Texas A & M University N-M-R Newsletter

No.140
MAY,1970

Deadline Dates: No. 141:   1 June 1970
                  No. 142:   6 July 1970

All Newsletter correspondence, etc., should be addressed to:

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

Uppsala universitet
Fysiska institutionen

University of Uppsala
Institute of Physics

BG GG

April 10, 1970

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

Ragnar A. Hoffman - Obituary

Dear Professor Shapiro,

We regret to inform you that the head of the NMR research group
at the Institute of Physics, Uppsala, Sweden, Dr Ragnar A. Hoffman
died on 12 March.

The important scientific work of Ragnar A. Hoffman is well re-
cognized in the NMR community. He started his research in high-
resolution NMR at this institute in 1957, primarily working on
the NMR spectra of aromatic compounds. The results were summarized
in his Ph.D. thesis "Proton magnetic resonance studies of unsa-
turated and aromatic compounds with particular regard to effects
of electron delocalization" which was put forward in 1960. He con-
tinued his work on the determination and interpretation of the NMR
parameters of unsaturated compunds, and this research resulted in
several important papers.

The double resonance techniques later attracted his interest. His
work in this field led to the developement of new methods and app-
lications of multiple resonance spectroscopy. This work also led
to an exstensive review article "High-resolution nuclear magnetic
double and multiple resonance" (together with Professor S. Forsén)
published in the series "Progress in Nuclear Magnetic Resonance
Spectroscopy".

During the last years Ragnar A. Hoffman became interested in the
study of relaxation effects and line-shapes in NMR. His work in
this field is incorporated in a comprehensive article "Line-shape
in high-resolution NMR" which has just appeared in the monograph
series "Advances in Magnetic Resonance". This paper has become
his last major contribution to the NMR literature.

Ragnar A. Hoffman also served as a teacher at this institute. With
his broad knowledge in physics, he was a skilful and inspiring
lecturer esteemed by his students and colleagues.

For us who had the privilege of collaborating with Ragnar A.
Hoffman in the research laboratory, he was a brilliant scientist,
always ready to discuss and clarify obscure questions, always
ready to try to penetrate the difficult problems in science.
Above all we will remember Ragnar as a personal friend, the loss
of whom we mourn, but who we will always remember with gratitude.

Yours sincerely

Bo Gestblom   Ola Hartmann   Sören Rodmar

ircha

**Institut
national
de recherche
chimique
appliquée**

établissement public à caractère
industriel et commercial,

12 quai Henri IV, Paris 4

rc Seine 58 b 7806

n° d'entreprise 971 75 104 9051

ccp Paris 9065 96 au nom
de l'agent comptable de l'Ircha

**Direction générale
Services de Paris**

12, quai Henri-IV, Paris-4ᵉ
téléphone : 272 82 70

Pr. B.L. SHAPIRO
Texas A. & M. University
College of Science
COLLEGE STATION TEXAS 77843

Paris, le   7 Avril 1970

Subject: Organo-phosphorus compounds (once more) - ^{13}C and
phospholes.

Dear BARRY,

Having been mute for some time and having seen a lot
of colors (nearly the full rainbow) around me, I find now time
to fill my pen up, just back from a trip. Mean while, our NMR
machine was not too lazy and to quote some observations, I pick
up ^{13}C resonance data, we have recently obtained on simple com-
pounds (vs. C_6H_6)

$(CH_3O)_3$ PO   +74.5 p.p.m.

$(CH_3O)_3$ PS   +73.4

$(CH_3S)_3$ PS   +110.4

$\left(\begin{array}{c} \rhd N \end{array} \right)_3$ P   +84.3 and 1045

$[(CH_3)_2N]_3$ PO   +91.5

$[(CH_3)_2N]_3$ P   +90.7

in all of these except the last no ^{31}P - ^{13}C coupling was obser-
ved (i.e. it is < 10 H$_z$ as spectra are directly observed with

. . . .

CAT enhancement). For 'hexametapyl', it was 17 Hz. This behavior is to be compared to relevant observations (W. McFARLANE, Proc. Roy. Soc., 306, 185 (1968)) on various $\underline{\underline{P}}$ O$\underline{\underline{C}}H_3$ groups for which ^{31}P - ^{13}C coupling $<$ 11 Hz or (H. ELSER, H. DREESKAMP, Ber. Busenges., 73, 619 (1969); W. McFARLANE, J.A. NASH, Chem. Comm., 1969, p. 913) on $\underline{\underline{P}}$ Si$\underline{\underline{C}}H_3$, Sn$\underline{\underline{C}}H_3$, Se$\underline{\underline{C}}H_3$, for which the same coupling is 13, 7.5 and $\lesssim$ 19.5 Hz. Thus, it appears that the modulus of carbon-phosphorus coupling through an heteroatom is not too sensitive to the heteroatom electronegativity, contrary to expectations that a reduced electronegativity would enhance the corresponding coupling.

Now, to come back to an interesting family I had briefly commented on in TAMU# 128.20, that of <u>phospholes,</u> we have
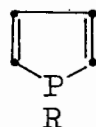
some additional data which may prove worth while. At that time, peak attribution of QUIN and BRYSON was only tentative and it was tempting to identify the observed proton-phosphorus couplings (13.9 and 39.5) with that known in vinyl phosphines (g$\underline{\underline{em}}$ + 11.7; trans +30.2). Actually, QUIN, BRYSON and MORELAND (J.Am. Chem. Soc., 91, 3308 (1969)) definitely assigned the greater coupling to the α proton and the smaller to the β one. This reversal respect to vinyl phosphines may be attributed to the aromatic behavior of such compounds. This attribution is in complete agreement with our observations on
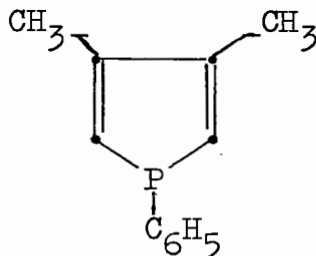
J ($\underline{\underline{P}}$ C $\underline{\underline{H}}$) 37.5 Hz

4 J ($\underline{\underline{P}}$ $\underline{\underline{H}}$)3.5 Hz

we have investigated as well

CH$_3$——————CH$_3$

J ($\underline{\underline{P}}$ C $\underline{\underline{H}}$) 30.5

4 J (P H) 2 Hz

P

S C$_6$H$_5$
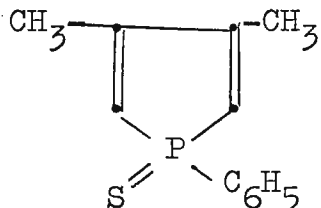
and for both of these, we have determined the relative sign of ^{2}J and ^{4}J ($\underline{\underline{P}}$ $\underline{\underline{H}}$) by spin decoupling. They are similar in the P$_{III}$ compound, opposite in the P(S) one. Due to the relative value of ^{2}J and ^{4}J, it is more likely that the ^{4}J sees its sign reversed; in such situations, an important (and sensivive)π contribution is to be expected and the relevant hyperconjugation at β—methyl would be 'turned over' by the hybridization change (not to speak of 'thru-space' contribution).

With my very best regards,

G. MAVEL

The Chemical Laboratory
University of Coimbra
Portugal

15th April 1970

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

H-H AND C-H COUPLING CONSTANTS IN NEUTRAL AND PROTONATED AZINES

Dear Professor Shapiro,

Thank you for your reminder.

We have obtained the H-H coupling constants of mono--protonated pyridazine and pyrimidine, as well as the one bond C-H coupling constants of protonated pyridine, pyridazine, pyrimidine and pyrazine, and have investigated additivity relationships for the H-H and C-H coupling constants of neutral and protonated azines.

It is found that there is good agreement between the observed values for the diazines and those calculated assuming that the effect per N atom, or NH^+ group, is the same as in pyridine, or pyridinium ion. The most significant discrepancies encountered regard $J_{H_4H_5}$ and $J_{C_4H_4}$ for pyridazine, which are appreciably larger than expected. This has been attributed to an appreciable shortening (of the order of 0.04Å) of the $C_4 C_5$ bond with respect to benzene.

Yours sincerely,

V.M.S. Gil   A.J.L.Pinto

CARLETON UNIVERSITY

OTTAWA 1, CANADA

PARTMENT OF CHEMISTRY

April 20, 1970

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

Dear Barry:

Long Range Shielding Effects of the C-H and C=O Bonds

We have recently reinvestigated the long range shielding effects of
the C-H and C=O bonds using 5α, 14α androstane and its mono-keto derivatives
as model compounds.

Since there is a conflict of opinions concerning the magnitude of the
C-H bond anisotropy (1-3) this parameter was a variable in the present study.
C-H and C=O dipole positions were varied independently along the respective
bond axes.

Calculations showed no preferred C-H dipole position (the best C=O
dipole location was found to be the midpoint of the bond in agreement
with earlier findings (2)). Values derived for the C-H bond anisotropy
were small. The geometric quantities in the McConnell equation for the
CH_2 group were small compared to those for the C=O bond. This makes
this system unsuited for a reliable evaluation of $\Delta\chi_{C-H}$ but for the same
reason a neglect of this term hardly affects the C=O bond shielding para-
meters. The geometric quantities in the equation for the magnetic and
electrostatic shielding mechanisms were obtained from measurements on
Dreiding models as well as from X-ray data. Two methyl group models were
used. The shielding effect at the average methyl proton position as well
as the average of the effect at 72 positions, 5° apart around the circle
of rotation of the methyl hydrogens, was calculated. It turned out that
improvements in the derivation of the geometric quantities hardly
affected shielding parameters and calculated shifts. In the table present
results are compared to previously derived C=O bond parameters.

- 2 -

TABLE 1

Method	$\Delta\chi^{CO}_{xy}$	$\Delta\chi^{CO}_{yz}$	$\Delta\chi^{CO}_{zx}$	k^{CO}
XR	30.7 ± 0.8	-9.4 ± 1.8	-21.3 ∓ 1.1	-9.1 ± 0.3
XA	31.7	-12.5	-19.2	-12.6
MR	26.2	-7.7	-18.5	-7.7
MA	26.7	-10.7	-16.0	-11.3
ref 1	27.0	-8.6	-18.4	-6.9
ref 2	25.7	-12.2	-13.5	-12.2

X: X-ray data used

M: molecular models used

R: rotating methyl group model

A: shielding effect at average methyl proton position

C=O dipole position 0.6 A from carbon.

The prediction of the shift of the C-19 methyl group in the C-11 ketone was 0.3 ppm too high. The oxygen atom approaches the methyl hydrogens to 2.3 - 2.4 Å. It is likely that in this case the methyl group is staggered as proposed earlier (2). It is also possible that van der Waals shielding makes a large contribution in this case.

References

1. J. W. ApSimon, P. V. Demarco, D. W. Mathieson, W. G. Craig, A. Karim, L. Saunders and W. B. Whalley. Tetrahedron 26, 119 (1970).

2. R. F. Zurcher, "Progress in Nuclear Magnetic Resonance Spectroscopy" J. W. Emsley, J. Feeney, and L. H. Sutcliffe, eds. Vol. 2, Pergamon, Oxford, 1967, p. 205.

3. J. Homer and D. Callaghan. J. Chem. Soc. (A), 439 (1968).

Yours sincerely,

J. W. ApSimon
Associate Professor

JWA/jt

Iwan N. Stranski-Institut
Institut für Physikalische Chemie
der Technischen Universität Berlin

1 Berlin 12, den April 22 nd, 1970

Tel: (0311) 3 4 4171

3 S

Prof. Bernard L. Shapiro

Department of Chemistry
Texas A & M University

College Station, Texas 77843
U. S. A.

Re. :   Possible errors in the calculation of association constants from
        chemical shift data and possible difficulties in sealing nmr tubes
        filled with halogenated hydrocarbon mixtures

Dear Professor Shapiro ,

The equation $(d\nu / dc)_{c=0} = 2 K_c (\nu_d - \nu_m)$, in the following named eq. (1),
which has been derived by Huggins et al. [1] is a frequently used formula to
evaluate association constants (K_c) for monomer-dimer-equilibria from the
initial slope $\left(\dfrac{d\nu}{dc} \Big|_{c = 0} \right)$ in a ν/c -diagram, with the resonance-sites of the
pure monomer, ν_m, and the pure dimer, ν_d. This is to certify that the above
cited relation (1) gives rise to erroneous results if it is applied to systems
having high association constants.

The concentration dependence of the chemical shift in a system with a monomer
dimer-equilibrium has been calculated for fast proton exchange using the well-
known relation:

$$\nu_{exp} = \left\{ \nu_m \cdot \left[\frac{1}{4 K_c} \left(\sqrt{1 + 8 K_c \cdot c_E} - 1 \right) \right] + \nu_d \cdot \left[c_E - \frac{1}{4 K_c} \left(\sqrt{1 + 8 K_c \cdot c_E} - 1 \right) \right] \right\} \Big/ c_E$$

where c_E is the total concentration of the associating species, and ν_{exp} is the
experimentally detected resonance-site of the associating proton.

[1]   C.M. Huggins, G.C. Pimentel, J.N. Shoolery
      I. physic. chem. 60 , 1311   (1956)

Model calculations with values which are typical for carboxylic acid, e.g. $K_c = 4000$ $1 \cdot mol^{-1}$ and $\nu_d - \nu_m = 600$ $c \cdot sec^{-1}$, have shown that only measurements at concentrations as low as 10^{-7} $mol \cdot 1^{-1}$ are able to yield the experimental association constants $K_c \approx 3950$ $1 \cdot mol^{-1}$. With concentrations, c_E, in the range of $1 \cdot 10^{-2}$ to $5 \cdot 10^{-2}$ $mol \cdot 1^{-1}$ taking the measurable chemical shift values as representing the initial slope, the calculated association constant is $K_c = 6$ $1 \cdot mol^{-1}$, a value which is far from being comparable with the original value of $K_c \approx 4000$ $1 \cdot mol^{-1}$. With an original association constant $K_c = 100$ $1 \cdot mol^{-1}$ and the same resonance difference for $\nu_d - \nu_m$ as above an association constant of $K_c = 16$ $1 \cdot mol^{-1}$ is obtained when using relation (1) in the concentration range $1 \cdot 10^{-2}$ to $5 \cdot 10^{-2}$ $mol \cdot 1^{-1}$. This result is in error by a factor of 6.

In nmr spectroscopy the lower limit of concentration is rather high, equation (1) will yield reliable values only for inferior association constants ($K_c < 10$ $1 \cdot mol^{-1}$). This is but only one reason why Parmigiani et al. [2] have calculated an association constant for the acetic acid dimerisation which is too small by a factor of approximately 400. For other reasons see Ref. [3].

Using carbontetrachloride and other halogenated hydrocarbons as solvents in nmr investigations of hydrogen-nuclei-exchange-reactions we came across another difficulty which is affiliated on the sealing of nmr tubes and we think it is worthwhile to be considered. Pouring the solution out into the nmr tube a thin film of carbontetrachloride (or another halogenated hydrocarbon) is attached to the inner wall of the nmr tube.
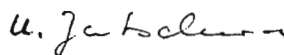
[2] A. Parmigiani, A. Perotti, V. Riganti
Gazz. chim. Ital. 91, 1148 (1961)

[3] U. Jentschura, E. Lippert
Ber. Bunsenges. phys. Chem. 74 , 7 (1970)

On sealing these nmr tubes, the solution being simply solidified in liquid
nitrogen, considerable amounts of hydrogenchloride could be produced by
the pyrolysis reaction of the C - Cl bond and consecutive reactions of the
pyrolysis products. This could be verified by the occurrence of acetyl
chloride in a mixture of acetic anhydride and halogenated hydrocarbons.
The acetyl chloride contamination was absent in unsealed mixtures and in
solutions which were distilled into the nmr tube on the vacuum line. No
efflorescence could be detected at the sealing-site of the nmr tube. Daylight
was excluded during all mixing, filling and sealing procedures in order to
prevent photolysis reactions of carbontetrachloride.[4] .

Sincerly yours

(E. Lippert)   (U. Jentschura)

[4]   S. Forsen
        Acta chem. Scand 14 , 231 (1960)

        U. Jentschura, E. Lippert
        Ber. Bunsenges. phys. Chem. 74 , 12 (1970)

Eidg. Technische Hochschule

Laboratorium für Organische Chemie

Zürich

8006 Zürich,　April 22, 1970 fo
Universitätstrasse 6
Tel. (051) 32 62 11

F. W. Wehrli
c/o Professor Dr. W. Simon

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

Heteronuclear Spin Tickling in the A_3X system of $^{13}CH_3\,^{12}CN$

Dear Professor Shapiro,

Heteronuclear tickling experiments have proved to be a useful method
for the indirect detection of resonance lines of nuclei of low magnetogyric
ratio such as ^{13}C (1). The following example is an illustration of the
general theory of double resonance in degenerate systems of the type A_mX_n,
given by Anderson and Freeman (2).

Extremely simple rules hold for predicting the double resonance behavior
if the perturbing rf filed H_2 is small compared to the spin - spin coupling
constant and if its frequency is identical with that of an X transition. In
this case all A multiplet lines should split up into submultiplets consisting
of 2S + 1 lines if S is the total spin of the X nuclei. Furthermore a residual line
appears in the center of each submultiplet if the total spin of the A nuclei is
greater than 1/2. In the case of an A_3X spin system, therefore, a subtriplet is
to be expected, with a distance of the two outer lines of $\gamma_c H_2/2\pi$ whenever H_2
is in exact resonance with one of the X transitions. Fig. 1*) shows a ^{13}C
satellite in the proton spectrum of acetonitrile, a) unperturbed, and b) and
c) with H_2 perturbing an outer and inner line of the ^{13}C quadruplet respectively.
The calculation of relative intensities yields a ratio of 1,5 : 7 : 1,5 and
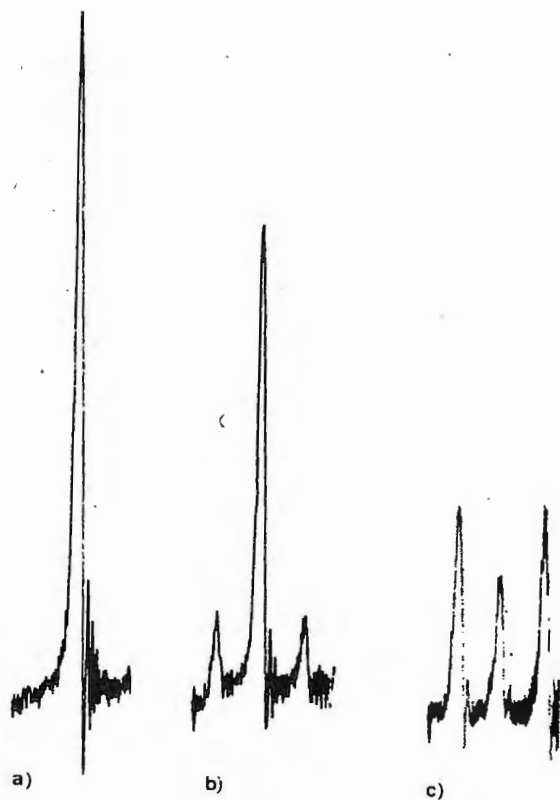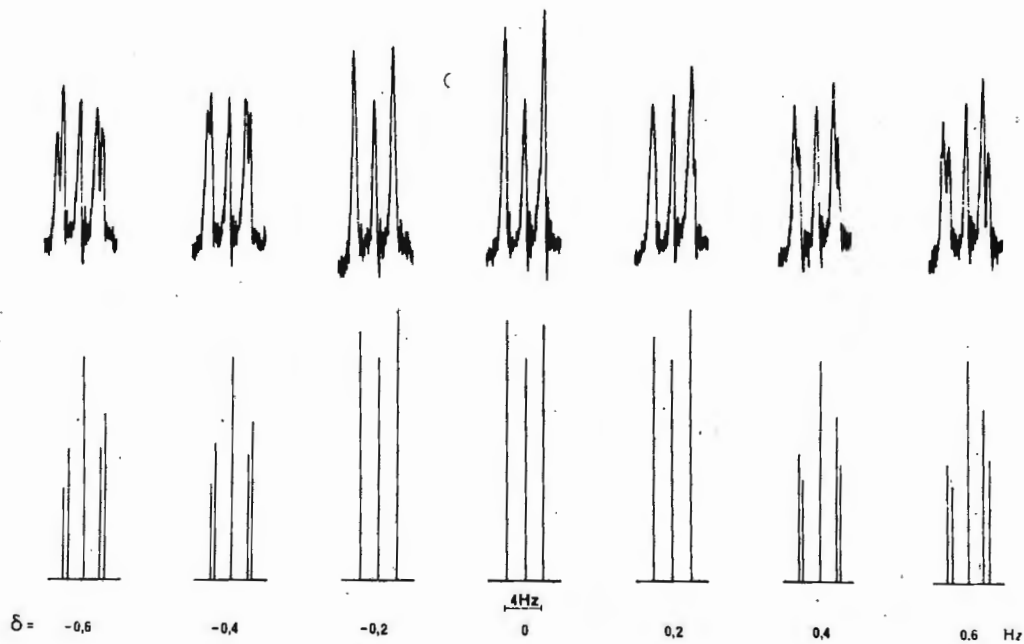3,5 : 3 : 3,5 in accordance with experiment.

Fig. 1

Fig. 2

$$\delta = \quad -0,6 \qquad -0,4 \qquad -0,2 \qquad 0 \qquad 0,2 \qquad 0,4 \qquad 0,6 \quad Hz$$
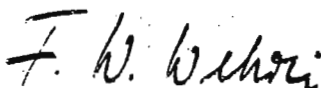
4Hz

*) All spectra were obtained on a Bruker-Spectrospin HFX-10 spectrometer.

Deviation from exact resonance causes changes in the relative intensities and finally further splitting of the outer subtriplet lines. The amount of this "secondary" splitting can be shown to be equal to the difference δ between the double resonance frequency and the ^{13}C transition frequency to be measured. This is illustrated in Fig. 2*) showing calculated and experimental spectra of a ^{13}C satellite line for different settings of the double resonance frequency near an inner line of the ^{13}C quadruplet. The results indicate that even for a very small frequency offset of less than 0.5 Hz from exact resonance, observable splitting of the outer subtriplet lines occurs. The method is therefore suggested to be applicable to highly accurate carbon shift determinations.

(1) R. Freeman & W. A. Anderson, J. Chem. Phys. 39, 806 (1963).
(2) W. A. Anderson & R. Freeman, J. Chem. Phys. 37, 85 (1962).

Sincerely yours,

F. W. Wehrli

F. W. Wehrli

P.S. Please credit this contribution to the subscription of Professor
Dr. W. Simon.

23 April 1970
1217 Birch
Richland, Wash.
99352

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

Post-doctoral Position Desired

Dear Barry,

I would appreciate your publishing this note in your newsletter.

I am interested in a post-doctoral position in either nmr or esr to begin within the next few months. As you know, my doctoral thesis was in nmr, and additional research experience has been gained in nmr since that time.

I will be happy to send full particulars, including a resume, a list of publications, and references to anyone interested.

Sincerely yours,

Jane

Jane L. Burdett

jb

UNIVERSITY OF ILLINOIS

Department of

CHEMISTRY AND CHEMICAL ENGINEERING

URBANA

61801

East Chemistry Building

April 24, 1970

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

<u>Low Temperature Enantiomeric Nonequivalence in</u>
<u>Asymmetric Hydroxylamines Employing Optically Active Solvents</u>

Having observed enantiomeric nonequivalence of tetrahedral amine oxides in 1-phenyl-2,2,2-trifluoroethanol (I) and similar solvents,[1] we became interested in the possibility of observing analogous phenomena in trivalent nitrogen compounds. Hydroxylamines are known to undergo slow interconversion of enantiomers ("degenerate racemization") at low temperatures[2,3] (see Fig. 1). Thus in chiral solvents the "enantiomers" may give different nmr spectra. Dr. K. Mislow's note to you of February 10, 1970 was the first report of this phenomenon for asymmetric trivalent nitrogen compounds (specifically aziridines).

Employing <u>d</u>-carbinol (I) enantiomeric nonequivalence does occur in O,N-dimethyl-N-benzylhydroxylamine (II) at low temperatures (see Fig. 2). Thus at -58° in deuterochloroform or <u>dl</u> carbinol (I) the N-methyl and O-methyl groups appear as singlets and the N-methylene as an AB quartet. The signal broadening in carbinol may be caused by increased viscosity. In active carbinol (I) enantiomeric non-equivalence is clearly evidenced by doubling of the N-methyl ($\Delta\nu$ = 5.8 Hz), O-methyl ($\Delta\nu$ = 6.7 Hz) and the high-field N-methylene ($\Delta\nu$ = 4.0 Hz).

An apparent application of this phenomenon is the study of compounds undergoing slow degenerate racemization which do not contain observably nonequivalent diastereo-topic groups. For example, by classical methods slow degenerate racemization could not be observed in O,N,N-trimethylhydroxylamine or O,N-dimethy-N-tert-butylhydroxyl-amine but could in principle be observed in chiral solvents. Similar results might be obtained for other types of compounds which exhibit slow degenerate racemization, e.g., sulfenamides and hydrazines.

Figure 3 depicts the change in amount of nonequivalence with temperature. Plots I and II represent, respectively, the AB nonequivalence for the N-methylene protons when deuterochloroform or a mixture of d,l carbinol and deuterochloroform is the solvent. Both plots I and II show a decrease in $\Delta\nu$ with decreased temperature after the original coalescence. This decrease is probably caused by changes in conformer populations with temperature.

Plot III is the chemical shift difference of enantiomeric O-methyl groups in deuterochloroform and <u>d</u>-carbinol (I). Plots similar to III result for N-methyl and N-methylene enantiomeric nonequivalence. The amount of nonequivalence increases with decreasing temperature, thus indicating a relation between this nonequivalence and conformer populations different from that in the AB nonequivalence.
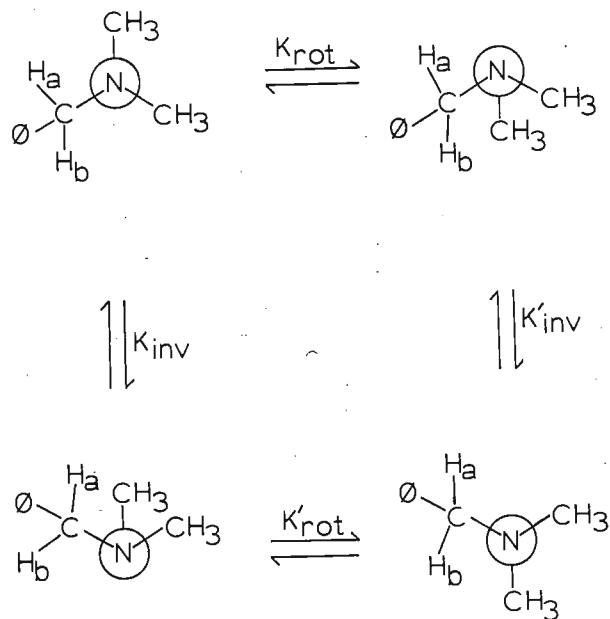
Ronald Muntz
W. H. Pirkle

Fig. 3. Dependence of Chemical Shift
Difference on Temperature
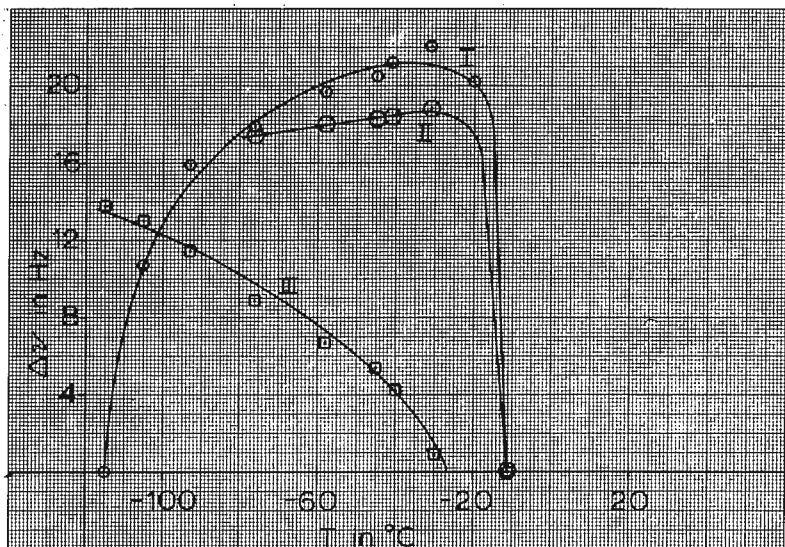
I = N-methylene AB nonequivalence in deuterochloroform
II = N-methylene AB nonequivalence in dl-carbinol and
     deuterochloroform
III = O-methyl nonequivalence in d-carbinol and deutero-
      chloroform

Fig. 1. Degenerate Racemization
of O,N,N-Trialkylhydroxylamines

Consecutive rotation and inversion
are necessary for interconversion of
enantiomers; therefore, either slow
rotation or inversion can lead to
nonequivalence.

1. W. H. Pirkle, S. D. Beare, and R. L. Muntz, J. Amer. Chem. Soc., 91, 4575
   (1969).
2. J. D. Roberts and D. L. Griffith, J. Amer. Chem. Soc., 87, 4089 (1965).
3. M. Raban, G. W. J. Kennex, Jr., and F. B. Jones, Jr., J. Amer. Chem. Soc.,
   91, 6677 (1969).

Fig. 2. NMR Spectra[a] of O,N-Dimethyl-N-Benzylhydroxylamine in Various Solvents[b]

NO CARBINOL

OCH$_3$

N–CH$_3$

NCH$_2$

$\underline{d}$l-Ø-CHCF$_3$
           OH

OCH$_3$

N–CH$_3$

NCH$_2$

$\underline{d}$-Ø-CHCF$_3$
        OH

OCH$_3$

N–CH$_3$

NCH$_2$
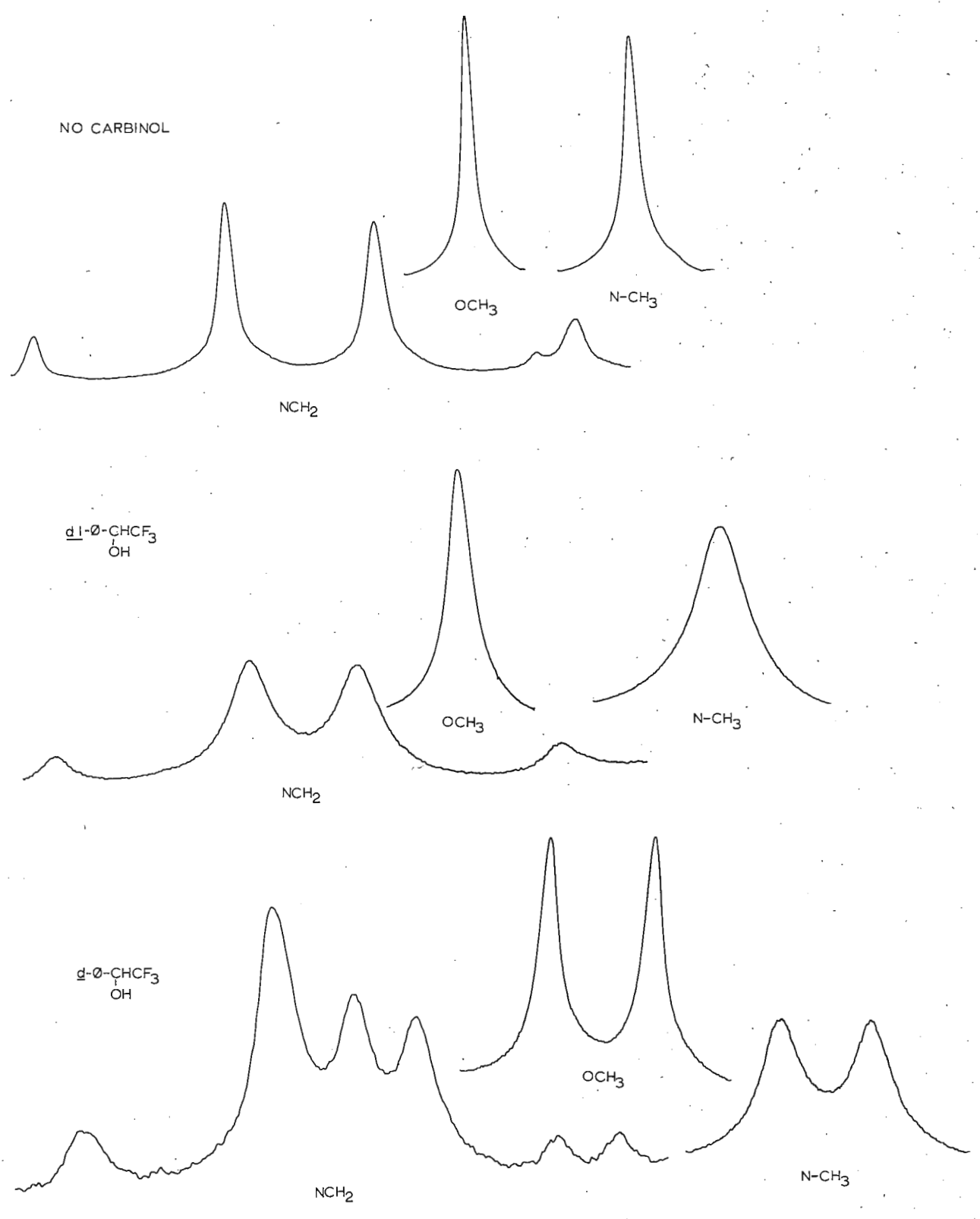
[a]Spectra run on Varian HA-100 spectrometer at –58° and a sweepwith of 50 Hz.

[b]The samples are composed of approximately four mmoles deuterochloroform, one mmole hydroxylamine, and in the last two cases, two mmoles of carbinol.

April 24, 1970

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

## Combination of NMR and IR Spectroscopy in Hydrogen Bonding Studies.

Dear Barry:

Recent work (1-3) has shown that 5-hydroxymethyl-1,3-dioxanes (I_a, R = H) with axial -CH_2OH groups do not show any intramolecular hydrogen bond in the IR. In order to explore this surprising finding, which is in contrast to the situation (4) in the acyclic analog 3-methoxypropanol-1, $CH_3OCH_2CH_2CH_2OH$, we synthesized the corresponding methyl compounds, Ib and IIb, R = CH_3, by a Grignard synthesis from the known (1) esters. The IR OH-stretching frequencies at 5×10^{-3} M concentration (measured in a 10-cm quartz cell) are shown under the formulations.

I
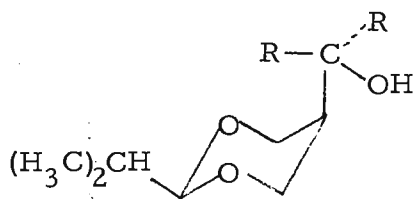
a R = H ($\tilde{\nu}$ = 3640 cm⁻)
b R = CH_3 ($\tilde{\nu}$ = 3622 cm⁻¹ s
            3639 cm⁻¹ sh
            3571 cm⁻¹ w)
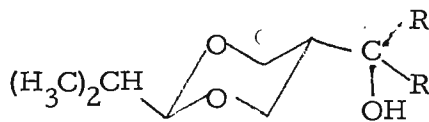
II

a R = H ($\tilde{\nu}$ = 3640 cm⁻¹)
b R = CH_3 ($\tilde{\nu}$ = 3616 cm⁻¹)
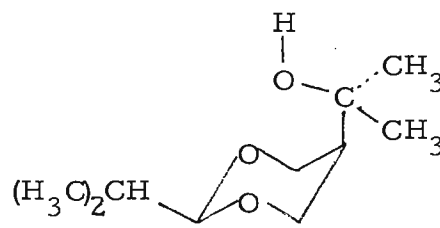
III

($\tilde{\nu}$ = 3571 cm⁻¹
corresponds to the
OH-down conformation)

The behavior of the NMR spectra of Ib and IIb upon dilution is of interest. When a solution of IIb in CCl_4 is diluted from ca. 1M (20%) to 5×10^{-3} M, the carbinol methyl groups shift from 71.2 to 68.7 Hz (from TMS at 60 Mhz). This change may be ascribed to the change in anisotropy of the medium

Professor Bernard L. Shapiro - 2 - April 24, 1970

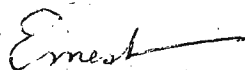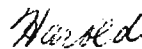upon dilution, since a similar shift (ca. 3 Hz) is observed for the isopropyl methyl signal in both Ib and IIb. In contrast, the carbinol methyl shift in Ib changes greatly, from 82.7 Hz to 68.7 Hz, as the concentration is changed from $1\underline{M}$ to $5x10^{-3}$ M. Such a large shift, other than of the O$\underline{H}$ itself, upon dilution of a CCl_4 solution is unusual. We ascribe it to the fact that at the highest concentration, Ib is strongly bonded intermolecularly (seen in the IR); such bonding forces the OH-group to the outside of the ring and the CH_3-group to the inside where it is known (5) to be subject to a downfield shift by the proximal ring oxygens. In dilute solution, however, where intermolecular hydrogen bonding no longer stabilizes conformation Ib, the dimethylcarbinol group turns with the OH inside (conformation III) and the chemical shift of the methyl group then becomes the same as in IIb.

It is surprising that, under these circumstances, the intramolecular hydrogen bonding in III is so weak. Clearly the OH-group is largely turned with the hydrogen up (and unbonded) rather than down (and bonded). We ascribe this to a combination of dipole repulsion and bond eclipsing forces which destabilize the OH-down (bonded) analog of conformation III. Data in the 3-tetrahydropyranmethanol series, to be published elsewhere, support this hypothesis.

Sincerely yours,

Ernest L. Eliel

Harold D. Banks

P.S. - Please credit this contribution to Dan Pasto's subscription.

1) E. L. Eliel and M. K. Kaloustian, Chem. Commun., 290 (1970).
2) P. Laszlo, personal communication and Tetrahedron Letters, in press.
3) J. Delmau, personal communication.
4) L. Kuhn, J. Amer. Chem. Soc., 76, 4323 (1954).
5) E. L. Eliel and M. C. Knoeber, J. Amer. Chem. Soc., 90, 3444 (1968).

CONSIGLIO NAZIONALE DELLE RICERCHE

ISTITUTO DI CHIMICA DELLE MACROMOLECOLE

20133 MILANO, 28th April 1970
VIA ALFONSO CORTI N. 12
TEL. 29.60.71

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

Dear Professor Shapiro,

We hope you will accept this contribution
to get on your mailing list.

Analysis of the Spectrum of Tetrabenzyltin

Although this spectrum is that of a very strongly coupled
system it has been possible to analyse it completely by
using the iterative program LAME (1).
Spectra (20% volume solution in CH_2Cl_2) were recorded five
times on HA-100 spectrometer, the r.m.s. error of the measured
frequencies being 0.05 Hz.
The r.m.s. deviation of the observed and calculated spectrum
was 0.07 Hz; with a maximum deviation of 0.2 Hz. All the
observable transitions were used for the iteration excluding
those of the CH_2 group (which gave a poorly resolved signal).
As a consequence, the analysis has been performed only on
the aromatic region; however all the parameters are pretty
well determined, including the benzylic couplings (the
largest parameter set error is 0.027; the largest correlation
coefficient is 0.52).
The results (Tab.1) can be compared with those of toluene
reported in ref. (2), the main feature being the upfield
shift ($\approx$0.3 ppm) of the ortho protons. Work is in progress
on similar compounds.

Sincerely yours,

L. Zetta, G. Gatti

(1) C.W. Haigh T.A.M.U. Newsletter No. 121, 54 (1968)
(2) M.P. Williamson, R.J. Kostelnik, S.M. Castellano
    J. Chem. Phys. <u>49</u>, 2218 (1968)

Parameter   (Hz.)   Prob. error

$W(1)=W(5) = 667.702$ 0.012

$W(2)=W(4) = 707.611$ 0.013

$W(3)=   692.615$ 0.017

$W(6)=   215.0$

$J_{12}=J_{45}= 7.569$ 0.020

$J_{13}=J_{35}= 1.264$ 0.015

$J_{14}=J_{25}= 0.644$ 0.020

$J_{15}=   1.861$ 0.020

$J_{16}=J_{56}=-0.526$ 0.020

$J_{23}=J_{34}= 7.420$ 0.016

$J_{24}=   1.384$ 0.020

$J_{26}=J_{46}= 0.249$ 0.027

$J_{36}=   -0.347$ 0.024

$J_{119_{SnCH_2}} =59.3$

$J_{117_{SnCH_2}} =57.0$
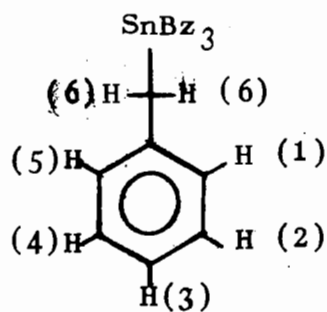
UNIVERSITY OF SUSSEX
THE CHEMICAL LABORATORY FALMER BRIGHTON BN1 9QJ
Telephone Brighton 0273 66755

29th April 1970

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

<u>Exchange Reactions of Donor-Acceptor Complexes</u>

Dear Professor Shapiro,

Here are a few notes on the first part
of a proton M.R. study of the system PMe_3, BMe_3 in toluene,
in which we have been looking at the kinetics of exchange
between the 1:1 donor acceptor complex and the free com-
ponent in excess [1]. Complex formation was taken to be
complete over the temperature range used ($-60^\circ C$ to about
$0^\circ C$), since (a) no lines from the deficient component
are seen at $-60^\circ C$, (b) a plot of line positions against
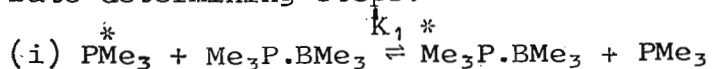composition at R.T. shows a discontinuity in slope at
1:1 mole ratio.

The proton spectra with excess PMe_3 have sharp
doublets at $-60^\circ C$ due to complexed ($\left| {}^2J_{PH} \right|$ = 9.3 Hz)
and free ($\left| {}^2J_{PH} \right|$ = 2.5 Hz) PMe_3, which exchange-broaden
and finally collapse, with increasing temperature, to one
doublet (the spacing of which shows that the above J's
are of opposite signs). Since the low temperature doub-
lets are first order, the line envelope was treated simply
as a pair of superimposed two-site problems according
to the method of McConnell (2). (This is confirmed by
a general density matrix treatment). The complexed BMe_3
signal was treated simultaneously as a further McConnell
two-site problem with equal populations, the $-60^\circ C$ doublet
($\left| {}^3J_{PH} \right|$ = 19.4 Hz) collapsing to a singlet at fast ex-
change. Slight additional broadening due to the quadrupolar
" B nuclei was accommodated by a T_2 term (3) applied to
81.2% of the complexed BMe_3 signal (^{10}B is taken to have
a negligible effect, having a larger quadrupole moment
and smaller coupling to methyl). The coalescence point
for each two-site exchange is different, giving three
per sample, doubled by use of spectra at 60 and 100 MHz.

Our iterative programme fits four parameters – (1)
chemical shift difference $\left| \nu_{complex} - \nu_{PMe_3} \right|$; (2) fre-
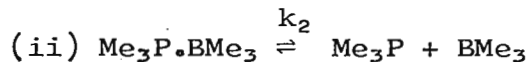quency alignment of the theoretical and calculated spectra,

– 2 –

to refer these to the same origin; (3) the T_2 mentioned above; (4) the mean lifetime of the complex τ_c. This is the only kinetic parameter needed, since the sample composition was known by condensing weighed amounts of the components directly into the N.M.R. tube. ($\tau_c [PMe_3] = \tau_{PMe_3}$ [complex] at equilibrium). Fairly accurate values

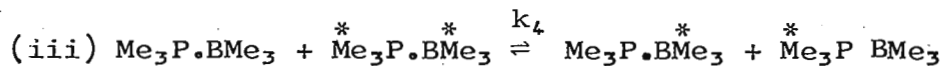of (1) were in fact known already from measurements on samples with 1:1 mole ratio and with no BMe_3.

Results on samples of varying composition, at the same temperature, were used to decide between possible rate-determining steps:

(i) $\overset{*}{PMe_3} + Me_3P.BMe_3 \overset{k_1}{\rightleftharpoons} Me_3P.\overset{*}{BMe_3} + PMe_3$

Rate $= k_1 [PMe_3][complex]$ $1/\tau_c = k_1 [PMe_3]$

(ii) $Me_3P.BMe_3 \overset{k_2}{\rightleftharpoons} Me_3P + BMe_3$

Rate $= k_2 [complex]$ $1/\tau_c = k_2$

(iii) $Me_3P.BMe_3 + \overset{*}{Me_3}P.\overset{*}{BMe_3} \overset{k_4}{\rightleftharpoons} Me_3P.\overset{*}{BMe_3} + \overset{*}{Me_3}P BMe_3$

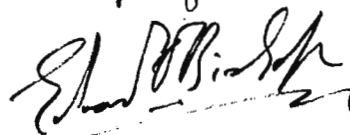Rate $= k_4 [Complex]^2$ $1/\tau_c = k_4 [complex]$

Some of the results are given below (for $-10^{\circ}C$), and clearly support the unimolecular mechanism (ii). This is also consistent with the Arrhenius activation energy of 14.0 kCals/mole (58.4 kJoules/mole), found by the temperature variation, which is similar to the gas phase dissociation energy of 16.47 kCals/mole [4].

Examples of both types (i) and (ii) mechanisms have been described in similar donor-acceptor systems [5]. In some cases there is evidence of different mechanisms with excess donor and with excess acceptor, and we are currently looking at the latter case (using BMe_3 spectrum) in this system, as well as varying the donor molecule.

Yours sincerely,

E.O. Bishop.

K.A. Alford

J.D. Smith.

[1] With Dr. J.D. Smith, Mrs. K. Alford and Dr. P.R. Carey.

[2] See e.g. Emsley, Feeney and Sutcliffe, " High Resolution N.M.R.", Vol.1, Ch.9, (1965).

[3] Cunliffe and Harris, Mol. Phys., 15, 413, (1968); Kintzinger and Lehn, ibid. 14, 133 (1968).

[4] H.C. Brown, J.C.S., 1248 (1956).

[5] J.P. Oliver and co-workers, Inorg. Chem., 4 1741; 7, 950, (1968); J.A.C.S., 89, 3970 (1967).

[complex]	[free PMe$_3$]	$\tau_c^{-1}(\sec^{-1})$
0.149	0.042	6.15
0.785	0.747	5.64
0.232	0.065	6.02
0.122	0.371	6.22
0.55	0.59	5.42
0.223	0.496	5.69
0.469	1.141	5.14
0.067	0.152	5.53
1.11	0.39	4.51
0.232	0.065	6.22

Data at -10°C. Concentrations are in molarities.

Dartmouth College HANOVER · NEW HAMPSHIRE · 03755

Department of Chemistry · TEL. (603) 646-2501

April 30, 1970

Dr. Bernard L. Shapiro
Department of Chemistry
Texas A&M University
College Station, Texas 77843
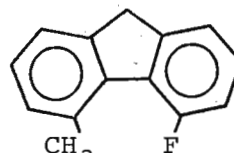
H-F Through Space Coupling

Dear Dr. Shapiro:

In a search for unambiguous examples of through-space spin-spin coupling, we have synthesized the first two members of a series of bridged biphenyls; namely, 1-fluoro-8-methyl-biphenylene (I) and 4-fluoro-5-methylfluorene (II). We now wish to disclose our results with these two compounds.
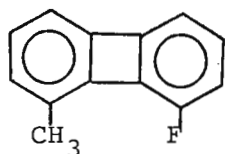
I.
$^6J_{HF} = 0$

II.
$|^6J_{HF}| = 8$ Hz

I shows a sharp singlet at 2.13 ppm ($CDCl_3$; 60 MHz) which is ascribed to the methyl group. On the other hand, II exhibits a <u>doublet</u> at 2.73 ppm similarly assigned to the methyl group but presumably split by the fluorine atom <u>six</u> bonds away $|^6J_{HF}| = 8$ Hz.

This apparently is the largest $^6J_{HF}$ yet observed. Because of the gross similarity between <u>I</u> and <u>II</u>, <u>except</u> for the methyl-fluorine internuclear distance (2.8 Å vs 1.4 Å) we believe that the splitting observed for II is best rationalized in terms of a through-space coupling mechanism.

Other members of the series where the methyl group is forced closer to the fluorine atom are in preparation.

Please credit this contribution to the account of P. R. Shafer.

Sincerely yours,

Gordon W. Gribble
Assistant Professor
of Chemistry

James R. Douglas

GWG/blw

UNIVERSITY OF CALIFORNIA, SANTA BARBARA

BERKELEY • DAVIS • IRVINE • LOS ANGELES • RIVERSIDE • SAN DIEGO • SAN FRANCISCO   SANTA BARBARA • SANTA CRUZ

DEPARTMENT OF CHEMISTRY
SANTA BARBARA, CALIFORNIA 93106

May 1, 1970

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

Nuclear Relaxation at the Active Site of α-Chymotrypsin

Dear Barry:

Recently we reported a study of the irreversible inhibition of the enzyme α-chymotrypsin by a series of trifluoromethyl substituted α-bromoacetanilides(I).[1]
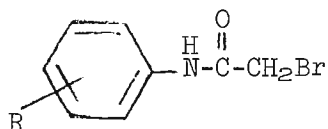
$$R = \underline{o}, \ \underline{m}, \ \underline{p}\text{-}CF_3$$

I

We have measured T_2 for these modified proteins using a Bruker 321S spectrometer operating at 56.4 MHz. and a Fabritek 1074 computer for enhancement of signal-to-noise ratio. Our results are collected below. For comparison, T_2 of the trifluoromethyl substituted inhibitors in acetone solution are also included.

The relaxation times for the inhibitors are not unusual and follow the same order with regard to substitution position, as that found in various halogen substituted benzotrifluorides.[2] The large decrease in T_2 of the enzymes is, of course, consistent with the molecular size of these materials. The results suggest that a CF_3 group at the <u>para</u> position of the inhibitor is considerably more restricted in its molecular motions than the same group at the <u>ortho</u> or <u>meta</u> positions. After pondering a scale model of the enzyme long enough, one can convince himself that a <u>p</u>-CF_3 group in the inhibitor can be buried deeply inside the active-site of the enzymes. Enforced interactions of this group with the protein could substantially decrease the molecular motions involved in nuclear relaxation and thereby decrease T_2. Trifluoromethyl groups at the <u>meta</u> and <u>ortho</u> positions appear to be more exposed to outside world where greater rotational freedom is possible.

T_2 for Trifluoromethyl Substituted Enzymes and Inhibitors

	T_2(sec.) at position		
	ortho	meta	para
Inhibitor	1.4	1.0	0.95
Modified α-chymotrypsin	0.04	0.016	0.006

2

Although clearly of a preliminary nature, our results suggest that n.m.r. may develop into a useful technique for probing the dynamics of the interactions between protein active sites and substrate-like molecules.

Sincerely yours,

E. W. Bittner

J. T. Gerig
Assistant Professor

1. E. W. Bittner and J. T. Gerig, J. Amer. Chem. Soc., 92, 2114 (1970).

2. A. S. Dubin and S. I. Chan, J. Chem. Phys., 46, 4533 (1967).

JTG:rt

University of New York at Buffalo

Density Matrix Treatment of Pseudocontact and Contact Shifts in Transsition Metal Complexes; Use of Fluke Synthesizer and PDP-8/I

Dear Barry:

I. Preprints of an article by Bruce McGarvey and myself on the calculation of contact and pseudocontact shifts are available to those interested in NMR studies of paramagnetic transition metal complexes. The paper (which is to appear in J. Mag. Reson.) gives an approximate density matrix method to deal with the following situations, to which formulae customarily used are not applicable[1]: 1. there is an appreciable contribution to the magnetic moment of the complex from unquenched orbital angular momentum; 2. there is appreciable orbital contribution to the paramagnetic shift from spin density at the ligand nucleus; 3. there is appreciable mixing of the ground electronic state and thermally populated excited states by the applied magnetic field.

II. We have modified our HA-60 system for field-frequency controlled heteronuclear operation. The system is patterned after the "MPC-60" system assembled by Davis and Wisnosky[2], with the following differences: 1. The frequency synthesizer used is a Fluke 633A; 2. The synthesizer is swept by the AX-08 "Laboratory Peripheral" of the Digital Equipment Co. "LAB-8" system (i.e. PDP-8/1 plus AX-08); 3. The HA-60 "Lock Box" (V-4354A) is used as the audio phase sensitive detector for the proton lock signal. We have used this system successfully for carbon-13 nmr studies of paramagnetic systems in which the concentration of carbon sites (i.e. unenriched) was a low as 1 M, and we could, without difficulty, go to lower concentrations.

I should add that the software available from DEC, as part of its noise averaging program, was not suitable for our system; we have been using a program developed by Dr. James Cooper, which is both convenient to use and versatile. I will be happy to give more details about the system to those interested. Any questions about the averaging program itself might better be addressed to Dr. Cooper at this address.

Sincerely,

Robert J. Kurland

1. a. H.M. McConnell and D.B. Chesnut, J. Chem. Phys. 28, 107 (1958).
   b. H.M. McConnell and R.E. Robertson, ibid. 27, 1361 (1958).
   c. J.P. Jesson, ibid 47, 579, 582 (1967).
2. D.G. Davis and D.E. Wisnosky, 9th ENC (1968).

Southern Research Institute

May 1, 1970

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

Title: Comment on a Paper on PMR Spectra of Nucleosides

Dear Barry:

Thank you for the reminder. As a payment on our subscription,
I would like to comment on a paper by Stevens and Fletcher[*] on the pmr
spectra of pentofuranose derivatives.

The paper has filled quite a need in extending and consolidating
information about the pmr spectra of isomeric furanose derivatives,
which have been so much less well understood than the derivatives of
six-membered ring sugars.

However, in the discussion of nucleosides their work was less
extensive, and it is to this portion that I would like to make an addition.
Their discussion was limited to the anomeric triacetates and tribenzoates
of the ribazoles (5, 6-dimethyl-1-ᴅ-ribofuranosylbenzimidazoles), about
which they state: "The signal for H-4 appears as a clearly defined
multiplet in the specta of the α-ribazole esters, whereas the signals for
H-4, H-5, and H-5' appear essentially as a single peak in the spectra of
the β-ribazole esters. The generality of these observations for anomeric
ribonucleosides has yet to be determined."

We have observed that this does indeed appear to be a general
phenomenon for 9-β-ᴅ-ribofuranosylpurines, as long as the OH groups
on the ribose moiety have been reacted to form either acetoxy or benzoyloxy
groups. However, in no case have we observed that H-4, H-5, and H-5'
appear approximately isochronous when the ribose retains its OH groups.

Similarly, when the sugar is 2'-deoxyribose, H-4, H-5, and H-5'
appear essentially as a broad single peak in the acetylated β-nucleosides,
but H-4 appears downfield and separate in the α-anomers. As with ribosides,

Prof. Bernard L. Shapiro
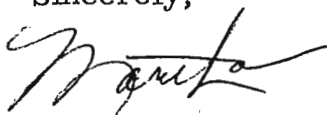May 1, 1970

Southern Research Institute

-2-

H-4 of both anomers appears separately when the OH's remain on the sugar.

This difference in appearance of the spectra, depending on whether the sugar OH's have been reacted or not, might be a solvent effect since customarily the blocked nucleosides are run in $CDCl_3$, while DMSO-d_6 is used for the corresponding unblocked compounds for reasons of solubility. However, in one case, we have the spectra of an acetylated β-nucleoside (sugar: 2'-deoxyribose) in both DMSO-d_6 and $CDCl_3$. H-4, H-5, and H-5' appear essentially isochronous in both solvents. Based on this one case, the difference does not appear to be a solvent effect.

It was good to see you again in Pittsburgh. Hope you both had a good trip back to Texas.

Sincerely,

Martha C. Thorpe, Research Chemist
Molecular Spectroscopy Section

MCT fh

*Stevens, J. D., and Fletcher, H. G., Jr., J. Org. Chem., **33** (5), 1799 (1968)

Author Index - TAMU NMR Newsletter No. 140

TAMU NMR Newsletter

Sponsors:

Abbott Laboratories
American Cyanamid Company
Bruker Scientific Inc.
W. R. Grace and Company
Japan Electron Optics Laboratory Co. Ltd.
The Lilly Research Laboratories, Eli Lilly and Company
Monsanto Company
Nuclear Magnetic Resonance Specialties, Inc.
Unilever Research (U.K.)
Union Carbide Corporation
Varian, Analytical Instrument Division

Contributors:

Badische Anilin- & Soda-Fabrik AG (Ludwigshafen, Germany)
The British Petroleum Company Limited (England)
The Dow Chemical Company
Eastman Kodak Company
Farbenfabriken Bayer AG (Germany)
Institut fur Physikalische Chemie der Techn. Hochschule Aachen (Germany)
International Business Machines Corporation
The Perkin-Elmer Corporation
The Procter & Gamble Company, Miami Valley Laboratories
Shell Development Company
University of Waterloo, Chemistry Department (Canada)