Texas A & M University
N - M - R
Newsletter

No. 160

JANUARY, 1972

Deadline dates: No. 161: 7 February 1972
No. 162: 6 March 1972

All Newsletter correspondence, etc. should be addressed to:

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

Monsanto

Monsanto Company
800 N. Lindbergh Boulevard
St. Louis, Missouri 63166
Phone: (314) 694-1000

December 3, 1971

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

Title: The Use of Noise-Modulated Partially Decoupled Spectra for Carbon-13 NMR Line Assignments.

Dear Barry:

Ernst has shown that in a decoupling experiment with random noise, the central line of a triplet, arising from the weak coupling of a nucleus of spin 1/2 with two different magnetically equivalent nuclei also of spin 1/2, is unaffected by the perturbation of the random noise. This line, which involves the antisymmetric spin states, stays sharp even when the decoupling is incomplete. This fact can be used to distinguish methylene-carbon from methine-carbon lines in ^{13}C nmr spectra. The technique can be effective even when single-frequency off-resonance decoupling experiments are indecisive in distinguishing methine from methylene carbon and when spin-lattice relaxation times from partially relaxed Fourier transform experiments are not simply related to the number of directly bonded protons. The former situation occurs whenever the methine- and methylene-carbon lines are, as in the spectra of many polymers, broad or poorly resolved, or are very closely spaced and arise from spin systems in which there are substantial long-range spin-spin interactions. The single-frequency off-resonance decoupled spectra do not then exhibit easily identifiable spin multiplet patterns. The latter situation sometimes occurs for polymeric elastomers such as poly(propylene oxide) in which the ^{13}C spin-lattice relaxation times are determined by the segmental motion of the chain which is distinctly anisotropic. The anisotropy destroys the simple inverse proportionality between the spin-lattice relaxation time of a main-chain carbon and the number of directly bonded protons, even though the dominant relaxation mechanism is dipolar.

Monsanto

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800 N. Lindbergh Boulevard
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Bernard Shapiro (2) Dec. 3. 1971

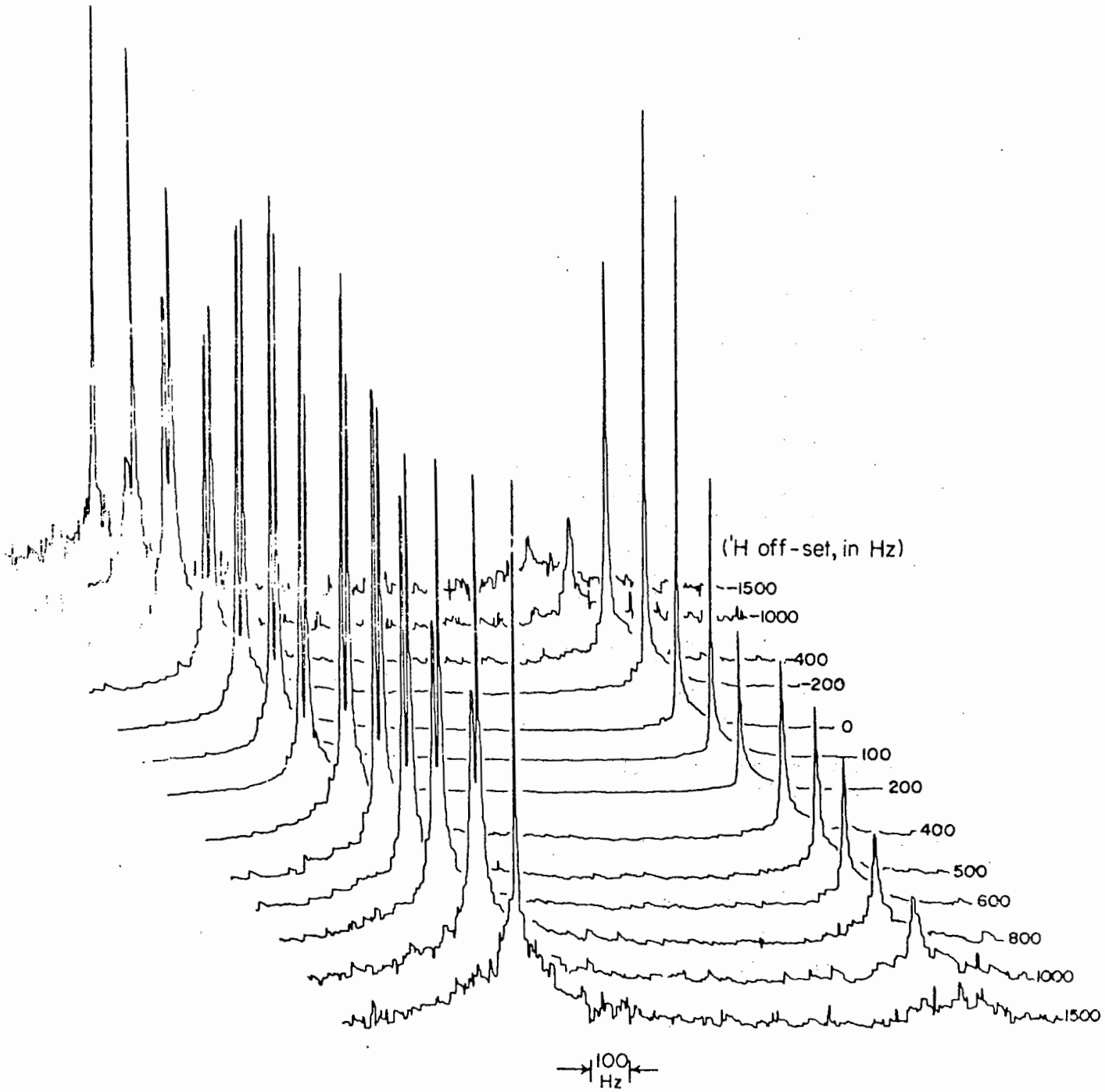
The use of noise-modulated, partially decoupled ^{13}C nmr spectra to distinguish methine- from methylene-carbon lines is illustrated by the spectra of propylene glycol, $HOCH_2CHCH_3OH$, shown in the figure. The spectra were obtained by Fourier transform methods using a Bruker HFX-90 spectrometer. A noise generator was used to phase modulate the ^1H rf producing an effective decoupling bandwidth which, for these experiments, was restricted to 500 Hz, but with less intense sidebands covering several times that width. A modest decoupling field intensity was used, $\gamma H_2/2\pi$ = 1800 Hz. For off sets of the ^1H rf of $\pm$ 1500 Hz, the effective decoupling has been reduced to the point where only the transition which involves the antisymmetric spin states is still sharp and easily observed. Similar results were obtained by keeping the ^1H rf on resonance and reducing $\gamma H_2/2\pi$ by about 15 dB. These results permit the straightforward identification of the higher field line of the low-field pair as due to the methylene carbon. Easily interpreted, simple multiplets with reduced couplings were not observed in the spectra of propylene glycol for a wide variety of unmodulated, off-resonance frequencies and decoupling field intensities, although for this particular system, the methine line could still be identified by the absence of a strong peak in the off-resonance spectra at the position of the lower field line of the decoupled low-field pair.

Please credit this contribution to the Monsanto subscription.

Sincerely,

Jacob Schaefer

bk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1500
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160-4

U.S. DEPARTMENT OF COMMERCE
National Bureau of Standards
Washington, D.C. 20234

December 3, 1971

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

Dear Dr. Shapiro:

Tom Farrar, of JEOL, has asked me to collaborate with him in writing the NMR article for Vol. 23 (1972) of the Annual Review of Physical Chemistry. The chapter will be limited to a discussion of pulse methods in NMR, relaxation mechanisms, especially spin-rotation, and Fourier Transform NMR. The manuscript should be completed by February, 1972. Naturally we are anxious to have the article as up to date as possible.

It would be of great service to the readers of the chapter, as well as to us, if you would kindly keep us informed in the next few months of your imminent publications, i.e. Journal and issue, and also send us preprints of your very recent work in NMR.

Please send your communications to the undersigned. Thank you for your cooperation.

Sincerely,

Marjorie S. Malmberg

MARJORIE S. MALMBERG
Polymer Crystal Physics Section

THE UNIVERSITY OF ROCHESTER
COLLEGE OF ARTS AND SCIENCE
RIVER CAMPUS STATION
ROCHESTER, NEW YORK 14627

DEPARTMENT OF CHEMISTRY

December 3, 1971

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

Title: ^{13}C FT Studies on a JEOL Spectrometer. Scalar Relaxation of ^{13}C by ^{14}N.

Dear Barry:

I recently had an opportunity to use the JEOL PFT-100 NMR spectrometer for a period of two weeks and I thought I would pass along a few comments on the system and an interesting ^{13}C spectra of formycin, a nucleoside antibiotic. The system consisted of the PFT-100 and a Nicolet 1085 computer. The instruments were surprisingly easy to operate and I was running spectra after a very brief introduction. When I was using the instrument the probe was capable of handling 8mm tubes and the lock signal was an internal (or capillary) deuterium lock. I have learned from Dr. Farrar that they now have a 10mm probe with external and internal lock capabilities. The resolution and stability of the instrument were excellent and I had no trouble maintaining lock on overnight runs. I did experience some difficulty with sample spinning in the variable temperature mode of operation. This was caused by a variation in the flow rate of the variable temperature air due to a dirty valve in the temperature regulator unit and when the latter problem was corrected the spinning problem disappeared. It was routine practice to blow a stream of room temperature air over the sample to help avoid excessive heating of the sample due to proton noise decoupling. This procedure maintained the sample temperatures about 22-25°C for most samples. However, when the concentration of protons was high the sample temperature rose, and for one sample that was dissolved in D_2O and NaOH the temperature was approximately 40-50°C. This illustrates the problem that will be encountered on all instruments for variable temperature studies during proton noise decoupling.

The most difficult aspect of the FT operation was learning how to correct the phasing in the transformed spectra. The Nicolet provides for both a zero order and first order linear phase correction and it took some time to get the correct parameters (my lack of experience). However, once the values were selected they did not change much from sample to sample unless one changed the magnetic susceptibility of the solvent such as going from DMSO-d_6 to D_2O. With practice the phasing becomes easier and it doesn't usually change much between samples.

The instrument performed very well for partial decoupling experiments. Figure 1 is a composite ^{13}C spectra of thymidine with proton decoupling (top)

and with partial decoupling (bottom). It is difficult to see on this compressed scale but the residual coupling is about 20 Hz for all couplings. The partially decoupled spectrum was the time average of 8192 pulses and the complete decoupling spectra was the sum of 7624 pulses. The line assignments (from Jones etal. PNAS 65, 27 (1970)), in order of increasing magnetic field, are C4, C2, C6, C5, C4', $\overline{C1'}$, C3', C5', C2', and CH_3. Note that the C2' overlaps the DMSO-d_6 peak. The concentration of thymidine was ~0.8 M. Nicolet was missing some software which would have made life more convenient (such as a program to print out the peak locations, etc.) but I understand that these are now available. The computer was not set up to control the pulse sequence so T_1 measurements had to be recorded as a series of single spectral measurements. The Butterworth filter (8-pole) on the JEOL pulse unit had a somewhat limited number of cutoff frequencies but if this was inconvenient the 4 pole Butterworth on the Nicolet 1085 could be used. The minimum setting for the interval, τ, was 0.01 seconds and I feel that this variable time should be adjustable to at least 0.001 seconds. These complaints are all relatively minor and overall I feel the instruments operated quite well and I was pleased with my results.

The carbon-13 spectrum of formycin is given in Figure 2. This compound is similar to adenosine except that the C8 and N9 in adenosine have been interchanged in formycin. Adenosine gives a normal C-13 spectrum (no appreciable broadening of any peaks) while in formycin we have two of the lines significantly broadened ($\Delta\nu 1/2 \cong 30$ Hz). This is due to scalar relaxation of the carbons by the Nitrogen-14 nucleus. The T_1 of the nitrogen is short due to quadrupole relaxation and the scalar coupling of the nitrogen to the carbon can be an effective relaxation process. If we assume that $J_{^{13}C-^{14}N}$ is ~10 Hz then the T_1 of the nitrogen is ~30 msec. These values seem reasonable but I welcome comments.

You will also note that there are only four carbons in the aromatic region and yet there are five carbons in the formycin base. On an expanded scale the low field broadened peak has a slight asymmetry that suggests the possibility of two overlapping resonances but I do not feel this is the case. I have more comments on this spectrum but this letter has gone on long enough already. I will conclude with a Table of the chemical shifts of formycin and Adenosine. Both samples were ~0.65 M in DMSO-d_6. The values given are in ppm downfield from DMSO-d_6.

Assignment	Formycin	Adenosine	Assignment
		-116.67	C6
C2	-112.09	-112.97	C2
C4?	-104.20 (broad)	-109.64	C4
C9?	- 99.17	-100.60	C8
C5?	- 83.52 (broad)	- 79.91	C5

Assignment	Formycin	Adenosine	Assignment
C4'	- 46.81	- 48.60	C1'
C1'	- 38.83	- 46.54	C4'
C3'	- 35.95	- 34.10	C3'
C2'	- 33.19	- 31.31	C2'
C5'	- 23.30	- 22.27	C5'

Sincerely,

Tom Krugh

Thomas R. Krugh
Assistant Professor of Chemistry

TRK:lcb

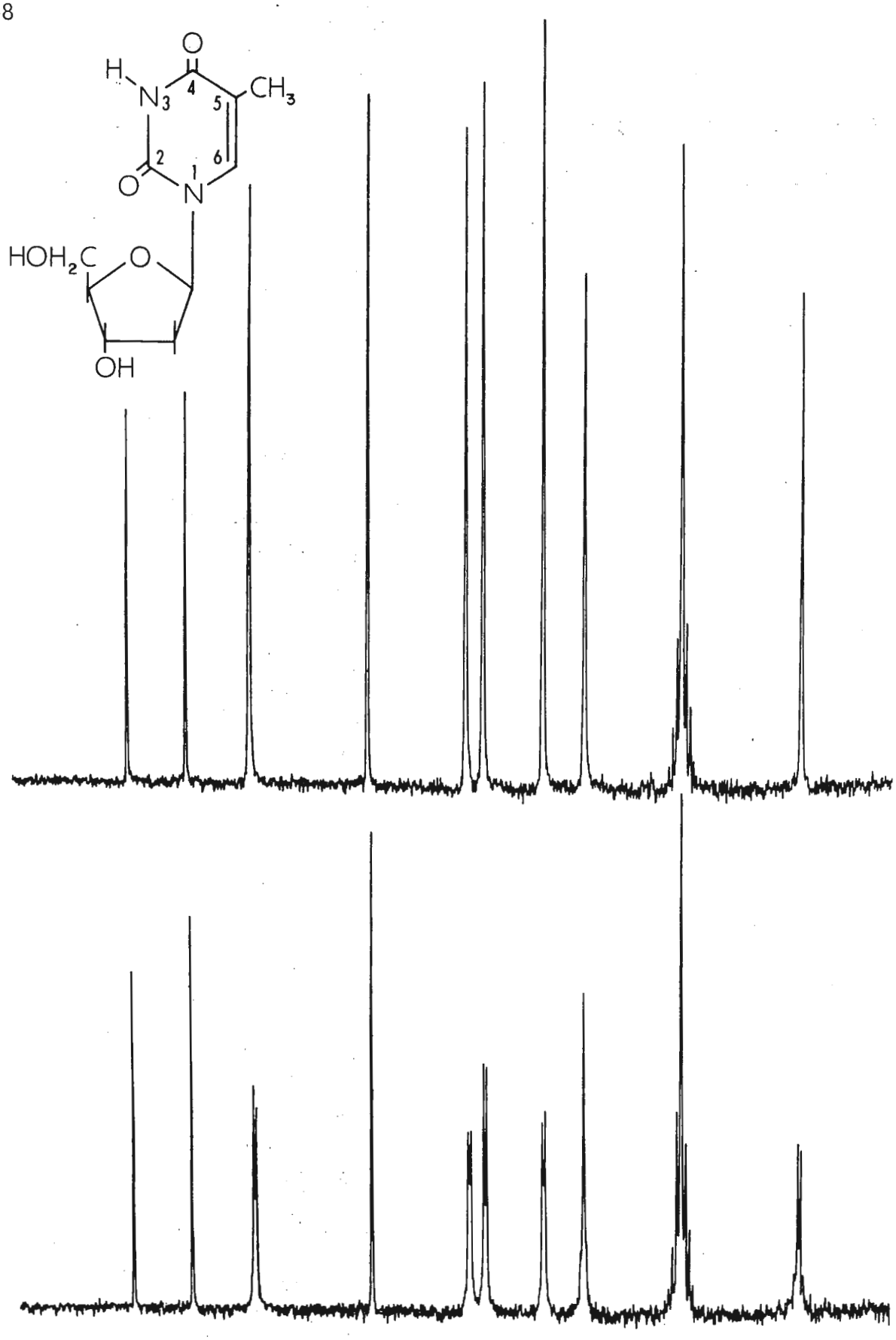

FIG. 1

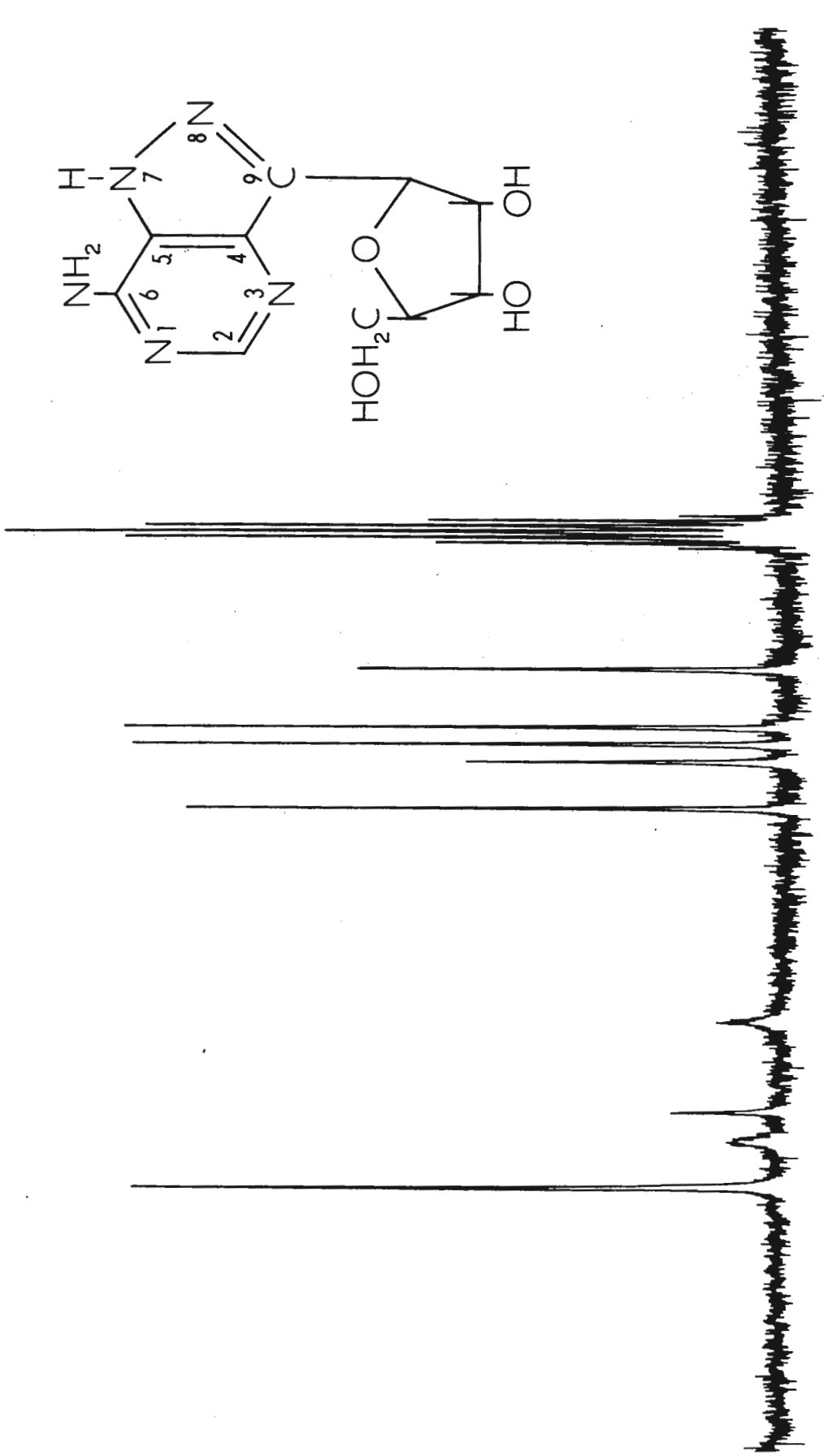

FIG. 2

160-10

COLORADO
STATE UNIVERSITY
department of chemistry
FORT COLLINS
COLORADO
80521

December 4, 1971

Re: ^{13}C NMR Symposium

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

Dear Barry:

I'd like to inform the readers of the Newsletter that we are organizing a symposium on ^{13}C NMR in conjunction with the Rocky Mountain Regional ACS Meeting, June 30-July 1, 1972, at Colorado State University. Although the meeting is nominally "regional", we hope that the combination of the excellent program of talks that we anticipate and the attraction of Colorado in the summer will induce interested researchers from many geographical areas to participate.

Anyone who is interested in more information on the symposium can obtain it by writing to me.

Sincerely,

Gary E. Maciel
Professor

GEM/mim

Unilever Research

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

CR/1235/as 12 Nov 71

Dear Dr Shapiro,

Spinning Device - Varian FT-100 Operation

To overcome sample spinning problems experienced when operating our HA-100 at low temperature, John Barzilay developed a simple device to exert a compensating downward air pressure on the spinner. This was reported in Analytical Chemistry 43, 160 (1971), and as a result of several requests we have had a small batch of these gadgets produced, which we can offer to interested parties at the cost price of D.fl. 145 (say $ 45). The device is also permanently fitted to our A-60 - although this is only feasible for those instruments having an HA-100 type spinner housing.

Since the end of January of this year we have been using an FT-100 accessory and 620i computer with our HA-100 for obtaining proton Fourier transform spectra. Apart from initial teething troubles during the installation period (about 4-5 weeks), the whole system has worked surprisingly well. We have found that even when it is not necessary to accumulate spectra use of the Fourier mode represents a useful time saving over the CW mode, so that almost all 100 MHz spectra are now obtained with the FT-100. During the necessary modification to our HA-100 system a low frequency filter had to be removed from the RF pre-amplifier. Initially this apparently had no ill-efects to normal CW use of the spectrometer, but over the months, with the system becoming slightly detuned, we have been troubled by increasing side bands when attempting homonuclear proton decoupling. We are hoping that things will be back to normal when the filter can be switched in for CW use.

One other inconvenience with the FT-100 is the appearance of a small inverted peak (approx. 6 Hz width at half peak height) at low field in all spectra. Since this also appears when no sample is inserted it is presumably a folded-back absorption from the probe itself.

Yours sincerely,

UNILEVER RESEARCH VLAARDINGEN

D.J. Frost J. Barzilay

160-12

Uppsala universitet
Fysiska institutionen

University of Uppsala
Institute of Physics

25.11.1971

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

Relaxation in an AB system

Dear Professor Shapiro,

We have studied the relaxation parameters in a strongly coupled two-spin system relaxed by an external catalyst. The line-shape analysis method developed by R.A. Hoffman was used. The ordinary slow-passage single resonance spectrum was recorded at successively higher rf amplitudes into the region of saturation of the spectral lines and the appearance of the double quantum transition. A corresponding set of theoretical spectra were calculated and plotted by a computer, and the relaxation parameters varied until a good fit with the experimental spectra was obtained.

The compound studied was fumaric acid monomethyl ester where the vinyl protons give a strongly coupled AB spectrum. The sample was doped with traces of a ferromagnetic compound. Assuming a random-field process being the dominant relaxation mechanism, we could calculate theoretical spectra. The computer program is quite general and gives the line-shapes for saturated and overlapping lines as well as for double quantum transitions. Some of the theoretical and experimental spectra at different rf amplitudes are shown here. One of the figures contains two theoretical spectra. They were calculated with slightly different strength of the random field relaxation interaction.

From these comparisons we determined the strength parameter and the correlation coefficient for the relaxation interaction at the two nuclear sites. The latter (r=0.65) is in good agreement with results from similar compounds.

We are planning to do some further work on line-shapes, and we intend to include other types of relaxation mechanisms in the present analysis method.

Sincerely yours,

Bo Gestblom

Ola Hartmann

Fysiska institutionen
Box 530
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Tel. 018-13 94 60

Institute of Physics
Box 530
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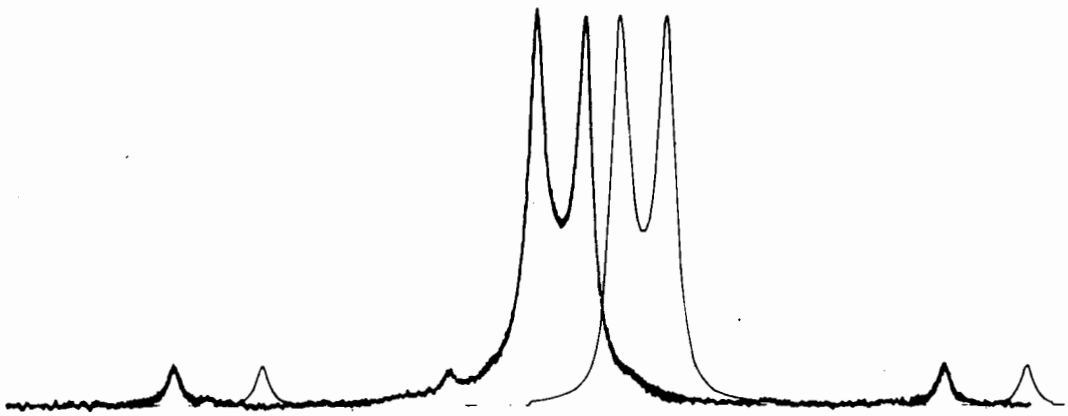
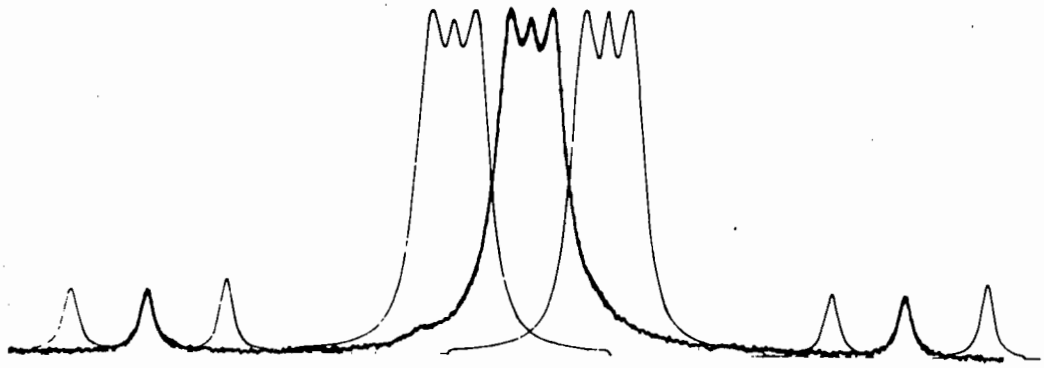
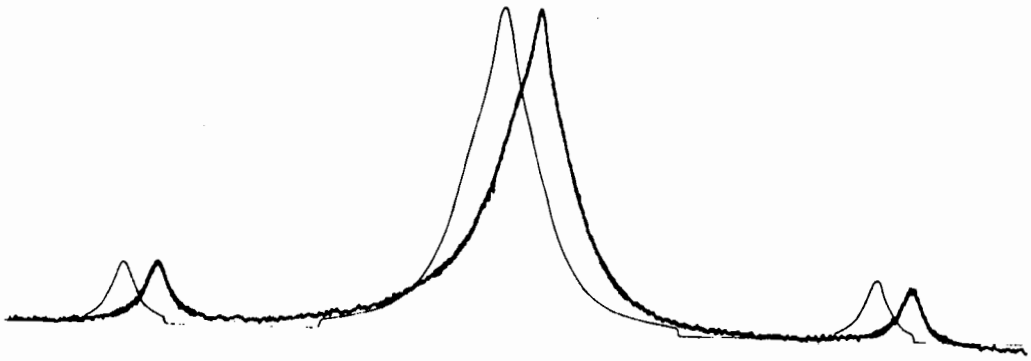






160-14

Doz. Dr. H. Dürr
Institut für organische Chemie
der Universität des Saarlandes
u. Dr. V. Formacek
Bruker Physik AG
Karlsruhe-Forchheim

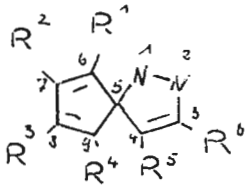
Saarbrücken, den 26.10.71
Telefon: 302.3409

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

Sehr geehrter Prof. Shapiro:

^{13}C- u. ^{1}H- NMR- Spektren von Spiro-pyrazolen

Seit einiger Zeit beschäftigen wir uns mit Spiro-pyrazolen vom Typ 1.



	R^1 - R^4	R^5	R^6
a	C_6H_5	CO_2CH_3	CO_2CH_3
b	C_6H_5	H	$CO_2C_2H_5$

Diese Verbindungen sind chemisch sehr schwer zu charakterisieren. Spektroskopische Studien sind infolge des hohen Substitutionsgrades ebenfalls unergiebig. Aus diesem Grunde haben wir die ^{13}C-NMR-Spektren von 1a und 1b aufgenommen.

Diese Messung wurde mit der Puls-Fourier-Transform-Methode (Bruker HX 90-Gerät) durchgeführt. Die Spektren sind in $CDCl_3$ aufgenommen. Als Locksignal wurde TMS eingesetzt. Zum Vergleich sind die ^{1}H-NMR-Spektren mit angegeben.

6.7.8.9-Tetraphenyl-3.4-bis-methoxycarbonyl-1.2-diaza-spiro[4.4]nonatetraen(1.3.6.8)

1a

6.7.8.9-Tetraphenyl-3-äthoxy-carbonyl-1.2-diaza[4.4]nona-tetraen(1.3.6.8)

1b

^{13}C-Spektren ($CDCl_3$)

C-Atom	$\delta^{13}C(H_2)$	$\delta^{13}C$(ppm)	C-Atom	$\delta^{13}C(H_2)$	$\delta^{13}C$(ppm)
3	3554.6	157.1	3	3303.1	145.9
4	3026.7	133.7	4	3009.0	132.9
5	2335.0	103.2	5	2390.0	105.5
6	3280.0	144.8	6	3197.3	138.6

Fortsetzung: ^{13}C-Spektren ($CDCl_3$)

	1a			1b	
C-Atom	$\delta\ ^{13}C(H_2)$	^{13}C(ppm)	C-Atom	$\delta\ ^{13}C(H_2)$	^{13}C(ppm)
7			7	3097.2	136.8
8	3069.3	135.6	8	3119.3	137.8
9	3262.0	144.1	9	3137.0	138.6

^1H-Spektren ($CDCl_3$)

Art der Protonen	τ (ppm)	Multiplizität	Art der Protonen	τ (ppm)	Multiplizität
arom. C-H	3.2-2.6	m	H-C=	1.65	s
CH_3	6.35	s	arom.C-H	2.7-3.2	m
			CH_2	6.25	q(7 Hz)
			CH_3	9.05	t

Interpretation des ^{13}C-Spektrums von 1a:

Nachdem eine Übereinstimmung zwischen den Literaturwerten[2] für die Phenyl-C-Atome und den gemessenen Werten festgestellt wurde,

C^{13}	C_1	o	m	p	
experim.	138.5	131.0	127.3	126.3	ppm
Lit.[2]	137.6	129.14	128.3	125.5	ppm

wurden die restlichen C-Atome des Ringskeletts zugeordnet.
Bei 2335 Hz (d.h. bei höchstem Feld) liegt das Spiro-C-Atom C^5. Bei tiefstem Feld ist es das C^3-Atom, das im Pyrazolring in unmittelbarer Nähe des N-Atoms steht. Die Lage dieses Peaks ist auf die elektronenanziehende Wirkung des Stickstoffs zurückzuführen. Bei 3262 und 3280 Hz befinden sich zwei Signale ähnlicher Verschiebung deren Flächen einem C-Atom entsprechen. Es handelt sich dabei - sehr wahrscheinlich - um die C-Atome 6 und 9. Eine genaue Zuordnung ist jedoch nicht möglich.
Bei 3069 Hz tritt ein Peak auf, dessen Verschiebung auf ein sp^2-C-Atom schließen läßt. Da die Fläche zwei C-Atomen entspricht, sollte es sich dabei um die C-Atome 7 und 8 handeln.
Das Signal bei 3026 Hz schließlich wird dem C-Atom 4 zugeordnet.
Die Signalintensitäten der einzelnen C-Atome sind durch Kern-Overhauser-Effekte und verschiedene Relaxationszeiten nicht alle gleich. Eine Übereinstimmung besteht jedoch innerhalb der Signale chemisch gleichartiger C-Atome wie der des aromatischen und des Spiro-pyrazol-Kerns.

(H.Dürr) (R.Sergio) (V.Formacek)

1) H. Dürr und L. Schrader, Z. Naturforsch. 24b, 536 (1969).
2) J. Mason, J. chem. Soc. (A) 1971, 1038.

Department of Chemistry

YORK UNIVERSITY

FACULTY OF SCIENCE

4700 KEELE STREET, DOWNSVIEW 463, ONTARIO

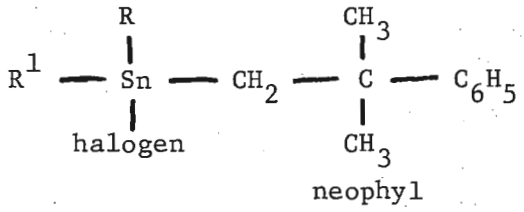
December 9, 1971.

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

NMR of Organo-Tin Enantiomers

Dear Sir:

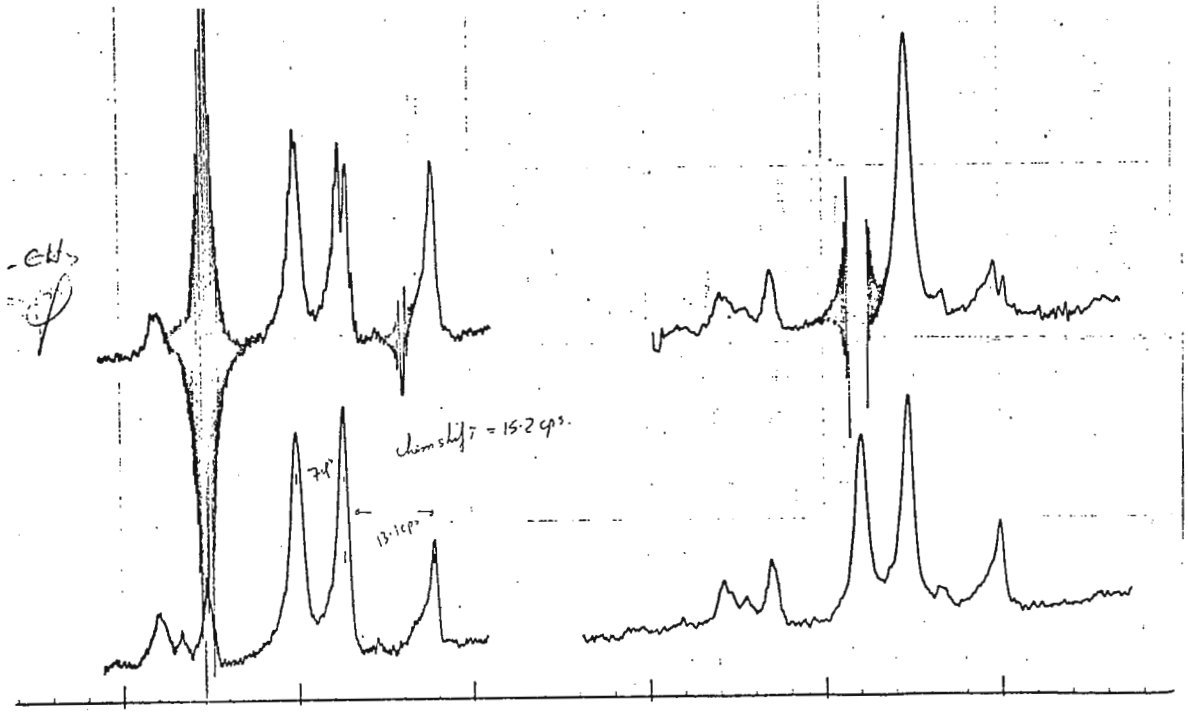
We were most interested in the recent newsletter (August) from Professor J.M. Anderson on exchange broadened NMR spectra of AB Nuclear Magnetic Double Resonance. The reason for this was our current interest in the nmr of dissymmetric tin complexes. In such complexes, anisochronous behaviour of methylene protons can be observed due to the inherent asymmetry of the molecules. This is a common enough phenomenon, well referenced in the literature. The only odd thing about the tin complexes is the requirement that at least one group must be a neophyl group. This is another story which we won't go into. The only other odd thing (and here the story really begins) is that except for one published case (Stynes & Allred, J.A.C.S. 93, 2666 (1971)) a halogen is also required. Thus diastereotopic nonequivalence is generally observed in tin complexes of the type



where R and R^1 are groups such as phenyl, methyl, butyl etc. Now in most cases the nonequivalence is of similar magnitude to the geminal coupling parameter resulting in ~ an AB spectrum. Further, often the outer weak transitions of the AB quartet are not seen, hence the interpretation of the spectra is open to charges of ambiguity. (We do have such a case but no charges were laid because we caught it in time ~ please read on.) It seemed appropriate to make use of our 100MHz decoupling facilities to prove the AB-ness of our spectra by tickling (the method of R. Freeman and W.A. Anderson, JCP 39 806(1963)). Tickle

we did, and thereby caught the aforementioned ambiguity and confirmed the AB-ness of a few other compounds. However, there is a problem as the exchange of enantiomeric forms of these compounds tends to be fast, and this is where Professor Andersons paper comes in, because now we know exactly what to expect in some of the cases where this begins to affect the spectrum. What we still don't really understand too well, although the basic groundwork has been laid down by Kaiser and others, is why we sometimes get a rather large Nuclear Overhauser Effect together with the double resonance splitting effect. A typical example is shown below for the methylene protons of tert-butyl phenyl neophyl tin iodide. It seems fairly clear that exchange can't be occuring at any great rate or we would get results similar to those of Prof. Anderson. So at the moment we are using it as a means of detecting possible stable enantiomers. Presumably these protons, buried inside the molecule, don't get relaxed too efficiently by normal methods other than via spin-spin interactions between themselves, hence have greater than normal sensitivity to perturbations of these neighbouring spin systems. We have noticed that at higher concentrations (where exchange via a bimolecular mechanism gets faster) this effect is greatly diminished. We would welcome any comments.

Another interesting feature of these complexes is the behaviour of the spin coupling constants. We have found that the ------; NO! we'll keep that for the next blue slip.



yours sincerely L. E. Holloway.

& S. A. Kandil

GENERAL ELECTRIC

CORPORATE RESEARCH AND DEVELOPMENT

GENERAL ELECTRIC COMPANY, RESEARCH AND DEVELOPMENT CENTER, P.O. BOX 8
SCHENECTADY, NEW YORK 12301, Phone (518) 346-8771

December 9, 1971

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

TITLE: CARBON -13 SPIN-LATTICE RELAXATION MEASUREMENTS; STRUCTURAL ANALYSIS OF AROMATIC COMPOUNDS

Dear Barry:

For the past six months we have been actively investigating ^{13}C spin-lattice relaxation behavior in intermediate size organic molecules. We have particularly been looking at substituted aromatic compounds.[1,2] Anisotropic molecular tumbling in these molecules results in very different spin-lattice relaxation times (T_1) for C-H carbons aligned and not aligned with preferred rotational axes. (See ref. 1 and 2.) C-H carbons having the C-H bond vector coincident with a preferred axis of rotation have shorter T_1 values than off-axis carbons. This rule facilitates cmr spectral assignments in aromatic compounds of intermediate complexity.

The FT cmr spectrum of 3-bromobiphenyl (Figure 1) has ten resonance lines. Five or six of the lines can be assigned based on chemical shift considerations. T_1 Values (in parentheses - Fig. 1) greatly facilitate remaining spectral assignments.

Carbons 4 and 4' have the shortest T_1, 0.76 sec, as a result of their alignment with the long biphenyl axis. T_1 For C-6 is shortened (0.96 sec) because it is para to the (heavy) Bromine. Both C-2 and C-5 are unaligned with any preferred axis of rotation (T_1 = 1.26 sec). As expected, rotation of the ring containing Bromine is slower than rotation of the other ring. This is evidenced by the longer T_1 values for the off-axis carbons on the latter (C-2' and C-3'; T_1 = 1.56 sec).

GENERAL ELECTRIC

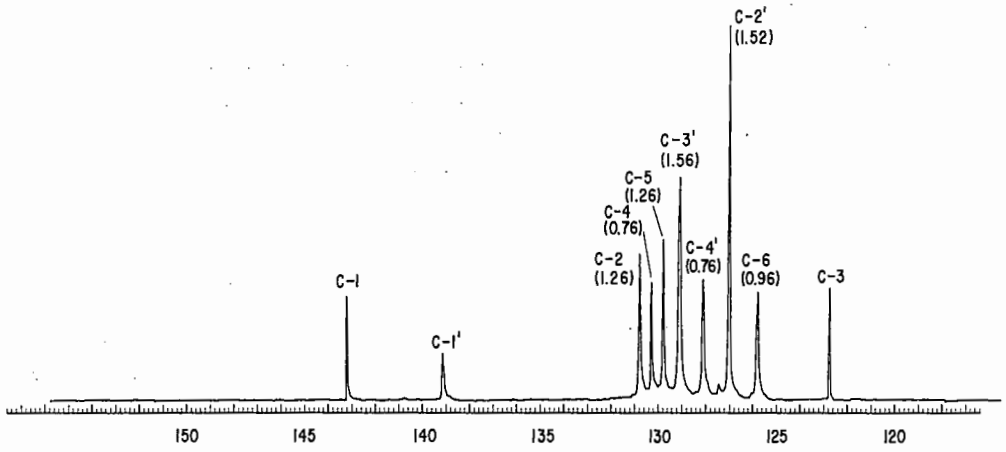
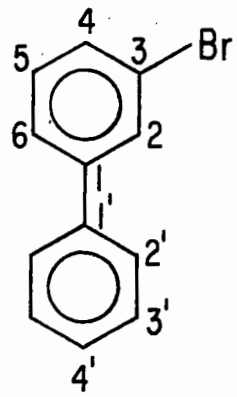


FIG. 1 FT CMR SPECTRUM OF 3-BROMOBIPHENYL. CHEMICAL SHIFTS RELATIVE TO TMS (T_1 IN PARENTHESES).



Best wishes,

George C. Levy

George C. Levy
Materials Characterization Operation

GCL/jmm

(1) G. C. Levy, Chem. Commun., in press.

(2) G. C. Levy, D. M. White, and F. A. L. Anet, J. Magn. Resonance, in press.

LABORATORIUM VOOR FYSISCHE CHEMIE

Toernooiveld
Driehuizerweg 200, Nijmegen
Telefoon (08800) 5 83 33

FACULTEIT DER WISKUNDE
EN NATUURWETENSCHAPPEN
KATHOLIEKE UNIVERSITEIT
NIJMEGEN, NEDERLAND

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

U.S.A.

Uw kenmerk | Uw brief van | Ons kenmerk

Datum December 10, 1971.

Onderwerp $Eu(DPM)_3$ - Induced shifts in cyclic polyethers.

Dear Professor Shapiro,

In an earlier contribution[1] we demonstrated the usefulness of Coronene$^-$, Na^+ ion pairs in THF solution as a shiftreagent for NMR spectra of polyethyleneglycoldimethylethers (glymes). Using Eu^{3+} or Pr^{3+} compounds as shiftreagents NMR spectra of the glymes were obtained, which were similar in shape to the spectra of the glymes attached to the sodium coronene ion pairs[2]. Attempts to measure NMR spectra of crown compounds (see structure formula in figures) complexed to sodium coronene were unsuccessful; however, interesting NMR spectra were obtained if the crown compounds were complexed to $Eu(DPM)_3$ (DPM = dipivalomethanato).

60 MHz.

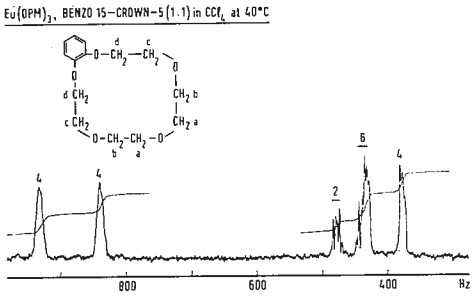
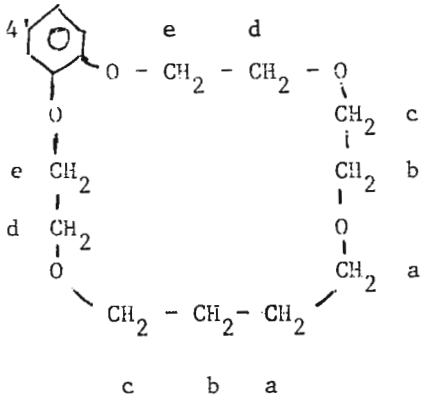


Fig. 1

Fig. 1 shows the effect of this compound on the spectrum of benzo 15-crown-5. In addition to the aromatic protonsignals found at about 420 and 440 Hz from TMS, four unresolved triplets are observed, each triplet representing two CH_2-groups. The intensities of the various peaks are indicated at the top of each peak. The NMR spectrum of benzo 18-crown-6 (the difference with the former compound is an extra CH_2CH_2O-group in the crown-ring) consists of four triplets and one singlet, apart from the

aromatic proton signals. Apparently the two CH_2-groups giving rise to a triplet are not adjacent ones, but are equally far removed from the aromatic ring.



In case of benzo 18-crown-6: the CH_2-groups b, c, d and e give rise to triplets, the CH_2-groups a give rise to a singlet.

Introducing a substituent (e.g. CH_3, Br, CH_3CO or vinyl) at the 4'-position in the aromatic ring yields even more detailed NMR patterns.

60 MHz.

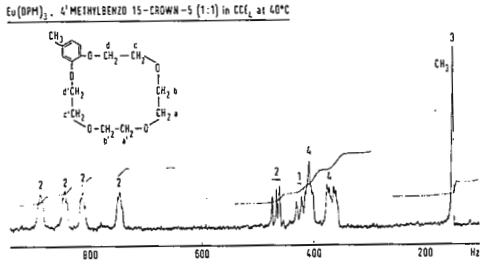


Fig. 2

As an example in fig. 2 is shown the NMR spectrum of 4' methylbenzo 15-crown-5: several triplets are split into two triplets, each triplet representing now one CH_2-group. These substituent effects are less pronounced in the 18-crown-6 compounds which we attributed to the larger flexibility of the crown-6-ring compared to the crown-5-ring.

Apparently a long-range shielding effect exist in these compounds, which becomes manifest by the enhancing influence of $Eu(DPM)_3$.

Sincerely yours,

(A.M. Grotens) (J. Smid) (E. de Boer)

1) E. de Boer, A.M. Grotens and J. Smid, TAMU NMR Newsletters 141 (1970).

2) A.M. Grotens, J. Smid and E. de Boer, Tetrahedron Letters, Nov. 1971.

A.M. Grotens, J. Smid and E. de Boer, J. Magn. Res., Febr. 1972.

University of Toronto
FACULTY OF PHARMACY
19 Russell Street
TORONTO 181, ONTARIO

December 10, 1971.

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

Dear Professor Shapiro:

^{13}CFTNMR Studies of Peptides

We are continuing our natural abundance ^{13}C Fourier Transform NMR studies on several biochemical systems,[1,2] including the amino-terminal 1-13, 1-15, and 1-20 (72, 79, and 92 carbon systems respectively) peptides of bovine pancreatic ribonuclease A (RNase A) and the 12 amino acid cyclic peptide, Bacitracin. Reported in Figures I and II are the respective aliphatic and aromatic/carbonyl resonance regions of the three RNase A peptides. These spectra were recorded on a Varian HA-100-12 system equipped for FT operation and utilizing a Varian 620-i 8K computer system. Within the last few months, the HA system has been replaced with a Varian XL-100-15 system again equipped for FT operation and in Figures III A and B are shown the respective aliphatic and aromatic/carbonyl ^{13}C resonance regions of Bacitracin as recorded on the XL system.

We have attempted detailed assignments of the carbon resonances in the RNase peptides using as a basis the ^{13}C chemical shifts of the individual amino acids comprising the peptides;[3] parameters describing the variation of amino acid chemical shifts as a function of the site of their incorporation in a peptide chain,[4] and difference spectroscopy. In Figures I and II, the tentative assignments in the 1-20 peptide are given. The excellent agreement between the free amino acid shifts (given by the stick diagrams in Figures I and II) and the peptide shifts, especially when the appropriate correction factors to the amino acid shifts when it is C- or N-terminal are considered,[4] provides evidence for the lack of any substantial secondary and tertiary structure in these peptides, in agreement with the circular dichroism and optical rotatory dispersion studies. An example of the agreement of the spectral details of the RNase amino-terminal peptides with smaller peptide systems is the resonance at 82.1 ppm (downfield from external CH_3I) in the 1-15 peptide and 80.9 ppm in the 1-20 peptide. These resonances are assigned to the β-carbon of serine (Ser) based on the difference between the spectra since 1-13 is devoid of Ser residues, 1-15 has one such residue, and 1-20 has three (apparently equivalent) Ser residues. According to the parameters derived by Christl and Roberts[4] from tripeptide systems, the β-carbon of a C-terminal residue is shifted downfield "on the average" 1.2 ± 0.6 ppm relative to the amino acid shift. Indeed the downfield shift of 1.2 ppm of the Ser β-carbon in the 1-15 peptide, where the residue is C-terminal, versus the 1-20 peptide where the residue is non-terminal is consistent with this finding (it is noted that the β-carbons of non-terminal residues in the tripeptides have substantially the same shift as in the free amino acids).

.../2

The presence of a thiazoline ring in Bacitracin formed by the amino terminal isoleucine and the adjacent cysteine residue and the unusual peptide linkage between the aspartyl γ-carboxyl group (residue #11) and the ε-amino nitrogen of lysine (residue #6) to form a 6 membered ring serve to produce deviations between some ^{13}C shifts in Bacitracin and the respective amino acid shifts. The most obvious example is the resonance at 97.1 ppm corresponding to the α-carbon of cysteine. The perturbation caused by formation of the thiazoline ring shifts this carbon ∿ 21 ppm downfield relative to the amino acid shift. We are in the process of attempting a more detailed analysis of the CMR spectrum of Bacitracin including relaxation studies.

Unfortunately, due to the large amount of "down" time associated with the XL installation in the first few months of its operation, we still are not in a position to discuss the merits of the XL system FT operation versus the HA system. However, the use of a heteronuclear lock is a blessing over the homonuclear lock required for FT operation on the HA-100. Furthermore, the necessity of including the CH_3I signal in the ^{13}C spectrum on the HA-100 dictated a spectral width and acquisition time unfavorable for best resolution. In addition, the problem of dynamic range associated with the intense CH_3I (90% ^{13}C-enriched) peak necessitated the use of block-averaging techniques essentially reducing the data table of the 620-i by half. These problems are circumvented with the XL system and the better resolution obtainable with more appropriate data acquisition times is evident in the Bacitracin spectrum. For example, note the large resonance at 148.6 ppm in the RNase peptides - this peak corresponds to the $C_{2,3,5,6}$ ring carbons of phenylalanine (Phe). In the Bacitracin, which also has one Phe residue, this resonance in the CMR spectrum is resolved into two peaks corresponding to the $C_{2,6}$ and $C_{3,5}$ carbons. The spectrum of the 1-15 peptide on the XL also reveals the presence of two such peaks with approximately the same separation as in Bacitracin.

With best wishes,

Sincerely,

Murray H. Freedman and James R. Lyerla, Jr., Faculty of Pharmacy, University of Toronto, Toronto, Canada, and Jack S. Cohen and Irwin M. Chaiken, National Institues of Health, Bethesda, Maryland.

P.S. In a competitive spirit, we wish to report that the record in our laboratory for the Varian "duck-shoot" program is currently held by Professor William Reynolds of the Department of Chemistry, who one dreary day, when the only working instrumental feature on the XL was the duck-shoot program, recorded 43 hits (wounded or killed) out of 50 ducks. We wonder how this stacks up against other laboratories - if indeed, other laboratories engage in such frivolity.

.../3

Footnotes:

1. M. H. Freedman, J. S. Cohen, and I. M. Chaiken, Biochem. Biophys. Res. Commun., 42, 1148 (1971).

2. J.S. Cohen, M. H. Freedman, and I. M. Chaiken, TAMU-NMR Newsletter, No. 149, 40 (1971).

3. W. Horsley, H. Sternlicht, and J. S. Cohen, J. Amer. Chem. Soc., 92, 680 (1970).

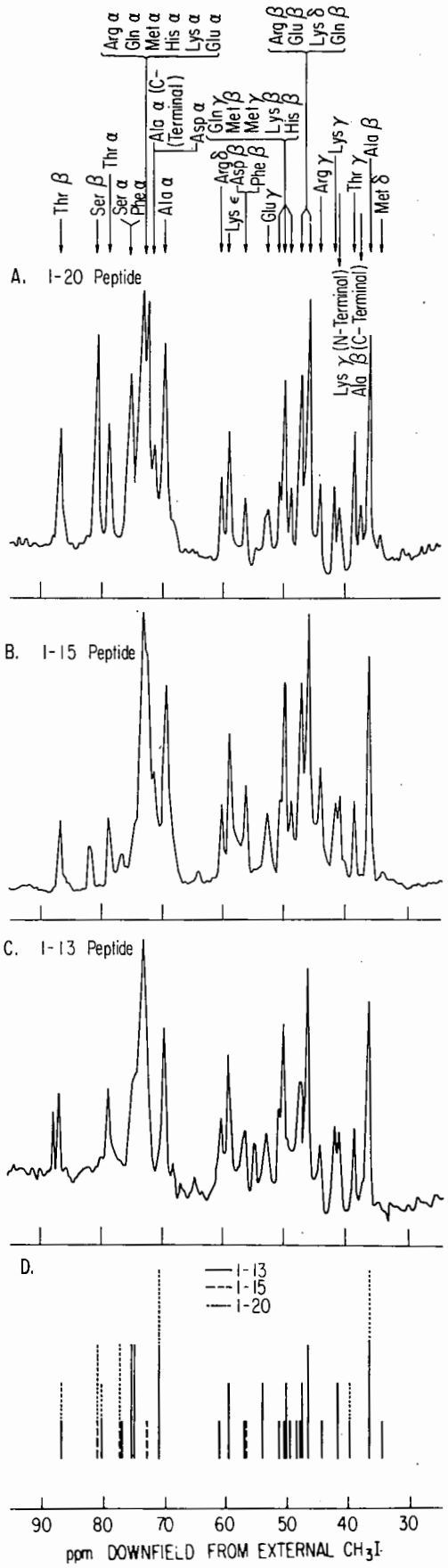
4. M. Christl and J. D. Roberts, J. Amer. Chem. Soc., in press (1972).

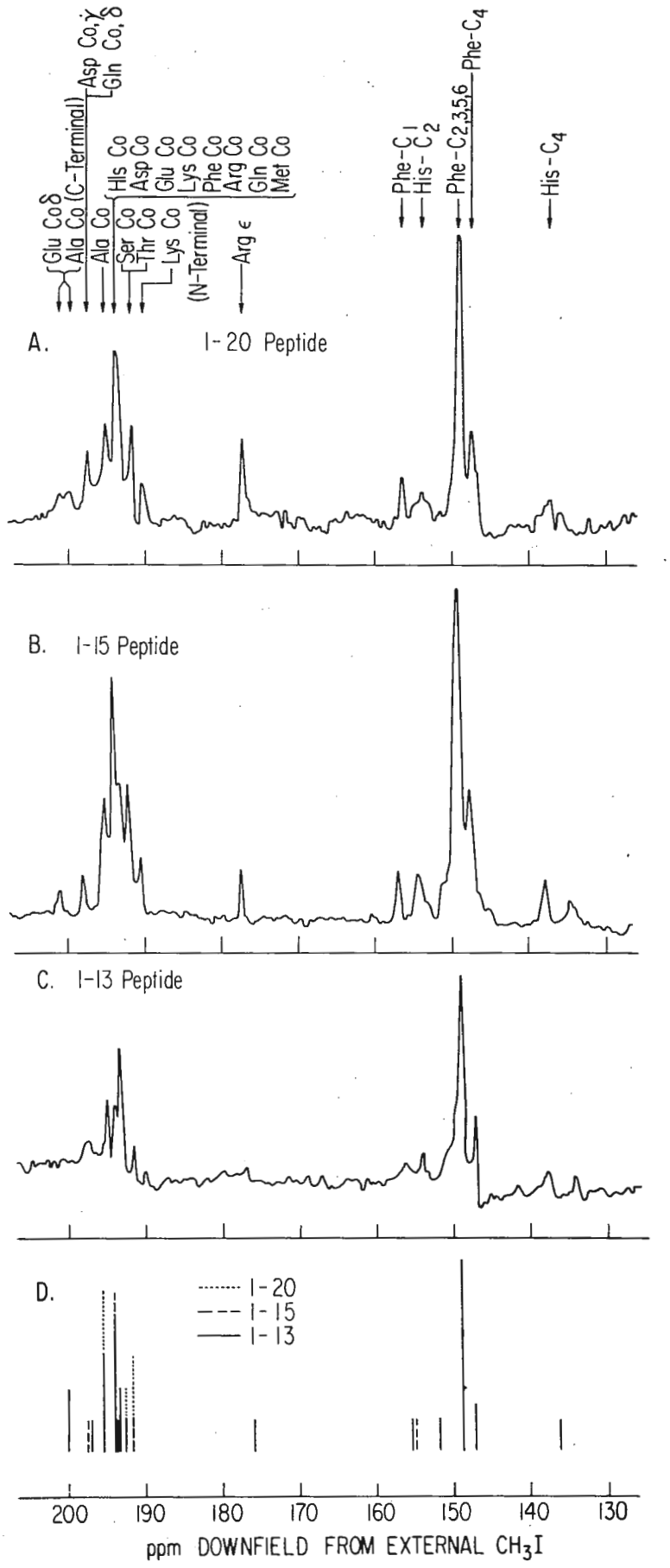
Figure Captions:

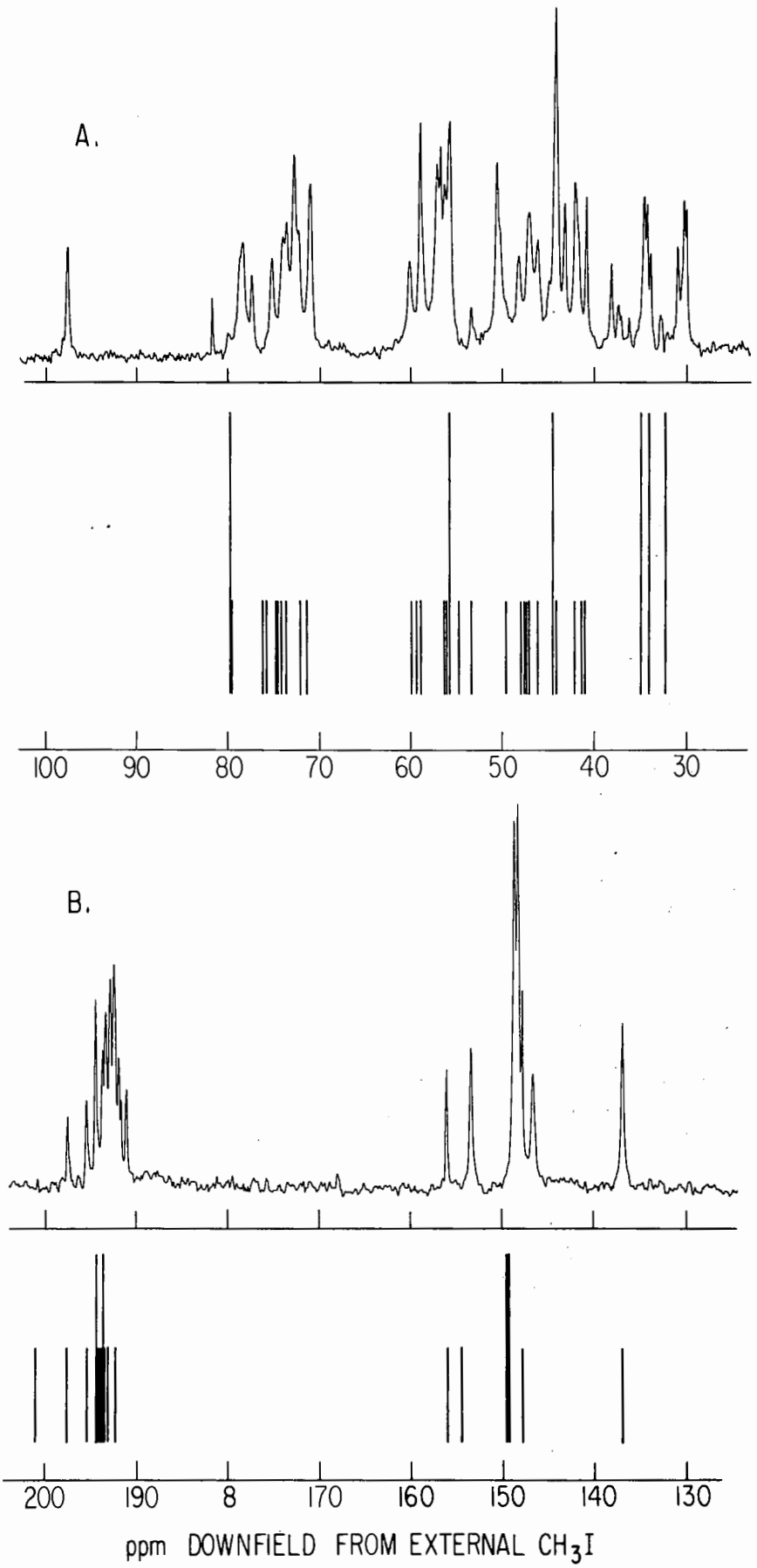
Fig. I A) The aliphatic region of the CMR spectrum of the amino-terminal 1-20 peptide of RNase A. The assignments in the peptide are listed above its spectrum. B & C) The respective aliphatic regions of the 1-15 and 1-13 amino-terminal peptides of RNase A. D) The stick diagram for the three peptides based on amino acid shifts. The spectrum of the 1-20 peptide represents 2000 blocks (250 pulses/block) of data accumulation on a 0.045 M solution at pH = 5.5 (∿ 20.6 hr time required). The spectra of 1-13 and 1-15 peptides represent 1500 blocks of data accumulation on 0.035 M solution at pH = 2.0 and 0.048 M solution at pH = 5.5 respectively (∿ 15.4 hr required for each spectrum).

Fig. II A-C) The aromatic/carbonyl region of the CMR spectra of the 1-20, 1-15, 1-13 amino-terminal peptides of RNase A. D) The respective stick diagram of this region based on the amino acid shifts. The assignments in the 1-20 peptide are listed above its spectrum. Peptide concentrations and running time are the same as for Fig. I.

Fig. III A) The aliphatic region of the CMR spectrum of Bacitracin and the respective stick diagram based on the amino acid shifts. The spectrum required 19,000 pulses on a 0.2 M solution at pH = 3.5 (∿ 2.1 hr required for the spectrum). B) The respective aromatic/carbonyl region of Bacitracin and the associated stick diagram.


Arg α
Gln α
Met α
His α
Lys α
Glu α
Arg β
Glu β
Lys δ
Gln β
Ala α (C-Terminal)
Asp α
Gln γ
Met β
Met γ
Lys β
His β
Thr β
Ser β
Thr α
Ser α
Phe α
Ala α
Arg δ
Lys ε
Asp β
Phe β
Glu γ
Arg γ
Lys γ
Thr γ
Ala β
Met δ
Lys γ (N-Terminal)
Ala β (C-Terminal)
A. 1-20 Peptide
B. 1-15 Peptide
C. 1-13 Peptide
D.
1-13
1-15
1-20
90
80
70
60
50
40
30
ppm DOWNFIELD FROM EXTERNAL CH3I


Glu Co δ
Ala Co (C-Terminal)
Asp Co, γ
Gln Co, δ
Ala Co
Ser Co
Thr Co
Lys Co
(N-Terminal)
Arg ε
His Co
Asp Co
Glu Co
Lys Co
Phe Co
Arg Co
Gln Co
Met Co
Phe-C1
His-C2
Phe-C2,3,5,6
Phe-C4
His-C4
A. 1-20 Peptide
B. 1-15 Peptide
C. 1-13 Peptide
D.
1-20
1-15
1-13
200
190
180
170
160
150
140
130
ppm DOWNFIELD FROM EXTERNAL CH3I


A.
100
90
80
70
60
50
40
30
B.
200
190
8
170
160
150
140
130
ppm DOWNFIELD FROM EXTERNAL CH_3I

ANALYTISCHE MESSTECHNIK

Kern- und Elektronenresonanz • Elektronische Messgeräte

SPECTROSPIN AG, CH-8117 ZÜRICH-FÄLLANDEN
Industriestrasse 26, Telefon (01) 85 48 55, Telex 54850

Fällanden, December 14th, 1971

Ihr Zeichen:
Unser Zeichen: Dr. K/eb

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

USA

Proton Fourier Transform Double Resonance

Dear Dr. Shapiro:

Bruker-Spectrospin has recently opened an application lab at Zurich, Switzerland. With this contribution we would like to initiate our subschribtion of TAMU-News Letters.

Thusfar homonuclear double resonance experiments have been restricted to CW-operating spectrometers. The adaptation of decoupling and tickling techniques for Fourier-Transform NMR work considerably extends its utility. Accordingly we have developed a time sharing method of homonuclear decoupling for FTNMR spectroscopy.

The sampling time of modern AD-converters is much shorter than the ordinary dwell times for recording free induction decays. This allows working with a receiver duty cycle of, say, 50 %. The period during which the receiver is turned off can be used for irradiation with a second transmitter frequency. The timing is achieved with a simple switching circuit triggered by the computer.

Proton Fourier Transform Double Resonance allows decoupling of various groups, saturation of disturbing solvent peaks or tickling experiments. A tickled spectrum of dibromopropionic acid is shown below.

Sincerely yours,

(Dr. H.P. Kellerhals) (M. von Moos)

H. Kellerhals M. von Moos

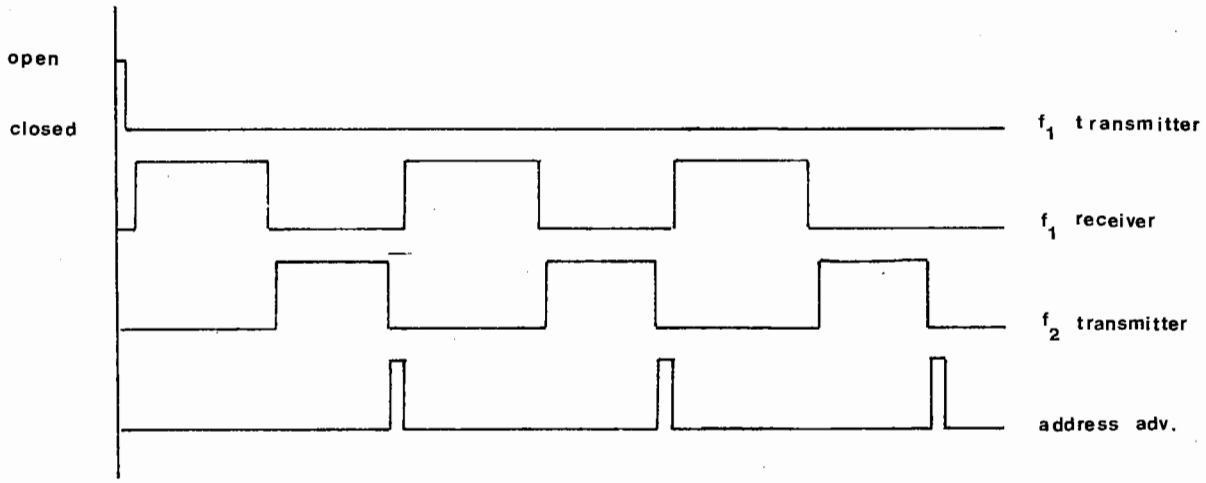


Fig. 1) Timing of double resonance experiments for FTNMR

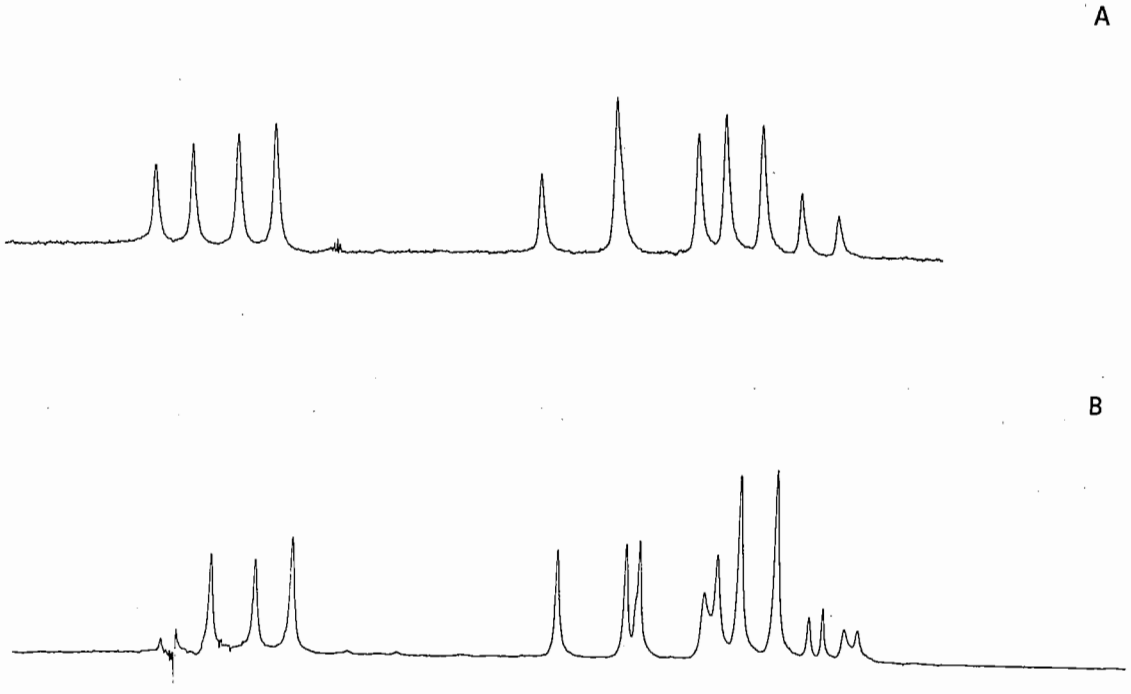


Fig. 2) FT spectra of dibromopropionic acid
A) normal spectrum
B) tickled spectrum

160-30

SECRETARIAT
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L'UNIVERSITE DE GENEVE
32, BOUL. D'YVOY
CH - 1211 GENEVE 4
SUISSE

TEL. 022 24.12.68

GJB/mp

GROUPEMENT AMPERE

LE PRESIDENT

Professeur Bernard L. SHAPIRO
Department of Chemistry
Texas A & M University
College of Science
College Station, Texas 77843

U.S.A.

Genève, le 14 décembre 1971

Cher Professeur Shapiro,

Merci de votre lettre de rappel du 6 décembre dernier.

1. NOUVELLES DU GROUPEMENT AMPERE.
   XVIIème Congrès Ampère - Turku (1972)
   1er Colloque spécialisé Ampère - Krakow (1973).
   Voir annexe.

2. TRAVAUX RECENTS DU DEPARTEMENT DE PHYSIQUE DE LA MATIERE CONDENSEE DANS LE DOMAINE DES RESONANCES MAGNETIQUES.

   a) par B. Borcard et G.J. Béné (Institut de Physique de la Matière Condensée, Université de Genève).
   Influence d'un gradient permanent axial sur les échos rotatoires à fréquence zéro.
   22, 786-789, 1971, Jour.Math. et de Phys. Appliquées (ZAMP).

   Résumé : Les auteurs étudient expérimentalement et donnent l'analyse théorique de l'influence d'un champ magnétique permanent et homogène, et surtout celle d'un gradient permanent ayant même symétrie que le champ générateur des échos rotatoires sur ce phénomène. On en déduit une méthode simple de détection et de mesure de faibles gradients magnétiques.

   b) G.J. Béné
   New spin echo techniques in the earth's magnetic field range.
   (Invited Lecture to the Fourth International Symposium on Magnetic Resonance, Rehovot and Jerusalem, August 24-31, 1971).

Résumé : The free precession, fundamental phenomenon of spin echo techniques is essentially non resonant. The spin echoes includes always 1) a coherent transitory state as starting point. 2) a dispersion of the elementary moments in the plane, perpendicular to the magnetic field. 3) a rotation by an angle α of the dispersion plane of the moments with respect to the magnetic field direction, and, 4) the observation of one or several echoes.

Stages 2) and 4) caused by the spreading of Larmor frequencies are passive ; in general, stages 1) and 3) are obtained by pulsed magnetic fields, in a suitable direction and of a certain duration, at the resonance frequency ω_0 of the nuclei in the magnetic field H_0 . In this sense, the spin echo techniques are derived from magnetic resonance.

We show phenomenologically, and illustrate by our experiments that stages 1) and 3) can easily be obtained in weak fields by non resonant methods. We can use the method of pulses at zero frequency, and have realized experimentally the rotary echoes in the laboratory reference frame.

These first results allowed us to analyse the various spin echo methods which can be deduced by a suitable choice of the axis of the pulses and by a rotation of the referential systems (dispersion plane of the moments and axis perpendicular to this plane) of an hypothetical experiment in which, the initial finite magnetization is subjected to a "pure gradient" (zero average field, but strongly inhonogeneous) whose axis of symmetry can be varied. Some new techniques of spin echoes are proposed and discussed.
The principal perturbations caused by a bad choice of pulse parameters or by the presence of residual permanent fields can, in this perspective, be quite simple analyzed and evaluated with precision.

c) par B. Borcard et G.J. Béné
ECHOS DE SPINS PAR INVERSION D'UN GRADIENT DE CHAMP MAGNETIQUE.
Séance SSP, Fribourg, 8-9-octobre 1971. A paraître HPA.

Résumé : Les auteurs décrivent une méthode nouvelle d'obtention d'échos de spins, dans laquelle on inverse seulement le gradient du champ magnétique appliqué.

Croyez, Cher Professeur Shapiro, à mes meilleurs sentiments.

Prof. G.J. Béné
Président du Groupement Ampère.

NOUVELLES DU GROUPEMENT AMPERE

XVIIème Congrès Ampère - Turku (1972).

Le 17e Congrès Ampère, organisé à Turku (Finlande) par notre collègue V. Hovi, Vice-Président du Groupement Ampère, aura lieu du 21 au 26 août 1972. La première circulaire relative à cette rencontre vient d'être distribuée. Nous recommandons à tous ceux qui seraient intéressés par le Congrès de Turku de se mettre sans retard en contact avec le secrétariat :

Mrs P. Somerkoski
Conference Office XVIIth Congres Ampere
University of Turku
Wihuri Physical Laboratory
20500 T U R K U 50

Finland

La seconde circulaire, qui sera distribuée en décembre 1971, contiendra une inscription ferme au Congrès de Turku. Rappelons que ce Congrès traitera des aspects physiques de la RMN et des phénomènes connexes.

1er colloque spécialisé Ampère - Krakow (1973).

Un 1er colloque spécialisé Ampère sera organisé du 28 août au 1er septembre 1973 par le Docteur J. Hennel de l'Institut de Physique nucléaire de Krakow (Pologne).

Les caractéristiques d'un tel colloque spécialisé sont les suivants :

- Environ 200 participants.
- Pas de sessions parallèles.
- Facilités pour discussions en petits groupes.
- Résumés détaillés distribués aux participants au début du colloque.
- Publication d'un compte rendu (exposés invités et communications).

Le sujet de cette rencontre sera "Nuclear Magnetic Resonance in solids : Pulse methods, High resolution, spin dynamics and related phenomena". Rappelons l'adresse de l'organisateur :

Docteur J. Hennel
Institut de Physique
ul Rodzikowskiego 152
K R A K O W 23

Pologne

à qui toutes informations peuvent être demandées.

THE UNIVERSITY OF TOLEDO / TOLEDO, OHIO 43606 / [419] 531-5711

College of Arts and Sciences
Department of Chemistry

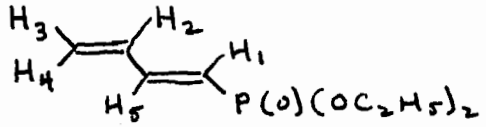
15 December, 1971

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

Analysis of the PMR Spectrum of Diethyl 1,3-Butadienylphosphonate

Dear Barry:

In a continuation of our interest in the spectra of vinyl-phosphorus systems and long-range phosphorus-proton couplings, we have recently completed an extensive analysis of the proton spectrum of diethyl 1,3-butadienylphosphonate.



The results are as follows:

ν_1	570.575	J_{14}	0.657	J_{34}	1.548
ν_2	642.140	J_{15}	16.731	J_{35}	-0.736
ν_3	540.683	J_{16}	18.101	J_{36}	2.882
ν_4	554.732	J_{23}	10.095	J_{45}	-0.803
ν_5	696.686	J_{24}	17.002	J_{46}	1.717
J_{12}	- 0.842	J_{25}	10.536	J_{56}	20.511
J_{13}	0.601	J_{26}	- 1.928		

The complete program LAOCN 3 was used for the final fit. All coupling constants are accurate to ±0.02 HZ and RMS error is 0.070. The calculated proton-proton coupling constants are in good agreement with the accepted values for the parent compound, 1,3-butadiene, indicating the phosphonate to possess an s-trans configuration. A manuscript covering these results is being prepared.

Best regards,

M. Mutter

Martin S. Mutter

Clay

Claibourne E. Griffin

INDIANA UNIVERSITY
Department of Chemistry
CHEMISTRY BUILDING
BLOOMINGTON, INDIANA 47401

December 15, 1971 TEL. NO. 812—

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

Title: Relative Merits of Low and High Magnetic Fields for Carbon-13 Fourier Transform NMR of Biopolymers

Dear Barry:

The dreaded pink sheet has arrived!

As everyone knows, if the "extreme narrowing limit" for relaxation applies, so that relaxation times are field-independent, a high resonance frequency provides better sensitivity than a low resonance frequency. This may or may not be the case for biopolymers in their folded conformation in solution, because the ratio T_1/T_2 may be much larger at high fields than at low fields, when the "extreme narrowing limit" does not hold. In addition, as pointed out by Kuhlmann, Grant, and Harris[1] the NOE in proton-decoupled ^{13}C spectra will change from 2.988 (assuming pure ^{13}C-^{1}H dipolar relaxation) for fast rotational reorientation to as little as 1.153 for slow reorientation. For "intermediate" values of the rotational correlation time, the NOE may change from a large value at low fields to a small value at high fields. We have done some calculations of T_1, T_2, and the NOE as a function of the rotational correlation time (τ_R) for a methine carbon which is part of a rigid sphere (approximately applicable to the α-carbons of native proteins). Some results are shown in Figs. 1-3, (where T_1, T_2, and τ_R are in seconds for three widely used magnetic field strengths (14.1, 23.5, and 51.7 kG). For a correlation time of 2×10^{-9} sec the NOE decreases very greatly when going from 14.1 kG to 51.7 kG. For a correlation time of 10^{-7} sec (expected for a protein of molecular weight 50,000-100,000), the NOE has the low value of 1.15 at 14.1 kG and 51.7 kG, so there is no change in S/N from NOE variations. But T_1 increases from about 0.126 sec at 14.1 kG to 1.67 sec at 51.7 kG (a 13-fold increase!), while T_2 remains unchanged at 0.0023 sec. Clearly the T_1/T_2 ratio is much less favorable at the high field, so that the S/N per unit time of signal averaging will be better at the low field.

The above considerations do not apply, of course, if rapid segmental motion dominates relaxation, as in denatured proteins. Neither are the results applicable directly to side-chains with fast internal rotation. We have done a theoretical analysis for a side-chain with one degree of internal motion attached to a spherical macromolecule (such as the methyl group of alanine in a protein). We have calculated

numerical results for T_1, T_2, and the NOE. More details in the form of a preprint[2] are available upon request.

Best Regards,

Adam

Adam Allerhand

References

1. K. F. Kuhlmann, D. M. Grant, and R. K. Harris, J. Chem. Phys. 52, 3439 (1970).
2. D. Doddrell, V. Glushko, and A. Allerhand, J. Chem. Phys., in press.

Fig. 1

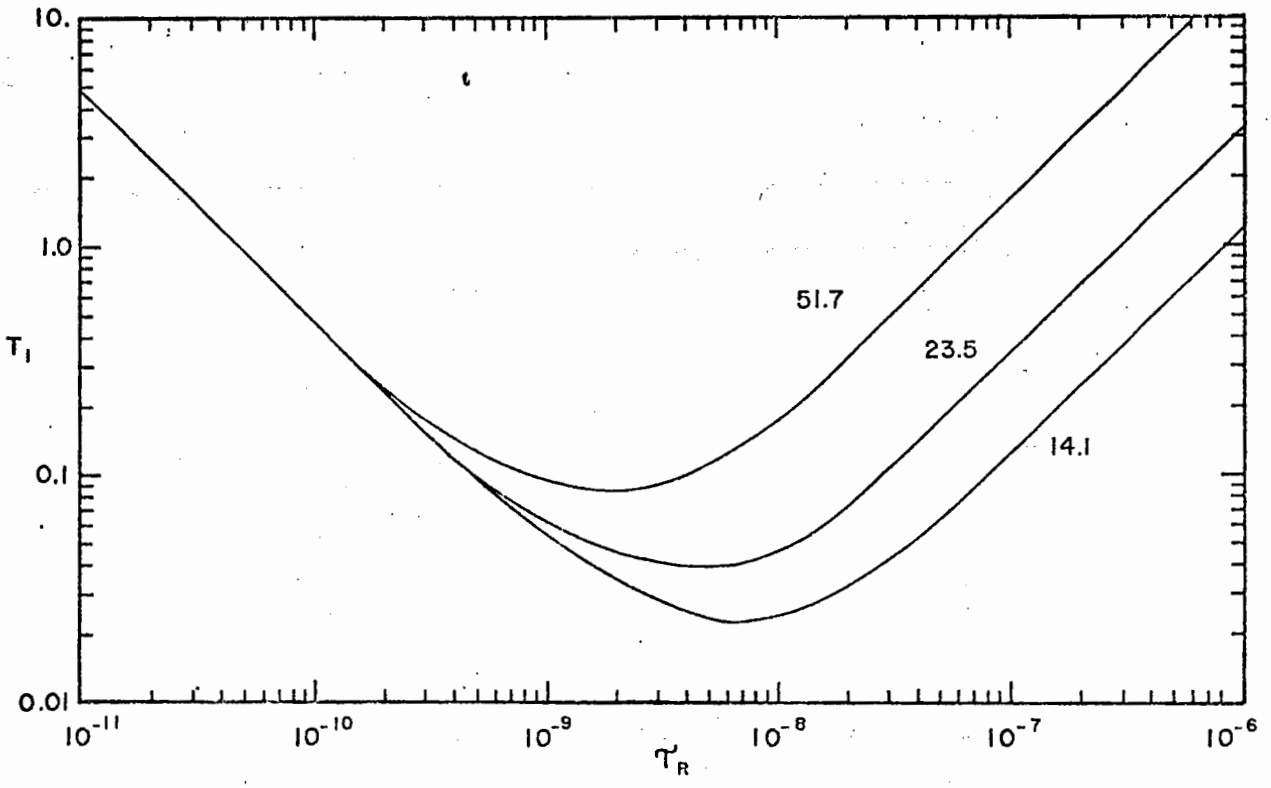


fig. 2

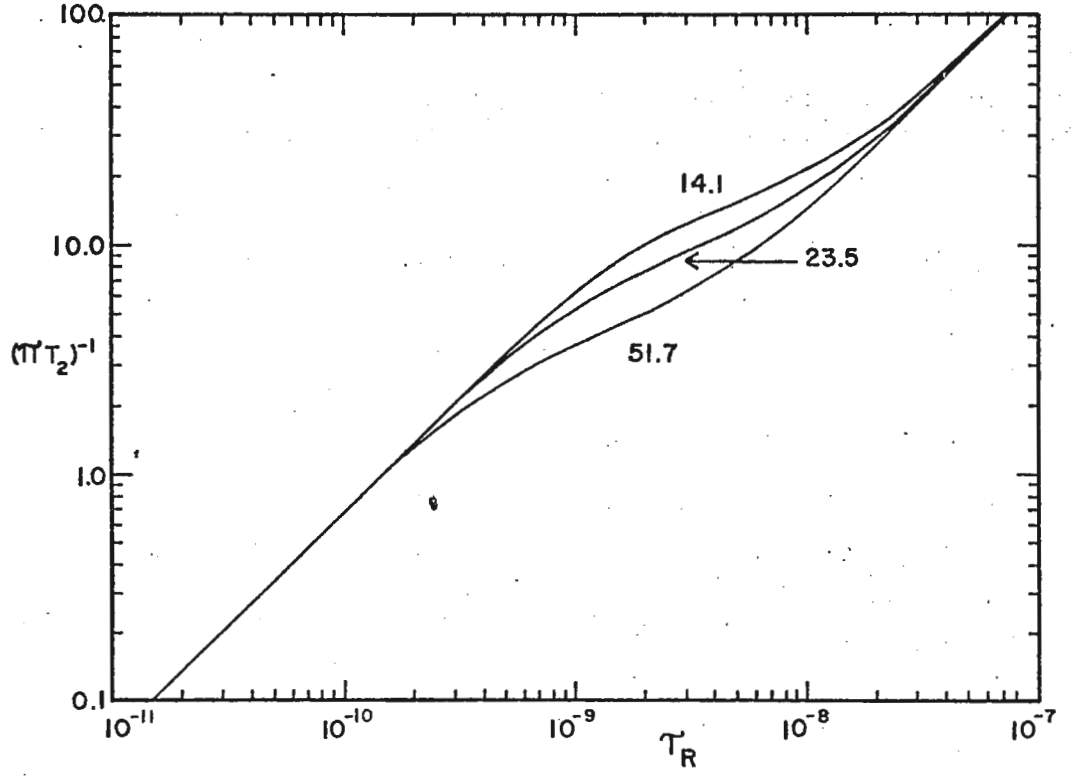
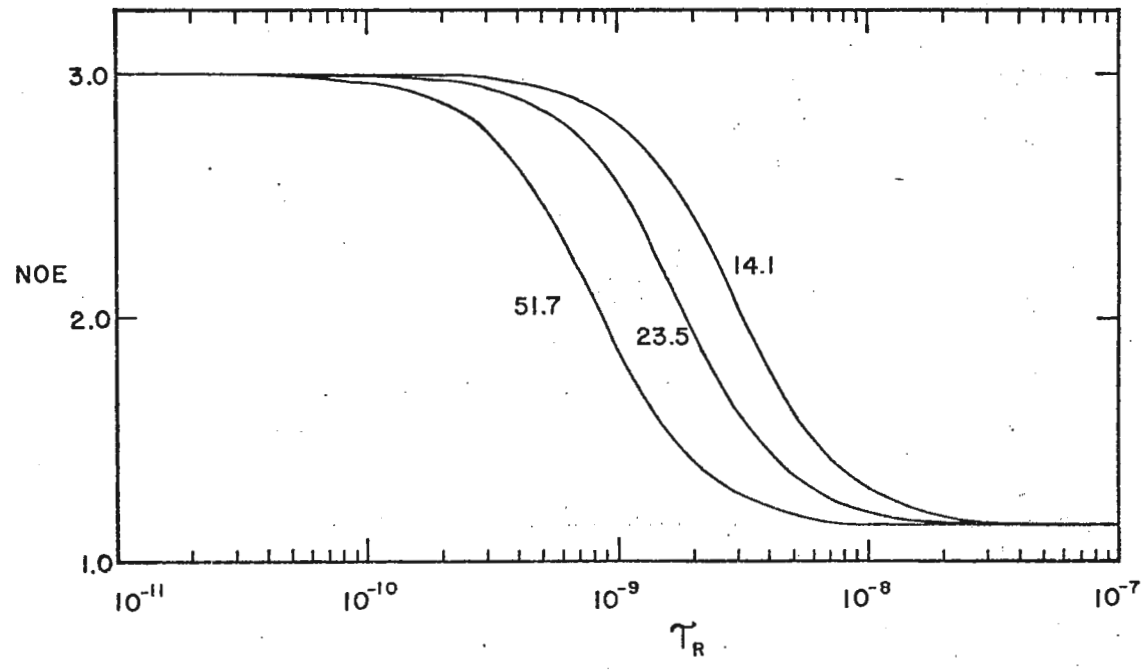

100
10.0
1.0
0.1
$(\pi T_2)^{-1}$
14.1
23.5
51.7
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
τ_R

fig. 3


3.0
2.0
1.0
NOE
14.1
51.7
23.5
10^{-11}
10^{-10}
10^{-9}
10^{-8}
10^{-7}
τ_R

Prof. Dr. Hanns Fischer

Physikalisch-Chemisches Institut
der Universität Zürich

CH-8001 Zürich
Rämistrasse 76
Telefon 01 / 32 26 20

December 15, 1971

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

Dear Dr. Shapiro:

CIDNP patterns are often calculated with the implicit assumption that the level populations of the products are simply proportional to the theoretically available population rates. Since experimental CIDNP patterns are mostly obtained under conditions for which the level populations are strongly influenced by relaxation processes as well as by the rates of population a more careful inclusion of relaxation in the calculation of CIDNP patterns is necessary if quantitative comparisons of experimental and theoretical results shall lead to support for one or the other formulation of the current radical pair theory. To do this the complete relaxation behaviour of the products must be known.

For the AB-proton system of $CHCl_2$-CHClCOOH in a 3:1 mixture of CH_2Cl_2 and $CH_2ClCOOH$ (J = 7 Hz, $\nu_0\delta$ = 140 Hz at H_0 = 23.5 kG) at 25°C we have determined the relaxation rates by studying time dependences of the four transitions (numbered 1 to 4 with increasing field) in the following way: In a first experiment the product was produced polarized in a reaction field H_r = 20 G by (5.0 ± 0.2) sec photolysis of dibenzoylperoxide in the mixture, then rapidly ($t_p \lesssim 1$ sec) transferred into the NMR-field H_0. The decay of the signals was observed at H_0. In the second experiment the reaction was carried out as before but with H_r = 21.0 kG, the sample was then stored for different times at a field of ≈ 2 G, the polarization measured later, immediately after rapid transfer. Analysis of the time dependences indicates

that the individual relaxation rates of the AB-system are practically independent of field strength and are caused by external fluctuating fields (intermolecular relaxation) as it would be expected for our case from the results of (1). Both protons relax with rates given by the usual relaxation matrix for external fields and $T_1 = (19.2 \pm 1.5)$ sec. The low field relaxation is compatible with a correlation factor $C = 0.67$.

Using these results we analyzed the experimental magnetic field dependence of the proton CIDNP (fig. 1) which was obtained by (5.0 ± 0.2) sec photolysis at various H_r, transfer into H_o in $t_r \lesssim 1$ sec and measurement of signal intensity (7 ± 1) sec after photolysis. In the analysis Adrian's high field CIDNP treatment (2) and the re-measured ESR-parameters (3) $\cdot CHCl_2$: $a_H = -16.8$ G, $a_{Cl} = 3.4$ G, $\cdot CHClCOOH$: $a_H = -19.96$ G, $a_{Cl} = 3.9$ G, and $g(\cdot CHCl_2) - g(\cdot CHClCOOH) = 1.3 \cdot 10^{-3}$ were applied. Adiabatic development of the states during transfer was assumed. Relaxation in H_r was treated in such a way as if all product molecules had been in H_r for 2.5 sec, relaxation during transfer was neglected, and relaxation in H_o (7 sec) was taken into account. The solid line in fig. 1 gives the result for the high field doublet. It is fitted with one scaling parameter to the experimental results. To save space we do not show the similarly excellent fit obtained for the low field doublet with the same scaling parameter.

The dashed curve shows the fit one would obtain with the same scaling factor for lines (3) and (4) if one assumed that all the lines decay with one unique time constant $\tau = T_1$. The influence of relaxation is most clearly seen for the points of zero-polarization, i.e. the crossing of line (4) and the field axis.

Sorry for the delay in sending our contribution.

Sincerely yours,

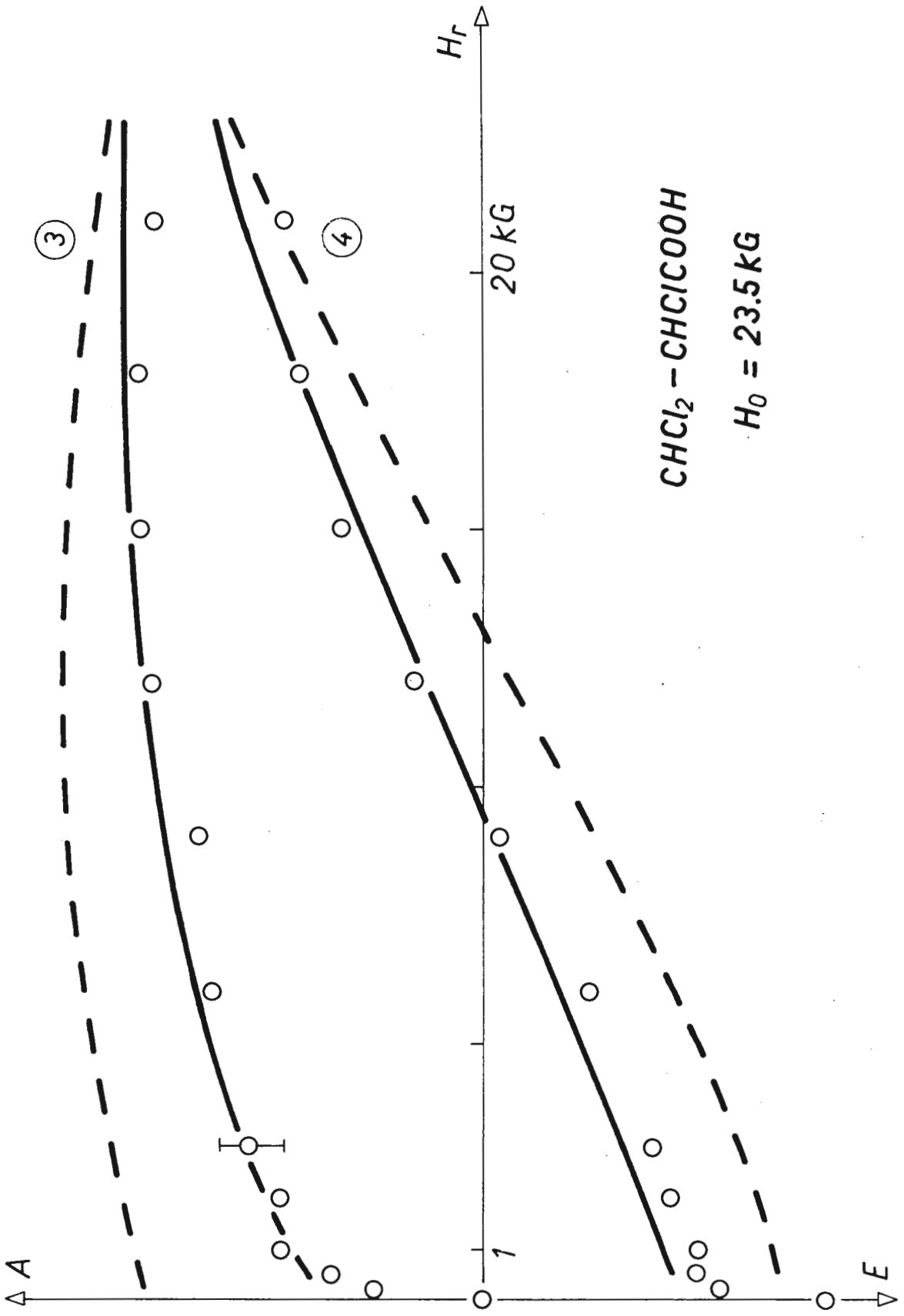
H. Fischer

Hanns Fischer Manfred Lehnig

(1) R. Freeman, S. Wittekoek and R.R. Ernst, J.Chem.Phys. 52, 1529 (1970)

(2) F.J. Adrian, ibid. 54, 70 (1971)

(3) H. Paul, unpublished


A
E
H_r
1
20 KG
3
4
$CHCl_2-CHClCOOH$
$H_0 = 23.5\,kG$

160-40

University of Waterloo

Waterloo, Ontario, Canada

Faculty of Science
Department of Chemistry

December 15, 1971

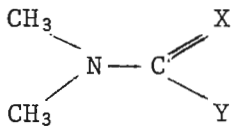
Dr. B.L. Shapiro, T.A.M.U. News,
Chemistry Department,
Texas A and M. University,
College Station, Texas 77843,
U.S.A.

Dear Barry:

The measurement of small couplings is a considerable experimental challenge that some labs have taken up. We feel we have an ideal series for such an endeavour. The long range coupling H-C-C-C-H in acetone of 0.54 ± 0.05 Hz (1) is well known and has been treated in an approximate theory (2).

We have noted a similar but smaller long range coupling (0.27 ± 0.05 H_3) in neat N,N dimethyl nitrosamine H-C-N-C-H. Assuming that the coupling is connected with π bonding at the nitrogen which also controls to a major degree the hindered rotation barrier about N-N in this case, then we should search for even smaller couplings H-C-N-C-H in molecules which have lower energy barriers. We have found another example and indications of a third case. The couplings and respective rotation barriers are:- N,N dimethyl nitrosamine $\Delta G^{\#} \simeq 23$ k cal $mole^{-1}$, $J_{H-C-N-C-H}$ 0.27 ± 0.05 H_3 (neat sample), $J_{H-C-N-C-H}$ disappears in 10 mole % solution in $(CHCl_2)_2$; N,N dimethyl thio carbamyl cyanide $\Delta G^{\#}$ = 23.5 k cals $mole^{-1}$, $J_{H-C-N-C-H}$ = 0.27 ± 0.05 H_3 in 1.5 mole % solution in $(CHCl_2)_2$. The latter coupling is temperature dependent and disappears above 130 deg. C. In N,N dimethyl formamide $\Delta G^{\#}$ = 21.0 k cals $mole^{-1}$ a long range coupling H-C-N-C-H is indicated by marked changes of resolution with solvent. No indication of long range coupling is seen in any amido type system with a barrier less than 21.0 k cals $mole^{-1}$.

If indeed there is a progressive decrease in long range coupling in a related series of molecules with solvents also playing a role, then in line with the magnitude of the hindered rotation barriers we might expect the coupling to decrease in the order:-



continued...

Dr. B.L. Shapiro. December 15, 1971

$X = S, Y = CN > X = O, Y = CN \sim X = O, Y = H > X = S, Y = F > X = O, Y = NCS \sim X = O, Y = CF_3 \sim X = O, Y = F > X = O, Y = N_3 > X = O, Y = CH_3 > X = O, Y = Cl > X = O, Y = Br$; etc.

Perhaps someone is interested in measuring coupling constants down to 0.01 Hz with expected solvent dependence.

With kind regards,

L.W. Reeves, R.F. Hobson,

LWR:lmb

References

1. J.R. Holmes et al. J.A.C.S. 83, 2959 (1961).

2. M. Karplus, J.A.C.S. 82, 4431 (1960).

160-42

EASTMAN KODAK COMPANY

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December 16, 1971

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

Caveat emptor, iterumque.
Or, more bugs in the Spectrosystem

Dear Barry:

We have been using the Varian Spectrosystem 100 for our signal averaging and have found that a serious error exists in the time averaging routine. The symptom we observed was a sharp discontinuity in the spectrum at a point of maximum (or near maximum) signal amplitude. This error might not be easily noticed in a very high resolution spectrum since it is likely to occur at the top of a peak, subtly producing a larger signal. However, for broad lines (such as from our protein solutions) it appeared as an obvious discontinuity.

This arises from an error in the Varian routine which does the signal averaging with an "average on overflow" technique. Since the computer word length is not sufficient to merely add each successive scan without overflowing, overflow is detected during a scan and

a) the input is scaled by 1/2,

b) each subsequent data point in memory being divided by two during the remainder of the scan,

c) at the end of the scan, all the data points up to the one which overflowed are divided by two.

We discovered that in Varian's teletype executive program No. 995122-00B, step (b) is erroneously omitted. Since the program does scale down the points up to the overflowed point at the end of the scan, a discontinuity in the spectrum results. This error repeats itself each time overflow is found during multi-scan averaging.

Kodak

Luckily, the cure was found by inserting only one word in the program in place of one instruction in this subroutine which was redundant. Listed below is the pertinent part of the program showing the change.

Address	Ins.	Mnemonic
2403	40315	,INR,
2404	40312	,INR,
2405	15000	,LDA, ← change to 42374 ,INR,
2406	4301	,ASRA, 1
2407	6130	,ERAI,
2410	100000	,0100000,

The arrow in the figure indicates the discontinuity in the protein spectrum. The broken line is the spectrum as correctly accumulated.

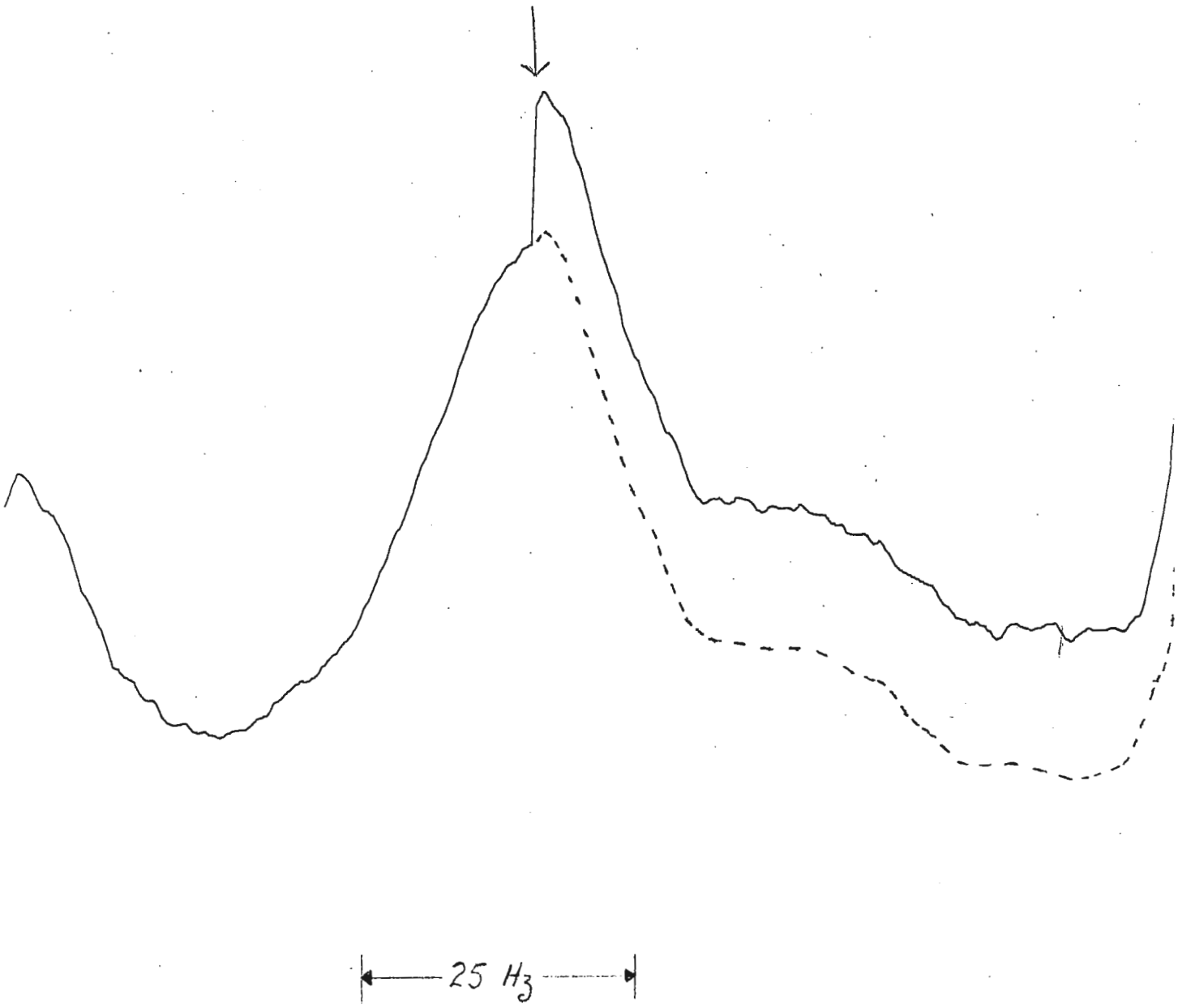
Best wishes for a Happy New Year.

Dick Graves Stan Gross Phil Rose

REG/CG/PIR/mg

160-44

~~400~~ ~~300~~ 2



8 scans, (single scan signal maximum adjusted to fill ADC)

University of Notre Dame
College of Science
Notre Dame, Indiana 46556

Department of Chemistry

December 20, 1971

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

Beyond the Coalescence Point

Dear Barry:

After getting over the surprise of having emerged unscathed from the recent exchange of broadsides concerning coalescence measurements in these venerable pages, I cannot resist the temptation to issue a commercial myself. I feel - perhaps wrongly - that certain crucial points have not been adequately emphasized by the various contributors.

Dnmr spectroscopists should be grateful to the mathematicians for having created the benevolent function called logarithm, known to swallow errors wholesale. Isn't it remarkable that with a rate constant off by as much as 100% and an error in the coalescence temperature (or any other temperature, for that matter) of 6° (imagine!), one still gets the free energy of activation to within about 5% in a typical situation? Here's how. The linearized relative statistical error in $\Delta G^{\ddagger}$ is given exactly by

$$(\sigma_{\Delta G^{\ddagger}}/\Delta G^{\ddagger})^2 = [\ln(k_B T/hk)]^{-2}(\sigma_k/k)^2 + [1 + \{\ln(k_B T/hk)\}^{-1}]^2(\sigma_T/T)^2,$$

or to a good approximation by

$$(\sigma_{\Delta G^{\ddagger}}/\Delta G^{\ddagger})^2 \approx [\ln(k_B T/hk)]^{-2}(\sigma_k/k)^2 + (\sigma_T/T)^2.$$

Take a typical case (T = 300 K, k = 100 s^{-1}) and find for the square root of the first term a value of 4% and of the second a value of 2%, which adds up to a total standard error of 4.5%, or, for a typical $\Delta G^{\ddagger}$ of 15 kcal/mol, to ± 0.7 kcal/mol. So, if one can be satisfied with this kind of precision (I hate to admit it, but such cases do exist), why bother about line shapes, questionable approximations, fine structure, accurate temperatures, good field homogeneity, relaxation, non-Lorentzian lines, temperature dependence of static parameters, etc, etc? Barring exceptional circumstances, the logarithm eats it all up!

Similarly, to get a free energy of activation correct to about 0.2 kcal/mol it is sufficient to have a single rate constant with an accuracy, say, of 25% at a temperature known to within 3^{o}. How easily this kind of accuracy is attainable depends on the case. In general, especially in the presence of complications, it would perhaps be advisable to do a little calculation. It needn't be a terribly sophisticated one; an approximate formula will probably do the trick in most instances.

But suppose now one is esoteric enough to desire decent values also for Arrhenius parameters or enthalpies and entropies of activation. Here the situation is dramatically different, as shown by an error analysis of the Arrhenius equation, which yields the following approximate expression for the standard error of the activation energy E_a:

$$(\sigma_{E_a}/E_a)^2 \approx [2T^2/(\Delta T)^2](\sigma_T/T)^2 + 2[\Delta(\ell nk)]^{-2}(\sigma_k/k)^2.$$

If the measurements cover a temperature range of $\Delta T = 20^{o}$, statistical errors of 25% in the rate constants cause an error of 26% in the activation energy, and an error of 3^{o} (at 300 K) introduces an error of 21% in E_a, for a combined error of 34% (± 5 kcal/mol for E_a = 15 kcal/mole). For $\Delta T = 60^{o}$ the corresponding numbers are 8.5%, 7%, 11%, ± 1.7 kcal/mol.

So how come that standard errors extracted from an Arrhenius or Eyring line are often found to be so unreasonably small? Must we blame the failure of the dnmr method on systematic errors and state categorically that a statistical analysis is not meaningful? Well, maybe. But not necessarily! I fear that the truth frequently turns out to be much simpler, and a great deal more embarrassing.

The crux of the matter is that there are two ways of calculating errors from an Arrhenius or Eyring line, a popular and an unpopular one. (It should not go unmentioned that authors with an aversion against mathematics have in addition devised various eyeballing procedures). In the first, one calculates the <u>precision of the fit</u> of the data points to a straight line. This procedure is perfectly adequate if, but only if, it is justified to assume that the statistical errors in the y coordinates of the individual data points are the same (their magnitudes don't matter), or at least approximately so. If this is not the case, one should carry out an explicit error propagation calculation, and then one might as well do things right and adopt Deming's method (instead of the "classical" Gaussian procedure), since it allows for errors in the y <u>and</u> x coordinates.

From the very nature of dnmr spectroscopy it is clear that the first method is hardly ever justified. For a two-line collapse or an $AB \rightleftharpoons BA$ exchange the weighting factors (proportional to the reciprocals of the variances) for the y coordinates are bound to be

smaller at the extremes of the rate range than around the coalescence point. As the above error analysis shows, we are thus faced with the unpleasant situation that careful line-shape analysis of simple spectra taken with all due precautions at carefully measured temperatures can give us very precise rate constants only in a range where they don't do us much good. The farther we move away from the coalescence region, the more valuable the points become in the statistics, but this beneficial effect is just about wiped out (or may actually be overcompensated) by the concomitant decrease in the weighting factors. In this context it should also be mentioned that a large chemical shift difference between the exchanging nuclei is indeed desirable from a quantitative point of view, but not necessarily sufficient in itself (fluorine, carbon-13 and supercon people should keep that in mind). What constitutes sufficient requirements is spelled out in a forthcoming paper in JACS (June 72).

To get rigorous values of the variances required for an error propagation calculation may not be a trivial task, but fortunately, rough estimates obtainable from a judgment of the relative sensitivity of the response of the calculated line shapes to changes in the rate constants, combined with the practical indistinguishability range of the match, go a long way. If all people would calculate their errors in this fashion, some might make a surprising, though not necessarily pleasant, discovery. I am willing to concede that this constitutes no progress, but it would certainly clear the air.

Finally, in view of all the inherent difficulties, is it really worth the trouble at all to go beyond the coalescence point? Clearly, there are cases where the answer must be no. Many dnmr spectroscopists nowadays seem convinced that it isn't worth it even in those cases where it appears technically feasible. Quite possibly, they are correct. But perhaps it would be wise not to be too dogmatic about it. For all we know at present, there may be very interesting information buried in activation entropies, for example, waiting to be discovered by fearless investigators who are not suffering from the production-line syndrome.

I apologize for expounding platitudes to those who have known about these things all along. I must admit that I was not fully aware of the pitfalls in the most commonly employed procedure for calculating errors from Arrhenius and Eyring lines until about two years ago, which was unfortunately after I had published a review article on the subject. Perhaps these belated confessions of a repentant sinner will still be of some use to a few.

Sincerely yours,

Gerhard

Gerhard Binsch

GB:mm

160-48
Institut für Organische Chemie
der Johann Wolfgang Goethe-Universität
Frankfurt am Main
Prof. Dr. H. Kessler

6 Frankfurt/M., den Dec. 20, 1971
Sandhofstr.
Telefon
(0611) 798-60 33

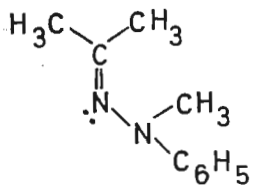
Professor Bernard L. Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas 77843
U S A

An unusual solvent effect on Z, E-topomerization of hydrazones

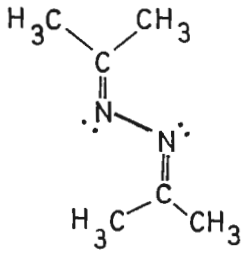
Dear Dr. Shapiro:

Your pink letter gave me an urgent remind but our move from Tübingen to Frankfurt took up a lot of time. That is the reason why I am so late this year.

Shvo and Nahlieli reported fast Z, E-topomerization[1] of the hydrazone I ($\Delta\nu$ = 18 Hz; T_c = 134°C; ΔG = 21.1 kcal/mol in hexachlorobutadiene)[2]. To our experience of substituent effects on inversion of nitrogen[3] the barrier should be much higher. From empiric calculations[4], which have been proved to be valid also for planar inversion of nitrogen, one gets an inversional barrier of about 50 kcal/mol.

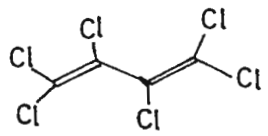
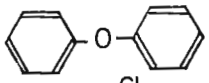
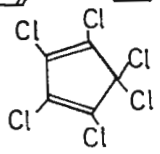
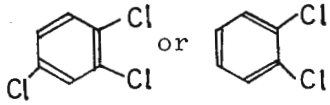
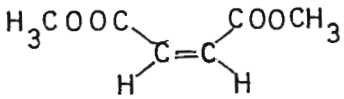
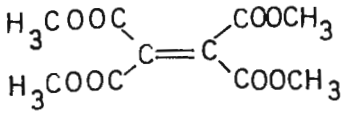


I



II

We therefore studied the influence of solvents[5] on the Z, E-topomerization of N-methyl-N-phenyl-acetone-hydrazone (I) as a representative example (table).

Solvent	T_c (°C)	
	120	
	> 190	no broadening
	95	
$Cl_2C{=}CCl_2$	135	
	> 190	broadening at 190
	> 190	sharp
	> 190	
$CHCl_2{-}CHCl_2$	186	

in all cases 10 - 12 Hz, all measurements 0.2 mol, NMR-Spectrometer Varian A 6o.

The table clearly shows that the coalescence temperature (T_c) of I strongly depends on the solvent used for measurements. The following experiments exclude plausible mechanistic possibilities:

1. The coalescence is not affected by the change of the nitrogen atmosphere to ordinary air (no oxygen catalysis).

2. Strong acids catalyze the topomerization, but traces of acids are not responsible for the coalescence. A coalescence at 120°C in diphenyl-ether requires o.2 mol trifluoro acetic acid per mol hydrazone.

3. No effect of (π-electron) acceptors such as tetracyanoethylene

or trinitrobenzene on T_c is observed.

4. Increasing concentration of I raises the T_c and vice versa in hexachlorobutadiene.

The specific catalytic effect of chlorine containing solvents is explained by a complex formed with the π-electrons of the imino-carbon and the chlor-atoms of the solvent, which facilitates the CN rotation.

The same effects have also been observed in compound II.

We are thankful for comments or other explanations.

Yours sincerely

H. Kessler

H. Kessler and A. Pfeffer*

*Chemisches Institut
Universität Tübingen

References

1) G. Binsch, E. L. Eliel and H. Kessler, Ang. Chem. Int. Ed. 10, 570 (1971).

2) Y. Shvo and A. Nahlieli, Tetrahedron Letters 1970, 4273.

3) H. Kessler, Ang. Chem. Int. Ed. 9, 219 (1970).

4) H. Kessler and D. Leibfritz, Tetrahedron Letters 1970, 4289, 4293, 4297.

5) For solvent effects on planar inversion of nitrogen see: H. Kessler and D. Leibfritz, Tetrahedron 25, 5127 (1969).

UNIVERSITY OF HOUSTON
CULLEN BOULEVARD
HOUSTON, TEXAS 77004
UNITED STATES OF AMERICA

DEPARTMENT OF CHEMISTRY

December 17, 1971

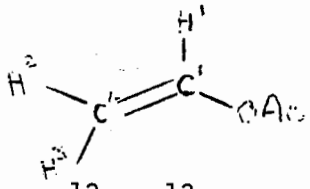
Professor B. L. Shapiro
Department of Chemistry
Texas A&M University
College Station, Texas 77843

Dear Barry,

^{13}C—H Coupling Constants in the Vinyl Portion of Vinyl Acetate

As part of the preparation of some hydrocarbons highly enriched in ^{13}C, Roger Knapp prepared a doubly labeled vinyl acetate. It has become a constant source of amusement to us to refer to the expected 108 line, first-order proton spectrum for mixture of vinyl acetates with enriched ^{13}C in the vinyl moiety. We were able to obtain all of the couplings listed in the table below by measurement of repeated line spacings. Any theoretician who might have an interest in more carefully determined numbers should get in touch with us.

We have revised the lanthanide-induced shift bibliography that we sent to a few people in September. The new one is "complete" through 15 November 1971 and is available on request.



Sincerely,

MRW

M. Robert Willcott

	$^{13}C_2$—$^{13}C_1$	$^{13}C_2$—$^{12}C_1$	$^{12}C_2$—$^{13}C_1$	$^{12}C_2$—$^{12}C_1$
J_{H1-H2}	6.4	6.5	6.5	6.4
J_{H1-H3}	14.1	14.1	14.1	14.1
J_{H2-H3}	1.4	1.4	1.4	1.4
J_{C1-H1}	193.0	—	193.0	—
J_{C1-H2}	6.5	—	6.5	—
J_{C1-H3}	7.8	—	7.9	—
J_{C2-H1}	10.4	10.4	—	—
J_{C2-H2}	163.0	163.0	—	—
J_{C2-H3}	160.0	160.0	—	—

160-52

UNIVERSITÉ DE LYON

LABORATOIRE DE SPECTROSCOPIE ET DE LUMINESCENCE

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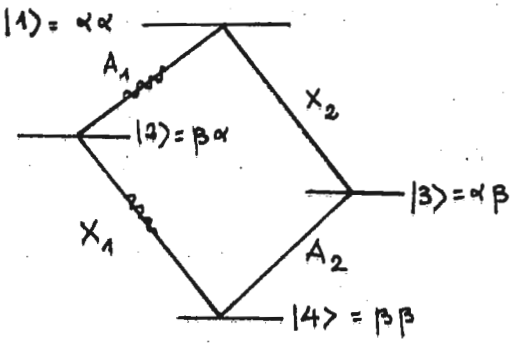
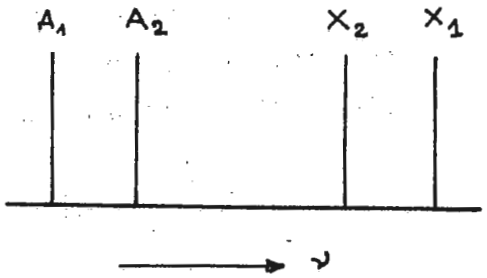
Cher Professeur Shapiro,

Titre : Observation de raies négatives dans une expérience de triple irradiation.

Nous nous intéressons actuellement à l'étude de différents paramètres de relaxation d'un système de deux noyaux AB. Pour cela nous avons mis au point un système de triple irradiation permettant de tracer un spectre RMN tout en irradiant simultanément deux raies de ce spectre. Nous présentons ici une expérience amusante de retournement d'une raie :

Considérons le système de 2 noyaux AX caractérisé par le diagramme d'énergie et le spectre de la figure (1,2.).





1. Diagramme des niveaux d'énergie 2. Spectre

La saturation de A_1 et X_1 avec des champs de radiofréquence H_2 et H_2' tels que $\gamma^2 H_2^2 (T_1 T_2)_{A_1} \gg 1$

et $\gamma^2 H_2'^2 (T_1 T_2)_{X_1} \gg 1$ a pour effet d'égaliser les populations des niveaux $|1>$, $|2>$ et $|4>$.

$N_1 = N_2 = N_4 = N_{sat}$, par suite :

$N_3 = N_o - 3 N_{sat}$.

Les intensités des raies X_2 et A_2, proportionnelles aux différences de population des niveaux mis en jeu, sont donc de signe contraire :

/...

$I(X_2)$ proportionnel à $N_{sat} - N_o/4$,

$I(A_2)$ " à $N_o/4 - N_{sat}$.

Nous avons effectué l'expérience sur le spectre des protons en position 2 du méthyl-4, dioxanne-1,3 à 100 MHz ($\Delta\nu/J = 6$).

Effectivement, sous triple irradiation, la raie A_2 du spectre apparaît renversée tandis que la raie X_2 voit son intensité diminuée. Ceci indique que la population du niveau $|3>$ est devenue plus grande que celle du niveau $|4>$ d'énergie plus faible.

Recevez nos sentiments les meilleurs.

J.C. DUPLAN J. DELMAU

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Herrn
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U S A

Präzision und Reproduzierbarkeit der Integration

Sehr geehrter Herr Professor Shapiro,

Wir untersuchen gegenwärtig, welche Faktoren die bei Routinemessungen erreichbare Genauigkeit der Integration von Protonenresonanzspektren beeinflussen. Da wir häufig quantitative Analysen durchzuführen haben, ist die Kenntnis dieser Faktoren für uns nützlich.

In einer ersten Untersuchung haben wir den Einfluss von Signalbreite, Signalgrösse und Integralamplitude an einem Gerät Varian A60A untersucht. Dazu haben wir das Spektrum einer Lösung von Naphtalin, Methylenchlorid, trans-Dekalin und Dioxan mit zwei verschiedenen Integralamplituden je zehn mal integriert. Die Konzentrationen der vier Komponenten wurden so gewählt, dass die Integrale von Naphtalin und Methylenchlorid gleich gross und etwa zehn mal grösser als die Integrale der beiden anderen Komponenten waren.

Damit erhält man für die Faktoren Signalbreite und Signalgrösse alle denkbaren Kombinationen:

Komponente	Signalbreite	Signalgrösse
Dioxan	klein	klein
Dekalin	gross	klein
Methylenchlorid	klein	gross
Naphtalin	gross	gross

Die Auswertung erfolgte nach einem faktoriellen Plan, wobei als vierter Faktor zur Kontrolle einer Wiederholung des gesamten Experimentes eingesetzt wurde. Dabei wurden die folgenden Resultate erhalten:

Der Wert des Integrals wird durch Signalbreite (Signifikanzschwelle 99%) und Signalgrösse (Signifikanzschwelle 95%) beeinflusst. Auch die Wechselwirkung zwischen diesen beiden Faktoren ist hoch signifikant (99%). Kleine breite Signale ergaben deutlich zu kleine Integrale.

Die Streuung der Einzelwerte der Integrale wird von allen drei Faktoren beeinflusst (Signalbreite: 95%; Signalgrösse: 99%; Integralamplitude 95%). Auch hier ist die Wechselwirkung zwischen Signalgrösse und Signalbreite signifikant (95%). Erwartungsgemäss ergab sich bei kleinen bzw. breiten Signalen eine vergrösserte Streuung. Ebenso ergab sich eine grössere Streuung bei der Integration mit grosser Amplitude.

Diese Resultate bestätigen die Vermutung, dass sich bei der Integration kleiner breiter Signale beträchtliche systematische Fehler ergeben. Dementsprechend sollen für genaue quantitative Analysen Referenz und Unbekannte sowohl bezüglich Signalbreite als auch Signalgrösse möglichst gut übereinstimmen.

Mögliche Verbesserungen der Genauigkeit und Präzision quantitativer Analysen sollen Gegenstand weiterer Untersuchungen sein, über die wir später berichten werden. Insbesondere wollen wir auch andere Gerätetypen (Varian HA100, Bruker-Spectrospin HFX-10 mit Puls-FTS-Zusatz, etc.) in die Untersuchung einbeziehen.

Mit freundlichen Grüssen

H. Meier

J. T. Clerc

E. Pretsch

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De Lairessestraat 174 - Telefoon 717451

AMSTERDAM, December 22, 1971

Uw ref.:

Onze ref.: 71120/JG/aa

Prof.Dr. B.L. Shapiro
c/o Texas A&M University
Department of Chemistry
COLLEGE STATION, Texas 77843
U.S.A.

Dear Professor Shapiro,

NMR of molecules, oriented in nematic solvents:

Recently, an investigation of NMR of molecules, oriented in nematic solvents has been accomplished (1). The first goal of this study was to investigate in which cases and under which conditions the NMR spectra provide reliable geometrical information. The neglect of pseudo-dipolar couplings, arising from anisotropy of indirect nuclear spin-spin couplings, has been studied and it has been shown that this neglect is not justified if *meta* and *para* fluorine-fluorine couplings in fluorine substituted benzenes are involved. The corresponding indirect couplings arise, at least partly, from anisotropic mechanisms. The same holds true for the geminal fluorine-fluorine coupling in 1,1-difluoroethene. In this case the tensor elements of the J-tensor could be determined.

The reported experiments do not give a clear picture about the anisotropy of the indirect *para* proton-proton and *ortho* fluorine-fluorine couplings in fluorobenzenes.

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The thesis (1) comprises experiments which have already been published by us as well as experiments which have not yet been published. A limited number of copies is available for anyone interested in this field and will be sent on request.

Sincerely yours,

J. Gerritsen

1. J. Gerritsen, thesis Free University, Amsterdam 1971.

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"Rotational Barriers"

Dear Dr. Shapiro,

As part of a study of rotational barriers in aromatic molecules we observed the effect of temperature on the n. m. r. spectrum of 3,5-dideuterio-4-dimethylaminobenzaldehyde in methylene chloride. For rotation of the aldehyde group in the same molecule previous workers have reported $\triangle G^{\ddagger}$ values at the coalescence temperature at 60 MHz of 10.8 kcal mol^{-1} in methylene chloride from the coalesence formula (1) and 10.5 kcal mol^{-1} in toluene and 10.2 kcal mol^{-1} in vinyl chloride from approximate formulas applied below coalescence (2).

We have carried out complete lineshape analysis of the 100 MHz spectra of the H_1 and H_2 protons from -20°C to 95°C. Lineshapes were generated by a program ABSHAPE for AB BA exchange based on the equations of Heidburg et al (3) and obtained from the Atlas N. M. R. Program library at the University of East Anglia. This program was modified to plot on the ICL 1934/6 graph plotter. The computer generated spectra were compared visually with experimental spectra to obtain the best fit. It was found that the chemical shifts were linearly dependent on temperature and the chemical shifts for the temperature range observed could be calibrated from the spectra obtained between -77°C and -95°C. At 100 MHz coalescence occurs at -62°C. Deuterium coupling was treated by assuming a constant change in line widths from those obtained at rapid exchange times to those observed at slow exchange. In the statistical treatment of results values obtained near the coalescence point were given the most weight.

From the Eyring plot, the results are $\triangle H^{\ddagger}$ = 10.5 kcal mol^{-1}, $\triangle S^{\ddagger}$ = -1.3 e.u., $\triangle G^{\ddagger}$ at -62°C (Tc) = 10.8 kcal mol^{-1} and $\triangle G^{\ddagger}_{300}$ = 10.9 kcal mol^{-1}. The small value obtained for the entropy of activation is as expected (4). However the exact value of the entropy

depends on whether the transition state for rotation has a structure in which the carbonyl group is perpendicular to the plane of the benzene ring.

The principle source of error in this treatment probably lies in the assumption of linear variation of line width. This problem is currently being approached from two angles. First for comparison purposes, the lineshapes of the undeuterated analogue are being calculated using the DNMR3 program of Binsch (5) obtained from the Atlas N. M. R. Program Library at the University of East Anglia. Secondly, the program DNMR3 is being modified to allow calculation of systems including atoms with spins different from 0. 5 and hence to directly calculate how the effect of the deuterium coupling on the line width varies with temperature.

Yours sincerely,

T. B. Grindley

A. R. Katritzky

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ИНСТИТУТ ХИМИИ
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Ul. Vavilova, 32, Moscow, USSR

« 28 » December 1971 г.

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Title: Ion-dipole Interaction in Biologically Active Cyclopeptidic Complexones by ^{13}C-NMR.

Dear Barry,

It had been already shown that the important information on the spatial structure and complexing mechanism of the stable alkali ion complexes of cyclic peptides and depsipeptides in solution can be obtained by ^{1}H-NMR. It is to be expected that the ^{13}C-NMR could provide new possibilities to such an end.

The distinctive characteristic of the complexes in question is the location of the ion within the central cavity of the cyclic molecule so that the former is held in place by ion-dipole interaction with those carbonyls that are oriented towards the center of the cavity. It was to be expected that with ion-dipole interaction of the type C=O...M^+ additional shift of electron density towards the oxygen will take place. This should decrease the ^{13}C screening only of those carbonyls that are sufficiently near the cation.

With valinomycin (36-membered cyclodepsipeptide [(D-Val—L-Lac—L-Val—D-HyIv)$_3$]) we have the following. There are four ^{13}C=O signals (Fig. 1a) of which , owing to symmetry of the chemical and spatial structure of the molecule [BBRC 34, 803 (1969); Chem. Nat. Prod., USSR, 1971, 221] , each should correspond to the carbonyls of three identical amino or hydroxy acid residues. Now, in the ^{13}C spectrum of the K^+ complex (Fig.1b) only one C=O signal falls within the C=O region of the non-complexed valinomycin spectrum (Table). But, since from

the structural considerations it follows that complexing should similarly effect the two ester C=O signals and similarly the two amide C=O signals, it is evident that all the ^{13}C=O resonances must have undergo a paramagnetic shift as a result of complexing.

The shifts of the two signals belonging to six C=O groups are quite considerable (3.1 - 5.5 ppm). These must be assigned to the ester carbonyls which, as had been established earlier, are engaged in strong interaction with the K^+ ion located in the molecular cavity (Fig. 2a). The shifts of the other two (amide) signals are smaller (0.5 - 1.9 ppm) that means that these carbonyls may only be participating in weak interaction with the cation because they take part in strong intramolecular H-bonding.

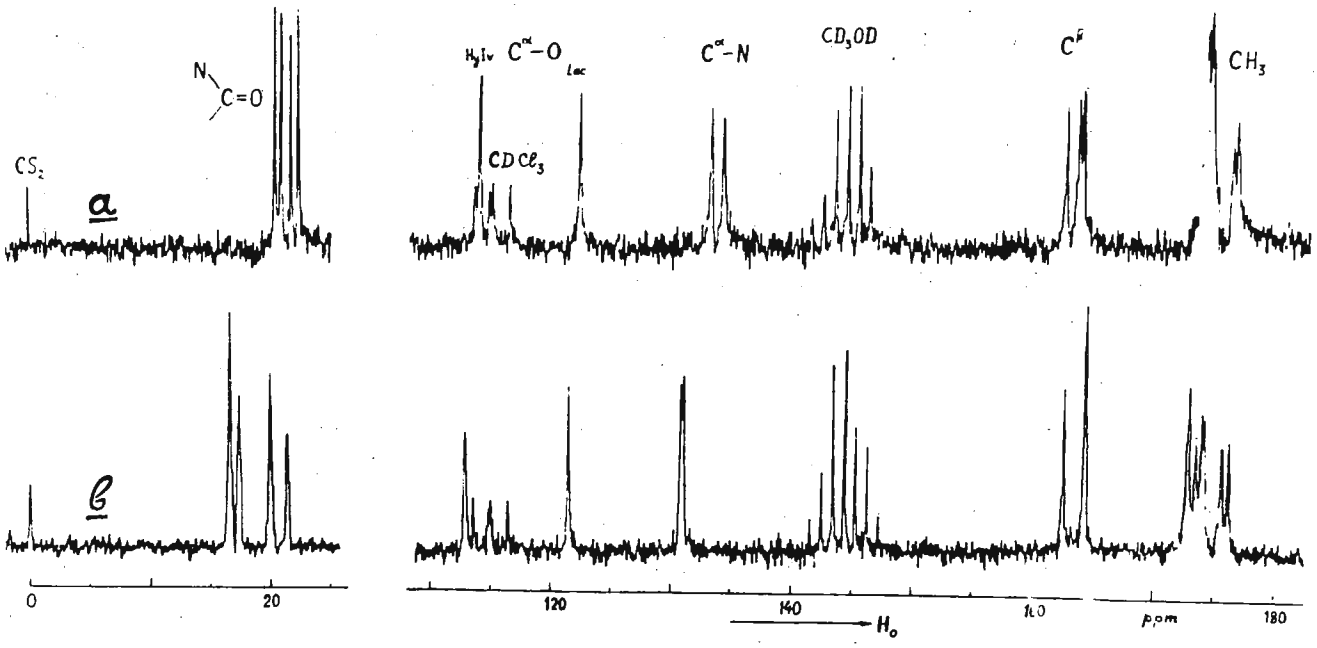

Fig.1. ^{13}C-NMR spectra of valinomycin (a) and of its K^+ complex (b). Bruker HX 90/13-18" FT-spectrometer.

Table. Carbonyl ^{13}C chemical shifts (ppm with respect to CS_2) for 200 - 300 mg solutions in 1.4 ml CD_3OD - $CDCl_3$(1:1).

	Compound	Na^+complex	K^+ complex
Valinomycin	20.4 20.9 21.7 22.8		16.8 17.3 19.8 21.2
Beauvericin	21.6 22.9	19.9 20.6	20.2 20.9
Val^6, Ala^9-antamanide	19.0 20.8 21.5 21.5 21.8	16.7 19.3 21.0 21.7 22.1	

In conformity with the theory of magnetic screening associated with electrostatic bond polarisation it follows that the induced chemical shift should diminish with decrease in the $C{=}O\cdots M^+$ angle from 180° to 90°. In enniatin (18-membered depsipeptides) complexes where all six carbonyls are symmetrically located around the central cation (Fig. 2b) these angles are much less than 180° [BBRC, 37, 668 (1969)] (in contrast with valinomycin where these are ~180°). Hence, despite the practically identical $O\cdots K^+$ distances in both types of complexes, the change in C=O resonances should be less for enniatins. In fact, in the K^+ complex of beauvericin —(L-Me—D-HyIv)$_3$ the C=O signals undergo less change in position (1.4 and 2.0 ppm) than that of the valinomycin complex (Table). When the K^+ is replaced by the smaller Na^+ ion a characteristic change occurs in the enniatin conformation, similar to the closing flower. This is connected with decrease in the $O\cdots M^+$ distance and a straightening out of the $C{=}O\cdots M^+$ angle both causing an increase in the positive charge electric field component directed along the carbonyl bond.

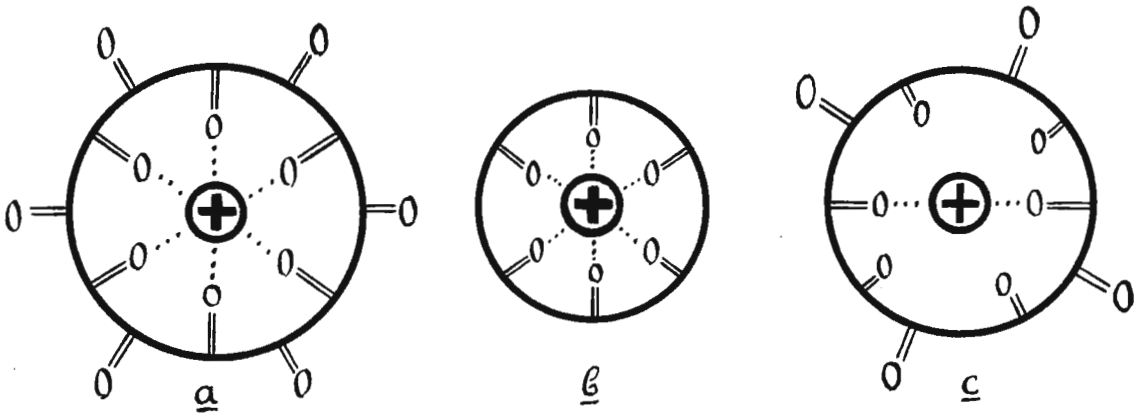

Fig. 2. Very schematic representation of spatial structure of the complexes of (a) valinomycin, (b) beauvericin and (c) antamanide.

As a result the C=O resonances for the Na^+ complex of beauvericin shift more to lower field (1.7 and 2.3 ppm) than for the K^+ complex.

In the ^{13}C spectrum of Na^+ complex of symmetric analog of antamanide (Val^6, Ala^9-antamanide)

$\overline{(L\text{-Val}—L\text{-Pro}—L\text{-Pro}—L\text{-Ala}—L\text{-Phe})_2}$ a significant shift to lower field ($\geqslant$ 2.3 ppm) is observed for only one C=O line corresponding to two symmetrically located identical amino acids residues (Table). The other four C=O signals are within the limits only -1.5 to +0.5 ppm. Hence the carbonyls of only two identical residues approach the cation located within the internal cavity of the cyclopeptide (Fig.2c). This conclusion is in complete agreement with the proposed conformation of Na^+ antamanide complex [BBRC, 42, 654 (1971)] .

Besides ion-dipole interaction shifts of the ^{13}C=O signal discussed above, marked changes are observed also in the positions of a number of other signals, which are obviously due to conformational rearrangement of the molecule on complex formation.

This work has been performed in collaboration with Drs. E.I.Fedin and P.V.Petrovskii from the Institute of Organoelement Compounds.

Sincerely yours,

Vladimir

Vladimir Bystrov

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