Texas A & M University N – M – R Newsletter

No. **259**

April, 1980

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DEADLINE DATES: No. 260   5 May 1980
                  No. 261   2 June 1980

All Newsletter Correspondence, Etc., Should be Addressed To:

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

CHEMICAL CENTER

Lund, Februari 29. 1980

PHYSICAL CHEMISTRY 2

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

Title: ^{43}Ca NMR in biochemistry.

Dear Barry,

As usual we are late with our contribution, but hopefully not too late.

During the last months we have been exploring the possibilities of using ^{43}Ca and ^{25}Mg NMR in studies of biological or biochemical interest. In these studies we have used our home built spectrometer with an Oxford instrument 6 Tesla wide bore magnet. To obtain optimal sensitivity we are using a probe with horizontal sample orientation. Figure 1 shows a spectrum of 1mM ^{43}Ca enriched to 60%.

After obtaining this encouraging sensitivity we have now continued to study Ca^{2+} and Mg^{2+} binding to Troponin-C, a component in the muscle protein system with a molecular weight of ca 18000. TN-C is known to bind two calcium ions very strongly and two other with a smaller binding constant. Figure 2 shows the ^{43}Ca line width as a function of pH with 3 fold excess of Ca^{2+}. Two pK_a:s are needed to simulate the pH dependence shown by the solid curve. (pK_{a1} = 4.8 and pK_{a2} = 6.0). These are in agreement with potentiometric data.

Figure 3 shows the temperature dependence of the linewidth of the ^{43}Ca signal for a sample with 0.75 mM Tn-C and 5.9 mM Ca^{2+}. The calculated linewidth used to draw the solid curve has been obtained by means of the McConnell eqn. for chemical exchange. The temperature dependence of the exchange time is given by

$$1/\tau = \frac{kT}{h} \cdot e^{-\frac{\Delta H^{\ddagger}}{RT} + \frac{\Delta S^{\ddagger}}{R}}$$

and the temperature dependence of the linewidth of the signal from calcium bound to the protein by

$$\Delta\nu_{1/2} = 1/\pi \cdot T_2 = Q\ \tau_{co}/e^{-\frac{\Delta G}{RT}}$$

The set of parameters used were: $\Delta H^{\ddagger}$ = 9.71 kcal/mol, $\Delta S^{\ddagger}$ = -10 cal/mol K, ΔG = 4.42 kcal/mol, τ_{co} = 4$\cdot$10^{-13} sec and Q = 5.97$\cdot$10^{12}

Inserted in Figure 3 is also the experimental ^{43}Ca signal at 219°K and the line calculated as shown above.

50 Hz

1 mM ^{43}Ca
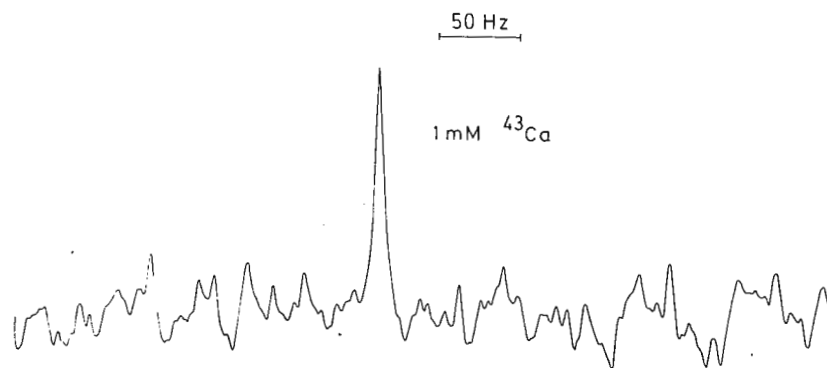
Figure 1. The ^{43}Ca spectrum of an aqueous solution of 1 mM CaCl$_2$ (60 % isotopically enriched) after 100 transients.
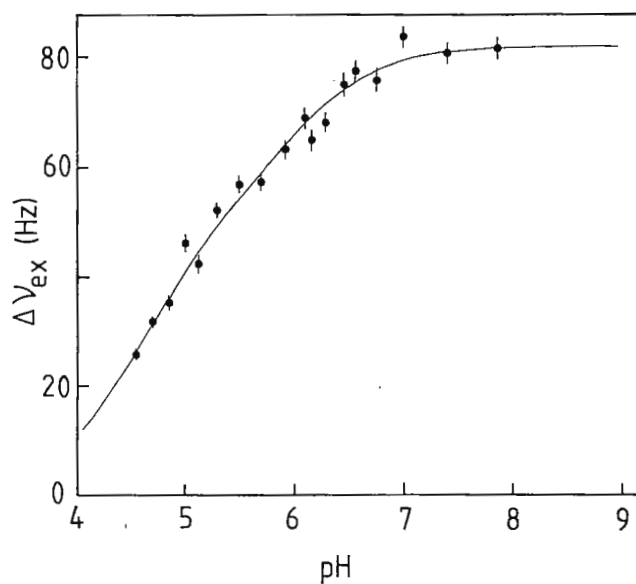
Figure 2. The pH dependence of the ^{43}Ca excess linewidth for a 5.9 mM CaCl$_2$ solution (60 % enriched) in the presence of 0.7 mM TN-C.
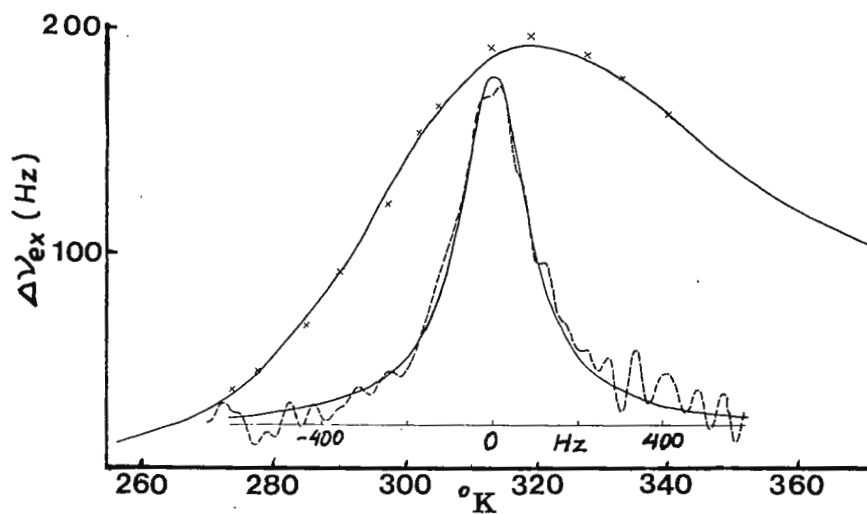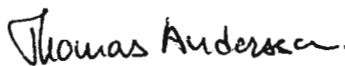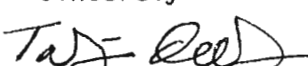
Figure 3. The tenperature dependence of the ^{43}Ca excess linewidth for a 5.9 mM CaCl$_2$ solution (60 % enriched) containing 0.75 mM TN-C.

Based on the results we have got so far we believe that the in NMR almost neglected nuclei, ^{43}Ca and ^{25}Mg can very well be used to obtain relevant information regarding biochemically interesting systems.

Sincerely

Thomas Andersson   Torbjörn Drakenberg   Sture Forsén

Carbon-13 NMR Shifts* of Thiocarbamates, S-Oxides, and S,S-Dioxides

		β	γ	β'
$CH_3CH_2CH_2XCON(\ n-C_3H_7)_2$	1 (X=S)	32.24	23.75	167.77
	2 (X=SO)	53.35	16.25	168.54
	3 (X=SO$_2$)	53.11	15.91	161.23
$Ch_3CH_2XCON(i-C_4H_9)_2$	4 (X=S)	24.60	15.51	167.60
	5 (X=SO)	45.26	6.92	168.06
	6 (X=SO$_2$)	46.48	6.76	161.82

*Shifts are expressed in ppm relative to TMS and the spectra were obtained in deuteriochloroform solutions on a Varian CFT-20 NMR spectrometer.

DE GUIGNÉ
TECHNICAL CENTER
WESTERN RESEARCH

Stauffer CHEMICALS

Stauffer Chemical Company

1200 S. 47th St. / Richmond, CA 94804 / Tel. (415) 231-1000 / TWX (910) 382-8174

March   12, 1980

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

Subject: "Carbon-13 NMR Studies of Thiocarbamates, S-Oxides, and S,S-Dioxides"

Dear Barry:

Recently McCrachren and Evans (J. Org. Chem., <u>44</u>, 3551 (1974)) reported that oxidation of thioalkylacetaldehyde dimethyl acetals to their corresponding sulfoxides and sulfones caused a large deshielding of β and β' carbons. The deshielding β_{SO} $(=\delta_{SO}-\delta_{S})$, β'_{SO}, β_{SO_2} $(=\delta_{SO_2}-\delta_{S})$, and β'_{SO_2} effects were in the range of 13.05 $\sim$ 23.14 ppm. In the case of sulfones, additional oxygen had little effect in shielding relative to the sulfides.

$$C-C-X-C-C(OCH_3)_2, \quad X=S, \ SO, \ SO_2$$
$$\gamma \ \beta \quad \beta'\gamma'$$
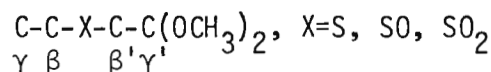
We have studied the carbon-13 NMR spectra of thiocarbamates and their corresponding sulfoxides and sulfones.

$$\overset{\overset{\displaystyle O}{\displaystyle \|}}{C}-C-X-C-N\diagup, \quad X=S, \ SO, \ SO_2$$
$$\gamma \ \beta \quad \beta'$$
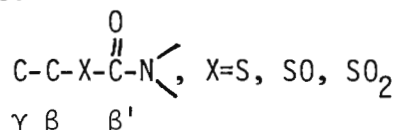
The chemical shifts of β, γ, and β' carbons in two thiocarbamates and their corresponding sulfoxides and sulfones are listed in the table.* The deshielding β_{SO} and β_{SO_2} effects in thiocarbamate sulfoxides and sulfones are comparable to that observed by McCrachren and Evans. However, there is only slight deshielding β'_{SO} effects in thiocarbamate sulfoxides. It is interesting to note that the β'_{SO_2} effects in thiocarbamate sulfones are shielding rather than deshielding relative to the parent thiocarbamates.

Sincerely yours,

C.K.Tseng

C. K. Tseng

D. J Bowler

D. J. Bowler

CKT/DJB:ams

attach

* See opposite page.

Koninklijke/Shell-Laboratorium, Amsterdam

Shell Research B.V.

Professor Bernard L. Shapiro

Department of Chemistry

Texas A & M University

College Station, Texas 77843

U.S.A.

Uw ref.:

Onze ref.: AG—

Amsterdam, 5th March 1980
Postadres: Postbus 3003, 1003 AA Amsterdam
Tel. via telefoniste (020) 20 91 11
Tel. rechtstreeks (020)
Hr/Mw

Dear Barry,

Conformational information from solid state NMR on the CXP-300

Since our previous newsletter, indicating measurements on our CXP-300
spectrometer from the middle of last year, various changes in the
magic-angle spinning probe have taken place. Bruker have redesigned
the spinning system, changing from "bullet" rotors to "mushroom"
rotors, and we ourselves have modified the angle adjustment. We are
now able to spin stably (in favourable cases) at speeds up to 6.5 kHz.
Even so, spinning sidebands still bother us at times (especially from
the Delrin we use as our rotor).

Recently, we have been exploring the use of high-resolution solid-state
^{13}C NMR in giving conformational information. As an example, we enclose
solid state and solution spectra of the Hantzsch ester.
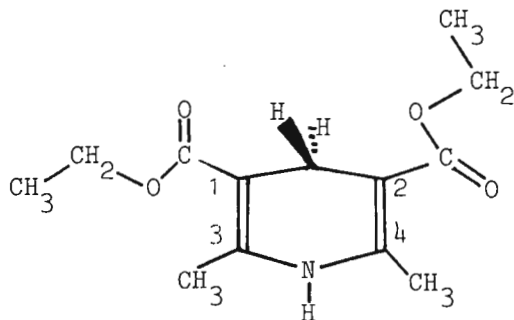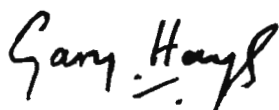
Its X-ray structure was recently determined (A.T.H. Lenstra et al.,
Bull. Soc. Chim. Belg. 88 (1979) 133) and it was found that disregarding
the protons, the complete skeleton was planar and the two double-bonded
oxygens of the carbonyl groups pointed in different directions, thus
lowering the apparent symmetry of the molecule. The question was whether
or not we could see this with solid-state NMR and by comparing the two
spectra one can easily see two doublets in the solid state - assigned to
the ring olefinic carbons - compared to singlets in the solution phase.
This tells us that olefinic carbons 1 and 2 are different and that 3 and
4 are different, whereas this would not be expected if both halves of the

Koninklijke/Shell-Laboratorium,Amsterdam

d.d.   Pag.

molecule were equivalent. It should be noted that the solid-state spectrum was obtained in a matter of minutes, while the spectrum of the solution phase had to be recorded over a much longer period (overnight), as the compound is not very soluble!

Yours sincerely,

KONINKLIJKE/SHELL-LABORATORIUM, AMSTERDAM
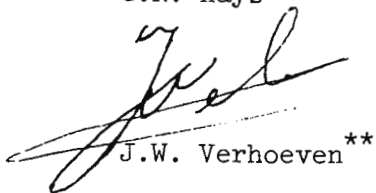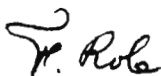
G.R. Hays   A.D.H. Clague   R. Huis   D.G. Gillies[*]

J.W. Verhoeven[**]   F. Rob[**]

[*] On sabbatical leave from Royal Holloway College, London
[**] University of Amsterdam

Enclosure

C=O

$=C\overset{*}{\underset{N}{\diagdown}}^{C}$

$=C\overset{*}{\diagup}\overset{C}{\underset{C}{}}$

DELRIN SAMPLE
ROTOR

CH_3(ETHYL)

CH_3(RING)

CH_2(ETHYL)

CH_2(RING)
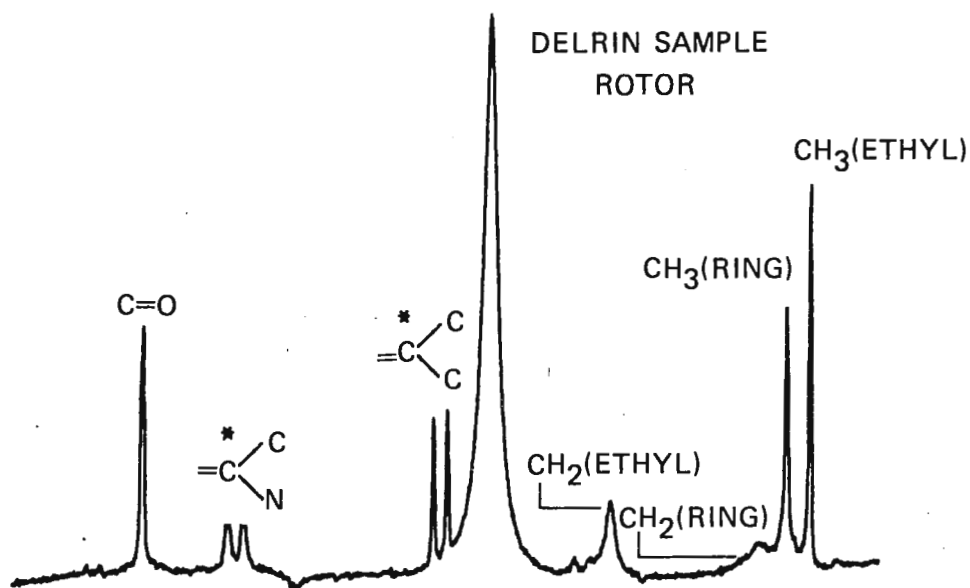
HANTZSCH ESTER: SOLID–STATE ^{13}C NMR SPECTRUM
(SAMPLE SPUN IN HOLLOW DELRIN ROTOR)

50 ppm

C=O

$=C\overset{*}{\diagup}\overset{N}{\underset{C}{}}$

$=C\overset{*}{\diagup}\overset{C}{\underset{C}{}}$

CH_2(ETHYL)

CH_3(RING)

CH_3(ETHYL)

CH_2(RING)
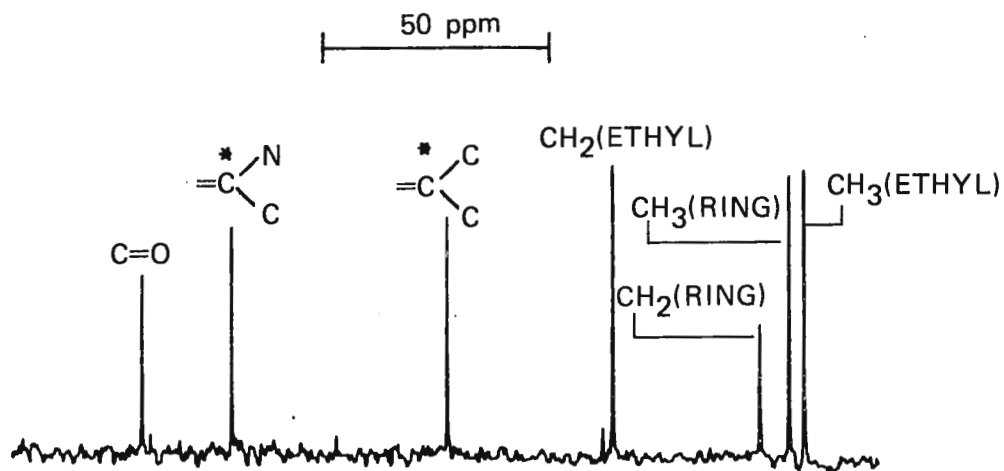
HANTZSCH ESTER: SOLUTION–STATE ^{13}C NMR SPECTRUM
(SOLVENT DMSO–d^6)

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WH-360 WB spectrum of a 0.002M solution of cholesteryl acetate (4.4 hours total time)

Imp

CDCl$_3$

90.6 MHz
^{13}C
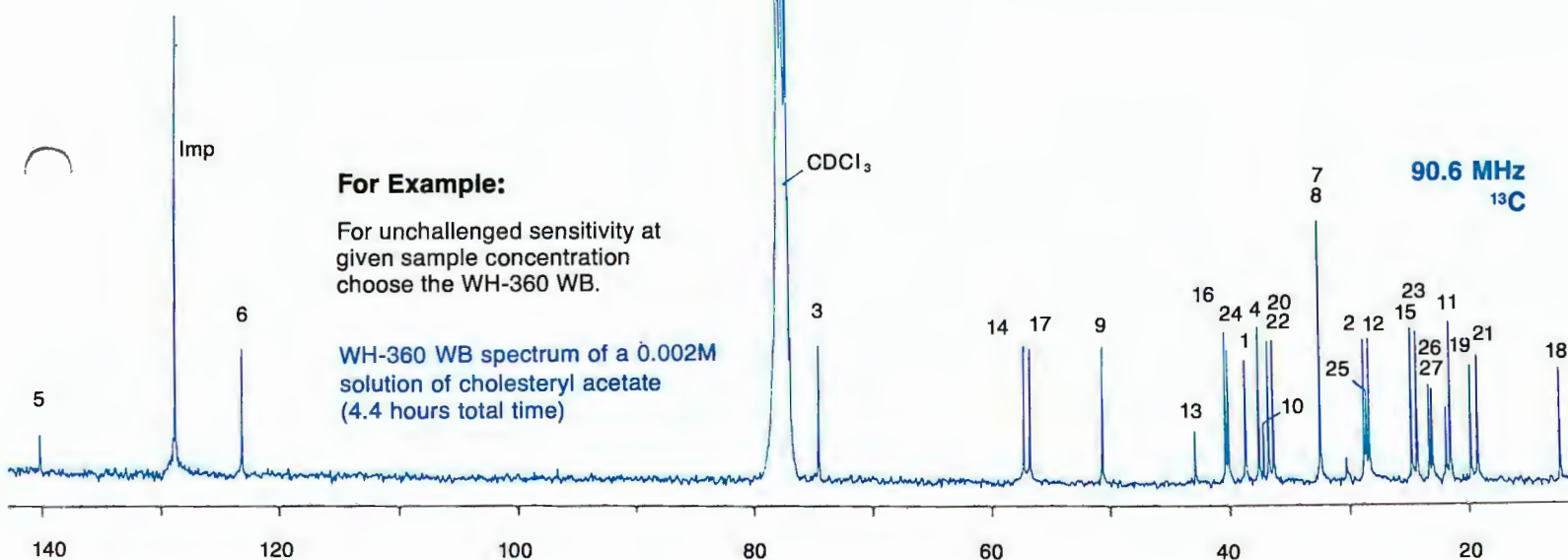
Whether your NMR needs are governed by scientific demands or budgetary constraints, Bruker is the only real choice. No other manufacturer offers as complete a product line as we do:
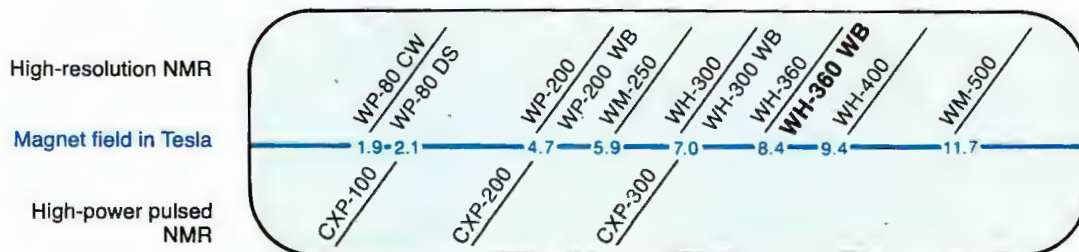
High-resolution NMR	WP-80 CW	WP-80 DS	WP-200	WP-200 WB	WM-250	WH-300	WH-300 WB	WH-360	**WH-360 WB**	WH-400	WM-500
Magnet field in Tesla	1.9-2.1	4.7	5.9	7.0	8.4	9.4	11.7
High-power pulsed NMR	CXP-100	CXP-200	CXP-300				

Attention, Nouvel intitulé du Laboratoire !

UNIVERSITÉ CLAUDE BERNARD LYON I

LABORATOIRE DE SPECTROSCOPIE HERTZIENNE

43, boulevard du 11 Novembre 1918
69622 VILLEURBANNE Cedex
Tél. (7) 889.81.24 / (secrétariat poste 3210 ou 3370)

T_1 et Zeugmatographie

Cher Docteur Shapiro,

Notre laboratoire s'intéresse actuellement aux applications de la R.M.N. à la biophysique :

- Obtention d'images par R.M.N en présence de gradient de champs (Zeugmatographie)

- Analyse de substances physiologiques grâce aux temps de relaxation T_1 et T_2.

Pour ces dernières déterminations, nous mesurons les temps de relaxation sur des échantillons contenus dans des capillaires placés dans des tubes R.M.N. de 5 ou 10 mm. Les mesures de T_1 par la séquence (π, τ, $\pi/2$, T) présentent une dispersion considérable pour un échantillon donné. Pour tester les valeurs de T_1 obtenues, il nous est apparu souhaitable d'examiner en même temps le T_1 d'un échantillon témoin placé dans un deuxième capillaire contenu dans le même tube de 10 mm. Un gradient de champs selon X permet alors d'examiner simultanément les résonances de l'eau propres à chaque capillaire et éventuellement de multiplier le nombre de mesures en multipliant le nombre de capillaires.

Pour vérifier la validité de cette méthode, nous avons mesuré T_1 sur deux échantillons identiques (cf. figure) et nous avons trouvé respectivement :

- tube A T_1 = 2,79 s
- tube B T_1 = 2,73 s
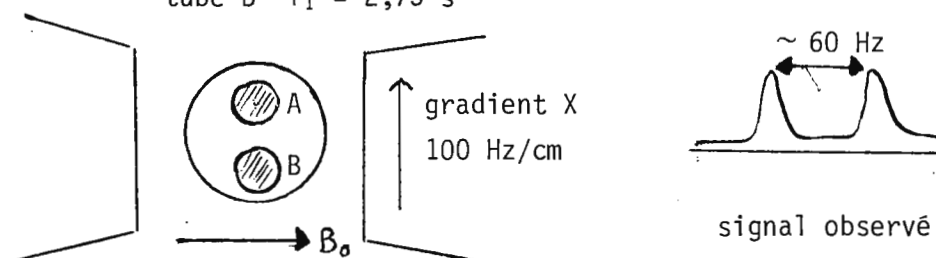
Un gradient faible (~ 100 Hz/cm) suffit à assurer une séparation des deux pics de 60 Hz, sans compromettre le fonctionnement du lock-interne-deuterium [$(CD_3)_2CO$ est placé dans l'espace entre les tubes]. Si l'on augmente le gradient (1000 Hz/cm ou plus) il faut recourir au lock-^{19}F-externe.

Outre son interêt pour des mesures simultanées de relaxation sur différents échantillons, ce type d'expérience permet de tester "les cartes de T_1" que l'on peut établir en imagerie R.M.N.

Recevez, cher Docteur Shapiro, l'expression de nos sentiments les meilleurs.

A. BRIGUET,   J. DELMAU,   J.C. DUPLAN,   R. TEYSSIER B. FENET

ISTITUTO DI CHIMICA
GENERALE ED INORGANICA

FACOLTA' DI SCIENZE

UNIVERSITA' DI TORINO

10125 TORINO. 27 February 1980
Corso Massimo d'Azeglio N.48
TEL.6505102·655831(2·3)

Professor B.L.Shapiro

Department of Chemistry

Texas A&M University

College Station, TX 77843

TITLE: Spectra of Metal Carbonyls at high ^{13}C abundance.

Dear Professor Shapiro,

the majority of the metal carbonyls requiry to be isotopically enriched to be amenable to ^{13}C studies; the 10-20% level is generally satisfactory. We are currently studying samples containing carbon-13 at an higher level with the following aims:

i) to observe the satellites subspectra in the cases in which the direct observation of the isotopomer producing the satellites is difficult;

ii) to extract additional informations from the appearance of the fine structure due to carbon-carbon coupling constants.

i is better achieved for a 25-35% enrichment and ii for an enrichment above 60%. We would like to mention some observations about the first point.

We have determined the $^1J(^{13}C-^{57}Fe)$(^{57}Fe: $I=\frac{1}{2}$, 2.19%, 2.92MHz at 21.14kG) for Fe-CO in several mono and polynuclear metal carbonyls and $^1J(^{13}C-^{187}Os)$(^{187}Os: $I=\frac{1}{2}$, 1.64%, 1.90MHz at 21.14kG) for Os-CO in $H_2Os_3(CO)_{10}$.

In all the samples studied CO's exchange occurs. Our observations were obtained for the iron derivatives in the fast exchange limit, then firstly point to the intramolecularity of the process. Secondly it is possible on the basis of the values of the coupling constants to distinguish between localized or internuclear CO's exchan-

ge for the polynuclear metal carbonyls which formula is a multiple of equivalent $M(CO)_n$ moieties. For instance among the molecules of the $Fe_2(CO)_6$ core containing one carbon-13 atom, 4.38% have one iron-57 atom; in half of them the iron-57 is directly bound to the carbon-13 atom, whereas in the other half the iron-57 and the carbon-13 atom are two bonds away. If it is assumed that the $^2J(^{13}C-^{57}Fe)$ are negligible, in the fast exchange limit the satellites of the unique CO resonance are a doublet either for localized or delocalized exchange. However in the case of localized exchange the satellites separation is double than in the other case. Our observations for $Fe_2(CO)_6S_2$ (see below) and for related systems show that the localized mechanism is operative for the CO's exchange since the values of $^1J(^{13}C-^{57}Fe)$ observed in the fast exchange limit are in the same range of those observed for mononuclear species (25-29 Hz).

S. Aime   L. Milone   D. Osella
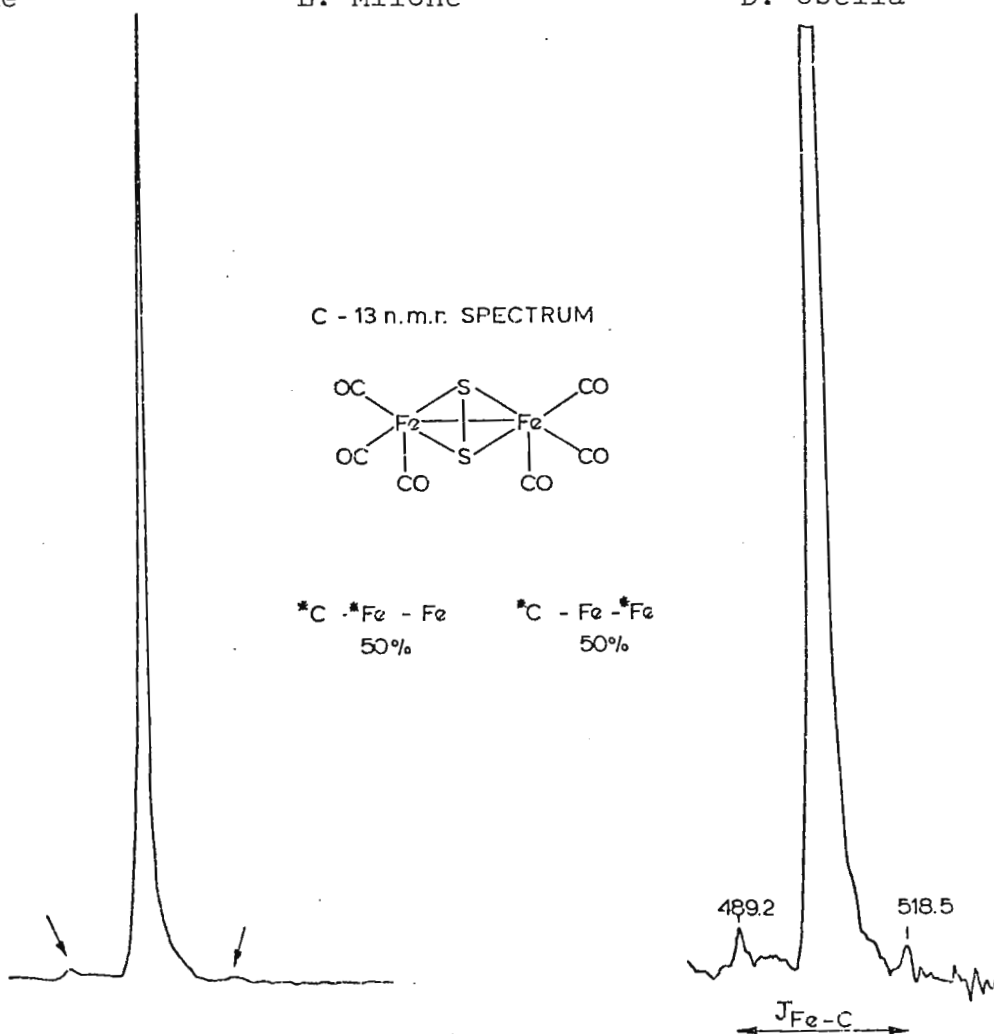
C - 13 n.m.r. SPECTRUM

*C -*Fe - Fe   *C - Fe -*Fe
50%   50%

489.2   518.5

J_{Fe-C}

SANDOZ, Inc.

February 28, 1980

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

Unexpected Simplicity in Proton-coupled ^{13}C-spectra

Dear Barry,

During the course of synthetic studies here at Sandoz, a number of compounds having the following substructure have been prepared:
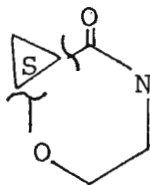
In trying to make the assignments, a curious effect in the ^{1}H-coupled carbon-13 spectrum was observed, as shown in the accompanying Figure. It appears that for one of the NCH$_2$ protons $^{2}J_{CCH}$ = ~ 0 Hz. From molecular models one notices that in each case one proton is near the plane of the carbonyl, the other almost parallel to the "p-orbitals". A naive view of this ^{1}H-coupled carbon spectrum might lead one to assume the following product had been made
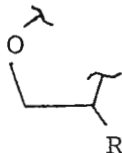
We are interested in learning if this effect has been seen in other systems and are curious to learn which proton is involved in the apparent ~ 0 Hz coupling constant.

Please credit this contribution to the subscription of S. Barcza, Sandoz, Inc.

Sincerely,

Michael Shapiro, Ph.D.
Unit Head NMR Laboratories

MS:rck
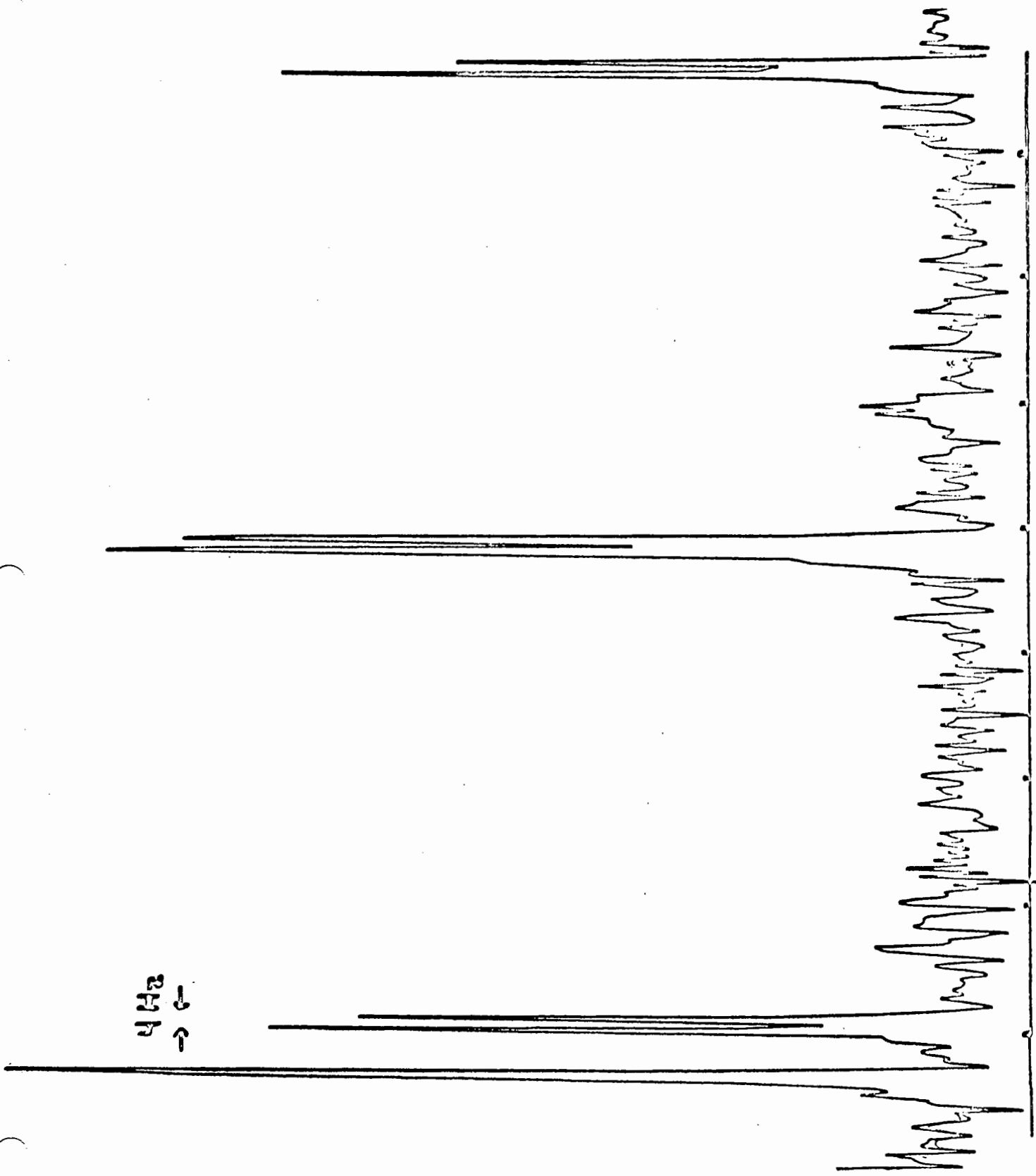
THE UNIVERSITY OF BRITISH COLUMBIA
2075 WESBROOK MALL
VANCOUVER, B.C., CANADA
V6T 1W5

DEPARTMENT OF CHEMISTRY

28 February, 1980

Prof. Bernard L. Shapiro
TAMU NMR Newsletter
Dept. of Chemistry
Texas A & M University
College Station, TX 77843 U.S.A.

LINEARIZED DISPA LINE SHAPE ANALYSIS

Dear Barry,

In the two years since we first proposed the DISPA (dispersion versus absorption) plot, we have analyzed some 16 distinct line-broadening mechanisms (see Fig. 1).[1] It is clear that the direction of displacement of a DISPA curve from its reference circle (i.e., the DISPA curve for a single Lorentzian line) can serve to identify (often uniquely) the line-broadening mechanism, using the data from a single spectrum (see reference 2 and papers cited therein).

Despite the demonstrated value of the circular display (and its dielectric analog, the Cole-Cole plot), there are obvious advantages to a linear display. Among several possible linearizations,[3] we have settled on the plot illustrated in Figure 2: the square of the DISPA radius versus square root of the frequency.
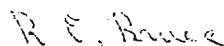
The plots in Fig. 2 were generated using a Bruker Aspect 2000 computer on our departmental WH-400 spectrometer. A listing of the Bruker assembler source file (written by Dr. R. E. Bruce) is available on request, and should appear shortly in the new Bruker user's newsletter. Alternatively, for anyone who sends us a blank disk cartridge (8-sector, for Diablo high-density model 30 series disk drive, IBM type 2315), we will return an initialized cartridge containing both ASCII and binary files, a test data set, and operating instructions. We are currently translating the Bruker program into Nicolet 1180 assembler language, and should have a corresponding Nicolet listing available shortly.

Best regards,

Alan G. Marshall   and   Robert E. Bruce
Associate Professor   Postdoctoral Fellow

1. A. G. Marshall and R. E. Bruce, J. Magn. Reson. 38, 0000 (1980).

2. F. G. Herring, A. G. Marshall, P. S. Phillips, and D. C. Roe, J. Magn. Reson. 37, 293 (1980).

3. R. E. Bruce and A. G. Marshall, submitted for publication.

LINEARIZED DISPA

Fig. 1. Characteristic displacement of a DISPA curve from its reference circle for 15 different line-broadening mechanisms. For example, (a) is an unresolved doublet, (b) is a Gaussian distribution in peak position, and (d) is a log-Gauss distribution in T_2. See ref. 1 for more details.
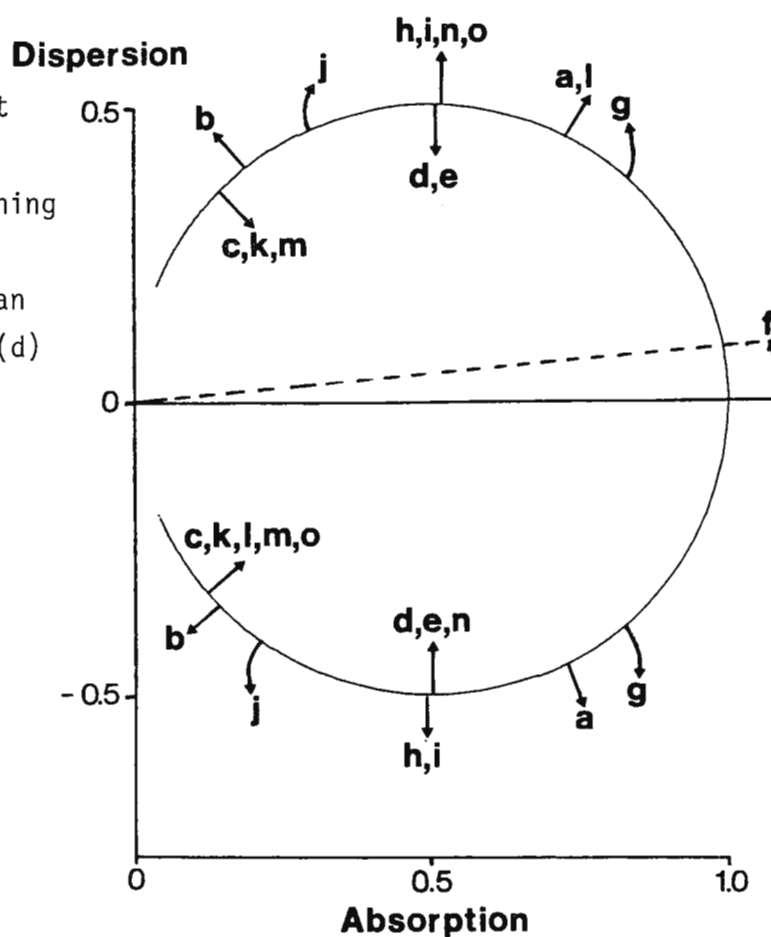
Fig. 2. Linearized plot of square of DISPA radius, versus square root of frequency from center of peak. Reference line ($R^2 = 1$) is for single Lorentzian line. Bottom curve is for superposition of two lines of different width. Top curves are for unresolved doublets of different separations. On-line data reduction is available to interested users.
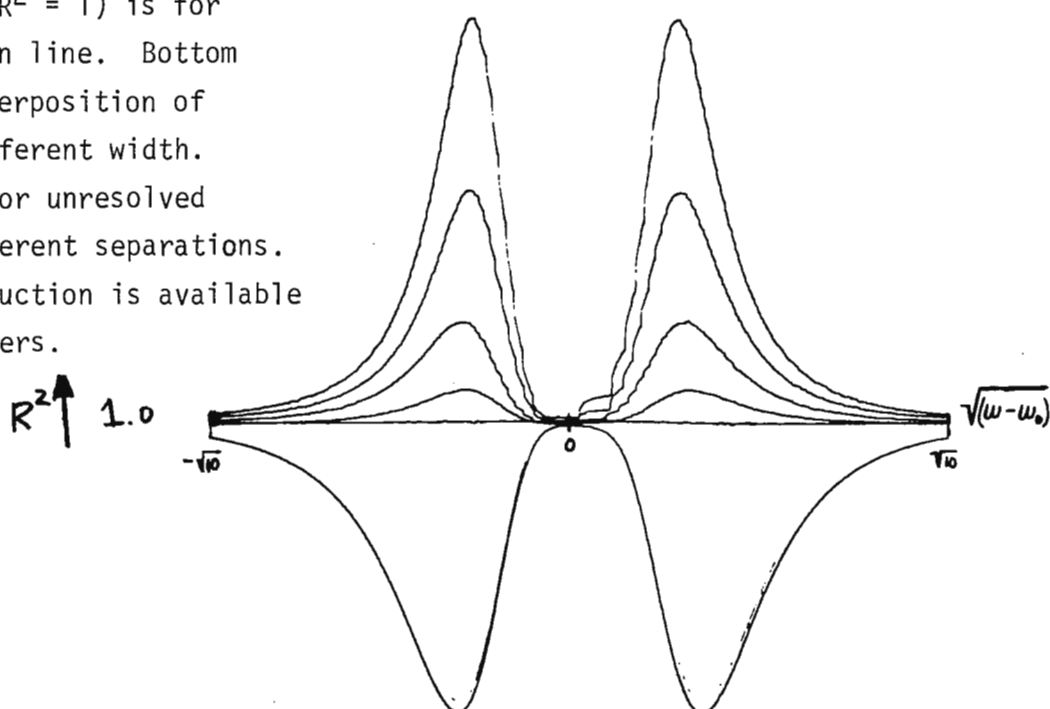
ISTITUTO SUPERIORE DI SANITA
    R O M A

Viale Regina Elena, 299
Tel 4990
Telegr : ISTISAN-ROMA

Rome, March 4th, 1980

Prof. B.L. Shapiro
Department of Chemistry
Texas A § M University
College Station, Texas 77843
USA

Title: ^{1}H NMR study of the interaction of RNase A with Cu^{++} in the presence of nucleotides.

Dear Prof. Shapiro,

in a previous paper (1), on the basis of the reassignment of the ^{1}H NMR C-2 histidine signals of the RNase A carried on in different laboratories, we were able to establish that at p^{2}H 5.5 the strongest site of interaction of the enzyme with Cu^{++} involves His-119.
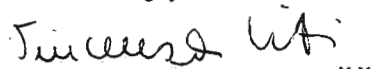
We are examining now, the interaction of RNase A with copper ions in the presence of 2'-CMP or 3'-CMP.

It is possible to observe (fig. 1) that when we add 2'-CMP to the solution RNase/Cu^{++} 84:1 M/M, p^{2}H 5.5, a competition between the two inhibitors is observable on His-119. In fact, His-12 is shifted to lower field as a function of nucleotide concentration and His-105 is not affected by 2'-CMP, as in the absence of Cu^{++}. On the other hand, as we can observe in fig. 1a, in the presence of only Cu^{++}, His-119 is not detectable because of its extreme broadening, but, progressively increasing the 2'-CMP concentration (fig. 1b, c, d), the signal shifts to lower field and becomes sharper until, at 2'-CMP to RNase A molar ratio 2:1 (fig. 1e) it reaches a linewidth of 8 Hz.

On the contrary, adding 3'-CMP to the solution of RNase A/Cu^{++} 84:1 M/M (Fig. 2) we can observe a shift of His-12 to lower field (less than in the case of 2'-CMP), while His-105 and in this case also His-119, remain very broad even at very high nucleotide concentrations.

Yours sincerely,

(Luigi Sportelli)[*]   (Vincenza Viti)[**]

(1) L. Sportelli and V. Viti (1979) Biochim. Biophys. Acta 580,100.

[*]Lab. delle Radiazioni, Ist. Sup. di Sanità, Roma (Italy)

[**]Lab. di Biol. Cellulare e Immunologia, Ist. Sup. di Sanità, Roma (Italy)

Please credit this contribution to the account of F. Podo.
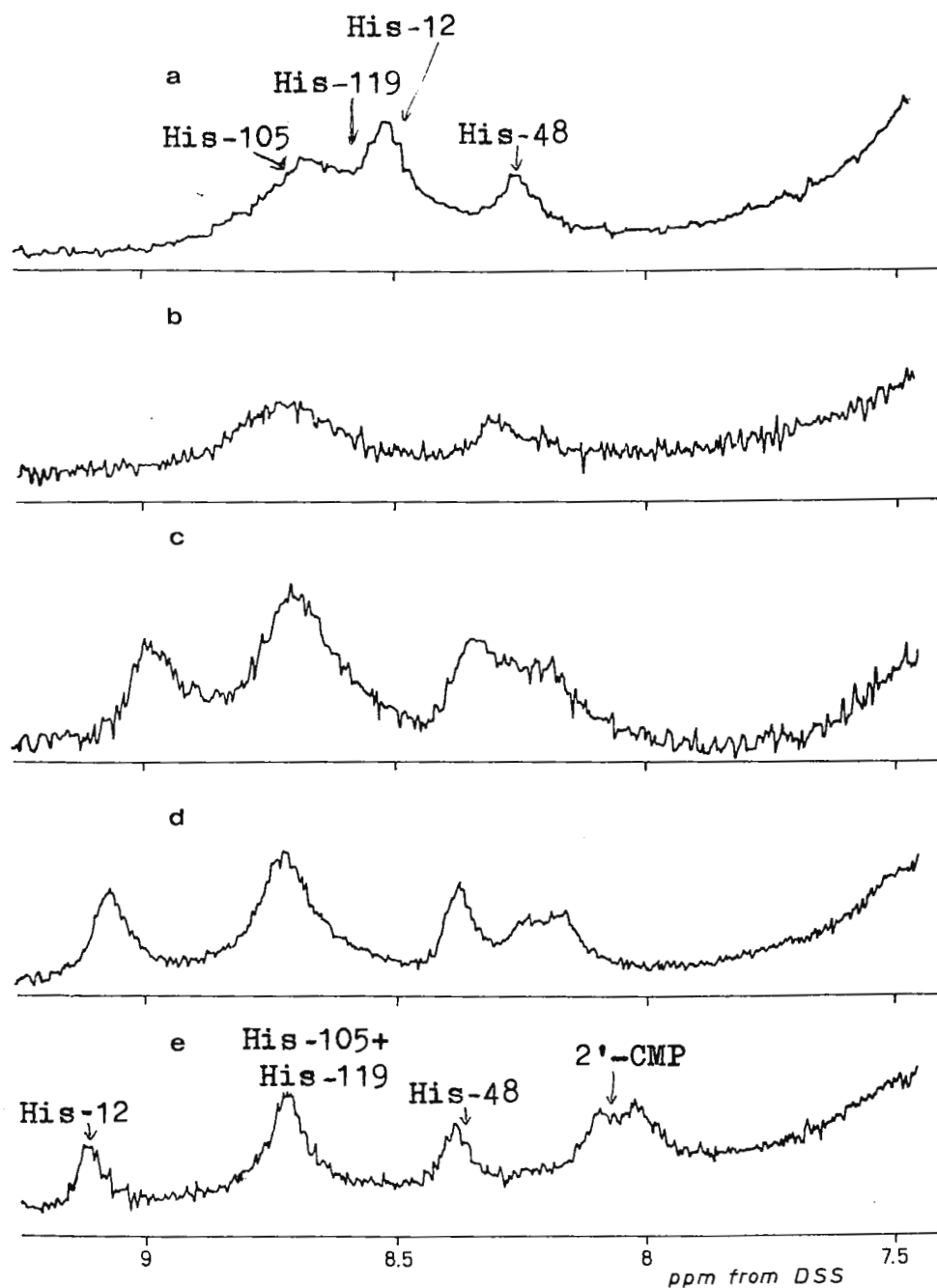
Figure 1
Effect of increasing amounts of 2'-CMP to the solution
RNase A-Cu^{++}84:1 M/M; a) no 2'-CMP; b) 2'-CMP0.2 M/M;c)
2'-CMP.0.5M/M;d)2'-CMP 1M/M;e)2'-CMP 2M/M.
(in b, c, d, e cases M/M indicates molar ratio between
2'-CMP and RNase A)
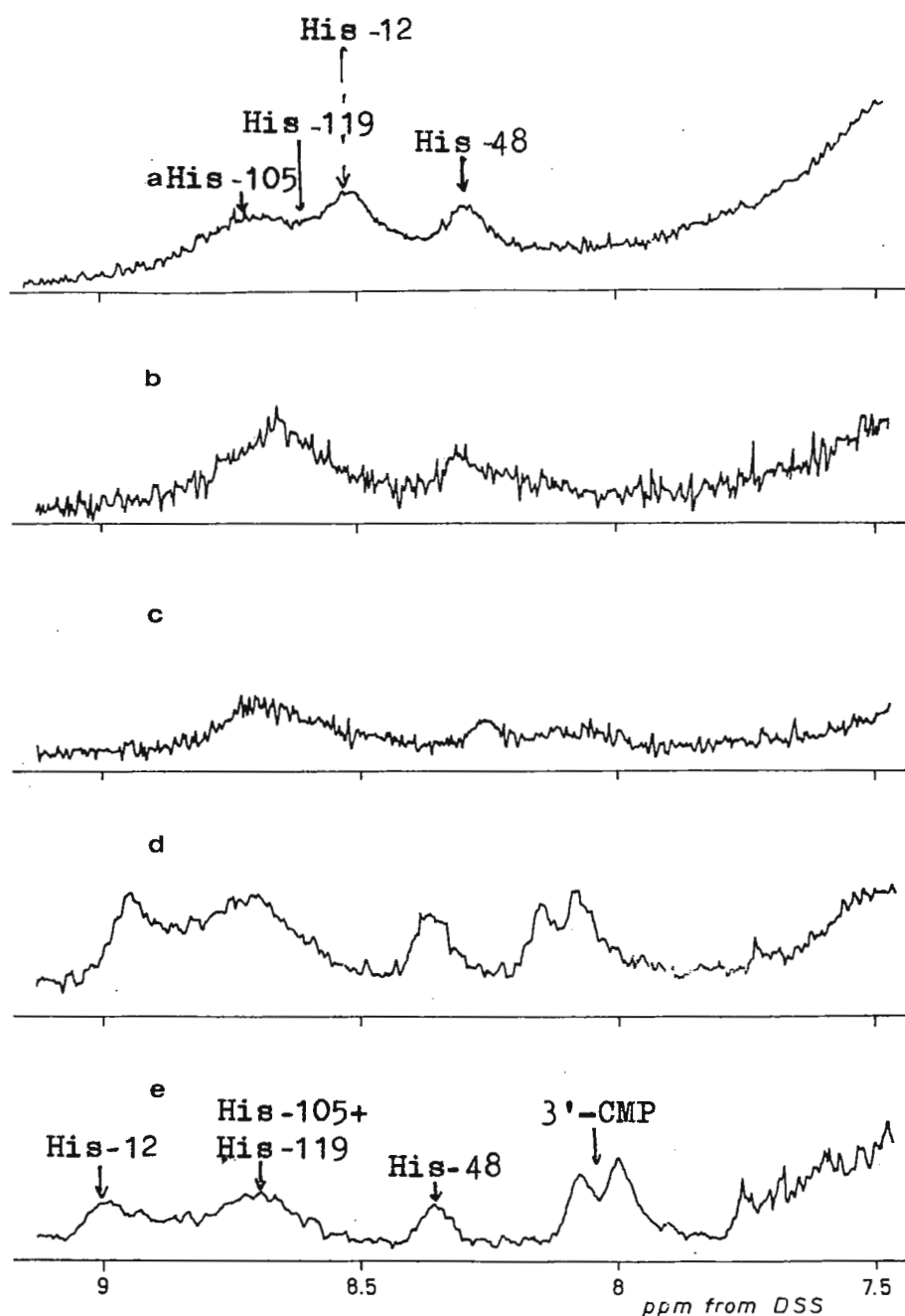
Figure 2

Effect of increasing amounts of 3'-CMP to the solution
RNase A-Cu^{++} 84:1   M/M; a) no 3'-CMP; b) 3'-CMP 0.2M/M;c)
3'-CMP 0.5M/M;d)3'-CMP 1M/M;e)3'-CMP 2M/M.
(in b, c, d, e cases M/M indicates molar ratio between 3'-CMP
and RNase A).

If you can't observe solids as readily as liquids on your superconducting FT NMR...

...you just don't have an XL-200!

50-MHz NMR Spectrum of Cured Neoprene
20 Minutes Accumulation
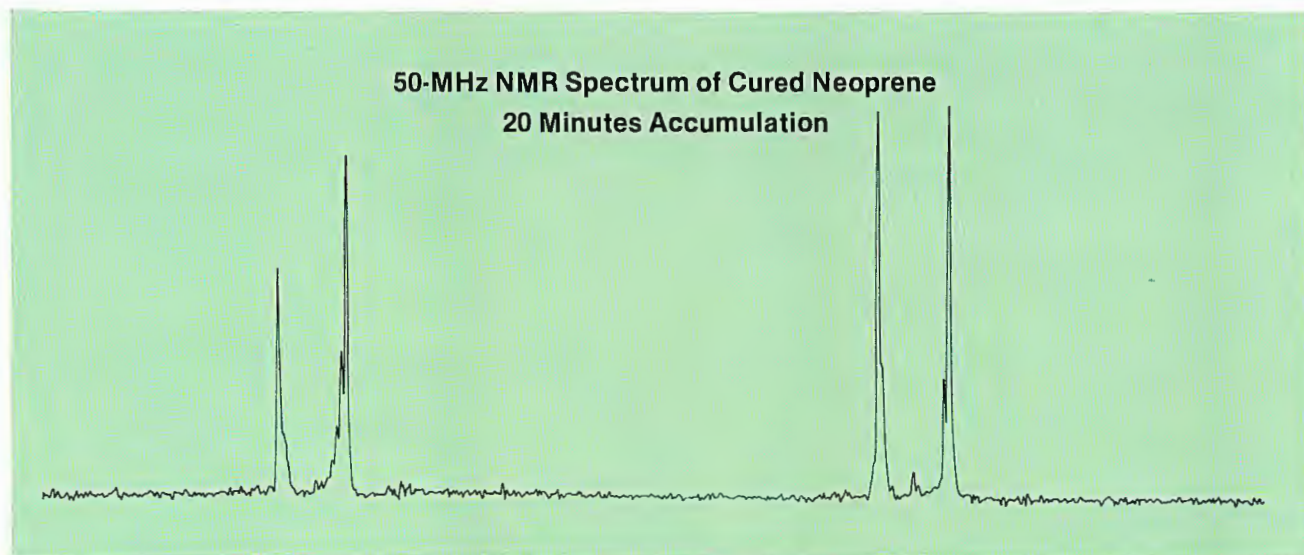
13C spectrum of cured neoprene with carbon black* in a Kel-F rotor using high-power gated decoupling (400 transients at 3-second intervals). The resolution has been enhanced by a Lorentzian-to-Gaussian transformation to bring out the fine structure. The width of the plot is 10 KHz.   *Sample courtesy of E.I. Du Pont de Nemours and Company

With the new ^{13}C solid-state accessory for the XL-200, you can spin solid or powdered samples at the magic angle, increase sensitivity using cross-polarization, and achieve efficient line narrowing with strong dipolar decoupling. Yet operation is surprisingly simple! You can introduce and eject the rotor pneumatically without disturbing the probe or the spinning axis adjustment. You monitor the spin rate on the spectrometer's built-in tachometer, just as in liquid-sample experiments. Front panel controls let you adjust optimal cross-polarization and decoupling conditions independently and conveniently.

There are other unique aspects to the XL-200 superconducting FT NMR Spectrometer, such as the data handling and spectrometer control system: a 13-bit ADC, which accommodates stronger signals on each transient; a standard 32K CPU, independent of the acquisition processor and programmed in PASCAL, a high-level, structured language; a built-in interactive 5M-word disk with dual platters; a large, flicker-free raster scan display.

The software, too, is exceptionally sophisticated. It permits multitasking (simultaneous acquisition, processing, printing, etc.) and queuing (automatic sequential execution of requested tasks) on the same or on different NMR experiments. You can also array parameters (up to three variables, including temperature) within a given experiment; generate your own convenient macro-commands;

create your own special or general-purpose pulse sequences in a simple, English-like code; even do your own computer programming in PASCAL.

Then there's the matter of the XL-200's broadband accessory which, with only a single probe for liquid samples, enables you to observe a host of nuclei (including ^{13}C) between 20 and 81 MHz. And there's the remarkable low-loss dewar system, which operates over three months on only 25 liters of liquid helium.

The XL-200 is in a class by itself— with a price tag and an operating economy that belie its advanced design.

varian

⬡ ROCHE ⬡

5 March 1980

Professor Bernard L Shapiro
Department of Chemistry
Texas A&M University
College Station
TX 77843
USA

Tricyclic Antidepressants - micelle formation

Dear Barry

In collaboration with Ray Abraham and Ken Lewtas (University
of Liverpool) we have been investigating the n.m.r. spectra
of a wide variety of drugs with antidepressant activity
(thymoleptics), e.g. imipramine hydrochloride (I), and their
interactions with various biologically relevant molecules
such as 5-hydroxy tryptamine and adenosine triphosphate. The
mechanism of action of these drugs, despite more than 20 years
research, is still much disputed. As a preliminary part of our
studies it was necessary to examine the self association
behaviour of imipramine, since "surface activity" and ability
to form micellar aggregates appears to be an important
characteristic of these drugs. Previous n.m.r. studies with
the phenothiazines e.g. promazine (II) indicated that these
compounds with neuroleptic activity have a critical micelle
concentration (CMC)[1]. More recently, several methods have
been reported for measuring the CMC of antidepressants, but
n.m.r. was not included in this study[2].

CH$_2$CH$_2$CH$_2$NMe$_2$HCl   CH$_2$CH$_2$CH$_2$NMe$_2$HCl
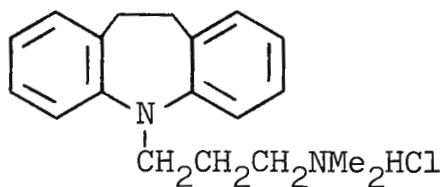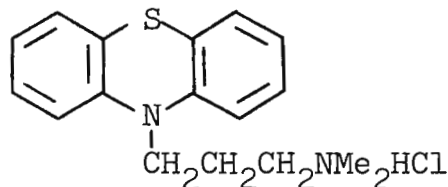
(I)   (II)

The concentration dependence of the ^{1}H chemical shifts of
imipramine in aqueous solution are shown in Figure 1, clearly
indicating a CMC of 0.03M, in good agreement with values
obtained by light scattering, conductivity and pH methods[2].
Similar curves with sharp CMC's were obtained for the side
chain protons. In the ^{1}H and ^{13}C spectra, micelle formation
is also reflected by line broadening at higher concentrations
or lower temperatures and by significant lowering of ^{1}H and
[13]C T_1 values, particularly for the quaternary carbons.

These are readily observed at 35°C for a 0.2M solution, but much less intense at 80°C or for a 0.02M concentration. As the proton most affected by aggregation is H-4 in the aromatic ring, this suggests perhaps that the molecules are stacked alternately in an offset manner as shown schematically (Figure 2). This stacking arrangement has been proposed previously for molecules of this type[1]. Experiments with a model compound, 3-dimethylamino propyl chloride showed no dilution effect on the chemical shifts, suggesting that association requires the hydrophobic phenyl groups to be present for true micelle formation.
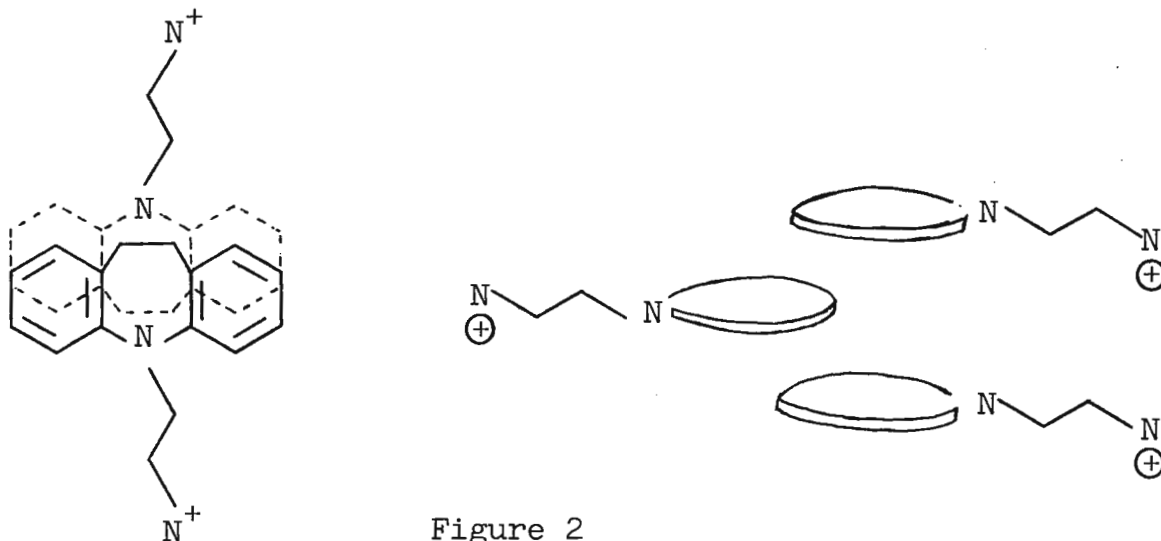
Figure 2

I hope this maintains our contribution for a few months.

sincerely

W A Thomas   I W A Whitcombe

1   See for instance D Attwood, A. T. Florence and J. M. N. Gillan, J. Pharm. Soc. 1974, 63, 988.

2   D Attwood and J Gibson, J. Pharm. Pharmac., 1978, 30, 176-180.

WAT/GER
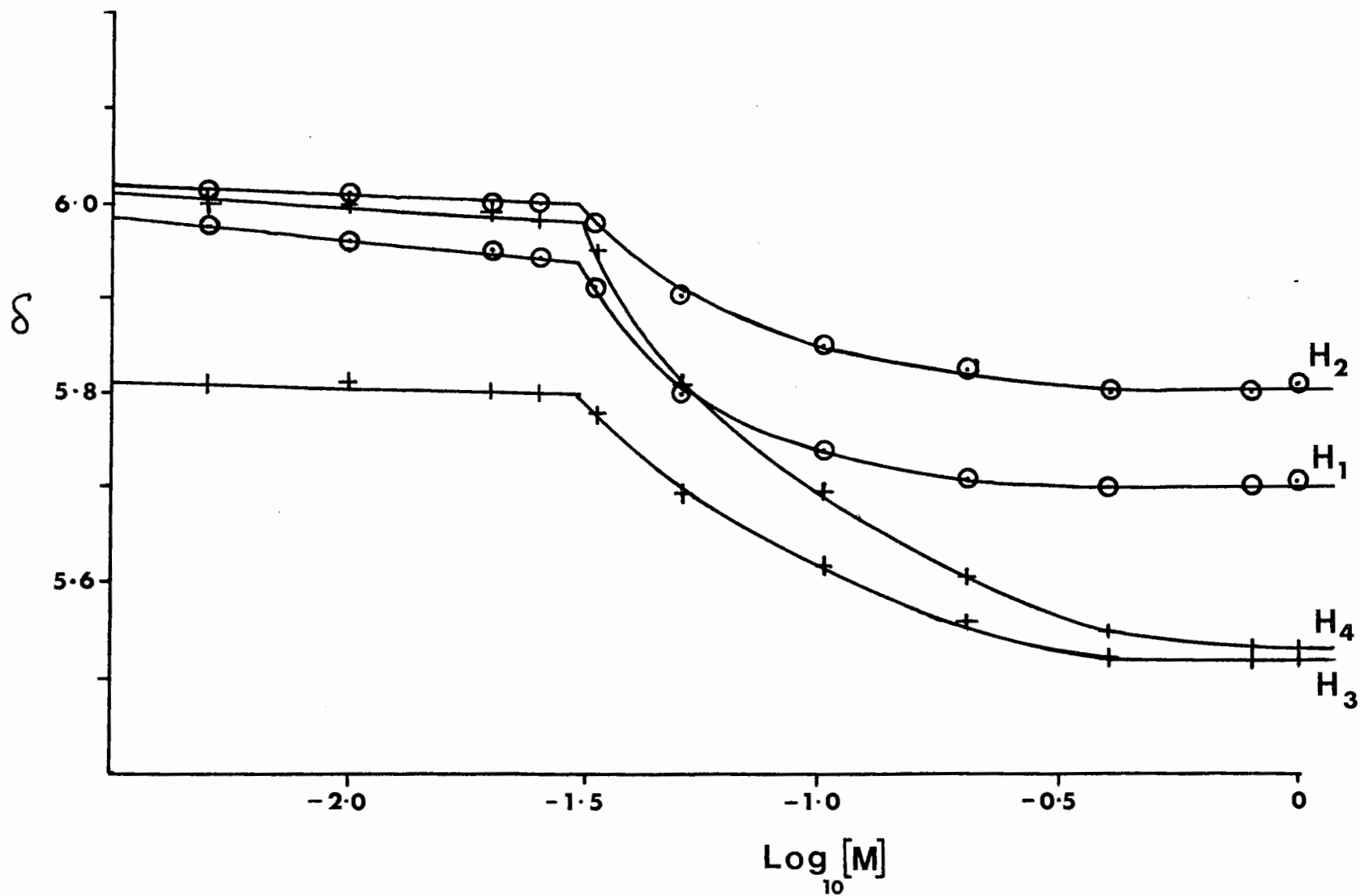
<u>Figure 1</u>   <u>Concentration dependence of the aromatic proton chemical shift</u>

<u>of Imipramine HCl in D$_2$O solution</u>

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GENERAL ELECTRIC COMPANY, RESEARCH AND DEVELOPMENT CENTER, P.O. BOX 8
SCHENECTADY, NEW YORK 12301, Phone (518) 385-2211

March 3, 1980

Professor B. L. Shapiro
Department of Chemistry
Texas A&M University
College Station, Texas   77840

Sensitivity of Silicon-29 Chemical Shift to Remote Structural Changes

Dear Barry,

A few years ago we reported the analysis of polydimethylsiloxane-bisphenol-A-polycarbonate (DMS-BPAC) block copolymers using ^{29}Si and ^{13}C NMR. In that paper, we noted that the silicon atom at the end of the silicone block is sensitive to the substituent on the other end of the BPA moiety, and two distinct silicon resonances were seen for Si^A and Si^A :
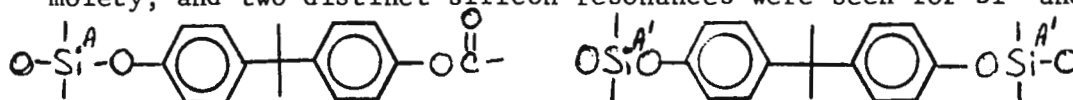
We have recently examined some model compounds and, again, have found the ^{29}Si chemical shift to be sensitive to substituents twelve bonds away:

δ_{Si} = 18.73

δ_{Si} = 18.58

δ_{Si} = 19.69

δ_{Si} = 19.51
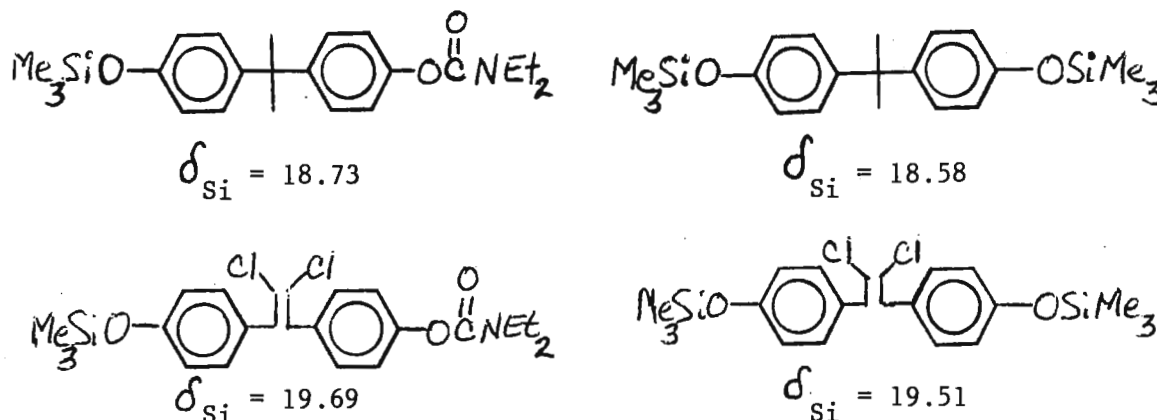
The results for these compounds prompted us to silylate some asymmetric bisphenols in which the two phenyl groups exhibit magnetic non-equivalence in the ^{13}C NMR. The ^{29}Si data are collected in the Table. It is interesting to note that in the ^{13}C spectra of 1a and 1d, C-4 is the only

GENERAL ⊛ ELECTRIC

phenyl carbon which resolves into more than one peak, yet in all of the ^{29}Si spectra the silicon atoms appear nonequivalent. These results will be included in a publication shortly.

Sincerely,

Elizabeth A. Williams
Chemical and Structural Analysis Branch
Materials Characterization Laboratory

Paul E. Donahue
Chemical and Structural Analysis Branch
Materials Characterization Laboratory

EAW:PED/ldr

1. E. A. Williams, J. D. Cargioli and S. Y. Hobbs, Macromolecules, 10, 782(1977).

GENERAL ⚙ ELECTRIC

<div align="center">

TABLE

^{13}C and ^{29}Si Chemical Shifts

of Trimethylsilyl Derivatives of some Asymmetric Bisphenols

</div>

$$\underset{\sim}{1}$$
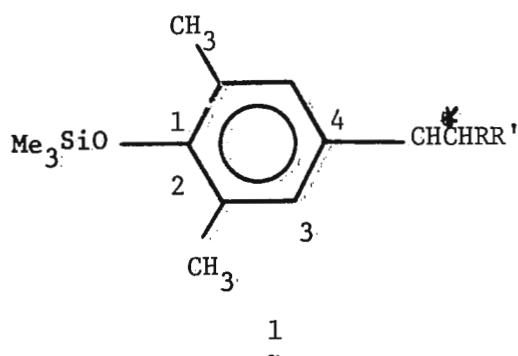
	R	R'	$\delta_{Si}{}^{a}$	$\delta_C(SiMe_3)^{a}$
a)	CH_3	$CH(CH_3)_2$	17.52 17.61	0.99
b)	CH_2CH_3	$CH(CH_3)_2$	17.37 17.60	0.97
c)	CH_3	C_6H_5	17.91 17.95	0.94 0.79
d)	CH_3	$CH(CH_3)CH_2CH_3$	17.67 17.80	0.95

[a] In ppm relative to Me_4Si. Positive values to low field

Professor V.F. Bystrov
USSR Academy of Sciences

Shemyakin Institute
of Bioorganic Chemistry

Ul. Vavilova 32
Moscow 117312 USSR

Professor Bernard L.Shapiro   March 11, 1980.
Department of Chemistry
Texas A & M University
College Station, Texas 77843
U.S.A.   Title: On NMR Study of Apamin
                                              Conformation

Dear Barry,

        In the course of conformational study of apamin (neurotoxic
octadecapeptide from bee venom) we have obtained its N^{ε} - pyrimidyl-
ornitine derivative: [Orn (Pyr)^{13}, Orn (Pyr)^{14}]-apamin. Formaly, by
doing this we decrease the pK_a value of 13th and 14th residues
(arginines in apamin have $pK_a > 13$) to observable range (pyrimidyl's
$pK_a \sim 3$). The dissociation of Orn (Pyr) residues was followed by pH
dependence of their aromatic protons and occured to be independent
(Hill coefficient $\underline{n}$ = 0.95) with the same pK_a 3.3. Ionisation of
at least one of these groups gives pronounced effect on position of
Leu^{10} δ-methyl resonances (0.11 and 0.05 ppm), assignment of which
is straightforward [1]. By comparison with results of conformational
calculation [2] we conclude that the effect is originated by Orn (Pyr)
residue in position 14.

        This piece of information shed some light on the disposition
of functionaly important arginine residues in spatial structure of
apamin. The papers on NMR study of apamin solution conformation are
now in preparation to be published in "Bioorganicheskaya Khimia".

                                Sincerely yours,

                                Vladimir

                                Vladimir Bystrov

1. V.F. Bystrov, A.S. Arseniev, Yu.D. Gavrilov, J.Magn.Res. 30,
   151 (1978).
2. E.M. Popov, P.N. Mel'nikov, Bioorganich.Khim. 5, 1471 (1979).

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(415) 497-6153

March 15, 1980

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

<u>Analysis of Relaxation in Proteins</u>

Dear Barry:

The prevalent approach in the analysis of NMR relaxation data towards motional and structural information about molecules is to assume a model for the molecular tumbling such as the rigid rotor,[1] spinning top on a rigid rod[2] or any of these extensions[3-5] and look for the best fit to one or two relaxation parameters (RP). The assumption of the model then allows the calculation of one or more correlation times τ_c to give some idea of the motion(s) present. This is an inherently unsatisfactory procedure because (1) it precludes the discovery of motions not foreseen by the model <u>a priori</u>; (2) the calculated τ_c will depend on the model chosen; (3) with a limited relaxation data set, a degeneracy of fits can exist and (4) while the models are obviously useful and can give excellent results when applied to small molecules,[2-5] they are not easily applied to macromolecules with multiple internal motions.

A good example of the ease with which one can be misled is the common assumption that α-CH groups in a protein are rigidly held and reflect only the overall τ_c of the protein.[6,7] Recent work suggests that this is not necessarily the case and it is therefore not surprising that the diffusional τ_c derived from NMR data for proteins such as BPTI and lysozyme have undergone repeated revisions.[6,8]

We therefore think that it is necessary to first look, with an unprejudiced or only a slightly prejudiced eye, for all possible motional frequencies that emerge from a large set of experimental relaxation data at various frequencies and <u>then</u> try to piece together a specific dynamic picture of the macromolecular structure. For this approach,[9,10] the appropriate general spectral density function $J(\omega)$ is

$$J_{ij}(\omega_j) = \sum_k{}' \frac{\alpha_k \overline{\lambda}_k}{\omega^2 + \lambda_k^2}$$

where k is the number of allowed motions, $\lambda_k = \tau_k^{-1}$ is the motional frequency and α_k is the relative contribution of each motion.

We have used this approach to analyze a large set of ^{13}C relaxation data at 2 field strengths for BPTI, a small protein (M.W. 6,500).[11-13] An Ile CH_3 group is shown in the table as an example:
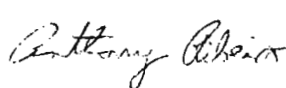
Peak	Field Strength	T_1	T_2	NOE	σ^2	λ_1 (Hz)	α_1 (%)	λ_2 (Hz)	α_2 (%)	λ_3 (Hz)	α_3 (%)
7.56 ppm	45MHz	.235	.055	1.55	0.000	6E8	7%	7E7	8%	3E11	85%
Ile^{18} or $^{19}_\delta$ CH_3	90MHz	.335	.090	1.50	0.003	6E8	4%	2E8	13%	1E11	83%

When k = 1 or 2, i.e., when one or two motions are allowed, the theory gives no simultaneous fits for all 3 parameters at one frequency. When three motions at the λ's and α's in the table are allowed, excellent agreement is found between calculated and experimental relaxation data. Over the cumulative analysis of forty resonances, we found that when the square of the variance $\sigma^2 < 0.01$, the experimental and calculated numbers are essentially identical.
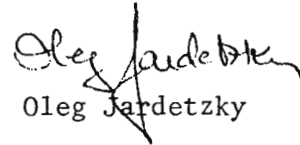
The excellent agreement between the two independent frequencies suggests a unique solution, i.e., 2 slow motions at ~10^8 Hz and one fast at ~10^{11} Hz contribute to the relaxation of the Ile group. λ_1 corresponds to the diffusional tumbling of the BPTI molecule as determined by light scattering. λ_2 could be either the diffusion about the minor axis of the pear-shaped molecule or a slow warp of the protein backbone or some other slow motion. λ_3 clearly represents side chain rotations.

The above approach usefully allows the separation of observed relaxation into number of motions present, their frequencies and relative contributions. No assumption of a specific model for the molecular tumbling is made. Indeed, the reverse process is possible. Given the motional frequencies, specific models may now be examined. This is an important point missed by several referees who suggested our papers not be published because they did not include specific and easily understood models. Fortunately, others saw the point of the whole procedure clearly.[11-13] We repeat that the whole point of an extensive data analysis as carried out above is that very often several specific models will fit a more limited data set (e.g. T_1 and NOE) equally well and singling one out can be totally misleading.

Sincerely,

Anthony Ribeiro   Oleg Jardetzky

1) Bloembergen et al., Phys. Rev. 73, 679 (1948).
2) Woessner, J. Chem. Phys. 36, 1 (1962).
3) Levine et al., Mol. Phys. 25, 497 (1973).

4) Wittebort and Szabo, J. Chem. Phys. 69, 1722 (1978).
5) Doddrell et al., J. Chem. Phys. 56, 3683 (1972).
6) Wuthrich and Baumann, Org. Magn. Res. 8, 532 (1976).
7) Opella et al., J. Amer. Chem. Soc. 96, 7157 (1974).
8) Dill and Allerhand, J. Amer. Chem. Soc. 101, 4376 (1979).
9) King and Jardetzky, Chem. Phys. Lett. 55, 15 (1978).
10) King et al., Biophys. J. 6, 103 (1978).
11) Jardetzky et al., Biochem. Biophys. Res. Comm. 92, 883 (1980).
12) Ribeiro et al., J. Amer. Chem. Soc. 102, In Press (1980).
13) Ribeiro et al., Applied Spect., In Press (1980).

ᐯᐯesleyan UNIVERSITY

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DEPARTMENT OF CHEMISTRY

March 11, 1980

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

<u>1980 Peter A. Leermakers Symposium</u>

Dear Dr. Shapiro:

This year's Leermakers symposium is titled "NMR in Chemistry and Biology-Echoes and New Focuses". I would like to invite all members of the NMR community, especially those in New England, to attend. The speakers and their topics are given in the announcement (see following page).

Sincerely,

Philip Bolton

DEPARTMENT OF CHEMISTRY
WESLEYAN UNIVERSITY

Wesleyan University, Middletown, Connecticut 06457

1980 PETER A. LEERMAKERS SYMPOSIUM
NMR IN CHEMISTRY AND BIOLOGY —
ECHOES AND NEW FOCUSES

Tuesday, May 13, 1980

9:00 a.m. PRESIDENT COLIN G. CAMPBELL, Wesleyan University

9:15 a.m. PROFESSOR EDWARD M. PURCELL, Harvard University: *The Beginnings of Nuclear Magnetic Resonance.*

10:00 a.m. DOCTOR RAY FREEMAN, Oxford University, England: *Two Dimensional Nuclear Magnetic Resonance.*

11:00 a.m. PROFESSOR PAUL C. LAUTERBUR, SUNY at Stony Brook: *Nuclear Magnetic Resonance in Three Spatial Dimensions.*

LUNCH

1:00 p.m. PROFESSOR JOHN S. WAUGH, Massachusetts Institute of Technology: *The Alchemy of Nuclear Spins: NMR in Solids.*

2:00 p.m. PROFESSOR MILDRED COHN, University of Pennsylvania: *Phosphorus-31 Studies of Some Enzyme Reactions.*

COFFEE

3:15 p.m. PROFESSOR ROBERT G. SHULMAN, Yale University: *High Resolution Nuclear Magnetic Resonance Studies of Cells and Tissues.*

4:15 p.m. PROFESSOR JOHN D. ROBERTS, California Institute of Technology: *Nitrogen-15 Nuclear Magnetic Resonance and Its Application to Proteolytic Enzymes.*

The Symposium will be held in the Science Auditorium, Science Center, Lawn Avenue

Please pre-register by notifying:
Lucille Blanchard
Department of Chemistry
Wesleyan University
Middletown, Connecticut 06457
(203) 347-9411

SADIS BRUKER SPECTROSPIN, Boîte Postale N 67160 WISSEMBOURG

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- Recherche Océanographique

Professor B.L. SHAPIRO
Dpt of Chemistry
Texas A & M University

COLLEGE STATION, Texas 77843
USA

N./Réf. 80 03 156 CB/MCH

V./Réf.

^{31}P NMR of P_4S_7

Wissembourg, le March, 4, 1980

Polysulfur cage compounds chemistry has received a great deal of attention and the P_4S_3, α and β P_4S_4, P_4S_9 and P_4S_{10} Phosphorus NMR data have already been published. All these compounds give clear cut spectra, readily amenable to first or second order analysis.

Interestingly enough, P_4S_7 is the only parent compound of the family whose 31P NMR spectrum is not available.

This compound is in fact very sparingly soluble in most common solvents ($\sim$0,4 g/l in CS_2), but the availability of high field supercon FT systems levels out this situation. On the other hand, even if a X ray structure of P_4S_7 has been published, only ^{31}P NMR can give some insight about the molecular geometry of this compound in solution ; such a solution behaviour of P_4S_7 being of some interest for inorganic and coordination chemistry chemists.

The ^{31}P spectrum of dissolved P_4S_7 in CS_2 is shown is fig. 1. Surprisingly, no $^2J_{P-S-P}$ coupling constants is detected on the spectrum, in contrast to

- β P_4S_4 ($^2J_{P1-S-P2}$ = 50,4 Hz, $^2J_{P2-S-P3}$ = 18,2 Hz)

- P_4S_3 ($^2J_{P-S-P}$ = 71 Hz)

- P_4S_9 ($^2J_{P-S-P}$ = 96 Hz).

Neither low temperature experiments, nor direct ^{31}P $\{^{31}$P$\}$ saturation transfer experiments gave apparent indications of an exchange process in the P_4S_7 molecule.

On the other hand, chemical shifts of the two groups of phosphorus fall within the expected range of P^{III} and P^{IV} shifts for such a cage compound, although no clear explanation of the difference between P^{III}, P^{IV} shifts from one compound to another has been formally rationalized.

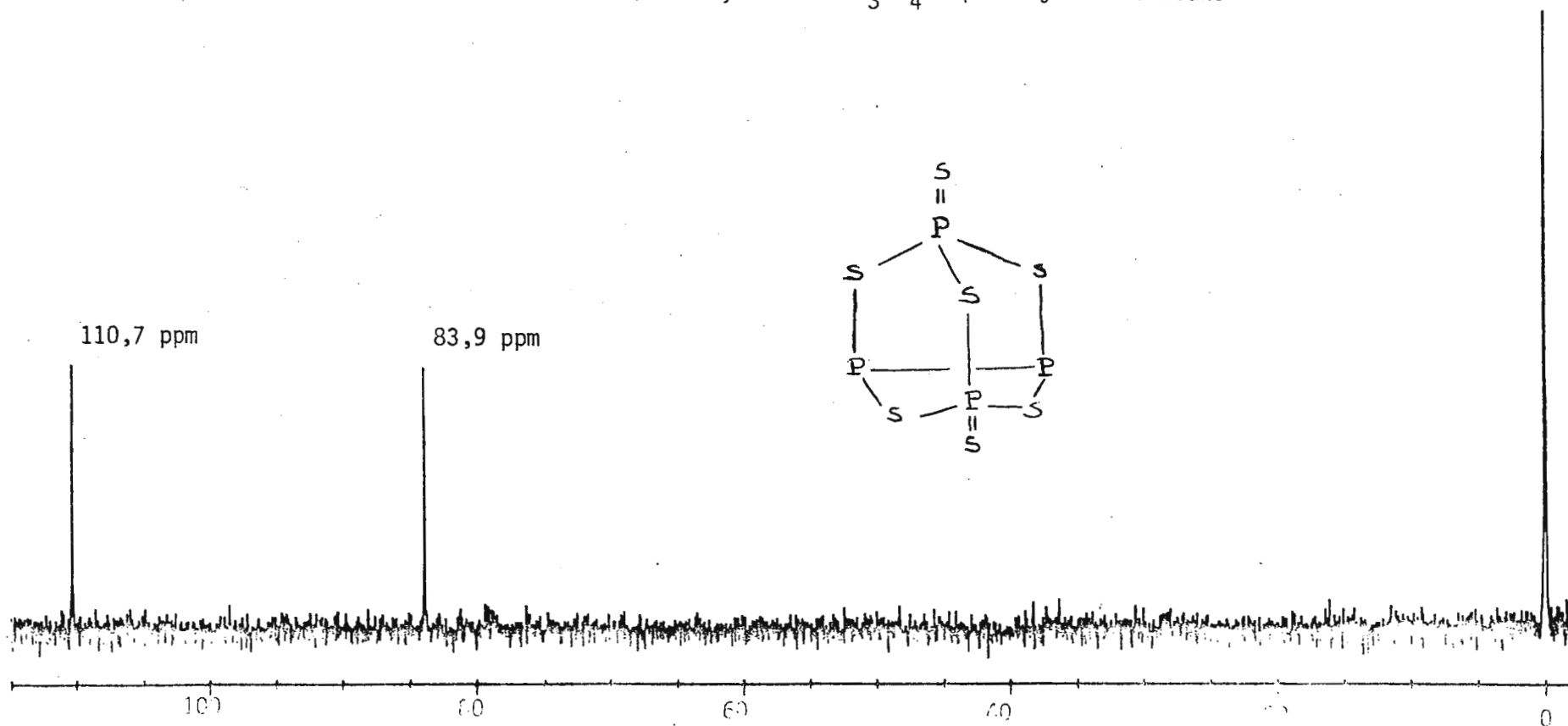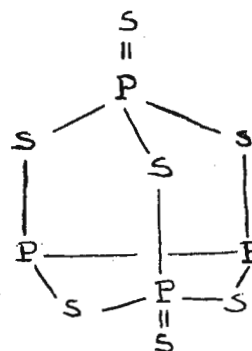A more detailed study including high resolution solid state 31P NMR will be soon published.

M.DEMARCQ

Centre de Recherches
UGINE KUHLMANN / LYON

C.BREVARD

Laboratoires d'Applications
BRUKER / WISSEMBOURG

101,2 MHz ^{31}P spectrum

of a solution (0,3 mg/ml) P_4S_7 in CS_2

40 sec. rep. rate, external D_3PO_4 capillary. 3 500 scans

110,7 ppm   83,9 ppm

The University of Liverpool

Professor Bernard L. Shapiro,
Department of Chemistry,
Texas A and M University,
College of Science,
College Station,
Texas 77843,
U.S.A.   6th March, 1980.

L.I.S. Determinations of Conformer Populations.

Dear Barry,

Derek Chadwick, Fernando Sancassan and I have been looking recently into the controversial question of the quantitative use of Lanthanide Induced Shifts (L.I.S.) in determining molecular conformations and energies.

We have recently shown that by utilisation of the L.I.S.'s for both ^{1}H and ^{13}C nuclei, use of a physically reasonable model for lanthanide ion binding and restriction of the number of variables defining the conformation of the system under study to a minimum, it is possible to refine, with considerable confidence, the solution conformations of a number of cyclic ketones, including cyclohexanone, 4-t-butyl cyclohexanone[1] and bicyclo [3.1.0] hexan-3-one.[2]

We now report that it is possible to extend this technique to the <u>direct</u> determination of conformer energies in solution. As previously, we restrict ourselves to cyclic ketones (2-,3- and 4-methyl-, and 2-chloro-cyclohexanones) with only one functional group capable of complex formation.

The binding model used was the two-site model in which the lanthanum ion populates two sites symmetrically disposed w.r.t. the plane bisecting the C.CO.C angle. The lanthanide populations in the two binding sites, the mole fractions of the conformers and the lanthanide coordinates (r, ϕ, ψ) were scanned for the best fit of observed vs calculated shifts, using the crystallographic agreement factor (R).

The figure summarises our results. The convergence of the program and definition of the populations is very reasonable, and this leads directly to $-\Delta G$ (axial $\longrightarrow$ equatorial) values of 1.8, 1.1 and 1.1 kcal/mole for 2,3 and 4 methyl cyclohexanone respectively,
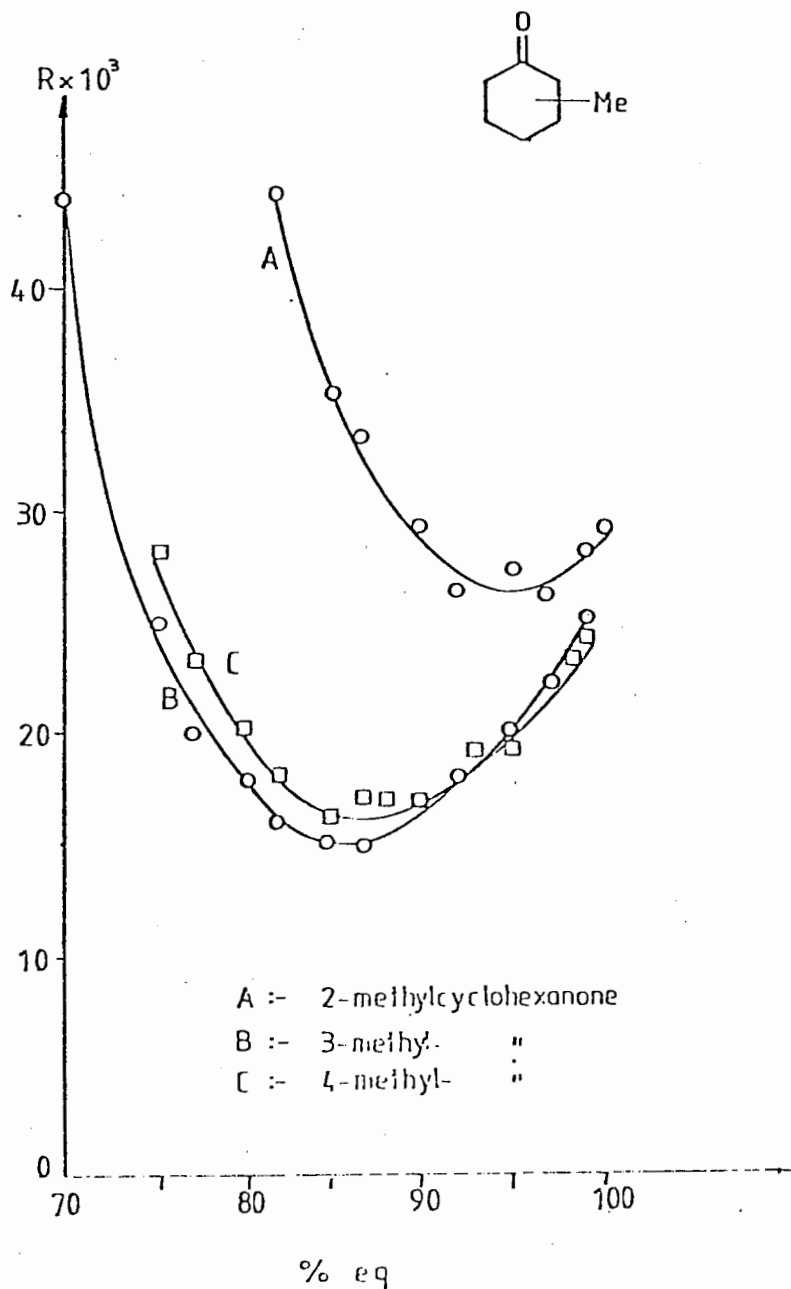
which compare well with previous literature values.

Yours sincerely,

Ray

Dr. R.J. Abraham.

1. R.J. Abraham, M.J. Bovill, D.J. Chadwick, L. Griffiths and F. Sancassan, Tetrahedron 36, 279 (1980).

2. R.J. Abraham, D.J. Chadwick and F. Sancassan, Tet. Letters 265 (1979).

A :- 2-methylcyclohexanone
B :- 3-methyl-   "
C :- 4-methyl-   "

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DEPARTMENT OF CHEMISTRY
TAMPA, FLORIDA 33620

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OXYGEN LONE PAIRS AND THE GEOMETRY OF SHIFT REAGENT--KETONE COMPLEXES

14 March, 1980

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

Dear Barry:

    In recent efforts to extend our shift reagent studies to other functional groups
we have investigated several substituted adamantanones ub the presence of EuFOD. The
experimental LIS were compared with values calculated using the pseudocontact equation
according to the "two-site model". For this model the predicted LIS are calculated on
the basis of two distinct complexes which afford a single time-average spectrum:
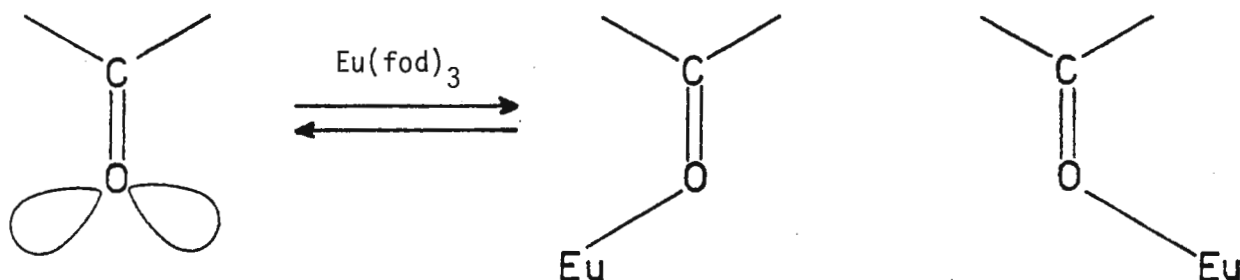
    The initial calculations assumed equal populations of the two isomeric complexes,
and we were surprised to discover that the optimum C-O-Eu angle was 180°. Even with
subsequent refinement of the calculations to permit unequal populations (as well as
different bond angles for each of the complexes) the optimum geometry was still
nearly linear.

    A check of the literature -- both experimental and theoretical -- quickly showed
that the common practice of drawing the lone pair orbitals on carbonyl oxygen in the
above manner -- i.e., as "rabbit ears" -- is simply not justified. Even in the case
of a symmetrical ketone the two lone pairs are not equivalent! One of the "lone pairs"
should be a mixture of oxygen s and p orbitals oriented along the carbon-oxygen axis,
and the other should be a pure p orbital which is perpendicular to the local plane of
the carbonyl group. (The actual molecular orbitals of course might not be localized
entirely on oxygen).

    Although the orbitals of the complex need not be the same as those of the free
ketone, it is clear that our experimental evidence is much better accommodated by the
"one-site model" for which simultaneous sigma and pi bonding would favor a linear
C-O-Eu array. (In the absence of symmetry, however, the "linearity" would be only
approximate).

$$Eu(fod)_3$$
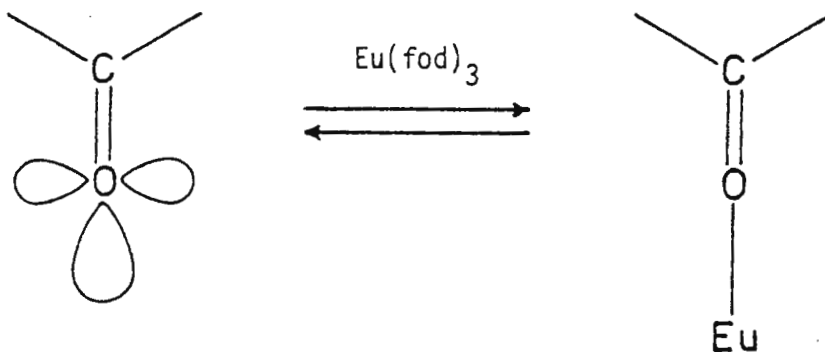
Our results for a variety of relatively rigid ketones are summarized below. The direction of distortion from linearity is indicated by the arrows, and the agreement factor is shown in parentheses.

180° (0.01)   163° (0.03)   170° (0.03)

155° (0.02)   170° (0.03)

170° (0.01)   175° (0.01)
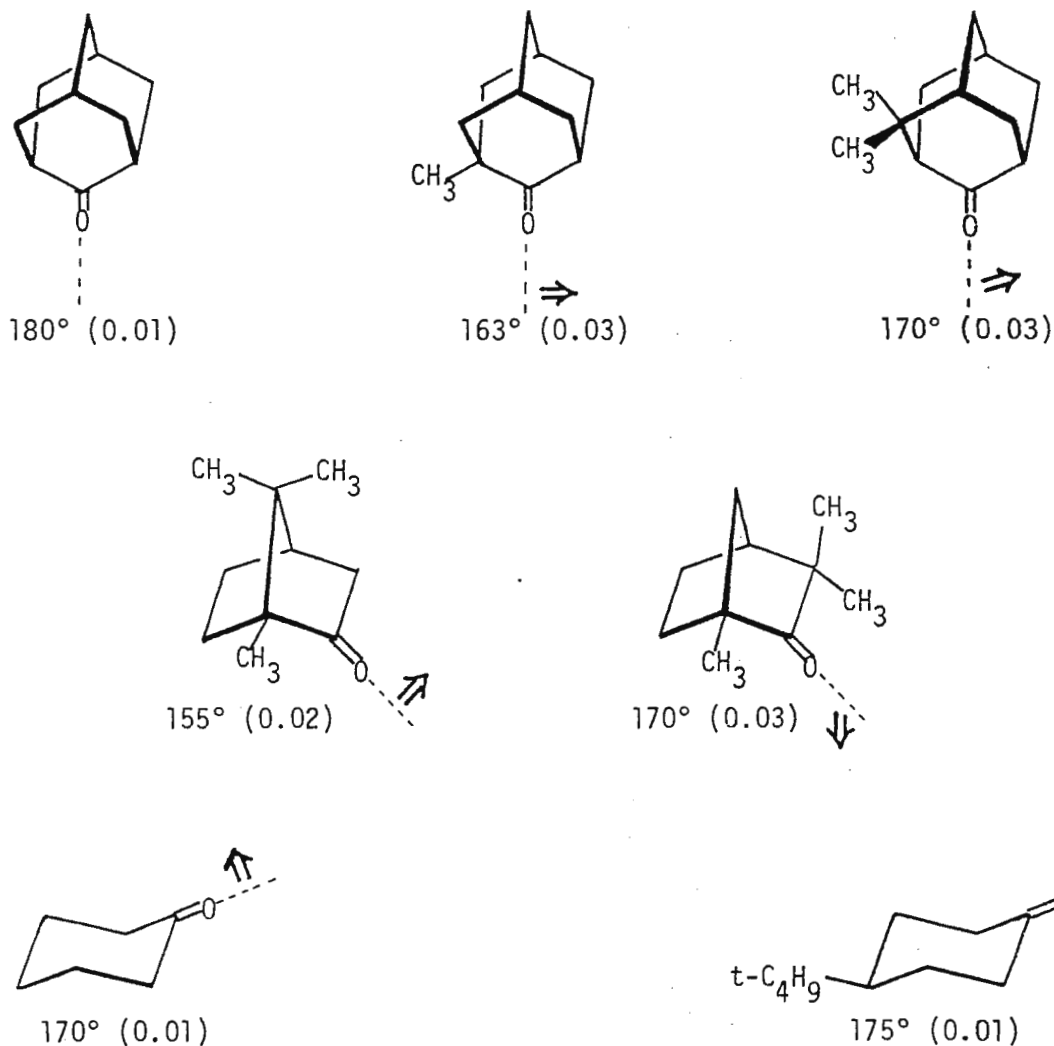
We have not been able to detect electronic perturbations of the "lone pair" orbitals with MO calculations, and the direction of the nonlinear distortion is in each case consistent with a steric effect.

Best regards,

Douglas J. Raber

GRIFFITH UNIVERSITY

Nathan, Brisbane, Queensland, 4111. Telephone (07) 275 7111. Telegrams Unigriff Brisbane

School of Science
Chairman: Dr. D. M. Doddrell

Ref: DMD:pc

10th March 1980

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

Dear Professor Shapiro:

Enhancement of ^{13}C Resonances in Paramagnetic Transition-Metal
Complexes Using Proton Polarization Transfer Spectroscopy

The S/N of ^{13}C spectra of paramagnetic transition-metal complexes
is usually significantly reduced compared to their diamagnetic
counterpart because the Nuclear Overhauser Enhancement (NOE) is
eliminated as the ^{13}C relaxation pathway is dominated by electron-
nuclear dipolar coupling. If there is a resolvable scalar coupling,
in principle, pulse sequence used to induce proton polarization
transfer of magnetization from proton to ^{13}C will yield ^{13}C spectra
with greatly increased S/N. The gain is γ_H/γ_C or a factor of ~ 4.
In its simplest form the sequence is

$$\frac{\pi}{2}(H,X \text{ axis})-\tau-\pi(H),\pi(C)-\tau-\frac{\pi}{2}(H,Y),\frac{\pi}{2}(C)-\Delta-(\text{decouple, acquire data})$$

τ, Δ are set at 1/4J. Another requirement is that $(2\tau + \Delta) \ll$
$T_1(H)$, $T_2(C)$.

Results showing that this idea works are given below. The S/N gain
is only a factor of two due to pulse imperfections.

(S/N) gain for the α, β, γ carbon resonances in pyridene on proton decoupling (NOE) and Polarization Transfer (PT) for varying amounts of added $Cu(AA)_2$

α-C	No $Cu(AA)_2$	2mg $Cu(AA)_2$	6mg $Cu(AA)_2$	30mg $Cu(AA)_2$
NOE	2.59	1.34	1.17	1.03
$T_1(S)$	16.0	2.6	1.9	0.4
PT	2.9	2.8	2.4	2.1
β-C				
NOE	2.5	1.7	1.6	1.2
$T_1(S)$	16.4	6.3	4.9	1.6
PT	2.6	2.5	2.5	2.6
γ-C				
NOE	2.6	1.8	1.7	1.2
$T_1(S)$	14.0	6.3	6.0	2.0
PT	2.6	1.9	2.4	2.2

We have used the pulse sequence to record ^{13}C of dicyanohemin with improved S/N. A paper is available on request.

Yours sincerely,

D.M. Doddrell

March 14, 1980

Dr. Barry L. Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas   77893
U.S.A.

Dear Barry:

Re: Lead-207 NMR to study Pb-complexes

We have recently been looking at the interaction of lead with some model systems using ^{207}Pb NMR in the hopes of unraveling some aspects concerning lead poisoning. Shown in the Figure are the Pb chemical shifts as a function of pH at three different Pb:acetylglycine ratios. ◑ = 1:1, △ = 1:2 and ◈ = 1:4. Equilibrium constants for the PbL^+ and PbL_2 complex can be extracted from this data by using a non-linear least squares curve fitting technique.

The large chemical shift range between uncomplexed (low pH) and complexed lead (high pH) shows that ^{207}Pb NMR will provide the chemist with a powerful technique for probing subtle molecular interactions.

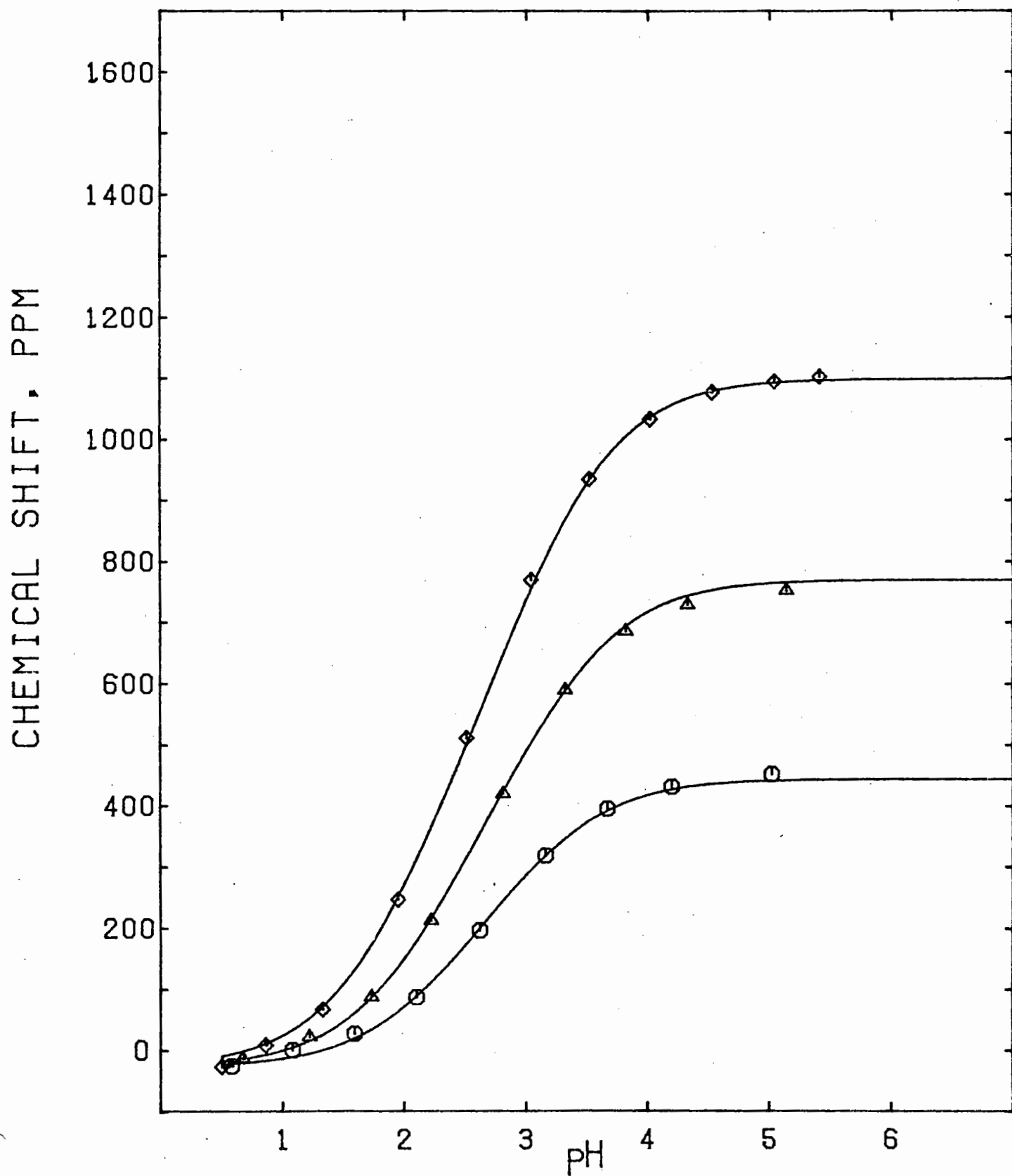Sincerely,

Tom Nakashima

Dallas Rabenstein

:aw
Enclosure

Figure: ^{207}Pb Chemical Shifts from Pb(NO$_3$)$_2$

TCU

TEXAS CHRISTIAN UNIVERSITY
Fort Worth, Texas 76129
817-921-7195

Department of Chemistry

March 21, 1980

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

The ^{2}H-NMR of Aqueous
Sodium Cholate

Dear Barry:

Recently, we have extended our NMR studies of steroid solution properties by looking at the ^{2}H-NMR of aqueous solutions of sodium 7-^{2}H-cholate at 23°. Because of instrument limitation, line widths were used to approximate T_2s. Since the aggregates observed were small, the assumption was made that the motional narrowing condition applied, i.e. $T_1 = T_2$. This is probably as good a system in which to use line widths as one is apt to find since the experimental values ranged from 50-200 Hz, and perdeuteroacetone was routinely found to be about 1.5 Hz. We were able to get a set of good ^{13}C T_1 values for 0.2M NaC and found these to compare very favorably with the ^{2}H-line width determined value (± 2%, $T_1(^2H) = T_1(^{13}C-H/15.6)$).

On the graph below, reciprocal T_1s are plotted vs viscosity. Applying the usual Stokes-Einstein approximation, one calculates at 0.01M the bile salt is monomeric. There is a linear change up to the viscosity corresponding to a 0.1M solution where an inflection point is found. At this point the cholate is in the form of a tetramer. The linear behavior with increasing cholate concentration corresponds to a monomer-tetramer equilibrium. Above this point, more complex behavior is observed as secondary micelles of higher aggregation numbers begin to form. No doubt also, we are getting above the region where this simple approach is valid.

Temperature studies up to 70° show that the tetramers present in a 0.1M solution preserve themselves. The change in relaxation time is entirely accounted for as a change in solution viscosity. This result stands in contrast to an earlier proton study, but there no attempt to account for spectral line widths on the basis of viscosity changes was made.

Yours sincerely,

Bill

W. B. Smith
Chairman/Chemistry Department

Plot of $1/T_1$ as a function of viscosity for aqueous sodium cholate. The error bars indicate $\pm 10\%$ and are not included where crowding of points occurs.
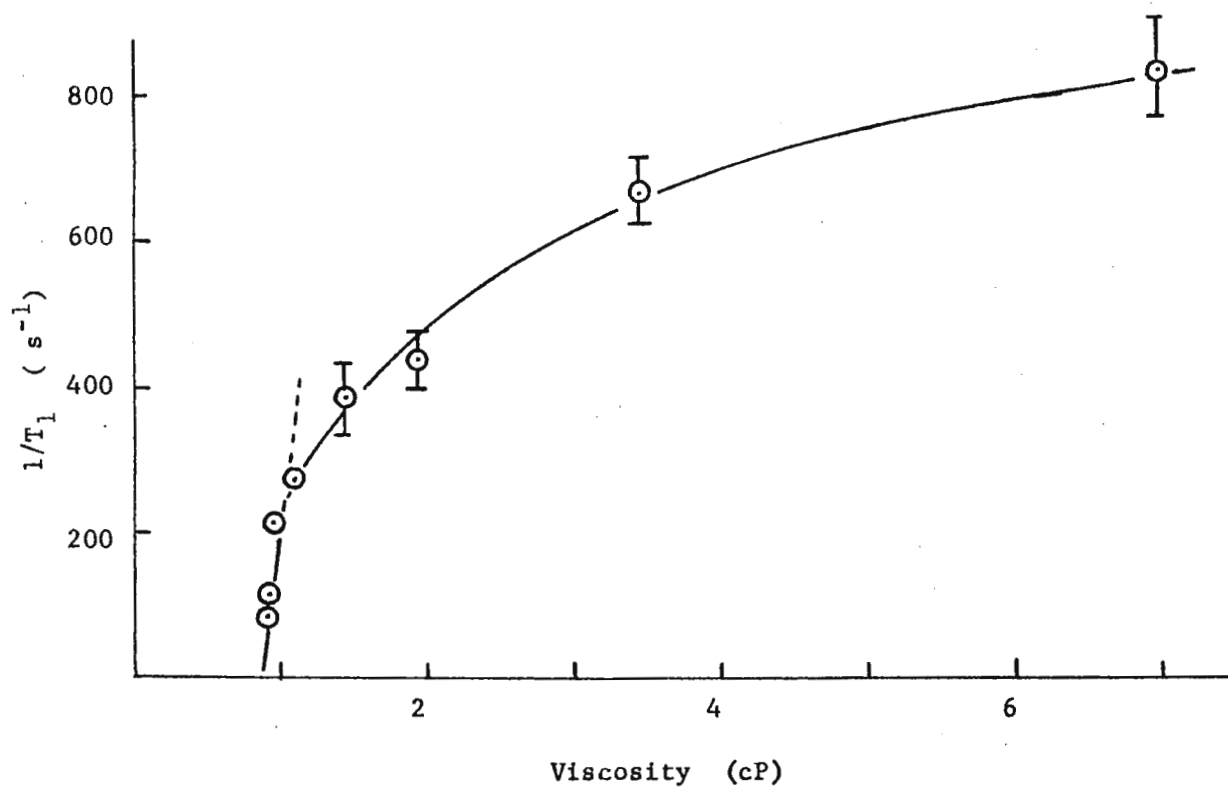
**UNIVERSITY OF
NEW BRUNSWICK**   Post Office Box 4400 \ Fredericton, N.B. \ Canada   E3B 5A3

Physics Department   Telex: 014-46-202
(506) 453-4723

March 27, 1980

Dr. B. L. Shapiro
Department of Chemistry   Five Birds with Two Stones
Texas A & M University
College Station, TX   77843

Dear Barry:

An echo following a single pulse is often an indication
that something is not quite right with the pulse, with the
electronics, or with the spectrometer adjustments. Yet things
can be adjusted to produce not only a single echo after a
single pulse but five echoes with two pulses (and more with
more pulses). An illustration is attached showing a phase -
detected off - resonance 640 msec time scan.

Irradiation is let loose at 1 on the thermally equili-
brated water sample, producing E.T. Jaynes' "λ-cone" precession
about the effective field (Phys. Rev. 98, 1099 (1955) until
the pulse terminates after 90 msec at $\overline{2}$. The free induction
decay follows duly at 3, and the first echo presents itself
at 4. Things seem quiet then until the second pulse (0.5 msec)
strikes at 5, inducing immediately another free decay at 6.
There follow four more echoes at 7, 8, 9 and 10. Echo 9 is
the usual two-pulse Hahn echo of the free induction decay
at 3, and 8 is the echo of echo 4. The mechanism forming
echoes 7 and 10 becomes obvious when the echo at 4 is under-
stood. It was first observed in 1955 by A. Bloom (Phys.
Rev. 98, 1105). His analysis was cast in doubt in 1972
(M.B. Stearns, AIP Conference Proc. 10(2), 1644) but has
since been restored to its original glory by V.P. Chekmarev,
M.I. Kurkin, and S.I. Goloshchapov (Zh. Eksp. Teor. Fiz. 76,
1675 (1979), engl. transl. Sov. Phys. JETP 49(5), 851 (1979).
Our experiments support the Soviet authors' analysis and
point to an amendment in form of the next term of their power
series expansion. We are preparing a more detailed report.

Sincerely yours,

R. Kaiser

RK:seb
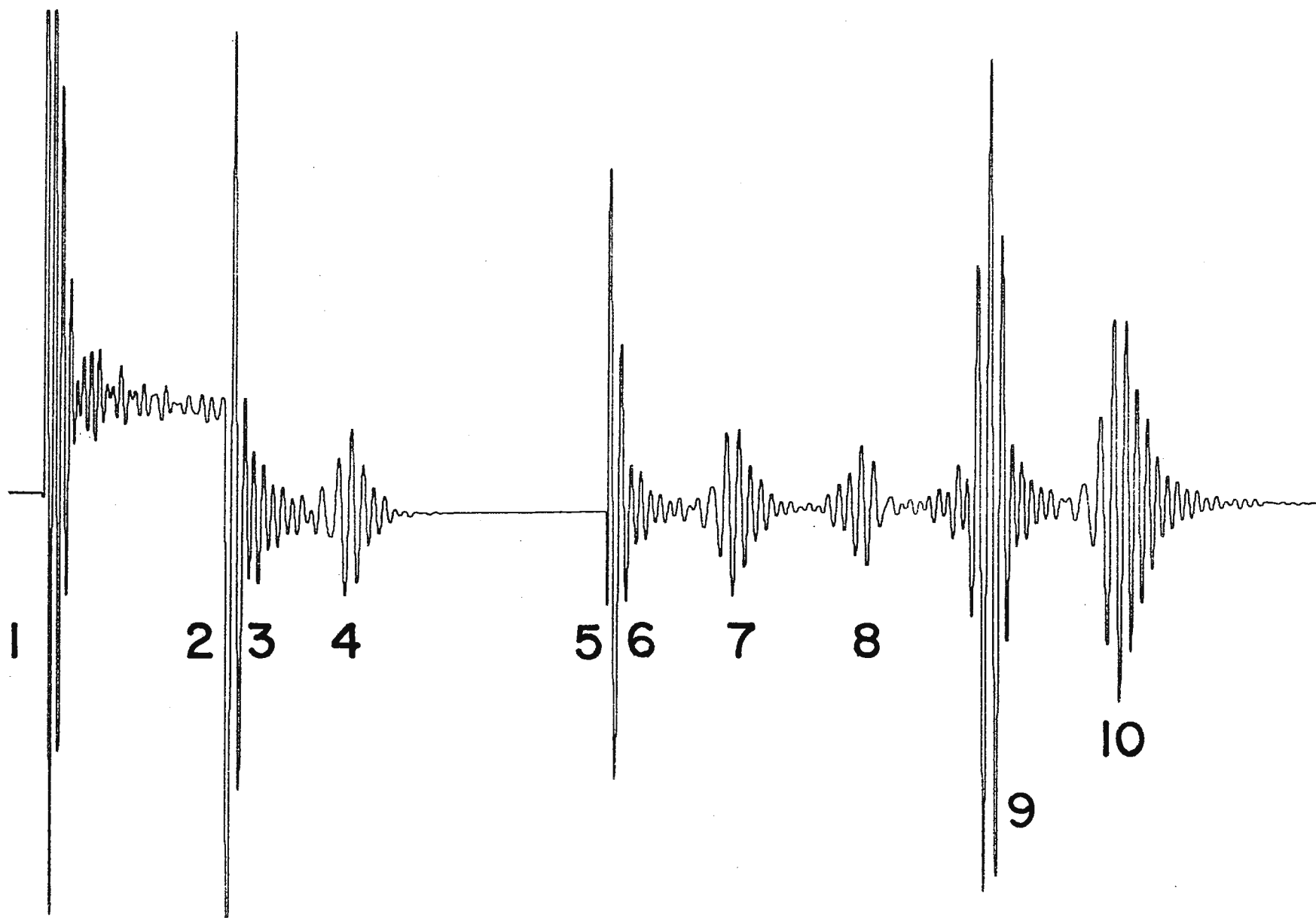
PURDUE
UNIVERSITY DEPARTMENT OF CHEMISTRY
March 31, 1980

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

Decouplers, Variable Temperature and Chemical Shifts

Dear Barry,

A few of your readers may be interested in some recent experience we have had with the influence of decoupling on variable temperature studies. The work was carried out on the Nicolet-360 in the Purdue Biological Magnetic Resonance Laboratory supported by NIH. Dr. Bob Peoples and Mr. John Kozlowski made the critical observations and did all the hard work.

We have been studying the pyramidal inversion in 7-phenylnorbornyl lithium in THF by carbon line broadening. Accurate temperature measurement is important to such work and we simply repeat Binsch's plea for the instrument manufacturers to design a well thermostatted probe with reproducible temperature control. Temperature measurement was made via the carbon thermometer of Led and Petersen - J. Mag. Res., 32, 1 (1978) and the internal thermocouple of the instrument. With the acetone/carbon tetrachloride in a coaxial 8 mm tube and the sample in the annulus of the 12 mm tube the following observations were made.

Decoupler (Watts)	Sample	Temp (thermocouple)	Temp (carbon)
off	THF	-68	-80
on (13)	THF	-65	-70
on (13.5)	LiBr(1M)/THF	-65	-52
off	LiBr(1M)/THF	-35	-43
on (13)	LiBr(1M)/THF	-35	-19

Once again we have made the standard observation that the instrumentally indicated temperature is only marginally related to the actual sample temperature. This should not be taken as a specific Nicolet problem. To our knowledge no instrument manufacturer or research worker has solved this problem. We would be delighted to learn that our knowledge is faulty. Further, the dependence of decoupler heating on ionic strength is again verified for non-aqueous solvents.

A recent improvement in the time constant for the temperature control circuit revealed another difficulty. When the decoupler is switched on there is an instantaneous rise in the indicated temperature. It appears that the thermocouple is acting as an rf sensor in addition to the standard thermal response. The implications for temperature control are obvious and we are working on a solution.

Perhaps a little chemistry may placate some of your more experienced readers who by now must be suffering from a severe case of deja vu. Our studies of 7-phenylnorbornyl lithium have shown that it is pyramidal and the two carbon bridges give separate resonances at -90°. The potassium and cesium salts are dramatically different. The chemical shift changes are much

Chemistry Building
West Lafayette, Indiana 47907

larger than I had anticipated especially at C1 and the meta carbon. We have interpreted this to mean that the anion in the cesium and potassium cases is planar. It is possible, in principle, that a species in a double minimum (pyramidal anion) should have different shifts from a species in a single minimum (planar anion). However we are unaware of an established case where the average chemical shift of two species in rapid equilibration is clearly different from the chemical shift in the symmetrical structure. Again, we would welcome correction on this point.
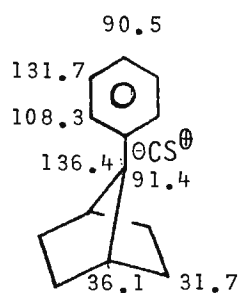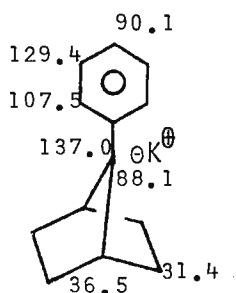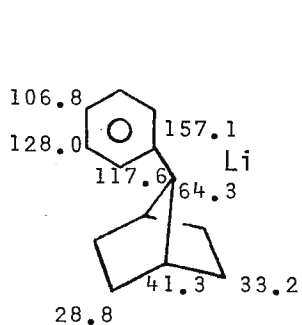
Yours sincerely,

Bob Santini   John Grutzner

BS/JG/gs

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V6T 1W5

DEPARTMENT OF CHEMISTRY

26 February, 1980

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

BIOPHYSICAL POSTDOCTORAL POSITIONS

Dear Barry,

Additional postdoctoral positions will be available in my laboratory, beginning in Summer or Fall, 1980. Salary will be approximately $12,700 per annum. The successful candidate(s) will be expected to participate in at least one of the following areas.

(A) Solution structure of ribosomal RNA. A concerted series of site-selective physical measurements (u.V., c.d., Raman, EPR, and ^1H, ^{19}F, and ^{31}P NMR using departmental 400 MHz and 200 MHz spectrometers) is designed to identify specific secondary and tertiary structural features of 5S RNA and 5.8S RNA from several species. The results will be used to refine the recently proposed "cloverleaf" RNA secondary structure (1,2) that we have been able to adapt to all 70-odd published 5S RNA and 5.8S RNA primary sequences.

(B) Dispersion versus Absorption (DISPA). This new graphical line shape analysis for NMR and EPR spectra appears to offer a simple way to determine the mechanism of line-broadening (e.g., unresolved splittings; multiple relaxation times; chemical exchange) using the data from a single spectrum (3-8). Our on-line, linearized (9) DISPA data reduction will be applied to polymer (RNA; gels), solvent (H_2O in tissues), and ion (^{23}Na) NMR, and also to EPR of spin-labels and coal samples.

(C) Perturbed Angular Correlations (PAC). We have recently reconstituted indium: porphyrins into apomyoglobin, to give a motional probe at the central metal atom of heme proteins (10). Extension to other heme proteins is planned.

1. G. A. Luoma & A. G. Marshall, PNAS 75, 4901 (1978).
2. G. A. Luoma & A. G. Marshall, J. Mol. Biol. 125, 95 (1978).
3,4 A. G. Marshall & D. C. Roe, Anal. Chem. 50, 756, 764 (1978).
5. A. G. Marshall, J. Phys. Chem. 83, 521 (1979).
6. A. G. Marshall & D. C. Roe, J. Magn. Reson. 33, 551 (1979).
7. F. Herring, P. Phillips, A. Marshall, & C. Roe, J. Mag. Res. 37, 0000 (1980).
8. A. G. Marshall & R. E. Bruce, J. Magn. Reson. 38, 0000 (1980).
9. R. E. Bruce & A. G. Marshall, submitted.
10. A. Marshall, K. Lee & P. Martin, J. Amer. Chem. Soc. 102 (5), 0000 (1980).

****

Interested candidates should send a curriculum vitae and three recommendation letters to:

Prof. Alan G. Marshall
Department of Chemistry
University of B.C.
Vancouver, B.C. V6T 1W5 CANADA

UNIVERSIDAD DE BUENOS AIRES
FACULTAD DE CIENCIAS EXACTAS Y NATURALES

Buenos Aires, March 5 1980.-

Prof. B.L. Schapiro
Dept. of Chemistry
Texas A & M University
College Station, Texas 77843
U.S.A.

Looking for a Disk on sale!

Dear Dr. Schapiro:

We are interested in buying a used (but working!)
NIC-294 Disk System, to add to our Nicolet NMR-812 Data System.

Since this comes usually with the Nicolet 1080 or
NMR-8xx data systems, we would eventually consider the purchase
of a whole system: computer, memories, terminals and disk (or disks!)

Perhaps some of your readers is planning to up-date
his system with the purchase of, say, the 1180 and would be interested
in selling the old 1080? Please write to the address given below.

Thank you very much for the space given to this letter.

Yours, sincerely,

V.J. Kowalewski

Address

Dr. V.J. Kowalewski, Professor
Departamento de Física
Facultad de Ciencias Exactas
1428, Buenos Aires-Argentina

TEXAS A&M UNIVERSITY

DEPARTMENT OF CHEMISTRY
COLLEGE STATION, TEXAS 77843

7 April 1980

TAMU NMR NEWSLETTER - BACK ISSUES AVAILABLE

In the twin hopes that some of our readers may wish to make their collection of TAMU NMR Newsletter issues more complete, and also help us with our storage problem, we would like to announce the availability of back issues of the Newsletter as follows:

Issues Available	Prices
Oct. 1978 - Sept. 1979	$50/yr*
Oct. 1977 - Sept. 1978	$40/yr*
1970 - Sept. 1977	$30/yr*

Single issues, as available (no academic or personal discounts):

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The above prices are net U.S. funds. Pre-payment with your order is required. Please make checks payable to Texas A&M University. All prices are post-paid at surface printed matter rates. If you desire first class mail delivery, you will be charged for the extra mailing costs.

The above prices are good until July 1, 1980.

B. L. Shapiro

BLS/ks