THE NMR NEWSLETTER

No. 478

July 1998

NUTS

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FORTHCOMING NMR MEETINGS

XIVth International Conference on Phosphorus Chemistry, Cincinnati. OH, **July 12 - 17, 1998**. For details, see Newsletter 468, 40.

NMR Symposium at the 40th Rocky Mountain Conference on Analytical Chemistry, Denver, CO, **July 27 - 30, 1998**. Contact: Dr. Robert A. Wind, Battelle/Pacific Northwest National Laboratory, P.O. Box 999, MS K8-98, Richland, WA 99352; (509) 376-1115; Fax: (509) 376-2303; Email: ra_wind@pnl.gov. See Newsletter 470, 8.

XVIIIth International Conference on Magnetic Resonance in Biological Systems, Tokyo Metropolitan University, **August 23 - 28, 1998**. Contact: Professor Masatsune Kainosho, Department of Chemistry, Tokyo Metropolitan University; +81-426-77-2544; Fax: +81-426-77-2525; e-mail: kainosho@raphael.chem.metro-u.ac.jp; http://icmrbs98.chem.metro-u.ac.jp

NMR Technologies: Development and Applications for Drug Design and Characterizations, Baltimore, MD, **October 29-30, 1998**; Contact: Jennifer Laakso, Cambridge Healthtech Institute, 1037 Chestnut St. Newton Upper Falls, MA 02164; 617-630-1300; Fax: 617-630-1325; chi@healthtech.com; http://www.healthtech.com/conferences/.

"NMR of Polymers and Biopolymers," Symposium at the 54th SouthWest Regional ACS Meeting, Baton Rouge, LA, **November 1-2, 1998;** Contact: members.aol.com/ACKolbert/symposium.html or e-mail to: mailto:ackolbert@aol.com" Xiaolian Gao at xgao@uh.edu .

NMR Spectroscopy of Polymers, Breckenridge, Colorado, **January 24-27, 1999**; an International Symposium Sponsored by the Division of Polymer Chemistry, American Chemical Society; Organizers: P. T. Inglefield and A. D. English: Registration contact: Neta L. Byerly, Division of Polymer Chemistry, Inc., Virginia Tech, 201 Hancock Hall, M.C. 0257, Blacksburg, VA 24061; 540-231-3029; Fax: 540-231-9452; email: nbyerly@vt.edu.

40th ENC (Experimental NMR Conference), Clarion Plaza Hotel, Orlando, Florida, **February 28 - March 5, 1999**;immediately preceding Pittcon in Orlando; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073; Email: enc@enc-conference.org.

continued on inside back cover

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

May 26, 1998.
(received 5/27/98)

Dear Barry,

We have been involved lately in characterizing numerous models of congestive heart disorders for evaluating efficacy of drug candidates. One of the critical issues in designing the studies is the necessity to evaluate the most relevant indices and how they relate to overall pharmacological actions of compounds. We have used cardiac-gated magnetic resonance imaging (MRI) as an interrogating tool for understanding physiological changes in heart structure and function serially.

The hemodynamic information (stroke volumes, etc) with appropriate estimates of blood pressure from the aortic arch, (i.e. afterload) can generate indices of (a) work done by the heart per beat to push a given stroke volume against the afterload i.e. the stroke-work (Joules/kg), (b) power required by the heart to achieve such stroke-work (Watts/kg) and (c) the intra-cardiac end-diastolic and peak systolic wall-tensions (DWT SWT respectively; Newton/meter) that develop to pump such stroke volumes into the aorta. Using MRI, differences between normo- and hypertensive rats were determined to evaluate these measurements. SHR and WKY rats (n=3-5/group) were imaged using a BRUKER 4.7T/40 cm imaging system with local transcievers gated to appropriate cardiac phases. Blood pressure recordings were obtained from the same animals. Cross-sectional areas of mid-ventricular heart sections were measured from the same anatomical site for all animals using the MRI data. Wall tensions were calculated using the Laplace equation ($T=Pr$). Calculated parameters for hypertensive rats expressed as a percentage of normotensive rats were: Stroke-Work (191%), Power (161%), Stroke volume (101%), Ejection Fraction (91%), SWT (240%*), DWT (206%*), Blood Pressure (sys/dias: 190%/186%) *$p<0.005$.

Results demonstrate that stroke-work, power requirements (both related to energy requirements of the heart), and intra-cardiac wall tensions between normotensive and hypertensive groups differ more than some of the hemodynamic parameters (stroke volume and ejection fraction).

Sincerely,
Sudeep Chandra Susanta
Sudeep Chandra and Susanta Sarkar

We acknowledge following members of CV pharmacology for valuable discussions : Drs. Robert Willette, Frank Barone, and Eliot Ohlstein

709 Swedeland Road, PO Box 1539, King of Prussia, PA 19406-0939. Telephone (610) 270 4800. Fax (610) 270 7777.

AMT

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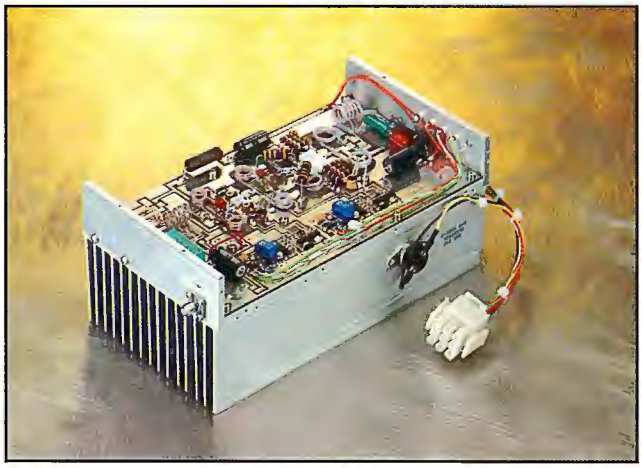
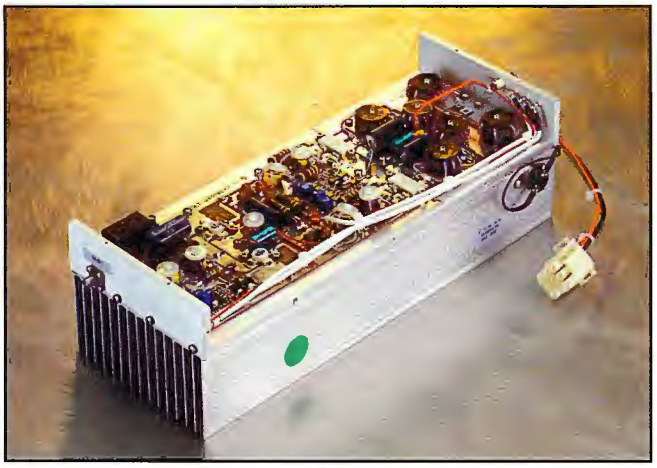


200 MHz to 500 MHz, 50 W, NMR Module



185 MHz to 500 MHz, 125 W, NMR Module

Model 4T70 – 25 MHz to 175 MHz, 7.0 kW, MRI Amplifier

SCIENTIFIC & MEDICAL PRODUCTS

AMT's scientific products are used extensively in Nuclear Magnetic Resonance (NMR) systems. These amplifiers cover the frequency ranges of 6 MHz to 950 MHz, with power levels as high as 2.0 kW peak power at 10% duty cycle.

AMT's medical products are employed in Magnetic Resonance Imaging (MRI) systems. These amplifiers cover the frequency ranges of 10 MHz to 200 MHz with power levels as high as 8.0 kW peak power at 10% duty cycle.

All amplifiers have dual mode capability and can be operated in either a pulsed or CW mode. Scientific and Medical customers include both OEM system manufacturers and end users.

SCIENTIFIC & MEDICAL PRODUCTS

COMPANY

AMT designs, develops and manufactures custom radio frequency (RF) and microwave power amplifiers for the wireless, scientific/medical and application specific industries. The company has been in business since 1984 and currently has over 60 employees, including 20 experienced engineers.

AMT has a worldwide reputation as a leading supplier of high power, solid state power amplifier products that operate at frequencies between 1 MHz and 3 GHz and provide RF power from several watts to several kilowatts. Its products are noted for their exceptional performance, highest quality and superior reliability.

The company's products are sold to numerous major corporations, universities and research centers throughout the world.

FACILITIES

AMT is located in Anaheim, California and occupies a 25,000 square foot facility allocated to engineering, manufacturing, quality assurance, marketing/sales, administration and finance.

Engineering areas include an R & D laboratory, a tool and die shop, mechanical design and drafting areas, an environmental testing laboratory and document control. The R & D laboratory is equipped with all of the latest design and testing equipment including intermodulation distortion simulators, network analyzers, spectrum analyzers, signal generators, noise figure meters and infrared (IR) scanners. The environmental testing laboratory includes equipment to simulate shock, vibration and thermal environments.

Manufacturing areas include a controlled access stock room, a 10,000 square foot assembly area and a production test area employing automatic testing. Also included is an environmental laboratory used for environmental stress screening of production products.

PRODUCTS

AMT's products vary in complexity from single modules, to rack-mounted amplifiers, to complete transmitter systems. The rack-mounted amplifiers and complete transmitter systems typically include detection/protection circuitry, built-in power supplies, front panel metering and digital and/or analog interface controls. Both forced air and/or water cooling are used, depending on the customer's requirements.

AMT's products feature highly reliable technical solutions designed for producibility and reliability. Producibility is enhanced through the use of surface mount components and circuit designs that eliminate the need for excessive alignment during the production cycle. High reliability is accomplished through the implementation of conservative thermal and RF circuit design and sophisticated self-protection schemes. Reliability is further enhanced during the design phase by employing detailed environmental testing.

These factors, along with computer driven automatic testing and environmental stress screening of the final product, ensure that the performance, quality and reliability meet AMT's exacting standards.

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May 22, 1998
(received 6/10/98)

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

The Application of DECRA to the solid state NMR spectra of mixtures.

Dear Dr. Shapiro:

We previously reported [1,2] the application of direct exponential curve resolution algorithm or DECRA to PGSE NMR data from multicomponent systems and shown that highly overlapped spectra can be resolved if the diffusivities of the components are different. The key to the success of DECRA is for the spectra of the individual components to decay exponentially, a condition fullfilled by typical PGSE data sets.

We have recently observed that DECRA can also be used in conjunction with a ^1H T_1-filter [3, 4] to cleanly separate the CP/MAS spectra of multicomponent solid mixtures. Efficient proton spin diffusion insures that each domain in a grossly phase-separated material or physical mixture has its own uniform ^1H T_1. The example given in figure 1 shows the separation of the ^{13}C CP/MAS spectrum of a mixture of glycine powder and polystyrene pellets into individual component spectra. DECRA treatment of the data offers the advantage of spectral separation even when the ^1H T_1 values of the components differ by as little as 20%. This and other advantages and variants of the DECRA analysis as applied to solid state NMR will be discussed in a forthcoming publication.

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Brian Antalek
bantalek@kodak.com

Willem Windig
windig@kodak.com

[1] B. Antalek, W. Windig, J. Am. Chem. Soc. 118, 1996, 10331-10332.
[2] W. Windig, B. Antalek. Chemom. Intell. Lab. Sys. 37, 241-254 (1997).
[3] N. Zumbulyadis, J. Mag. Res. 49, 329 (1982).
[4] N. Zumbulyadis, J. Mag. Res. 53, 486 (1983).

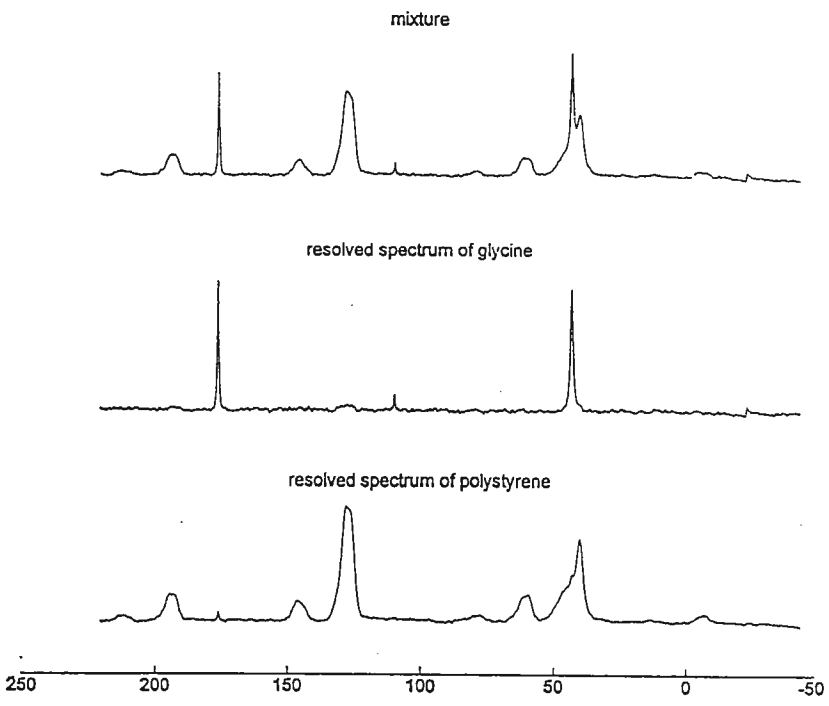


Fig. 1

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

DUNCAN M. SMITH
Molecular Structure Group
e-mail: duncan@amgen.com

June 8, 1998
(received 6/10/98)

Selective Use of Selective Decoupling

Dear Barry,

The constant time $^{1}H/^{13}C$ HSQC (CT-HSQC) experiment[1] is a very useful tool in the assignment of protein resonances. The sign of the peaks is determined by whether the number of attached aliphatic carbons is odd or even. This enables peaks due to Gly α, Thr β and Met ε to be readily identified as they produce negative peaks in regions otherwise dominated by positive ones.

Fig. 1 shows the Cα/Hα region of the 500MHz gradient $^{1}H/^{13}C$ CT-HSQC on a sample of 2mM $^{13}C/^{15}N$ ubiquitin pH 5.1 in D_2O at 298K. The data was acquired on a Bruker DRX500 with a Nalorac z-gradient 5mm triple resonance probe. Negative peaks are shown as a single contour. The Gly α resonances are clearly visible between 44 and 46 ppm, and the Thr β resonances between 68 and 73ppm. The remaining resonances are due not only to non-Gly α, but also to Ser β and Pro δ.

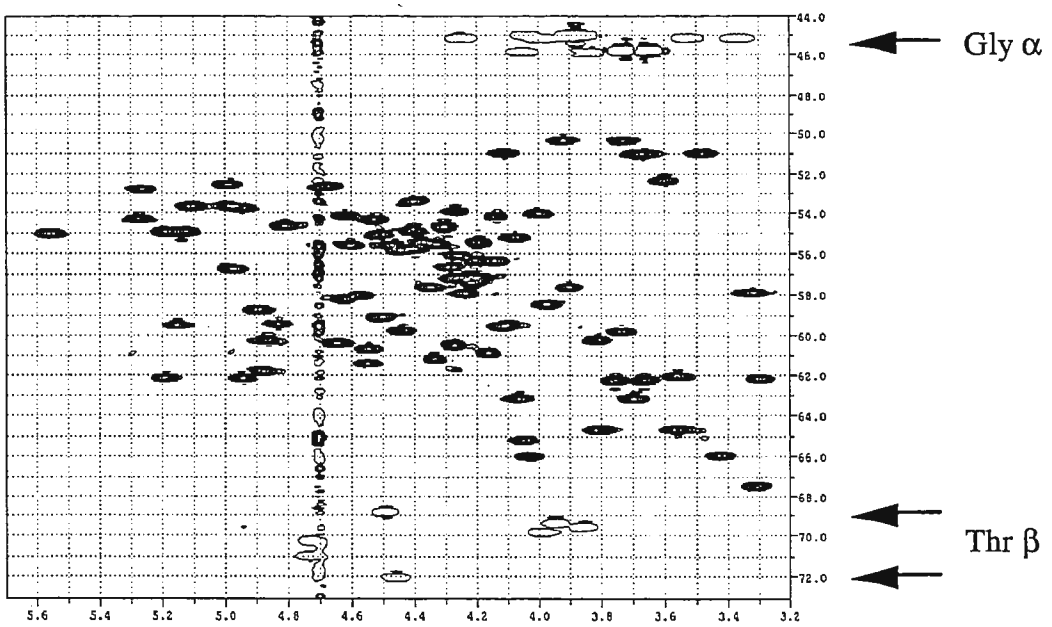


Fig. 1: Expansion of lowfield region of $^{1}H/^{13}C$ CT-HSQC of ubiquitin with Seduce decoupling of carbonyl region.

A simple method to identify the Ser β and Pro δ resonances is to re-run the experiment without Seduce decoupling of the carbonyl region. This leaves the $^{1}J_{C\alpha CO}$ coupling of ~55Hz visible as a splitting in the ^{13}C dimension. Carbons that are more than 1 bond away from a carbonyl do not exhibit a splitting due to the smaller long-range coupling constants.

Fig. 2 shows a CT-HSQC acquired without Seduce decoupling. Three times as many scans per FID were acquired so the lowest contour level is 3 times higher. The majority of the resonances are clearly split by the coupling to the carbonyls. However, the resonances due to the 3 Ser βs are now readily identifiable at 62.3, 63.2 and 64.8ppm. In addition, the resonances due to the 3 Pro δs are also easily picked out at 50.4, 51.0 and 51.05ppm.

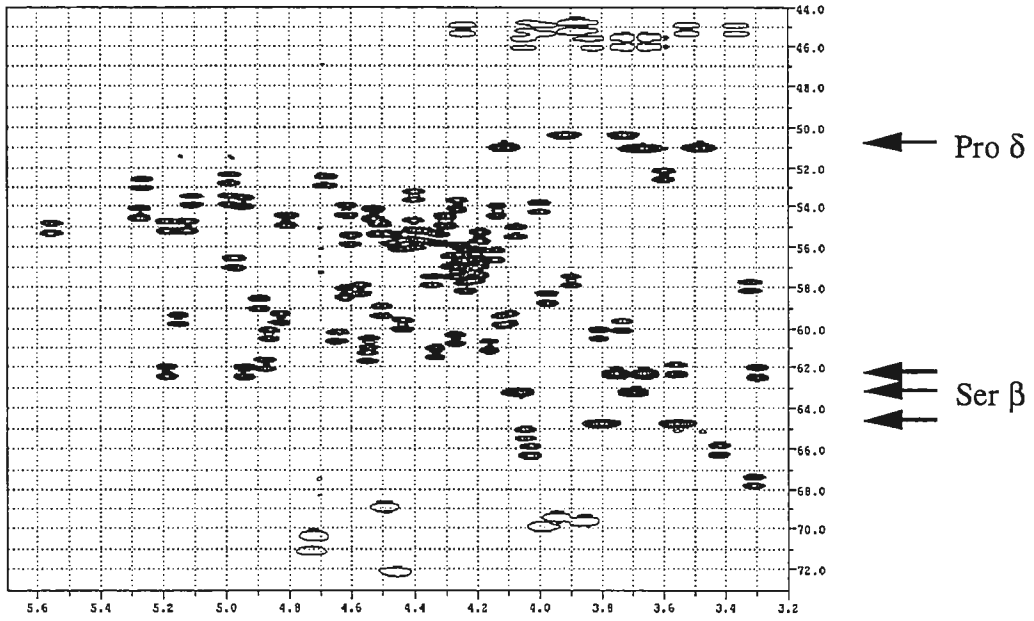


Fig. 2: Same region as fig. 1 without Seduce decoupling of the carbonyl region and showing splitting of resonances except Thr/Ser β and Pro δ.

This is a simple method for the identification of the chemical shifts of certain residue types, and provides useful starting points for the analysis of other datasets. It is equally applicable to the identification of other carbons adjacent to carbonyls in Asn, Asp, Gln and Glu residues.

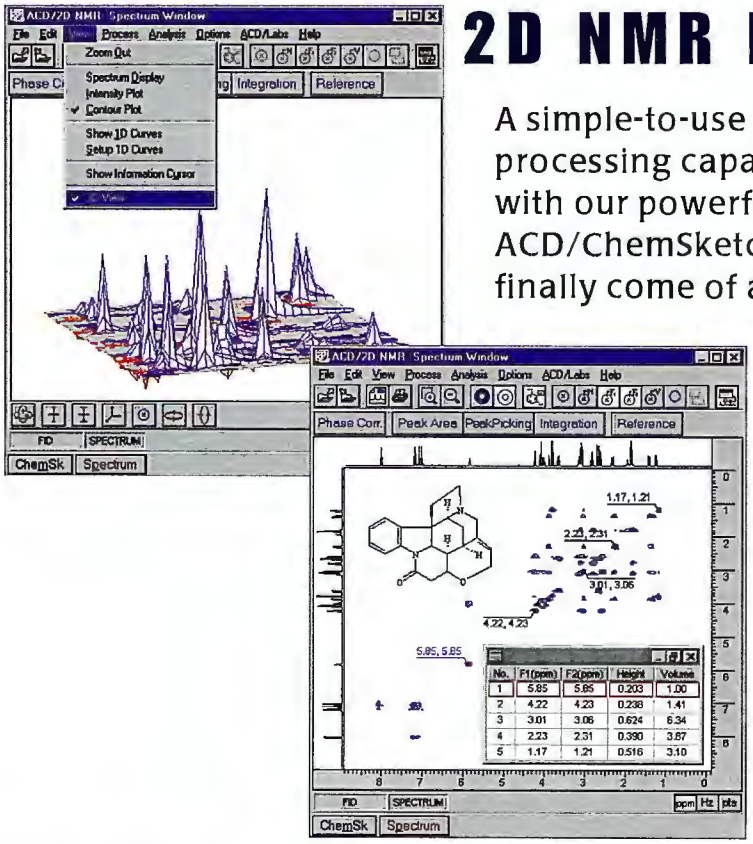
Duncan M Smith

1. G Vuister & A Bax, J. Mag. Reson. **98**, pp428-35 (1992)

NMR IR UV-Vis MS Raman

The Expanding Universe of
Advanced Chemistry Development

2D NMR Processor



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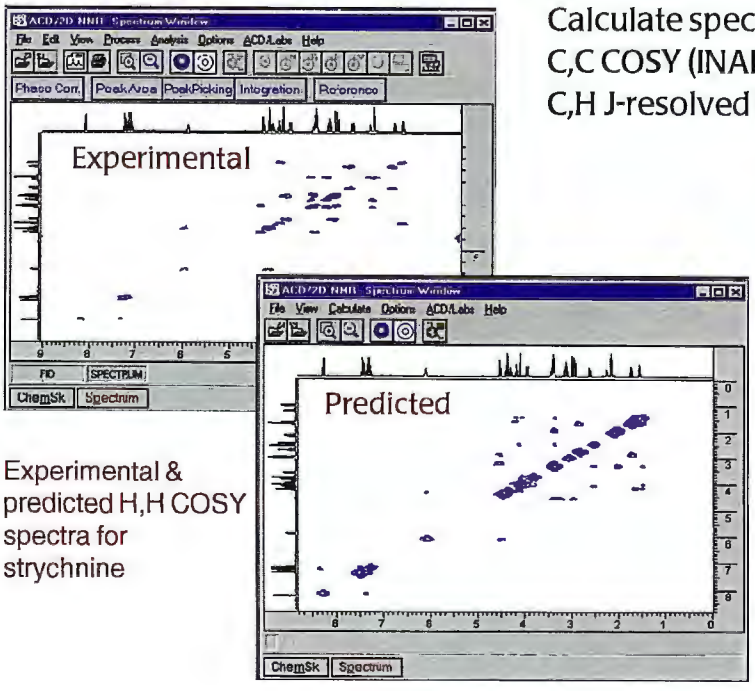
5. **Attach chemical structure** and additional data to the spectrum;
6. Attach 1D spectra to the spectrum;
7. Print spectra and create reports using all the power of ACD/ChemSketch.

2D NMR Predictor



Experimental & predicted H,H COSY spectra for strychnine

Calculate spectra of some 2D experiments: H,H COSY; C,C COSY (INADEQUATE); C,H COSY (HETCOR); H,H and C,H J-resolved Display data as intensity or contour plots

Additional features (will be released in Autumn'98):

- View tables of shifts and coupling constants
- Possibility to correct chemical shift or coupling constant values and recalculate the spectrum

Optionally:

- Use direct or all coupling constants for C,C COSY and C,H J-resolved experiments
- Use ^{1}J-^{3}J constants or all coupling constants for H,H COSY and H,H J-resolved experiments
- Use first-order or higher-order interactions for prediction of the H,H J-resolved experiment
- Use heteronuclear couplings for all the experiments

See reverse side for contact information

The Expanding Universe of

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Process raw NMR spectral data using a wide array of tools.
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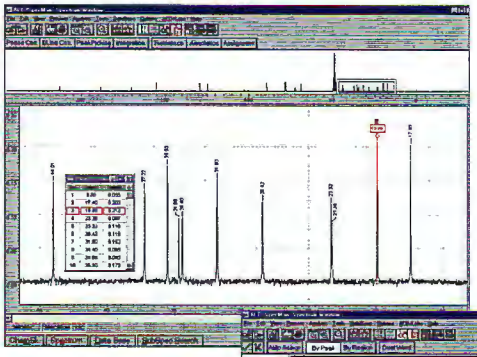
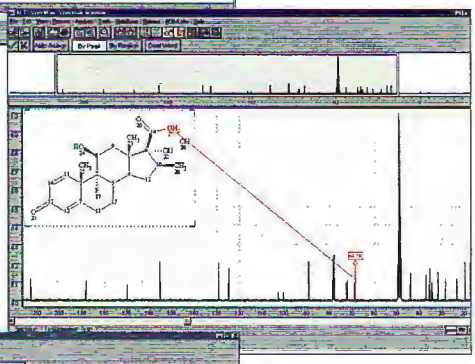
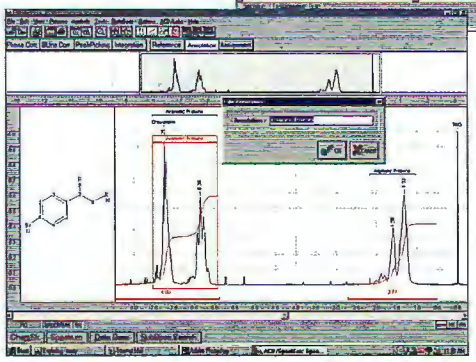


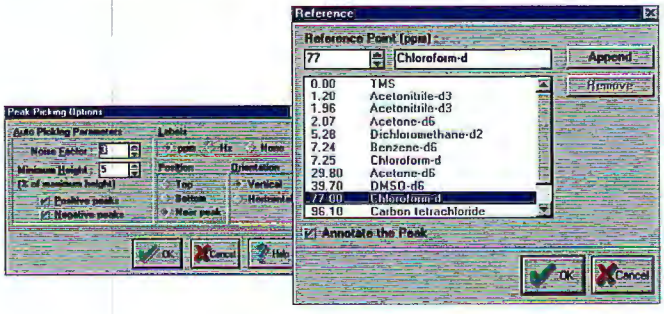
Standard display showing zoom window and peak table



Assign a spectrum by selecting either peak or region - simply select the nucleus and drag towards the peak



On-screen annotations: ideal for identifying solvents, impurities, and polymer details including sequencing and tacticity



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- Complete NMR processing capabilities including Import filters for Varian, Bruker, Jeol, Chemagnetics, WinNMR, Nuts, Lybrics, JCAMP, etc.
- Fourier Transform, phase correction, baseline correction, peak referencing, peak integration, and peak picking
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IN REPLY REFER TO:

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

29 May 1998
(received 6/8/98)

^{129}Xe NMR Investigation of Carbon Black Aggregate Morphology

Dear Barry:

Recently, we have applied one- and two-dimensional ^{129}Xe NMR methods to investigate the morphology of reinforcement carbon blacks. Interestingly, we observe a wide range in chemical shifts among different samples, and we attribute these differences primarily to variations in *aggregate* structure.

Figure 1 shows the ^{129}Xe NMR spectrum of a physical mixture of three "normal" ASTM fillers: N110 (1.89 g), N347 (3.00 g), and N472 (1.00 g). The blend quantities represent the amounts necessary to yield equal surface areas of each component according to their ASTM D3037 N_2 adsorption values. The peak at $\delta \approx 0$ppm corresponds to xenon atoms which are very weakly adsorbed. The next farthest upfield peak ($\delta \approx 53$ ppm) corresponds to N347 adsorbed ^{129}Xe atoms, followed by N110 ($\delta \approx 68$ ppm) and N472 ($\delta \approx 94$ ppm) adsorbed xenon.

We interpret the observed variations in ^{129}Xe NMR chemical shift in terms of the relative pore sizes *within the aggregate structure.* Thus, the aggregate voids of sample N472 are smallest, followed by fillers N110 and N347. Additionally, we use the integrated NMR peak intensities of each sample as a measure of their relative unoccupied aggregate volume. It is therefore possible to calculate the relative aggregate densityof each sample, and the so called "structure" of the aggregate (which depends primarily on aggregate density). Figure 2 shows a plot of relative aggregate volume (from ^{129}Xe NMR peak intensity) versus aggregate "structure" (ASTM D2414 dibutyl phthalate absorption) for each sample. The ratio of aggregate volume:aggregate surface area is also used to calculate the relative linear void dimensions, and found to be consistent with our assignments based on chemical shift.

Finally, using two-dimensional ^{129}Xe NMR exchange spectroscopy, we calculate the approximate exchange times of xenon atoms between filler samples. Figure 3 shows the 2D spectrum obtained with an exchange time of 100 ms, where exchange is apparent between all filler pairs except N472 and N110. The absence of exchange between these two samples is attributed to their relatively small aggregate void size (as indicated by their downfield ^{129}Xe NMR chemical shifts and volume:surface area ratios). When the exchange time is reduced to 6 ms, no evidence of exchange between any of the samples is apparent.

Please credit this contribution to the Naval Research Laboratory.

With best regards,

Ken

K.J. McGrath
Code 6122
Naval Research Lab
Washington, DC 20375-5342
mcgrath@ccf.nrl.navy.mil

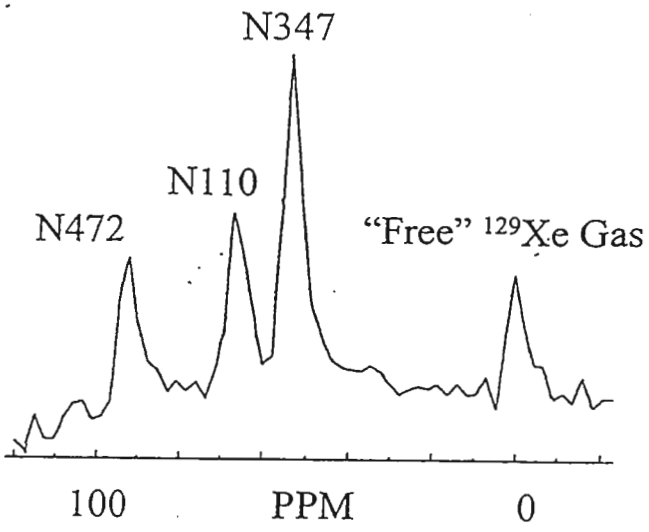

Figure 1: ^{129}Xe NMR Spectrum of CB Blend

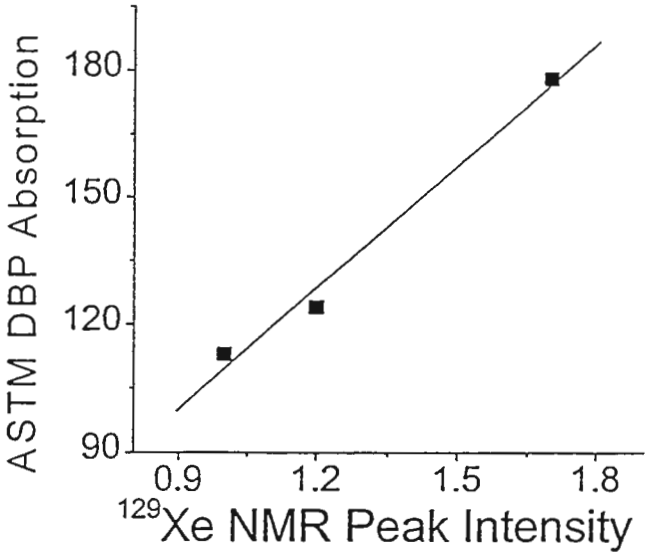

Figure 2: ^{129}Xe NMR vs. ASTM "Volume"

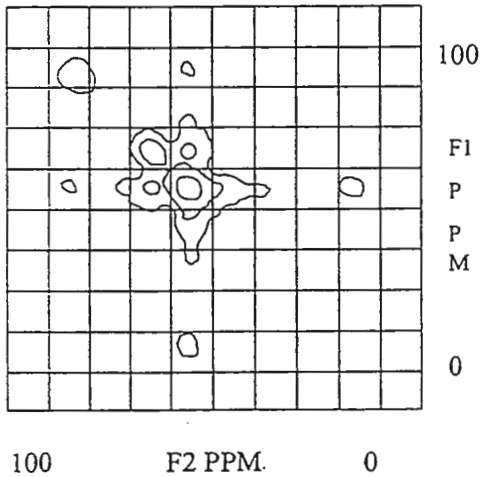

Figure 3: 2D ^{129}Xe NMR Exchange Spectrum

(100 ms exchange time)


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answer the
questions of
tomorrow
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Bruker continues to be the world's leader in NMR magnet technology based on our extensive experience and proven record of success. One of our great achievements of this decade is the UltraStabilized™ cooled technology developed in the early 1990's for the 750 MHz magnets. Since then, we have been perfecting this technology and have applied it to the 800 UltraStabilized magnet series.

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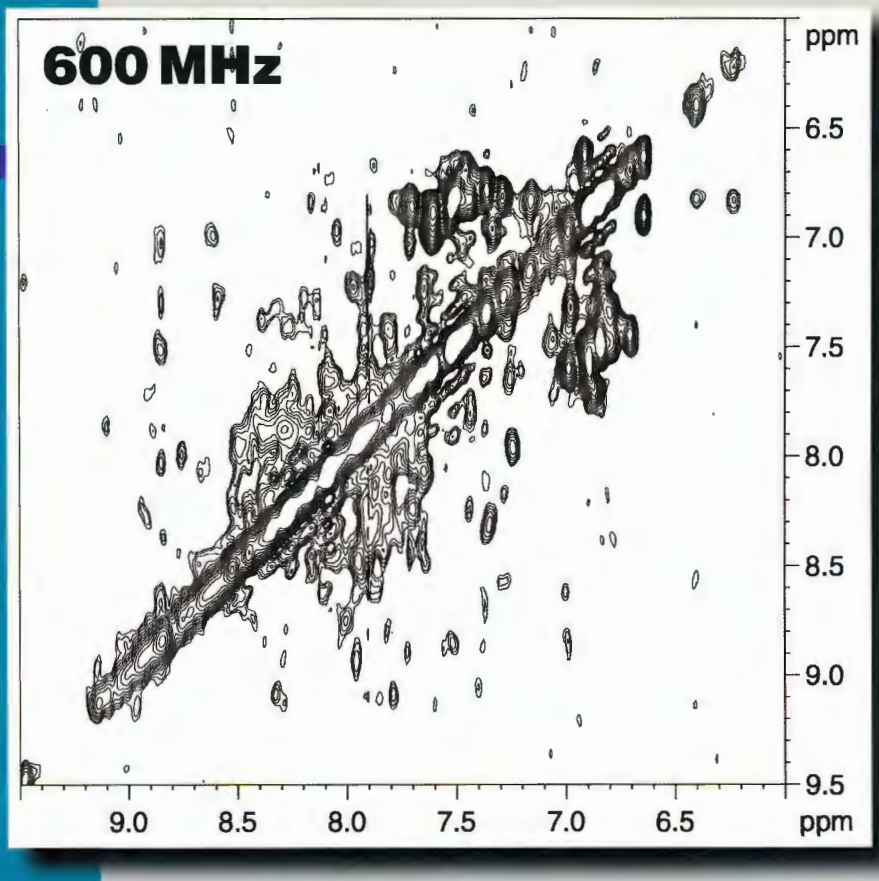
800 UltraStabilized in operation at the University of Maryland Baltimore County. *Photo courtesy of UMBC.*



Comparison of the first ^1H-^1H plane of NOESY-HSQC exper
labeled protein in 95% H_2O / 5% D_2O with buffer. *Spectra co*

Bruker's patented cryostat de reduced temperature and am

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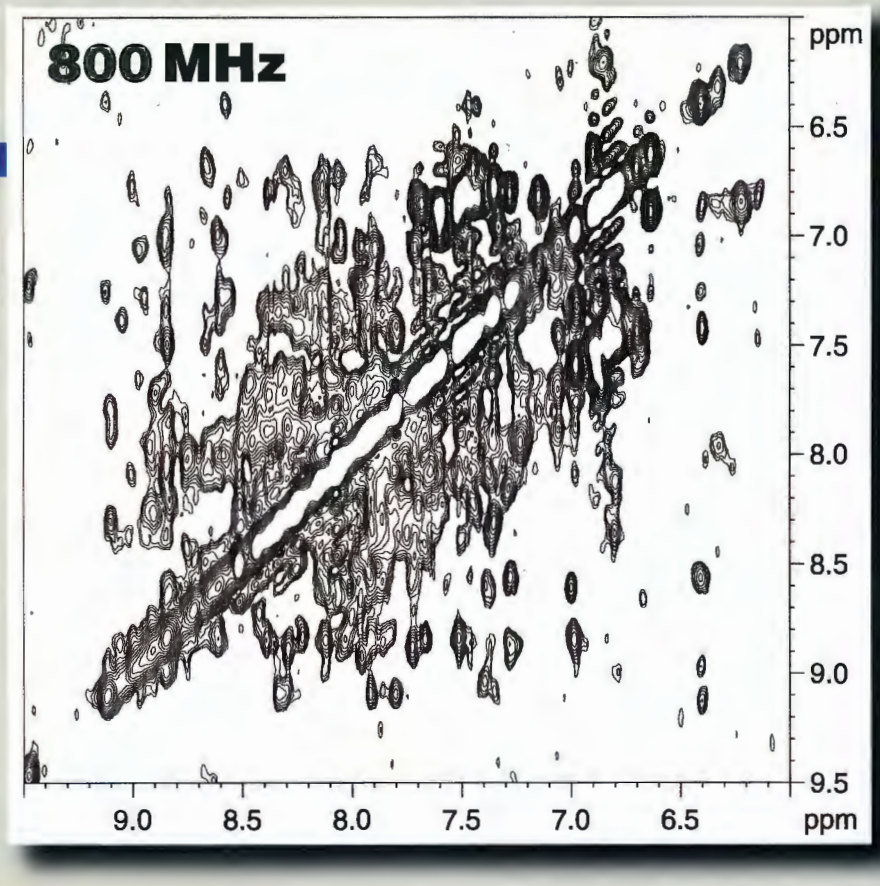

ments performed under identical conditions: 1mM ^{15}N-
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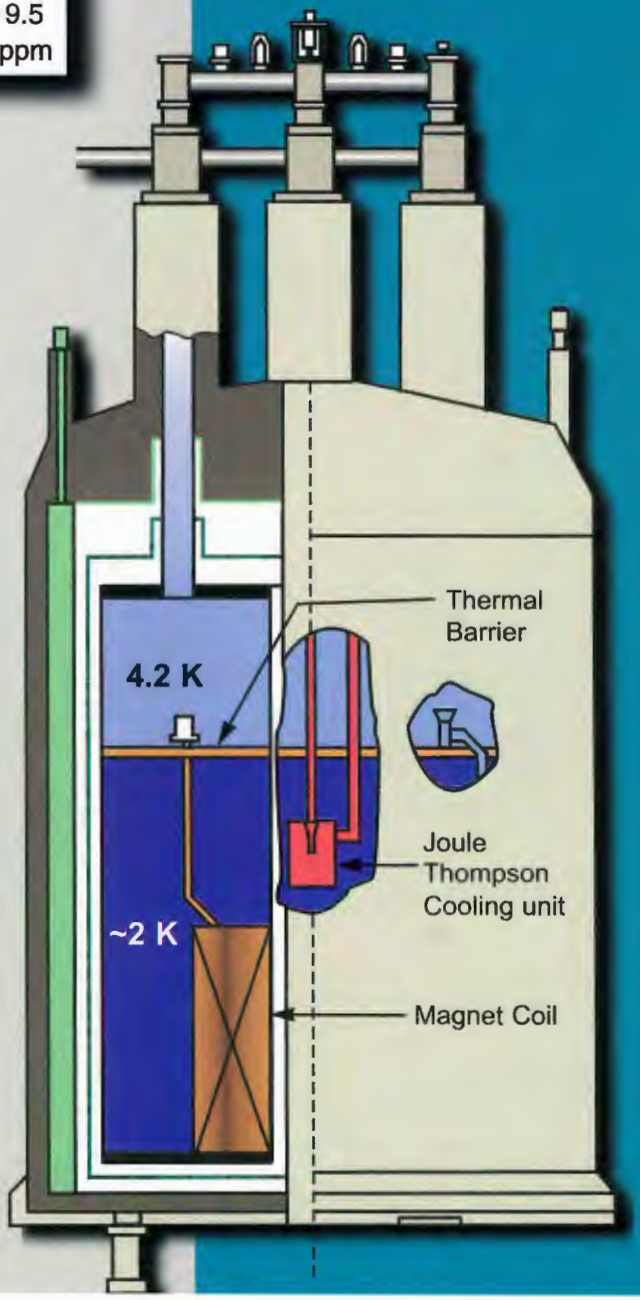

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Leonard D. Spicer, Director
Anthony A. Ribeiro, Manager

919 684 4327
919 613 8887

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

June 1, 1998
(received 6/4/98)

Re: ^{13}C NMR Spectral Simplifications of Fluoralkyl Chains from ^{19}F decoupling at High Field

Dear Barry,

We have recently explored heteronuclear ^{19}F decoupling capabilities on our Varian Unity 600 spectrometer to obtain ^{13}C NMR data on fluoroalkyl compounds. Heteronuclear ^{19}F decoupling is currently not in general use as many NMR spectrometers are not equipped with this capability. Ideally, ^{13}C NMR spectral simplification from heteronuclear ^{19}F decoupling could be accomplished at low decoupler power levels so that heating of the sample is minimized. Early NMR studies (90MHz or lower B_0 Zeeman field) on fluoroalkanes using noise decoupling recorded two separate ^{13}C spectra, first with the ^{19}F decoupler set at the CF_3 resonance and then at the midpoint of the CF_2 resonances (1). Wide-band heteronuclear ^{19}F decoupling for the recording of a single ^{13}C spectrum required the use of very high power (50W) decoupler units (2,3). At 50 W decoupler power, a rapid stream of nitrogen gas was used to cool the decoupling coil (3). It is unclear to what extent sample heating affected the data.

There is ~60 ppm separation between CF_3 and CF_2 ^{19}F signals in fluoroalkyls, and Fig. 1A shows the 564 MHz ^{19}F NMR spectrum of the fluorinated alcohol, CF_3-$(CF_2)_4$-CF_2-CH_2CH_2OH recorded using a 5mm Varian triple resonance probe with high band coil tuned for ^{19}F detection. 60 ppm is ~34 kHz at 600 MHz B_0 field, or ~6X the 6 kHz needed to span a 10 ppm ^1H window. The fully coupled 150 MHz ^{13}C NMR spectrum (Fig. 1B) reveals a complex pattern of >50 resolved lines between 106 and 122 ppm with $^1J_{CF}$ and $^2J_{CF}$ couplings of ~280 and 33 Hz for the six fluorinated carbons (C3-C8). Since $^1J_{CF}$ is ~2X $^1J_{CH}$ and ^{19}F shifts span ~6X ^1H shifts, complete wide-band heteronuclear ^{19}F decoupling of fluoroalkyl chains is taken to be ~12 times more difficult to achieve than complete ^1H decoupling of alkyl compounds.

We measured the continuous-wave (CW) decoupler output on our Unity 600 using a Bird Thruline Wattmeter terminated with a 50 ohm load and fitted with either 1W 425-850 MHz or 5W 400-1000 MHz crystals. As decoupler power increased from 28 to 49db (maximum recommended by Varian), the wattmeter readings increased from 20 mW to 1.6W. Calibration of the decoupler field strength in the triple resonance probe by off-resonance decoupling gave $\gamma H2$=5753 Hz at 49 db, i. e. an effective decoupler bandwidth of ~23 kHz, which is obviously less than the 34 kHz between CF_3 and CF_2 signals at 600 MHz field. When the decoupler is set at the midpoint between CF_3 and CF_2 signals and broadband Waltz-16 decoupling is applied, only a partial simplification of the fluoroalkyl ^{13}C NMR spectrum is achieved (Fig. 1C). GARP-1 decoupling (4) programmed through the wave form generator at lower power (47db, 1.1W) however sufficed to simultaneously decouple the CF_3 and CF_2 regions and all fluorinated carbon signals collapse to singlets (Fig. 1D), except for the C3 signal at 118.8 ppm which is a triplet with a small $^2J_{CH}$ coupling from the C2 CH_2.

Single frequency CW decoupling of the -130 ppm CF_2 ^{19}F multiplet (Fig. 1E) removes the $^2J_{CF}$ coupling from the 118.1 ppm resonance which now collapses to a simple quartet with a $^1J_{CF}$ coupling (Fig. 1E). This identifies the 118.1 ppm signal as the CF_3 (C8) resonance, and also confirms that the most upfield ^{19}F resonance arises from the CF_2 next to the terminal CF_3 group, a generalization previously made from substituent effects on ^{19}F chemical shielding (5). The C6 CF_2 group (linked to C7) is also identified as the sharp triplet at 111.2 ppm, as it retains a $^2J_{CF}$ coupling from the C5 CF_2 group. Single frequency CW decoupling of the lowest field CF_2 at -117 ppm (Fig. 1F) collapses the C3 118.8 ppm "triplet-of-triplets" to a simple triplet. This also removes a $^2J_{CF}$ coupling from the C4 CF_2 which is now identified at 111.7 ppm.

Single frequency CW decoupling of the -85 ppm CF_3 ^{19}F resonance removes the $^1J_{CF}$ coupling from the 118.1 ppm "quartet-of-triplets" which now appears as a simple triplet with $^2J_{CF}$ coupling (Fig. 1G). C7 at 109.4 ppm now appears as a "triplet-of-triplets" with its own $^1J_{CF}$ coupling and a $^2J_{CF}$ coupling from the C6 CF_2. On limiting the decoupler (42db, 320mW power) to excite only the -120 to -130ppm CF_2 region, two simple quartets result at 118.1 and 109.4 ppm with $^1J_{CF}$ and $^2J_{CF}$ couplings. These quartets clearly arise from the terminal CF_3 and adjacent CF_2 groups.

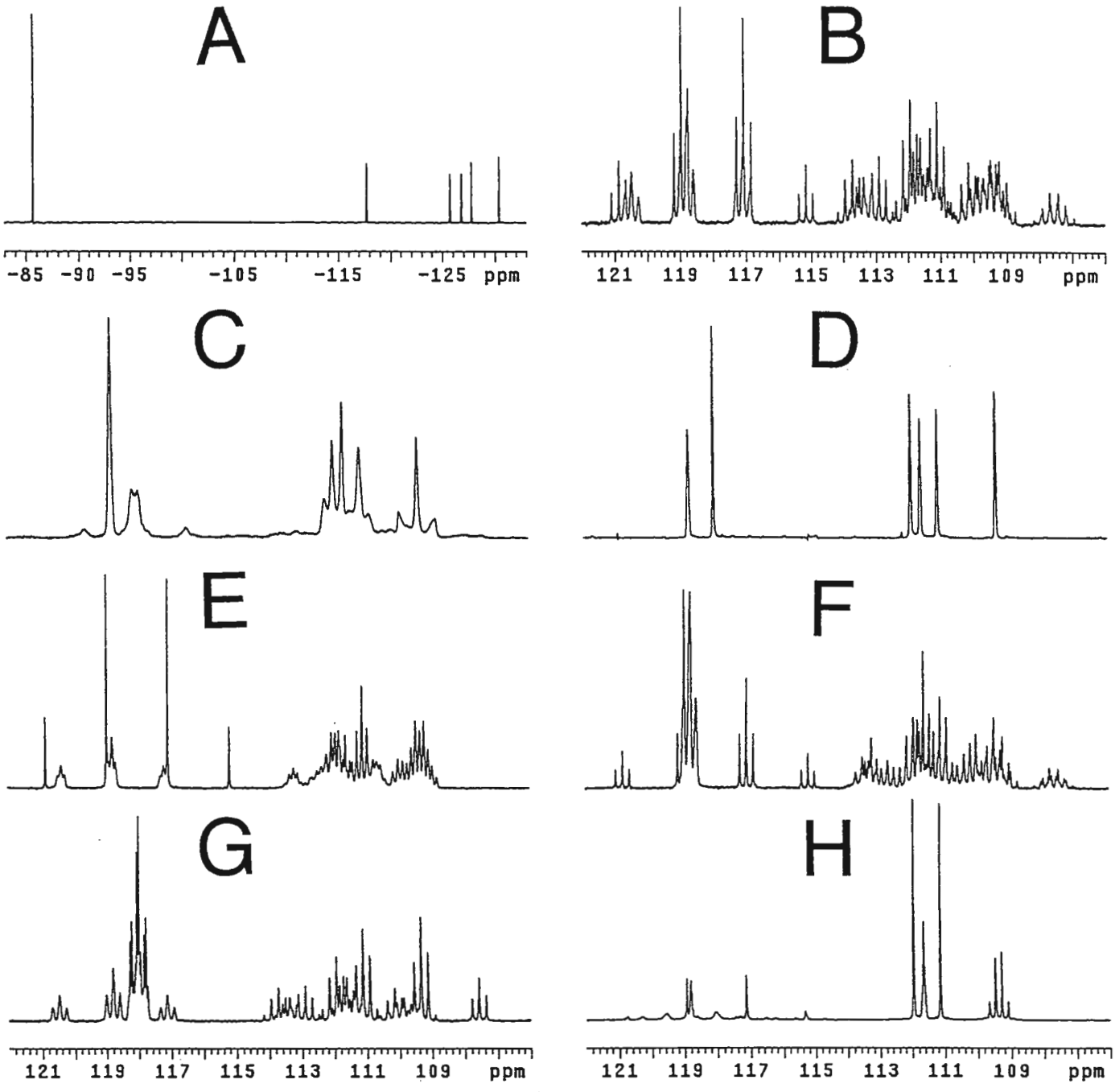
The ^{13}C NMR resonances shown (Fig. 1B-H) have linewidths ~4Hz, digital resolution of 0.59 Hz/pt and are processed with 1 Hz line broadening. The 1W level for heteronuclear ^{19}F decoupling appears to be reasonable to minimize heating effects in the sample. The selective ^{19}F decoupling exploiting two- as well as one-bond effects for the ^{13}C NMR spectral simplification achieves a complete ^{13}C NMR assignment for the fluorinated alcohol. .

Regards,

TONY

Anthony A. Ribeiro (A^2R)
ribeiro@tweety.mc.duke.edu

1. Lyerla and VanderHart J. Am. Chem. Soc. 98, 1697 (1976).
2. Hamza et al. J. Magn. Reson. 42, 227 (1981).
3. Ovenall and Chang J. Magn. Reson. 25, 361 (1977).
4. Shaka et al. J. Magn. Reson. 64, 547 (1985).
5. Brey and Brey, Encyclopedia of NMR, Vol. 3, 2063 (1996).



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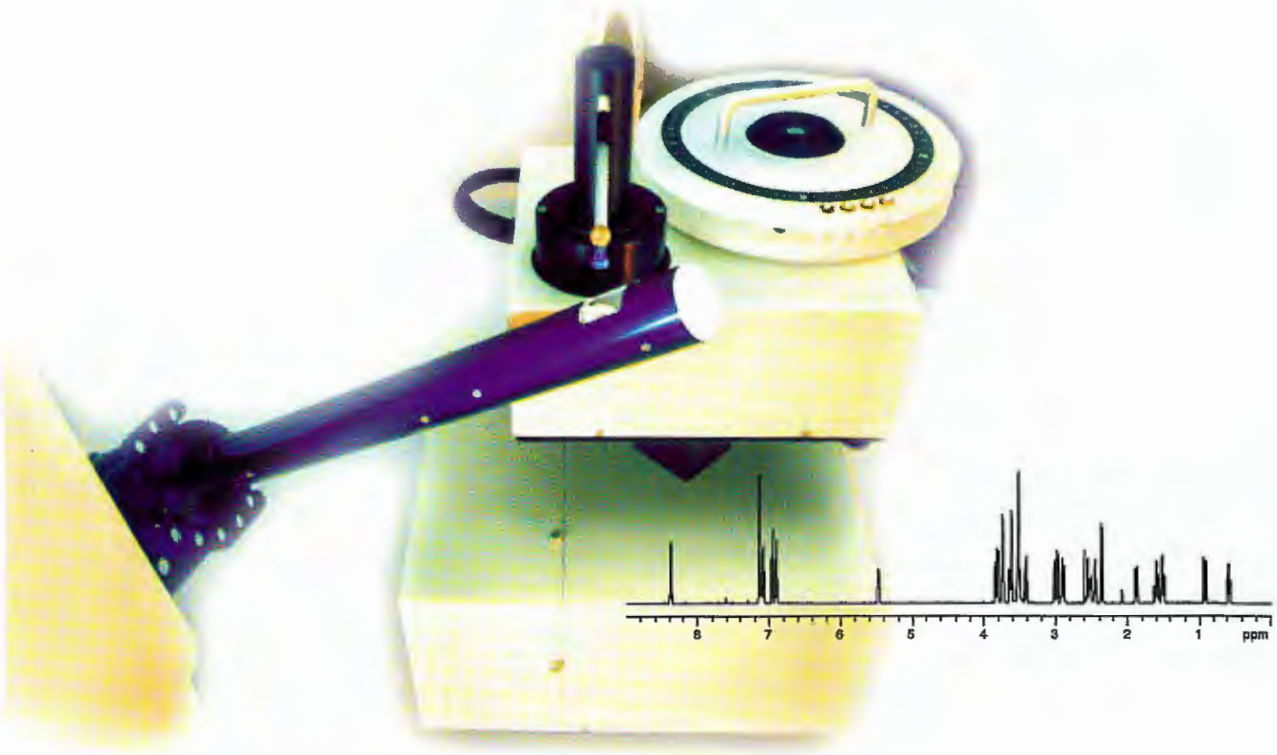

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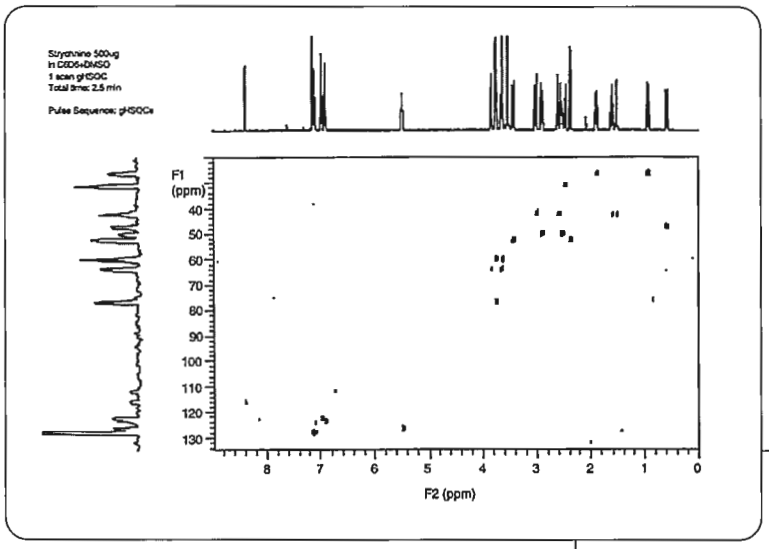
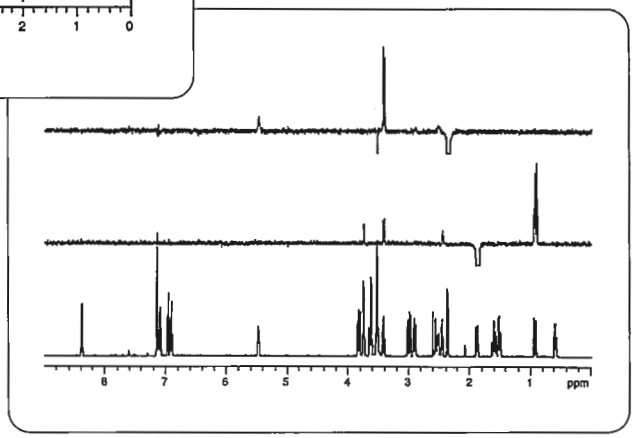


Gradient Selected ^{1}H-^{13}C HSQC
Total acquisition time is 2.5 minutes
Sample: 0.5 mg strychnine in C_6D_6/DMSO-d_6



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Sample: 0.5 mg strychnine in C_6D_6/DMSO-d_6

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May 27, 1998
(received 6/1/98)

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

Re: MAS-NMR of Solvent-Swollen Plant Polymers

Dear Barry:

In recent years, magic-angle spinning (MAS) ^{1}H and ^{13}C NMR techniques have been used to examine peptides and drug candidates bound to solvent-swollen solid-phase synthesis resins; these methods offer significant potential for applications in combinatorial chemistry and drug discovery.[1,2] The use of solvent swelling to enhance mobility and MAS to minimize magnetic susceptibility line-broadening can dramatically improve the resolution of the resulting NMR spectra, making it possible to monitor the syntheses *in situ*, without time-consuming purification steps. Rather than examining the small molecules, we have drawn upon prior ^{1}H spectral studies of the resins themselves[3] to focus on solid biopolymer supports with intrinsic mobility and significant interactions with various solvents. In particular, we are seeking to obtain high-resolution spectra of swelled plant cuticular polymers using MAS methods.

Presented below are preliminary results for suberin, a solid biopolymer blend isolated from wound-healing potatoes.[4] This agriculturally important protective material is thought to possess spatially separated domains that consist of polysaccharides, aromatics (phenolics) and aliphatics (fatty acids). Each constituent is blended or connected to the others, in ways not yet established. As expected, the traditional ^{1}H NMR spectrum of suberin is broad and featureless even with MAS at 8 kHz, as shown in **Fig. 1a**. The rigidity of the dry polymer is confirmed by the retention of large dipolar coupling effects and consequent breadth of the spectral pattern.

What happens after swelling the suberin sample for a day in chloroform? Without spinning, the ^{1}H NMR spectrum remains broad (**Fig. 1b**), but with 8-kHz MAS there appears a forest of sharper peaks (**Fig. 1c**). Though well short of the resolution typical in a solution-state NMR spectrum, these data make it straightforward to distinguish the three domains in suberin: aliphatics at 0.9-2.4 ppm; polysaccharides at 3.5-5.3 ppm; and aromatics at 6.2-8.0 ppm. The sharpest singlet has a linewidth of 24 Hz, compared with 1-2 Hz for liquid water in our Doty XC5 CPMAS probe. So far, we have obtained the best resolution enhancements across the spectrum with $CDCl_3$ as the swelling solvent.

A variety of other useful ^{1}H NMR experiments are also feasible with this approach. COSY and NOESY results in the $CDCl_3$-swollen suberin sample are shown in **Figs. 2a** and **2b**. With COSY, through-bond correlations within each structural type are clearly observable and may be analyzed in detail. The NOESY spectrum shows correlations between the aliphatic and polysaccharide domains, but none of the anticipated cross peaks[4] are found between aromatic protons and the other two chemical types. This anomaly is attributable to preferential swelling of different domains by the solvent. For instance, $CDCl_3$ will solvate the aliphatics readily and the polysacharides to some degree, but the solvent may fail to penetrate the heavily crosslinked

---

[1] Fitch, W. L. *et al.*, *J. Org. Chem.*, 59 **(1994)** 7955-6.
[2] Keifer, P. A. *et al.*, *J. Mag. Reson., Series A.*, 119 **(1996)** 65-75.
[3] Keifer, P. A. *J. Org. Chem.*, 61 **(1996)** 1558-9.
[4] Yan, B. and Stark, R. E., *Macromolecules*, 31 **(1998)** 2600-5.

networks in which the phenolic suberin moieties are thought to be located. This hypothesis is supported by the relative peak intensities in the MAS ^{1}H NMR spectrum **(Fig. 1c),** since the aliphatic peaks are large and sharp whereas aromatics that are known to be compositionally important in suberin[5] can barely be seen. Under these conditions, it becomes more difficult to observe NOESY corsspeaks that involve aromatics.

Out current efforts to improve this protocol include the use of solvent mixtures and variation of the temperatures for solvent swelling and NMR spectral acquisition, respectively. Suggestions are also welcome from the readership of the *Newsletter*.

Sincerely yours,

Bin Yan
Postdoctoral Research Associate

Ruth E. Stark
Professor of Chemistry
Email: stark@postbox.csi.cuny.edu

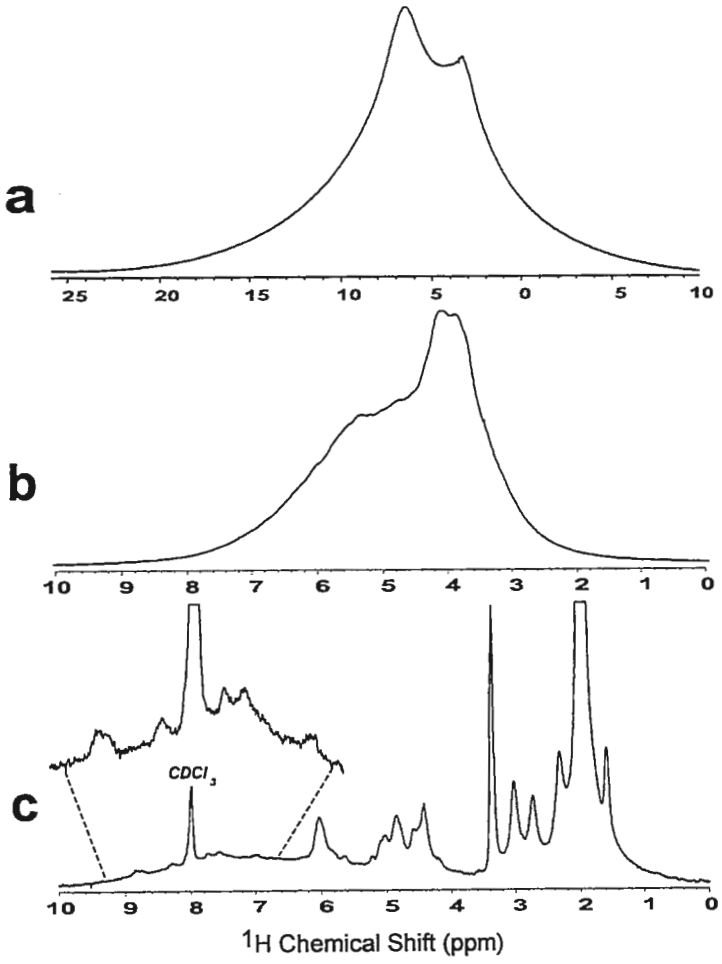

Figure 1. *300 MHz ^{1}H NMR of suberin samples. (a) dry, MAS=8 kHz; (b) swollen in $CDCl_3$, static; (c) swollen in $CDCl_3$, MAS=8 kHz. All spectra were obtained using a 5 mm XC5 probe from Doty Scientific Inc.*

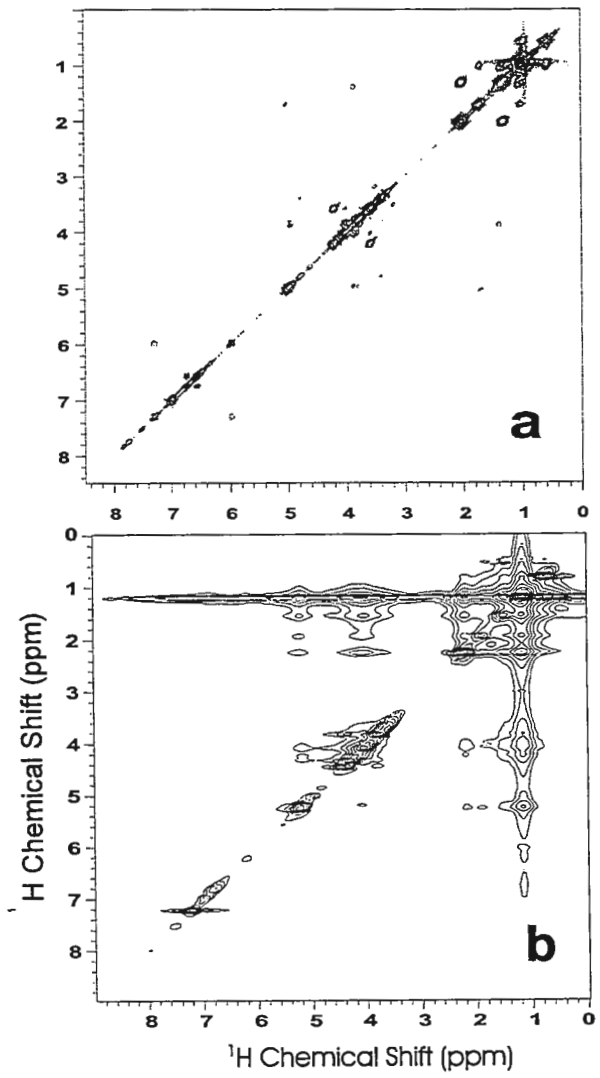

Figure 2. *2D NMR of swollen suberin (MAS at 8 kHz). (a) COSY; (b) NOESY (mixing time 150 ms).*

[5] Garbow, J. R. *et al., Plant Physiol.*, 90 **(1989)** 783-7.

Lilly

Lilly Research Laboratories
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Lilly Corporate Center
Indianapolis, Indiana 46285
(317) 276-2000

8 June, 1998
(received 6/11/98)

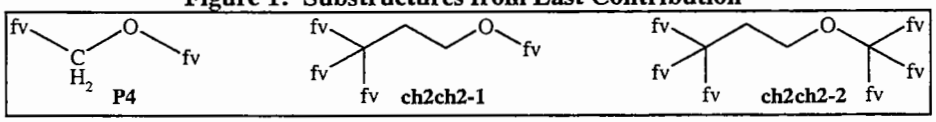
CASE Programs and the Mysteries of Free Valences

Dear Barry,

I will continue my discussion of Computer Assisted Structure Elucidation (CASE) programs[1,2] with a discussion of free valences and the difference in the ways in which the DENDRAL programs and MolGen handle them.

In the DENDRAL programs, free valences could be satisfied by attachment to "heavy atoms" only. That is, attachment to hydrogen was forbidden. Thus, substructure **P4** in Figure 1 could not become an O-methyl or a hydroxymethyl group during structure generation. There was a bit of a trap here. By default with this definition, specifying the location of one free valence implied that *all other sites* in the substructure were to be "filled out" with protons. This was sometimes easy to forget, especially since the "drawings" presented by these programs did not explicitly show these protons. For example, the DENDRAL representation of **P4** would be "-C-O-". However, once one got used to this convention it was very convenient, since it fit very neatly the NMR spectroscopist's view of substructures.

Figure 1: Substructures from Last Contribution[2]



Of course there were occasions when this rather rigid definition was not appropriate. Especially before the days of the DEPT experiment there were times when one wasn't entirely sure just how many protons were attached to each site of a substructure. In such cases one used the tool HRANGE to specify the range of protons possible at each site. With large substructures the specification of the number of protons at each site could become tiresome and also provided the user with ample opportunity to make mistakes. Because I am pretty good at making mistakes, I used the free valence definition whenever possible, but the flexibility afforded by the HRANGE tool was convenient at times.

Flexibility is also available in MolGen, but the defaults are different. In MolGen free valences can be satisfied by any atom, including hydrogen atoms. In the example from last month[2] we had defined **ch2ch2-1** (Figure 1) as one of the GoodList substructures in the MolGen analysis. MolGen can in principle expand **ch2ch2-1** to an O-propyl or a hydroxyethylene group. In fact there were too few remaining protons to fill out the quaternary carbon of **ch2ch2-1** to make a methyl group, but attachment of the oxygen atom to hydrogen was possible, and because of this we got twice as many candidate structures (6) from MolGen as we got (3) from GENOA.

The problem is solved, in both GENOA and MolGen, by simply telling the programs *everything* that we know about the substructure. For example, we know that the oxygen atom of **ch2ch2-1** is not attached to a hydrogen atom. We can probably assume that it is not attached to oxygen, since that would lead to a peroxide. Therefore, with the constraints inherent in the molecular formula, it must be attached to carbon.

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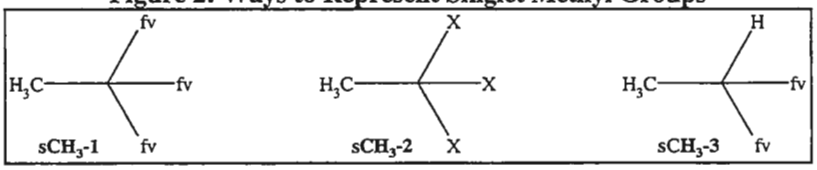
[1] See NMR Newsletter, March 1998, #474, p. 5.
[2] See NMR Newsletter, April 1998, #475, p. 29.

We don't know how many protons are attached to that carbon, or even its hybridization, but with the default free valence definition of MolGen the substructure **ch2ch2-2** provides the constraint we want. With this substructure added to GoodList, MolGen gets the same final three structures that GENOA does.

Let's go through another example of free valences. One of my favorite compounds for testing these programs is borneol. If one inputs the molecular formula of borneol ($C_{10}H_{18}O$) into MolGen and hits the "start" button, one gets a total of 95,312 structures.[3] If you put in the multiplicities of all the carbon resonances, which is very easy to input in version 3.5 with the "H-distribution" window, the number of structures is reduced to 8,295. If one uses the carbon chemical shift data to forbid MolGen from forming any multiple bonds (again, easy to do in MolGen) one gets 2191 structures. If one looks at some of these structures,[4] one sees some strained bicyclic systems that one could probably safely put on BadList, and perhaps other substructures that could be ruled out on the basis of chemical shifts. But again it is more efficient to put in positive evidence if we have it.[2] For example, we know from the proton spectrum that the three methyl carbons must be attached to quaternary carbons, so let's try to explain that to the program (Figure 2).

Figure 2: Ways to Represent Singlet Methyl Groups



By now we know that **sCH$_3$-1** will not work. Since free valences can be satisfied by protons as well as other atoms, **sCH$_3$-1** can be seen to represent methyl singlets, doublets, or triplets. Thus we should not be surprised by the fact that putting three **sCH$_3$-1** groups on GoodList has no effect on the number of structures generated. **sCH$_3$-2** uses X atoms, which by definition can be anything but proton. But putting three **sCH$_3$-2** substructures on GoodList leads to no structures passing the constraints! I am not sure why this happens, and neither is anyone I have asked. I suspect that this results from pushing the overlapping capabilities of substructures on GoodList in MolGen too far. The DEPT data tell us that there are three quaternary carbons and three methyl groups in borneol. Thus, two of the methyls must be attached to one of the quaternary carbons. Putting three **sCH$_3$-2** groups on GoodList implies three methyls and three quaternary carbons, and perhaps the program is unable to recognize the necessity to overlap a couple of the latter.

But with a program as powerful as MolGen, there is always a work-around. The one I chose was to define **sCH$_3$-3** and put it on BadList. **sCH$_3$-3** specifies that the methyl is attached to a carbon bearing at least one proton; i.e., a doublet methyl. Since free valences can be satisfied by hydrogen atoms, **sCH$_3$-3** could also represent a methyl triplet. By putting this substructure on BadList, one rules out all methyls except those attached to quaternary carbons. Structure generation with this constraint leads to 306 structures.

MolGen is a good CASE program, but it is of the type that I have begun to call a "classical" CASE program. It leaves all the spectrum interpretation to the molecular structure chemist. In addition, even after the human has a clear idea of the constraint he wants to give to the program, there can still be problems "translating" this information to the program, as we saw in the example above with borneol. In my next contribution I will describe an alternative program, one that I call a "non-classical CASE program.

Doug Dorman
doug_dorman@lilly.com

[3] Don't try to look at these structures by hitting the "Results" button. With this many structures, this crashes the program.

[4] With "only" 2,191 structures the program does not crash.

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System Weight (kg) Including Cryogen's	120	315	391	133	325	399	1050	400	610	625	1200

NMR Operating Frequency (MHz1H)	600		750	800		900	
Field Strength (Tesla)	14.0		17.6	18.8		21.1	
Nominal Room Temperature Bore Access (mm)	51	89	51	63		63	
Magnet Type (Standard or shielded)	Actively Shielded	Standard	Standard	Standard	(2.2K) Pumped	(2.2K) Pumped Standard	(2.2K) Pumped With Iron Shield
Field Stability (Hz/hour 'H)	<10	<12	<15	<15	<15	<15	<15
Axial 5 Gauss Stray Field Contour (Metres)	2.5	5.0	7.6	8.69	6.3	12.2	8.73
Radial 5 Gauss Stray Field Contour (Metres)	1.75	3.9	6.1	6.89	5.0	9.7	3.81
Cryostat Type	T5FB	T4FBL	T6	T6L	T7	T8	
Minimum Helium Refill Interval (Days)	120	90	60	60	60	60	
Cryostat Helium Refill Volume (Litres)	101	60	187	216	328	1200	
Minimum Nitrogen Refill Interval (Days)	15	15	14	14	14	15	
Nitrogen Refill Volume (Litres)	136	100	137	162	167	1800	
* Minimum Operational Ceiling Height (Metres)	3.16	3.4	3.78	3.97	3.97	8.75	
System Weight (kg) Including Cryogen's	1180	1200	3000	4000	4000	18000	

Room Temperature Shim Specifications

Shim Type (Model)	Number of Channels	Dimensions	
		External Diameter (Cryostat Bore Size)	Internal Diameter (NMR Probe Diameter)
23/54/45	23	54mm	45mm
18/89/73	18	89mm	73mm
26/89/73	26	89mm	73mm
28/51/40	28	51mm	40mm
40/51/40	40	51mm	40mm
29/51/45	29	51mm	45mm
36/63/51	36	63mm	51mm

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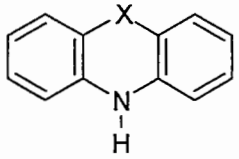
June 10, 1998
(received 6/19/98)

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

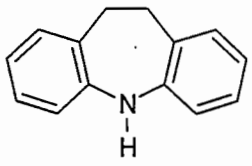
Deuterium-induced carbon-13 isotope shifts in cross-conjugated systems

Dear Professor Shapiro:

The deuterium induced ^{13}C isotope shifts for a structurally varied group of 21 nitrogen-containing benzoheterocyclic systems, labeled at the NH position, have been measured in DMSO-d_6. The analyzed compounds included bridged diphenylamines, benzolactams, 4-quinolinone, acridinones, carbazoles and indoles (Scheme). The variations of two-bond isotope effects ($^2\Delta$) are function of the competitive nitrogen lone-pair delocalization into the two neighboring unsaturated systems (α and α') [1-4]. A dependence between the δN*H* with the arithmetic mean of $^2\Delta C\alpha$ and $^2\Delta C\alpha'$ is evidenced (Figure). Exclusion of **5** –for which the formation of an azepine ring anion with 8 π-electrons on deprotonation makes the NH proton less acidic– and **13** improves considerably the quality of the correlation, to give $r = 0.90$. The least-squares equation is $^2\Delta(C\alpha + C\alpha')/2$ (ppb) = -25.53 δN*H* (ppm) + 146.5.



X	
1	CH_2
2	S
3	O



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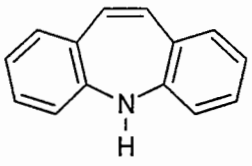

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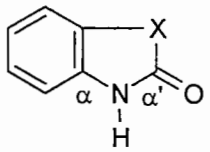
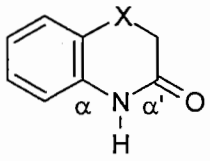
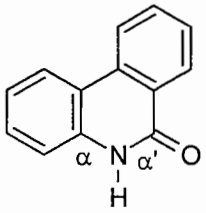


X		X	
6	CH_2	**8**	O
7	S	**9**	CO



X	
10	CH_2
11	S
12	O



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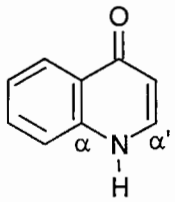

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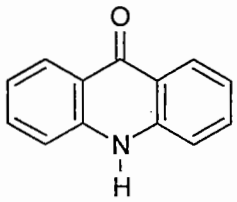

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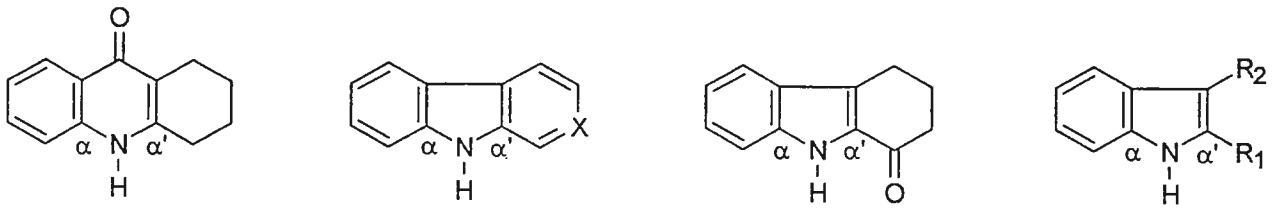


16

	X
17	CH
18	N

19

	R_1	R_2
20	COMe	H
21	H	COMe

Scheme. Structural formulae of bridged diphenylamines **1-5**, benzolactams **6-13**, 4-quinolinone **14**, acridinones **15**, **16**, carbazoles **17-19** and indoles **20**, **21**.

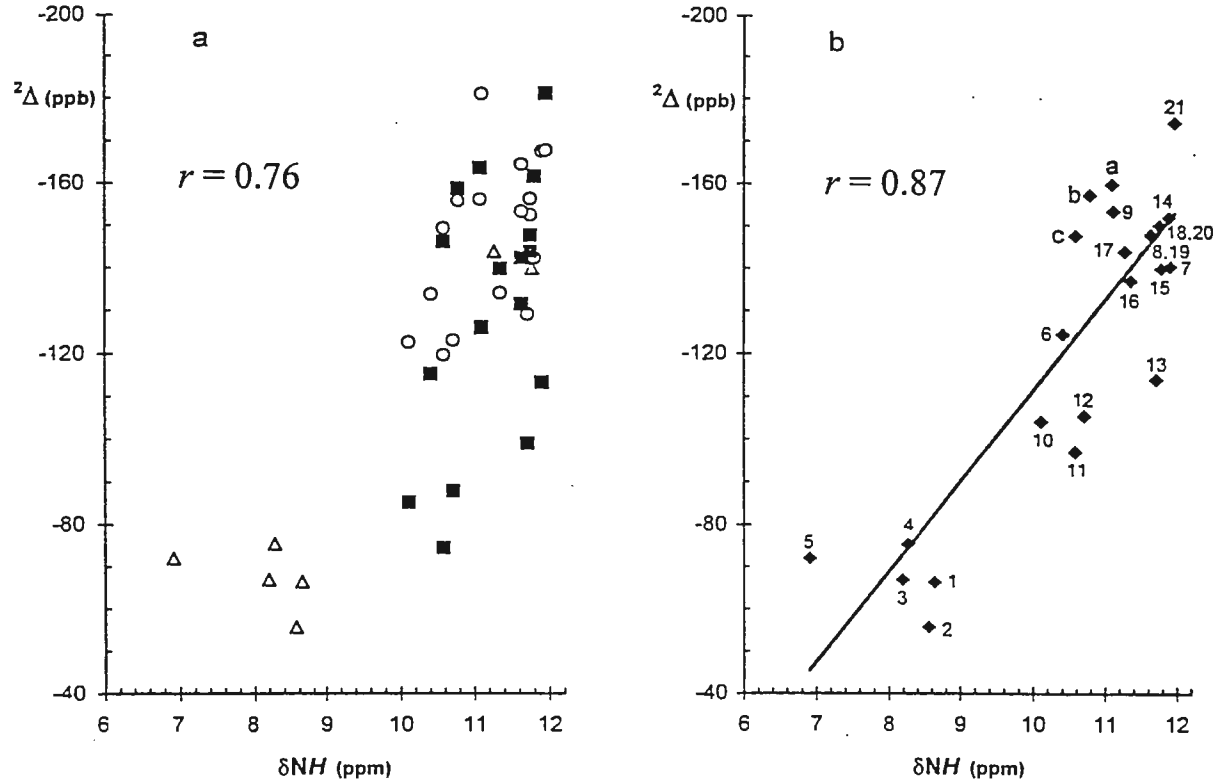


Figure a): Plot of $^2\Delta$ vs. δNH. Symmetrical molecules (Δ), Cα (o), Cα' (■). b): Plot of $^2\Delta$(Cα + Cα')/2. The plot includes data for indole (a), tetrahydrocyclopent[*b*]indole (b) and tetrahydrocarbazole (c).

1. Morales-Ríos, del Río, Joseph-Nathan, *Magn. Reson. Chem.* **27**, 1039 (1989).
2. Morales-Ríos, Joseph-Nathan, *Magn. Reson. Chem.* **29**, 49 (1991).
3. Morales-Ríos, Pérez-Alvarez, Joseph-Nathan, Zepeda, *Magn. Reson. Chem.* **32**, 288 (1994).
4. Morales-Ríos, Joseph-Nathan, Wrackmeyer, Kupce, *Magn. Reson. Chem.* **31**, 238 (1993).

Sincerely yours,

Martha S. Morales-Ríos

Pedro Joseph-Nathan

ARGONNE NATIONAL LABORATORY
9700 South Cass Avenue, Argonne, Illinois 60439

June 11, 1998
(received 6/25/98)

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

Re: **MRI Investigation of Anomalous Solvent Diffusion in Polymers**

Dear Barry,

In recent years, MRI methods have proved useful for studying solvent transport behavior in polymers and coals. For instance, time-resolved MRI has been used in our lab to distinguish between Fickian and Case II swelling dynamics [Cody & Botto, *TAMU nmr Newsletter*, **424**, 25 (1994)]. Recently we have observed anomalous swelling behavior in cross-linked rubber samples, for which the swelling dynamics are found to be intermediate between Fickian and Case II diffusion. Our results are unusual given that swelling of rubbers in typically Fickian in nature. The samples were cross-linked copolymers of poly(isobutylene)-co-poly(paramethyl-styrene) (PIB/PMS), kindly provided by Jeff White at Exxon Chemical. The mole % concentrations of PIB and PMS in the polymers were 97% and 3%, and Tg = -73°C and 101°C for PIB and PMS, respectively. Thus, the samples have largely 'rubber-like' properties at room temperature.

Images of cyclohexane uptake in samples were recorded *in situ*. The sample was contained inside a glass cross that was constructed from 5mm NMR tubes and held in place with Kel-F holders. The holders were free to slide leaving the samples unconstrained as they swelled. Samples were cut longer than they were wide with approximate dimensions 1 x 1 x 10 mm. By imaging a slice perpendicular to the long axis, swelling in two dimensions could be observed.

Front velocity and concentration profiles are diagnostic of the type of swelling behavior. Fickian transport is characterized by an exponentially decreasing solvent front that moves as the square root of time, while a sharp solvent front moving linearly with time is characteristic of Case II diffusion. Figure 1 shows the progression of cyclohexane in three PIB/PMS samples having different cross-link densities. Sample 1 is the most cross-linked while sample 3 is the least cross-linked. The points were fitted to the equation $p = v \cdot t^n$, where p = position of solvent front, t = time and n is an exponent (n = 0.5 for Fickian and n = 1.0 for case II). The fits gave values for n of 0.70, 0.86 and 0.87 for samples 1, 2 and 3, respectively. These values are indicative of anomalous swelling behavior.

Figure 2 presents MRI images and the corresponding front profiles for sample 2. Brighter pixels indicate greater signal intensity. Diffusion weighting was employed in the images on the right as a means of eliminating signal from bulk cyclohexane. The diffusion coefficient of cyclohexane imbibed in the polymer was found to be smaller (by a factor of ca. 2) than that in the bulk solution. The relatively sharp front profiles observed indicate non-Fickian swelling.

Valtier and coworkers [Valtier, M.; Tekely, P.; Kiene, L.; Canet, D. *Macormolecules*, **1995**, *28*, 4075-4079] noticed another difference between Fickian and Case II swelling. They found that the 2D contour of the diffusion front reflects the initial shape of the object if the swelling is Case II. However, the diffusion contour quickly becomes circular in the case of Fickian swelling. In our samples, 2D contours retained the original object shape until the end of the swelling process. This indicates that swelling dynamics are closer to case II.

Observation of bright regions near the solvent front in the diffusion-weighted images is also interesting. The profiles obtained reflect gradients in the self-diffusion coefficients of cyclohexane across the sample. The data imply that the polymer network is relaxing slowly behind the solvent front. We intend to explore this property in more detail in the future.

Sincerely,

David Gregory

David M. Gregory
Chemistry Division

Robert E. Botto
Chemistry Division

Figure 1

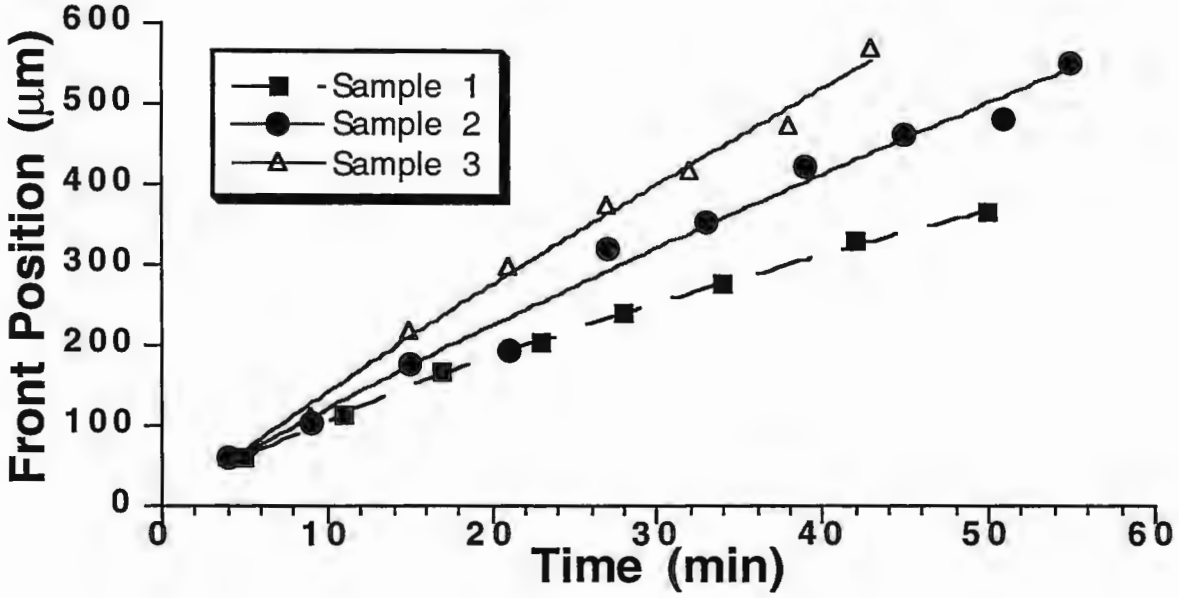
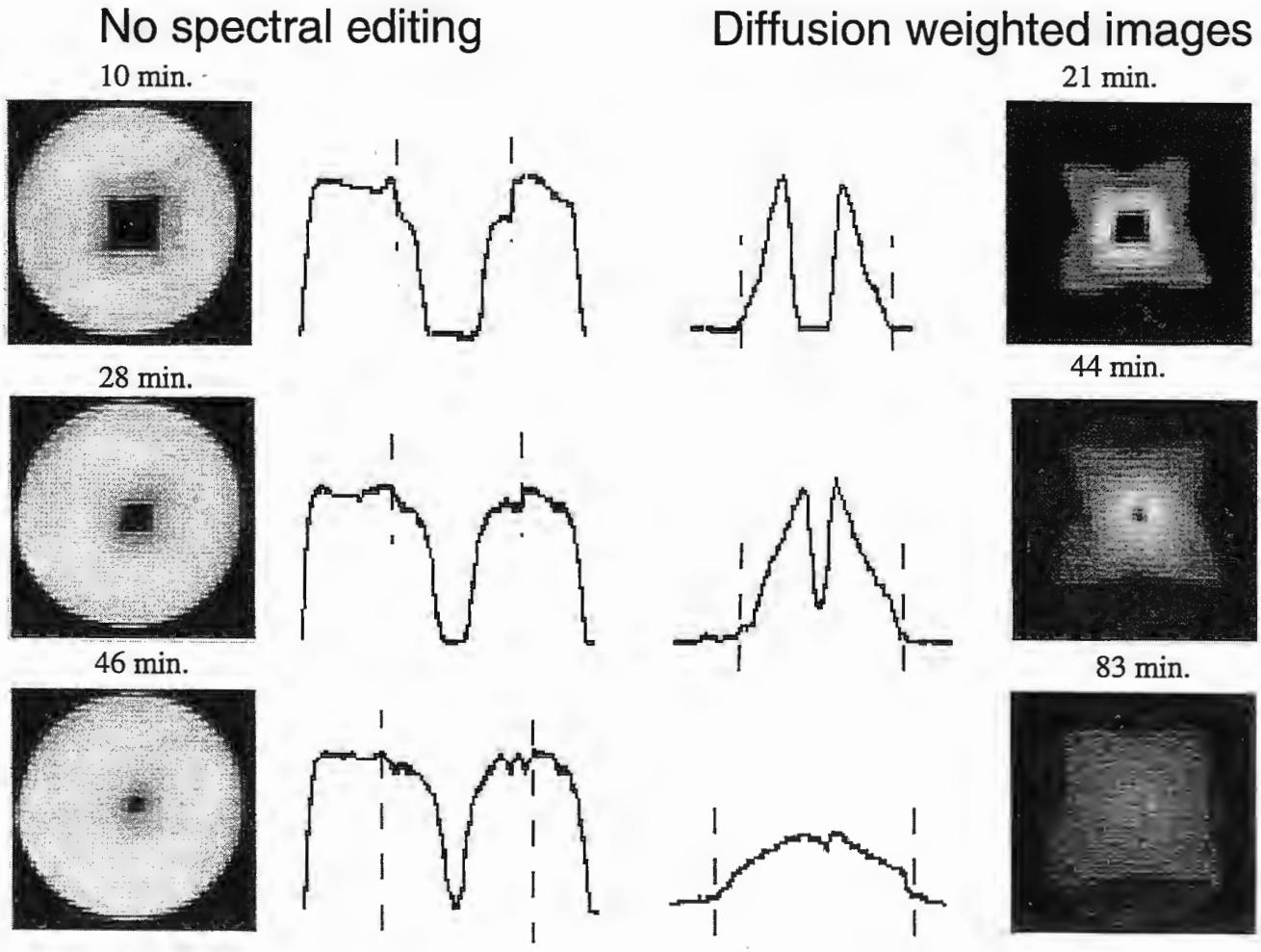


Figure 2



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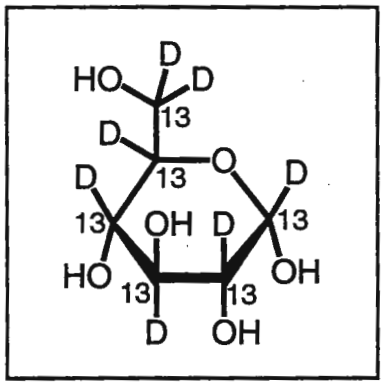

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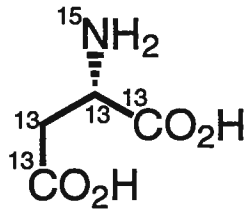
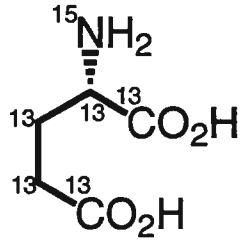
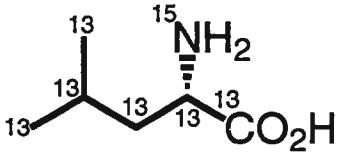


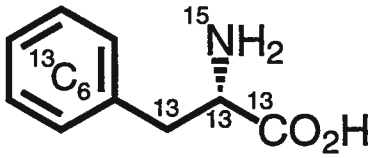
L-Aspartic Acid-$^{13}C_4$,^{15}N



L-Glutamic Acid-$^{13}C_5$,^{15}N



L-Leucine-$^{13}C_6$,^{15}N



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L-Glutamic Acid-$^{13}C_5$,^{15}N
L-Glutamine-$^{13}C_5$,$^{15}N_2$
Glycine-$^{13}C_2$,^{15}N
L-Isoleucine-$^{13}C_6$,^{15}N
L-Leucine-$^{13}C_6$,^{15}N
L-Lysine-$^{13}C_6$,$^{15}N_2$
L-Phenylalanine-$^{13}C_9$,^{15}N
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June 25, 1998 (received 6/26/98)

Emerging Figures of Merit for NMR: Choosing the Right Probe for the Job

Dean L. Olson, Paul F. Molitor, Michael E. Lacey, Jonathan V. Sweedler
School of Chemical Sciences, University of Illinois at Urbana-Champaign

Dear Barry and *NMR Newsletter* Readers,

In light of recent advances and applications in NMR for trace analysis [1-4], new figures of merit are emerging [4] for users to evaluate and compare relative probe performance for a particular application [5]. Here, we present a few helpful definitions and interpret them with respect to common NMR experiments.

NMR users are accustomed to an expression of *S/N* for a given analyte concentration, such as 0.1% ethylbenzene in $CDCl_3$, or 40% dioxane in C_6D_6. This performance parameter can be more explicitly defined as the concentration sensitivity

$$S_c = \frac{S/N}{C \cdot t^{1/2}}$$

where C is the sample concentration, and the $t^{1/2}$ term normalizes for the total experiment time by incorporating into a single variable the acquisition time, number of transients, pre-delay, etc. Such a definition, however, may not tell the whole story for a probe which has been designed for mass-limited samples. In such a case, a more relevant indicator of probe performance is the mass sensitivity

$$S_m = \frac{S/N}{mol \cdot t^{1/2}}$$

where the mole amount is the portion of the sample which lies within the NMR coil observe volume, V_{obs}. The V_{obs} and sample concentration are used to compute the moles of observed sample.

We now consider some cases where sample mass is and isn't limiting to the analysis. The first example derives from product literature for a probe designed for trace analysis. In a recently received advertisement for the Nalorac SMIDG SUBMICRO™ probe, a proton spectrum is included which was acquired on a total sample of 172 μg of sucrose in 23 μL of D_2O (21.8 mM) in the 1.7 mm o.d. sample tube. The single-scan *S/N* = 193 for the anomeric proton on a 600 MHz spectrometer with an acquisition time of 4.1 sec. Since the total sample volume equals the observe volume in this example, the sensitivities (with appropriate units) are easily computed and appear in Table 1.

Suppose an analyst wants to know what the result would be for the same sample mass in a 5 mm probe. A good comparison is to acquire an identical spectrum on a sucrose concentration which

corresponds to the same mass of sucrose (172 μg) dissolved in the observe volume of the 5 mm probe. Based on a coil length of 16 mm and a tube i.d. of 4.2 mm, V_{obs} = 222 μL (2.26 mM sucrose). The anomeric proton S/N = 136 for a single scan on our 600 MHz Varian INOVA™ spectrometer using the Varian 5 mm proton detection probe. We used the same data acquisition and processing parameters and have presumed that line width and shape are comparable; the resultant sensitivities appear in Table 1. Clearly, the mass sensitivity is better for the SMIDG probe, but the concentration sensitivity is better for the 5 mm Varian probe.

An additional figure of merit to consider especially when comparing NMR probes for use as detectors in separations like LC-NMR, CE-NMR, and CEC-NMR [6], is the limit of detection (*LOD*) defined in terms of the concentration or mass of sample which yields a $S/N = 3$. These values are affected by the experiment time as well, so that

$$LOD_c = \frac{3 \cdot C \cdot t^{1/2}}{S/N} \qquad \text{and} \qquad LOD_m = \frac{3 \cdot mol \cdot t^{1/2}}{S/N}$$

where the mole quantity again refers to that amount of sample in the observe volume. These values appear in Table 1 for the two previous probes. The *LODs* are consistent with the earlier conclusions, but also allow the user to compute the approximate mass or concentration of sample needed to acquire a given S/N in a particular probe.

Our research focuses on developing sensitive NMR detectors for mass-limited conditions using solenoidal microcoils fabricated directly on capillaries. For a microcoil wound on capillary with a 357 μm o.d. and V_{obs} = 5 nL [7], the S/N = 32 for the sucrose anomeric proton. The data were acquired on a 300 MHz spectrometer using acquisition and analysis conditions different from the previous two examples. Though the total experiment time is 60 sec, a time-normalized comparison can still be made. The figures of merit for sucrose in the microcoil are included in Table 1. In comparison to the other two probes, these performance indicators show that the microcoil achieves the highest S_m and requires the smallest sample size, but is limited in S_c . It should be noted that a significant improvement in S_c and a proportionate decrease in LOD_c for the microcoil can be attained by increasing V_{obs} [8]. Users should bear in mind that the possibility of radiation damping becomes greater in a more mass-sensitive probe.

To conclude, performance comparisons for NMR probes employed under different analytical situations are easily rendered using the figures of merit described here. These performance criteria are readily obtained and quite useful in choosing a probe for a particular analysis. An additional consideration is the total sample amount available to the analyst and how it can be most effectively prepared to generate an acceptable result. For instance, in the cases of the 5 mm probe and the microcoil, only a fraction of the total sample (the observe factor) lies within V_{obs}. Consequently, this may require the use of a speciality tube, susceptibility matched plugs, or additional sample. A mass-limited condition probably calls for the greatest S_m, which is usually the probe with the smallest coil. A situation which is not mass-limited, or where the sample already exists in a relatively large volume and can't be concentrated, would benefit by using the probe with the largest S_c, which will usually have the biggest V_{obs} . Determination of the figures of merit described here help guide the user in choosing the most appropriate NMR probe for the job.

References

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Table 1.

Figure of Merit	Varian 5 mm	Nalorac SMIDG	Microcoil
S_c (S/N • mM^{-1} • $sec^{-1/2}$)	30	4.4	0.0083
S_m (S/N • μmol^{-1} • $sec^{-1/2}$)	134	190	1660
LOD_c (mM • $sec^{1/2}$ •S/N^{-1})	0.10	0.69	360
LOD_m (nmol • $sec^{1/2}$ •S/N^{-1})	22	16	1.8

Please credit this contribution to Dr. Vera Mainz, Director of the Varian-Oxford Instruments Center for Excellence in NMR (VOICE Lab) at the School of Chemical Sciences, University of Illinois.

Best regards,

Dean L. Olson Paul F. Molitor Michael E. Lacey Jonathan V. Sweedler

THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER
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The Mary Nell and Ralph B. Rogers
Magnetic Resonance Center

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

June 10, 1998
(received 6/16/98)

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

^{39}K Noise at 4.7 Tesla

Dear Barry,

Recently, I decided to expand my horizons a little and do ^{39}K NMR as well as ^{23}Na relaxation experiments, in spite of the 200-fold loss in sensitivity. Potassium is an extremely important biomedical ion (as well as sodium) but researchers have reported a decrease in ^{39}K NMR "visibility" with lowering B_0. With this in mind, I decided to set up ^{39}K experiments. Because of the short T_2 of the satellite transition (spin I = 3/2), I decided to use the wideline probe on our Bruker MSL-200 with 4.7 T super-wide-bore (15 cm) vertical magnet. Later on, if our new Varian INOVA 300 MHz console ever achieves ^{39}K functionality, I hope to check the B_0 dependence reported for biological tissue.

I had expected a weak signal, but the initial S/N was unexpectedly low. By tweeking the electronics, such as the duplexer, I achieved "reasonable" signal strength; but, the signal was just too noisy, with a noise level that changed hourly. Because the ^{39}K signal is at 9.339 MHz, it was in the range of my portable short wave radio. With it, I found extremely intense noise around 9.3 MHz all over the lab, but especially strong at the magnet and even stronger at the console. I went next door to the new clinical Phillips MRI machine and found that one of the monitors emits very strong 9.3 MHz noise. I found the same noise at the two GE/Omega consoles in two other labs, at the monitor of my office PC (486, 66 MHz), and at the monitor of my home PC (Pentium II, 266 MHz). However, I did not find such noise (either at 9.3 MHz or at 14 MHz) at the SUN computers of the two Varian INOVA consoles or at the monitor of a Dell 90 MHz Pentium computer in the computer room. Because such r.f. noise is so prevalent and extremely strong, it is a real problem. I had similar problems twenty years ago with the TI Silent Writer terminal on the Nicolet computer used to control a home-made NMR spectrometer, but that noise was around 13.3 MHz.

Obviously, shielding/filtering is important for the probe, pre-amp, r.f. cables (RG-58 cables are leaky), power leads to the pre-amp, cables to the magnet shims, etc. I am making headway on the problem, but I would appreciate advice from others who may have had similar problems.

Sincerely,

Don

Donald E. Woessner
dwoess@mednet.swmed.edu

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• GE QE-300, including dual 1H/13C electronics, $^{1}H/^{13}C$ switchable probe.	$45,000.
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June 1, 1998
(received 6/6/98)

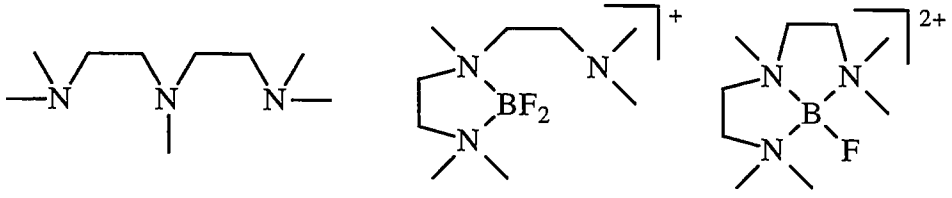
Dr. B. L. Shapiro,
THe NMR Newsletter,
966 Elsinore Court,
Palo Alto, CA 94303, USA.

title: **NMR of fluoroboron cations including $^{11}B,^{19}F$ HETCOR**

Dear Barry:

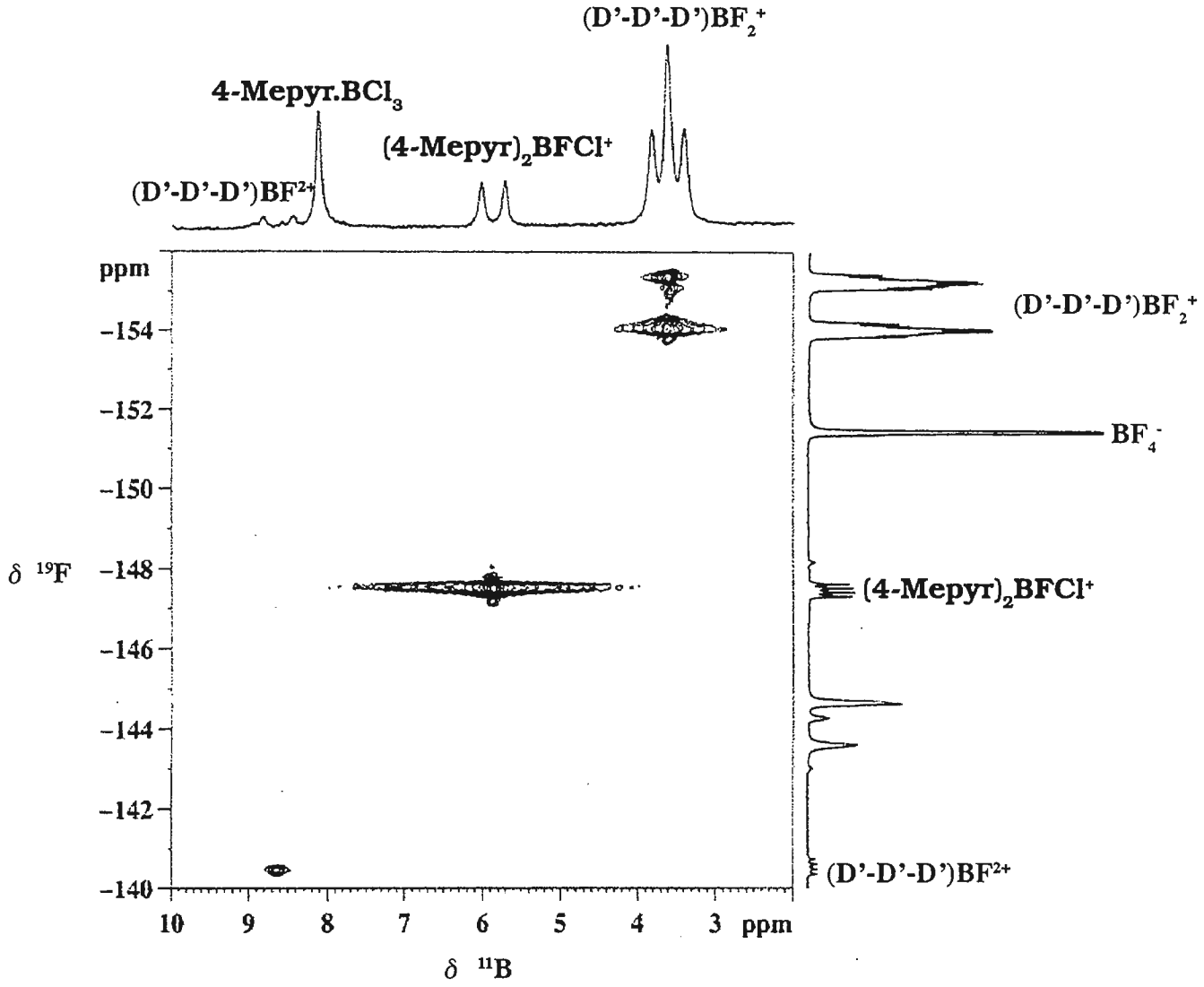
Our ^{19}F and ^{11}B nmr studies of the formation of fluoroboron cations ($D_2BF_2^+$ and D_3BF^{2+}; D = various Lewis bases[1]) have recently been given a major boost from the capabilities of McMaster University's Bruker DRX-500 instrument. Its full ^{19}F capability, which allows a wide range of X nucleus-fluorine 2D experiments, was installed to extend the work of Gary Schrobilgen's research group at McMaster, which is a leader in inorganic fluorine chemistry and has many interesting multinuclear nmr studies to its credit. We do our routine work at Brock University on our "workhorse" 12-year-old Bruker AC-200 (for solution work) and our 2-year-old Bruker DPX-300 (for MAS), and have access to the McMaster DRX-500 when necessary. One very simple advantage of the DRX-500 is that we can obtain 1D ^{19}F and ^{11}B spectra in rapid succession: important because many of our systems are highly reactive and change with time.

We have been working on the synthesis of fluoroboron cations involving chelating donors, few of which are known. These are best made by ligand displacement from easier-to-prepare fluoroboron cations such as $pyr_2BF_2^+$ (readily isolable as its PF_6^- salt[1]) or ligand **and** Cl^- displacement from adducts such as $pyr.BF_2Cl$. Two displacements by a single bidentate ligand give the desired chelated-donor difluoroboron cations. Similar approaches starting from pyr_3BF^{2+}, pyr_2BFCl^+, or $pyr.BFCl_2$ and involving three displacements should give fully chelated BF^{2+} cations of tridentate ligands such as pentamethyl-diethylenetriamine (**I**).



I **II** **III**

The Figure shows a portion of the $^{11}B,^{19}F$ HETCOR spectrum of the complex system resulting from reaction of I with the adduct system 4-methylpyridine.BF_3 + BCl_3, which was already complex and contained species such as 4-Mepyr.$BFCl_2$ (formed by halogen



redistribution) and 4-Mepyr$_2$BF$_2^+$ (formed by displacement of Cl$^-$ from 4-Mepyr.BF$_2$Cl by further 4-Mepyr). Adding I causes further displacements, and new species incorporating I appear. Of particular interest is the ^{11}B signal at 3.5 ppm which correlates with **two** ^{19}F signals at -152.2 and -154.1 ppm. This is consistent with the tridentate ligand coordinating to boron via its centre N and one of its terminal N's to give **II** in which the centre N is chiral, making the BF$_2$ fluorines prochiral and magnetically nonequivalent. This is confirmed by the F,F COSY spectrum: of all of the many ^{19}F signals, arising from many different species, only these give cross peaks, confirming that the two fluorines are present in the same molecule. The one-bond ^{11}B-^{19}F coupling constants of the magnetically nonequivalent fluorines are appreciably different (32.9 and 37.6 Hz). The two-bond ^{19}F-^{19}F coupling constant of 61.2 Hz is consistent with the relatively few reported examples of two-bond FBF coupling (e.g. $B_2F_7^-$, 95 ± 10 Hz[2a]; $(PhCH_2NMeEt)_2BF_2^+$, 72 Hz[2b], D*BF$_2$X (X = Br, I), 33-49 Hz[2b]). The Figure also shows the emergence of what we believe to be the first fully-chelated tridentate-ligand fluoroboron species, **III**.

We thank Dr. Don Hughes and Mr. Brian Sayer for assistance and the Department of Chemistry, McMaster University, for instrument time. We also thank Prof. Alex Janzen, University of Manitoba, for discussions leading to our work on these systems.

Yours sincerely,

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Leipzig, 17.06.98
(received 6/24/98)

Tricoordinate Zincates

Dear Barry,

The structures of organometallic reagents important in synthetic procedures are continually studied under the assumption that a better knowledge of the ground state structures of the reagents will lead to improved control in the reactivity (e.g. selectivity) of their reactions. We have studied by NMR spectroscopy ^{13}C- and ^{6}Li-labeled methyl cuprates to address further the much debated topic of "higher order" organocuprates *vs.* "lower order" organocuprates.[1] An identical coupling pattern is observed in the ^{1}H and ^{1}H-coupled ^{13}C spectra for all three of the ^{13}C labeled organocuprates Me_2CuLi (**1**), Me_3CuLi_2, (**2**), and $Me_2Cu(CN)Li_2$ (**3**) with the following coupling constants: $^{1}J_{CH}$ = 109.5 Hz, $^{2}J_{CC}$ = 21 Hz, $^{3}J_{CH}$ = -0.8 Hz, and $^{4}J_{HH}$ = 0 Hz (see Figure 1a). We have recently published results[2] indicating that the predominant solution structures of organocuprates **2** and **3** are lower-order in nature, and the dimethyl-cuprate core resembles that found for **1**.

Our attention has now turned to the homologous zinc reagents.[3] The neutral Me_2Zn (**4**) reagent shows a similar coupling pattern ($^{1}J_{CH}$ = 116.1 Hz, $^{2}J_{CC}$ = 15.3 Hz, $^{3}J_{CH}$ = -0.1 Hz, and $^{4}J_{HH}$ = 0 Hz) to isoelectronic **1** (see Figure 1b). However, unlike the copper system, treatment of Me_2Zn with another equivalent of MeLi results in formation of a higher-order zincate Me_3ZnLi (**5**) as evidenced by the change in the proton coupled ^{13}C NMR spectrum (Figure 2a). This coupling pattern was simulated (Figure 2b) using the WIN-DAISY simulation program and refined on the experimental spectrum to give the following coupling constants: $^{1}J_{CH}$ = 110.9 Hz, $^{2}J_{CC}$ = 14.0 Hz, $^{3}J_{CH}$ = 0.6 Hz, and $^{4}J_{HH}$ = 0.4 Hz. We are currently further investigating this zinc system.

Sincerely yours

[T. A. Mobley] [S. Berger]

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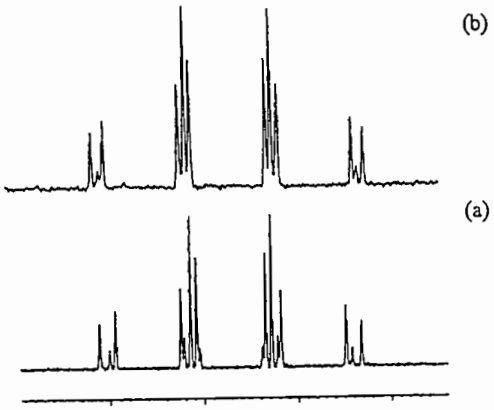

Figure 1. ^{1}H-coupled ^{13}C NMR of fully ^{13}C-labeled (a) Me_2CuLi (1) and (b) Me_2Zn (4)

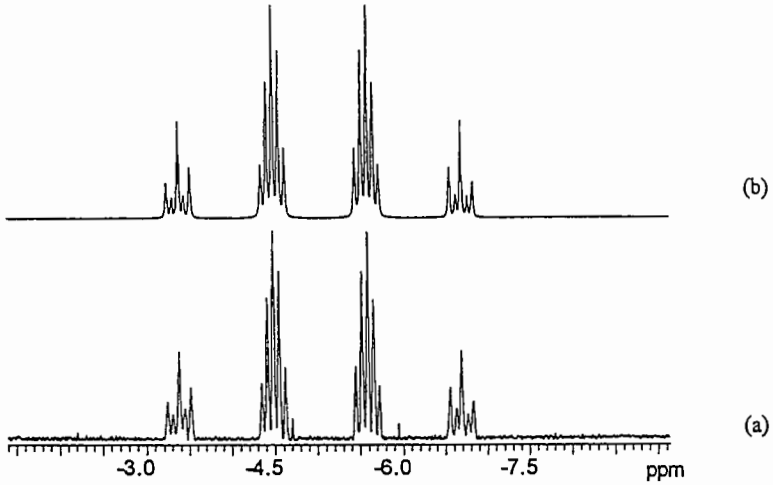

Figure 2. ^{1}H-coupled ^{13}C NMR of fully ^{13}C-labeled Me_3ZnLi (5) (a) experimental and (b) calculated.

Continued from p. 40

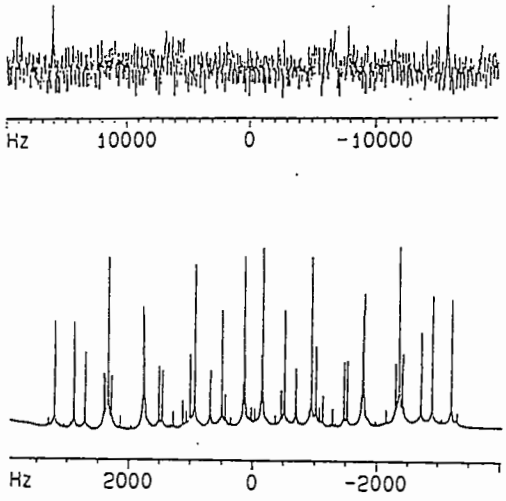

Fig. 1

Top trace : ^{2}H NMR spectrum of Benzene in the natural abundance oriented in phase ZLI-1114

Bottom trace : ^{1}H NMR spectrum of Benzene oriented in phase ZLI-1114 under identical condition

SOPHISTICATED INSTRUMENTS FACILITY
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May 25, 1998
(received 6/22/98)

Natural Abundance ^{2}H NMR of Oriented Molecules

Dear Barry,

In the last decade, the field of NMR of oriented molecules appeared to have reached a saturation point as far as the structural studies are concerned with only a few significant applications. This is essentially due to spectral complexity with increase in the number of interacting nuclei. Now it has once again become an active field due to several recent developments such as the discovery of thermotropic liquid crystals of low order parameter (1), the use of lyotropic liquid crystals as solvents for large biomolecules (2) and the use of high magnetic fields for aligning molecules (3). Another development in this direction is the possibility of recording natural abundance ^{2}H NMR spectra of pure liquid crystals (4). We have recently extended this method to record the natural abundance deuterium NMR spectra of dissolved molecules (5). These latter developments may be expected to aid the analyses of complex proton spectra.

The top trace of Fig.1 shows the ^{2}H NMR spectrum of benzene in the natural abundance oriented in MERCK phase ZLI-1114. The spectrum was obtained on a Bruker AMX-400 NMR spectrometer using a 10 mm diameter sample tube in about 18 hours. A quadrupole split doublet with a separation of 31.952 KHz is observed. This corresponds to an order parameter in the plane of the benzene ring equal to 0.1084 (obtained using a value of 196.5 KHz for the ^{2}H-quadrupole coupling constant). From this information, the dipolar coupling between the ortho protons of benzene was derived as –852.1 Hz.

The proton spectrum of the same sample under identical conditions is shown in * Fig.1 (bottom trace). The analysis of the spectrum using the standard techniques also gives a value of –852.1 Hz for the ortho H-H dipolar coupling in benzene.

The results demonstrate that the natural abundance deuterium NMR spectra of molecules dissolved in liquid crystals can be obtained within reasonable time on the present day spectrometers. Such studies can be used to derive information which can enhance the utility of the NMR spectroscopy of oriented molecules particularly when applied to complicated systems.

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* The figure is on p. 39.

C.L. Khetrapal K.V. Ramanathan N. Suryaprakash S. Vivekanandan

(C.L. Khetrapal) (K.V. Ramanathan) (N. Suryaprakash) (S. Vivekanandan)

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The NMR Newsletter - Book Reviews

Book Review Editor: István Pelczer, Dept. of Chemistry, Princeton University, Princeton, NJ 08544

"NMR Spectroscopy: Processing Strategies"

(an interactive course)

by

Peter Bigler

VCH Verlagsgesellschaft, Weinheim, Germany, 1997; 249 pages, ISBN 3-527-28812-0
$99.00 (hardcover); A CD-ROM for working with sample spectra is provided.

Distributed processing of NMR data is widespread, which means that the chemist obtains or collects FIDs, and has her/his own software to process these files. Some manufacturers have integrated spectral processing, analysis and interpretation tools. It means different programmers, different philosophies, different layouts, etc. This programmed learning book by Peter Bigler is clearly written for the novice, the non-specialist, although experts may also find useful hints on matters hidden by the usual users manual. The book fulfills a real need for an up-to-date introduction to NMR data processing, and provides an in-depth understanding of the advanced processing strategies necessary for a fruitful application of modern multidimensional NMR. Clearly the book can be welcomed by Bruker instrument users. It is written for explaining the sometimes bewildering and diverse software tools which lack an easy-to-learn, but still sufficiently detailed, users' manual. The practitioners who read this book and proceed with the worked examples "Check It's" as they occur in the text, will be rewarded with a proper functional understanding of NMR data processing/analysis at a level that will allow them to derive full benefit of this spectroscopic method.

Software facilities are, of course, always being upgraded, and for this reason any text can be easily outdated. Anticipation of forthcoming books in this series (e.g. Modern Spectral Analysis, Data Acquisition and Intelligent Data Management, in part written by Bruker people) makes this piece of work valuable for those who wish to learn the whole game from zero knowledge to full structure elucidation.

The practical summaries of basic 1D and 2D experiments typical for applications by organic chemists are very useful. Since this is a programmed introduction, first you have to install the software, then proceed with tasks of increasing complexity. This explains for example the reverse order of processing and display/plot chapters. The book can be used also for educational purposes, most efficiently in combination with the Bruker's manual. However, to a certain extent, the half-German/half-English abbreviated commands, e.g., StrukEd. are annoying. The same is true for mixed language snapshots of the Windows screens.

Continued

The book consists of six Chapters, as follows:

1. Introduction: Outlines the specific aims of the book, providing the readers with basic theoretical and practical knowledge, as well as expert guidance on processing strategies in NMR spectroscopy.

2. Your Personal "PC NMR Processing Station": Includes hints for installation of 1D/2D WIN-NMR and the GETFILE file transfer protocol. However, it seems that network problems, if such arise, should be deferred to the expert.

3. Modern Homo- and Heteronuclear 1D and 2D NMR Experiments: A short overview: Simplified theoretical descriptions, pulse sequence figures (as plotted by the NMRSIM module), application field, examples of spectra, and a useful collection of recommended readings are provided.

4. How to Display and Plot 1D and 2D Spectra: Assuming that processed spectra are available, a step-by-step description is given, based on pull-down menus and commands.

5. How to Process 1D and 2D NMR Data: Provides the fundamental concepts of NMR data processing. Many examples of 1D and 2D applications are presented at both basic and advanced levels to help the readers assess an overall mastery of the processing strategies.

6. NMR Data of an Unknown Oligosaccharide: For a self-test, a real situation of structure elucidation is provided. At this final stage, the reader can check her/his skill with the different processing tools in applying them to the structure determination of an unknown oligosaccharide.

Following Chapter 6 are a glossary and a subject index.

A few items of practical importance deserve be mentioned, such as explanation of linear prediction, multiplet analysis (which can be useful for teaching first order analysis), diagonal removal from 2D spectra, and efficient 1D WIN-NMR serial processing. Some things seem to be missing, however, such as preferred settings for ftp in Getfile, or are not explained clearly enough. In the Open menu, for example, how the Hosts should be defined: is it the NFS the remotely defined Host? Also, in T_1 analysis, if you are not aware that the variable delay list format is different in UXNMR and WIN-NMR, you are lost.

In summary, we believe that the book provides a very useful and practical treatise of data processing strategies employed in modern NMR spectroscopy, and is a very welcome addition to existing software manuals. Practical NMR courses organized at universities, technical schools, etc., can derive full benefit of the material presented in the book.

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

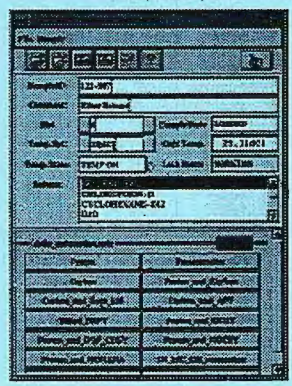
Forthcoming NMR Meetings, continued from page 1:

Spin Choreography - a symposium in appreciation of Ray Freeman, Cambridge, England, **April 8-11, 1999**; web site: http://mchsg4.ch.man.ac.uk/mcmr/RF.html; fax: c/o M.H.Levitt +46-8-15 2187; email: mhl@physc.su.se.

41st ENC (Experimental NMR Conference), Asilomar Conference Center, Pacific Grove, CA, **April 9-14, 2000**; Contact: ENC, 1201 Don Diego Avenue, Santa Fe, NM 87505; (505) 989-4573; Fax: (505) 989-1073; Email: enc@enc-conference.org.

Additional listings of meetings, etc., are invited.

How To Run JEOL's Eclipse+ Spectrometer



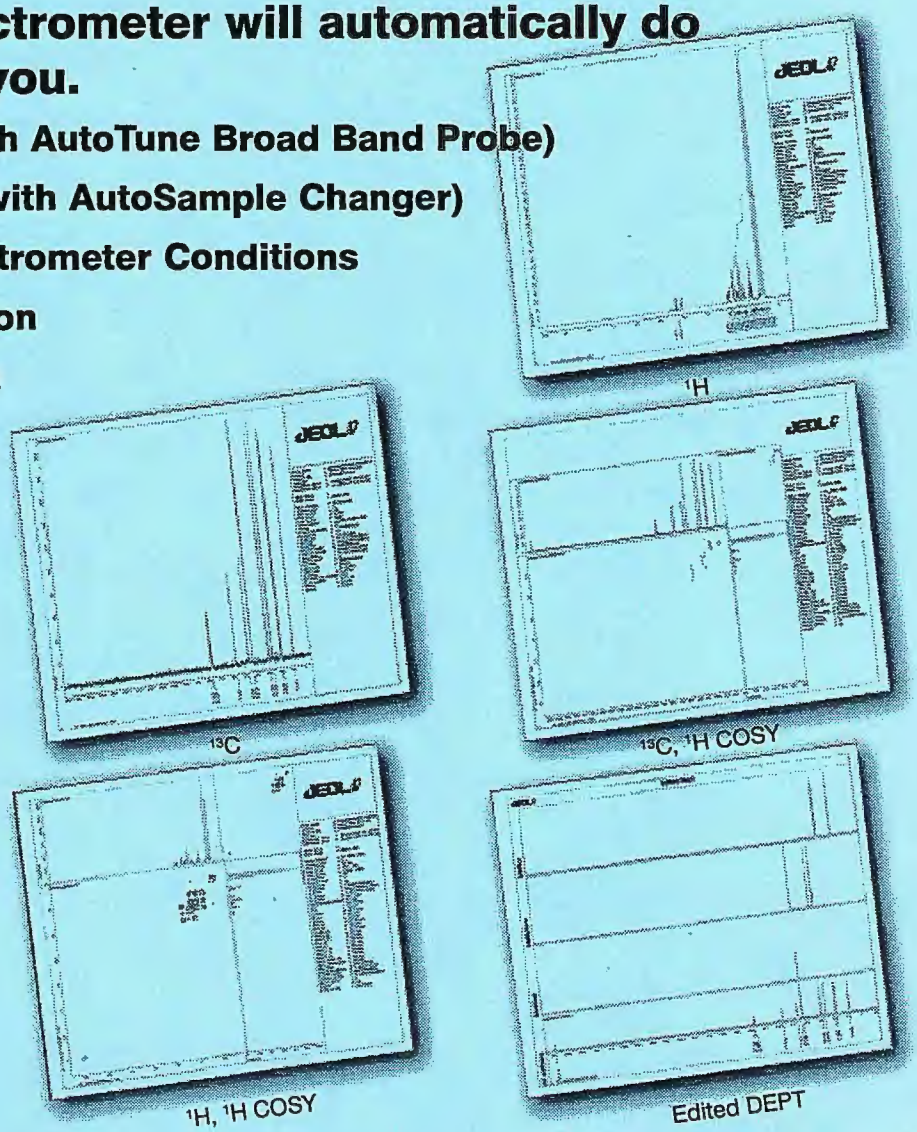
Step 1: Enter your sample name and the solvent.

Step 2: Click the mouse button on the data you want.

Step 3: Walk away with your data.

JEOL's Eclipse Spectrometer will automatically do everything else for you.

- ✔ Auto Probe Tuning (with AutoTune Broad Band Probe)
- ✔ Auto-sample Control (with AutoSample Changer)
- ✔ Auto Selection of Spectrometer Conditions
- ✔ Auto Baseline Correction
- ✔ Auto Data Presentation
- ✔ Auto Phase Correction
- ✔ Auto Digital Filtering
- ✔ Auto S/N Monitoring
- ✔ Auto Queue Control
- ✔ Auto Receiver Gain
- ✔ Auto Data Storage
- ✔ Auto Referencing
- ✔ Auto Processing
- ✔ Auto Peak Picks
- ✔ Auto Integration
- ✔ Auto Plotting
- ✔ Auto Shim
- ✔ Auto Lock



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