Texas A & M University N–M–R Newsletter

No. 199

April, 1975

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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 INSTITUTE

UNIVERSITY OF AARHUS

DEPARTMENT OF ORGANIC CHEMISTRY
HANS JØRGEN JAKOBSEN

8000 Århus C, Denmark March 10, 1975
Telephone (06) 12 46 33   HJJ/EL

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

Dear Professor Shapiro,

^{34}S Induced Isotope Shift in the ^{13}C NMR Spectrum of CS_2.
Selective Population Transfer (SPT) in ^{29}Si FT NMR.

With only a few days left before I shall leave Scandinavia
in order to spend a $\frac{1}{2}$-year sabbatical in NMR labs in the USA
(University of Florida) and Canada (UBC, Vancouver), I send
you this contribution which I hope may be of interest to
some of your readers.

On shimming the 15 inch magnet of our XL-100
spectrometer for optimum resolution using the
12 mm ^{13}C insert and internal deuterium lock
we generally use the $^{13}CS_2$ resonance from a
80% v/v solution of non-enriched CS_2 (99.9%
purity) in acetone-$\underline{d_6}$ as a resolution test.
With this set-up we have found that a sensi-
tive indication of maximum resolution and
best lineshape is the observation of a small
peak on the high-field side of the ordinary
signal (Fig.1). The two peaks have an inten-
sity ratio of about 10:1 and are separated
by 0.009 ± 0.001 ppm (0.22 ± 0.03 Hz). It has
been concluded that this chemical shift dif-
ference is a ^{13}C isotope shift induced by
^{34}S (4.2% natural abundance) and that the small
peak is the spectrum of naturally present
(8.4%) $C^{34}S^{32}S$.

1 Hz
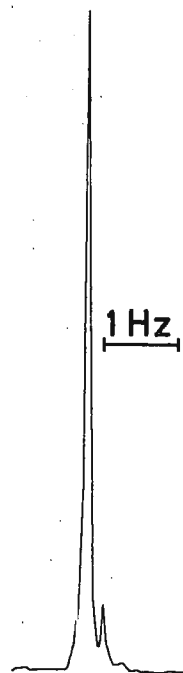
Fig.1. ^{13}C FT NMR spectrum of CS_2 (one
transient; line-width at half-height:
0.08 Hz). The intensity ratio of the
$^{13}C^{32}S_2$ and $^{13}C^{34}S^{32}S$ signals is c.10:1

Fig.1

Finally, we are currently extending the Selective Popu-
lation Transfer (SPT) FT NMR method (i.e., applying selec-
tive π pulses to ^{1}H transitions prior to excitation of the

observed resonances by a strong non-selective $\underline{H}_1$ rf pulse),
described in our latest newsletter (TAMU NMR $\underline{\underline{188}}$, 44) and
elsewhere[1] for sensitivity enhancement and determinations
of signs of coupling constants, to the observation of nuclei
other than ^{13}C. Prompted by the increasing interest in na-
tural abundance ^{29}Si FT NMR and the problem of negative nu-
clear Overhauser enhancements (NOE) for $^{29}Si-\{^1H\}$, we enclose
(Fig.2) some of the SPT FT spectra obtained for this low na-
tural abundance (4.7%) nucleus (J.Amer.Chem.Soc., in press).
Fig.2a shows the intensity enhancements observed in the ^{29}Si
FT NMR spectrum of $(CH_3)_4Si$ (TMS), while Fig.2b shows deter-
mination of the relative signs for some of the couplings in
$[(CH_3)_2SiH]_2O$ (TMDS) from its ^{29}Si FT NMR spectrum using
SPT.

Sincerely yours,

Hans Jørgen Jakobsen   Svend Aage Linde   Rigmor S. Hansen

---

[1] S.Sørensen, R.S.Hansen, and H.J.Jakobsen, J.Magn.Resonance
14, 243 (1974). H.J.Jakobsen, S.Aa.Linde, and S.Sørensen,
J.Magn.Resonance 15, 385 (1974). A.A.Chalmers, K.G.R.Pach-
ler, and P.L.Wessels, J.Magn.Resonance, 15, 415 (1974);
Org.Magn.Resonance, 6, 445 (1974).
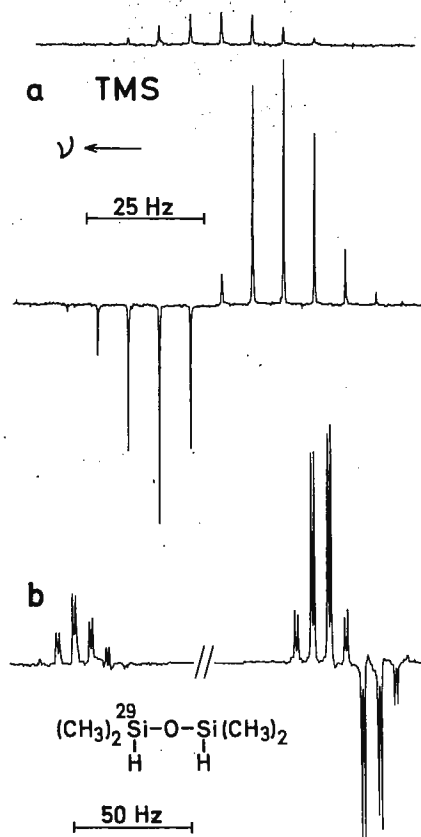
Fig.2

Fig.2. ^{29}Si FT NMR spectra of TMS
(a) and TMDS (b). (a) Upper part:
Normal proton coupled spectrum
($^2J_{Si-H} = 6.62$ Hz); lower part:
SPT spectrum obtained after a SPT
π pulse has been applied to the
high frequency line in the ^1H doub-
let spectrum; $\tau = 1.3$ sec, $\gamma\underline{H}_2/2\pi =$
0.38 Hz. For both spectra acquisi-
tion time: 16 sec, transients: 100,
and otherwise identical experimen-
tal conditions. (b) Relative sign
determination of coupling constants
from the SPT spectrum of TMDS
($|^1J_{Si-H}| = 205.4$ Hz, $|^2J_{Si-H}| =$
7.12 Hz, and $|^3J_{Si-H}| = 1.26$ Hz).
Selective SPT π pulses have been
applied to the lowest frequency
line in the $^{29}Si-CH_3$ satellites in
the ^1H spectrum (doublet of doublets,
$|^2J_{Si-H}| = 7.12$ Hz and $|^3J_{H-H}| = 2.8$
Hz). The spectrum shows that $^3K_{H-H} \times$
$^1K_{Si-H} > 0$ (K_{ij}: reduced coupling con-
stants). $\tau = 1.3$ sec, $\gamma\underline{H}_2/2\pi = 0.38$
Hz, acquisition time: 4 sec, and
transients: 300.
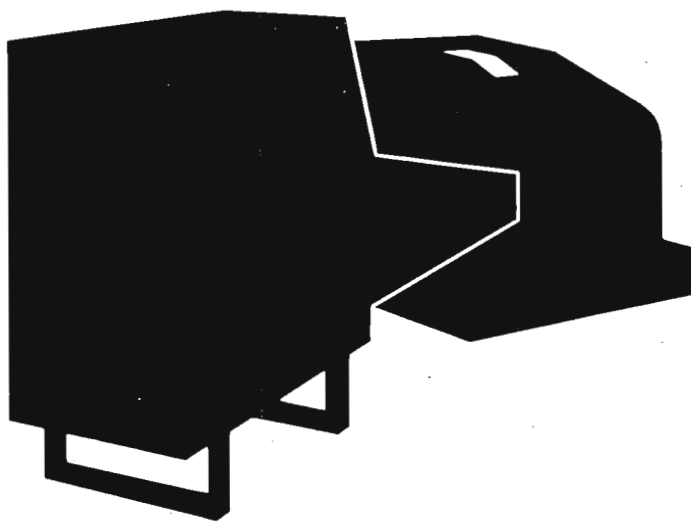
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RESEARCH CENTER | Stauffer | **Stauffer Chemical Company**
CHEMICALS

Dobbs Ferry, New York 10522 / Telephone (Area Code 914) OWens 3-1200

March 10, 1975

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

Dear Barry:

Title: A Bruker Broadband Multinuclear Spectrometer

Within the past month, with a great deal of help from D. Traficante, we have completed the modification of our Bruker HFX-90-Digilab NMR 3S FT system to multinuclei operation a la Traficante and Simms, J. Mag. Res. 15, 484 (1974). Our pleasure over the performance of the system has prompted this letter.

Our original system had FT capabilities for ^{13}C and ^{31}P only and the instigation to investigate the multinuclei approach was fostered by the desire to acquire ^{29}Si capabilities. Since we already had a frequency synthesizer, equipments costs for the extended capability were very little more than those for a single additional nucleus. Being in an industrial environment, another important consideration was the ease of changing from nucleus to nucleus. As you well know, the present "multinuclear" spectrometers, realistically, require the better part of a day to become operational on another nucleus. In our modified system, this changeover is accomplished in 1-2 minutes and the spectrometer is never taken out of lock. Needless to say, this results in very efficient sample through-put.

With the broad-band insert we can cover a frequency range of 6 to 38 MHz, with excellent sensitivity over that range. S/N for ^{13}C of a single 90° pulse of decoupled benzene was 240/1 with no real effort made for maximum field homogeneity. A typical plot of the ^{13}C spectra of benzene vs. pulse width is shown in Figure 1. In addition, the natural abundance ^{2}H spectra of H_2O is shown. Again, this was obtained without any attempt to maximize pulse width, delay, homogeneity, etc., and I am sure is a poor indication of the optimum performance. In an aside, one might comment that the low sensitivity ($< 1/100$ as sensitive as ^{13}C) and large amounts of deuterated solvents available in NMR laboratories require great care to ensure against contamination of a sample. Unfortunately, we discovered this the hard way.

Stauffer Chemical Company

Professor B. L. Shapiro
March 10, 1975

There are a couple of minor differences between our system and
the published one. We gate the 36.4 MHz rather than the 30 MHz
simply because our gated 30MHz was not clean. Also, for ^{31}P operation
only, we use the 36.4-MHz signal from the spectrometer and by-pass the
mixer amplifier (mixer 2, Fig. 2, J. Mag. Res.) since, with the original
approach, we always observed a ^{31}P signal even though no phosphorus was
present. Apparently this was arising from the 72 MHz of the frequency
synthesizer beating against the 36 MHz from the spectrometer. In any
event, the above technique avoids the problem.

Thus, with this modification, we have about 71 nuclei at our
beck and call which should be sufficient for some time to come. We do
hope to use this same approach for ^{19}F and ^{1}H with the narrow-tuned
H & F inserts. However, this does present much more stringent filter-
ing requirements. Please credit this letter to C. K. Tseng's account.

Sincerely yours,

David H. Marr

DHM:bs
Enclosure

Natural Abundance ^2H
in H_2O
1500 pulse
30° tip ∠

FIGURE 1

^{13}C C_6H_6 $\{^1H\}$

199-6
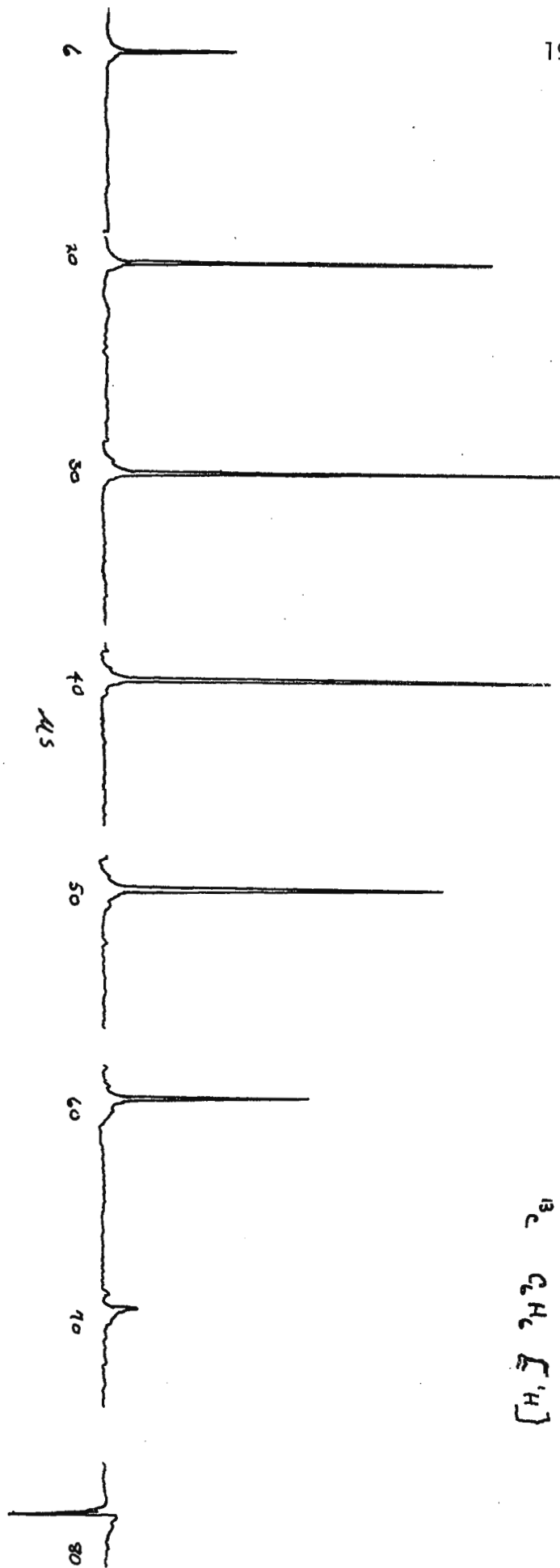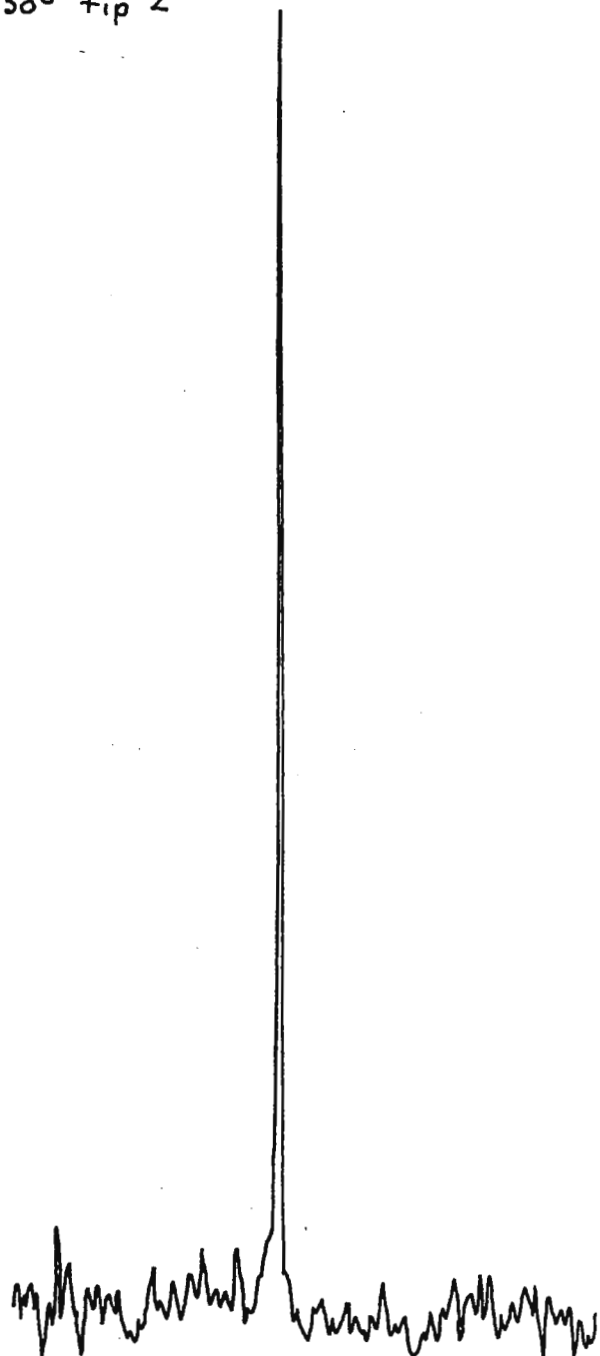
LABORATORIUM VOOR FYSISCHE CHEMIE

Toernooiveld
Nijmegen
Telefoon (080) 55 88 33

FACULTEIT DER WISKUNDE
EN NATUURWETENSCHAPPEN
KATHOLIEKE UNIVERSITEIT
NIJMEGEN, NEDERLAND

Professor Bernard L. Shapiro

Department of Chemistry

Texas A & M University

COLLEGE STATION, Texas 77843

Uw kenmerk	Uw brief van	Ons kenmerk	

Datum March 12, 1975

Onderwerp Fermi contact shifts, observed for solvent ^{13}C
nuclei in solutions of alkali aromatic ion pairs.

Dear Professor Shapiro,

At present we are investigating the ^{13}C NMR spectra of solvents, in the presence of alkali aromatic ion pairs. In the figure the ^{13}C NMR spectra are shown of 1,2-dimethoxyethane (DME), in which 1M neutral biphenyl (Bp) has been dissolved (fig. a) and of DME in the presence of 1M biphenyl mononegative ion (fig. b). As the figure shows the presence of the negative ions causes a considerable shift of the ^{13}C NMR spectrum to low field. The ^{13}C resonance positions of the CH_3 and CH_2 groups are shifted 30.2 and 16.8 p.p.m, respectively, so that the quadruplet of the $^{13}CH_3$ partly overlaps with the triplet of $^{13}CH_2$. The down field shift of the ^{13}C spectrum indicates that a positive spin density resides on the ^{13}C nuclei of the solvent nuclei. This can be brought about by spin polarization effects and/or direct overlap effects of the orbital containing the unpaired electron with the ^{13}C nuclei of the solvent molecule. From our Na NMR experiments on the same system [1] we know that we are dealing with loosely bound ion pairs, in which the Na ion is solvated by DME. This picture favours spin density propagation onto the solvent nuclei, the ^1H nuclei as well as the ^{13}C nuclei. That spin density can be present on the proton nuclei has been demonstrated before on similar systems [2]. For the system discussed here, the averaged contact proton shift of DME at 34^oC is only 1.0 p.p.m to low field (one peak being observed), indicating that the ^{13}C NMR spectra reveal more information about the structure of the ion pairs in solution than the corresponding ^1H spectra.
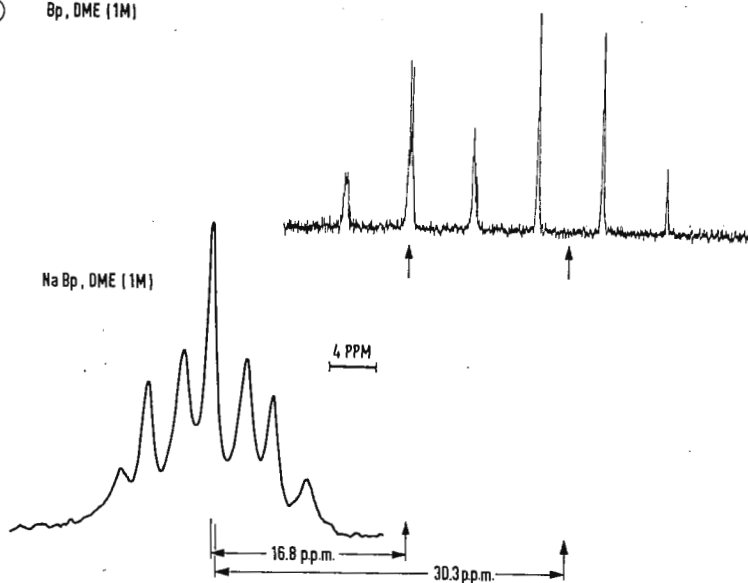
^{13}C NMR spectrum of DME at 38°C

a) in the presence of 1M neutral biphenyl (Bp)

b) in the presence of 1M NaBp

The vertical arrows indicate the resonance positions
of the $^{13}CH_2$ and $^{13}CH_3$ groups.

In a 1M solution of biphenyl mononegative ion in DME free as well as DME molecules bound to the ion pair will be present. Since at 38°C an averaged ^{13}C NMR spectrum is observed for DME (see figure), rapid exchange takes place between bound and free DME molecules. This exchange reaction does not lead to equal contact shifts of the two chemically different ^{13}C nuclei, which points to the presence of well defined ion pair structures.

We are extending our experiments to other solvents and other alkali aromatic ion pairs. In this way we hope to obtain additional information about the structure of the ion pairs in solution, supplementing data from previous alkali NMR experiments, carried out on the same system.

References

[1] G.W. Canters and E. de Boer, Mol. Phys., 27, 1185, 1973; ibid, 27, 665, 1974.

[2] E. de Boer, A.M. Grotens, J. Smid, J. Am. Chem. Soc., 92, 4742, 1970.

E. de Boer   G.P.M. van der Velden   J. van Dongen Torman

UNIVERSITY OF WALES

University College of Swansea

Department of Chemistry

J. H. Purnell M.A. Sc.D.
Professor of Physical Chemistry and
Head of Department.
A. Pelter Ph.D.
Professor of Organic Chemistry.
J. H. Beynon Ph.D. D.Sc. F.R.S.
Royal Society Research Professor.

SINGLETON PARK SWANSEA SA2 8PP
UNITED KINGDOM
TEL SWANSEA (0792) 25678

Professor B. L. Shapiro   13th March 1975
Department of Chemistry
Texas A and M University
College Station, Texas 77843
U.S.A.

Dear Professor Shapiro,

XL 100/620L/disc system performance; ^{13}C nmr study of gem-diol forms of carbohydrate ketone derivatives.

We have recently had installed an XL 100 spectrometer with 620L 16K computer and disc, and although we still have a few teething troubles we are pleased with the system's performance. For example, we have resolved (Fig. 1) lines 6 and 9 (using the numbering of ref 1) in orthodichlorobenzene after an overnight accumulation using an internal deuterium lock, despite an interface fault which caused the loss of some of the FID. We find the automatic storage of an FID on the disc when an accumulation is interrupted an extremely useful facility.

The organic research in this department covers a wide spectrum, and our last newsletter (ref 2) concerned peptides. My own interest is carbohydrates and one of our current projects concerns ketone derivatives (see for example ref 3). The existence of aldulose derivatives in the gem-diol forms is relatively common, and ^{13}C nmr is a very convenient way of studying the equilibria; the carbonyl and quaternary carbons being readily identified in the off-resonance proton decoupled spectra. Compounds 1 and 2 represent aldulose derivatives that exist, in D_2O solution, in gem-diol and ketone forms respectively, and compound 3 (ref 4) exists as an equilibrium mixture with the ketone predominating. The chemical shifts (in ppm) measured from dioxan (as internal reference), which is assigned a value of 67.4 on the TMS scale, are given in paretheses for the carbonyl/gem-diol carbons.

Please credit this subscription to Claude Haigh's account.

Yours sincerely,

J. M. Williams.

1. F.A. Bovey, Nuclear Magnetic Resonance Spectroscopy, Academic Press, 1969, page 123.
2. J.S. Davies, R.J. Thomas, and M.K. Williams, TAMU NMR, 1974, 189, 8.
3. J. F. Batey, C. Bullock, J. Hall, and J.M. Williams, Carbohydrate Research, 1975, 40, in press.
4. G. Hutchinson, unpublished work.

Fig. 1 Spectrum obtained with resolution enhancement and a 32K transform. Measured width: 100 Hz; plotted width: 25 Hz.
Observed spacing = 0.05 Hz.

1

(100·4)

2

(207·5)

3

(213·2)

(95·9)

Dear Professor Shapiro:

REDUCTION OF WATER CONTENT AND ELIMINATION OF THE HYDROCARBON IMPURITY IN CDCl$_3$

Overnight FT accumulations on a third generation spectrometer (XL-100, PFT-100, WH-90) should be sufficient to detect signals from samples in the 5-10 µg range in a 5 mm tube and in 0.3-0.4 ml solvent. At these low levels and extended observation times, even trace contaminants in solvents can produce objectionably large peaks. Deuterochloroform, unless specially processed, shows lines from water and the almost ubiquitous hydrocarbon impurity (i.e., "grease peaks") after relatively few pulses. Since CDCl$_3$ is widely used and is the solvent of choice for many of our metabolite samples, some attention has been given to reducing these extraneous signals to unobtrusive levels.

Much if not all of the hydrocarbon in commercial CDCl$_3$ preparations arises from the polyethylene liner used in screw cap bottles. Purchasing the solvent in sealed glass ampoules and storing in a glass-stoppered vessel effectively eliminates this problem. A polyethylene stopper is to be avoided since it has been demonstrated that hydrocarbon contamination can occur in a short time without direct physical contact between the solution and the polyethylene source.

Attempts to control the size of the water line were initially hampered by desorption of water from the wall of the NMR tube. Since this process is relatively slow, it is not particularly evident in accumulations of an hour or so. For overnight or weekend experiments, however, the increase in area can be substantial. This is illustrated in figures I and II which represent tracings of the same "100%" CDCl$_3$ sample obtained within 20 minutes after introduction into the NMR tube (I) and after 23 hours (II)[a]. A further twofold increase over the 23 hour signal occurred after six days. This problem can be circumvented by preconditioning the NMR tube with D$_2$O. A technique that I found satisfactory is to keep about 1 ml D$_2$O in the NMR tube overnight, decant, wash with a small amount of a polar deuterated solvent (e.g., CD$_3$OD, acetone-d6) to remove most of the residual water, dry briefly with a stream of dry nitrogen and store in a D$_2$O atmosphere. When CDCl$_3$ was examined in a D$_2$O-equilibrated tube, the increase in the water peak over a 20 hour interval was trivial. It follows from this finding that an initial D$_2$O pretreatment of the glass vessel used to store the CDCl$_3$ should also be carried out.

----

[a]Similar increases of the TMS signal were observed occasionally indicating that residual amounts of this species can also be adsorbed on to the glass surface. The effect in our laboratory is probably exaggerated because of the relatively large amounts of TMS required for CW operation of the HA-100 instrument. One might therefore expect that our tubes have close to a maximum sorbed concentration of the standard.

In addition to preconditioning tubes, it is of course important to store the CDCl$_3$ over molecular sieves. Figure I illustrates the level to which the water peak can be reduced with Davison: Grade 514, Type 4A sieves. The sieves were taken directly from the bottle without going through an activation procedure. Further significant reduction can be achieved by a D$_2$O exchange of the residual water in the dried solvent stock. Figure III represents a tracing of "100%" CDCl$_3$ which had been equilibrated with D$_2$O and then dried for two hours over sieves before analysis. Compared with I, the water line has been reduced about two and one-half fold. It is estimated that the residual HDO in the 0.4 ml specimen used in III is less than 5 µg or about 2 µg expressed as the H$_2$O equivalent. Since this operation was not carried out in a dry box there is little reason to suppose that the water content is as low as it is possible to attain. For most applications, however, this level of water is already trivial.

It should be stressed that all of the foregoing measures serve only to minimize the contributions by the solvent and container vessels to the water signal. To minimize the pickup of extraneous water during sample preparation it may be necessary to:

1. D$_2$O equilibrate any glassware used for sample transfer;
2. remove any H$_2$O adsorbed on the sample by drying or D$_2$O exchange;
3. carry out all operations in a dry box.

Byron H. Arison, Ph.D.
Department of Biophysics
Merck Institute for Therapeutic Research
Rahway, New Jersey 07065
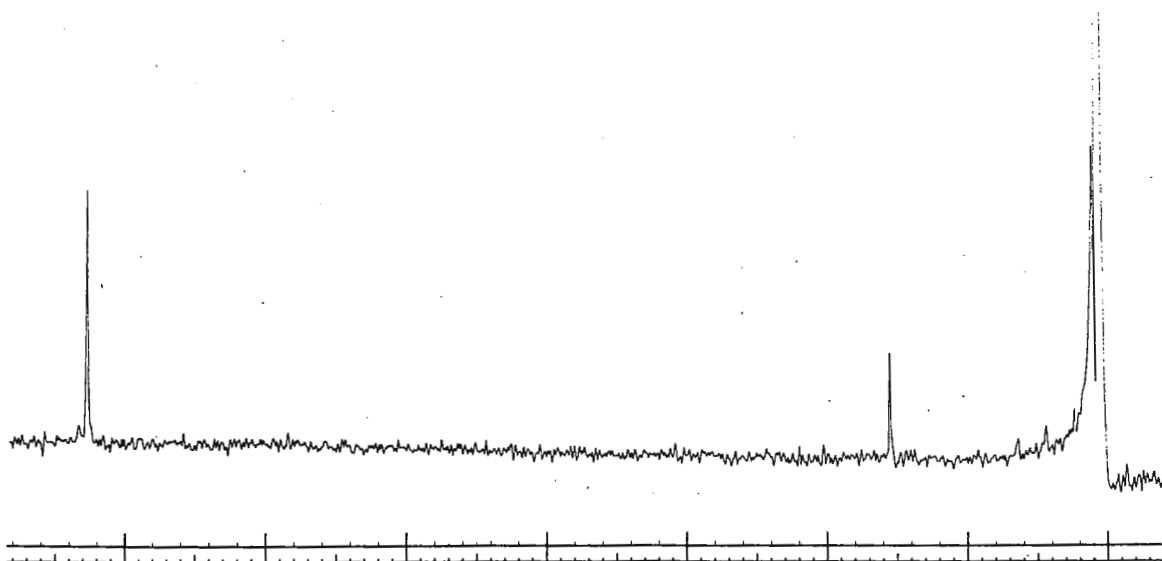
FIGURE I: "100%" CDCl$_3$, sieve dried; 1000 transients; accumulation completed 20 minutes after introduction into NMR tubes.
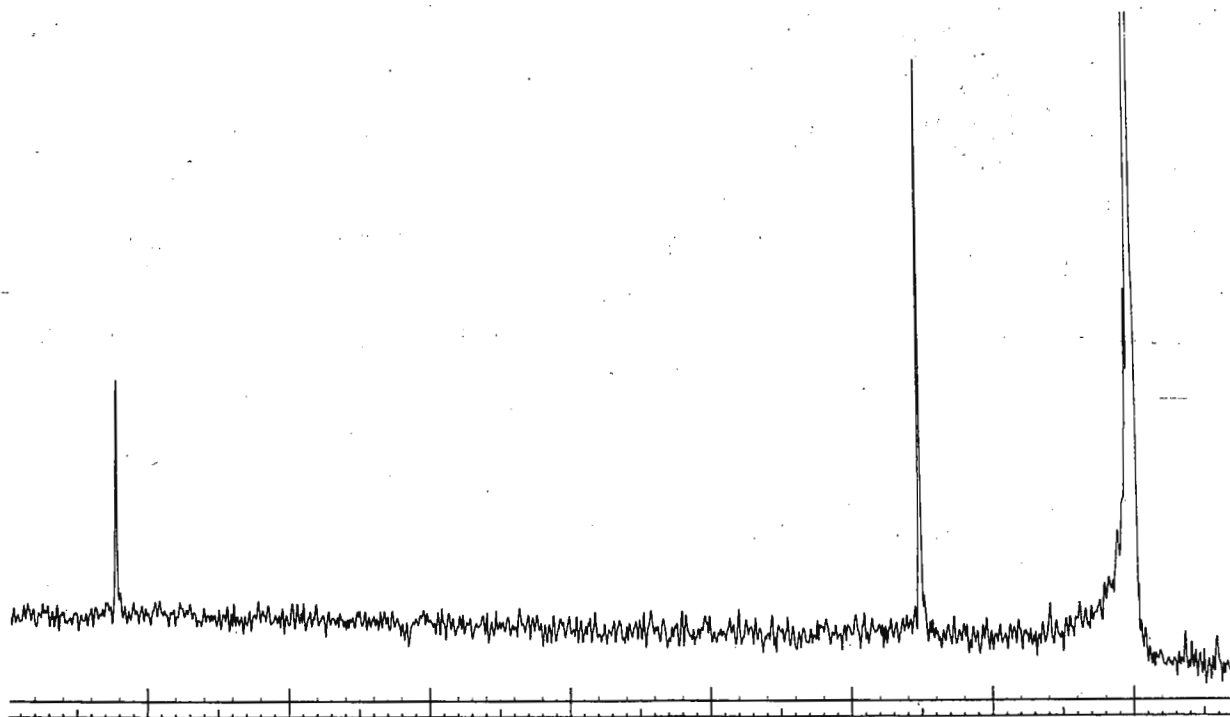
FIGURE II: "100%" CDCl3, sieve dried; 250 transients; accumulation completed
23 hours after introduction into NMR tube.
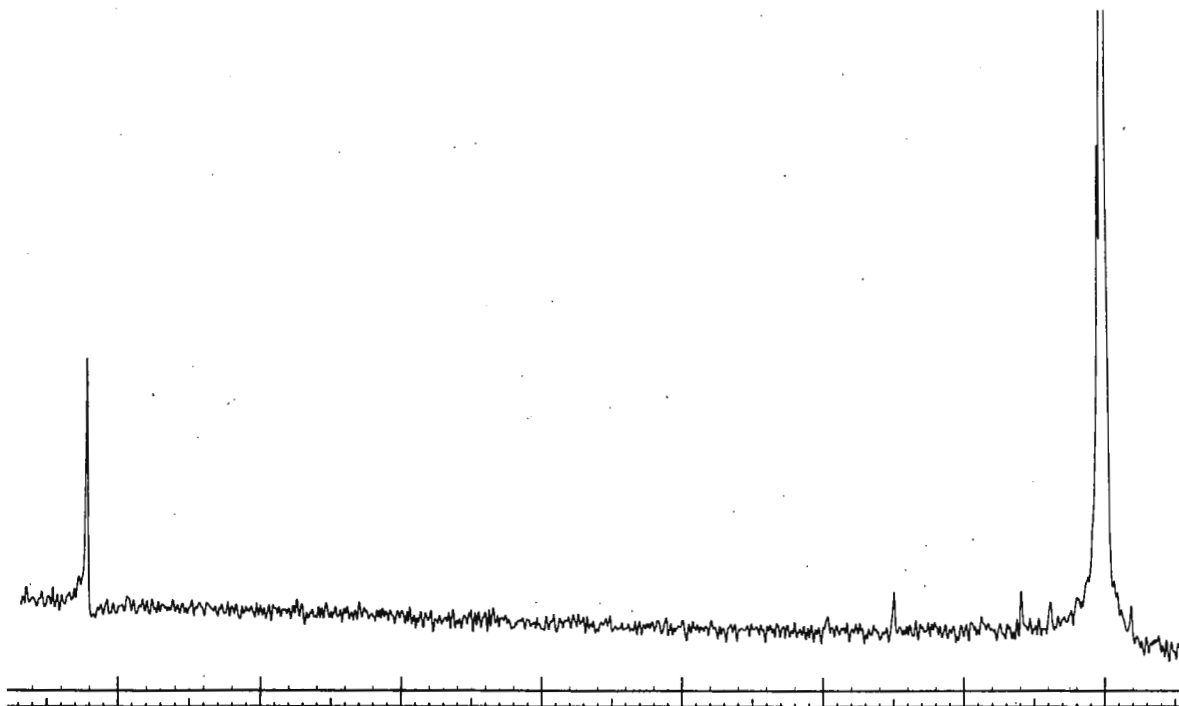
FIGURE III: "100%" CDCl3, D2O equilibrated, sieve dried, 1000 transients.

University
of Strathclyde

Department of Pure and Applied Chemistry

Thomas Graham Building,
295 Cathedral Street, Glasgow G1 1XL Tel: 041-552 4400

17th March, 1975.

Professor Bernard L. Shapiro,
Texas A and M. University,
College of Science,
College Station Texas 77843,
U.S.A.

Dear Barry,

    We have recently installed a JEOL-PS-100-PFT-100 system
and in the process of trying it out we have run ^{13}C spectra
on lunarine hydrate in $CDCl_3-CD_3OH$ and some related compounds.
We were trying to see if T_1 measurements would allow us to
detect any relatively free motion of the spermidine moiety in
the macrocyclic ring.   The preliminary results seem to
indicate that the macrocyclic ring is rigid however.   The
tables show chemical shifts (relative to TMS=0) and T_1's for
all the carbons in lunarine and in spermidine hydrochloride
(II) and spermine hydrochloride (III) (both these in D_2O).

        Kind regards,

                    Yours sincerely,

                    Peter

                    Peter Bladon.

LUNARINE (I)

C	δ	T_1 (sec)	C	δ	T_1 (sec)
1	88.2	0.21	14	110.1	0.18
2	50.8	0.14	15	166.4	3.25
3	209.4	2.54	16	31.2	0.12
4	50.8	0.14	17	27.4	0.13
5	50.8	0.14	18	39.1	0.13
6	50.1	1.94	19	41.8	0.11
7	129.5	2.43	20	26.8	0.13
8	160.8	4.27	21	28.5	0.13
9	120.5	0.19	22	35.5	0.09
10	124.8	0.21	23	166.4	3.25
11	132.8	2.37	24	121.6	0.18
12	132.4	0.18	25	146.3	0.20
13	139.4	0.20			

SPERMIDINE 3HCl (II)

C	δ	T_1 (sec)
1	37.5	2.05
2	24.5	1.55
3	45.4	1.38
4	47.9	1.29
5	23.5	1.59
6	24.7	1.83
7	39.7	1.77.

SPERMINE 4HCl (III)

C	δ	T_1 (sec)
1	37.5	1.67
2	24.5	1.35
3	45.4	1.06
4	47.8	0.75
5	23.5	0.85

$$\overset{+}{H_3N}.\overset{1}{CH_2}.\overset{2}{CH_2}.\overset{3}{CH_2}.\overset{+}{NH_2}.\overset{4}{CH_2}\overset{5}{CH_2}.\overset{6}{CH_2}.\overset{7}{CH_2}\overset{+}{NH_3} \quad 3Cl^-$$

(II)

$$\left[\overset{+}{H_3N}.\overset{1}{CH_2}.\overset{2}{CH_2}\overset{3}{CH_2}\overset{+}{NH_2}.\overset{4}{CH_2}.\overset{5}{CH_2}\right]_2 \quad 4Cl^-$$

(III)

(I)
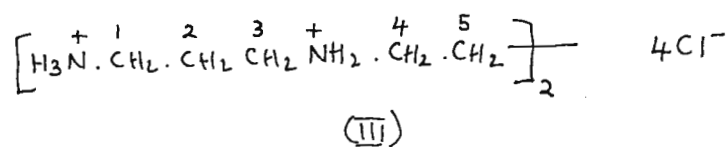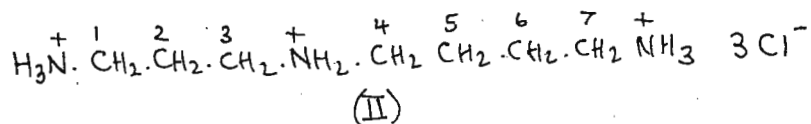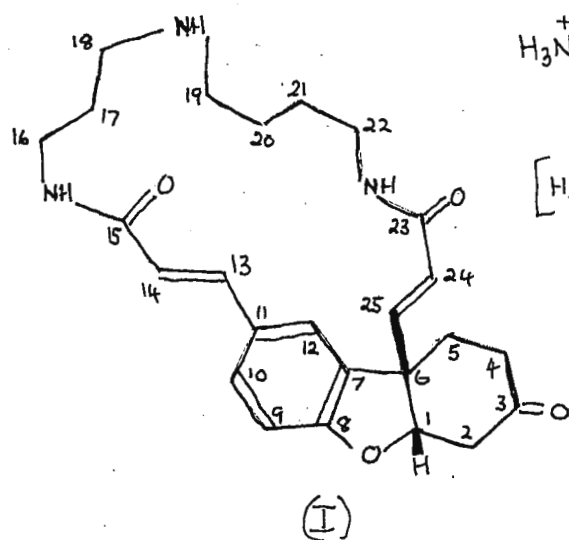
Université de Nancy I

LABORATOIRE

DE CHIMIE THÉORIQUE

Case officielle N° 140 - 54037 NANCY Cedex
Tél. 27.00.24 (Poste 2049 et 2051)

NANCY, le   March 17, 1975
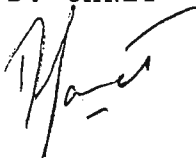
Professor B.L. SHAPIRO
Department of Chemistry
Texas A & M University

COLLEGE STATION, Texas 77843

U.S.A.

Dear Professor Shapiro,
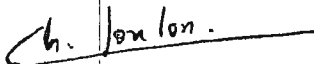
For rare spins (such as oxygen-17 in natural
abundance) investigated by FT NMR, the achievable
S/N ratio is often limited by the computer word
length. Even with computer words containing 20 bits,
saturation is rapidly reached and the final result
may contain too much noise. We have written a program
which obviates this difficulty. When saturation is
reached after n scans, the accumulated interferograms
are normalized to the A/D converter size (in that way
the vertical resolution is not altered). They are then
transferred to a second memory block and the operation
is repeated until a convenient S/N ratio is obtained.
In the second zone, one adds in fact independent inter-
ferograms of which S/N ratio is improved by $\sqrt{n}$, compared
to a single scan. In that way accumulations are carried
out <u>as long as desired</u> (with the <u>same vertical resolution</u>)
and the final S/N ratio is improved by $\sqrt{N}$, N being the
total number of scans. This program is written in assembly
language and runs on a Nicolet 1080 which is interfaced
to a Bruker HX.90. The figure shows a typical example of
results obtained in this way (the experiment lasted about
three hours).

Yours sincerely,

D. CANET   C. GOULON-GINET   J.P. MARCHAL

2500Hz
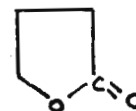
Natural abundance ^{17}O spectrum of γ-Butyrolactone   (370,000 scans)

SYNTEX RESEARCH
DIVISION OF SYNTEX CORPORATION
3401 HILLVIEW AVENUE
PALO ALTO, CALIFORNIA 94304

14 March 1975
AR/616

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

Single Frequency $^{13}C-\{^1H\}$ Decoupling in Aromatic Systems

Dear Barry:

I recently had the opportunity to measure the ^{13}C nmr spectrum of
cyclazine and in order to confirm the assignments a number of single
frequency decoupling experiments were carried out. I find this
technique quite useful especially for carbohydrates (on which more
will be said later) and usually no difficulties are encountered.
In this case, however, the ^1H chemical shifts were determined from
a spectrum measured several years ago on a relatively dilute solu-
tion (approximately 20 mg/ml) while the ^{13}C spectrum was measured on
a more concentrated solution (1 gm/ml) and consequently the single
frequency decoupling would not work. The ^1H spectrum was remeasured
on the same solution used for the ^{13}C nmr spectrum and with the re-
vised ^1H chemical shifts, the ^{13}C chemical shift assignments were
confirmed without further problems.

We have subsequently used this technique on a number of aromatic
systems and noted a considerable concentration dependence on the ^1H
chemical shifts which could easily lead to errors in assignments. As
a consequence of these observations, all samples on which this
technique is to be used have both the ^1H and ^{13}C spectra measured on
the same solution. Some data for cyclazine are listed in the Table.

Sincerely yours,

Michael L. Maddox, Ph.D.
Staff Researcher
Institute of Organic Chemistry

MLM:lo

Attachment

CHEMICAL SHIFTS OF CYCALZINE						
	1,4	2,3	5,7	6	2a	4a,7a
^{1}H dilute	7.31	7.62	7.97	7.71		---
^{1}H conc.	7.10	7.43	7.63	7.32		
^{13}C conc.	110.01	117.18	112.59	119.83	126.75	130.16
$^1J_{C-H}$	173.9	171.7	165.4	161.2		
$^3J_{C-H}$	4.7	4.6	7.5		8.3	8.3 3.8
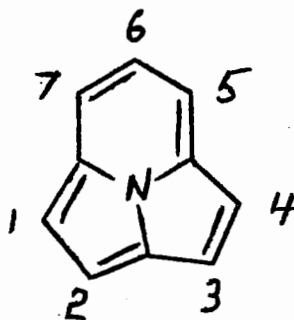
Stingy

Fisher Deuterated Solvents have such outstanding isotopic and chemical purity, it's against their nature to make NMR spectrum contributions.

The stingiest Fisher Deuterated Solvents have an unsurpassed 100.0 atom % deuterium — ideal for critical NMR work. Not one atom of hydrogen is present to alter your spectrum. Seven commonly-used solvents are Fisher one-hundred-percenters: Acetone-d6, Benzene-d6, Chloroform-d, Deuterium Chloride (20% solution in D_2O), Deuterium Oxide, Methyl Sulfoxide-d6, and Pyridine-d5. Their exceptional purity eliminates masking even in the most sensitive Fourier Transform systems.

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Fisher Deuterated Solvents, the stingy ones, are available at your local Fisher branch. Delivery, within days.

Fisher Scientific Company

Department of Chemistry   The Florida State University
                                Tallahassee, Florida 32306

-March 12, 1975

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

   Title: "Postdoctoral Position Available; Biophysical NMR Spectroscopy'

Dear Barry:

Sufficient research funds have appeared to allow me to take on one
additional postdoctoral fellow this next year. The research area
will include physical and biophysical multi-nuclei nmr work on both
our Bruker HFX-90 and HX-270 spectrometers. Experience in nmr in-
strumentation design considerations is helpful but not required.

Our current instrumentation at FSU is quite versatile, having two
field (21 and 63 kilogauss) capability for ^{13}C and ^{1}H Fourier trans-
form or cw nmr. Each instrument is interfaced to a versatile Nicolet
1080 series computer with a disc-augmented memory. Equipment is being
assembled to change over the HFX-90 to a frequency-synthesizer based
FT spectrometer. Our instrument development program is supported by
excellent machine and glass shops, etc.

The research programs in my group at present are largely in the area
of molecular dynamics and ^{13}C relaxation. New efforts are starting
in the areas of interactions between small molecules and complex bio-
logical systems, in electron-nuclear relaxation, and in studies of
liquid structure.

The research is largely interdisciplinary and the fellow will interact
closely with the other members of my group. This position is available
any time after July 1st. The initial stipend will be $7800-$9000 per
year depending on qualifications. Appointment for a second year is
available by mutual agreement.

Interested persiblings[1] should write to me. They should also have one
or two letters of recommendation forwarded to me.

Sincerely,

George C. Levy
Associate Professor

[1]It has been pointed out that the word persons is still inherently sexist

HARVARD UNIVERSITY

DEPARTMENT OF CHEMISTRY

12 Oxford Street
Cambridge, Massachusetts 02138
U.S.A.

March 5, 1975

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

Dear Barry,

The Department of Chemistry at Harvard University is looking for a Manager to take charge of its magnetic resonance facilities. Qualifications for the position include a M.Sc. or Ph.D. in Chemistry with expertise and experience in high resolution NMR, facility with NMR and ESR instrumentation, electronics and computer programming, and knowledge of chemical and physical applications of NMR and ESR. The level of expertise should be sufficient to qualify the candidate for appointment as a Senior Research Associate at Harvard University.

The duties consist of responsibility for the operation and maintenance of the NMR and ESR facilities in the Chemistry Department including consultation with qualified users in the design and execution of experiments, training and supervision of users, and supervision of instrument operation and maintenance. It is expected that the manager will be involved in collaborative work with members of the department on special research problems including instrument development. The equipment consists of an A-60, T-60, HA-100(FT), XL-100, V-4300 ESR and new CFT-80 NMR and E9 ESR spectrometers arriving this year. Also there is an Electronics Technician who works only on NMR equipment.

The salary will be commensurate with the applicant's experience. Harvard is an Equal Opportunity Employer.

Interested persons should send a copy of their resume to

Brian D. Sykes, Chairman of Instrument Committee
Department of Chemistry
Harvard University
Cambridge, Massachusetts   02138

Yours sincerely,

Brian D. Sykes
Associate Professor of Chemistry

Universität Regensburg
FACHBEREICH CHEMIE
Albrecht Mannschreck

8400 REGENSBURG,
Universitätsstraße 31 — Postfach
Telefon (0941) 9431

943 2186

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

Configuration of Open-Chain Compounds RCHD-CDMe-COX
via Different Lanthanide Shifts of Diastereotopic Protons. ——
Postdoctoral Position

Dear Professor Shapiro,

we have studied the <u>configuration of open-chain compounds</u> in collaboration[1] with *V. Jonas* and *T. Burgemeister*, the samples originating from *H. Simon*, Technische Universität München. He sent us one (optically active) stereoisomer $\underline{1}$ of $H_5C_6C^3HD\text{-}C^2DMe\text{-}C^1ONH_2$. Its configuration at C^2 was known to be ($\underline{R}$), the C^3 configuration was of interest. The latter can be determined by comparison with the racemate $\underline{\underline{2}}$ of $H_5C_6CH_AH_B\text{-}CHMe\text{-}CONH_2$: Assignment of the shifts of H_A and H_B in $\underline{\underline{2}}$) steric positions would solve the problem[2]. (to

	R	$\bar{\delta}(H_A)$	$\bar{\delta}(H_B)$	$\bar{\delta}(Me)$
Unknown stereoisomer $\underline{1}$ of	0	2.97	–	1.18,s
$H_5C_6CH_AD\text{-}CDMe\text{-}CONH_2$	o.248	5.20,s	–	2.45,s
Racemate $\underline{\underline{2}}$ of	0	3.2-2.6,complex abs.		1.17,d
$H_5C_6CH_AH_B\text{-}CHMe\text{-}CONH_2$	0.250	5.25,dd	4.41,dd	2.50,d

$$R = \left[Eu(fod)_3\right]/\left[amide\right], \; CDCl_3, \; 35^o$$

In **2** one of the methylene protons, i.e. the one named H_A, is shifted much more by Eu(fod)$_3$ than H_B (table). From the Newman projections of **2** (only the (R) enantiomer being shown), it is seen that H_A and H_B in conformation (R)-**2c** must be shifted very similarly. On the other hand, (R)-**2a** will be populated more than (R)-**2b** which suffers unfavourable non-bonding interactions[3]. In conformation (R)-**2a**, however, one of the methylene protons is situated more closely to the europium atom. Accordingly, this proton has to be named H_A in the Newman projections, which means that the shifts of H_A and H_B in **2** are assigned to steric positions [4,5].
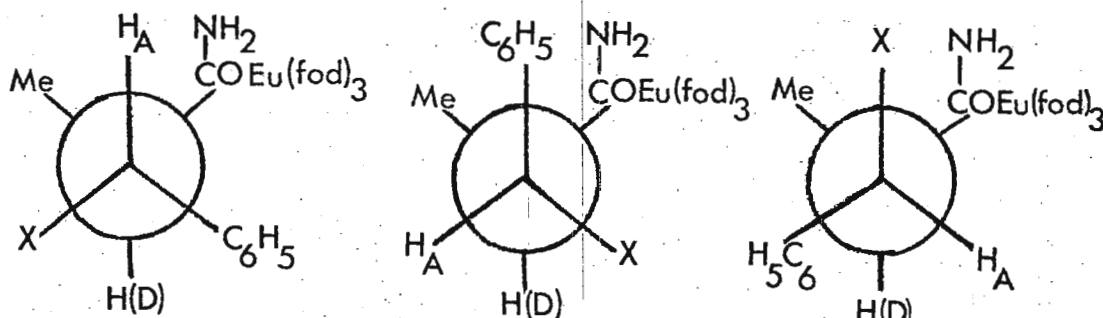
X = D :	**1a**	**1b**	**1c**
X = H_B :	(R)-**2a**	(R)-**2b**	(R)-**2c**

Concerning **1**, the table proves that it is obtained by formal replacement of H_B, not H_A, in **2** by deuterium. Therefore, since the configuration at C^2 of **1** was known to be (R), its C^3 configuration is as shown in the Newman projections, i.e. (R), too.

A similar procedure yielded the configuration of a stereo-isomer of MeCHD-CDMe-COOH. This method should be a general one for assigning diastereotopic groups (and for determining the corresponding configurations) provided one knows, which conformation out of two preponderates.

A <u>postdoctoral position</u> in our group has to be filled. The holder of this position should mainly do research in the field of chiral association complexes[6]. Anyone interested should write to me.

Moreover, we are continuing our work on non-planar butadienes[7] and on intramolecular migrations[8], including some ^{13}C measurements. We have some access to an XL-100 spectrometer (CW, FT; ^{1}H, ^{13}C) and have just received a WH-90 machine (FT; ^{1}H, ^{13}C) of our own.

Sincerely yours,

Albrecht Mannschreck

Albrecht Mannschreck

---

1) Forthcoming publication; preprints available.

2) This problem cannot be solved by looking at the averaged vicinal coupling constants because $H_5C_6CH_AH_B-CH_CMe-CONH_2$ (2), in the presence of $Eu(fod)_3$, showed $^3J_{AC} \approx {}^3J_{BC} \approx 7$ Hz.

3) This assumption is supported by results for similar systems[4].

4) Cf.G.E. Wright, Tetrahedron Lett. 1973, 1097.

5) Cf. V.F. Bystrov, S.L. Portnova, T.A. Balashova, S.A. Koz'min, Yu.D. Gavrilov, and V.A. Afanas'ev, Pure Appl.Chem. 36, 19 (1973).

6) A.Mannschreck, V.Jonas, and B.Kolb, Angew.Chem. 85, 994 (1973); Angew.Chem.Int.Ed.Engl. 12, 909 (1973), and references cited therein.

7) A.Mannschreck, V.Jonas, H.-O.Boedecker, H.-L.Elbe, and G.Köbrich, Tetrahedron Lett. 1974, 2153.

8) A.Mannschreck, H.Dvořák, and T.Burgemeister, TAMUNN 187, 5 (1974).

PURDUE UNIVERSITY
DEPARTMENT OF CHEMISTRY
CHEMISTRY BUILDING
WEST LAFAYETTE, INDIANA 47907

March 18, 1975

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

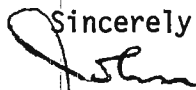Title: Insertion of a ^{13}C-labeled Amino Acid into a Protein by Reverse Proteolysis

Dear Barry:

Isotopic substitution appears to be the cleanest method of simplifying nmr spectra of proteins for the purposes of resolving nuclei of interest or making definite assignments. One can, of course, add a nuclear or electronic spin label by chemical modification, but in doing so it is difficult to determine the extent to which the system under study may have been perturbed. Isotopic substitution into native protein structures should produce the minimum disturbance. Previously this has been done by feeding isotopically labeled amino acids to micro organisms which incorporate the label into proteins of interest[1-4] or by peptide synthesis.[5] The latter approach has been confined to short peptides incorporated into a semi-synthetic enzyme composed of two non-covalently bound peptides.

We present here a new approach to protein labeling for nmr spectroscopy based on the manipulation of equilibria of reactions catalyzed by proteolytic enzymes. The basic idea was developed by Robert W. Sealock and Michael Laskowski, Jr.,[6] who changed an internal residue of the protein soybean trypsin inhibitor from L-arginine to L-lysine. What we have done is to remove the internal L-arginine and replace it with a synthetic ^{13}C-L-arginine with the ^{13}C-label in the guanidino carbon. The unzipping of the protein by the two proteolytic enzymes trypsin and carboxypeptidase B and the zipping-up catalyzed by the same enzymes is illustrated in Figure 1. The loose ends are held together conveniently by a disulfide bridge. Normally the proteolytic equilibria greatly favor the middle form with the maximum number of bonds cleaved. The zipping-up steps are driven along by removing the product of the reaction (resynthesized trypsin inhibitor) by binding it to excess trypsin, which can be removed subsequently in a fast step that does not allow unzipping.

^{13}C-nmr spectra of unlabeled and labeled soybean trypsin inhibitor are shown in Figure 2. The pulse Fourier transform spectra were obtained at 25 MHz using 50 mg of protein in a 5 mm tube. 32,250 pulses were accumulated with a repeat time of 2 sec. The relaxation time for the peak is consistent with our understanding that arginine-63 is a freely-rotating surface residue. Its chemical shift is identical (within experimental error) to that of free arginine.

Sincerely yours,

John L. Markley
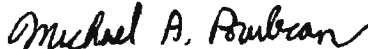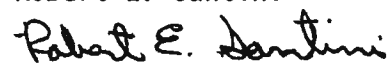
Mary E. Welch

Michael A. Porubcan

Robert E. Santini

Michael Laskowski, Jr.

Professor B. L. Shapiro
March 18, 1975

References:

[1] H. L. Crespi, R. M. Rosenberg, and J. J. Katz, Science 161, 795 (1968).

[2] J. L. Markley, I. Putter, and O. Jardetzky, Science 161, 1249 (1968).

[3] D. T. Browne, G. L. Kenyon, E. L. Packer, H. Sternlicht, and D. M. Wilson, J. Am. Chem. Soc. 95, 1316 (1973).

[4] M. W. Hunkapiller, S. H. Smallcombe, D. R. Whitaker, and J. H. Richards, Biochemistry, 12, 4732 (1973).

[5] I. M. Chaiken, J. S. Cohen, and E. A. Sokoloski, J. Am. Chem. Soc. 96, 4703 (1974).

[6] R. W. Sealock and M. Laskowski, Jr., Biochemistry 8, 3703 (1969).

P. S. Please credit this to the Purdue account in Prof. N. Muller's name.

Figure 1

Figure 2

Eidgenössische Technische Hochschule Zürich

Laboratorium für Organische Chemie

CH-8006 Zürich,
Universitätstrasse 16
Tel. (01) 32 62 11

199-30

March 18th, 1975

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

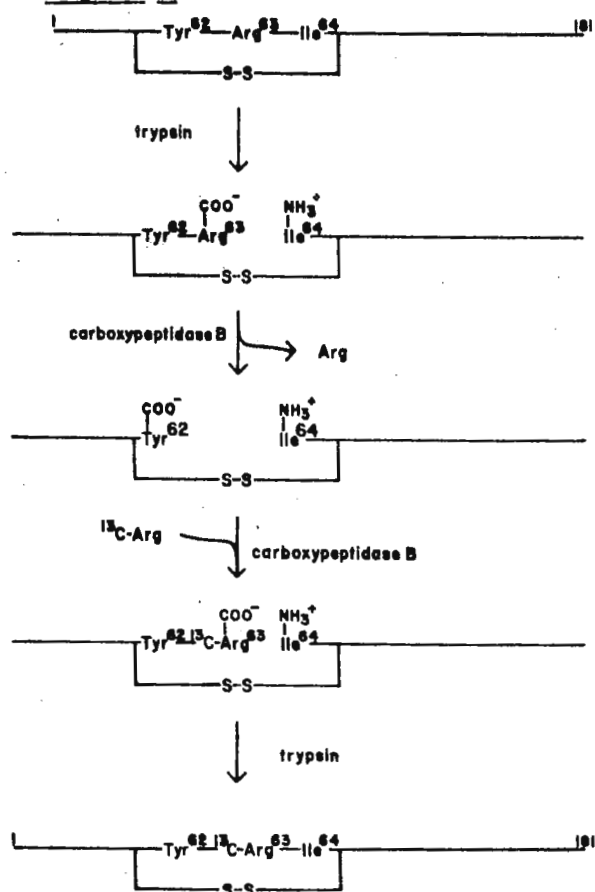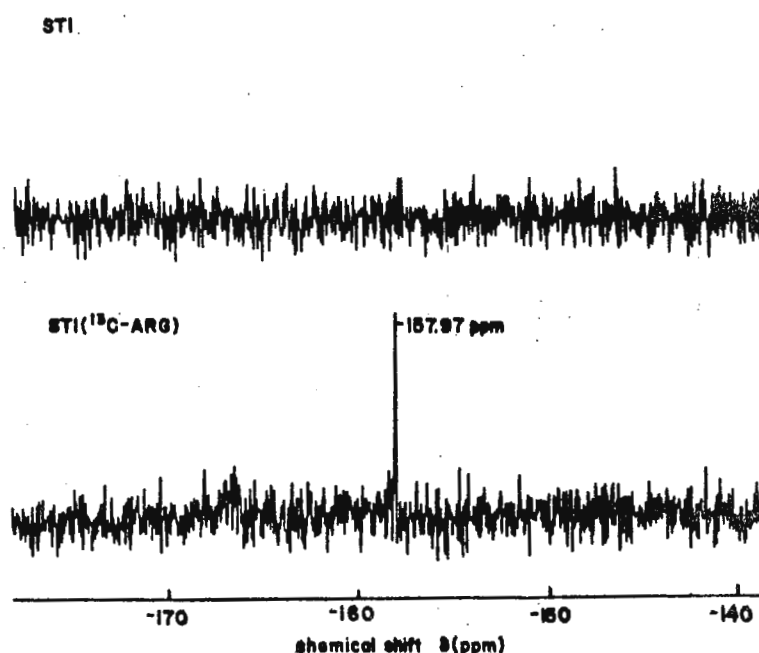Ion Exchange Between Free and Complexed Ionophores

Dear Professor Shapiro,

Some aspects of the design of carriers for alkali and alkaline earth
metal cations are discussed in a paper we submitted for publication
lately [1]. One of the conditions an ion carrier has to fulfill
is that the kinetics of the ion exchange processes involved are
fast or at least comparable with the kinetics of the diffusion
processes of the membrane system [2]. Although at present absolute
quantitative statements in this respect cannot be made, some infor-
mation on the rate of the exchange processes involved may be obtained
by NMR spectroscopy of the corresponding ligands in bulk systems.

In Fig. 1 ^{13}C-NMR spectra of some ligands in mixtures with their com-
plexes are given ($CDCl_3$, 40°C). Since the corresponding signals of
ligand and complex are averaged for the ion carriers in Fig. 1A and
1B the mean life-times of the complex and ligand are much smaller
than about 0.02 sec. In contrast the exchange rate for the macro-
heterobicyclic ligand [3] (Fig. 1C) is considerably smaller (mean
life-time of complex and ligand well above 0.2 sec.). The macrotetro-
lide monactin (an ion carrier antibiotic) shows some line broadening
(Fig. 1D) and therefore represents an intermediate situation.

Yours sincerely,

D. Ammann   R. Büchi   E. Pretsch   W. Simon

[1] E. Pretsch, R. Büchi, D. Ammann and W. Simon, Ringbom Memorial
    Publication, in press.

[2] W. E. Morf, E. Lindner and W. Simon, Anal. Chem., in press.

[3] J. M. Lehn, Structure and Bonding 16, 1 (1973)

38710

Figure 1

^{13}C-NMR Spectra of Some Ion Selective Ligands in Equilibrium with their Preferred Ion Complexes

199-32

~60 % complex (Ba(SCN)₂)   1c

3* 2*

3

2

1*

SCN⁻
(folded)

1

90   80   70   60   50   40   30   20   10   0   PPM

~60 % complex (NH₄SCN)   1D

9,9*

5,5*

4,4*

3* 6*

8*

2*2

7*

7

10*

3

8

10

1*

1

180   160   140   120   100   80   60   40   20   0 PPM
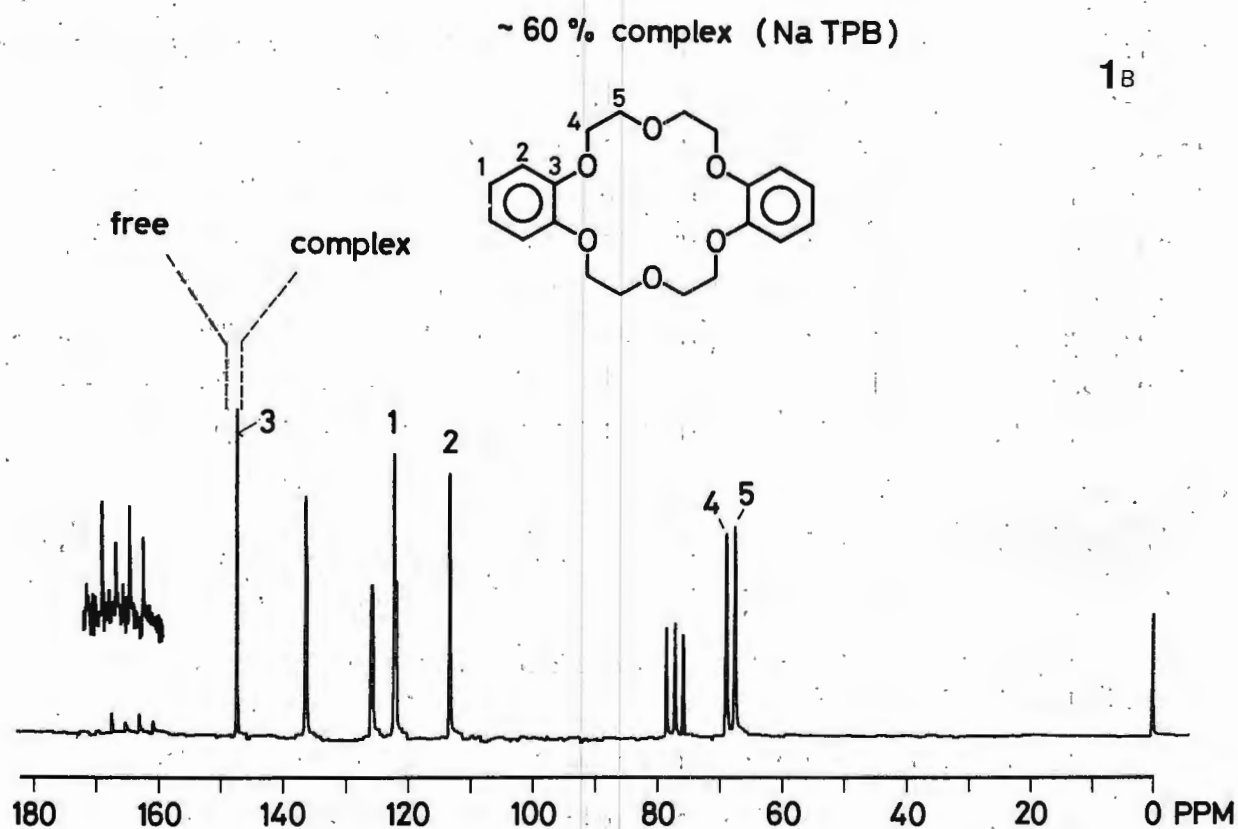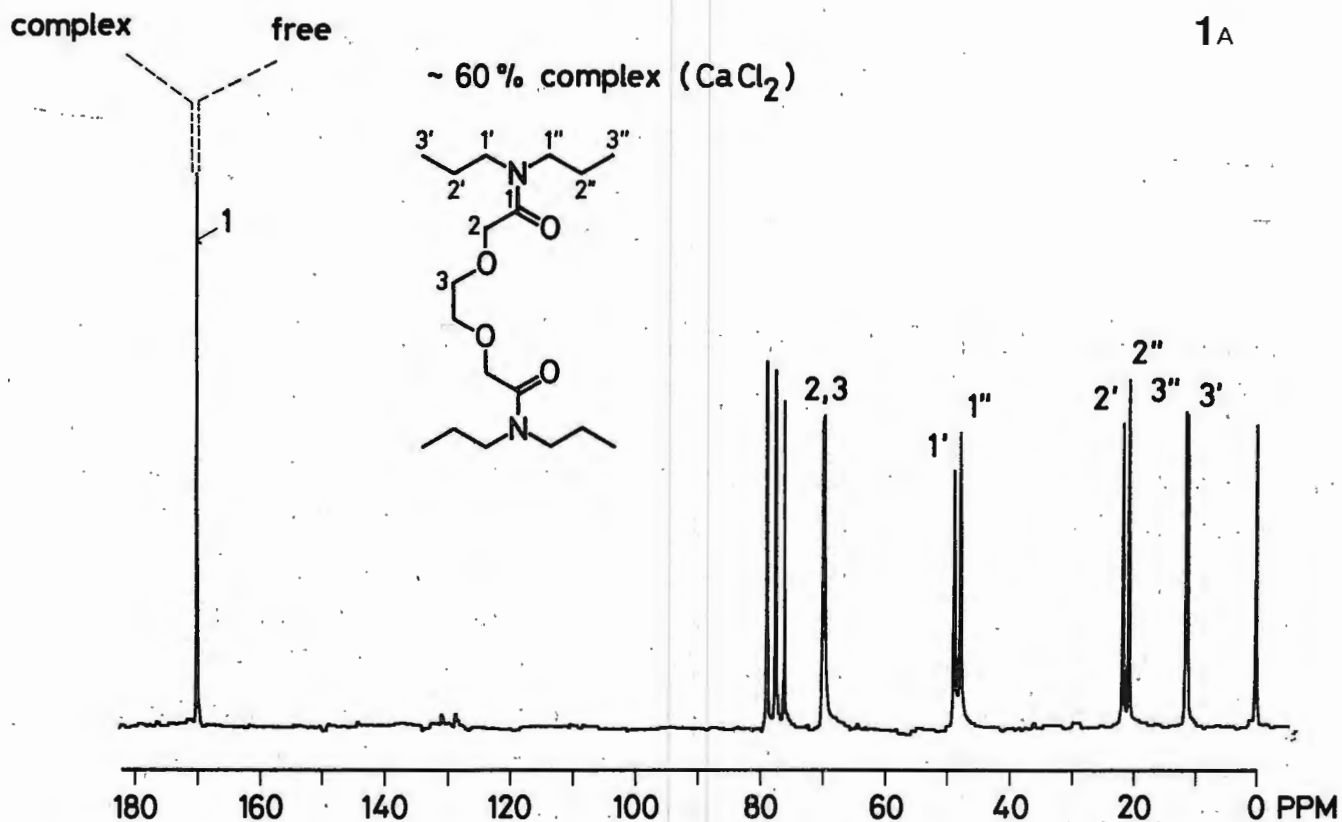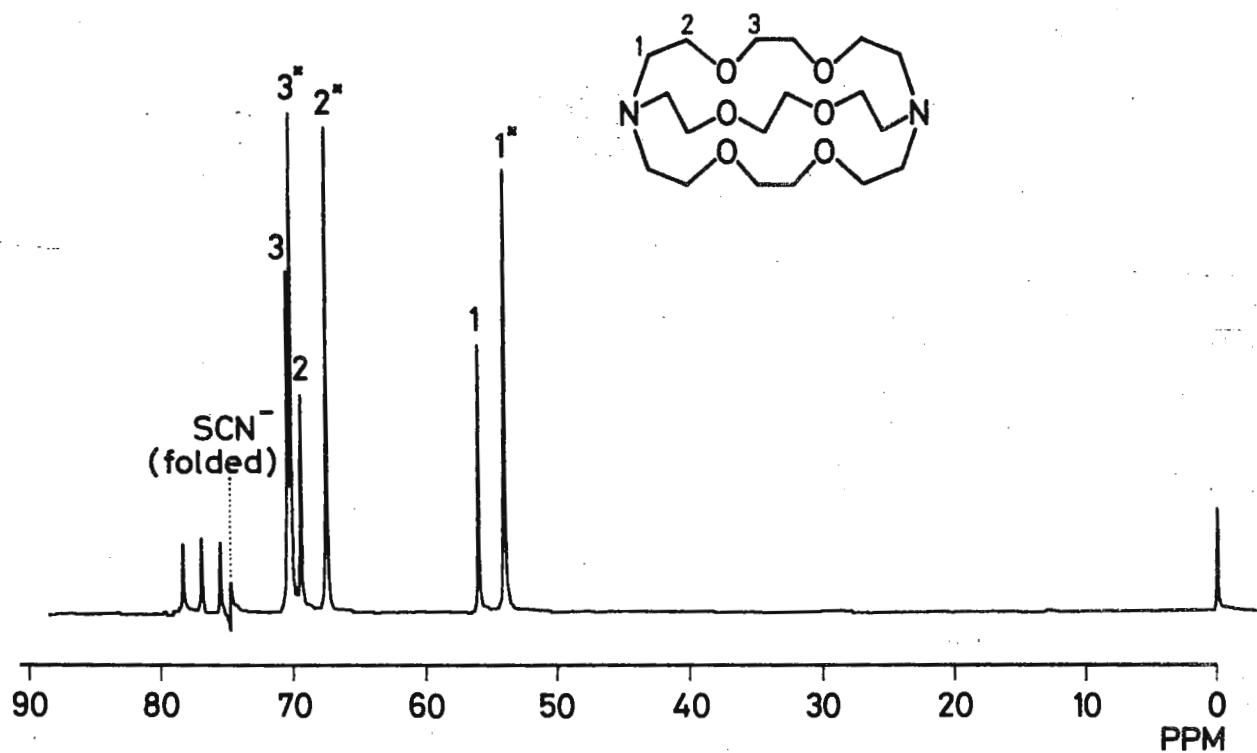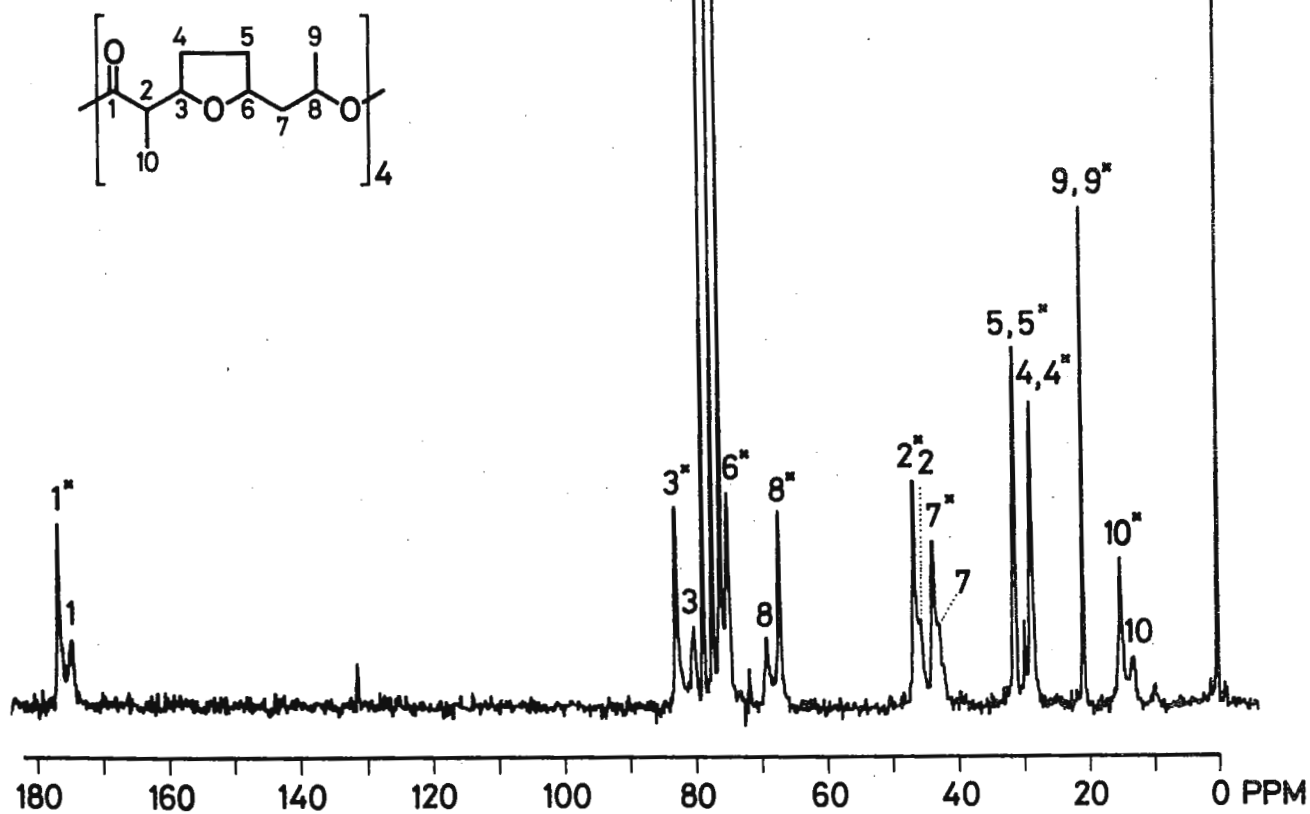
Southern Research Institute

KETTERING-MEYER LABORATORY

2000 NINTH AVENUE SOUTH
BIRMINGHAM, ALABAMA 35205
TELEPHONE 205-323-6592

March 18, 1975

Prof. Bernard L. Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas 77843

Title: ^{13}C NMR Spectra of Isomeric 4-Methylcyclophosphamides

Dear Barry:

Several months ago we obtained the ^{13}C nmr spectra of cis- and trans-isomers of 4-methylcyclophosphamide. They were separated by Dr. R. F. Struck of the Organic Chemistry Research Department of Southern Research Institute. This is the first report that isomers of substituted cyclophosphamides have been obtained separately.
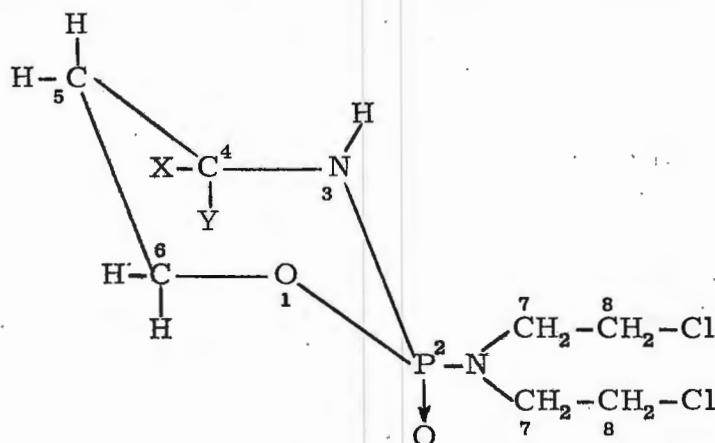
I (trans-)   X = CH$_3$, Y = H
II (cis-)   X = H, Y = CH$_3$
III   X = H, Y = H

Chemical shifts and the appropriate carbon-phosphorus coupling constants are given below for the two 4-methylcyclophosphamides and for cyclophosphamide itself, III. Assignments of the individual peaks were confirmed in all cases by the ^{1}H-coupled spectra.

Prof. Bernard L. Shapiro
March 18, 1975

Southern Research Institute

     The assignment of configuration to the two isomers was based on a consideration of carbon-phosphorus coupling constants. We assumed that the P → O bond is axial, and the bulky bis(2-chloroethyl)amino group equatorial. This has, indeed, been shown to be the case in the solid state for III,[1] and for 4-ketocyclophosphamide[2] and 4-peroxycyclophosphamide.[3] Since an equatorial methyl group at C-4 would be expected to exert a smaller change on the ring bond angles than an axial 4-methyl, we expected the carbon-phosphorus couplings of C-4 and C-5 of the trans-isomer, I, to be more like those of III than the corresponding couplings of the cis-isomer, II, would be. This appears to be substantiated by the data, and the assignments were made.

	Compound					
	I		II		III	
Carbon	δ	$|J_{CP}|$	δ	$|J_{CP}|$	δ	$|J_{CP}|$
4	48.35	2.7	48.44	3.7	41.48	2.4
5	33.53	7.3	33.70	3.7	25.84	6.1
6	66.47	7.3	66.42	7.3	67.78	6.1
7	49.05	4.9	49.19	4.9	48.95	4.9
8	42.21	2.4	42.40	---*	42.33	1.2
CH_3	23.19	7.3	24.11	12.2		

*Not resolved.

     Chemical shifts are in ppm downfield from internal TMS on solutions in $CDCl_3$, and are good to ± 0.02 ppm. $|J_{CP}|$ is in hertz, and is good to ± 0.3 for I and II, ± 0.6 for III.

Sincerely,

Martha C. Thorpe
Senior Chemist

MCT:jkw

1. S. Garcia-Blanco and A. Perales, Acta Cryst., B28, 2647 (1972).

2. N. Camerman and A. Camerman, J. Amer. Chem. Soc., 95, No. 15, 5038 (1973).

3. H. Sternglanz, H. M. Einspahr, and C. E. Bugg, J. Amer. Chem. Soc., 96, No. 16, 4014 (1974).

THE WEIZMANN INSTITUTE OF SCIENCE

REHOVOT · ISRAEL   רחובות · ישראל

ISOTOPE DEPARTMENT   March 18, 1975   מחלקת איזוטופים

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

Dear Barry:

In the February 1975 issue of TAMU-NMR-Newsletters C.A. Reilly presents ^{13}C spectra of
$CDCl_3$ in which he notes that addition of $Cr(acac)_3$ "always broadens the central line (due
to ^{13}C coupling with 0 spin state of D) more than it does the outer two lines (coupling
to +1 and -1 spin states of D)", and he asks,"Why does this happen?"

This selective broadening may be explained by considering the extra contribution to the
^{13}C lineshape from the T_1 relaxation of the neighboring deuterium nucleus (Abragam, p.
501). The effect is analogous (but not equivalent) to exchange of deuterium between
different $CDCl_3$ molecules resulting in frequency switching between the ^{13}C triplet
components. Addition of the paramagnetic $Cr(acac)_3$ molecules enhances the longitudinal
relaxation rate of the deuterium, thus increasing the switching rate. This relaxation
mechanism which results in $\Delta m_I = \pm 1$ transitions between the deuterium levels only, differs
from the quadrupolar relaxation of the deuterium which affects both the $\Delta m_I = \pm 1$ and ± 2
transitions. Neglecting the contribution of the latter mechanism (which appears to be very
small indeed) and considering only the dipolar relaxation of the deuterium, T_{1D}, the line-
shape of the ^{13}C resonance can straightforwardly be computed from the following equations:

$$\frac{dG_{\pm}}{dt} = [i(\omega_0 - \omega \pm J) - \frac{1}{T_2} - \frac{1}{T_{1D}}] G_{\pm} + \frac{1}{T_{1D}} G_0$$

$$\frac{dG_0}{dt} = [i(\omega_0 - \omega) - \frac{1}{T_2} - \frac{2}{T_{1D}}] G_0 + \frac{1}{T_{1D}} (G_+ + G_-)$$

where $1/T_2$ is the linewidth of the ^{13}C resonances in the absence of effect from deuterium
and G_+, G_0 and G_- are the ^{13}C magnetizations corresponding to the deuterium m_I states +1,
0 and -1.

Prof. B.L. Shapiro

In the slow relaxation rate limit ($T_{1D} J \gg 1$), which is clearly fulfilled by the spectra presented by Reilly, these equations yield three Lorentzians at ($\omega_0 + J$), (ω_0) and ($\omega_0 - J$) with corresponding widths ($1/T_2 + 1/T_{1D}$), ($1/T_2 + 2/T_{1D}$) and ($1/T_2 + 1/T_{1D}$). Thus shortening of T_{1D} results in selective broadening of the ^{13}C triplet components - the central line being broadened by twice the amount of the outer lines. Physically this effect can be understood by noticing that the center line "exchanges" with two other lines while the outer lines each "exchange" with just one other singlet. This selective broadening is opposite to that expected from quadrupole relaxation of deuterium, where the outer ^{13}C peaks should broaden more than the central one (because of the $\Delta m_I = \pm 2$ transitions).

With best regards

Sincerely yours,

Zeev Luz

ZL/ca

P. S. Please credit this contribution to Jacques Reuben's account.

DOW CHEMICAL U.S.A.

March 21, 1975

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

Dear Barry:

UNEQUAL C-13 LINE WIDTHS IN DEUTERIUM SPLITTING PATTERNS

Charlie Reilly's recent puzzlement about greater broadening of the inner line ($m_D = 0$) over the outer lines ($m_D = \pm 1$) in the C-13 spectrum of $CDCl_3$ doped with $Cr(acac)_3$ intrigued me (this newsletter, No. 197, February, 1975, p. 13).

This could be the result of partial deuterium decoupling via deuterium relaxation induced by the $Cr(acac)_3$. The deuterium undergoes transitions $m = 1 \rightleftharpoons m = 0$ and $m = 0 \rightleftharpoons m = -1$ at equal rates. This would cause the $m = 0$ state to have half the lifetime of the $m = \pm 1$ states. In the "slow exchange" limit, broadening of the C-13 lines would reflect inversely the deuterium lifetimes, so that the broadening induced by this mechanism would be twice as great for the center ($m_D = 0$) line as for the outer ($m_D = \pm 1$) lines of the C-13 spectra.

Reilly's most extreme illustration of the effect is consistent with the above mechanism, assuming that the T_1 value(s) for C-13 has not become so short that C-13 relaxation contributes much to the broadening. Thus,

Induced broadening:
  Outer lines ($m_D = \pm 1$)
    5.5 - 3.5 = 2.0 Hz
    5.2 - 3.2 = 2.0 Hz   =   <u>2.0 Hz</u>

  Inner line ($m_D = 0$)
    6.8 - 3.0 =   <u>3.8 Hz</u>

  Ratio inner/outer = 3.8/2.0 =   1.9   (2.0 theor)
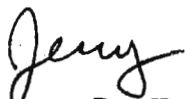
Prof. B. L. Shapiro   March 21, 1975

Naturally, the T_1 values for the individual C-13 lines should be determined to decide whether this mechanism alone causes the effect.

The phenomenon should be general for splitting patterns by nuclei which have $I \geqslant 1$. Certainly one would anticipate it in the carbon-13 spectra of other deuterated solvents, so that the outer lines of a multiplet pattern would be sharper than the inner lines. Observing the phenomenon requires that this mechanism dominates other sources of line broadening.

Yours truly,

Jerry P. Heeschen
Analytical Laboratories
574 Building

nhc

UNIVERSITÉ D'OTTAWA   UNIVERSITY OF OTTAWA

**DÉPARTEMENT DE CHIMIE**

OTTAWA ONTARIO
CANADA K1N 6N5

**DEPARTMENT OF CHEMISTRY**

March 21, 1975

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

Dear Barry:

^{13}C   I'd like to present a summary of work by Bruce Grindley on the spectra of five conformationally fixed nitrosopiperidines and application of the derived substituent parameters to the determination of the conformational properties of syn and anti N-nitroso-2-methylpiperidine. For the model piperidines, the ^{13}C shifts of those carbons used for conformational analysis are given with the sturctures below.
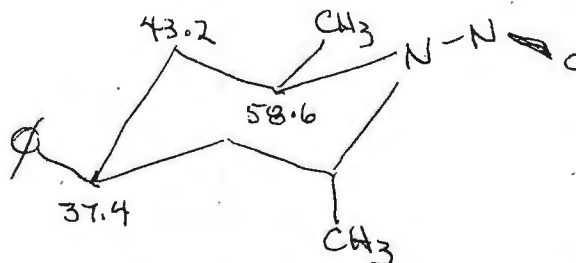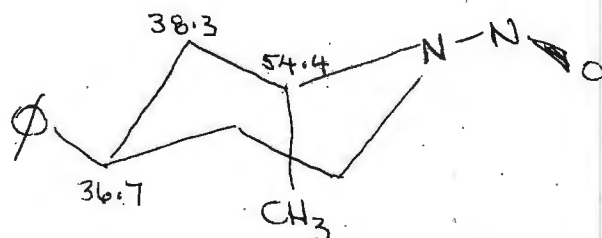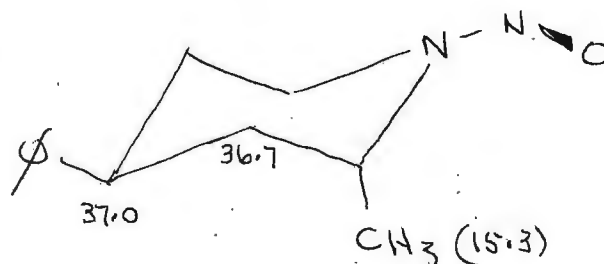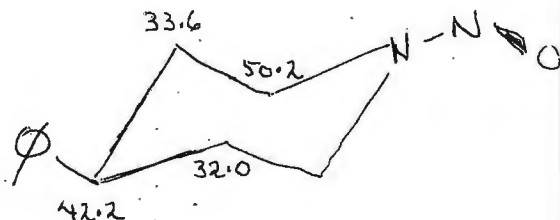
From this data, a number of methyl substituent parameters are obtained which, in conjunction with the shifts of N-nitrosopiperidine, can be used to predict several shifts in the syn and anti isomers of N-nitroso-2-methylpiperidine as follows:
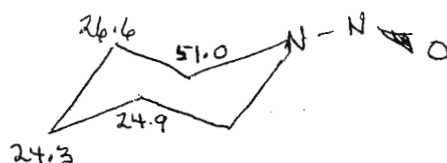
Predicted ^{13}C Shieldings

	Observed	% Axial Conformer
	$C_3 = 29.7$	
	$C_4 = 19.3$	96
	$C_6 = 46.9$	> 100
	$C_2 = 56.4$	57
	$C_3 = 33.1$	64
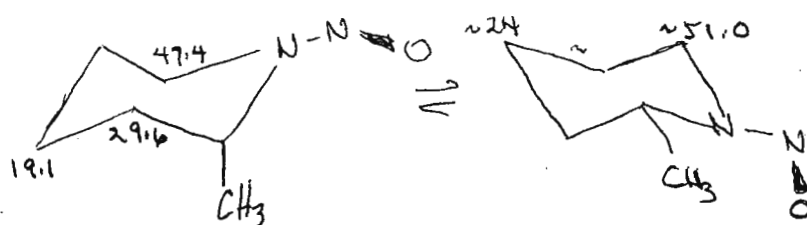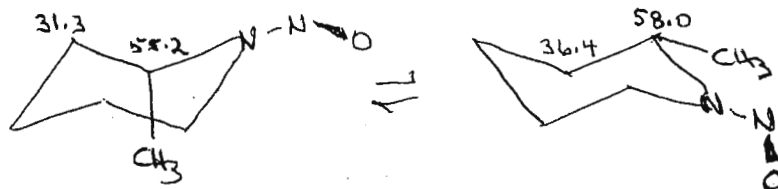
It can be concluded that the <u>syn</u> isomer adopts the axial conformation exclusively, while the <u>anti</u> isomer has 60 ±5% of the axial form. These conclusions differ appreciably from those of Forrest et al. (J.A.C.S., <u>96</u>, 4286 (1974)) based on lanthanide-induced shift data. It is our opinion that ^{13}C data provides a more reliable assessment of the conformational equilibrium.

Best regards,

R.R. Fraser.

RRF:cmg

Conformational Analysis by ^{13}C NMR

Department of Chemistry

BROCK
University

St. Catharines, Ontario

March 25, 1975.

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

Dear Professor Shapiro:

BRUKER WP-60; POST DOC POSITIONS

Our Bruker WP-60, which was the first North American installation apart from Bruker's demonstrator, is now running routinely on ^{1}H, ^{13}C, ^{19}F and ^{31}P. After some initial teething troubles we are achieving resolution and sensitivity well in excess of specifications on all four nuclei, and find we are changing nuclei three or four times/week. With Bruker's help we modified the PAPS control so that it could be used with the multi-pulse generator (MPG) as well as in the previous SPG mode. This modification permits use of PAPS for T_1 measurements and for experiments where the accurate pulse width of the MPG are needed.

FT in fluorine is a pleasure after years of searching for widely separated lines by CW methods. Between the use of 20-50 KHz sweep width search spectra (surprisingly useful even with computer limited resolution), and the 50 KHz of F_1 offset to zero in on each cluster of peaks; an hour's work is now done in minutes. For proton decoupling in the ^{19}F spectra we could use either the hetero-decoupler with appropriate filters to keep the 60 MHz out of the 56.4 and 62.5 MHz lines (more of a problem at 14 than at 21 K gauss), or more conveniently, we simply used the ^{1}H pulsed homo-decoupler, which, since it is essentially time shared, causes no problems.

A note to potential Bruker ^{19}F users. On WH and WP instruments, the computer set F_1 offsets move in the opposite direction to that for other nuclei since the offset is added to the proton frequency in the console. I.e., for ^{1}H, 60MHz + ΔR_1

for ^{13}C, 60 + ΔF_1 -45 = 15 MHz + ΔF_1
for ^{31}P, 60 + ΔF_1 - 35.7 = 24.3 MHz + ΔF_1
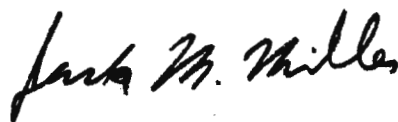But for ^{19}F, 116.4 - (60 + ΔF_1) = 56.4 MHz - ΔF_1

Since ^{19}F FT systems are only now becoming popular, not all field engineers are aware of this, and much head scratching can result. The manually switched 10 KHz steps offset the 116.4 MHz and therefore move in the normal direction.

Our first major modification this summer will be to wind a second decoupling coil on each of our inserts for triple irradiation and multi-nuclei decoupling work. By rebuilding our old NMR Specialities HD-60 heterodecoupler from our A-60 (^{11}B, ^{14}N, ^{19}F and ^{31}P CW and BB decoupling) for use with the WP-60, we will be able to decouple these nuclei and protons simultaneously.

In addition to calculating NMR spectra we've also used the data system for calculation and plotting of theoretical photoelectron spectra and expect to feed IR interferograms to the system for FT and plotting. We have even had a psychologist request us to do FT work on tape recorded EEG data, so all in all the WP-60 is getting a good workout and is proving reliable.

We have several teaching PDF positions available in the department this coming year, one of which will be in the area of NMR.

Yours sincerely,

Jack M. Miller,
Associate Professor.

JMM/jh

UNIVERSITY OF CALIFORNIA, SAN DIEGO

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DEPARTMENT OF CHEMISTRY   POST OFFICE BOX 109
REVELLE COLLEGE   LA JOLLA, CALIFORNIA   92037

March 27, 1975

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

Title: Explanation of the Cr(AcAc)$_3$ effect on the ^{13}C triplet in CDCl$_3$.
Painless solid state conversion of V2100 magnet power supply.

Dear Barry,

We were delighted to see Charlie Reilly's pretty ^{13}C spectra of Cr(AcAc)$_3$
doped CDCl$_3$ [TAMU-NMR 197, 13 (1975)] and believe that the following
provides the answers to Charlie's three questions:

1)   Why does the center line (m$_D$ = 0) of the ^{13}C-D triplet broaden more
than the outer lines (m$_D$ = ±1) when Cr(AcAc)$_3$ is added?

Answer: The spin-lattice relaxation of D (R$_{1D}$) caused by Cr(AcAc)$_3$ may
be described as a "random fluctuating field" mechanism, i.e., a rank
one tensor interaction which allows only Δm = ±1 transitions for D. The
four transitions, 0 → ±1 and ±1 → 0 have equal probability of occurring,
and the rate out of m = 0 is therefore twice that out of the m = ±1 states.
The scalar coupling then causes a transverse dephasing rate, R$_2$, of the
^{13}C lines, which is twice as large for the center line as for the outer
two lines. Subtracting "free" CDCl$_3$ line widths from "doped" in Charlie's
upper and lower spectra gives 2:3.8:2 Hz. Very nice. For the skeptic
we offer the following slightly more rigorous, liberal dose of hair:

We can describe the effect of a paramagnetic agent as an isotropic random
fluctuating field of average square strength $\overline{\omega^2} = \gamma_D^2 \overline{H^2}$ and therefore

$$\mathcal{H}(t) = \vec{\omega}(t) \cdot \vec{I} = \omega_z(t) I_z + \omega_x(t) I_x + \omega_y(t) I_y$$

with $\omega_z = \omega_x = \omega_y = \frac{1}{\sqrt{3}} \omega$.

For the D transition rate as usual

$$W_{i \to j} = \int_{-\infty}^{\infty} \overline{\langle j | \mathcal{H}(t) i \rangle \langle j | \mathcal{H}(t+\tau) i \rangle^*} e^{-i\omega\tau} d\tau$$

and by using

$$I_x = \frac{1}{2}(I_+ + I_-)$$
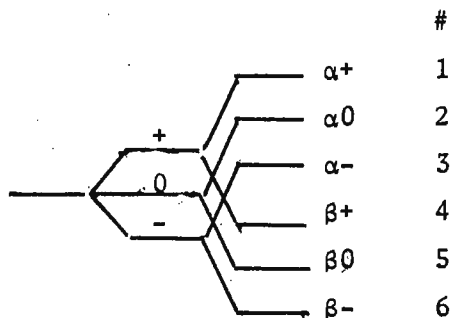
$$I_y = \frac{1}{2i}(I_+ - I_-) \quad \text{and}$$

$$I_\pm |I,m\rangle = \sqrt{I(I+1) - m(m\pm1)} \, |I,m\pm1\rangle$$

we get
$$W_{i \to j} = \frac{1}{2} \langle j|I_+ + I_-|i\rangle^2 \int_{-\infty}^{\infty} \overline{\omega_z(0)\omega_z(\tau)} \, e^{-i\omega\tau} d\tau$$

$$= 2 \int_0^\infty \overline{\omega_z^2} \, e^{-|\tau|/\tau_c} e^{-i\omega\tau} d\tau$$

$$= \frac{2}{3} \overline{\omega^2} \tau_c \equiv R_{1D} \quad \text{for} \quad \omega\tau_c \ll 1$$

for all transitions.

For the effect on the ^{13}C consider the spin states where the arrows are the observed ^{13}C transitions

	#
α+	1
α0	2
α-	3
β+	4
β0	5
β-	6

In a Liouville representation of the density matrix elements which correspond to ^{13}C spectral magnetizations <u>only</u>

$$\dot{\underset{\sim}{\sigma}} = (\underset{\approx}{R} - i\underset{\approx}{\Omega})\underset{\sim}{\sigma}$$

where in the rotating frame

$$\underset{\approx}{\Omega} = \begin{pmatrix} J_{CD} & 0 & 0 \\ 0 & 0 & 0 \\ 0 & 0 & -J_{CD} \end{pmatrix}$$

and the matrix elements of $\underset{\approx}{R}$ are

$$R_{abcd} = J_{acbd} - \frac{1}{2} \delta_{ac} \sum_s J_{sbsd} - \frac{1}{2} \delta_{bd} \sum_s ascs \quad .$$

The transverse relaxation rates for the three ^{13}C lines σ_{14}, σ_{25} and σ_{36} are given by R_{1414}, R_{2525} and R_{3636}, and non-zero J's (spectral densities) are those involving D transitions equal to $\frac{2}{3}\omega^2\tau_C = R_{1D}$. A little algebra results in

$$\begin{pmatrix} \dot{\sigma}_{14} \\ \dot{\sigma}_{25} \\ \dot{\sigma}_{36} \end{pmatrix} = R_{1D} \times \begin{pmatrix} i \cdot \dfrac{J_{CD}}{R_{1D}} - 1 & 1 & 0 \\ 1 & -2 & 1 \\ 0 & 1 & -i \dfrac{J_{CD}}{R_{1D}} - 1 \end{pmatrix} \begin{pmatrix} \sigma_{14} \\ \sigma_{25} \\ \sigma_{36} \end{pmatrix} \quad .$$

This result may be compared with the transverse ^{13}C dephasing caused by the scalar coupling to D when D is relaxing by quadrupolar interaction for which $\Delta m = \pm 2$ transitions are allowed:

$$\begin{pmatrix} \dot{\sigma}_{14} \\ \dot{\sigma}_{25} \\ \dot{\sigma}_{36} \end{pmatrix} = \frac{R_{1Q}}{5} \begin{pmatrix} \dfrac{5iJ_{CD}}{R_{1Q}} - 3 & 1 & 2 \\ 1 & -2 & 1 \\ 2 & 1 & \dfrac{-5iJ_{CD}}{R_{1Q}} - 3 \end{pmatrix} \begin{pmatrix} \sigma_{14} \\ \sigma_{25} \\ \sigma_{36} \end{pmatrix} \quad .$$

The diagonal R elements (which are the only ones contributing to the line widths) here predict a line width ratio of 3:2:3. Often, this ratio is almost masked by inhomogeneity, but careful line width measurements usually reveal a difference (as in Charlie's spectra 3.5:3.0:3.2 Hz). While we refuse to come up with an explanation for the 3.5 vs. 3.2 for the outer lines, the 0.2 - 0.4 Hz difference between outer and center lines is precisely what is expected since T_{1D} in $CDCl_3$ is of the order of 1 sec.

2) How general is this phenomenon?

Answer: As general as the occurrence of significant contributions from rank one relaxation mechanisms on a spin to which ^{13}C is coupled. Other agents would be O_2 and lots of intermolecular D-H interactions, but they would be less effective and the quadrupole pattern would in general dominate. Above calculations can easily be extended to 2,3,-many,if anyone has the desire. We have just recently completed a lot of them for spin $\frac{1}{2}$ nuclei. The different line broadening effects can of course be useful for something or other.

3) Are the T_1's of all spin states shortened similarly?

Answer: The ^{13}C T_1's are not affected by the above, but could of course be affected (equally) by $Cr(AcAc)_3$ directly. The ~1:2:1 ratio observed says they are not, but, then, more accurate data are probably required.

For information, data and general theory we give credit (without ranking!) to Slichter; Abragam; Redfield; Gutowsky, Vold and Wells; Shoup and Farrar (T_2 ^{13}C in chloroform) Huntress (T_{1D} in $CDCl_3$) and quite a few others.

Grtle and Bob

R. R. and R. L. Vold

mb

P. S. With great pleasure we announce the extremely painless conversion of our V2100B magnet power supply to solid state. Rolf Tschudin built the pass bank for us, came to San Diego, and had it installed and running in a couple of hours. So far it has been functioning without any problems at all.

N O T I C E

This contribution appears as sent to us, despite the fact that it exceeds our 3-page maximum for contributions. This should not be construed as a removal of the length restriction, for the seriousness of our financial situation is unresolved. Special dispensations like the present one are occasionally given, but only when a) space could not be saved by reformatting, and the work is sufficiently interesting and b) at least one of the authors is a beautiful and charming member of the female persuasion. For all other cases, we are forced for economic reasons to return to >3-page contributions for condensation.

B. L. Shapiro, M.C.P.
4/1/75

**EIDGENÖSSISCHE
TECHNISCHE HOCHSCHULE ZÜRICH**

**Laboratorium
für Physikalische Chemie**

8006 ZÜRICH, March 10, 1975
Universitätstrasse 22
Telefon (01) 32 62 11

Prof. Dr. B. L. Shapiro
Department of Chemistry
Texas A+M University
College Station, Texas

TWO-DIMENSIONAL SPECTROSCOPY

Dear Barry,

In 1971, J. Jeener has formulated the idea of pulse pair
Fourier spectroscopy (Ampère International Summer School II,
Basko Polje, unpublished). As we could not yet find results
of an experiment of this kind in literature, we recently tried
the experiment with some success.

Pulse pair Fourier spectroscopy is an alternative to
double resonance. It characterizes the nonlinear properties of
spin systems and permits, for example, to trace out the energy
level diagram in a manner similar to a tickling experiment.
One measures the response to a pair of 90° pulses with separation
t_2 as a function of the time t_1 elapsed after the second pulse.
By varying the pulse separation t_2, one obtains a two-dimensional
impulse response $h(t_1, t_2)$:
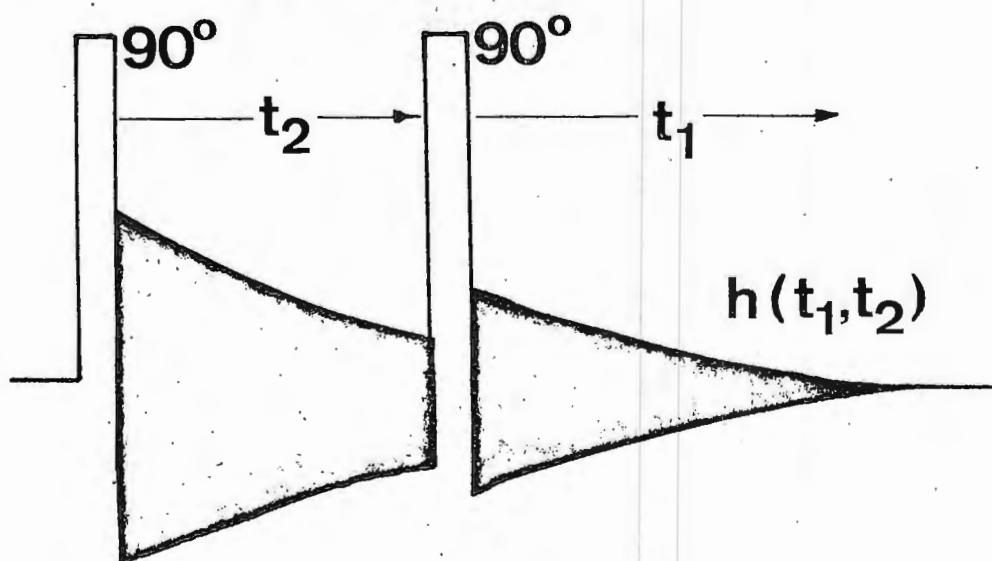
The 2D Fourier transform of $h(t_1, t_2)$ produces a 2D spectrum in a manner analogous to Fourier Zeugmatography (TAMU-NMR Letter 191, 36). An example of a low resolution 2D spectrum of 1,1,2-trichloroethane is given in the following figure. It consists of two peaks on the f_1 axis which represent the original spectrum, peaks on the diagonal and off-diagonal peaks which contain the "double resonance" information. In this example, they demonstrate at least that the two peaks belong to the same spin system.
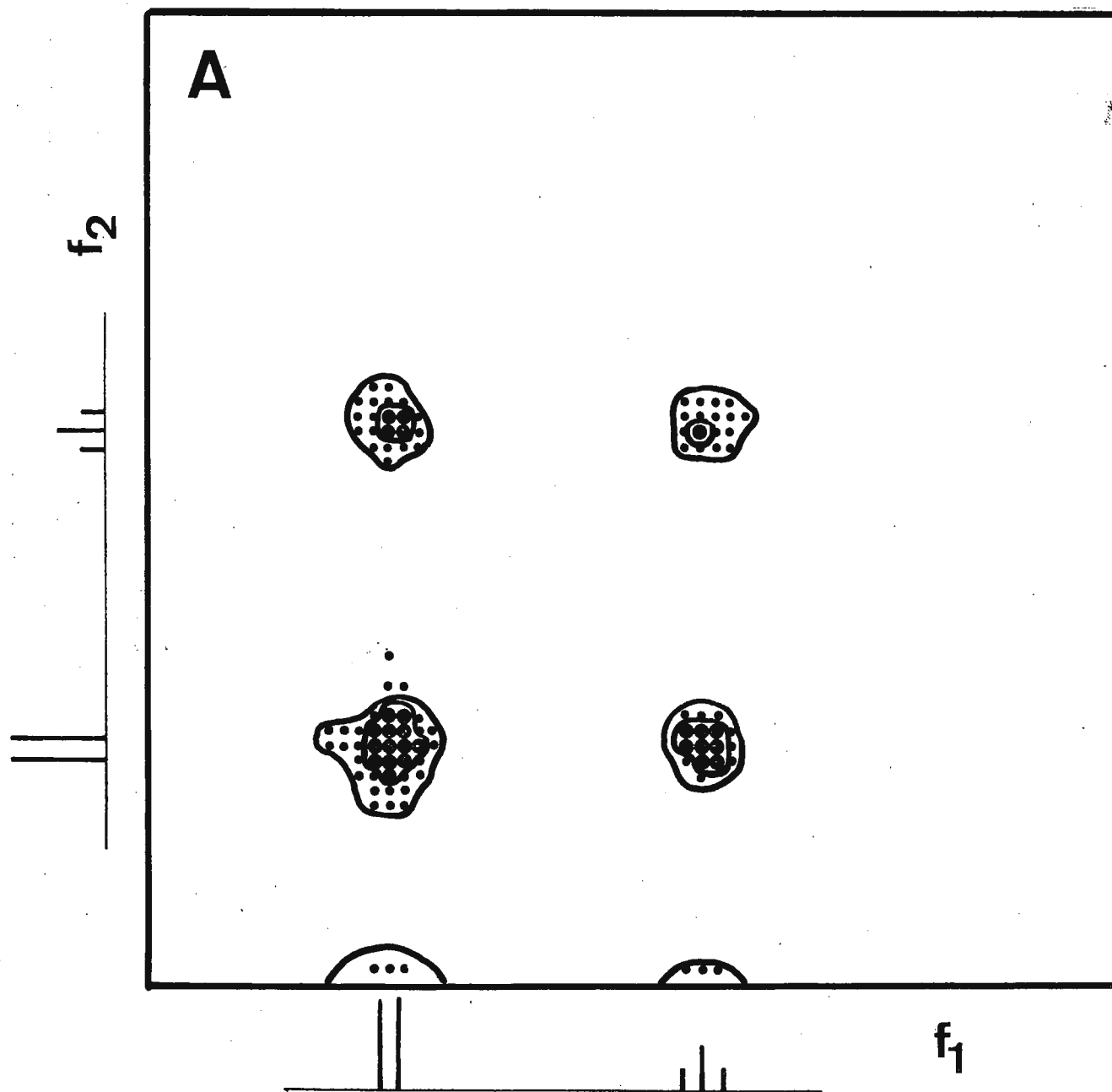
More detailed information can be obtained by means of a blow-up of a partial 2D spectrum. The next figure gives the enlarged lower left corner of the above figure showing the CH_2 doublet.
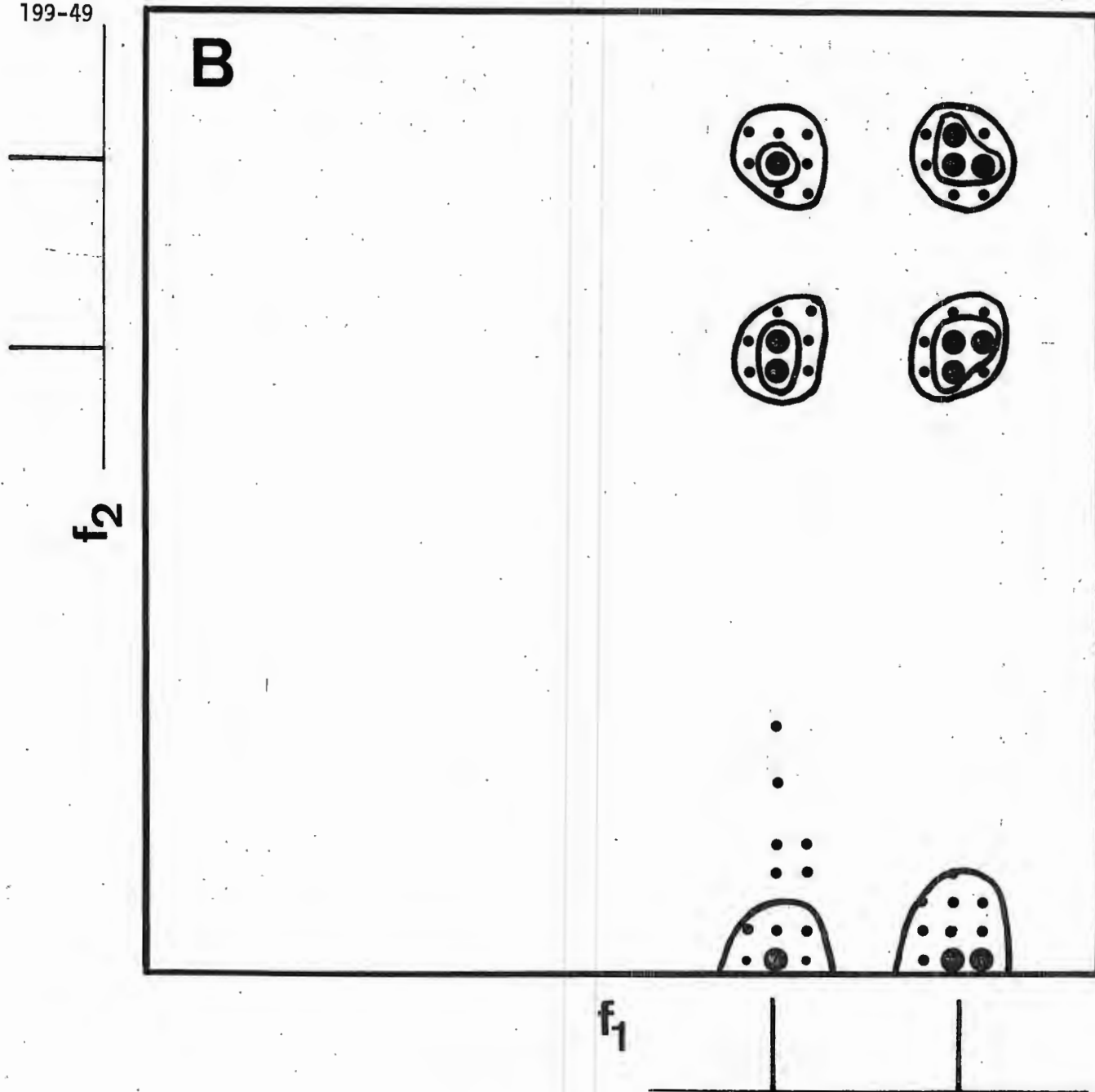
These spectra are preliminary in several respects. First
of all, resolution is severely limited by the available computer
memory. A 64x64 data matrix was used. Secondly, the absolute
value of the 2D spectrum is plotted disregarding phase infor-
mation which may be of particular interest. This experiment
has several further interesting aspects which we presently
are investigating.

Sincerely yours

Richard

Richard R. Ernst

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

Sesto, 29.1.1975

da citare nella risposta ....

Subject : "NMR Study of the Meerwein.Pon-
dorf reaction"

Dear Prof. Shapiro,

we have recently studied the reaction between acrolein and
sec. butyl alcohol in presence of aluminum sec. butyloxide
as catalyst to give methyl ethyl ketone and allylic alcohol.

$$CH_2 = CHCHO + CH_3CH\ Et \quad \xrightarrow{\quad Al[OCH(CH_3)Et]_3 \quad}$$

$$\xrightarrow{\qquad} \quad CH_2 = CHCH_2\overset{\ominus}{O} \ + \ CH_3CO\ Et$$
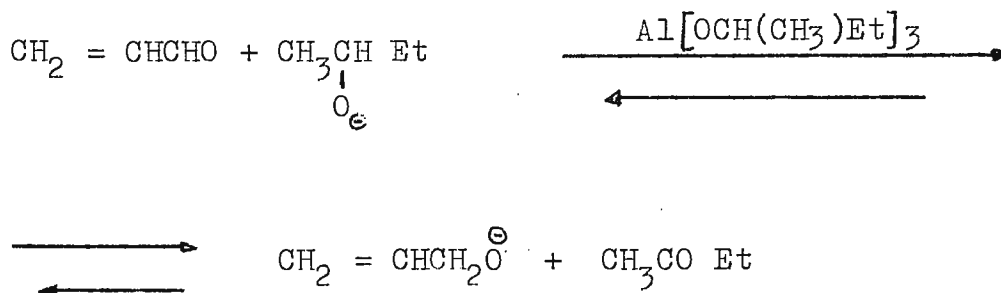
The reaction was studied at various temperatures in large
excess of sec. butyl alcohol. The NMR technique was used as
the analytical tool to follow the reaction. A typical 60 MHz
of a reaction mixture is shown in the herebyattached figure.
For the reaction mixture shown in figure the starting con-
centrations were ca. 1 x 10^{-3} acrolein moles/g sec. butyl al
cohol and ca. 0.1 x 10^{-3} catalyst moles/g sec. butyl alcohol.

Mod. 10827/02 - 11.000 - 7-67

A and C are the resonances of the aldeidic proton and of the methyl protons due to acrolein and methyl ethyl ketone respectively. B and D are on the contrary the absorptions of the internal standards used to evaluate the concentrations of acrolein and of methyl ethyl ketone. Pyrazine (B) and hexamethyldisiloxane - HMDS (D) have been used as internal standards. The decrease of acrolein concentration and the increase of methyl ethyl ketone concentration have been determined for different reactions. Rate constants (K) have been consequentely obtained at various temperatures. It was possible to conclude that the reaction order is 1st order relative to acrolein at any temperature. In addition, activation parameters could be measured. Making use of the well - know Eyring equation :

$$K = \varkappa (K_B T/h) \exp (-\Delta H^*/RT) \exp (\Delta S^*/R)$$

and plotting ln (K/T) versus 1/T to give a straight line with the slope $-\Delta H^*/R$ and the intercept ln $(\varkappa K_B/h) + \Delta S^*/R$, the following values of enthalpy and entropy of activation (ΔH^* and ΔS^*) were obtained :

$$\Delta H^* = 9.0 \quad K \text{ cal/mole}$$
$$\Delta S^* = -37.8 \quad \text{cal/mole } °K$$

yours sincerely,

L. Cavalli, G. Cancellieri, L. Valtorta

SOCIETA' ITALIANA RESINE
CENTRO RICERCHE ANALISI - SEAN SESTO -
Via Trento, 106 - 20099 SESTO S.G. (MI)
ITALIA

$$CH_2 = CHCHO + CH_3CH\ Et \quad \xrightarrow{\quad} \quad Al[OCH(CH_3)Et]_3$$
$$\underset{O^{\ominus}}{} \quad \xleftarrow{\quad}$$

$$\xrightarrow{\quad} \quad CH_2 = CHCH_2\overset{\ominus}{O} + CH_3CO\ Et$$
$$\xleftarrow{\quad}$$
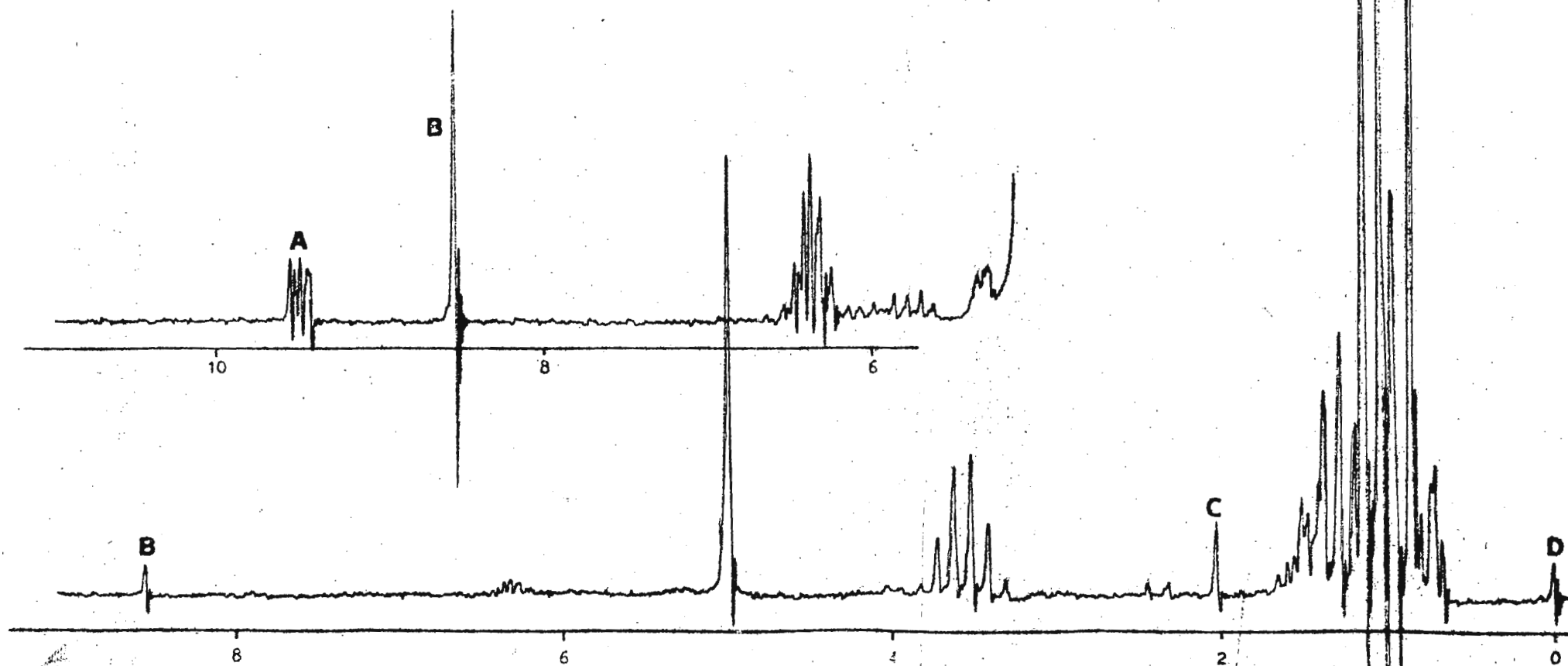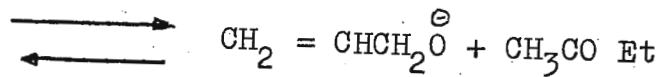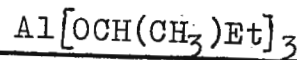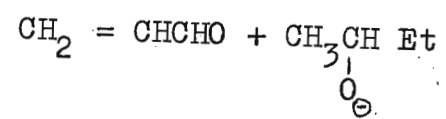
Fig. 1

LILLY RESEARCH LABORATORIES

DIVISION OF ELI LILLY AND COMPANY · INDIANAPOLIS, INDIANA 46206 · TELEPHONE (317) 636-2211

April 1, 1975

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

Title: Assignment of ^{13}C Resonances

Dear Professor Shapiro:
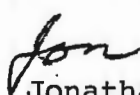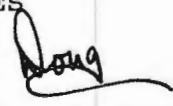
The standard method of "off-resonance coherent wave decoupling" (ORCWD) has been used for several years to assign carbon resonances. While this method is quite useful in smaller molecules, many of the compounds that we deal with yield spectra which are too complex to analyze in this manner. Also, while ORCWD is effective in distinguishing "doublets and quartets" from "singlets and triplets," further discrimination is commonly difficult. While working with the dimeric indole alkaloids, we developed a method which has proven a useful addition to the tricks of assigning carbon resonances.

From some T_1 measurements on some of the more easily available alkaloids, we found that the following T_1 values obtained: singlets, $\geqslant 1$ sec.; methyls, ca. 0.5 sec.; and doublets and triplets, 0.1-0.2 sec. Using an inversion-recovery pulse sequence with $\tau = 0.35$ sec. (= 0.5 ln2), the methyl resonances are very nearly nulled. At the same time, the singlets are inverted and the doublets and triplets are upright. Thus, by comparison with a ^{13}C nmr spectrum collected in the normal fashion, this method easily distinguishes these three groups of carbon resonances. The final distinction between doublets and triplets can be effected by ORCWD. We commonly collect ORCWD spectra in the inversion-recovery mode also, since this trick leads to significant simplification of some of the more crowded regions of the spectra.

While this method was originally developed for the dimeric alkaloids, we have subsequently applied it to a number of compounds of the molecular weight range 500-2000. With smaller molecules, molecular flexibility leads to much greater variation in T_1 values and the method fails. Fortunately, the smaller molecules can be generally analyzed by ORCWD directly.

Best regards,

LILLY RESEARCH LABORATORIES

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

JWP/DED:vr