D.W.

Texas A&M University N-M-R Newsletter

No. 220

January, 1977

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DEADLINE DATES: No. 221: 7 February 1977
No. 222: 7 March 1977

All Newsletter Correspondence, Etc. Should Be Addressed To:

Dr. Bernard L. Shapiro
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Texas A&M University
College Station, TX 77843 U.S.A.

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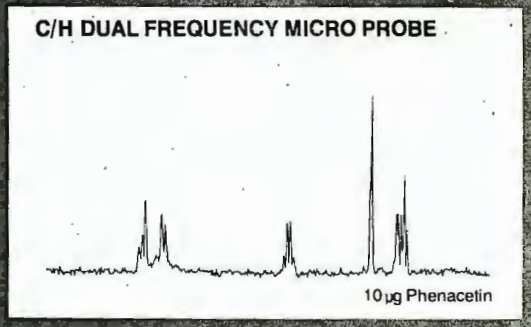

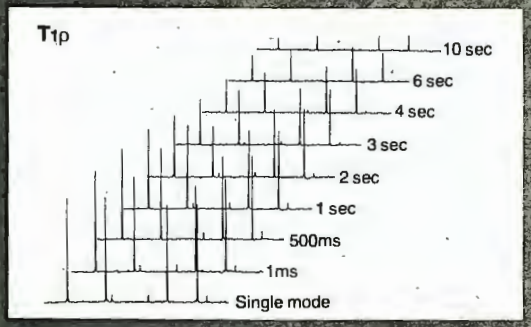

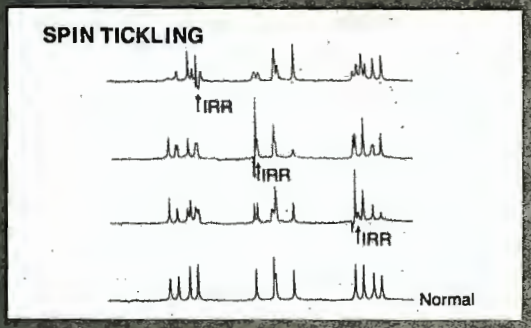

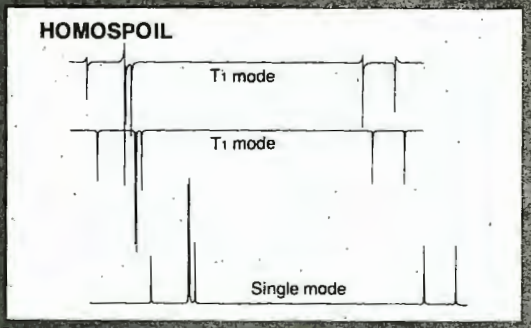

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Prof. V.Bystrov
USSR Academy of Sciences
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Moscow 117312 USSR

November 29, 1976

Professor Bernard L.Shapiro
Department of Chemistry
Texas A & M University
College Station, TX 77843
U.S.A.

Title: Aromatic Signal Assignment for Neurotoxin Short Protein

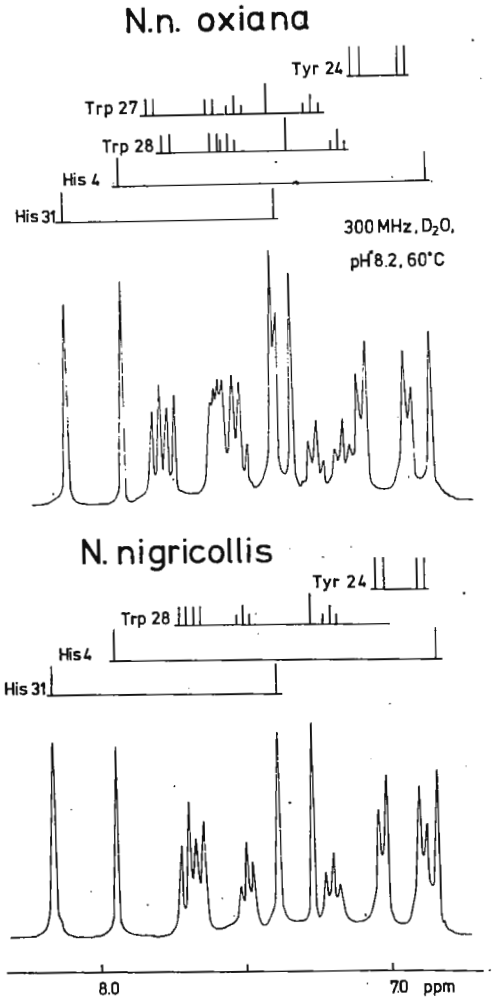
Dear Barry,

We have assigned the aromatic proton signals in the NMR spectrum of neurotoxin II Naja naja oxiana - the short protein (61 amino acid residues) isolated from Central Asian cobra venom. The two tryptophan and one tyrosine multiplets were identified by double resonance.

For the two histidine assignments we made use of different isotope exchange rates of the imidazole C_2H hydrogens in D_2O - T_2O (1.5 mCi) solution (pH 8.0). After incubation for 40 hours at 40°C the NMR spectrum shows that due to deuterium incorporation the intensity of the low field C_2H signal decrease by 30% and of the high field signal - by 75%. Accordingly the same differentiation has to be observed for radioactive tritium incorporation at the C_2 position. Thus the labelled neurotoxin II sample was digested by tripsin and the fragments were separated by Sephadex chromatography. The two isolated fragments with 1-15 and 27-32 residues, which contain His-4 and His-31 respectively, show different radioactivity, the first being $\sim$3 times more radioactive. This means that the His-4 has more mobile C_2H hydrogen and thus the high field signal is assigned to this histidine residue.

RECEIVED FEB - 7 1977

To assign the tryptophan residues we have compared the neurotoxin II spectra with the homologous protein - α-toxin from South African cobra Naja nigricollis. This toxin contains only one triptophan residue (Trp-28) which is invariant for all short neurotoxins, including neurotoxin II. The indole NH signal of α-toxin has very similar pH and exchange behaviour as one of the neurotoxin II NH signals, namely, their chemical shifts show two inflections at pH 3.2 and 6.0 and their line width do not broaden up to pH 8.5. The corresponding tryptophane C_2H and C_4H (or C_7H) chemical shifts also depend on pH in the range 3 - 6.5 pH.



The results of our assignment are summarized on the Figure for both neurotoxins.

With best wishes for the New Year,

Vladimir

Vladimir Bystrov

The University of Western Ontario

Department of Chemistry
Chemistry Building
London, Canada
N6A 5B7

December 14, 1976.

Dr. Bernard L. Shapiro,
Department of Chemistry,
Texas A and M University,
College Station, Texas 77843,
U. S. A.

Dear Dr. Shapiro:

A SIMPLE METHOD FOR OBTAINING PHASE ALTERNATED SEQUENCES ON A CFT-20.

This letter is to initiate my subscription to TAMU NMR Newsletter.

Recently, Dr. Doddrell pointed out the necessity for using a phase alternated pulse sequence to overcome difficulties associated with imperfect pulses during the measurement of short relaxation times.[1] For instruments not provided with phase alternating hardware, modifications may be made using double-balanced mixers and associated logic circuitry.[2,3] I would like to report a very simple method which A.M. Ferguson and I have developed for the CFT-20.

As shown in the diagram, the 3.3μH choke (L32 in Varian Schematic 87-144-78) is replaced by a hand-wound autotransformer, in which the section that replaces the choke also has an inductance of 3.3μH. This transformer was contructed from a small, ferrite toroid of material suitable for operation at 20 MHz. A bifilar winding was used with the start of one winding being connected to the finish of the other winding to provide a centre tap. By careful adjustment of the number of turns in the windings, two signals of equal intensity and each with overall gain of unity are available, with one signal being 180° phase shifted relative to the other. Though it was not required, further trimming could be achieved by fitting trim capacitors to each output.

Switching is achieved with a reed relay switch, the logic control for which is derived from EXC477. All of the components used in this modification are mounted on a piece of Veroboard (2x3 cm) and attached at right angles to the transmitter card, thus avoiding the need for connecting cables.

The previously spare execution line 477, available as a latched output on the E-bus card, is operated by a set of software modifications using about twenty words of memory. The relay is activated prior to the pulsing for every even-numbered transient just before the delay time (LT) between the inverting (TT) and observing (PW) pulses. The relay is reset at the end of the phase compensation delay following the observe pulse. The ADC output is complemented for the collection of data from every second transient by means of a software

complement instruction.

The only precaution which needs to be taken is to ensure that the LT delay between the inverting and observing pulses is not less than about 0.002s, so that the switch has adequate time in which to operate. For routine spectra, the inverting pulse (TT) is set to zero.

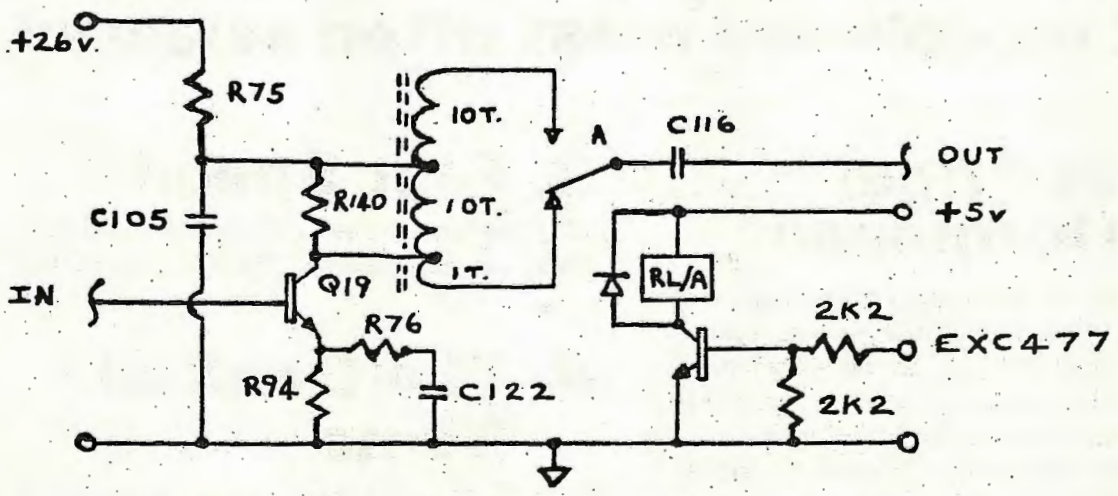
Details of the software modifications are available on request.

Yours sincerely,

J.W. Blunt.

(on study leave from University of Canterbury, Christchurch, New Zealand, until June 1977).

1. D.M. Doddrell and D.T. Pegg, TAMU NMR, 208, 5 (1975).
2. J.D. Cutnell, H.E. Bleich, and J.A. Glasel, J. Magn. Resonance, 21, 43 (1976).
3. R.E. Santini and J.B. Grutzner, Anal. Chem., 48, 941 (1976).



Modifications to 20 MHz Pulse Amplifier of CFT-20 to Achieve Phase Alternation.

(Those items prefixed with C, R or Q are existing components.)

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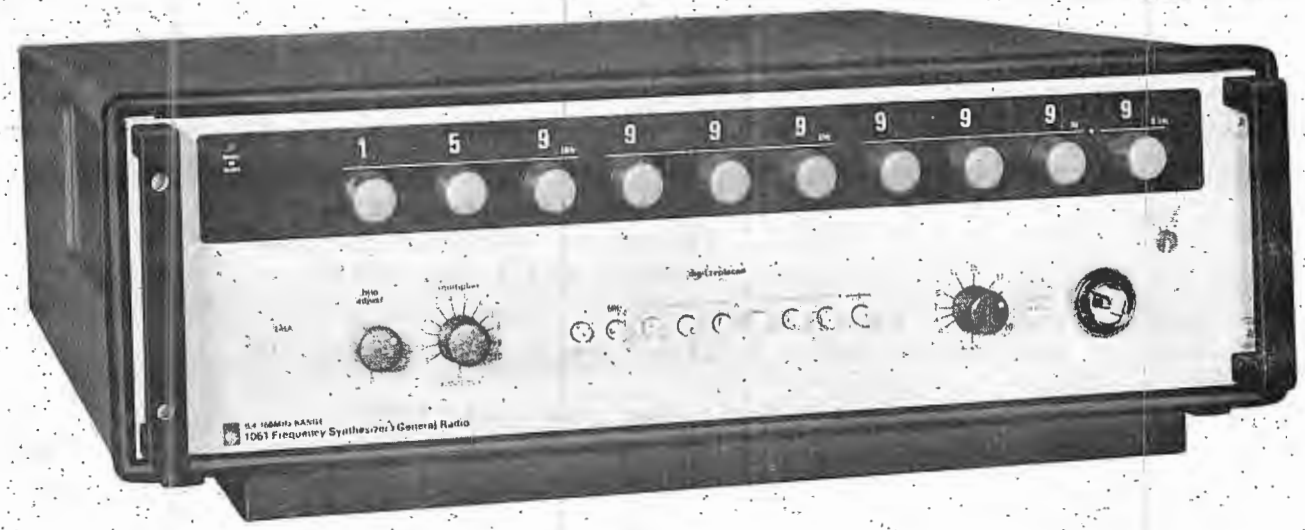

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File Référence

December 16, 1976

Prof. B.L. Shapiro
Department of Chemistry
Texas A and M University
College Station, Texas 77843
U.S.A.

Dear Barry,

XL-100 Modifications

Please excuse my long delay in contributing to the newsletter. We have received an XL-100A and TT 100A and are busy getting acquainted with them. Our first modification was to replace the 15,400,960 Hz crystal with the output from a frequency synthesizer. A fixed frequency, 10 MHz, from the synthesizer is also used to synchronize the frequency counter. This modification is useful for large offsets from a lock resonance while maintaining calibrated sweeps.

Because of the crystal filter in the voltage controlled oscillator the spectrometer offset circuit only locks in a certain span of offset frequencies, corresponding to a range of output frequencies. For a different master oscillator frequency the offset frequencies for which lock occurs are changed so that lock occurs for the same range of output frequencies as previously. This corresponds to a different part of the spectrum. The offset span remains constant but the range may be varied to cover spectral regions of interest. This is particularly useful for fluorine resonance studies on inorganic fluorides.

When the master oscillator frequency is changed a different code of pushbuttons must be used for the gyrocode to lock properly. This can be calculated by the program of R. Codrington of Varian Associates, with the appropriate change in the master oscillator frequency. I have written a similar program in assembler language for the 1180 Nicolet computer and will provide listings on request.

We have constructed a divider and mixing network to generate 15,400,000 Hz from the standard 10 MHz output of the synthesizer and normally use this as the deuterium master frequency. This has the advantage of making the variable frequency of the synthesizer available for observation of other nuclei.

Yours truly,

S. Brownstein.

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14th December, 1976.

Professor B.L. Shapiro,
Department of Chemistry,
Texas A and M University,
COLLEGE STATION. Texas. 77843.
U.S.A.

Dear Professor Shapiro,

Temperature Dependence of Proton Spin-Lattice Relaxation Times in Some Paramagnetic Transition-Metal Complexes.

We have been interested for some time now in the mechanisms of electron spin relaxation in solution. We have always assumed that rotational reorientation (time constant τ_R) modulated the magnetic parameters of the complex and caused electron spin relaxation (1,2). Of course, our probe into the electron spin relaxation is its affect on the measured nuclear spin relaxation (T_1). T_1 is dominated by electron-nuclear dipolar coupling. Whether the Redfield limit holds ($\tau_{e2} > \tau_R$) or not for the electron spin relaxation, the overall electron-nuclear dipolar interaction time (τ_c) is given by $\tau_c = k\tau_R$ and thus $T_1^{-1} \alpha \tau_R$. A temperature dependence study of T_1 should therefore give E_R, the rotational activation energy. For some metal acetylacetonate complexes, E_R is approximately constant (see below)

E_R[a]	M	
9.2	$Cu(AA)_2$	
8.4	$Fe(AA)_3$	
10.9	$Cr(AA)_3$	AA = Acetylacetonate
10.8	$Pd(AA)_2$[b]	
10.4	$Co(AA)_3$[b]	

[a] In kJ mol^{-1}. [b] Diamagnetic.

While for others, the data plot is non-linear and the measured activation energy much lower.

E	M
3.6	$Ru(AA)_3$
2.2	$V(AA)_3$
1.3	$Mn(AA)_3$

Professor B.L. Shapiro,
Department of Chemistry

14th December, 1976.

We conclude that rotational reorientation may not be the dominant time process in solution, the magnetic parameters of the complexes being modulated at rate much faster than τ_R.

Yours sincerely,

D.M. Doddrell

1. D.T. Pegg and D.M. Doddrell, Aust.J.Chem., 29, 1869 (1976).

2. D.T. Pegg and D.M. Doddrell, Chem.Phys.Letts., 42, 607 (1976).

220-9

University of Nottingham

Department of Chemistry

UNIVERSITY PARK NOTTINGHAM NG7 2RD
TEL. NOTTINGHAM 56101

HB/MJS

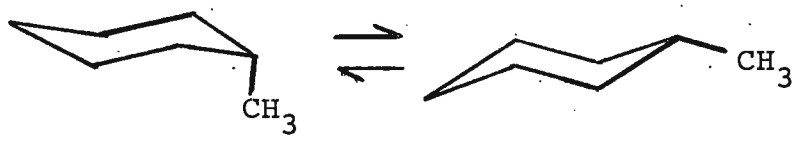
14th December 1976

Dr. B.L. Shapiro,
Department of Chemistry,
Texas A and M University,
College Station,
Texas 77843,
U.S.A.

Dear Dr. Shapiro,

Dynamic Range in ^{13}C P.F.T.N.M.R.

In our studies of conformational equilibria we frequently encounter situations in which the minor conformation constitutes 1% or less. If the energy of activation for the interconversion is relatively small, so that a particularly low temperature is required to slow the inversion rate, the equilibrium generally becomes further biased ($\Delta G^{o} = -RT\ln K$; $\Delta G^{o} = \Delta H^{o} - T\Delta S^{o}$). However, by analysis of (^{13}C-methyl) methylcyclohexane ($1 \rightleftharpoons 2$) by pulsed Fourier transform N.M.R., we have been able to measure accurately the equilibrium constant K (= 2/1) at 172K (K = 164) and at 149K (K = 427)[1].



(1) (2)

In P.F.T.N.M.R., the maximum possible pulses (and therefore maximum possible signal to noise) is a function of computer word length and digitiser resolution.[2] Our Nicolet computer has a 20-bit word length and a maximum 9-bit digitiser resolution. In the experiment at 172K, the final S/N for the methyl signal of (2) was 10,560 and for the methyl signal of (1) was 45. Had we, for example, used a computer with a 16-bit word length and 12-bit resolution on the digitiser, the final S/N for the methyl signal of (1) could not have exceeded 4.5, leading to a considerable reduction in the accuracy of integration.

University of Nottingham

Department of Chemistry

UNIVERSITY PARK NOTTINGHAM NG7 2RD
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14th December 1976

Dr. B.L. Shapiro,

We had hoped to extend this work to accurate measurements of equilibrium constants between 1000 and 10,000. (A free energy difference $-\Delta G^{o}$ of only 2Kcal. $mol.^{-1}$ leads, at 120K, to an equilibrium constant of about 4000, so that the situation is not exactly rare.) However, the available computer is quite unable to determine equilibrium constants over 1024. Any useful extension to equilibrium constants of 5000 requires a 24-bit word length with 12-bit digitiser resolution, whilst further extension to 10,000 requires a 32-bit word length with 16-bit digitiser resolution. End of story?

Yours sincerely,

Harold Booth, Jeremy R. Everett.

Dr. Harold Booth,
Jeremy Everett.

(1) Chem. Comm. 1976, 278.

(2) J.W. Cooper in Topics in Carbon-13 NMR, Vol. 2, p.391 (ed. G.C. Levy).

Remember this ad?

We ran this ad in mid-1972 when six of us formed Transform Technology Incorporated with the help of Nicolet Instrument Corporation. Now, less than four years later we have over three dozen employees and are now a Nicolet operating division, known as Nicolet Technology Corporation.

What has happened since our first ad? Well, we don't mind tooting our horn by pointing out that NTC has become established as a leader in the development of FT NMR equipment. We have developed, produced and installed scores of FT accessories for use on instruments such as the XL-100, HR-220, T-60, R-12 and R-32. In fact, for over a year we have been the leader in U.S. sales of FT data systems. Now we're working on becoming the leader in overseas sales as well.

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You can be sure that we are actively working on new "firsts." For example, we'll be demonstrating a complete Fourier Transform Mass Spectrometer very soon. To repeat the closing statement from our original ad—write or call collect to discuss your requirements. Maybe we can work together to add another "first."

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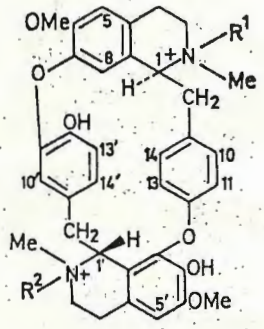
December 16, 1976



Professor B. L. Shapiro
Department of Chemistry
Texas A and M University
College Station, Texas 77843

Dear Barry:

"Some CMR Assignments of (+) - Tubocurarine Chloride"

We have recently had occasion to examine the CMR of (+) - tubocurarine chloride (1). Previous PMR work (TAMUNMR 162-24) noted that the protons on the para-substituted aromatic ring H-10, H-11, H-12 and H-14 are sharp at ambient temperature, but broaden at higher temperatures. CMR studies also show analogous results in that four protonated carbon resonances broaden at higher temperatures (marked * in figure).

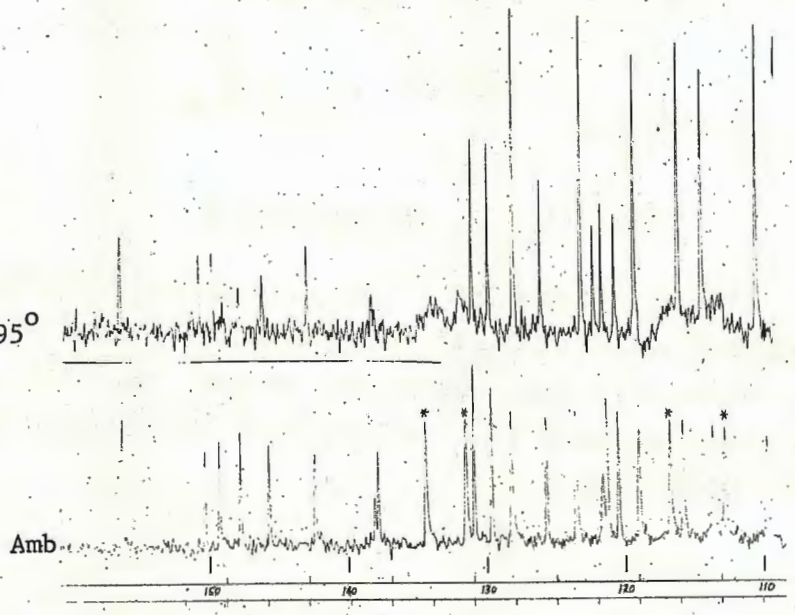
The unusual elevated temperature broadening is a consequence of hindered rotation of the para-substituted aromatic ring. The disappearing resonances are then easily assigned to the four protonated carbons on the para-substituted aromatic ring. A single frequency decoupling experiment of H-8 at 5.10 ppm has assigned another carbon. With the use of model compounds and substituent effects most carbons are now assigned with a fair degree of certainty. These assignments will appear in the future when complete.

Sincerely,

Ruth Stanaszek

Ruth Stanaszek
NMR Lab, D-482

msg



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Professor C.L.Khetrapal

December 17, 1976

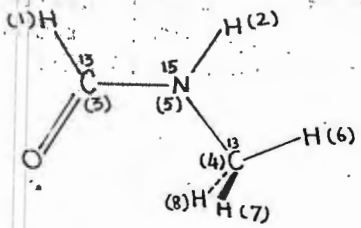
Professor Bernard L. Shapiro
Department of Chemistry
Texas A & M University
College Station, TX 77843
U S A

Title: NMR of ^{13}C and ^{15}N isotopically enriched N-Methyl Formamide

Dear Professor Shapiro,

Before your pink note follows the blue, I would like to report some of our recent results.

We have investigated the NMR spectra of the title compound in isotropic and nematic phases. The spectra indicate the presence of cis and trans ^{15}N-methyl(^{13}C)-formamide(^{13}C), cis and trans ^{15}N-methyl formamide(^{13}C) and trans ^{15}N-methyl(^{13}C)-formamide (structure 1) in a sample obtained from Merck, Sharp and Dohme of



Structure 1

Canada. Trans ^{15}N-methyl(^{13}C) formamide(^{13}C) is present to the major extent and detailed analyses have been undertaken only for such species. In the isotropic phase, the ^{13}C and the ^{1}H spectra were studied whereas in the nematic phase only the PMR spectrum has been investigated.

An interpretation of the various direct dipolar couplings indicates significant non-planar distortions around the nitrogen atom provided influences of molecular vibrations are neglected. The dihedral angles H(1)-C(3)-N-H(2) and H(1)-C(3)-N-C(4) describing the non-planar distortions have been estimated to differ by 11 $\pm$ 4° from the values of 0° and 180° for a completely planar configuration.

The direct dipolar couplings D_{46}, D_{56} and D_{67} provide the HCH bond angle and the angle which the line joining nuclei 5 and 6 makes with the bond connecting the nuclei 4 and 5, irrespective of whether the three bonds meeting at the nitrogen atom lie in one plane or not. Neglecting the influences of molecular vibrations and the anisotropic contributions of indirect couplings, these values are determined as 108.5° and 30.7° respectively.

Yours sincerely,

C.L. Khetrapal

C.L. Khetrapal

220-15

University of East Anglia

School of Chemical Sciences
University of East Anglia
Norwich NR4 7TJ, ENGLAND
Telephone Norwich (0603) 56161
Telegraphic Address UEANOR NORWICH

From Dr. R. K. Harris
Dr. K. J. Packer

20th December, 1976

Dear Barry,

HIGH-RESOLUTION NMR OF THE SOLID STATE - POSTDOCTORAL POSITION AVAILABLE

For the last fifteen months we have been building a spectrometer-computer system designed to routinely achieve high-resolution for solid-state samples using the three techniques now becoming standard, viz. (i) dipolar decoupling, (ii) cross-polarisation between abundant and rare spin species, and (iii) rapid spinning about the "magic angle". The system is based on a Bruker BE 38 magnet, gating/phase-shifting units and power amplifiers, interfaced to a Nicolet 1180 computer and pulse programmer. Much of the remaining electronics has been built in our laboratory. Currently techniques (i) and (ii) have been satisfactorily tested; attached is a $^{13}C\{^{1}H\}$ cross-polarized spectrum of the usual test sample, powdered adamantane, obtained using our equipment. Soon we expect to be able to turn to applications. Out of the many areas of obvious application of these new techniques we are commencing with studies of solid polymers and adsorbed species.

For further development of the system and to carry out the applications work we expect to be employing a post-doctoral fellow (possibly two), to join the present team of six research workers in October 1977. Suitably qualified people interested in joining us are invited to write to one of us in the near future.

With best wishes,

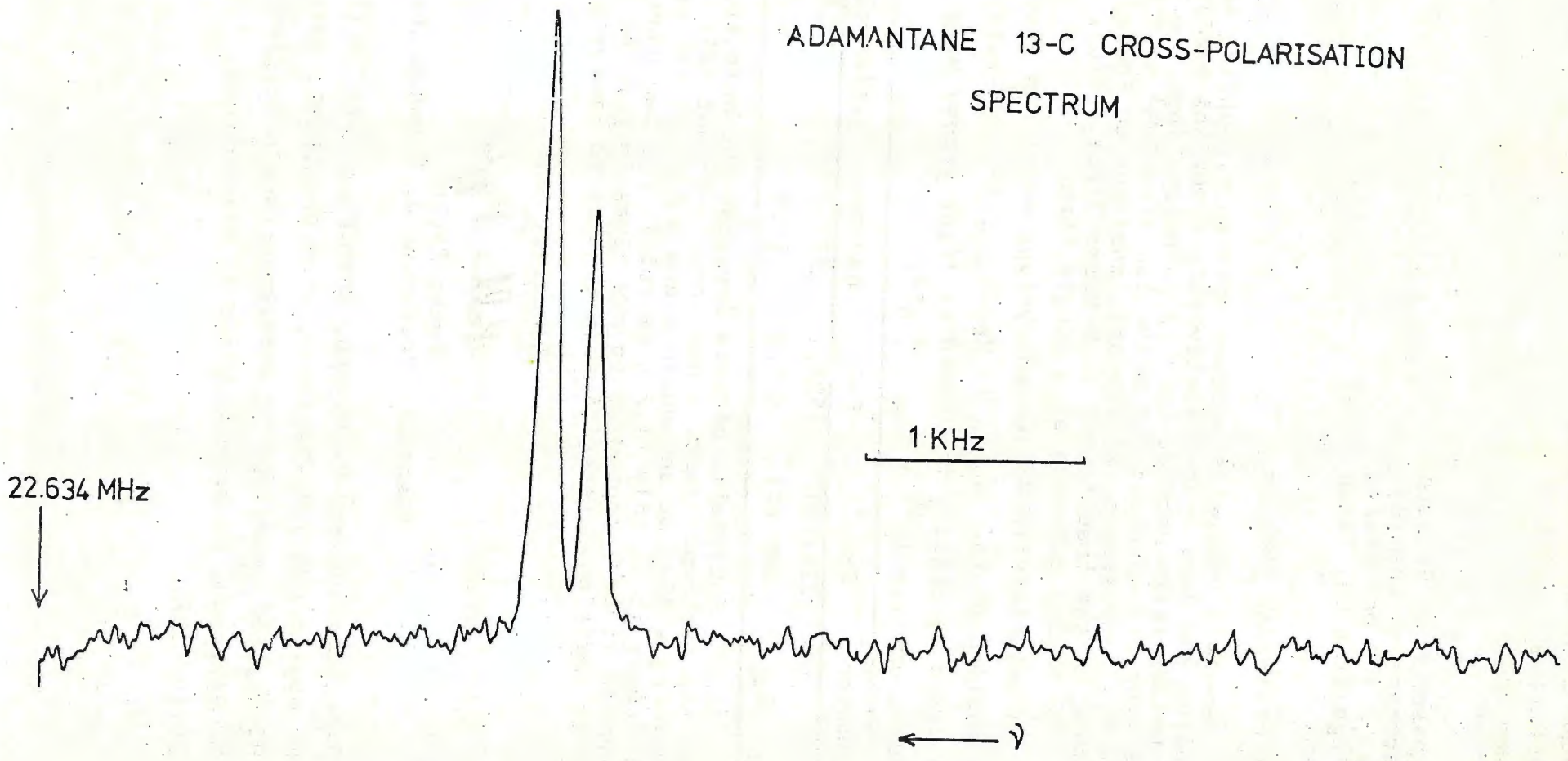
Yours sincerely,

Robin Ken

R. K. Harris K. J. Packer

Dr. B. L. Shapiro,
Department of Chemistry,
College of Science,
Texas A & M University,
College Station,
Texas 77843,
U.S.A.

KJP/RKH/KJS


ADAMANTANE 13-C CROSS-POLARISATION
SPECTRUM
1 KHz
22.634 MHz
ν

220-16

INSTITUTIONEN FÖR FYSIKALISK KEMI
Department of Physical Chemistry
ÅBO AKADEMI Porthansgatan 3-5
SF 20500 Åbo 50 Finland

December 29, 1976

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

Dear Professor Shapiro,

Ramsey's theory of nuclear spin-spin coupling assumes L-S coupling and uses a non-relativistic hyperfine Hamiltonian. As our relativistic Hartree-Fock calculations indicate large deviations from L-S coupling for molecules like AuH[1] or TlH[2], I have recently completed a relativistic analogue to Ramsey's theory[3]. Instead of the traditional four terms J(1a), J(1b), J(2) and J(3) the new theory consists of a single term.

A relativistic Pople-Santry-type model was also constructed and applied on the $^1J_{Hg-C}$ in $Hg(CH_3)_2$. The non-relativistic limit was taken by letting the speed of light become very large. The results are (in 10^{19} $m^{-2}kg\ s^{-2}\ A^{-2}$)

Parameter	Exp.[4]	Rel.	Non-rel.	Ratio rel/non-rel.
K	1264(2)	1524.1	571.7	2.67
$K_{\parallel} - K_{\perp}$	599(44)	535.4	164.5	3.25

Thus relativistic effects increase the anisotropy even more than the isotropic part. A new, negative isotropic cross term K_{s-p} involving s AO:s at one nucleus and p AO:s at the other one appears. For $^1K_{Hg-C}$ it is only -1.7 % of total. For two heavy sp^3 hybridized elements it is expected to be six times larger. At the non-relativistic limit the present theory reduces to Ramsey's and $K_{s-p} = 0$.

Sincerely yours,

Pekka Pyykkö

Pekka Pyykkö
Associate Professor of Quantum Chemistry

1 J.P. Desclaux and P. Pyykkö, Chem.Phys.Lett. 39(1976)300.
2 P. Pyykkö and J.P. Desclaux, Chem.Phys.Lett. 42(1976)545.
3 P. Pyykkö, submitted to Chem.Phys.(North-Holland).
4 C. Schumann, H. Dreeskamp and K. Hildenbrand, J.Magn.Res. 18(1975)97.

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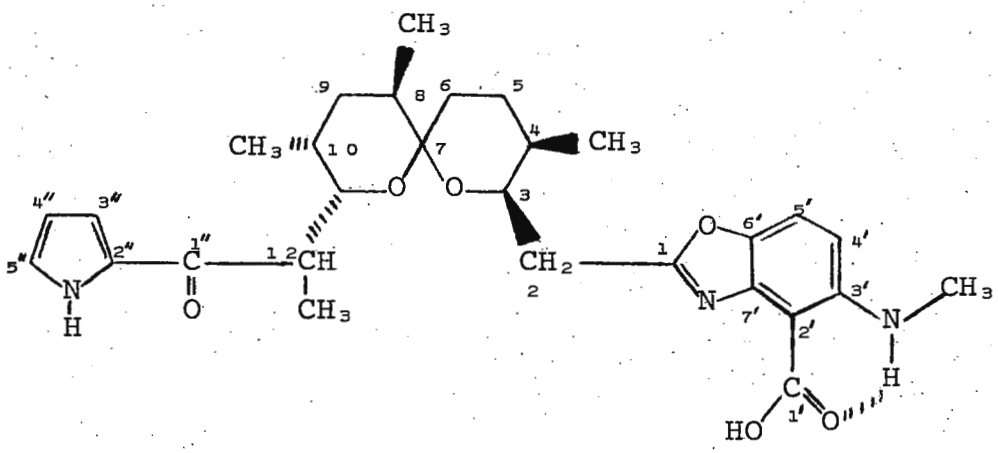
December 21, 1976

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

Dear Professor Shapiro:

"Carbon Resonance Assignments for A23187"

The fermentation product A23187[1] is unique among the polyether ionophores in its specificity for divalent and trivalent metal ions. This has led to very active interest in the compound and to literally scores of requests for samples. Perhaps scientists working with A23187 would find an assignment of its carbon resonances useful.



The assignments are based on (1) comparison of the spectra of A23187 and those of model compounds and derivatives, (2) selective proton decoupling, and (3) "long range" (i.e., 2 and 3 bond) ^{13}C-^{1}H coupling constants. The last method was particularly interesting when used in conjunction with D-exchange of the two N-protons. This led to the predicted simplification of the pyrrole carbon resonances. Also, the resonance of C(4') went from a doublet of doublets (NH) to a sharp doublet (ND).[2] The assignments shown in the Table have served us well now for eighteen months and have stood the tests of several derivatives.

---

[1] M. O. Chaney, P. V. Demarco, N. D. Jones, and J. L. Occolowitz, J. Amer. Chem. Soc., 96, 1932 (1974); M. O. Chaney, N. D. Jones, and M. Debono, J. Antibiot., 29, 424 (1976).

[2] F. W. Wehrli, J. Chem. Soc. Chem. Commun., 663 (1975).

A23187 is very soluble in organic solvents but is essentially insoluble in water. These properties, plus its affinity for polyvalent ions, may make it useful in removing paramagnetic metal ions from aqueous solutions. Indeed, we have used A23187 in clearing Cu^{++} and Mn^{++} from solutions of aminoglycosides, but we have not measured enough relaxation times to determine how effective it is with trace amounts of metal ions.

Sincerely,

LILLY RESEARCH LABORATORIES

Doug Dorman Jon Paschal

Douglas E. Dorman, Ph.D., Jonathan W. Paschal
Physical Chemistry Research

DED/JWP:vr

TABLE: ^{13}C NMR Spectra of A23187 Free Acid and Its Calcium Salt

Position	A23187 Free Acid	$(A23187)_2$ Ca
1	166.1	168.3
2	32.3	32.1
3	68.3	70.8
4	28.7	29.0
CH_3(4)	11.4	11.7
5	25.7	25.3
6	25.4	25.1
7	98.5	98.1
8	32.4	32.1
CH_3(8)	16.2	16.1
9	35.2	35.2
10	28.3	28.0
CH_3(10)	10.8	10.8
11	72.8	74.5
12	42.5	42.6
CH_3(12)	13.2	11.1
1'	168.2	172.1
2'	97.9	105.9
3'	150.8	151.1
4'	108.4	108.6
5'	116.9	113.3
6'	140.8	140.8
7'	141.6	141.7
CH_3(N)	30.0	30.4
1"	193.9	197.4
2"	133.1	134.1
3"	116.4	121.0
4"	110.1	110.6
5"	124.5	129.9

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H. Günther

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Prof.Dr.B.L.Shapiro
Dept. of Chemistry
Texas A & M University
College Station, Texas 77843

U S A

Systematic Nomenclature for $^{13}C,^{1}H$-Coupling Constants in Hydrocarbons.

Dear Barry:

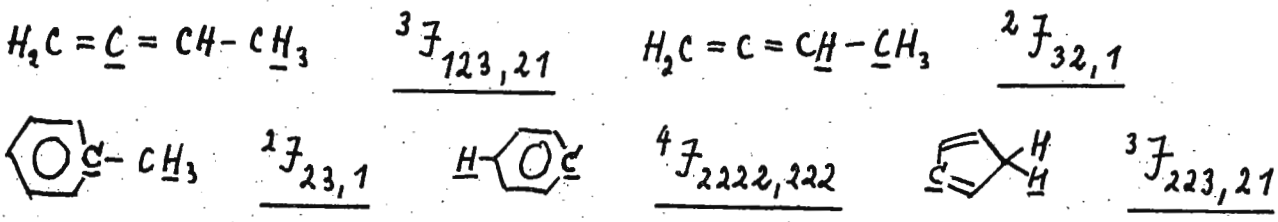
Recently, the interest of C-13 NMR spectroscopists has shifted more strongly to $^{13}C,^{1}H$ coupling constants and we hope to report soon on a contribution to this field.

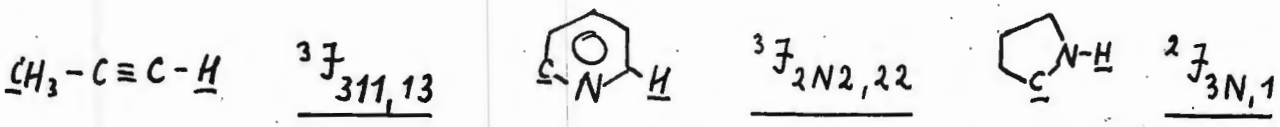
Looking at the data already in the literature one gets the impression that it has generally not been fully realized that coupling pathways available for $^{13}C,^{1}H$-spin,spin interactions are much more multifarious than those for H,H coupling constants. Especially the simple notation used today (^{1}J, ^{2}J etc.) does not include any detailed information about the coupling pathway, i. e. the type of carbons and the bonds involved, except if the specific structural fragment is given in parenthesis. We therefore have looked into the possible structural arrangements more systematically and as a result propose a nomenclature that gives the information mentioned above.

Taking only hydrocarbons, hybridization at the carbon atoms can be sp, sp^2, or sp^3. On the basis of simple permutation rules 3 types of one-bond C,H coupling constants, 9 types of two-bond C,H coupling constants, and 27 types of three-bond C,H coupling constants result. Not all of them are, however, physically meaningful. On the other hand, additional arrangements arise because of the possibility to join two carbons by a single, double, or triple bond. The summary of the final 38 combinations we found is given in Scheme 1 together with the appropriate code. This code gives the hybridization indices of the carbons (klm; 1 for sp, 2 for sp^2, and 3 for sp^3) and after the comma the bond orders of the CC-bonds involved (ij; 1 for single, 2 for double and aromatic, 3 for triple bond). The code is then used as subscript:

$$^{n}J_{klm,ij}$$

A few examples will help to illustrate the system:

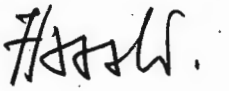




The last examples demonstrate how an extension to structures containing heteroatoms is possible.

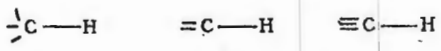
Judging from Scheme 1, there is plenty of research ahead!

Sincerely yours,



S C H E M E 1

Code Coupling over one bond: $^{1}J(^{13}C,^{1}H)$



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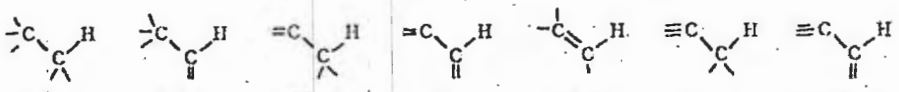
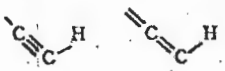
Coupling over two bonds: $^{2}J(^{13}C,^{1}H)$

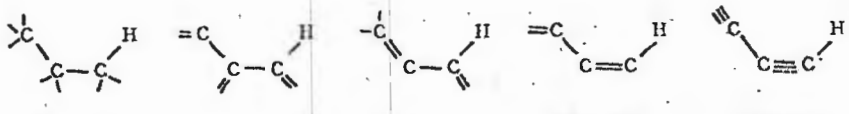


kl,i 33,1 32,1 23,1 22,1 22,2 13,1 12,1

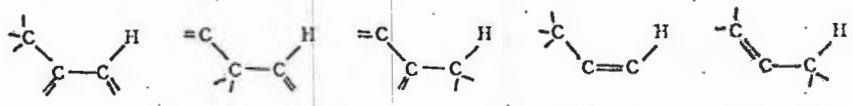


kl,i 11,3 12,2

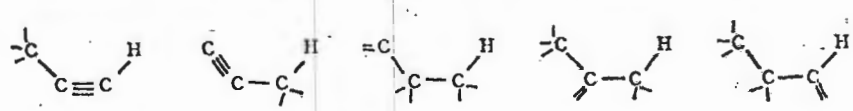
Coupling over three bonds: $^{3}J(^{13}C,^{1}H)$



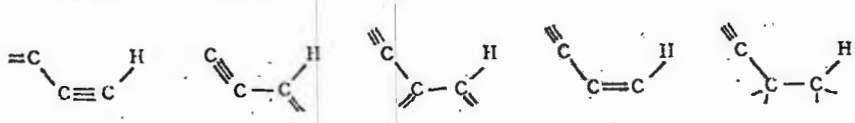
klm,ij 333,11 222,11 222,21 222,12 111,13



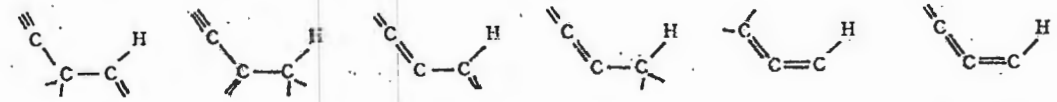
klm,ij 322,11 232,11 223,11 322,12 223,21



klm,ij 311,13 113,31 233,11 323,11 332,11



klm,ij 211,13 112,31 122,11 122,12 133,11



klm,ij 132,11 123,11 122,21 123,21 212,22 113,22

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DEPARTMENT OF CHEMISTRY
SANTA BARBARA, CALIFORNIA 93106

December 28, 1976

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

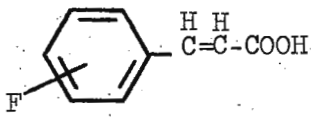
"Fmr Studies of Fluorocinnamoylchymotrypsins"

Dear Barry:

We are still battling with the enzyme α-chymotrypsin and can report the following nmr results. Bender and co-workers have nicely elucidated the mechanism of chymotryptic catalysis as regards the hydrolysis of cinnamoyl ester and amides. A minimal mechanism for this process is represented below where [E···AL] is an enzyme-substrate complex within which the acyl

$$E + AL \rightleftharpoons [E\cdots AL] \underset{+L}{\overset{-L}{\rightleftharpoons}} \hat{E}A \underset{H_2O}{\overset{H_2O}{\rightleftharpoons}} [E\cdots A] \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} E + A$$

group of the substrate is transferred to the serine-195 residue of the enzyme to give $\hat{E}A$. Hydrolysis of EA affords an enzyme-product complex, [E···A], which can reversibly dissociate to regenerate the free enzyme. We have used a series of monofluorinated cinnamoyl groups (I) in an examination of the enzyme forms $\hat{E}A$ and [E···A] by fluorine magnetic resonance spectroscopy and some results are given in Table I. The substantial differences in enzyme-induced chemical shift effects cannot easily be ascribed to changes in the protein structure if x-ray crystallographic evidence is accepted and we believe



I

that these variations must arise from differences in the way the fluorocinnamoyl moieties are bound in the active site of the enzyme. The fluorocinnamate groups have a plane of symmetry and can potentially bind to the asymmetric specificity pocket of chymotrypsin in two ways. We suggest as a possible explanation of our results that one of these complexes is formed immediately after hydrolysis of $\hat{E}A$ and has enzyme-cinnamoyl interactions identical to those found in $\hat{E}A$, but that this complex is not favored thermodynamically relative to the other. Thus,

the last part of the above mechanism would be written

$$\ldots \hat{EA} \rightleftharpoons [E\cdots A] \rightleftharpoons E + A \rightleftharpoons [E \sim A]$$

where [E ~ A] represents the dominant but "unproductive" product-enzyme complex observed in our fmr studies of "[E···A]". We hope to solidify this argument by means of $^{19}F\{^{1}H\}$ nuclear Overhauser effect experiments which are in progress.

Sincerely yours,

B. A. Halley
Research Assistant

Tom

J. T. Gerig
Associate Professor

TABLE I - α-Chymotrypsin-Induced Chemical Shift Effects[a]

	o-F	m-F	p-F
Acylenzyme, $\hat{EA}$ [b]	-0.2	-4.1	-7.0
Enzyme-Cinnamate Complex, [E···A] [c]	-2.4	-1.8	-2.7

[a] Chemical shifts in ppm, determined at 94.1 MHz.

[b] At pH 3.9 in 6% acetonitrile/water at 25°, 0.1 M acetate buffer.

[c] At pH 6.2 in 0.14 M phosphate buffer at 25°.

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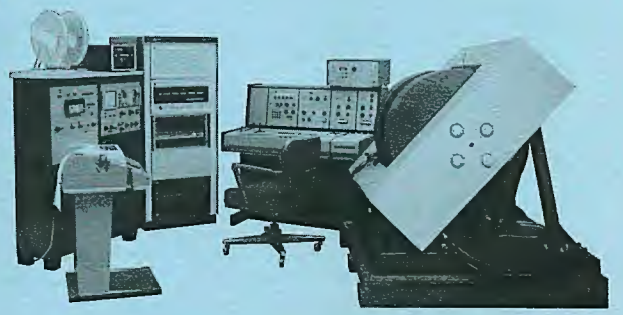
^{13}C Spectra 10 Times Faster

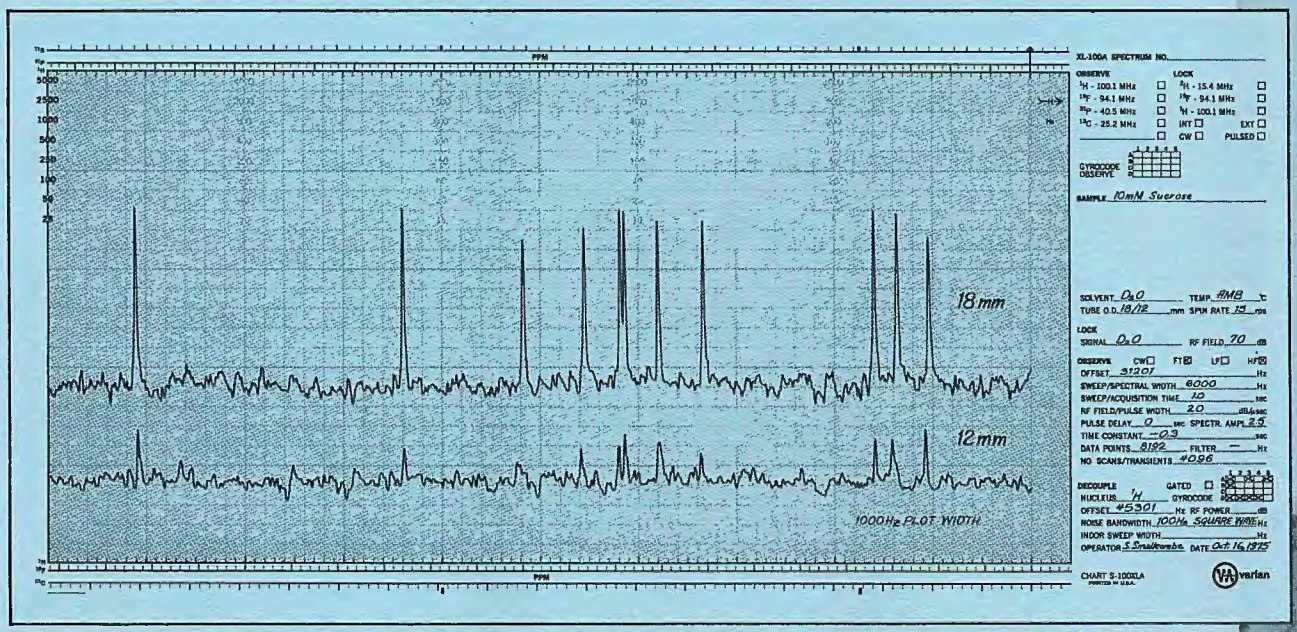
Now Varian XL-100 users can run natural abundance ^{13}C spectra at millimolar concentrations. Varian's new V-4418 Variable-Temperature Probe accommodates 18-millimeter sample tubes and boosts sensitivity to over three times that of the standard 12-mm probe. Compare the two spectra of 10 mM sucrose — clearly this new probe could extend the application of ^{13}C NMR to entirely new areas of chemical research.

The V-4418 is Varian's latest offering to the scientist who needs ^{13}C spectra of samples of limited solubility or limited molarity; or who studies certain equilibria and requires low concentration; or who works with relaxation properties that are best studied at low concentration. The V-4418 lets him use samples less concentrated by a factor of 3, or reduces the time required for an experiment by a factor of 10 — with results second to none.

Not only is the **absolute sensitivity** of the V-4418 Probe outstanding, it also offers excellent **sensitivity per milliliter** of solution, an important asset if you study scarce or expensive (most often both) macromolecules. The Probe develops its full sensitivity potential with 6 milliliters, a volume only three times that required with the standard 12-mm probe!

And that's not all. When the V-4418 Probe is used together with the recently introduced single-sideband filter, overall sensitivity of the XL-100 increases by a factor of 5. Or, in terms of time savings, these combined capabilities reduce a formerly 24-hour experiment to a routine 1-hour run.





Compare these two broadband proton-decoupled carbon spectra of 10 mM sucrose in D_2O, one using an 18-mm sample, the other the standard 12-mm sample! Data were accumulated for 4096 transients, with a one-second acquisition time and a 90° pulse.

Sample tube shown actual size.

For further information contact your local Varian representative or write to:
Varian Instruments, 611 Hansen Way,
Box D-070, Palo Alto, CA 94303.

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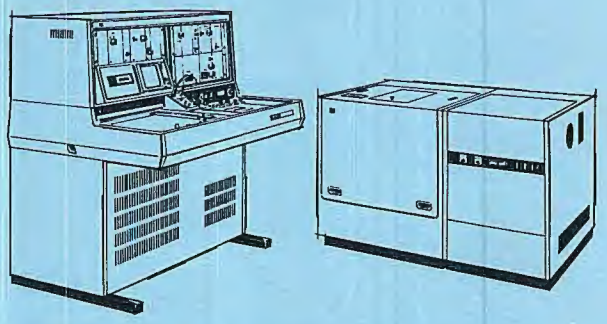
Low Cost — Routine ^{13}C System

The FX60 features:

- $^{13}C/^{1}H$ Dual Frequency 10, 5, 2mm V.T. Probes
- (LPCS) Light Pen Control System
- Built-in Proton-HOMO/HETERO decoupler
- RF crystal filter detection system
- 12 bit AD/DA for increased dynamic range
- INTERNAL and EXTERNAL locking modes
- 8, 16 and 32K word data collection
- Built-in Read/Write Cassette System
- ^{19}F, ^{31}P, ^{15}N extensions are available



Comprehensive 60 and 100 MHz Systems

The FX60Q & FX100 features:

- (DQD) DIGITAL Quadrature Detection System
- Dual Frequency variable temperature probes
- 4-channel DIGITAL phase shifters (DPS)
- Comprehensive auto-stacking system
- Computer based pulse programmer
- CPU Expandable to 65K words (MOS)
- 2-channel 12 bit AD/DA
- $T_1\rho$/spin locking system
- Disc storage systems
- Multi-Frequency HOMO/HETERO decoupling capabilities
- Multi-Frequency observation

For detailed brochure, demonstration or information, phone or write . . .

JEOL

Analytical Instruments, Inc.

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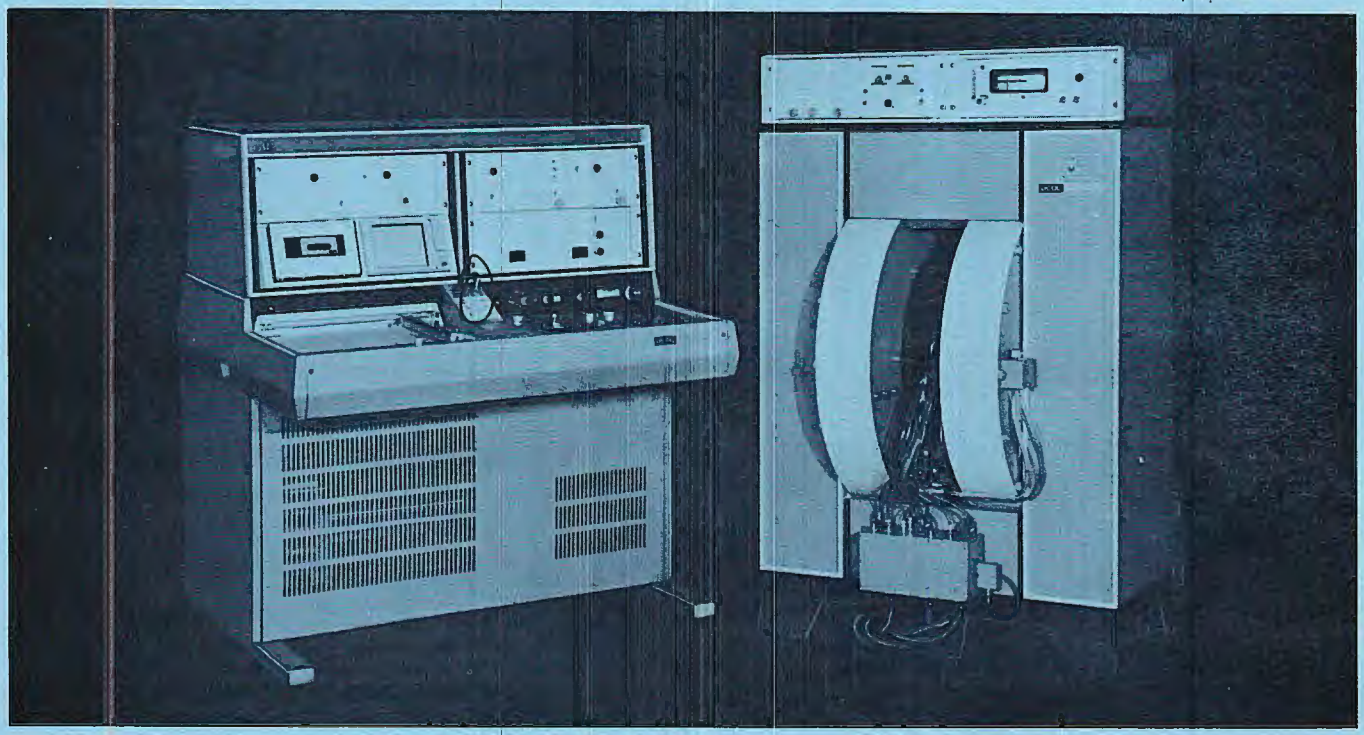
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