of analogue molecules. This distance has been adopted as a reference, because the conformation of the sugar moiety is constant for all daunomycin analogues studied (2).

[e] Measured at 300 MHz, 25°C, $CDCl_3$. Accuracy within ± 0.05 Hz.

[f] Accuracy ± 0.1 Hz.

The interproton distance values, Table 1, were obtained by the usual equation given for extreme narrowing and isotropic molecular motions. That the overall motion of the molecule is isotropic resulted from the ^{13}C N T_1 values for all protonated carbons (excluding methyl groups), which are equal within the experimental error. Consequently internal motions such as rotation or ring inversion are either negligible or not contributing to the relaxation process. The correlation time derived by ^{13}C experiments is equal to 4.9×10^{-11} s, assuming a predominant contribution from directly attached protons and a C-H distance of 1.1 Å. This value has been used to calculate an interproton reference distance ($r_{4'-5'}$ = 2.52 Å), which is in good agreement with those obtained by molecular mechanics calculations (2.41 Å) and by X-ray analyses of daunomycin (2.38, 2.33 Å) and of the analogue carminomycin (2.45 Å)(*).

The glycosidic linkage geometry has also been expressed in term of the rotational angles ϕ = H(1')-C(1')-O(7)-C(7) and ψ = C(1')-O(7)-C(7)-H(7), which were derived from the experimental distances of Table 1 by using a model geometry generated by molecular mechanics calculations. A starting geometry was created by standard bonds lengths and angles; the sugar moiety was then rotated, changing systematically the torsional angles ϕ and ψ, in order to find the best agreement between the experimental and calculated interatomic distances (Figure 2), which occurs for ϕ = 42° and ψ = -10°. The preferred conformation is shown in Figure 3.

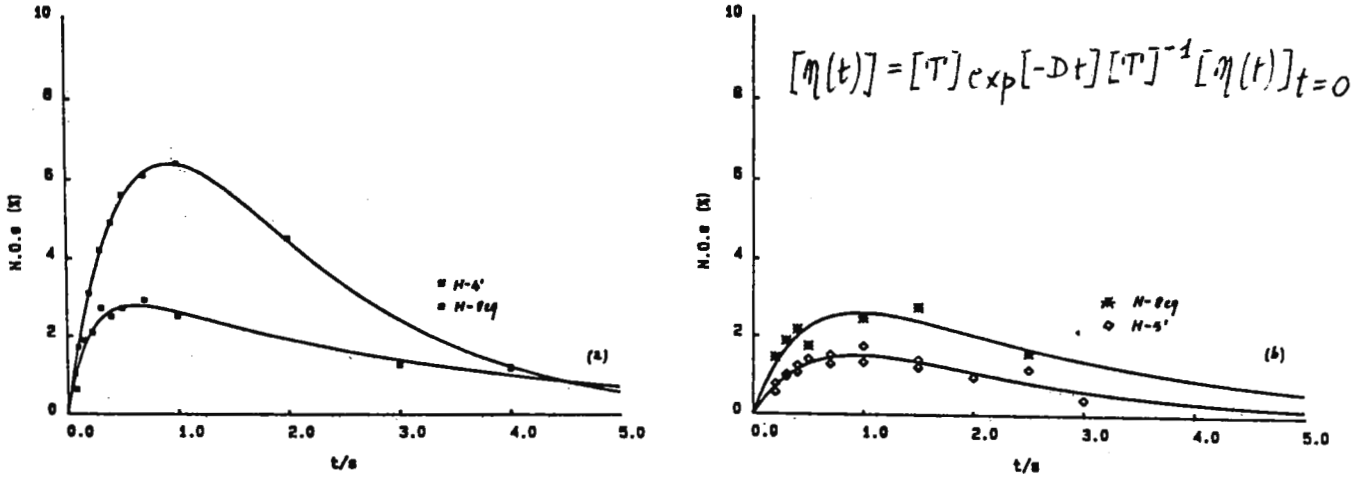


Figure 1. Examples of the transient NOE experiments; (a) inversion of H-5', (b) inversion of H-9. [T] is the matrix formed by the eingenvectors of the relaxation rates matrix and [D] is the diagonalized relaxation matrix.

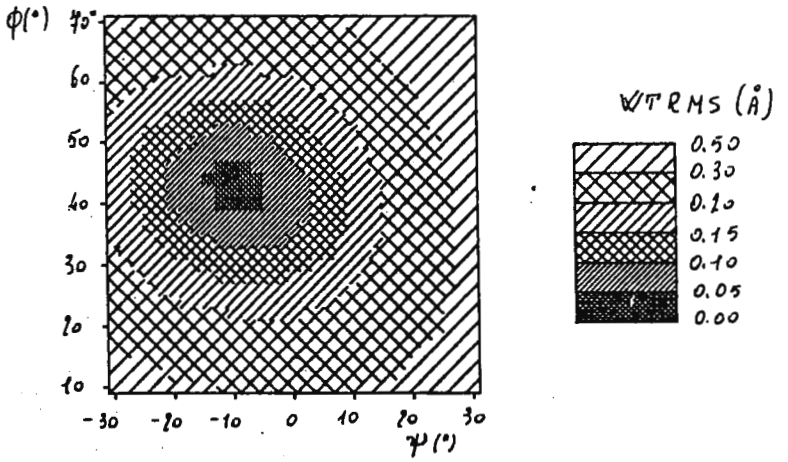


Figure 2. Weighted Root Mean Square (WTRMS) of deviations between computed and experimental distances ($r_{5'-9}$, $r_{5'-8eq}$ and $r_{1'-7}$), as functions of ϕ and ψ angles.

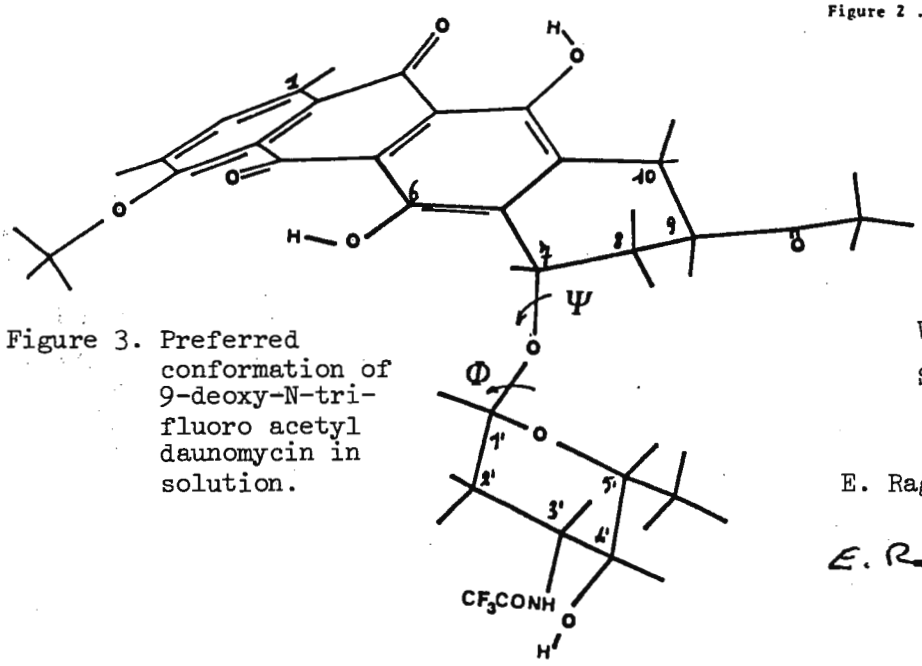


Figure 3. Preferred conformation of 9-deoxy-N-trifluoro acetyl daunomycin in solution.

With best greetings.

Sincerely Yours,

E. Ragg R. Mondelli

(1) R.Mondelli, E.Ragg, G.Fronza, J.Chem.Soc.Perkin Trans. II, 27 (1987).
(2) R. Mondelli, E. Ragg, G.Fronza, A.Arnone, J.Chem.Soc. Perkin II, 15 (1987)
(*) References quoted in (1)

POSITIONS AVAILABLE

Varian Associates Instrument Group is a major producer of analytical instruments and associated equipment used in laboratories around the world. Our NMR Spectrometers provide problem solving capabilities in a diverse field of applications ranging from Basic Chemicals and Materials Science to biomedical and biotechnological research to in-vivo spectroscopy and imaging. We currently have openings in our Florham Park, New Jersey, office for Applications Chemists.

You will be responsible for customer support, technical assistance for sales, and NMR applications research and development. Travel requirements will be 25% to 40%. The successful candidate will have a PhD in the life sciences, experience in liquids analysis in biochemical applications, problem solving capabilities, and knowledge of Varian Spectrometers desirable. Management experience is also a plus.

At Varian, you will enjoy a competitive salary and benefits package, plus a balance of business, science and people that make for satisfying growth. For confidential consideration, please send your resume to: Kathy Brainerd, Varian Associates, Inc., 505 Julie Rivers Road, Suite 150, Sugar Land, TX 77478

An Equal Opportunity Employer M/F/V/H

UNIVERSITÉ DE LAUSANNE

INSTITUT DE CHIMIE ORGANIQUE

Rue de la Barre 2 – CH-1005 Lausanne
Téléphone (021) 44 42 50

Post-Doctoral position

We are looking for an experienced NMR spectroscopist to join our team. We are currently working on various 2D methods for studying cross-relaxation (NOE), effects of cross-correlation between different mechanisms, and relaxation induced coherence transfer. New 2D methods are also under development to make automated analysis by pattern recognition more reliable. Candidates with a background in solid-state NMR or with an interest in biological applications would also be welcome. Equipment includes AM 400, WH 360, Aspect 1000, Aspect X32, VAX 8550. Salary in the range of Sfr. 3'000.- to 4'000.- per month (ca. $ 2'000 to 2'600) will be provided by the Swiss National Science Foundation.

Geoffrey Bodenhausen

Geoffrey BODENHAUSEN

Texas A&M University NMR Newsletter - Book Reviews

Book Review Editor:
William B. Smith, Texas Christian University, Fort Worth, Texas.

"Principles of Nuclear Magnetic Resonance in One and Two Dimensions"

by

Richard R. Ernst, Geoffrey Bodenhausen, and **Alexander Wokaun.**

Oxford University Press, 200 Madison Avenue, New York, New York 10016;
1987; 610 pages; $98.00.

If one were to name those books making fundamental contributions to NMR spectroscopy, no doubt one would start with the books by Abragam, by Pople, Schneider, and Bernstein, and by Emsley, Feeney, and Sutcliffe - all 'bibles' in the field. The present volume, written by three of the leaders in the development of modern pulse NMR theory and practice, may well fall into the same landmark category.

After a brief introductory chapter, the physics of nuclear spin systems is explored, with the aid of density matrix theory. Chapter Three demonstrates the manipulation of the nuclear spin Hamiltonian as applied to double resonance and multiple pulse sequences. Chapter Four covers one-dimensional Fourier spectroscopy. Linear and non-linear response theory are covered from both a classical and quantum mechanical view.

Multiple quantum transitions and coherences are discussed in Chapter Five as a background to two-dimensional spectroscopy, which is the subject matter of Chapters Six through Eight. Chapter Nine covers dynamic process such as chemical exchange and cross-relaxation. Chapter Ten reviews the background and principles of NMR imaging. In view of the recent diatribes written by proponents of the various imaging techniques, the treatment here is with an even hand and no obvious prejudices.

W.B.S.

THE UNIVERSITY OF ROCHESTER
MEDICAL CENTER
601 ELMWOOD AVENUE
ROCHESTER, NEW YORK 14642
AREA CODE 716
SCHOOL OF MEDICINE AND DENTISTRY · SCHOOL OF NURSING
STRONG MEMORIAL HOSPITAL
DEPARTMENT OF BIOPHYSICS

September 21, 1987
(received 9/28/87)

Professor Barry L. Shapiro
Department of Chemistry
Texas A&M University
College Station, Texas 77843

RF Homogeneity

Dear Professor Shapiro:

We have been looking into B_1 mapping and uncovered some features of general interest. In the usual pulsed Fourier transform NMR experiment, the signal from any point in the probe depends on the specific pulse sequence and the ability of the probe to create and detect transverse magnetization at that point[1]. We call the ability to detect a signal the receive function. The spatial dependence of the receive function is proportional to the signal generated in the probe from a unit current flowing in a small coil moved about within the probe. By reciprocity this function must be proportional to the ability of the coil to set up a field B_1 at the point of the small coil. Thus, the receive function is proportional to $B_1(x,y,z)$ where x,y,z are Cartesian coordinates within the probe.

The ability to create transverse magnetization is dependent on a transmit function which for a simple 90°-FID sequence is $\sin(\gamma B_1(P^{1/2}, x,y,z)t)$ where P is the power of a pulse of length t and γ the gyromagnetic ratio. For the case of an ideal spin-echo pulse sequence, i.e., instantaneous rotation of all spins and the evolution of spin packets to a uniform distribution about the z axis before the application of the 180° pulse, the transmit function is $\sin^3(\gamma B_1(P^{1/2}, x,y,z)t)$. (See figure). Reality may be nearly square pulses of finite length, or in imaging application cases an apodized sinc function pulses. In either case a deviation from the $\sin^3$ dependence may be observed as seen in the figure below. The functional dependence in these cases is best determined on an individual basis using a numerical integration of the Bloch equations.

These relations may be utilized in conjunction with imaging hardware to generate B_1 field maps[2]. We fill the volume of the resonator with a uniform concentration water phantom of known T_1 and T_2. The rf power level is adjusted to obtain an image in which at least one region is rotated by the required 90° and 180°. All others, depending on the homogeneity of B_1 within the resonator, are rotated by equal or lesser amounts. Under conditions of a fixed transmitter power setting the ratio $B_1(x,y,z)/B_{1max}(x,y,z)$ may be replaced with $(B_1(P^{1/2}, x,y,z)/B_{1max}(P^{1/2},x,y,z))$. The normalized RF magnetic field for a fixed power level will be related to the signal, S, by the transcendental function $S/S_{max}=(B_1(P^{1/2},x,y,z)/B_{1max}(P^{1/2}, x,y,z))\sin^3(\gamma B_1(P^{1/2},x,y,z)t)$. A straight-forward computer program may then be used to convert an intensity image into a B_1 image.

Continued...

(1) D. I. Hoult, P, C. Lauterber, J. Magn. Reson., 34, 425 (1979).

(2) J. P. Hornak, J. Szumowski, and R. G. Bryant, Submitted to Magn. Reson. In Medicine, 1987.

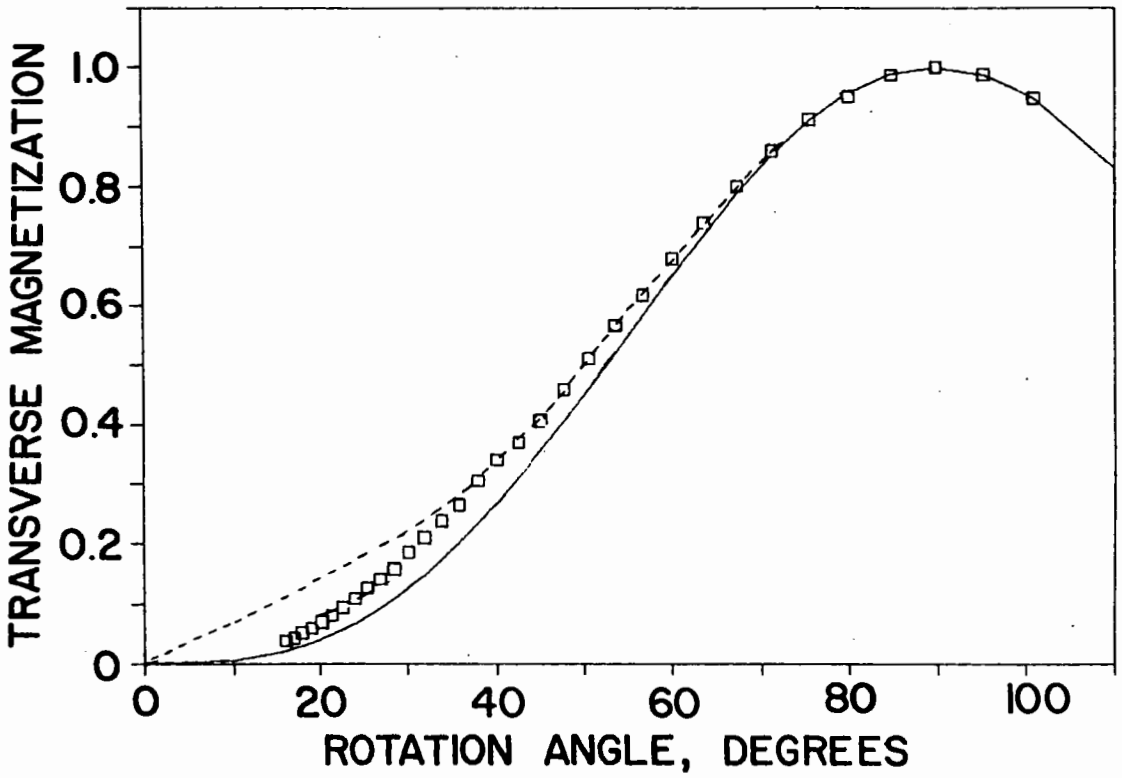


Figure 1. A comparison of the experimental ☐ and computed dependence of spin echo transmit function on a GE Signa imager. The solid line corresponds to the assumption of instantaneous RF pulses. The dotted line results from a numerical integration of the Bloch equations with an apodized sinc RF pulse, spin relaxation, and an experimentally measured lineshape.

Sincerely,

Joseph P. Hornak
Joseph P. Hornak
Assistant Professor

Robert G. Bryant
Dean's Professor

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
National Institutes of Health
Building 2, Room B2-02

National Institute of Diabetes a
Digestive and Kidney Diseases
Bethesda, Maryland 20892

Professor Bernard L. Shapiro
966 Elsinore Court
Palo Alto, California 94303

September 28, 1987
(received 10/2/87)

Dear Barry:

TITLE: DRAIN PIPE FILTER

To eliminate some annoying spikes and clean up the signal on our NT 500, we have constructed a very low loss bandpass filter for protons. It consists of a coaxial resonator made from 2 sections of copper water pipe, has an insertion loss of <0.1 db and goes between the probe and the preamp. Tuning is by center screw. Bandwidth and match can be set by changing the shape and size of the wire loops. The inside surfaces should be cleaned of any oxide layers. The filter can be built for other frequencies by scaling the height proportional to 1/f (i.e. 6.96" for 360 MHz).

Instead of the expected small loss in signal-to-noise ratio, we actually found an improvement in sensitivity of about 10%. The filter is particularly useful for ^{1}H-detected heteronuclear shift correlation experiments where it prevents the high power X-decoupling from reaching the ^{1}H preamplifier.

Sincerely,

R. Tschudin

Rolf Tschudin
Laboratory of Chemical Physics

Legend to Fig. 1 & 2:

1. Copper pipe, 3" i.d., 3 1/4" o.d., 5" long.
2. Copper pipe, 3/4" i.d., 7/8" o.d., 4 9/16" long.
3. Base plate, copper, 4" x 4" x 1/16", corners rounded.
4. Top plate, copper, 4" x 4" x 1/16", corners cut off.
5. End cap, copper or brass, 7/8" dia.
6. Tuning screw, 1/4-32, 1 1/4" long, brass.
7. Positive contact spring, 1/4" i.d., bronze or steel.
8. Washer, 1/4", brass.
9. Tie rods, 1/8" dia. brass, 5 1/4" long, both ends threaded. 5-40 for 1/4". 8 of.
10. Nuts, 5-40, brass. 16 of.
11. Rubber feet. 4 of, glued to corners of base plate.
12. BNC Bulkhead connectors. 2 of.
13. Solder lugs, copper. 2 of.
14. Wire loops, #18 bare copper wire, ~2 1/2" long. 2 of.
15. Screw, 4-40, brass.
16. Disk, 1/2" dia., 1/16 thick, brass or copper.

FIG.1
TOP VIEW
HALF SCALE

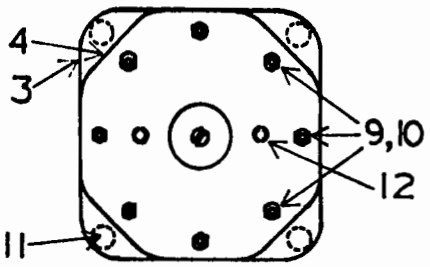
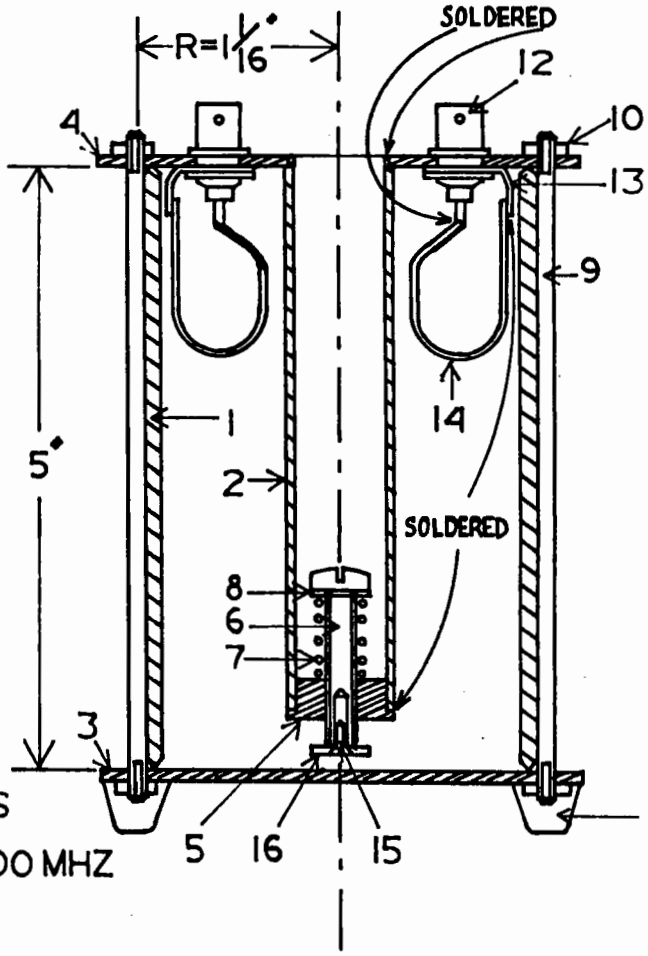


FIG.2
SECTION
FULL SCALE



LOW LOSS
FILTER, 500 MHZ

ACHTUNG HOMEBUILDERS

We have a superconducting solenoid, 220 MHZ, VARIAN Ser. #114, bare, with persistence switches, but no dewar, power supply or control unit. We are willing to donate it to a worthy cause. If interested, please contact the undersigned.

Yours very truly,

Rolf Tschudin
Laboratory of Chemical Physics
(301) 496-2692

State University of New York
Health Science Center
Syracuse

College of Medicine

Department of Radiology
Division of Radiological Sciences
(315) 473-8470

October 9, 1987
(received 10/16/87)

Dr. Bernard L. Shipiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, CA 94303

Dear Barry:

We had an interesting experience in our laboratory. Joop van Nesselrooij, a visiting scientist studying pituitary tumors in rats, was positioning an animal in the bore of our 2 Tesla imaging instrument when he became aware of a pain in his left thumb. The intensity of the pain was found to be correlated with the proximity of the thumb to the bore of the magnet.

The accompanying X-ray (negative) explains the source of the discomfort -- a small metal chip located just under the thumbnail. The history of this thumb is that it was involved in an accident 20 years ago when our researcher was repairing his car. A metal spring snapped him in the thumb, apparently driving this ferrometallic fragment under the nail.

It was recently removed surgically and we believe this to be the first documented experiment involving adiabatic demagnetization by surgical intervention (ADSI).

Sincerely,

Nikolaus M. Szeverenyi

Joop van Nesselrooij

Bruker delivers.

Again.

Since its foundation in 1960, Bruker has continued to make major contributions to the field of commercial analytical instrumentation, especially NMR:
1963: World's first pulsed NMR spectrometer.
1967: World's first truly multinuclear high resolution NMR spectrometer.
1969: Introduction of Fourier transform techniques for NMR.

Since then Bruker has entered the fields of FT-IR, NMR Imaging (MRI), and in-vivo spectroscopy.

We introduced a fiberoptics link for high-speed data transfer and ultra-fast array processors for the new generation of NMR data processing systems.

Then in 1986 we introduced the first microscopy accessory for NMR.

And now Bruker announces the 600 MHz high resolution NMR spectrometer.

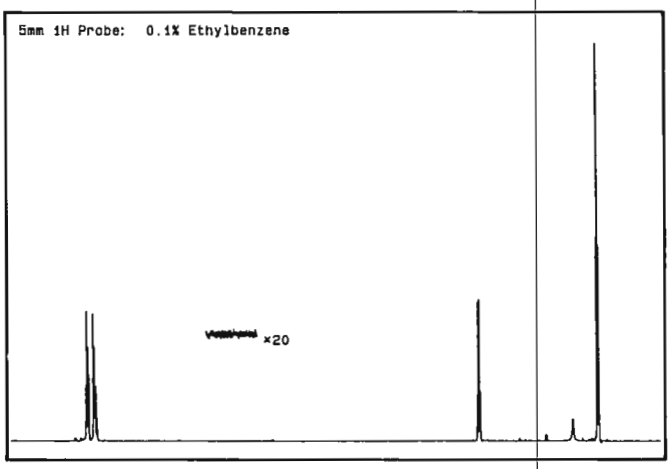
In short, no other manufacturer has advanced NMR as significantly as Bruker. And no one delivers as complete a line of systems and accessories for research and routine NMR, and as comprehensive a support package:
From hardware to software, from technical service to applications support. Bruker delivers. To find out more, drop us a line or use the reader service card.

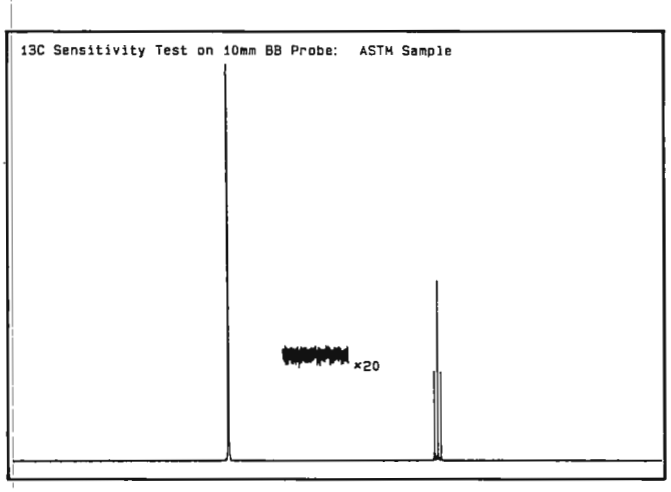
Bruker Instruments, Inc.
Manning Park, Billerica, MA 01821

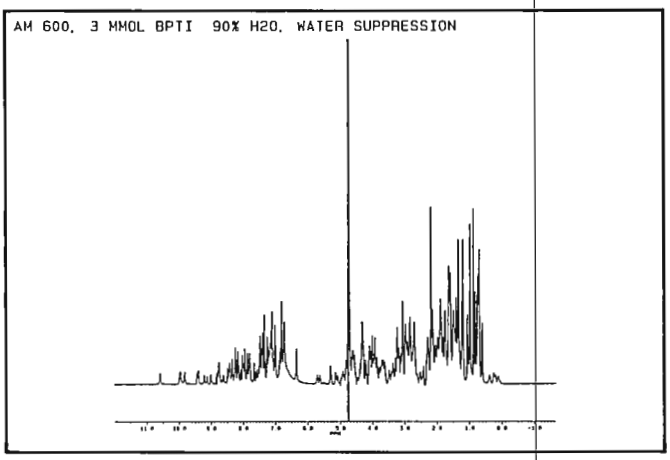
In Europe: Bruker Analytische Messtechnik GmbH, Silberstreifen, D-7512 Rheinstetten 4, W. Germany

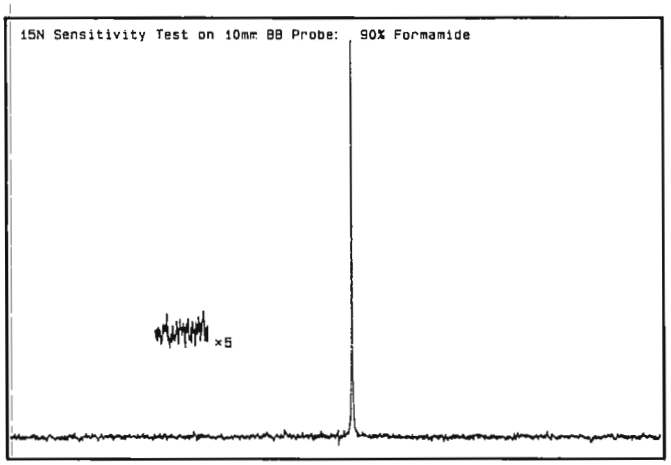
BRUKER *NMR Systems designed to solve problems.*

AM 600 NMR Spectra









Current AM 600 specifications (subject to change):

Probehead	Nucleus	Test	Value
^{1}H selective (5mm)	^{1}H	lineshape	10/20
		S/N	600:1
Broadband (5mm)	^{13}C	S/N (ASTM)	220:1
		S/N (10% EB)	180:1
		lineshape	6/15
	^{15}N	S/N (FORM)	25:1
Broadband (10mm)	^{13}C	S/N (ASTM)	650:1
		S/N (10% EB)	375:1
		lineshape	6/15
	^{15}N	S/N (FORM)	80:1
Resolution (all probes)			0.25 Hz

Magnet drift: ca. <40 Hz/hr

EB = ethylbenzene with ^{1}H decoupling
ASTM = 60% C_6D_6 in dioxane
FORM = Formamide (^{1}H decoupling without NOE)
LINESHAPE: ^{1}H = $CHC1_3$ linewidth at height of ^{13}C satellite/at 20% this level
^{13}C = C_6H_6 linewidth at 0.55%/0.11% of peak height

NMR FT-IR DATA SYSTEMS BRUKER NMR IMAGING EPR MS

Australia: BRUKER (Australia) Pty. Ltd., Earlwood, New South Wales, Tel. 02-5589747
Belgium: BRUKER SPECTROSPIN S.A./N.V., Bruxelles, Tel. (02) 7 36 11 38
Canada: BRUKER SPECTROSPIN LTD., East Milton, Ontario, Tel. (416) 876-4641
England: BRUKER SPECTROSPIN LTD., Coventry, Tel. (0203) 463770
France: SADIS BRUKER SPECTROSPIN SA, Wissembourg, Tel. (088) 94 98 77
India: BRUKER INDIA SCIENTIFIC Pvt. Ltd., Andheri (West), Bombay, Tel. 22 62 72 32
Italy: BRUKER SPECTROSPIN SRL, Milano, Tel. (02) 23 50 09, 2 36 40 69
Japan: BRUKER JAPAN CO. LTD., Ibaraki, Tel. 0298-52-1234
Netherlands: BRUKER SPECTROSPIN NV, Wormer, Tel. (75) 28 52 51
Scandinavia: BRUKER SPECTROSPIN AB, Åkersberga, Sweden, Tel. (07 64) 6 80 60
Spain: BRUKER ESPANOLA S.A., Madrid, Tel. 341-259-20-71
Switzerland: SPECTROSPIN AG, Fällanden, Tel. 182-59-111
W.-Germany: BRUKER ANALYTISCHE MESSTECHNIK GMBH, Rheinstetten, Tel. 0721-5161-0
BRUKER ANALYTISCHE MESSTECHNIK GMBH, Karlsruhe, Tel. 0721-5967-0
BRUKER-FRANZEN ANALYTIK GMBH, Bremen, Tel. 0421-8700-80
USA: BRUKER INSTRUMENTS, INC., Billerica, MA 01821, (617) 667-9580
Regional Offices in Chicago/IL, Wilmington/DE, Houston/TX, San Jose/CA

TH Delft

Delft University of Technology

Department of Applied Physics

P.O. Box 5046
2600 GA Delft, The Netherlands

Lorentzweg 1
2628 CJ Delft, The Netherlands
University switch board:
(015) 789111
Telex 38151 hbthd nl

Prof. B.L. Shapiro
966 Elsinore Court
Palo Alto, California 94303 USA

Your reference and date	Our reference	Office telephone	Date
		781025	Oct. 13, 1987
Subject			(received 10/21/87)

IN VIVO PROTON WATER-SUPPRESSED SPECTROSCOPIC IMAGING OF RAT BRAIN

Dear Professor Shapiro,

We develop methods for localised in vivo NMR spectroscopy (MRS) on the brain of non-anesthetised rats in order to monitor concentration changes of a number of metabolites simultaneously during for instance pathological processes. Spectroscopic Imaging (SI) [1] for the 3 spatial dimensions separately with water suppression is done to achieve optimal positioning and dimensioning of the Volume of Interest (VOI) for localised MRS measurements.

Conscious rats with surface coils implanted chronically onto the top of the bare skull are restrained in a head-body holding device [2]. On our homebuilt 7T spectrometer we use a Hore [3] $1\bar{1}$-$2\bar{2}$ spin echo water suppression sequence with an echo time of 136 msec and the spectral window centered on the resonance of N-acetyl aspartate at 2.02 ppm. 1-D spatial information is phase-encoded by incrementing the amplitude of a gradient pulse, given after the $1\bar{1}$ pulse, symmetrically around 0 in 48 steps. Combined EXOR- and Cyclops phase cycling (8 steps) is done. With a repetition time of 2 sec, sufficient signal-to-noise ratio (S/N) is obtained in 15 minutes.

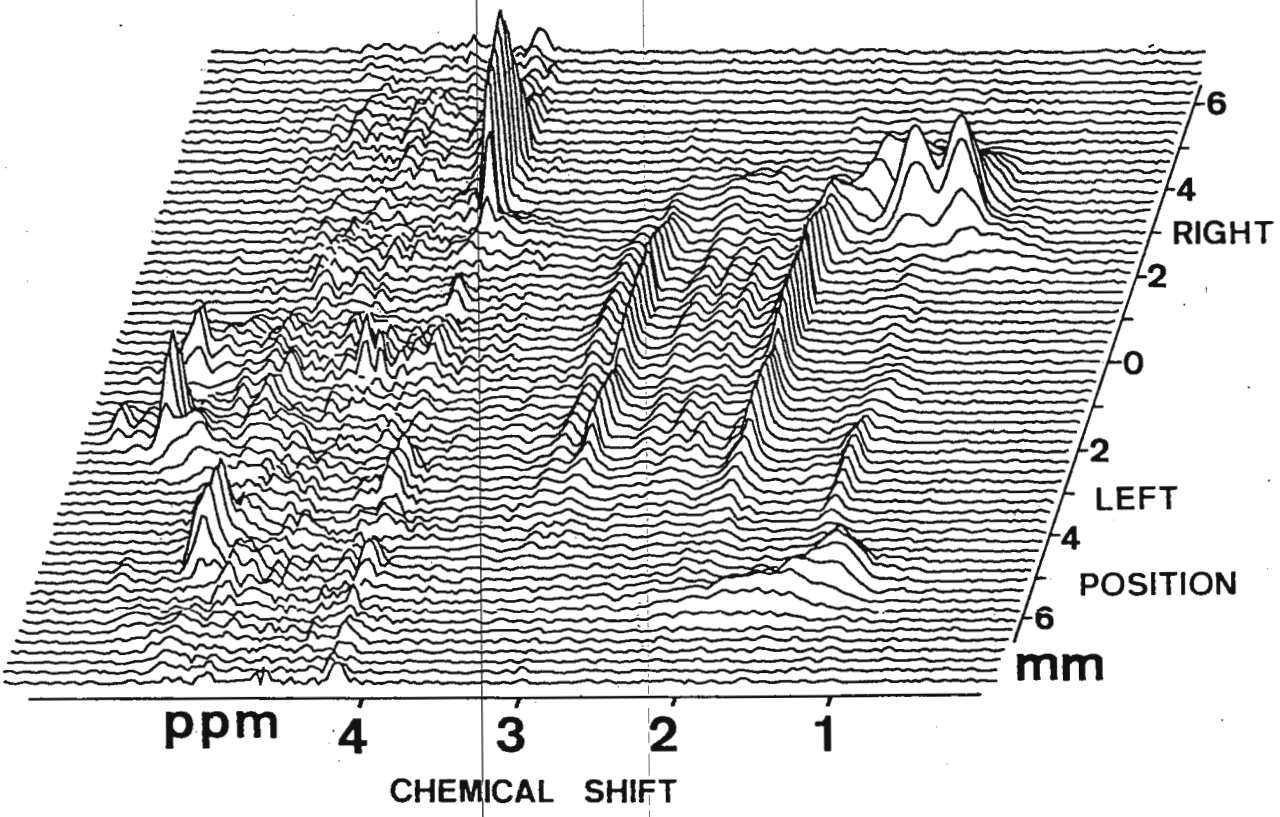
In one of our experiments we used a rat which had a localised lesion in one hemisphere of the brain. As a result of this, the animal frequently lost its balance. Effects of this lesion can be seen in the SI shown in the figure which we took from this rat. It shows spectra from sagittal slices, going from the left to the right side of the brain (0=midline position). In the chemical shift dimension, main contributions are from: water (above 4 ppm), choline compounds (3.2 ppm), creatine compounds (3.0 ppm), (N-acetyl)aspartate (2.6 ppm), glutamine (2.4 ppm), glutamate (2.3 ppm) and N-acetyl aspartate (2.0 ppm). Lipids (1 to 2 ppm) appear to be localised at extreme left and right positions. The interesting thing is that we can see lactate (1.3 ppm) elevated in the left hemisphere, while the other metabolites have reduced intensities compared to the right hemisphere, where hardly any lactate seems to be present.

Obviously, Spectroscopic Imaging can be a very helpful tool in getting a spatial overview of the metabolic state of tissue and in checking out possible localisation artifacts.

References
1. A.Maudsley, S.Hilal, W.Perman, H.Simon, J.Magn.Res. 51, 147 (1983).
2. N.Deutz, W.Bovee, R.Chamuleau, J.Neurosci.Meth. 16, 157 (1986)
3. P.Hore, J.Magn.Res. 55, 283 (1985)

Albert de Graaf

Wim Bovée



In vivo spatially 1-D water-suppressed proton Spectroscopic Image at 7T of the brain of a rat with a localised lesion in the left brain hemisphere.

ISOTEC INC.
A Matheson Company
Stable Isotopes for Research and Industry

October 18, 1987

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

POSITIONS AVAILABLE

Dear Barry:

As you know, several of my former coworkers and I are now with Isotec, comprising the core of our labelled compound operation. Isotec Inc. has been in business for eight years, separating and enriching He-3 and the other noble gas stable isotopes as well as the stable isotopes of carbon, nitrogen and oxygen; for the last couple of months, we have been completing our synthesis labs and producing stable isotope labelled compounds.

Because of this new product line, we have a number of job openings. We are looking for several good chemists with organic synthesis backgrounds (B.S., M.S. and Ph.D. levels), preferably with some experience using stable isotopes in syntheses. Since a number of your readers have employed such people in their labs, although usually for short periods, I thought they might be able to recommend some suitable candidates.

We are also looking for two salespeople. One, for an "inside" sales position, would report to Maureen Kalloo, and would handle phone orders and customer requests by interfacing with the lab and the outside world. A person with a B.S. in chemistry is preferred, but others with related backgrounds will be considered. The other opening is for an "outside" salesperson who would report to me. This person will probably not travel during the first six months, but would then be expected to travel extensively to promote our line of stable isotope labelled compounds (including NMR solvents) to the research community. Clearly, a knowledge of NMR and/or mass spectrometry would be an asset. The candidate should have a B.S. or M.S. in organic chemistry; previous technical sales experience would be very useful. Further details about any of these positions can be obtained by calling me at (800) 448-9760. Isotec is owned by Matheson Gas Products and employees are offered the full range of company benefits.

For those who worry about the important things in life, there will be an Isotec Suite at the ENC--in the style to which they have become accustomed.

Best Regards,

Myra

Myra Gordon, Manager
Sales and Marketing
Labelled Compounds

3858 Benner Road, Miamisburg, Ohio 45342 U.S.A. • Phone 513/859-1808
Telex 288278 • Fax (513) 859-4878 • Easy Link 62014510

THE ROCKEFELLER UNIVERSITY
1230 YORK AVENUE • NEW YORK, NEW YORK 10021-6399

14 October 1987
(received 10/19/87)

Dr. Bernard L. Shapiro
TAMU NMR Newsletter
966 Elsinore Court
Palo Alto, California 94303

Dear Dr. Shapiro:

"Natural Abundance $^{1}H\{^{15}N\}$ Spectra of
Bovine Pancreatic Trypsin Inhibitor"

With the development of ^{1}H detected heteronuclear chemical shift correlation spectroscopy, detection of ^{15}N spectra has become possible for peptides and small proteins at natural abundance. Use of nitrogen chemical shifts of backbone and side chain amides for structural investigation requires essentially complete assignments. In addition, there has recently been considerable interest in studying ^{15}N enriched proteins, and further improvements in understanding the origin of the variation of chemical shifts with primary, secondary, and tertiary structure are likely to be of general use. We have attempted a complete assignment of the $^{1}H\{^{15}N\}$ spectra at natural abundance from bovine pancreatic trypsin inhibitor (BPTI), a small (MW 6500) rigid protein which has been the molecule of choice for extensive proton NMR studies.

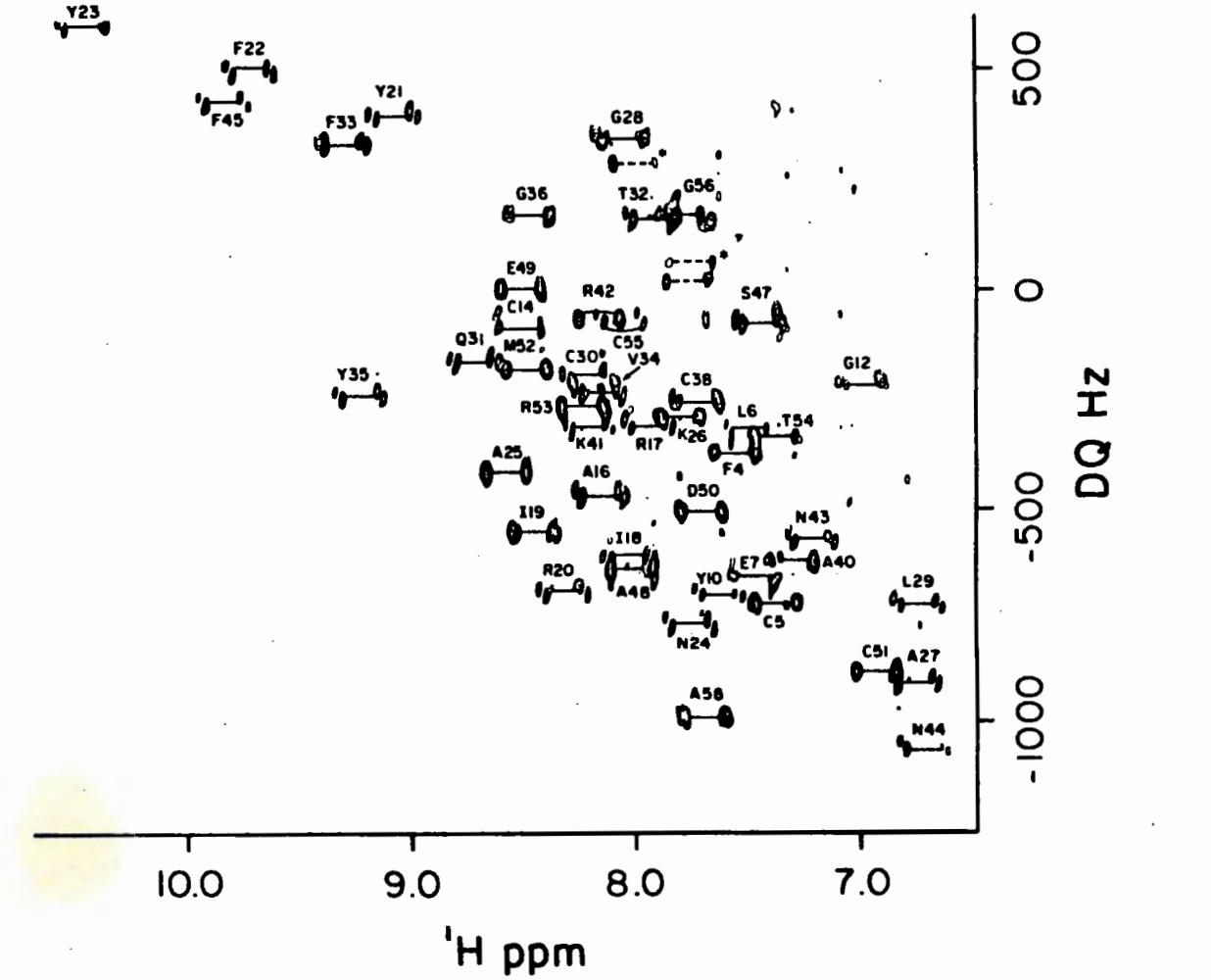
We have shown that a sufficiently accurate assignment of the ^{15}N chemical shifts in a small protein is practical at natural abundance. The correlation of this data to secondary structural features produces some qualitative relationships which are commented on in a fuller description to appear in JACS; further NMR studies on compounds with known structural data are necessary to separate the multiple factors contributing to chemical shift deviations arising from conformational effects.

Sincerely,

John Glushka

David Cowburn

Figure - $^{1}H\{^{15}N\}$ heteronuclear double quantum spectrum of BPTI in 10% D_2O/90% H_2O, pH 4.6, 23 mmol., at 68° C. The proton carrier frequency was at 8.77 ppm relative to internal trisylylpropionic acid reference. The data matrix was 4096 x 128 with acquisition times of 680 ms and 16 ms for t_2 and t_1 respectively. For each t_1 block, 1200 accumulations were taken, with an interacquisition delay of 100 ms, for a total accumulation time of 33 hours. The data were processed with a gaussian function applied to t_2 and zero filling to 512 points in t_1. Doublets split by $^{1}J_{NH}$ couplings are joined with a line and labelled with their assignment. Peaks labelled with a star are thought to belong to slowly exchanging Asn 43 and 44 carboxamides. Missing from this plot are signals from D3, K15, G37, R39, K46, and G57, D3, R39, and K46 were observed at other temperatures; K15, G37, and G57 remain unassigned.



FACULTY POSITION - The Department of Chemistry of Jackson State University invites applications for a tenure track position effective, January, 1988. The area of specialization is open; however the candidate must have research experience in modern NMR techniques and have a commitment to teaching. Candidates with experience in the application of NMR to biological or material sciences research will be favored. Departmental NMR facilities include a new widebore GN300 spectrometer. Duties include teaching general chemistry and undergraduate and M.S. level courses in the area of specialization and establishing a research program. Send curriculum vitae, statement of research interests, teaching goals and three letters of recommendation by November 30, 1987 to:

Dr. Richard H. Sullivan
Chair
Department of Chemistry
Jackson State University
Jackson, MS 39217

Prof. V.F.BYSTROV
USSR Academy of Sciences
Shemyakin Institute of Bioorganic Chemistry
Ul. Miklukho-Maklaya, 16/10
117871 GSP Moscow V-437
USSR

September 15, 1987

Title: 2D NMR Solution Structure of Scorpion Long Neurotoxin

Professor Bernard L.Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas
USA

Dear Barry,

Recently we finalized the NMR study of mammalian neurotoxin M_9 isolated from the *Buthus eupeus* Central Asian scorpion venom. The toxin consists of 66 amino acid residues with four disulfide bonds and belongs to the family of "long" scorpion toxins.

The 500 MHz proton 1D NMR spectra revealed two slowly exchangable conformations, relative content of which is pH and temperature dependent, apparently originated by the *cis-trans* isomerisation of one of five X-Pro peptide bonds (presumably, Leu^8-Pro^9).

The spatial structure of the M_9 conformer predominant above pH 1.5 was studied at pH 2.5-3.0, 30°C. For this conformer nearly complete residue specific signal assignment was obtained in phase-sensitive COSY and NOESY (τ_m=0.2s) proton spectra with digital resolution 0.4-3 Hz/point (ω_2) and 5-6 Hz/point (ω_1) [Bioorg. Khim. (USSR) *12* (10) 1306 (1986)]. The obtained results on sequential and sequentially distant NOE's, ^3J(HN-C$^\alpha$H), and deuterium exchange rates of peptide NH groups (H-bonding) were used as input data for the modified distance geometry algorithm with pseudoatomic representation [*ibid, 11* (9) 1192 (1985)].

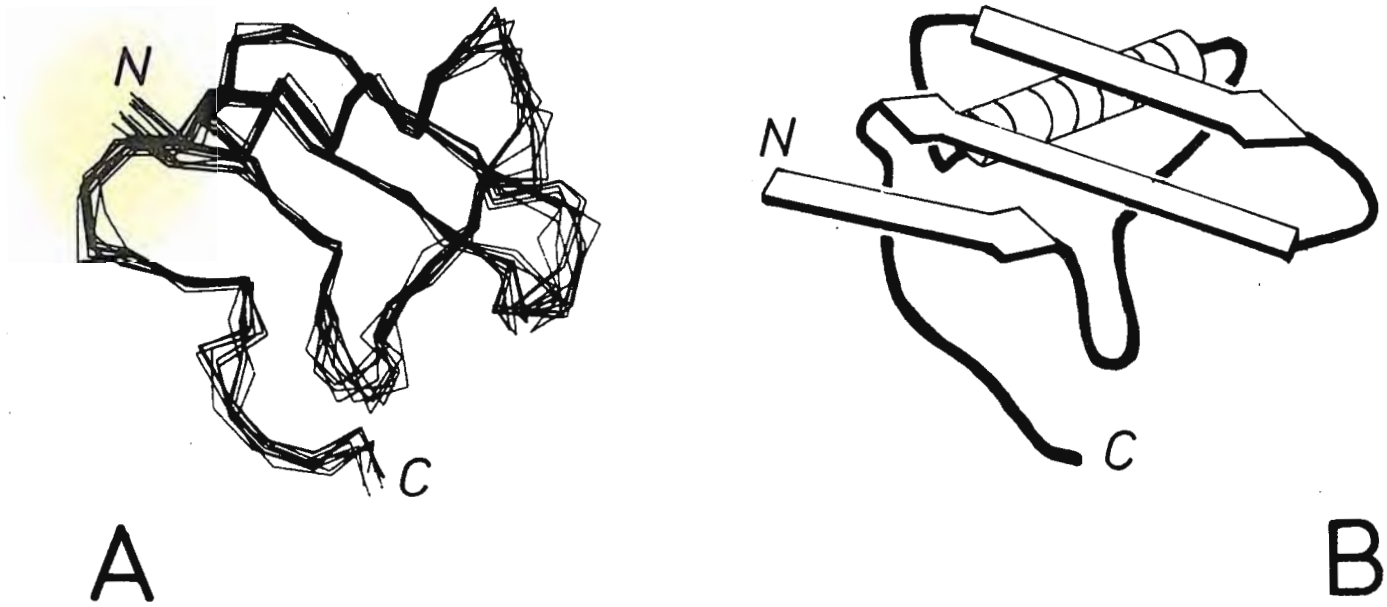
The ten spatial structures that are consistent with experimental constraints with the lowest error function are shown in Fig. A. For these structures the average root-mean-square deviation of coordinates of α-pseudoatoms is 2.1±0.2 Å and for both α- and β-pseudoatoms is 2.3±0.3 Å. In Fig. B the structure is presented in a highly schematic form to demonstrate the main features,which are the 2.5-turn α-helix (residues 22-31) in the central part of the polypeptide and the three-stranded antiparallel β-structure (residues 1-5, 35-40 and 46-52). All five X-Pro bonds are in the *trans*-configuration.

The obtained conformation resembles the X-ray structure of scorpion insectotoxin v-3 *Centruroides sculpturatus*, which exhibits different sort of activity and has low sequence homology. Both toxins demonstrate similar conformational motif with "short" insectotoxin I_{5A} *Buthus eupeus* (35 residues, four disulfide bonds) [*ibid*, 9 (6) 768 & (12) 1667 (1983), and *FEBS Lett.* *165* (1) 57 (1984)] in orientation of the α-helix relative to the β-sheet.

The paper is presented to the *Biophysical Chemistry*.

Yours sincerely,

Vladimir Bystrov Vladimir Pashkov Vladimir Maiorov



(A) The α-pseudoatom backbone of ten calculated neurotoxin M_9 structures consistent with the NMR data. The structures are superimposed so as to minimize the root-mean-square deviation of the α-pseudoatoms with respect to the arbitrary chosen structure in the calculated set.

(B) Schematic presentation of the neurotoxin M_9 spatial structure. Tree arrows correspond to the three-stranded antiparallel β-sheet and a cylinder - to the α-helix.

Positions of the N- and C-termini are indicated. The disulfide bonds are omitted for clarity.

TEXAS A&M UNIVERSITY
NMR
NEWSLETTER

No. 350
November 1987

Table of Contents, cont'd.

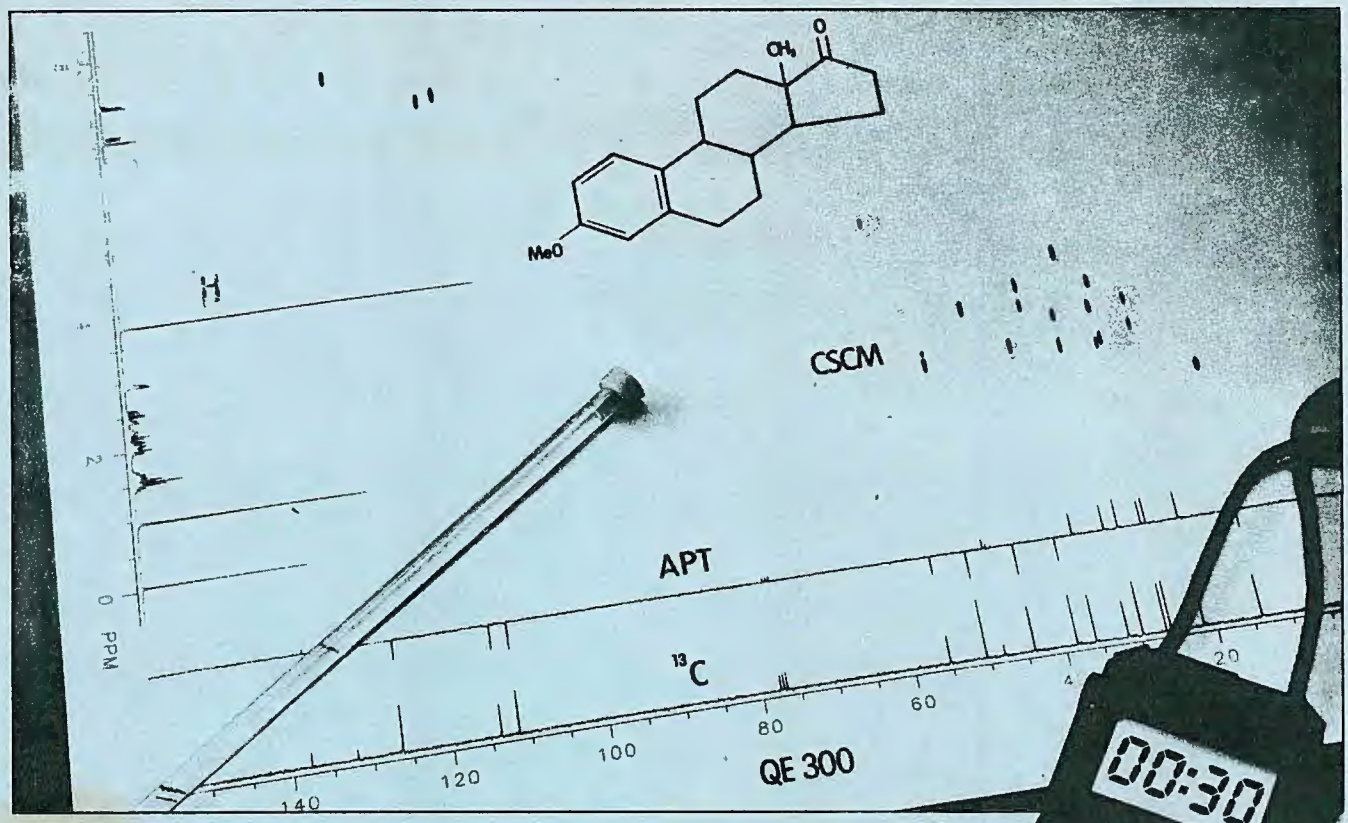
* * * * * * * * *

Sponsors of the TAMU NMR Newsletter

During the past year, the following companies have been Sponsors of the TAMU NMR Newsletter, in virtue of providing significant funding above that required for subscriptions. This form of support of the Newsletter is invaluable - indeed, vital - and we are most pleased to draw this special attention to their generosity.

Abbott Laboratories
The British Petroleum Co., Ltd. (England)
Bruker Instruments, Inc.
Cryomagnet Systems, Inc.
Eastman Kodak Company
E.I. du Pont de Nemours & Company, Inc.
General Electric Company, Medical Systems Group, NMR Instruments
IBM Instruments, Inc.
Intermagnetics General Corporation
JEOL USA, Inc., Analytical Instruments Division
The Lilly Research Laboratories, Eli Lilly & Company
Millipore Corporation, Waters Chromatography Division
The Monsanto Company
The Procter & Gamble Company, Miami Valley Labs
Programmed Test Sources, Inc.
Shell Development Company
Spectral Data Services, Inc.
Unilever Research
Union Carbide Corporation
Varian, Analytical Instrument Division

May we hope that additional companies, other organizations, and even individuals can find a way to join these special supporters of the Newsletter? Details on request.



GE Performance!

^{1}H, ^{13}C, APT, and 2D NMR in ½ hour - automatically!

The GE QE-300 does it all — faster than any other NMR spectrometer.

A ^{1}H spectrum, ^{13}C spectrum, an attached proton test (APT), and a ^{1}H-^{13}C chemical shift correlation map (CSCM). All these analyses can be performed in as little as ½ hour, on as little as 50 mg. of sample, for most organic compounds. And the QE-300 does them all – automatically.

With the NMR industry's most advanced automation.

This performance is made possible by the QE-300's automated software, hardware, and powerful MACRO programming capability.

Set-up starts with *Autolock*. Lock on as little as 10% $CDCl_3$ in a 5 mm tube.

Use *Compushim* for touching-up spinning shims or complete shimming with both spinning and non-spinning gradients using the lock signal or observe FID.

Autogain optimizes the receiver gain independently for sequential ^{1}H and ^{13}C acquisition.

After data acquisition, *Autophase* accurately phases ^{1}H and ^{13}C spectra.

And finally, the analysis is completed with *Autointegrate*.

All these routines can be called up from QE-300 MACROs. In fact, any QE-300 operation, including pulse programs, can be implemented via MACROs for automatic, unattended sample analysis.

And the most complete package of hardware accessories.

The QE-300 is available with the industry's most reliable, highest capacity (100 positions!) *Automatic Sample Changer*. Plus, you can add an array processor, a variety of hard disks, and switchable probes for even higher sample throughput and performance.

Structural elucidation simplified.

For many organic molecules, the four experiments presented above will be all you need to determine or confirm molecular structure. For more complex applications, GE/NMR offers an extensive ^{13}C library with outstanding search capability. This library contains data from over 10,000 compounds and is currently being expanded using a QE-300 in operation at the Aldrich Chemical Company.

High throughput and performance demonstrated.

Get all the facts on the GE/NMR QE-300. Better yet, arrange for a demonstration. Call the GE/NMR group at (415) 490-8310. Or write General Electric Company, NMR Instruments, 255 Fourier Avenue, Fremont, CA 94539.

GENERAL ELECTRIC

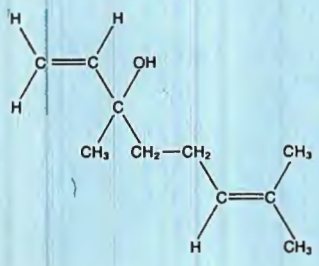
JEOL'S GX-FT NMR Systems

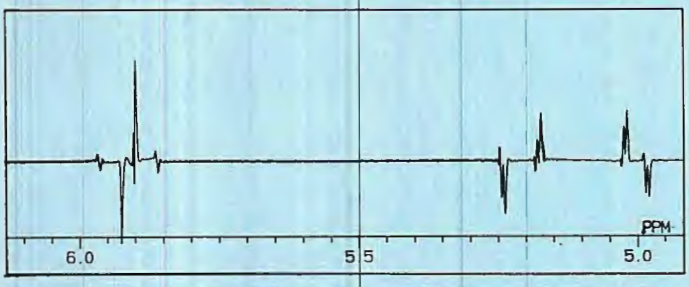
Subject: Automation

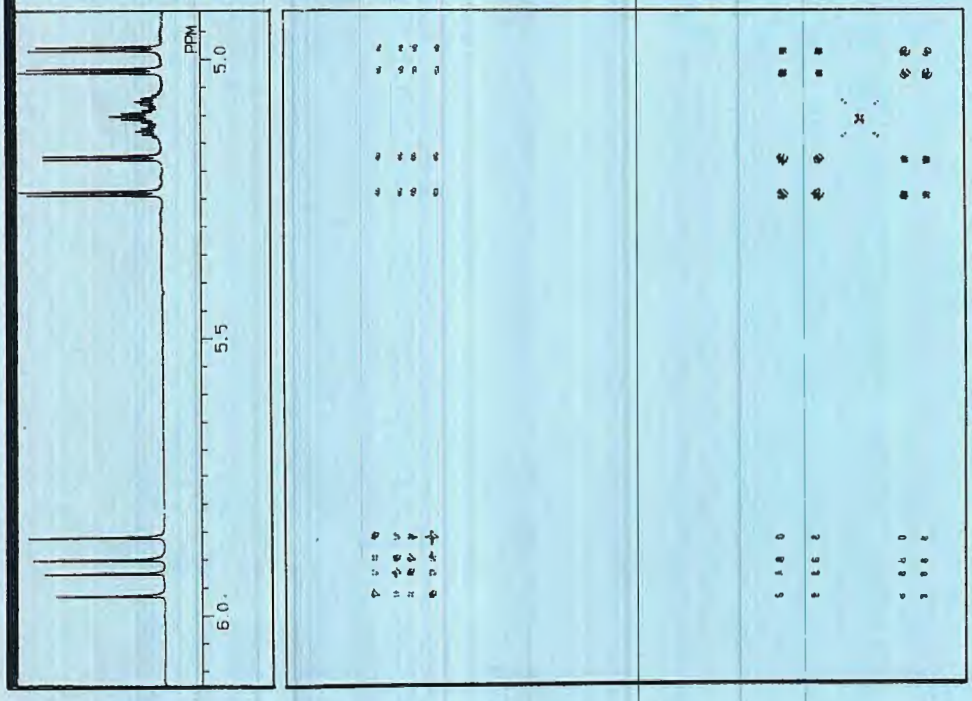
One of the more than 200 (and growing) automated routines available on the GX-Series; the data illustrates a Double Quantum Filter Phase Sensitive Cosy on the downfield section of Linalool run on a GX-270/WB (89mm) MHz spectrometer. From the moment you load the sample, spinning, lock, shimming, acquisition, transform, phase correction, and plotting are totally automated. Should you need something not already in our menu a few strokes on the keyboard will put it there.

So whether your requirements are for routine or research, the GX-FT NMR is an instrument that you should consider when evaluating FT-NMR Systems.

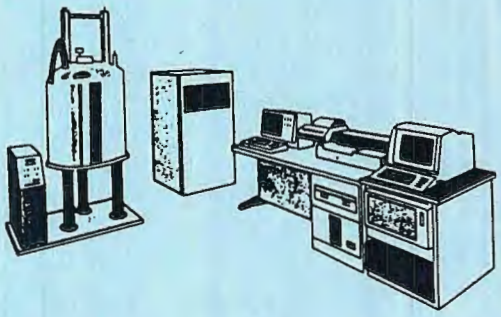
Linalool







The GX Series FT-NMR Spectrometer



For further information call:

JEOL

Serving Advanced Technology

11 Dearborn Road, Peabody, MA 01960
(617) 535-5900