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These restrictions apply equally to both the actual Newsletter participant-recipients and to all others who are allowed access to the Newsletter issues. Strict adherence to this policy is considered essential to the successful continuation of the Newsletter as an informal medium of exchange of NMR information.
Deadline Dates: No. 147: 7 December 1970
No. 148: 4 January 1971

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

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

The survey of computer program usage which was initiated in the spring of 1969 has now been completed. Questionnaires were distributed to conferees at the recent Gordon Conference on Magnetic Resonance and to participants at the ENC meeting of 1969. Also, a questionnaire was published in the TAMUNMRN. This effort was supplemented by Dr. E. Lustig of the Food and Drug Administration who made available the responses to an earlier questionnaire. A collection of programs was also provided by Professor R. K. Harris.

A report has been prepared in which 44 programs are listed. The information has been updated by the authors of the individual programs in the summer of 1970. We conclude that at present the most satisfactory method of distributing these programs is through the Quantum Chemistry Program Exchange (Q.C.P.E.) at Indiana University. Many of these programs are presently listed by Q.C.P.E, and we have included the appropriate catalog numbers.

The report has now been forwarded to Dr. T. C. Farrar, Chairman of ASTM Sub-Committee E-13.7. Dr. Farrar plans to have copies of the report available for distribution. Requests should be sent to:

Dr. T. C. Farrar  
U. S. Department of Commerce  
National Bureau of Standards  
Washington, D. C. 20234

Sincerely yours,

C. S. Johnson, Jr.  
Chairman of the Task Group on Computer Applications of Sub-Committee E-13.7
Cher Professeur Shapiro,

Dans le cadre d'un travail sur le comportement en RMN des pyrazolines-2, nous avons été amenés à analyser le système AA'BB' des protons 4 et 5 de ces composés.

Il est apparu alors que le passage de 60 à 100 MHz, en diminuant le rapport $J/V_0$, conduit à la disparition de certaines transitions de faible intensité nécessaires à l'obtention de certains paramètres avec une précision correcte.

Ainsi, le spectre dans le deutérochloroforme à 100 MHz de la formyl-1 phényl-3 pyrazoline-2, I, ne présente (fig. 1a) aucune transition entre les deux demi-spectres. Analyssé comme AA'BB'X au moyen de LAOCN 3 (1), nous obtenons les paramètres du Tableau 1a. On constate que les deux constantes de couplage géminales sont données avec une grande imprécision.

Le même échantillon, à 60 MHz, donne un spectre (fig. 1b) présentant trois petites transitions dans la partie centrale, le doublet appartenant aux protons B car $J(AX) \approx 0$.

L'analyse conduit aux valeurs du Tableau 1b. Cette fois, toutes les constantes de couplage ont une précision comparable.

Fig. 1a

C_6H_5

CCl_3

100 MHz

Fig. 1b

60 MHz
<table>
<thead>
<tr>
<th>Tableau I</th>
<th>Tableau II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formyl-1 phényl-3 pyrazoline-2</td>
<td>Acétyl-1 phényl-3 pyrazoline-2</td>
</tr>
<tr>
<td>a) 100 MHz</td>
<td>b) 60 MHz</td>
</tr>
<tr>
<td>W (Hₐ)</td>
<td>318,902</td>
</tr>
<tr>
<td>W (Hₐ’)</td>
<td>393,921</td>
</tr>
<tr>
<td>W (Hₓ)</td>
<td>884,0</td>
</tr>
<tr>
<td>J (AA’)</td>
<td>-19,753</td>
</tr>
<tr>
<td>J (BB’)</td>
<td>-14,212</td>
</tr>
<tr>
<td>J (AB)</td>
<td>12,353</td>
</tr>
<tr>
<td>J (AB’)</td>
<td>7,725</td>
</tr>
<tr>
<td>J (BX)</td>
<td>1,153</td>
</tr>
<tr>
<td>RMS ERROR</td>
<td>0,070</td>
</tr>
</tbody>
</table>

* Erreur probable sur les paramètres donnée par LAOCN 3.
** Déplacements chimiques et constantes de couplage en Hertz (Réf. TMS).
*** Ces déplacements chimiques n'ont pas été introduits dans l'itération.

Dans le cas de l'acétyl-1 phényl-3 pyrazoline-2, II, nous avons effectué l'analyse uniquement à 60 MHz, en négligeant l'interaction des protons B avec le groupe méthyle [J(AX) = 0, J(BX) = 0,42 Hz mesuré sur le méthyle]. Ceci nous a conduit à ne pas utiliser que les transitions de la partie AA' et seulement quelques unes de la partie BB', uniquement pour calculer v(B). Le résultat obtenu est dans le Tableau II.

Veuillez croire, cher Professeur Shapiro, à l'assurance de nos sentiments les meilleurs.

J. ELGUERO  
A. FRUCHIER

PS. L'un d'entre nous (Alain Fruchier) souhaite aller la prochaine année scolaire (sept. 1971 - Jul. 1972) dans un laboratoire pour approfondir ses connaissances en RMN. Toute suggestion d'un laboratoire pouvant l'accueillir sera la bienvenue.
Milano, September 10th, 1970

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

NMR Spectra of \( \Delta^3 \) - and \( \Delta^4 \) -pyrrolin-2-one

Dear Professor Shapiro,

We have analysed the \( H \) spectra of \( \Delta^3 \) - and \( \Delta^4 \) -pyrrolin-2-one \( ^{1} \) (inseparable mixture of I and II 2:1), including sign determination of all coupling constants, made by tickling and triple resonance experiments.

\[
\text{I} \quad \begin{array}{c}
\text{N} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{N}
\end{array}
\]

\[
\text{II} \quad \begin{array}{c}
\text{N} \\
\text{H} \\
\text{O} \\
\text{H} \\
\text{N}
\end{array}
\]

The spin systems are of type \( A_2XYZ \) and the results are reported in fig. 1.

The interest in these compounds is in part due to the presence of the pyrrolic ring in many important natural substances, like vitamin B\(_{12}\), bile pigments, antibiotics. Moreover these small molecules show long-range couplings, which are important data for testing the predictions of the current theory \(^{2}\). As a matter of fact, there are still insufficient experimental data, particularly concerning the small cyclic systems, and only few examples of positive \( J_{\text{allyl}} \) in non aromatic molecules \(^{1,2,3}\).

Moreover these compounds are very apt to show the potential of sign determination for structural purpose, and are convincing examples that the relatively small long-range couplings should always be characterized by their signs, if one wants to use them for structural determinations.

In \( \Delta^4 \)-pyrrolin-2-one II, we have measured a positive allylic type coupling of +1.58 Hz, across the heteroatom, between the NH and the vinylic hydrogen (\( J_{XZ} \)), both lying on the same plane. This is in agreement with the theoretical formulation of a \( C \)-electron mechanism for a transoid allylic coupling in a...
planar \( \phi = \phi' = 180^\circ \) conformation\(^{(2)}\). The two interacting protons are indeed in a "W" arrangement.

\( 4J_{1,3} \) in pyrrole, involving proton on the nitrogen atom, is 2.45 (4) Hz, and the sign is reported\(^{(5)}\) to be positive. The larger value of \( 4J \) in pyrrole could be explained with the possibility of a "double" path of coupling, which lacks in \( \Delta 4 \)-pyrrolin-2-one.

The \( \sigma \)-electron mechanism for the 4-bond coupling \( J_{XX} \) in \( \Delta 4 \)-pyrrolin-2-one \( \Pi \), can be in some way supported by the same value found for \( J_{YZ} \) ( +1.50 Hz ) in \( \Delta 3 \)-pyrrolin-2-one \( \Pi \). \( J_{YZ} \) in \( I \) involves the same fragments as \( J_{XX} \) in \( \Pi \), with the same substituents and geometry; and the only difference is the lack of the double bond.

The other allylic transoid couplings are negative as expected by \( \phi = 120^\circ \).

The substitution of \( \text{NH} / \) group in molecule \( I \) with \( \text{C} \) (6) or \( \text{O} \) (7) does not affect the allylic coupling \( J_{AX} \).

\( \text{sincerely yours} \)

R. Mondelli

---

\(^{(1)}\) The chemical part will be published in Tetrahedron.

\(^{(2)}\) The full paper on NMR has been submitted to Organic Magnetic Resonance


acetone-d$_6$

$$J_{AY} = 1.75 \text{ Hz}$$
$$J_{AX} = 1.95$$
$$J_{XY} = 6.75$$
$$J_{XZ} = 4.01$$
$$J_{YX} = 4.93$$
$$J_{YZ} = 0.00$$
$$J_{ZX} = 1.58$$
$$J_{YX} = 1.98$$

**Fig. 1**
Ligand Exchange by NMR, a Double Rate Process.

We are currently setting up an NMR group at York, comprising interested chemistry & biology faculty, and would like to start a subscription to Newsletter with this opening communication.

Ligand exchange reactions of metal alkoxides are being examined by NMR, in particular the process of self-alcoholysis which lends itself to NMR because of its rate. Thus the exchange between tert-butyl alcohol and titanium tert-butoxide can be studied via line shape measurements of the alcohol group protons. The exchange can be expressed in an overall form as

\[ \text{M(OR)}_4 + \text{RO}^\cdot \text{H} = \text{M(OR)}_2(\text{OR}') + \text{ROH} \]

Line shapes are computer fitted, the programme designed for a Watfor compiler (FortranIV). As a short cut to initial fitting the programme searches out line widths at 1/4, 1/2, and 3/4 height, shift difference between maxima and max/min peak height ratios. Complete line shapes can be called for on a plot subroutine.

The choice of solvent is a particular problem. It must have and adequate temperature range, must not contain ligating groups to compete with the alcohol, and should have little or no specific solvent effect. Such solvents are saturated hydrocarbons which unfortunately have resonances in the same region as the tert-butyl group. A compromise is an aromatic ring with hydrocarbon substituents or propylene carbonate. It is interesting to note that metal alkoxides exhibit downfield shifts (relative to TMS) in aromatic solvents instead of the more usual upfield solvent shift. Allowance has to be made for the temperature variation of the shift by extrapolation from lower temperatures at which exchange effects are negligible.

The exchange is observed to be catalysed by both acid and base which can both be found as impurities in the system; acid coming from the
glass (washing with NaCl solution prior to distilled water seems to suppress this source); base being produced by partial hydrolysis of the alkoxide via trace amounts of water which are exceedingly difficult to remove. However, an unusual feature of the kinetics appears to be unfolding with reasonable consistency. The Arrhenius plot of rate against temperature shows two distinct portions, corresponding to two activation energies. The plots always show a low energy, low temperature portion of activation energy around 4kcal, and most show a high energy high temperature portion, activation energy around 18kcal, when appropriate temperatures can be reached. Owing to continuing difficulties with catalytic effects the order of reaction is not clear, except that the low energy route is probably at least bimolecular and the high energy route nearer unimolecular. This would fit the necessary change of activation entropy (given by the intercepts) which require a higher (negative) entropy for the low temperature process than for the high temperature one. We could thus be observing the change from an associative mechanism to a dissociative one. Arrhenius plots of this type are also observed in systems where tunnelling can occur, but are relatively rare for ligand exchange at metal atoms.

![Arrhenius Plot](image)

Yours sincerely,

C. E. Holloway
C. E. Holloway
R. Ward.
Bernard L. Shapiro  
Department of Chemistry  
Texas A & M University  
College Station, Texas 77843

16 October 1970

Dear Barry:

Now that there is at last a worthy competitor (Keithley 800 series) for the PAR lock in amplifiers, I am certain that many are already being applied in n.m.r. laboratories. One such application is on the Varian HR 220 (presently with Dan Urry at UAB, Birmingham) where we used the Keithley with success in locking the spectrometer and also during frequency sweep experiments.

One characteristic deficiency, however, is lack of variable DC amplification and very high output impedance. This means, of course, that the 10v full scale dynamic range of the detector cannot be fully utilized on the 1v Varian recorder, and that the signal is distorted by impedance mismatch. The DC amplifier integrator shown in the attached figure alleviates this problem and also allows integration of the n.m.r. signal.

Amplifiers shown are Zeltex 148 and 148C Chopper stabilized operational amplifiers and a Zeltex B-10 booster necessary for full range drive into the 75 ohm 50 db (1 db/step) precision attenuator.

Circuit operation is straightforward. The 148-B10 combination is unity gain inverting while the 148C is in a gain of -5 configuration. Therefore, the attenuator would be set at 34 db for full scale on the recorder with full scale out from the Keithley.

Sincerely,

Dennis E. Wisnosky

DEW/dlb

Enclosures
DC AMPLIFIER / INTEGRATOR

Pin number on board

Trim pots 20 turn precision
All resistors 1% 1/2 watt
5µf capacitor 5% polystyrene
D. E. Wisnosky 01970
Dear Barry:

Having received your warnings about my impending excommunication, I hasten to offer the following contribution:

**COMMENTS CONCERNING REPLACEMENT OF 304TL TUBES WITH TRANSISTORS**

The rising replacement cost of the set of 8 regulator tubes in the V 2100 magnet power supply has led us to a consideration of alternatives. Two methods have been reported in the Newsletter: Substitution of a single watercooled 3CW 5000 TL tube (v. Parmakovitch, TAMUNMR 128, 18) or construction of a transistorized regulator section (W.H. Stegemann, TAMUNMR 131, 1). We have chosen the second alternative and have copied Mr. Stegemann's design fairly closely.

The problem with any transistor replacement for the 304 TL's is the low breakdown voltage of transistors as compared with the voltage drop required across the regulator section. This voltage drop must be large enough to act as a buffer for line voltage variations and to eliminate the ripple voltage from the 3 phase push-pull rectifier section. We have found the 16 stages of Stegemann's circuit to be adequate as buffer for line voltage variations, but we observed rather large 60 Hz and 120 Hz ripple components (which must result from some unexplained asymmetry in our rectifier or 3-phase line) and we have added an input choke to the 4 μf capacitor ripple filter at the rectifier output. After construction of the transistorized regulator we first had high frequency oscillations.
in the current regulation feedback loop. These could be suppressed by shaping the frequency response at the reference resistors. The circuit then showed good regulation and stability and seemed entirely satisfactory.

It had been in operation for 8 months when a catastrophic breakdown of most of the 2N3055 power transistors occurred while the magnet was being operated at a 6% higher field for F$^{19}$ spectrometry. Other components (except power line fuses) appear to be undamaged, the galvanometer in the Superstabilizer was protected with Si diodes (R.W. King, TAMUNMR 118, 54). We suspect that the breakdown may have been triggered by a line voltage transient caused perhaps by nearby construction work. We are now rebuilding the regulator with Zener diodes from the collector of the 2N3055 power transistors to the base of the driver transistor (BC 140) in each stage, in order to limit the voltage across each stage to a safe value.

We have also replaced the 872A mercury rectifier tubes with high voltage diodes (W.B. Monitz, 10th ENC 1969), and the 8 volt mercury reference batteries with a small power supply and IC regulator. No difficulties have been encountered with these modifications.

With best regards,

Sincerely yours,

R. Kaiser, Professor

/cwp
To: Dr. B. L. Shapiro,  
Department of Chemistry,  
Texas A & M University,  
College Station,  
Texas 77843,  
U.S.A.

Low temperature non-equivalence in a doubly asymmetric hydroxylamine

Recent interest in the slow interconversion of enantiomeric hydroxylamines\(^1\)\(^2\)\(^3\) prompts us to report our results with a doubly asymmetric hydroxylamine, O, N-dimethyl-N-1-phenylhydroxylamine (I). At ambient in CDCl\(_3\), the 100MHz spectrum of I showed the expected C-Me doublet at \(\delta 1.40\) (J\(_{H-CH_3} = 7.0\) Hz), and N-Me and O-Me singlets at \(\delta 2.44\) and 3.43 p.p.m. respectively; the tertiary proton appeared as a quartet at 3.60 p.p.m.

At -40° C the C-Me protons appeared as a quartet centred at \(\delta 1.41\)  
(\(\delta_{Me_A} - \delta_{Me_B} = 13.5\) Hz), the N-Me protons as a doublet at 2.48 (\(\Delta\delta = 25\) Hz) and the O-Me protons as a doublet at 3.42 p.p.m. (\(\Delta\delta = 32\) Hz). The coalescence temperature for all three groups of non-equivalent protons was ca -5°C (ca. -20 at 60 MHz). We interpret these results as follows:

The doubly asymmetric hydroxylamine is a mixture of two diastereomeric ("dl") pairs (1 \(\sim\) 4).
1. 2.

N-inversion and C-N rot

1.

N-inversion and C-N rot

3.

4.

1 and 2 diastereomers; 3 and 4 diastereomers; 1 and 4 enantiomers; 2 and 3 enantiomers.

Inversion of configuration at nitrogen (and rotation about the C-N bond) converts a member of one diastereomeric pair into a member of the other pair, (e.g. 1 → 2). Thus at 24° inversion is so rapid that the separate methyl resonances assignable to the two diastereomers are not observed, but at -40° the diastereomeric pairs are well defined in the n.m.r. The above interpretation is oversimplified in that it takes no account of rotation about the O-N bond. Strictly, in order for the system to be totally degenerate three energy barriers must be surmounted, viz: N-inversion, rotation about the C-N bond and rotation about the
N-O bond. These three processes would convert 1 into the enantiomer of 3 and 3 (a diastereomer of 1) into the enantiomer of 1, i.e. lead to complete degeneracy and hence the simple n.m.r. The doubling of the N-Me and O-Me resonance signals reported for 1, was not observed with 0,N-dimethylbenzylhydroxylamine$^1$, O-methyl-N-isopropylbenzylhydroxylamine$^{2,3}$ or O-isopropyl-N-methylbenzylhydroxylamine$^{2,3}$. This suggests that the decreased rate of N- inversion is the principal factor involved in the appearance of separate diastereomer resonances at low temperatures, although the slowing down of rotation about the N-C and N-O bonds may help to accentuate the chemical shift difference between the signals.

The original integrated spectrum at -40° indicated that the diastereomeric pairs were present in approximately equal quantities. Recent experiments with a freshly prepared sample of 1 however, definitely showed unequal populations of the diastereomers (ratio 2 : 1) at -40° for all three diastereotopic methyl groups. Subsequent experiments on the same sample failed to confirm this result and gave spectra very similar to those obtained originally. This unexplained anomaly is currently under investigation and so far it appears that the effect is connected with the age of the sample.

We should like to thank Dr. D. Z. Denney (Rutgers University, New Brunswick, N.J.) and PCMU (Harwell) for the 100MHz spectra recorded on varian HA 100 spectrometers.

Basel, October 22, 1970

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

Dear Barry,

We have developed a computer program (SHAPE) for the iterative calculation of geometry and degree of orientation of a molecule from its direct couplings using a weighted-least-squares method.

The number of magnetic nuclei in the molecule should not exceed eight. The direct coupling is defined according to Saupe (Z. Naturforsch. 20A, 572 (1965)); a pseudo-dipolar part is not taken into account.

Descriptions of the program and listings are available upon request.

Sincerely yours,

P. Diehl  P.M. Henrichs  W. Niederberger

[Signature]

P. Diehl  P.M. Henrichs  W. Niederberger
Professor Bernard L. Shapiro,

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

Dear Dr. Shapiro,

School of Chemistry, University of Bradford, Bradford 7, Yorkshire, England.

21st September, 1970.

K.D.B. and B.J. have examined the p.m.r. spectra of over 40 9-substituted fluorenes in CDCl₃, acetone-d₆, and dimethylsulfoxide-d₆. In view of the correlations often encountered between chemical shifts and substituent electronegativities, we have taken the opportunity of combining the shifts, $\delta_a$, (and also the shifts, $\delta_{a,rel}$, relative to the parent) with those of other 9-fluorenes in the literature in an attempt to assess their dependence on polarizability, dipole moment, Hammett constants and related quantities.

While $\delta_{a,rel}$ tends to increase with mutually-consistent group electronegativity, $E$ [Wells, Prog. Phys. Org. Chem. 6, 111 (1968)] of the shifts for -CH₃, -CH₂OH, and -CH₂OCH₃ are smaller, and those for -OH and -F somewhat larger, than expected. Further, -Br and -Cl have much bigger shifts than for the average line, -F is on the line, and -OP₃ has a much smaller shift; anisotropy of $\beta$ appears to have a surprisingly small effect. Deviations from linearity are less if $\delta_a$ is plotted against group electronegativity, $E$, determined by p.m.r.; the mean gradient is 1.2 p.p.m./gp unit.

When $\delta_a$ in 9-K-fluorenes is plotted against $\delta_{CH_3}$ in CH₃R (and much the same is true for a graph against $\delta_{CH_3}$ in PhCH₂R), nearly all the points are below the line of unit gradient drawn through R=H, evidently substituents have less effect on H-$\delta_a$ shifts in fluorenes than in methane and toluene. Electronegativity apart, we detected no correlation between $\delta_a$ and any of the following: $Q$ [as used, for example, by W.S. Smith et al., J. Phys. Chem. 74, 812 (1970)]; Hammett constants $\sigma^+$, $\sigma^-$, and $\pi$ group dipole moment; and the substituent bulk (as given by cubes of radii).

Of the aromatic chemical shifts, $\delta_4$ tended to shift to higher fields with "polar" Hammett constant, $\sigma^+$, and $\delta_1$ to lower field with $-\Delta\pi$ and with substituent size. Otherwise, $\delta_1$ and $\delta_4$ appeared independent of $Q$ (see reference above to W. S. Smith, et al.), group $E$, dipole moment, and other Hammett constants.

The most divergent points in the graph of $\delta_4$ against $\sigma^+$ are for 9-fluorofluorene (6.0 ppm instead of 0.2, and 9-cyanofluorene (0.02 instead of 0.20 predicted from the $\sigma^+$-value). Calculations with models of fluorene and its 9-F, 9-Cl, and 9-Br derivatives suggested that, in order for electric-field effects to make a substantial contribution to H-4 shielding, constant B in the equation

$$\sigma_B = -3BP^2\delta,$$

(where $P$ is the C-R bond polarizability, $I$ is the ionisation potential of $R$, and $d$ is the distance between $R$ and the proton) would have to be of opposite sign and many times larger than proton shieldings require.

K.D.B. is now at School of Chemistry, University of Leeds, England, and B.J. is moving to Dept. of Chemistry, University of Durham, England.

Yours sincerely,

K. D. Bartle  B. J. Dale  D. W. Jones  R. S. Matthews
There has just appeared convincing evidence that the 9-substituent in 9,10-dihydroanthracenes is pseudo-axial [J. B. Stothers et al., J. Am. Chem. Soc., 92, 5912 (1970)]. Presumably steric interaction of the 9-substituent with the aromatic peri protons is sufficient to force the substituent out of the pseudo-equatorial position.

In view of these results, it would be of interest to ascertain the effect of one aromatic ring, i.e., whether the peri proton of one ring would be sufficient to force the substituent into the pseudo-axial position. We have already collected data that can answer this question -- we have investigated the nmr spectrum of 1,4-dihydro-1-naphthoic acid and have discovered that indeed the carboxylate group is pseudo-axial.

Using a Jeolco PS-100 nmr spectrometer and the Laocoon III program, the following parameters were obtained for 1,4-dihydro-1-naphthoic acid:

- Chemical shifts $H_1$-$H_5$ respectively: 5.45, 3.93, 3.75, 6.53, 6.37.
- Coupling constants $J_{AB}$: $J_{12}$ 4.59; $J_{13}$ 1.22; $J_{14}$ 3.93; $J_{15}$ 3.93; $J_{23}$ 9.62; $J_{24}$ 1.24; $J_{25}$ 2.97; $J_{34}$ 4.60; $J_{35}$ 2.44; $J_{45}$ 21.92.

The relative magnitudes of the vicinal [$J_{12}$, $J_{34}$, $J_{35}$] and allylic [$J_{13}$, $J_{24}$, $J_{25}$] coupling constants are convincing evidence [M. Karplus, J. Chem. Phys., 30, 11 (1959); M. Barfield, J. Chem. Phys., 41, 3875 (1964)] that $H_1$ is pseudo-equatorial, and that the carboxylate group is therefore pseudo-axial.

Sincerely,

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

ANALYSIS OF A 'DECEPTIVELY SIMPLE' ABX SPECTRUM USING SOLVENT PERTURBATIONS; DMSO BEWARE!

Dear Barry:

Thank you for commencing my subscription to the NMR newsletter. Our laboratory is primarily interested in applications of NMR to biological problems. We have a Varian XL-10015, equipped to study \(^1\text{H}, ^{13}\text{F}, ^{31}\text{P}, \) and \(^{13}\text{C}, \) in continuous wave and Fourier transform modes. We are particularly interested in making contact with people who have written NMR or ESR programmes for the Varian 8K 620i computer.

Recently George Neville, Barry Blackburn, Roxanne Deslauriers, and I have been studying the conformations of amphetamine drugs such as amphetamine HCl. We have been using the couplings between the methylene and methine hydrogens to monitor rotamer populations about the CH\(_2\)-CH bond. Usually the CH\(_3\) and CH hydrogens constitute a normal ABX or ABC system which can be handled conventionally using LAOCOON III. In the case of amphetamine HCl, however, the CH\(_2\) region of the spectrum consisted of only two lines - a 'deceptively simple' spectrum\(^1,2\), which defied a proper analysis. By studying the spectra in various mixtures of DMSO-D\(_6\) and D\(_2\)O, we were able to change the relative rotamer populations and obtain analyzeable spectra. Extrapolation of the coupling constants and chemical shifts from mixed solvents to pure D\(_2\)O looked as below. Spectral simulation
using the extrapolated parameters gave good agreement with the observed spectrum, and thus permitted analysis of the rotamer populations under the required solvent conditions.

Finally, a word of caution regarding the use of DMSO-D$_6$ as a solvent for phenolic compounds. In recent studies of dipeptides containing tyrosine we have several examples of extraneous peaks developing with time in the aromatic hydrogen region, presumably due to reaction of DMSO-D$_6$ with the hydroxyl group of tyrosine.

Yours sincerely,

Ian C.P. Smith

ICPS: pg


October 23, 1970.

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

Dear Professor Shaiiro,

Would you please publish the following announcement in the NMR Newsletters:

Announcement

The Fourth International Symposium on Magnetic Resonance (25th anniversary of nuclear magnetic resonance) will take place at the Weizmann Institute of Science, Rehovot and the Hebrew University, Jerusalem, Israel, on August 23 - 31, 1971.

Among the invited speakers are:

F. Bloch & E.N. Purcell
W.A. Anderson (Palo Alto)
E.R. Andrew (Nottingham)
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M. Cohn (Philadelphia)
P. Diehl (Basel)
S. Fujiwara (Tokyo)
R.M. Golding (Kensington)
H.S. Gutowsky (Urbana)
E.L. Hahn (Berkeley)
K. Hausser (Heidelberg)
G. Hertz (Karlsruhe)
Prospective participants should address inquiries to the organizing committee. Participants interested in presenting papers at the symposium are invited to do so. Brief summaries should be submitted prior to April 1st, 1971.

The 1971 symposium will emphasize basic nuclear magnetic resonance and its applications. However, contributions in electron spin resonance, quadrupole resonance, cyclotron resonance, ferromagnetic resonance and acoustic magnetic resonance are invited.

All correspondence should be addressed to:

Executive Committee,
The Fourth International Symposium on Magnetic Resonance,
The Weizmann Institute of Science,
Rehovot, Israel.

Thank you in advance for your cooperation.

Yours sincerely,

Daniel Fiat

Daniel Fiat.
November 8, 1970

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

Dear Dr. Shapiro:

AN INDIRECT NUCLEAR OVERHAUSER EFFECT VIA CHEMICAL EXCHANGE

An NMR investigation of 9-(2',4',6'-trimethylphenyl)xanthene, I, was recently completed in this laboratory. At ambient temperature (+3°C.) the NMR of I exhibits three resonances at 1.60, 2.27 and 2.53ppm due to the methyl substituents at positions 2', 4' and 6', respectively, and a singlet at 5.98ppm due to H₉; the aromatic protons are centered near 6.88ppm. As shown in I, steric interactions force the 9-aryl ring to be approximately perpendicular to the xanthyl moiety leading to a very different magnetic environment for the two ortho methyls. Upon raising the temperature the signals for these two methyl groups, Me-2' and Me-6', broaden and eventually coalesce at 95°C. The barrier to methyl magnetic equilibration was attributed to hindered rotation about the 9-aryl bond.

During the course of that study, nuclear Overhauser effect experiments were carried out to substantiate chemical shift arguments which assigned the low field Me-6' as being syn to H₉. These experiments were performed on a Varian HA-100 operating in frequency sweep mode using a thoroughly degassed CDCl₃ solution of I.
Irradiation of the Me-6' signal resulted in a 23.0% enhancement in the integral of $H_9$. Irradiation of the spatially more distant high field Me-2' resulted in a 14.5% polarization of $H_9$. This latter NOE can be attributed to a small but detectable chemical exchange between Me-2' and Me-6' which transfers the partially saturated Me-2' group at a rate fast compared to the methyl relaxation time. The Me-4' resonance provided a convenient standard and upon saturation yielded a -0.4% change in $H_9$.

Solution of the appropriate coupled equations under steady state conditions yields the following expression for the indirect N.O.E. effect ($H_9/H_9^0$) of Me-2':

$$\frac{H_9}{H_9^0} = 1 - \frac{\tau}{\rho} \frac{Me^{o}-6'}{H_9^0} \quad (S-1)$$

where $S = \frac{T_{1,6}}{T_{1,6}^0} = \frac{Me^{o}-6'}{Me^{o}-6'}$ with $\frac{1}{\tau_T} = \frac{1}{T_{1,6}} + \frac{1}{T_{\text{exchange}}}$

and $\sigma$ and $\rho$ represent the sum of various relaxation rates for which the dominant contribution is due to the interaction of $H_9$ and Me-6'. Upon irradiation of Me-2', the ratio, Me-6'/Me-6', was measured directly and found to be 0.259. Substitution of this value into equation 1 predicts a positive polarization of 17% for $H_9$ upon irradiation of Me-2', in reasonable agreement with the observed value.

Sincerely yours,

Don T. Dix
Research Chemist

S. V. McKinley
Research Chemist

HH, HF and FF Couplings in Fluoroethanes.

Dear Barry,

We have just finished an investigation on the solvent dependence of the N.M.R. spectrum of 1,2 difluoro and 1,1,2-trifluoro ethane and these results, with those of the 1,1,2,2-tetrafluoroethane (Mol. Phys. 19, 265 (1970)) give the \( J_{HH} \), \( J_{HF} \) and \( J_{FF} \) couplings of the discrete rotamers of all the simple fluoroethanes capable of exhibiting rotational isomerism.

However, a number of these couplings are averages over the two equivalent rotamers. We assume that the value of a given coupling in one rotamer is identical to the similarly oriented coupling in the other rotamer of the same compound. The couplings obtained in this way are shown in parentheses in the figures.

Some general trends may be noted.

Increasing fluorine substitution gives a progressive but very non-linear decrease in \( J_{HH} \) and \( J_{HF} \), which is much larger when the fluorine is introduced at the CH end of the CH.CF fragment.

In difluoroethane \( J_{HH} \) varies from 0 to 6.2 Hz, depending on the orientation of the F nuclei, but increasing fluorine substitution even out these effects to give \( J_{HH} \approx 1.5 \text{ to } 2.0 \text{ Hz} \).

\( J_{FF} \) is very dependent on fluorine substitution, varying from \(-30\) to \(-6 \text{ Hz} \) but in contrast \( J_{FF} \) shows no dependence at all and is relatively constant at \(-13 \text{ to } -5 \text{ Hz} \).

Yours sincerely,

Dr. R.J. Abraham.
FIGURE 5, $J_{HH}$ COUPLINGS (Hz) IN FLUOROETHANES
FIGURE 6, $3J_{HF}$ COUPLINGS IN FLUOROETHANES
\[ \text{FIGURE 7, } J_{HF} \text{ COUPLINGS IN FLUOROETHANES} \]
Dr. B. L. Shapiro
Dept. of Chemistry
Texas A and M University
College Station, Texas 77843

November 3, 1970

13 C Spectra of Ethyl Pyridines

Dear Barry:

I was interested in Ray Freeman's recent letter (TAMU Newsletter No. 143) in which he presented his pen-shaking Fourier Transform experiments with 2-ethyl pyridine. He assigned the C3 and C5 resonances on the basis of his 13C relaxation time measurements.

I have checked Ray's assignment by the old-fashioned (but reliable) method of selective proton decoupling. First, the CH2 decoupled spectrum of the 4 ring protons (Figure 1) at 100 MHz was analyzed by a standard iterative procedure to give the proton shifts (relative to internal HMDSX): HC5: 6.86 ppm; HC3: 6.94 ppm; HC4: 7.35 ppm; HC6: 8.11 ppm. The assignment of the proton resonance multiplets was readily made by comparison of the spectrum in Figure 1 with the ABX spectrum obtained (Figure 2) by irradiating HC6 in addition to the CH2 protons. 13C resonances at 22.65 MHz from C3 and C5 are shown in Figure 3 for four slightly different irradiating frequencies (reduced decoupling power) in the neighborhood of the proton resonances at 6.86 and 6.94 ppm. The calculated frequencies required to decouple the protons on C5 and C3 were -7912 and -7904 Hz (calculated from the measured value of -8529 Hz required to decouple the protons in HMDSX). It is clear that the resonance on the left shows maximum sharpness at -7899 Hz whereas the one on the right shows maximum sharpness at -7910, i.e., the assignment must be as shown in the figure. These resonances are not as sharp as usually found in such selective decoupling experiments because at the low decoupling power necessary here, C5 is only partially decoupled from the proton on C6 to give a doublet whereas C3 is only partially decoupled from this proton as well as from the protons in the ethyl group. This latter observation is also consistent with the assignment shown in Figure 3. This assignment is opposite to that made by Ray on the basis of his T1 measurements.
The $^{13}$C resonances in 3-ethyl and 4-ethyl pyridines have also been assigned by selective proton decoupling. The chemical shifts are given below.

<table>
<thead>
<tr>
<th></th>
<th>CH$_a$</th>
<th>CH$_b$</th>
<th>C2</th>
<th>C3</th>
<th>C4</th>
<th>C5</th>
<th>C6</th>
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<tr>
<td>HMDSX</td>
<td>2-0</td>
<td>150.2</td>
<td>123.9</td>
<td>135.8</td>
<td>123.9</td>
<td>150.2</td>
<td></td>
</tr>
<tr>
<td>Pyridine</td>
<td>--</td>
<td>--</td>
<td>150.2</td>
<td>123.9</td>
<td>135.8</td>
<td>123.9</td>
<td>150.2</td>
</tr>
<tr>
<td>2-Et Pyridine</td>
<td>13.8</td>
<td>30.6</td>
<td>158.5</td>
<td>122.1</td>
<td>136.2</td>
<td>121.0</td>
<td>149.5</td>
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<tr>
<td>3-Et Pyridine</td>
<td>15.5</td>
<td>26.4</td>
<td>149.9</td>
<td>139.6</td>
<td>135.5</td>
<td>123.8</td>
<td>147.6</td>
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<tr>
<td>4-Et Pyridine</td>
<td>14.3</td>
<td>28.2</td>
<td>150.0</td>
<td>123.3</td>
<td>152.5</td>
<td>123.3</td>
<td>150.0</td>
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Sincerely yours,

C. A. Reilly
FIG. 1  CH$_2$ Decoupled Spectrum of Protons on C3, C4, C5 of 2-Ethyl Pyridine
FIG. 2. CH₂ and HCC Decoupled Spectrum of P(AH) in C₃, C₄, and C₅.

792.8 Hz
727.6 Hz
696.8 Hz
680.3 Hz

1797
**SHELL DEVELOPMENT CO.**

**13C-NMR-**

**EMERYVILLE, CALIF.**

**22.63 MHz**

**SAMPLE**

2-Ethyl Pyridine

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<tr>
<th><strong>SOURCE</strong></th>
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<td><strong>INTERNAL STANDARD</strong></td>
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<td><strong>STABILIZATION</strong></td>
<td>C6F6 EXT CAP</td>
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**BRUKER HFX-90 SPECTROMETER**

| **SCAN WIDTH SETTING** | 20 Hz/cm |
| **SCAN TIME SETTING** | 500 sec |
| **SCAN RATE** | 2.4 Hz/sec |
| **SCAN TIME** | sec |
| **SCAN RANGE** | TO Hz |
| **NUMBER OF SCANS** | 1 |
| **RF UNITS:** | |
| $f_0$ | $-54$ db |
| $f_1$ | $-28$ db |
| $f_2$ | $-36$ db |
| **FREQUENCY OF $f_2$** | N.O.T.A.E. Hz |
| **DECOUPLING MODE:** | | |
| **SELECTIVE** | |
| **BB MOD** | |
| **OPERATOR** | CAR |
| **DATE** | 10/20/70 |

**REMARKS**

HMDSX at 4329 Hz

" Decouples at -8529 Hz"
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