Texas A&M University
N-M-R Newsletter

No. 222

March, 1977

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DEADLINE DATES: No. 223: 4 April 1977
No. 224: 2 May 1977

All Newsletter Correspondence, Etc. Should Be Addressed To

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

AUTHOR INDEX - TAMU NMR NEWSLETTER NO. 222

JEOL

JEOL LTD. 1418 Nakagami Akishima Tokyo 196 Japan
Telephone. (0425)43-1111 Cable JEMSCOPE TOKYO Telex: 0-2842-135

February 1, 1977

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

Dear Professor Shapiro,

^{1}H and ^{19}F DOUBLE IRRADIATION IN ^{13}C OBSERVATION

In ^{13}C observation of fluorocompounds, C-H and C-F couplings make the spectra quite complex and there is often great difficulty in making unambiguous assignments. Many NMR spectroscopists have wished to decouple ^{19}F and ^{1}H at the same time in ^{13}C observation, but double irradiation of ^{19}F and ^{1}H presents certain problems.

a. The frequencies are very close
b. J_{C-H} and J_{C-F} are relatively large
c. ^{19}F has a large range of chemical shifts

In order to meet this need for F/H double decoupling, we have developed a special ^{13}C probe for the FX-100. With this letter, we enclose several ^{13}C spectra obtained with this new ^{13}C probe in our laboratory.

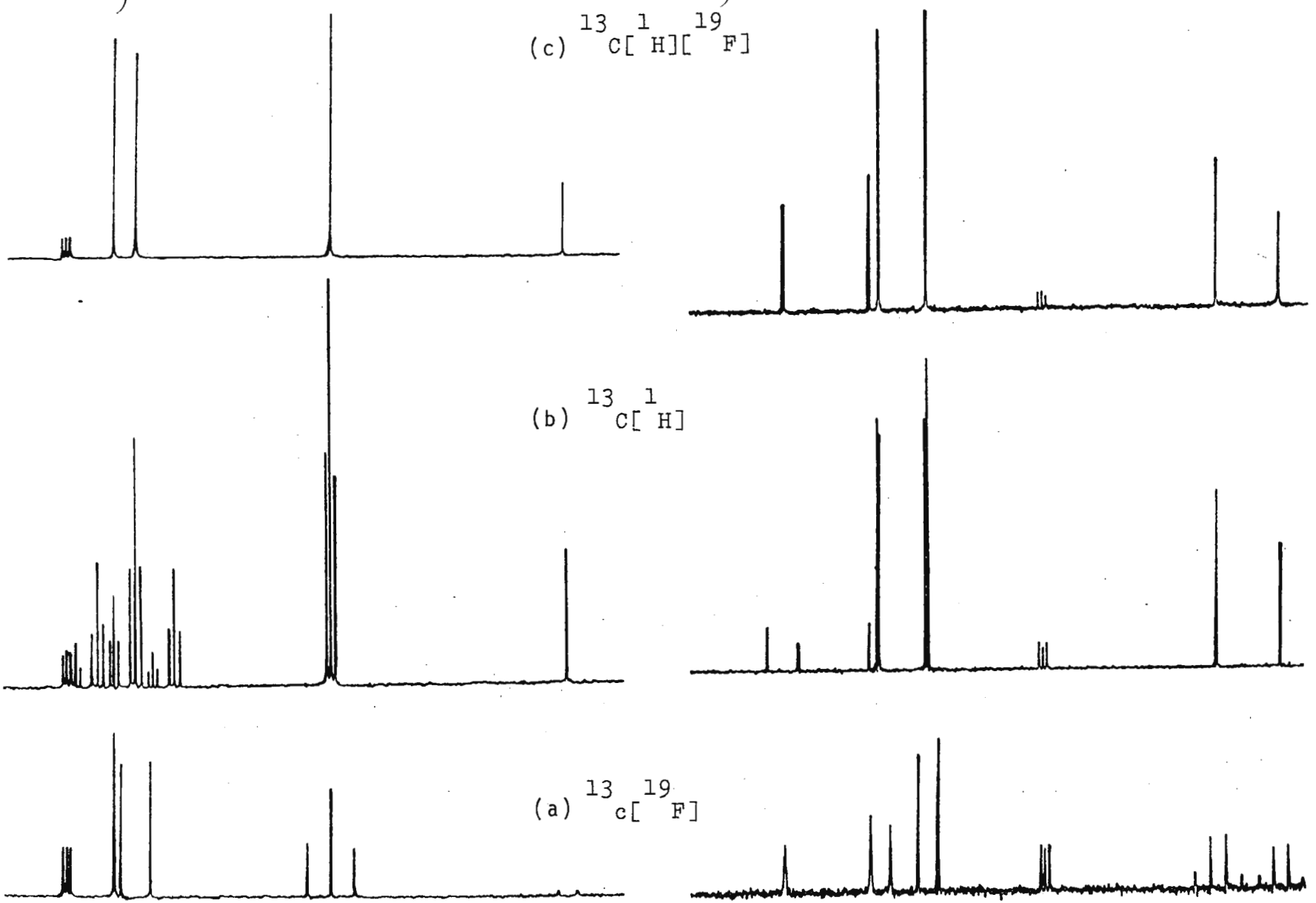
1. 2,2,3,3,-tetrafluoropropanol(ca. 50% in benzene-d6)
   spectrum width: 4000Hz
   reference: TMS
2. para-fluorotoluene(ca. 50% in chloroform-d)
   spectrum width: 5000Hz
   reference: TMS

20-Watt power amplifiers were used for both ^{1}H and ^{19}F irradiation, and 1000Hz and 5000Hz noise modulation was applied for ^{1}H and ^{19}F irradiation respectively in our experiments. The sample tube was 5mm in this special ^{13}C probe.

Sincerely yours,

S. Shimizu M. Imanari

Application Laboratry
Analitical Instrument Division



[1] 2,2,3,3,-tetrafluoropropanol [2] p-fluorotoluene

Carbon-13 spectra of 2,2,3,3,-tetrafluoropropanol and para-fluorotoluene.
(a) F-19 decoupling, (b) H-1 decoupling, (c) H-1 and F-19 decoupling.

Department of Chemistry

The Florida State University
Tallahassee, Florida 32306

February 14, 1977

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

Dear Barry:

This contribution contains 2 parts:

(1) POSTDOCTORAL (OR SIMILAR) OPENING FOR NMR INSTRUMENTATION SPECIALIST

(2) COMMENTS ON 3 PARAMETER NON-LINEAR FITTING PROCEDURES FOR CALCULATION OF T_1's FROM IRFT AND FIRFT DATA

1. We have an opening available now for an instrumental postdoctoral fellow or other specialist interested in helping to design and build new spectrometer sub-systems. We are currently constructing a modular, large sample 35kG spectrometer, which will be used for ultra-high Sensitivity FT nmr studies of dilute solutions and hard-to-observe nuclides. Other work will include redesign of Bruker HFX-90 and HX-270 probe and preamplifier systems, as well as several NMR-computer interfacing projects

The successful candidate will work with another instrumentation specialist in our laboratory. He will be able to spend up to 50% of his time on current research projects in physical and organic chemistry and molecular biology.

This appointment is for 1 year but may be renewed by mutual agreement. The stipend will be $9,000 - $13,000 depending on qualifications. The position is available immediately but a spring or summer starting date is satisfactory. Applicants should write to me, including a vitae. Also, candidates should arrange for two letters of recommendation to be forwarded to me.

George Levy

2. Use of a non-linear three parameter fitting procedure for analyzing inversion-recovery T_1 measurements.

For conventional inversion-recovery T_1 measurements, with the waiting time between 180°-τ-90° pulse sequences of order of 4 or 5 T_1, including one τ of this magnitude (corresponding to the equilibrium magnitization, A) does not increase the total experimental time severely. Therefore, the usual data reduction technique, involving a semilogarithmic plot of the differences between A and signal intensities $S(\tau)$ is a reasonable choice. However, if the pulse sequence repetition rate (waiting time) is greatly reduced, as in the fast inversion recovery method,[1] and the T_1 is long, the measurement of A (which is still necessary if the semilogarithmic plot is to be used) may take a very large share of the total experimental time. Therefore, the next logical step in reducing the time necessary for a T_1 determination would be omitting the measurement of A.[2] In order to obtain this additional time-saving, it is, however, necessary to replace the semilogarithmic plot method of data reduction by a non-linear least-squares fitting procedure. For an ideal experimental case the signal intensities may be fitted to an exponential expression involving two parameters: A and T_1. This method is, however, very sensitive to systematic errors, such as mis-adjusted pulse angles, frequency offset between the carrier and the resonance, etc. Much more satisfactory results can be obtained using a three parameter expression of type

$$S(\tau) = A + B \exp(-\tau/T_1) \qquad (1)$$

with A, B and T_1 being adjustable parameters. Obviously, in order to define the above function properly, the experimental data cannot cover an arbitrarily narrow range of short τ's. Using two different statistical criteria we have investigated the dependence of the accuracy of FIRFT measurements of T_1 as a function of the waiting time and the longest τ included (τ_{max}). Experiments have been performed for ^1H resonance in a 2% acetone solution in $CDCl_3$ at 270 MHz. We have found that shortening the FIRFT waiting time has no significant effect on the accuracy. On the other hand, a too short τ_{max} can result in a large increase for the uncertainty of calculated T_1 values. On the basis of our results, it appears necessary to use τ values covering a range up to at least 1.5 or 2 T_1 for the most accurate determination of T_1's. Inclusion of such τ's is also motivated by dynamic range and signal-to-noise considerations.

The combination of FIRFT and non-linear least-squares fitting procedure is now routinely used in our laboratory (the on-line Nicolet 1080 minicomputer performs the least-squares fit, making manual intensity measurement unnecessary) and it has proved a very powerful tool for efficient T_1 measurements. As an example, the total time required for the measurement of a 90 second T_1 for ^{15}N at natural abundance in neat acetonitrile was 11.5 hours (using this procedure with τ_{max} = 140 sec). Including one τ of 450 sec and keeping everything else constant would give an experimental time of 19.5 hours. A conventional inversion-recovery experiment with the same number of acquisitions would take a prohibitive 96 hours. (All experiments on a Bruker HX-270, 15 mm tube.) This nitrogen does not undergo efficient dipolar relaxation; the NOE is expected to be very low. (However, we have not yet performed that experiment.) More typical ^{15}N T_1 experiments in this laboratory require 0.5 - several hours for neat and concentrated (≳4M) solutions. In favorable cases (short T_1 and full NOE) we can obtain reasonably accurate natural abundance ^{15}N T_1's on 1M solutions in under 3 hours.

Warmest regards,

George C. Levy
Associate Professor

Jozef Kowalewski*

*Swedish Natural Science Research Council Postdoctoral Fellow, 1976, at Florida State University. Permanent address: Department of Physical Chemistry, Arrhenius Laboratory, University of Stockholm 10405 Stockholm, Sweden.

[1] D. Canet, G. C. Levy, and I. R. Peat, J. Magn. Resonance, 18, 199 (1975).

[2] See T. K. Leipert and D. W. Marquardt, ibid, 24, 181 (1976), and M. Sass and D. Ziessow, ibid, 24, in press.

222-5

The University of Sydney

N.S.W. 2006

Department of Organic Chemistry

TELEPHONE: 692 1122.

IN REPLY
PLEASE QUOTE:

February 3, 1977

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

Dear Barry

DYNAMIC NMR : PROBLEM OF VARIATION OF $\Delta\nu$ WITH TEMPERATURE

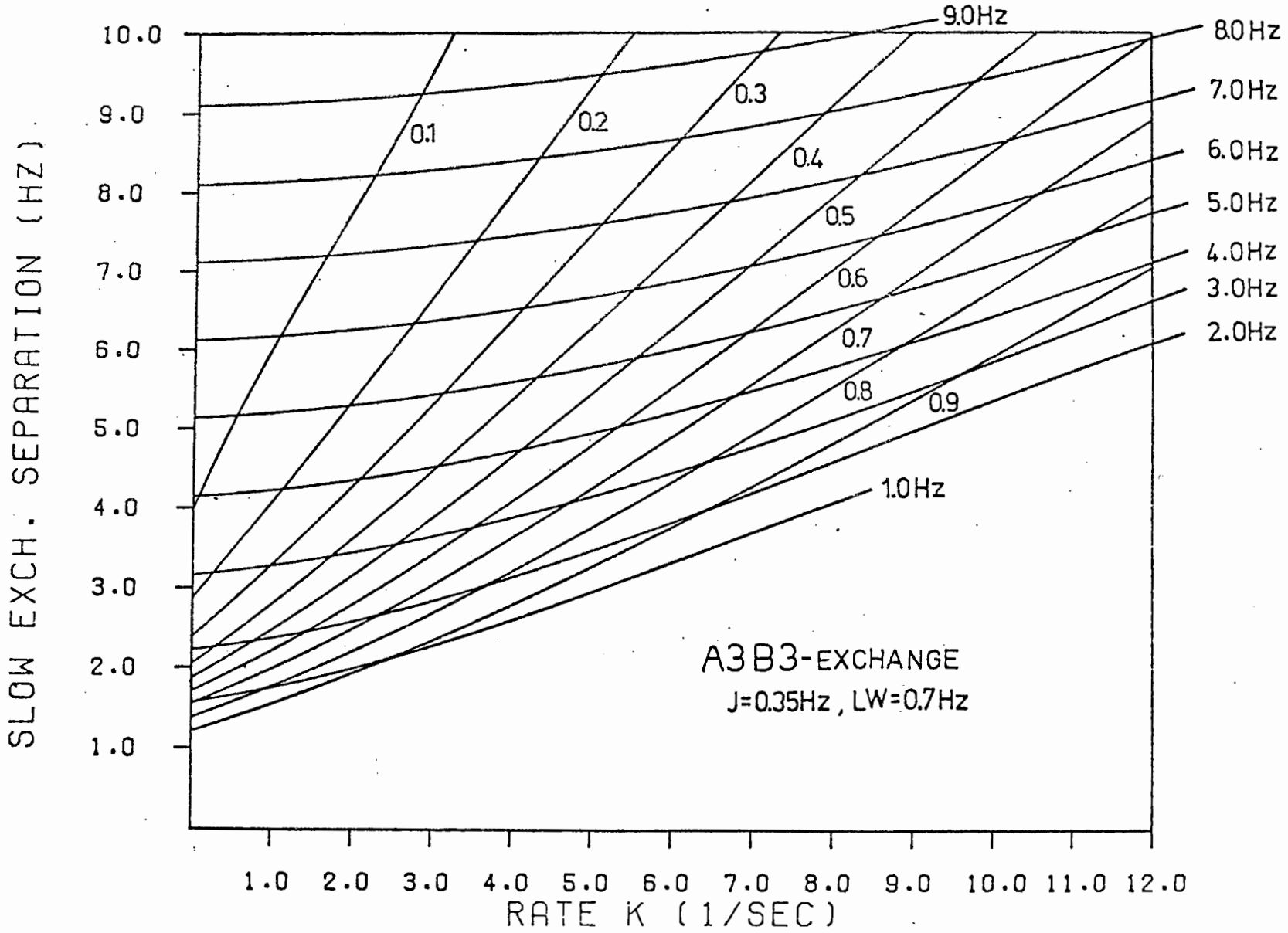
In connection with Dynamic NMR studies in these laboratories, we have examined a number of exchanging systems with equal populations where there were very significant variations in the inherent chemical shifts ($\Delta\nu$) with temperature. Line-shape analysis can cope in principle with such problems, but each match becomes a two-dimensional problem, i.e., one searches by varying $\Delta\nu$ as well as the rate of exchange. One can either use an iterative fit computer program or search for a visual match by varying $\Delta\nu$ as well as the rate of exchange.

A series of computations revealed that the Woodbrey-Rogers parameter (min/max) forms a family of curves when presented on a plot of inherent $\Delta\nu$ (slow exch. separation) against rate (k). The lines denoted 0.1 to 0.9 in figure opposite are values of min/max for a particular system (A_3B_3) with fixed values of line width (LW) and coupling constant (J). Similarly, the apparent line separation (lines marked 1.0 to 9.0 Hz in figure) form another family of curves on an identical plot. It can be seen that for the intermediate exchange region the superimposed plots form a grid and that for any experimentally obtainable set of the two values (min/max and apparent line separation) there is a single intersection which permits us to obtain at once both k and $\Delta\nu$. A computer program developed in these laboratories will draw grids corresponding to that shown here for other systems.

With best regards

Yours sincerely

S. Sternhell


SLOW EXCH. SEPARATION (HZ)
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
9.0Hz
8.0Hz
7.0Hz
6.0Hz
5.0Hz
4.0Hz
3.0Hz
2.0Hz
1.0Hz
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
A3B3-EXCHANGE
J=0.35Hz, LW=0.7Hz
1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0 10.0 11.0 12.0
RATE K (1/SEC)

The University of Manitoba

Department of Chemistry
Winnipeg, Manitoba
Canada R3T 2N2

February 22, 1977.

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

Dear Dr. Shapiro, i.e., Barry,

SMALL BARRIERS TO INTERNAL ROTATION

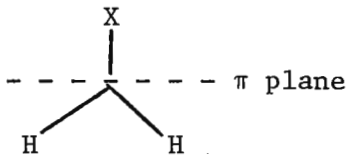
The established line shape methods are applicable from about 6 to 25 kcal/mole and depend on the dephasing of magnetization as spin magnetic moments are transferred between sites of different Larmor frequencies by internal rotational motions. Under the usual experimental conditions the NMR line shapes are insensitive to the dephasing process if it is controlled by barriers as small as 2 kcal/mole.

However, if the conformational dependence of certain nuclear spin-spin coupling constants, J, is known it follows that a solution of the hindered rotor problem (Mathieu equations, say) will yield the expectation values of J as a function of the internal barrier, of the reduced moment of inertia, and of the temperature. If maxima and minima of J can be established theoretically or experimentally, a measurement of J establishes both the low-energy conformation and the barrier height (note that one is discussing a barrier and not a ΔG difference between two conformers separated by a barrier).

The basic theory is not new, having been applied in microwave and ESR spectroscopy; although the constraints of the NMR experiment demand modifications of the treatment. The method is described in [redacted] Can. J. Chem. 54, 1322 (1976), and is seen to be applicable to barriers which are predominantly twofold in nature (this limitation could be removed if the functional form of J were better known, in general). Such barriers have now been measured for some twenty benzene derivatives and are tabulated below. The tabulation refers to the conformations 1 to 8.

When comparisons are available, our results often agree with thermodynamic, far infrared, Raman or ESR data (for related radicals). These methods are not available here but the measurements have been supplemented by extensive MO calculations at the INDO, MINDO/3, and ab initio STO-3G levels (4-31G calculations are not really practicable for these molecules).

February 22, 1977,
Dr. Bernard Shapiro.



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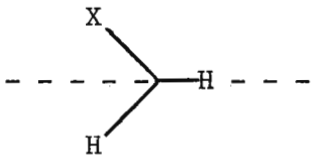

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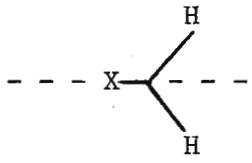

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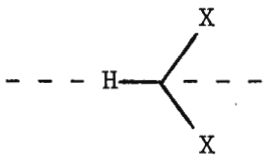

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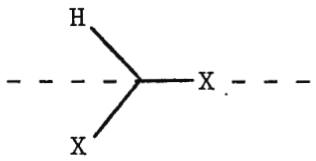

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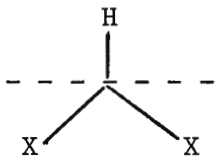

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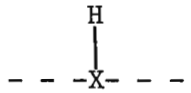

8

Group	Low	High	Barrier (kcal/mole)	Group	Low	High	Barrier (kcal/mole)
$-CH_2CN$	-	-	<0.2	$-SiH_2CH_3$	1	3	0.8 ± 0.4
$-CH_2NH_2$	-	-	<0.2	$-CH_2SH$	1	3	1.7 ± 0.2
$-CH_2OH$	-	-	<0.2	$-CH(CH_3)_2$	4	6	2.0 ± 0.2
$-CH_2F$	3	1	0.26 ± 0.05	$-SiH(CH_3)_2$	4	6	1.0 ± 0.3
$-CH_2Cl$	1	3	2.1 ± 0.4	$-SiHCl_2$	4	6	1.0 ± 0.3
$-CH_2Br$	1	3	>3	-CH(cycloprop)	4	6	2.0 ± 0.2
-	-	-	-	$HC=CH_2$	7	8	1.6 ± 0.3
$-CH_2I$	1	3	>3	-OH	7	8	>3.5
$-CH_2CH_3$	1	3	1.2 ± 0.1	-SH*	7	8	1.1 ± 0.3
-	-	-	-	-SeH	7	8	0.35 ± 0.25

*For p-X-C_6H_4SH the barrier about the C-S bond varies from 2.8 kcal/mole for X=NO_2 to 0 ± 0.3 kcal/mole for X-NH_2 (6 compounds), based on $^4J_o^{H,SH}$.

Clearly, our measurements need to be checked by, say, relaxation measurements. We hope to do so when an FT spectrometer becomes available in the next year. Furthermore, we hope to use the technique of "J spectra" (J. Chem. Phys. 54, 301 (1971)) again on an FT machine, to increase our accuracy of measurement and thus to determine solvent perturbations of these small barriers as well as temperature effects on the couplings.

The present approach complements the relaxation methods of Grant (J. Phys. Chem. 79, 2031 (1975)) and of Ellis (J. Am. Chem. Soc. 97, 5685 (1975)), which have been applied to methyl group rotational barriers.

If these barrier measurements are generally correct, they will give an additional reason for the extensive work on long-range spin-spin couplings carried out here over the past ten years. Any errors in our barriers could be traced back to errors in two assumptions only, if necessary.

Keep warm,

Ted Schaefer,
Professor.

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DEPARTMENT OF CHEMISTRY, M-016
LA JOLLA, CALIFORNIA 92093

February 14, 1977

Dr. B.L. Shapiro, Dept. of Chem., Texas A & M Univ.
Dear Barry: I will have a post-doctoral position available beginning this summer in Pittsburgh; tthe work will involve application of internuclear Overhauser effects to small-molecule-protein binding. Interested parties should write or phone - Aksel Bothner-By, M001, UCSD, La Jolla, CA 92093, tel. 714-452-4187.

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February 11, 1977

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

Dear Professor Shapiro: XL-100 Modifications

My letter is directed mainly to XL-100 owners. The following paragraphs were problems that needed attention and the solutions.

We have about 35 students on our XL-100 that is equipped with a Gyro Code Multi-nuclei (field conversion). When changing from one nuclei to another, the students were required to retune the pulse amp. cards via the "RF Indicator Meter" as outlined in the manual. To eliminate the need of all this tuning, we placed colored marks on the variable capacitors (on pulse amplifier card) to represent the proper tuning of the various nuclei. The students now open the side plate, set the proper color for the desired nuclei, and close the side plate.

Our C.A.P.S. modification required that every time a different nuclei was selected on the "R.F. Module", a cable had to be changed in the "F.T. R.F. Module." We changed our system so that the output of the C.A.P.S. card is delivered to pin A1 of P1918 (print 87-109-816). The students now have complete control of C.A.P.S. on all nuclei from the teletype keyboard.

Our recent attempt at N^{15} resulted in poor signal-to-noise. Upon checking with different people at Varian, each seem to have his own tuning method. After gathering all the information, I used the following method and got over 50 to 1 using the Varian standard.

a. To start, tune the N^{15} exactly as you would the C^{13}.
b. Preset R26 (lock preamp) to full cw.
c. Completely retune the observe preamp, with lock preamp in place.
d. Retune C20 of lock preamp.
e. Set R26 for a null as in C^{13}.

Sincerely,

Clarence Gust
Instructor

CG:fs

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Dr. SHAPIRO
Department of Chemistry
Texas A. & M. University
College Station, Texas
U.S.A.

RÉFÉRENCE A RAPPELER : c/DRF/COP-77-53/mjc

VOTRE RÉF.

VOTRE LETTRE DU

GRENOBLE LE 10 février 1977

Dear Dr. Shapiro, Reproducible T_1 measurements

In line with our interest in organophosphorus compounds, we have initiated a programme of ^{31}P relaxation time measurements. Since part of our interest in spin lattic relaxation times is concerned with extracting conformational and geometrical information, we have paid some attention to obtaining reproducible if not "accurate" values. Most of the known technical problems involved in such measurements have been treated in the literature [1,2].

We have used the unmodified inversion recovery pulse sequence, making measurements at between twenty to fourty different pulse intervals interspaced with measurements of S_∞ , the equilibrium magnitisation every four or five spectra.

To obtain a good digital line definition, we work with a maximum spectral width of 1,000 Hz, using zero filling where convenient, and artificially broaden our lines with an exponential filter.

Because inhomogeneities in the r.f. field over the sample volume can cause serious errors, we employ sample cells which restrict the volume of the sample to the homogeneous region of the r.f. field. All samples are routinely degassed with at least four to five cycles of the freeze-pump-thaw process at pressures below 10^{-4} torr.

Although T_1 is best extracted by fitting the experimental data to an exponential curve [3,4], we find plotting the normal linear semi-log plot whilst the experiment is proceeding a good way of monitoring possible sources of error.

Random errors manifest themselves by a uniform scattering of points about the straight line and by random fluctuations in S_∞. Long term spectrometer instabilities are often indicated by a chronological change in S_∞ together with a slight curve in the semi-log plot. Inhomogeneities in the r.f. field also tend to gently curve the

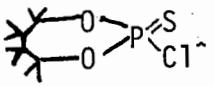
C.E.N.G. IMP. N° 1 - A - 1-72

data as does working close to receiver saturation conditions. If a good straight line is not obtained, then there is no point in continuing until the source of error has been eliminated.

It is well known that the value for T_1 obtained from the null signal pulse interval is far more sensitive to systematic errors than the value for T_1 obtained from the semi-log plot. Knowing S_∞ , T_1 null may be easily accurately obtained from the semi-log plot. We find that a useful criterium for a reliable experiment, after a good straight line, is that T_1 null should be not more than 10%-15% less than T_1 slope. If it is, something is wrong. Similarly, when the data has been exponentially fitted, the values for T_1 and S_∞ obtained should be very close to T_1 slope and the experimentally obtained value for S_∞.

When these conditions are satisfied, we have obtained T_1 values with a reproductibility of around 2%. Whether these values are truly accurate is another question, but we do feel provided care is taken, accuracies much better than the standard $\pm$ 10% often quoted can be routinely obtained.

Below are some ^{31}P relaxation times obtained under condition of proton noise decoupling from neat liquids in 5 mm microcells at 32°C, on a Varian XL.100 and a Brüker WP.60 spectrometers, with literature values where available :

Compound	XL.100 T_1	WP.60 T_1	Lit.
$P(OMe)_3$	6.8	6.9	6.0 [5]
$P(Me)_3$	3.4	3.4	
$P(NMe_2)_3$	11.4	11.2	
P Ph Cl_2	11.3	11.5	10.0 [6]
	12.3	12.4	

(1) G.C. LEVY and I.R. PEAT, J. Magn. Res., 18, 500 (1975).

(2) I.M. ARMITAGE, H. HUBER, D.H. LINE, H. PEARSON and J.D. ROBERTS, J. Magn. Res., 15, 142 (1974).

(3) D.L. DE FONTAINE, D.K. ROSS and B. TERNAI, J. Magn. Res., 18, 276 (1975).

(4) T.K. LEIPERT and D.W. MARQUARDT, J. Magn. Res., 24, 181 (1976).

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(6) S.J. SEYMOUR and J. JONAS, J. Chem. Phys., 54, 487 (1971).

Sincerely yours,

J.B. ROBERT(+) J. TABONY (++)

(+) Université Scientifique et Médicale de Grenoble
(++) Institut Laue-Langevin, Grenoble

JEOL

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February 22, 1977

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

Dear Professor Shapiro,

"^{13}C NMR of Micro Melts"

We are often confronted with not only the problem of limited sample quantity, but also with severely limited solubility. These cases can be very frustrating since neither large diameter nor micro tubes are applicable.

In exploring alternate techniques for sample preparation, we considered running small amounts of sample simply melted in the sample tube. This method is often possible since many organic compounds melt under 180°C without decomposition.

We have tested this technique as shown using the dual variable temperature microprobe equipped with external deuterium lock. Glass capillaries (1.8mm diameter) were used requiring about 20 µl of molten sample.

In the examples attached we have run 5mg of cholesterol in 20 µl of $CDCl_3$ (3000 scans, 30 minutes) for comparison and then a five minute and a thirty minute accumulation of 20 mg of cholesterol neat at 160°.

There is some broadening due to viscosity effects and also very noticable changes in the chemical shifts of compounds in the melt relative to solution. We have also run cholestanol (160°), cholesterol palmitate (100°) and methyl palmitate (100°) under melt conditions with excellent results.

Sincerely yours,

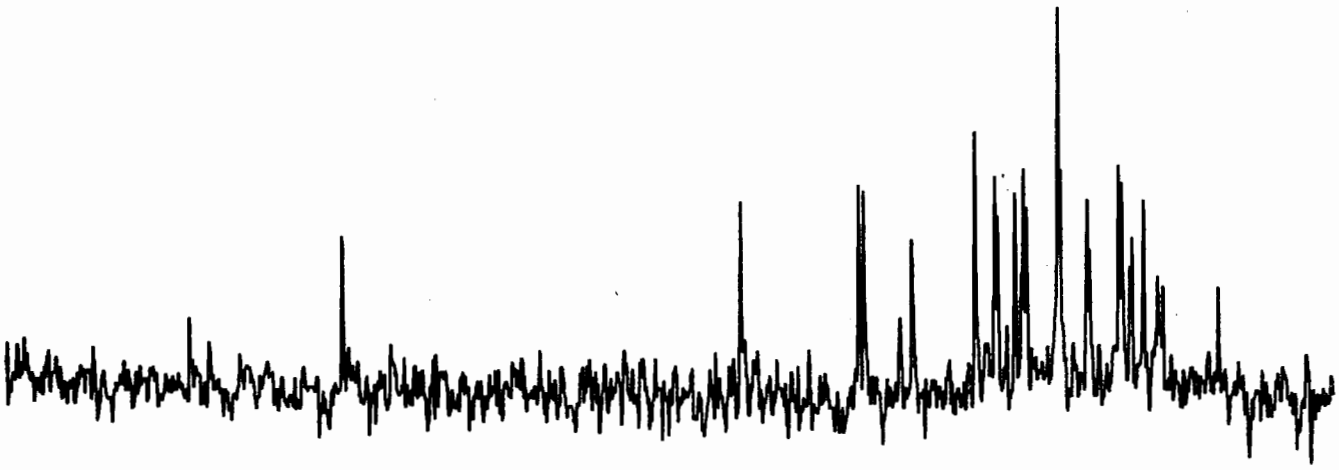
Ralph K. Goto Mike

Dr. Ralph H. Obenauf
Mgr., Applic. Labs.

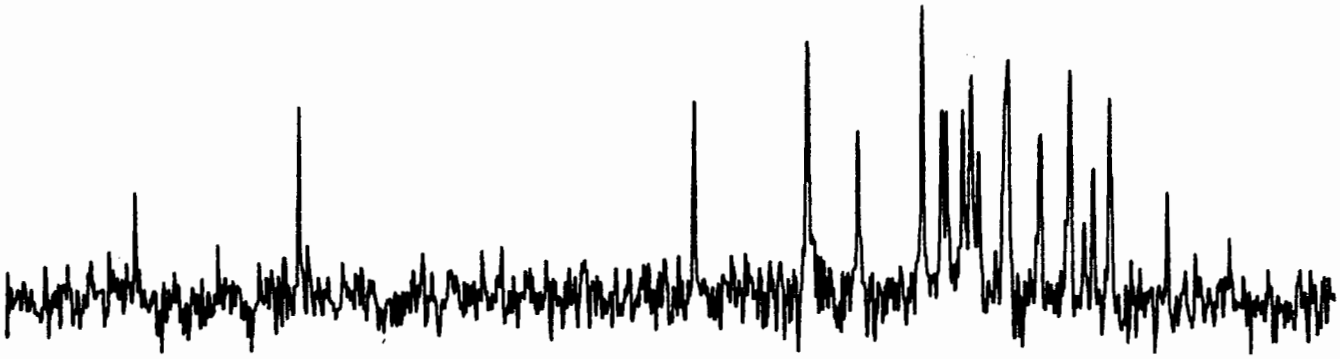
Mr. Koji Goto
Mgr., Tech. Dept.

Dr. Michael Albright
NMR Application Chemi

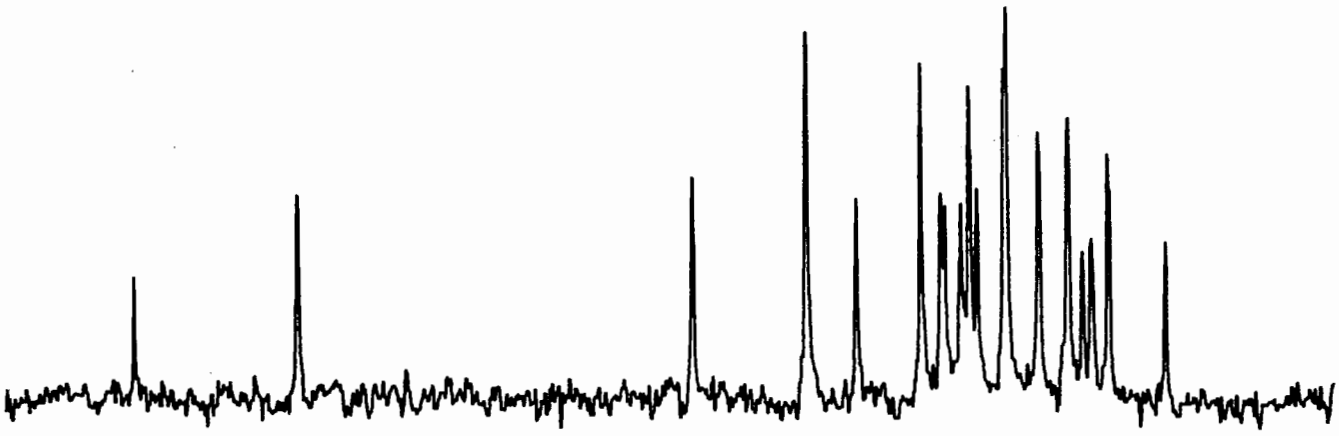
/nc



A. 5mg Cholesterol, 20 ul $CDCl_3$, 3000 scans, 30 minutes



B. 20mg Cholesterol neat (160°), 500 scans, 5 minutes



C. 20mg Cholesterol neat (160°), 3000 scans, 30 minutes

Monsanto

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

February 23, 1977

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

MAGIC ANGLE SPINNING AND POLARIZATION TRANSFER IN CROSS POLARIZATION NMR

Dear Barry:

A possible conflict would seem to arise between the requirements of line-narrowing by magic-angle spinning at frequency ω_s, and those of the spin-exchange process by which the rare spins are polarized in cross polarization nmr: the latter depends on an effectively static dipole-dipole interaction H_{IS} between rare and abundant spins, and the sample rotation can render this interaction oscillatory. In certain situations (roughly speaking when the condition $|H_{II}| >> \hbar\omega_s$ can be satisfied), this feature is unimportant. As we will see, this is true since the modulation of H_{IS} by I-I dipolar fluctuations overwhelms the additional coherent modulation by relatively slow spinning.

However, spinning at the magic angle can significantly modify the rate of polarization transfer from abundant to rare spins in proton enhanced NMR experiments on solids, if the spinning speed is greater than or comparable to the static dipole-dipole interaction among abundant spins in the rotating frame. In adamantane, this fact can be strikingly demonstrated experimentally. As shown in the figure, the cross-polarization transfer rate, T_{CH}^{-1} as a function of Hartmann-Hahn mismatch, breaks up into a collection of sidebands separated by the spinning frequency.

In collaboration with John Waugh, we have developed a semi-quantitative explanation for this behavior. Briefly, spinning has two effects. First, it provides a 100% AM on H_{IS} so that secular IS transfer occurs in the neighborhood of a Hartmann-Hahn mismatch of $\pm\omega_s$, $\pm 2\omega_s$, but not for a perfect Hartmann-Hahn match. This is true regardless of the size of H_{IS}. For a powder, the ratio of the first and second sidebands is $\sqrt{2}$. The second effect of spinning is to modulate the characteristic <u>frequencies</u> which H_{II} imposes on H_{IS}. That is, the dipolar fluctuations of the abundant spins are modulated. The

Prof. B. L. Shapiro February 23, 1977

modulation index of this FM is determined approximately by the ratio of the spinning frequency to the I-I interaction in the rotating frame. Thus, each AM sideband breaks up into an FM pattern. This analysis leads to a prediction of the relative centerband intensity to the intensities of the sidebands in the T_{CH}^{-1} *vs* mismatch plot of 1: 2.1: 1.7: 0.4: 0.05, in reasonable agreement with the average experimental values of 1: 2.4: 1.6: 0.3: 0.05.

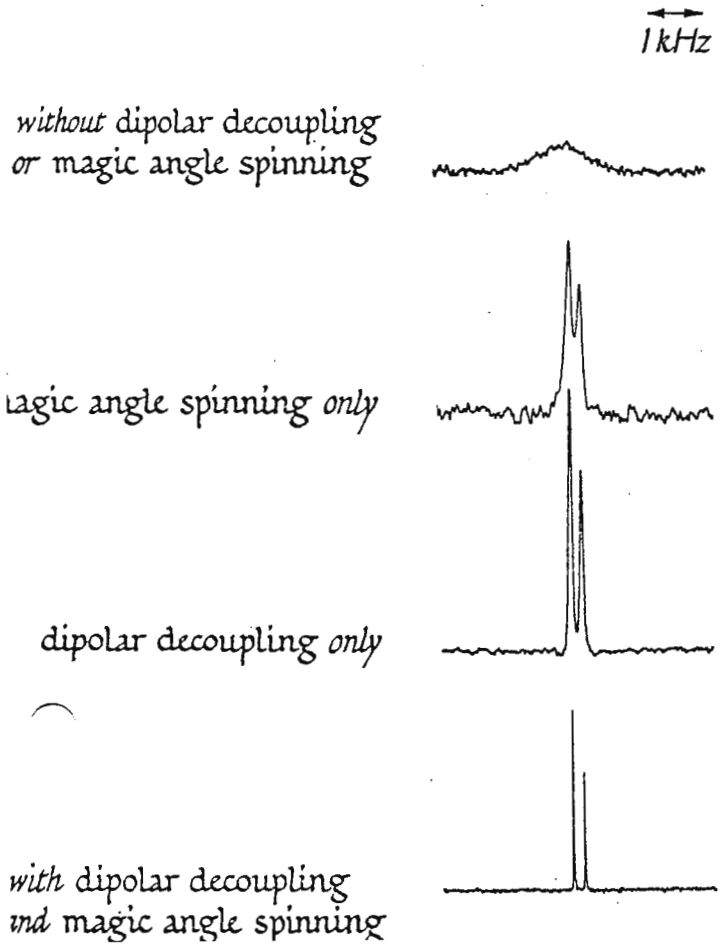
This analysis also gives us some insight into why spinning has so little effect on cross-polarization transfer rates in systems with strong I-I dipolar interactions. Such systems have a T_{CH}^{-1} *vs* mismatch non-spinning width arising from dipolar fluctuations substantially greater than practical spinning speeds. Thus the AM associated with spinning produces sidebands that fall within the T_{CH}^{-1} width, while the FM has such a high modulation index that no observable sidebands of significant intensity are produced. We can also use our analysis to approach the question of the effect of molecular motion on transfer rates. But there are lots of complications.

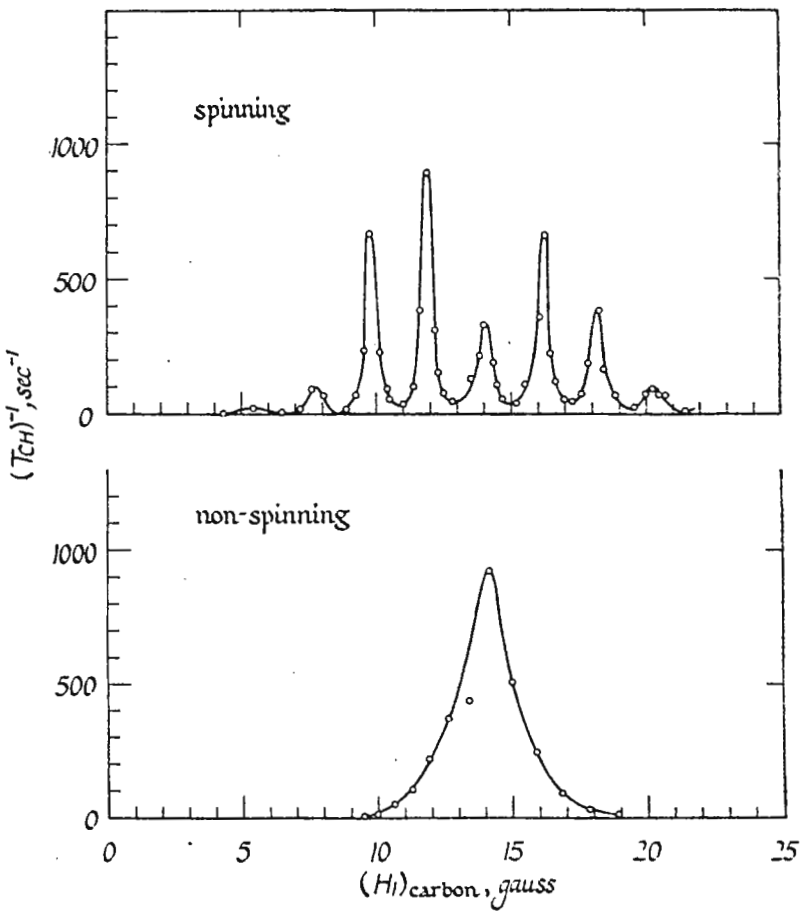
Sincerely,

Jacob Schaefer Jake

E. O. Stejskal Ed.

adamantane





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DÉPARTEMENT DE CHIMIE ORGANIQUE
Professeur B. ROQUES
(C N R S) E R A 07613

Paris, February 4th, 1977

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

Dear Professor Shapiro,

^{13}C NMR study of the rotational barrier in para dimethylamino π (tricarbonylchromium) benzaldehyde I (1).

There is an apparent discrepancy between the electron withdrawing effect of the $Cr(CO)_3$ group in π (tricarbonylchromium) arenes as shown by MO calculations, physicochemical measurements, chemical reactivity etc... and the absence of significant changes in the transmission of substituent effects in the complexed rings as determined by NMR (2) (3). So, we have measured the barrier to rotation about the carbonyl-C_1 arene bond in I in order to estimate the changes in conjugaison between the ring and the aldehydic carbonyl group under complexation. For this purpose, we have used ^{13}C NMR which has been shown of great interest in the determination of low rotational barriers (4).

^{13}C NMR spectra were recorded on a VARIAN XL 100 spectrometer with solution of *c.a* 0.5 M of free II and complexed I molecules in CD_3COCD_3 between 20°C and -103°C (figure 1).

The activation parameters were obtained by complete lineshape analysis and compared with those of the free compound. Table I.

	$T_c(C_2)$ °C	$\Delta\nu(C_2)$ Hz	$\Delta G_{T_c}^{\neq}$ Kcal.Mole^{-1}	$\Delta H^{\neq}$ Kcal.Mole^{-1}	$\Delta S^{\neq}$ cal.Mole^{-1}.des^{-1}
(I)	-82	188	8.6±0.2	8.2±0.2	-2.2±2
(II)	-50	220	10.2±0.2 ★	11.5±0.2 ★	+6.0±2 ★

★ $\Delta G_{T_c}^{\neq}$ = 10.6, $\Delta H^{\neq}$ = 11.0, $\Delta S^{\neq}$ = +1.7 in $CHCl_2F + CCl_2F$ (5)

Table I. Activation parameters for (I) and (II).

A significant decrease of *c.a* 1.5 Kcal/mole is observed for $\Delta G_{T_c}^{\neq}$ under complexation. Several explanations may be advanced to these results.

a) Torsion of the CHO group out of the plane of the aromatic ring due to the $Cr(CO)_3$ moiety. However this assumption is not in accordance with X ray data on similar derivatives.

b) Electron withdrawing effect of the $Cr(CO)_3$ group which could decrease the rotational barrier. This is in opposition with recent data indicating the absence of significant perturbation in the π system under complexation (2) (6).

c) Stabilization of the transition state in the complex compared to the free molecule by an interaction between the negative oxygen of the CHO group and the chromium tricarbonyl moiety. This hypothesis is in accordance with the sign changes in the ΔS term between the free and the complexed derivatives.

In order to obtain more additionnal information, it would be of interest to determine the barriers in a serie of p.substituted π (tricarbonylchromium) complexes by ^{13}C NMR at very low temperatures.

Sincerely yours ;

S. COMBRISSON T. PRANGE B.P. ROQUES

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2. Roques B.P., Segard C., Combrisson S. and Wehrli F. J. Organometal. Chem., 73 (1974) 327.

3. Bodner G.M. and Todd L.J. Inorg. Chem., 13 (1974) 360.

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5. Drakenberg T. , Jost R. and Sommer J. Chem. Comm. (1974) 1011.

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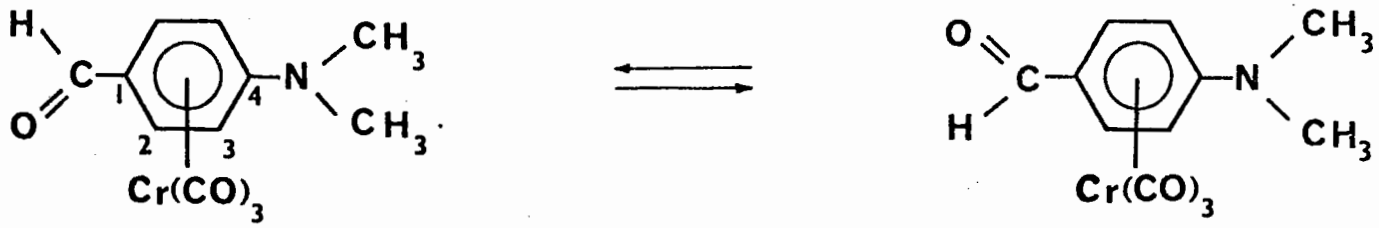
H
C
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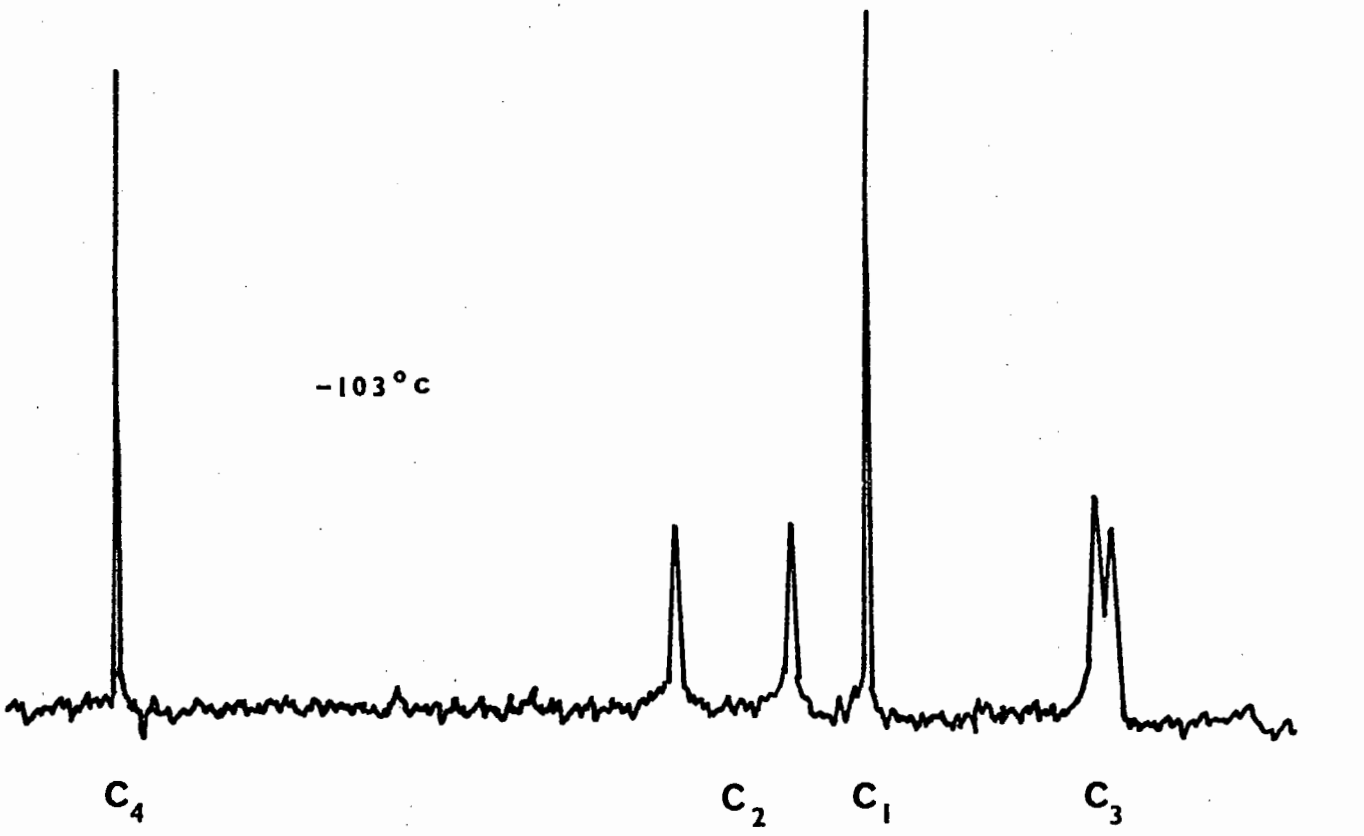
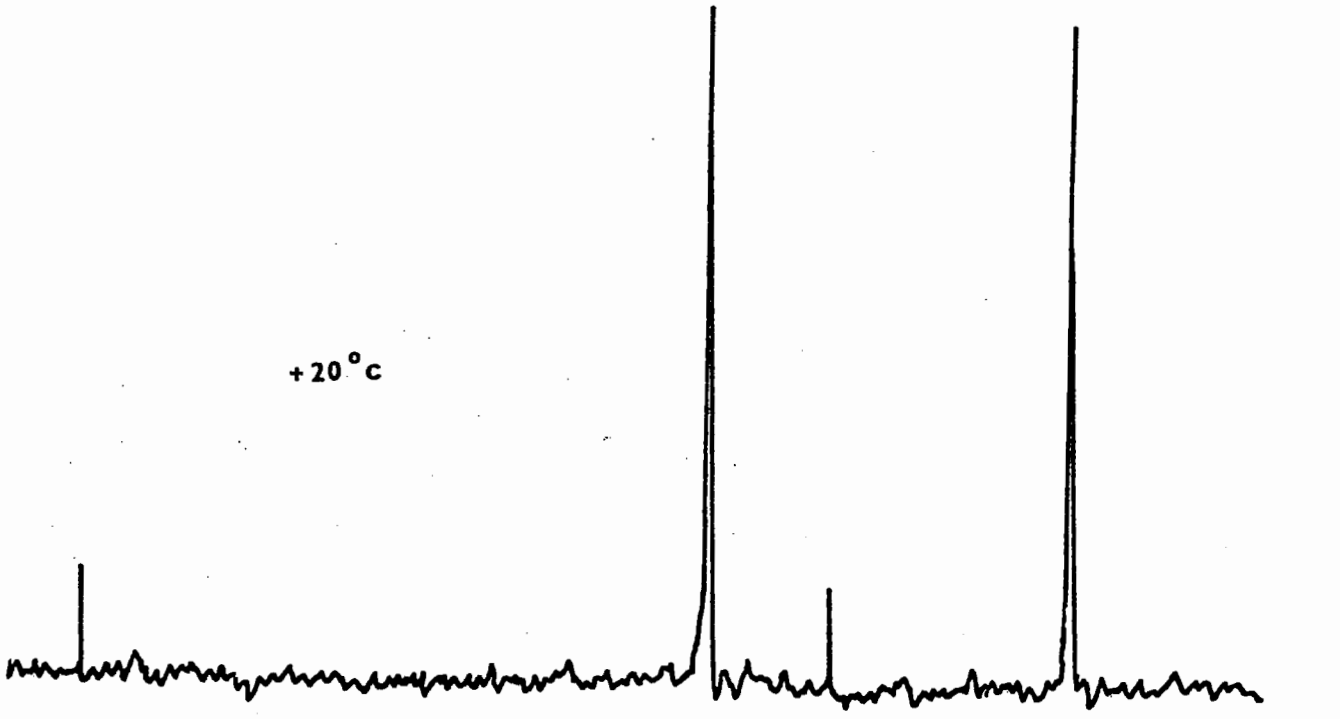
Cr(CO)3


-103°c
C4
C2
C1
C3


+20°c
125
100
75
δ ppm

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

Your reference

Our reference

Date Feb 24 1977

Dear Professor Shapiro

ACCURACY MEASUREMENTS OF SELECTIVE EXCITATION SUB-PULSES

Several recent publications have described selective excitation of spectral regions (1) or lines (2) with sets of sub-pulses prior to each acquisition. A weak pulse repeated at τ msec will selectively excite a line at τ^{-1} KHz from the irradiation frequency. We wish to describe some test results on our standard FTNMR spectrometer, a JEOL PFT-100P fitted with a PG 100 programmeable pulser. With a 90° pulse length of 15 to 20 μsec for various nuclei, any more than ten sub-pulses per excitation will reduce the length of the individual sub-pulse to the same order as the pulse rise-time. In Fig. 1, overlaid oscilloscope pulse profiles indicate the rise-time to maximum power as being 3.0 μsec.

So what is the spectroscopic effect of a very short pulse, how reproducible is this effect, and how does this relate to the power and shape of the pulse-profile? Furthermore, how accurate is the interpulse time when control is executed by sequential access to three 16-bit addresses for the pulse, delay and loop-counter each with its associated time/number control parameter? We performed 40.3 MHz ^{31}P-FTNMR observations on 85% H_3PO_4 in a 10mm tube with 5, 10 or 100 sub-pulses per acquisition and with τ set to the theoretical value. The signal-noise ratio per sub-pulse excitation relative to the 90° pulse (Fig. 2) showed very rapid increase until at 1.7 μsec an apparently linear relationship to the 90° pulse was established. This related to the power of the pulse quite well.

(1) B L Tomlinson and H D W Hill, J.Chem.Phys.59,1775(1973).

(2) G Bodenhausen, R Freeman and G A Morris, J.Magn.Resonance 23,171(1976).

reproducibility of signal height with ten 1.5 μsec sub-pulses prior to one acquisition. Potential deviation due to all manner of causes was anticipated, but signal height showed the very small standard deviation of 0.8%, a deviation of each sub-pulse excitation of ±2.5% on average. Given that a 1.5 μsec pulse is on the rapidly changing part of Fig. 1, this seemed very satisfactory. Finally, the same sample was excited with 200×0.9 μsec sub-pulses giving a theoretical zero-to-zero bandwidth of 9 Hz. After correcting the phase, the absolute signal-noise ratio was measured at a series of τ values (Fig 3) and found to be a maximum between 578 and 579 μsec. With a theoretical τ value of 579 μsec, the delay incurred in the pulser control was negligible. Therefore, accurately selective excitation is possible with our spectrometer without any modification.

Best wishes

Ian O'Neill Brian Stuart

C P Richards

IAN K O'NEILL
COLIN P RICHARDS
BRIAN STUART

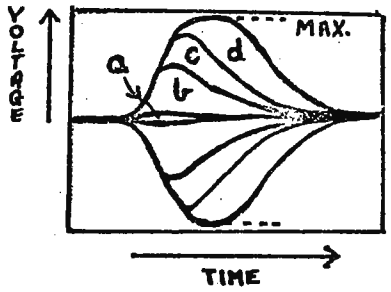


FIG. 1 Voltage / Time profiles for :—
a 1.0 μsec pulse c 2.0 μsec pulse
b 1.5 μsec pulse d 3.0 μsec pulse

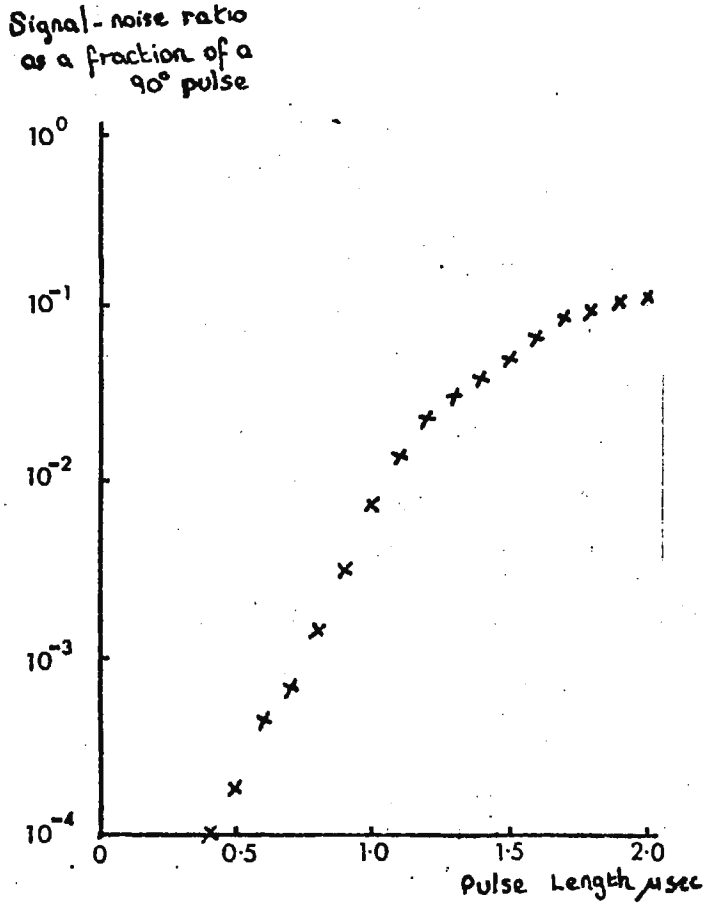


FIG.2 Spectroscopic effect of one pulse.

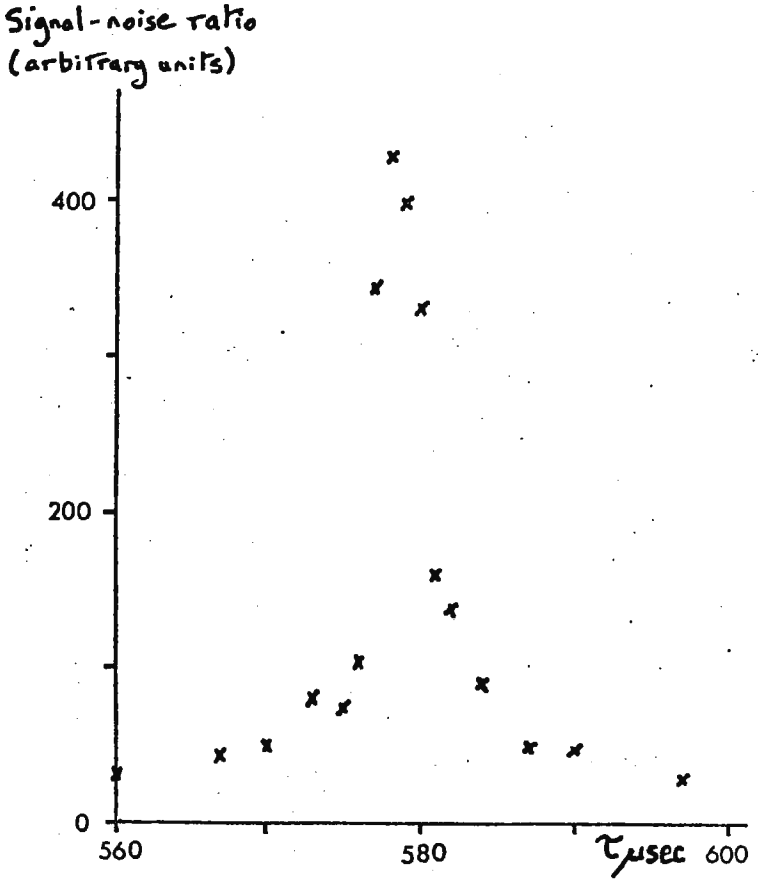


FIG.3 S/N as function of τ. Theoretical τ = 579 μsec.

THE PROCTER & GAMBLE COMPANY

MIAMI VALLEY LABORATORIES

P. O. BOX 39175
CINCINNATI, OHIO 45247

February 17, 1977

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

Dear Professor Shapiro:

Our Bruker HX-90 Multinuclei FT spectrometer is equipped for ^{19}F field/frequency stabilization (lock). This internal ^{19}F lock system has been satisfactory for observing all nuclei with the exception of protons. We have experienced difficulties in obtaining quality proton spectra because of an apparent RF interference between the ^{19}F (85 MHz) lock and ^{1}H (90 MHz) observation channels during single coil FT experiments. This interference not only produced peak distortions in the proton spectra but also decreased the sensitivity of the FT experiment. We have recently eliminated this problem by replacing the ^{19}F stabilization with deuterium (14 MHz). This conversion to ^{2}H lock was accomplished with minimal spectrometer system alterations through the adoption of the scheme already employed for multinuclei detection on our HX-90 (L. R. Isbrandt, TAMU NMR Newsletter 212-30). Our only expenditures were the purchase of a proton/deuterium sample insert and a deuterium stabilization matching network.

As the block diagram of this ^{2}H stabilization arrangement shows, the ^{19}F transmitter output of the spectrometer is mixed with 71 MHz derived from a frequency synthesizer to produce the 14 MHz deuterium resonance frequency. The probe detected ^{2}H signal is again mixed with 71 MHz and the sum frequency of 85 MHz is subsequently amplified through the existing ^{19}F preamplifier and stabilization channel circuitry.

Initial experiments indicate that the large difference between the proton and deuterium frequencies virtually eliminate spectral problems arising from pulse generated distortions. An additional benefit gained by this conversion is the elimination of the ^{19}F lock reference capillary from the NMR tube. This has eliminated the problem of spinning sidebands and increased the signal-to-noise because of the increase in sample volume.

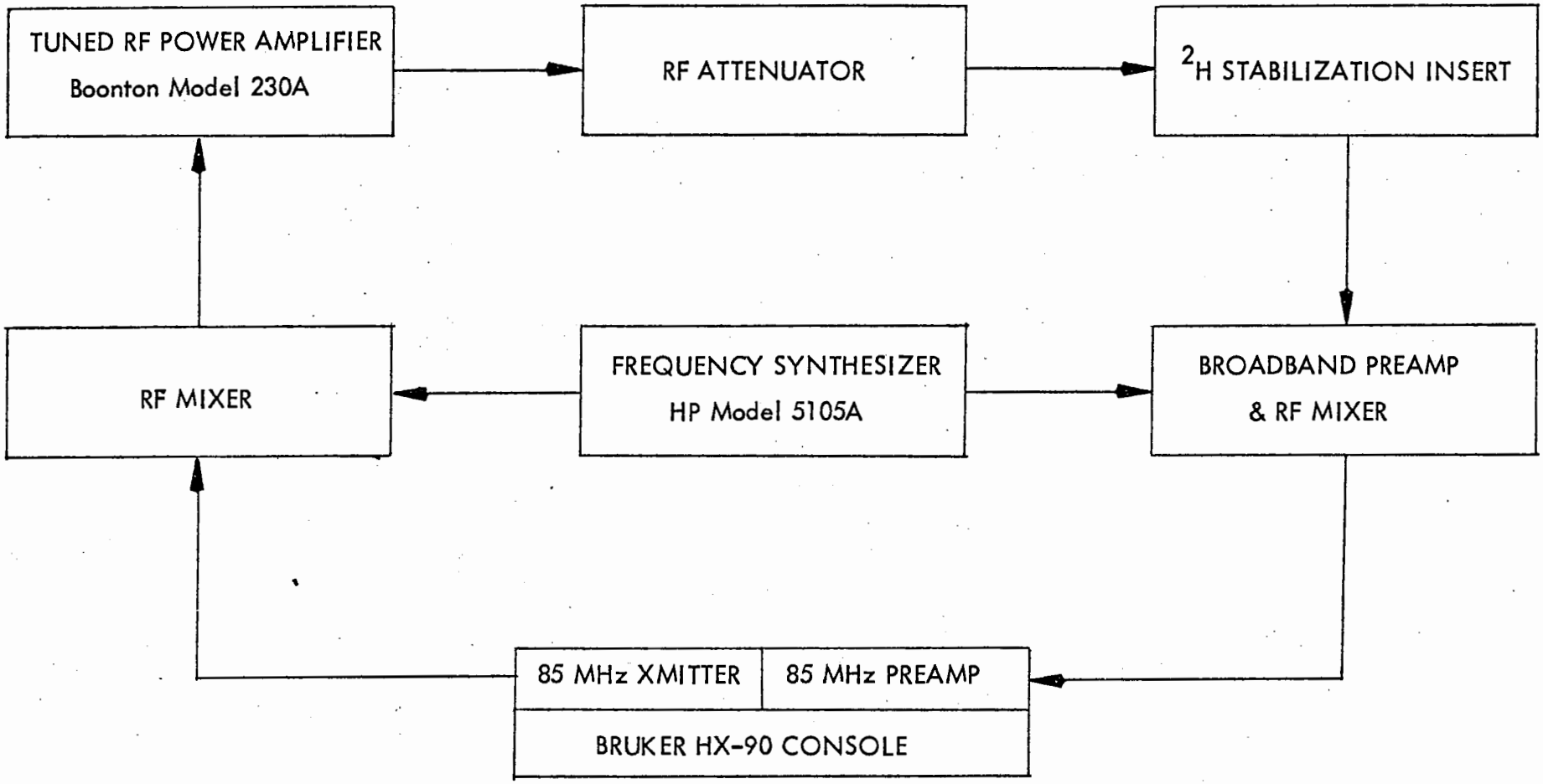
Sincerely yours,

THE PROCTER & GAMBLE COMPANY
Research & Development Department

Charles D. Sazavsky

Charles D. Sazavsky
Miami Valley Laboratories

pas
Encl.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Department of Chemistry

February 28, 1977

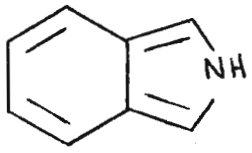
Professor B.L. Shapiro
Department of Chemistry
Texas A & M University
College Station, Texas 77843

Dear Barry:

To resuscitate my moribund subscription, I offer the following, abstracted from the Ph.D. thesis of Dr. Elsamma Chacko:

THE AROMATICITY OF ISOINDOLE

The well-documented chemical instability of isoindole seemed inconsistent with numerous theoretical studies which indicate it to



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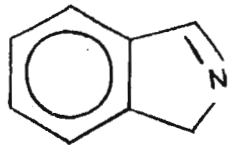
be aromatic, and prompted us, in collaboration with Dr. Joseph Bornstein of our department, to undertake an NMR study whose goals were to provide evidence for or against its aromaticity.

"Isoindole", produced by flash vacuum pyrolysis according to the method of Bornstein et al., consists of a nonequilibrium mixture of isoindole (1) and its tautomer, isoindolenine (2). At -40° in either



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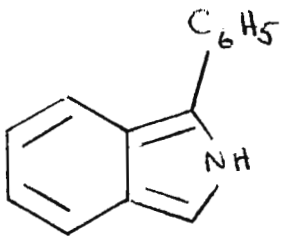
toluene-d_8, acetone-d_6 or acetonitrile-d_3, we were able to observe a slow, irreversible transformation of 2 into 1. Eventually no trace of 2 was detectable. Addition of D_2O to 1 resulted in loss of the NH resonance, but even after prolonged standing at room temperature, no incorporation of deuterium into the adjacent positions occurred. In contrast, in 1-phenylisoindole (3), which exists in mobile equilibrium with ca. 5% of the isoindolenine 4, deuterium



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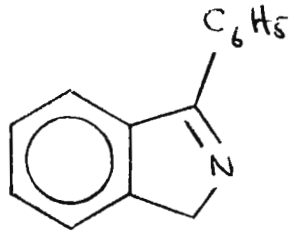

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incorporation into position 3 at room temperature is instantaneous, complete and reversible. These results indicate 1 to be considerably more stable than 2 and argue strongly for its aromaticity.

These and other results relating to the electron distribution in isoindole will appear shortly in Tetrahedron Letters. Preprints are available.

Sincerely,

D.J. Sardella
Associate Professor of Chemistry

DJS/beg

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

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Datum January 31, 1977

Onderwerp
High resolution NMR of modified tRNA's.
Tertiary structure determination.

Dear Professor Shapiro,

In this letter we present some recent ^{1}H 360 MHz NMR experiments on transfer ribonucleic acids (tRNA's). These biological macromolecules play a crucial role during protein synthesis; they consist of 75-85 nucleotides, interlinked by phosphodiester bonds, while their molecular weight is approximately 28 x 10^3.

For one of these species, phenylalanine specific tRNA from yeast, the 3-dimensional structure has recently been solved by X-ray crystallography and it turns out to be hold together by hydrogen bonds. A number of so called tertiairy hydrogen bonds between residues far apart in the secondary structure (fig. 1) is important for maintaining the 3D-conformation. Moreover, they are important during protein-nucleic acid and nucleic acid - nucleic acid recognition reactions. We are particularly interested to know whether these are present in solution in accordance with the X-ray results.

Generally, imino protons involved in hydrogen bonding can be observed by NMR between 15 and 11 ppm downfield from DSS. According to the crystal structure 7-methyl-guanine at position 46 (^{7}mG) is base-paired to guanine at position 22, while the latter also participates in a normal Watson-Crick base pair with the complementary cytidine at position 13. In this interaction imino protons are involved, as is shown in fig. 2.

Therefore, the ^{7}mG was selectively removed from the tRNA by chemical modification and ^{1}H spectra of the intact material and the ^{7}mG-

deficient material were recorded and subsequently substracted. The results given in fig. 3 reveal that one ^{1}H-resonance is lost at −12.5 ppm after modification, indicating that the structure, deduced from the crystal data, is also present in solution.

The presence in solution of this hydrogen bond could be confirmed in an independent way by experiments performed on another tRNA-species, i.e. E. coli $tRNA^{Metf}$, where we obtained analogous results, except for a difference in resonance position which amounts to 1.1 ppm. Using ring current calculations this difference could be explained on the basis of structural differences between the two tRNA's.

With best regards,

P.J.M. Salemink T. Yamane C.W. Hilbers

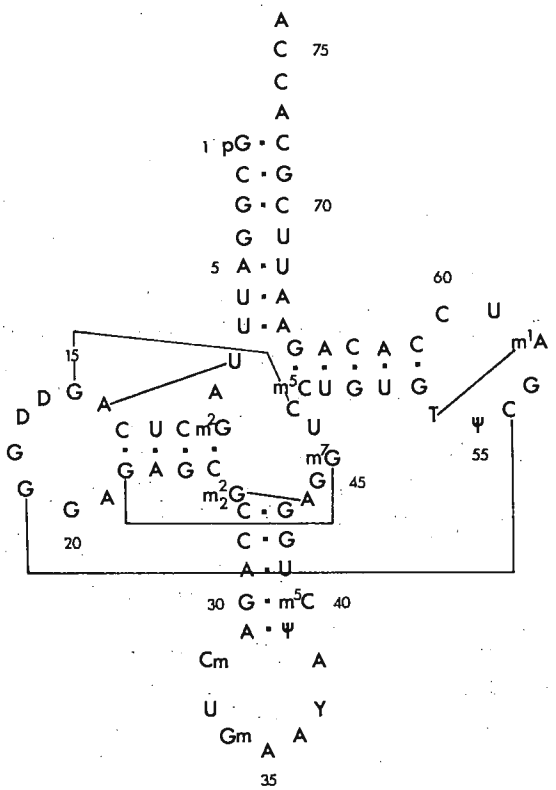

Fig. 1.
Primary structure of yeast $tRNA^{Phe}$ folded into a clover-leaf. Solid lines represent tertiary interactions expected to be visible in the NMR spectrum. Dots represent secondary Watson-Crick hydrogen bonds. Numbers indicate positions of the bases in the primary structure.

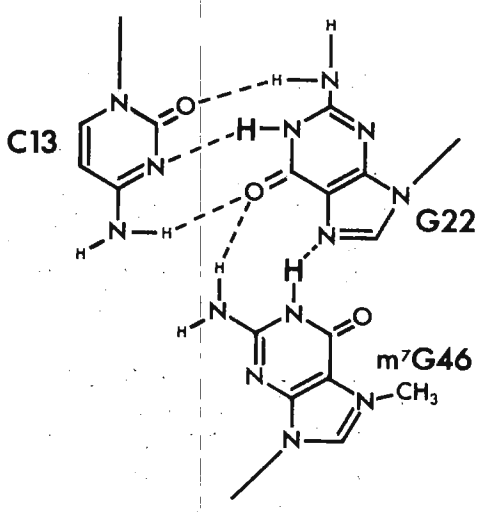

Fig. 2
Triple interaction between $^7mG_{46}$, G_{22} and C_{13}. The hydrogen bond between $^7mG_{46}$ and G_{22} discussed in the text is pressed in capital.

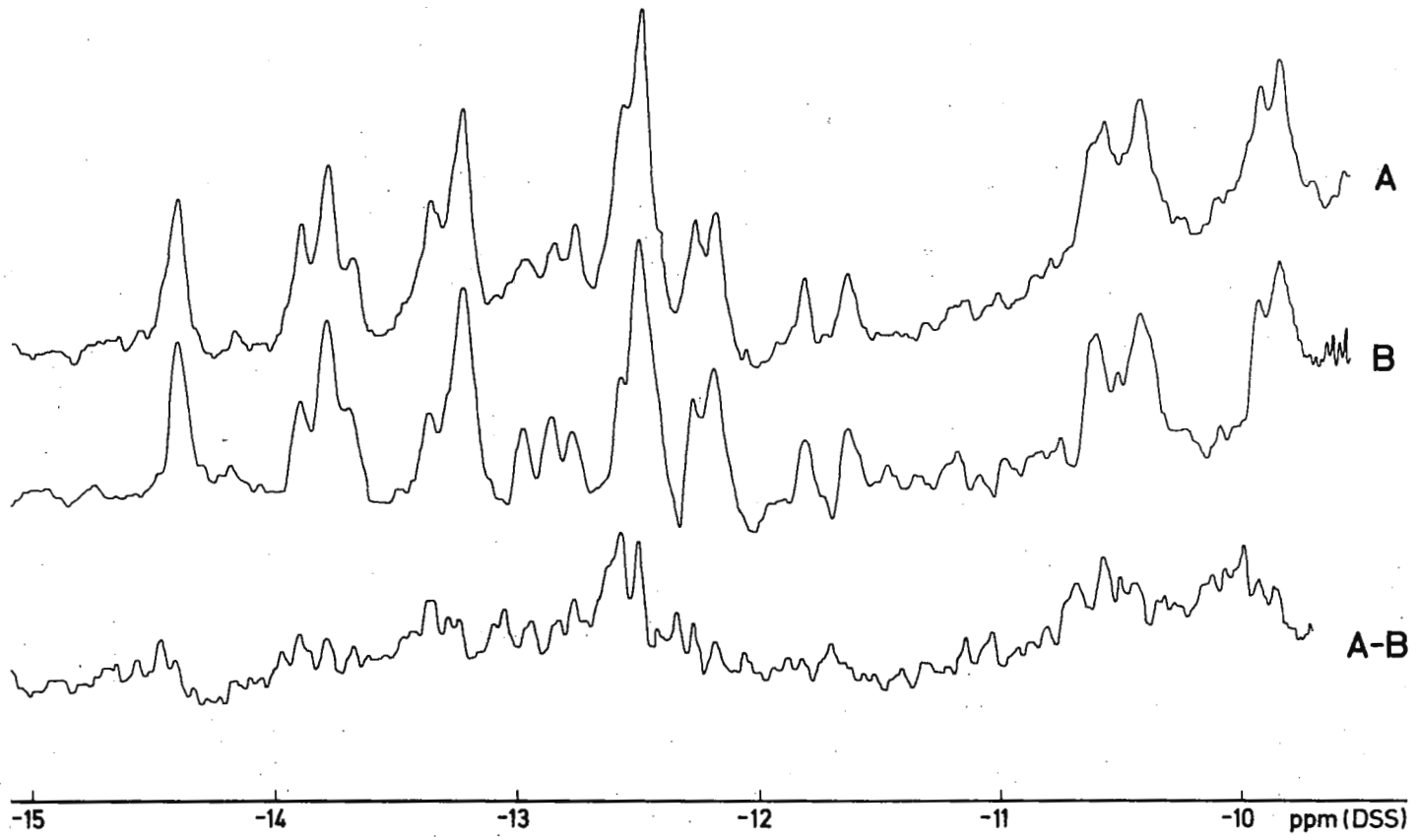

Fig. 3
^{1}H 360 MHz NMR spectra recorded at 35°C.
a = intact yeast tRNA^{Phe}. b = yeast tRNA^{Phe}, in which ^{7}mG has been removed by chemical modification. a-b = difference spectrum.

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the Medical Center / SCHOOL OF MEDICINE / COMPREHENSIVE CANCER CENTER

JOHN R. DURANT, M.D., DIRECTOR (205) 934-5077

March 2, 1977

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

Dear Barry:

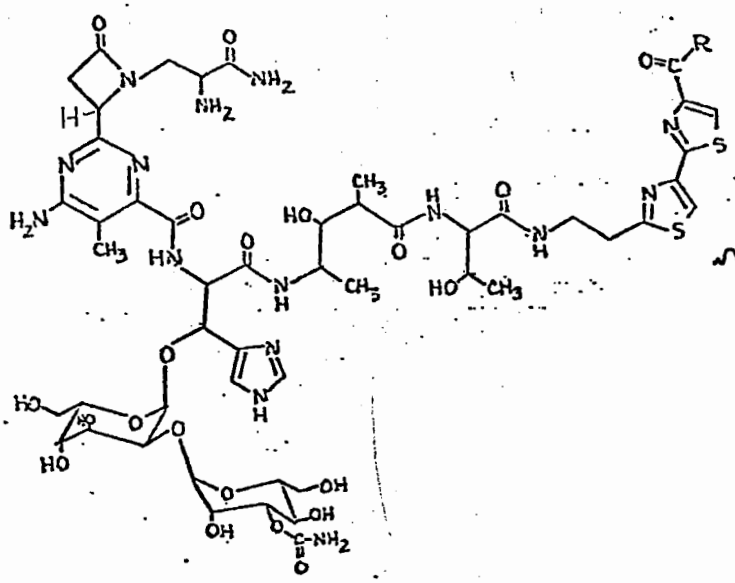
In response to your final "pink note" we would like to describe some of our current research on the bleomycins (BLM). This family of water soluble glycopeptides isolated from streptomyces verticillus exhibit both antibiotic and antineoplastic action (1). The structure of these drugs is shown in Figure 1. Bleomycin complexes of various radioactive metals ($^{57}Co^{2+}$, $^{67}Ga^{3+}$, $^{111}In^{3+}$, $^{160}Yb^{3+}$) have been used as tumor scanning agents in the detection and staging of a wide variety of solid tumors and malignant lymphomas (2). Models for the structures of some of the metal-BLM complexes have been proposed by Murakami et al. (3).

We have just completed the ^{1}H NMR assignments of the commerically available BLM, Blenoxane, which is composed of approximately 70% A_2 and 25% B_2 with smaller amounts of other congeners (4). As part of a detailed ^{1}H NMR study of the interaction of BLM with various metal ions, we have gathered the preliminary data shown here. Figure 2 shows the aromatic region of Blenoxane titrated with gallium (Ga^{3+}) at pH 7.0. Note that by the addition of 0.58 equivalents of Ga^{3+}, a set of shifted peaks are observed in spectrum (c) of Fig. 2. The observation of two sets of peaks in spectrum (b) of Fig. 2 clearly indicate that there is "slow exchange" of BLM between its free and bound state. By the comparison of the integrated intensities of the free and bound C_4 protons of histidine in the presence of various relative concentrations of Ga^{3+}, we find that the metal complex has the empirical formula $Ga(BLM)_2$. Since the corresponding Cu^{2+} and In^{3+} complexes of BLM have been shown to have a 1:1 stoichiometry (5), we conclude that different metals must occupy different binding sites on BLM. We are currently trying to ascertain which functional groups on BLM are involved in binding the Ga^{3+}. We hope to be able to report on these results in the near future.

Sincerely yours,

Francis Chang — Jerry Glickson — Bob Lenkinski

References: (1) H. Umezawa, Biomedicine, 18, 459(1973); (2) D.L. Lilien, S.E. Jones, R.E. O'Mara, S.E. Salmon & B.G.M. Durie, Cancer, 35, 1036(1975); (3) H. Murakami, H. Mori, and S. Taira, J. Theor. Biol., 42, 443(1973); (4) D. Chen, B.L. Hawkins, and J.D. Glickson, Biochemistry, submitted (1977); (5) A.D. Nunn, J. Antibiotics, 29, 1102(1976).



BLEOMYCIN	R
A_1	$-NH(CH_2)_3\overset{O}{\overset{\|}{S}}CH_3$
A_2	$-NH(CH_2)_3\overset{+}{S}(CH_3)_2$
$A_{2'-a}$	$-NH(CH_2)_4NH_2$
B_2	$-NH(CH_2)_4NH-\overset{NH}{\overset{\|\|}{C}}-NH_2$
A_5	$-NH(CH_2)_3NH(CH_2)_4NH_2$
A_6	$-NH(CH_2)_3NH(CH_2)_4NH(CH_2)_5NH_2$
BLEOMYCINIC ACID	$-OH$

Fig 1

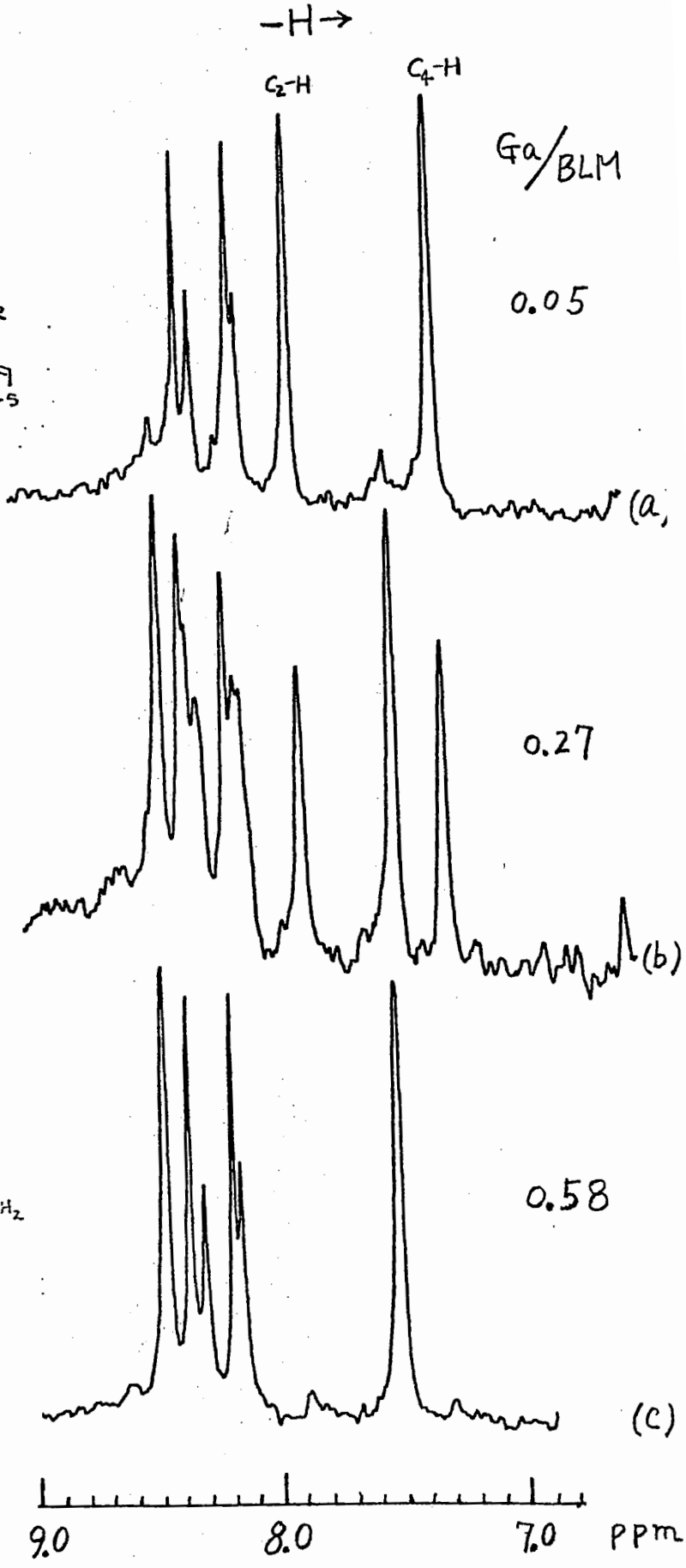


Fig 2

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Dept. of Chemistry
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28th February 1977

Onderwerp

Dear Professor Shapiro,

Exchange effects via T_1 relaxation

Your blue reminder prompted us to the following contribution. It is a well known fact that exchange rates, τ^{-1}, can be determined by line shape analysis (LSA) of NMR spectra. A disadvantage of this method is that only the small temperature range where exchange effects are visible in the spectrum is experimentally accessible. Beyond this range τ^{-1} can be determined by the spin echo technique[1], non selective T_1 measurements[2], and a double resonance technique[3]. In this letter I want to discuss a method where the longitudinal magnetization after a selective perturbation is used to monitor exchange effects between two sites, A and B.

If the total longitudinal magnetization, $M_{Z_A} + M_{Z_B}$, is inverted by a non selective π pulse[2], one only gets information about the exchange rate if the average lifetimes τ_A and τ_B and the T_1 values in the absence of exchange, T_{1_A} and T_{1_B} are in the range $T_{1_B} < \tau_A, \tau_B < 5T_{1_A}$. In organic liquids, however, this not often is the case, as there most times $T_{1_A} \simeq T_{1_B}$. The Forsén-Hoffman[3]

1. N. Boden, in Determination of Organic Structures by physical methods, volume 4, eds. F.C. Nachod, J.J. Zuckerman, Academic Press, 1971.
2. H. Strehlow, J. Frahm, Ber. Bunsenges. Phys. Chem. 79, 57 (1975).
3. S. Forsén, R.A. Hoffman, J. Chem. Phys. 39, 2892 (1963).

method can be used to determine exchange rates in the range where $\tau \simeq T_{1A}, T_{1B}$. Between this range and the temperature range accessible by the LSA method there often is a gap.

In this gap τ^{-1} can be determined by inverting the magnetization in one of the exchanging sites, say M_{Z_A}, by a selective π pulse. The return of M_{Z_A} to its equilibrium value is then given by

$$M_{O_A} - M_{Z_A}(t) = C_1 e^{-r_1 t} + C_2 e^{-r_2 t}$$

$$r_{1,2} = \tfrac{1}{2}\left(\frac{1}{\tau_{1_A}} + \frac{1}{\tau_{1_B}}\right) \pm \tfrac{1}{2}\sqrt{\left(\frac{1}{\tau_{1_A}} - \frac{1}{\tau_{1_B}}\right)^2 + \frac{4}{\tau_A \tau_B}}$$

$$\frac{1}{\tau_{1_{A,B}}} = \frac{1}{T_{1_{A,B}}} + \frac{1}{\tau_{A,B}}$$

$\tau_{A,B}$ is the average lifetime in site A or B respectively.
The slope at time zero of the recovery curve on a logarithmic scale is given by

$$r_3 = \frac{-C_1 r_1 - C_2 r_2}{C_1 + C_2} = \frac{1}{\tau_{1_A}}.$$

r_1, r_2, r_3, the ratio C_1/C_2 and the relation $M_{O_A}/\tau_A = M_{O_B}/\tau_B$ can be used to determine τ_A, τ_B, T_{1A} and T_{1B} reasonably well experimentally if r_1 and r_2 differ by a factor 5 or more. Examples at 67 and 93°C are given in the figure for a 5% solution of dimethylformadride (DMF) in DMF-d7.

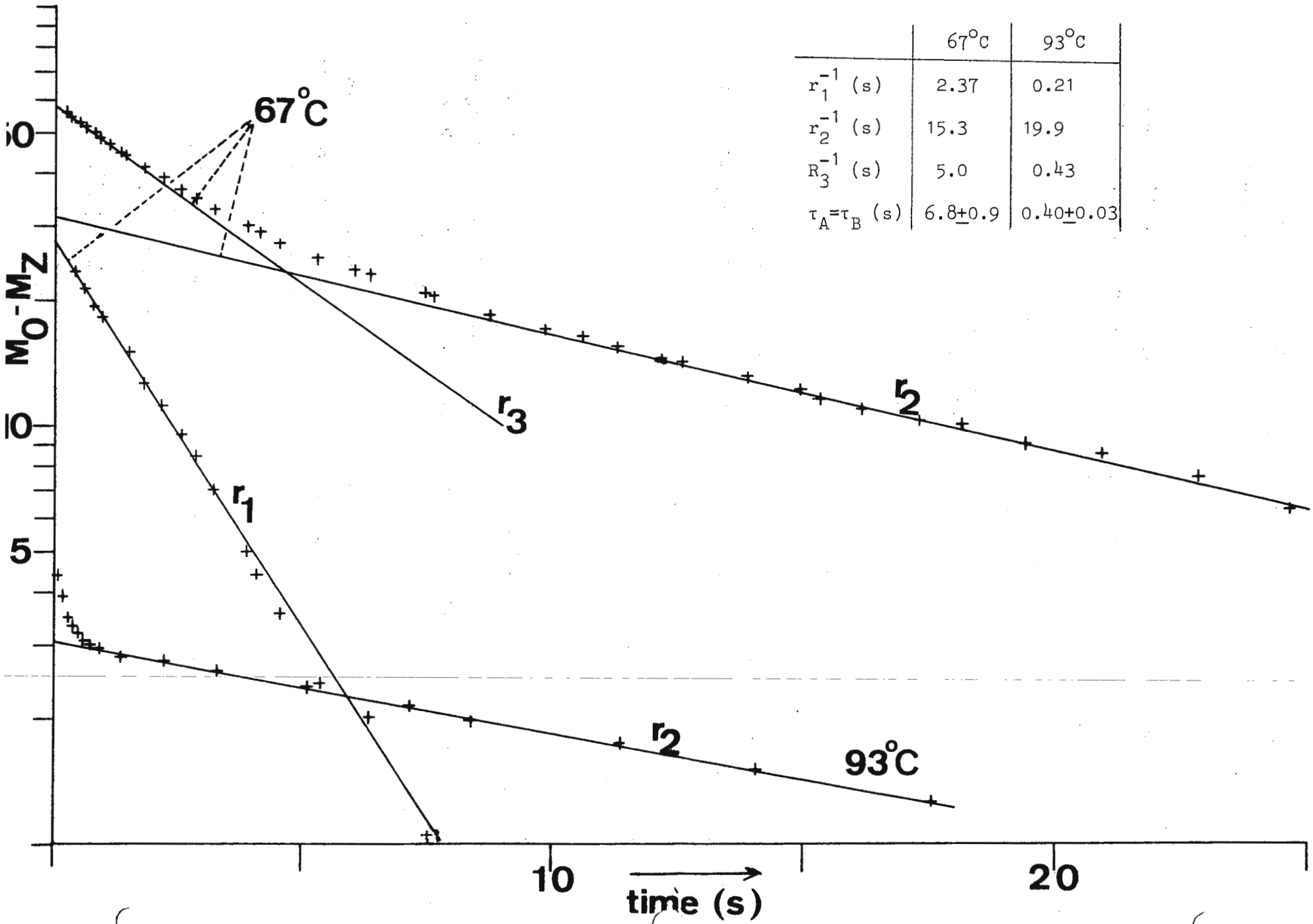
This method can therefore by used with success supplementary to the LSA method in order to extend the temperature range over which τ^{-1} values can be determined. This may lead to more reliable kinetic and thermodynamic parameters.

Please credit this contribution to the account of Prof. J. Smidt.

Sincerely yours,

Dr. W.M.M.J. Bovée

$M_{O_A} - M_{Z_A}(t)$ versus the time for DMF at two temperatures



	67°C	93°C
r_1^{-1} (s)	2.37	0.21
r_2^{-1} (s)	15.3	19.9
R_3^{-1} (s)	5.0	0.43
$\tau_A=\tau_B$ (s)	6.8±0.9	0.40±0.03

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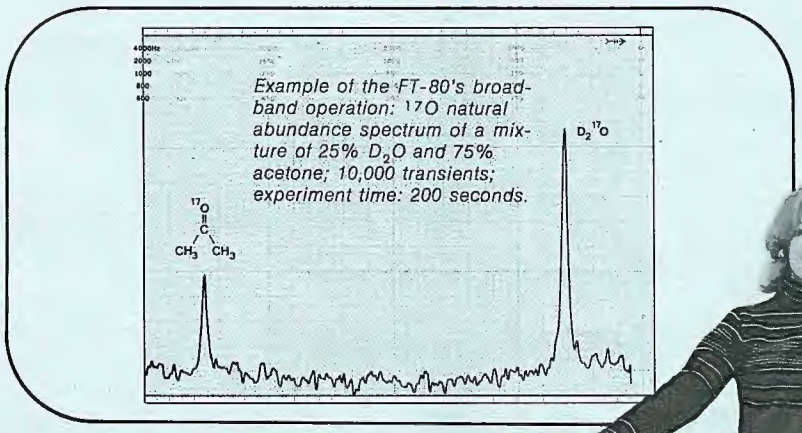

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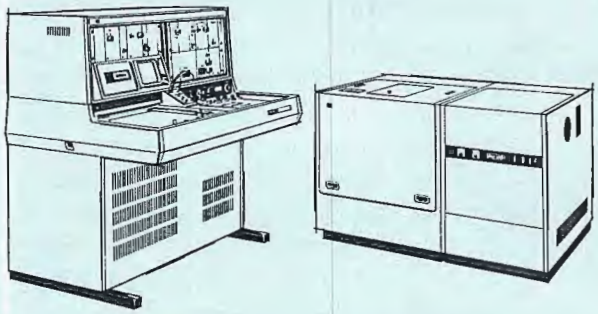

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