Mailed: July 30, 1962

Monthly Ecumenical Letters from Laboratories Of N-M-R

No. 46

DEADLINE FOR NEXT ISSUE
August 27, 1962

VARIAN associates

Professor A. A. Bothner-By
Director of Research
Mellon Institute
4400 Fifth Avenue
Pittsburgh 13, Pennsylvania

Dear Dr. Bothner-By:

THE "TICKLING" EXPERIMENT

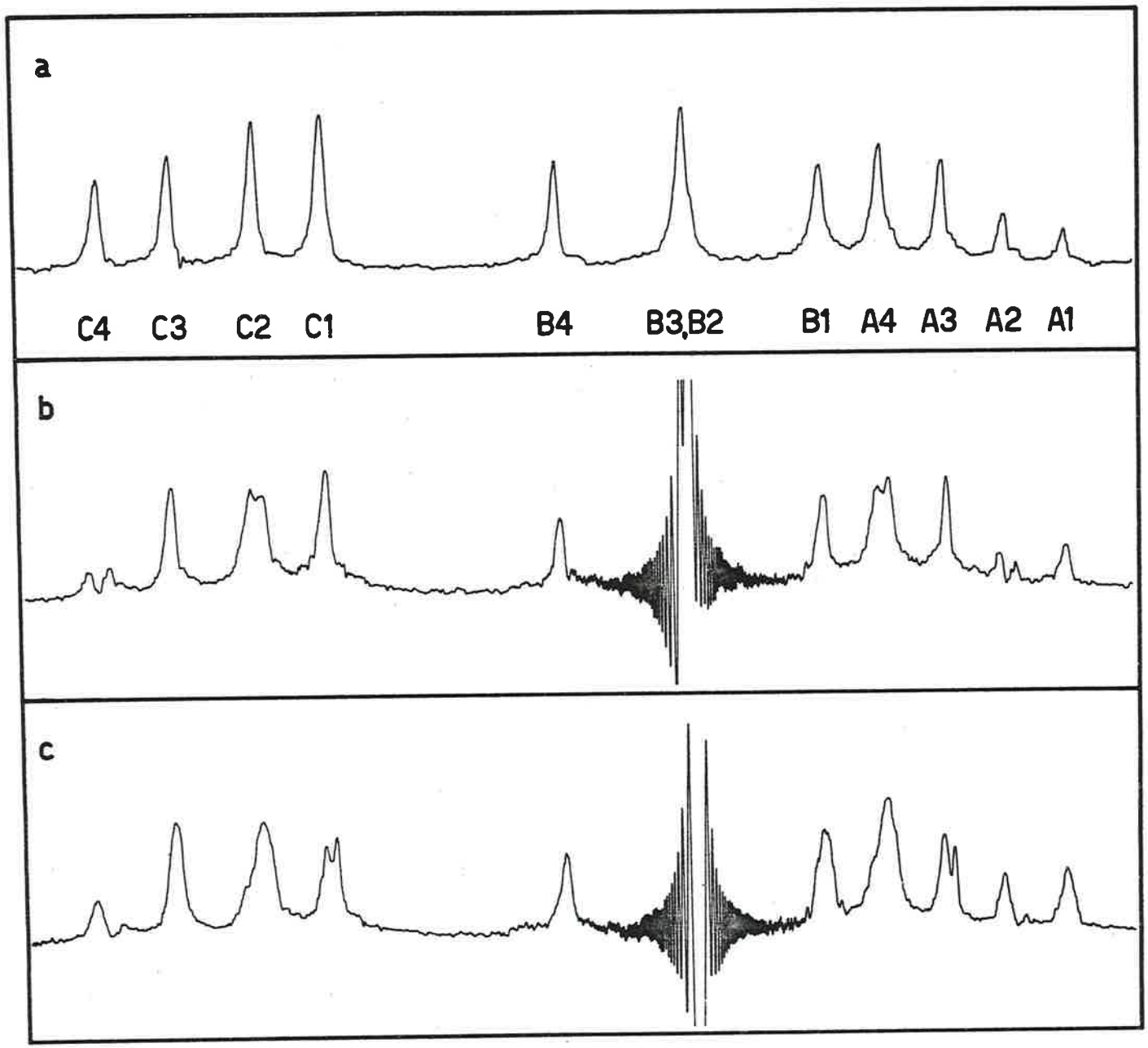
For some time now we have been investigating the use of very weak perturbing fields (H_2 at ω_2) in proton double resonance experiments. There appear to be several interesting applications of this technique, one of which is the refinement of the double irradiation method of finding relative signs of spin coupling constants, which was mentioned by Dr. Anet in the last issue of this Newsletter. Perhaps readers would be interested in a brief outline of one other by-product of this research.

Weak irradiation of just a single line in a high resolution spectrum causes a splitting of any other transitions that have an energy level in common with the perturbed transition. For instrumental reasons these doublets are sometimes broad and sometimes sharply resolved, and as might be expected the form of a sharp doublet is extremely sensitive to the setting of ω_2, since $\gamma H_2/2\pi$ is now of the order of the observed line width rather than of the order of a coupling constant. So much so, that the method may be used not only to detect the presence of two lines in an unresolved doublet but also to measure their separation. Furthermore in many cases an estimate of their relative intensities can be made, for the expression for the observed splitting contains the same matrix element that determines the intensity of the perturbed line.

Our example is that old favorite 2:3 dibromopropionic acid (see Newsletters 41 and 43), chosen because we know the energy level assignment and the relative signs of the spin couplings from previous work. Figure 1a shows that lines B3 and B2 are unresolved in this particular sample. Our theory predicts all the observed splittings, but in particular indicates that irradiation of B3 should give well-resolved doublets for A2 and C4 (Fig. 1b) while irradiation of B2 should give well-resolved doublets for A3 and C1 (Fig. 1c). (In these lower traces the investigating frequency sweeps through ω_2 giving a beat pattern in the region of lines B3 and B2.) The optimum settings of ω_2 differed by 0.4 cps. We believe that smaller separations could be measured in this way provided that ω_2 could be measured sufficiently accurately, for example by measuring 100 periods on a counter. The relative intensities are given by the square of the ratio of the splittings observed in Figs. 1b and 1c, obtained at constant H_2, and indicate that B3 is about seven times as strong as B2. It is already possible to measure the chemical shift of a hidden resonance line by the more brutal spin decoupling method, but this new technique should make it possible to plot out quite a complex spectrum normally hidden by overlying resonances.

Yours sincerely,
Ray Freeman Wes Anderson
R. Freeman and W. A. Anderson
Instrument Division

RF/WAA:iw



Ray Freeman and Wes Anderson, Figure 1

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE • BETHESDA 14, MD.

NATIONAL INSTITUTES OF HEALTH
Tel: 656-4000

May 25, 1962

Dr. Aksel A. Bothner-By
Mellon Institute
Pittsburgh 13, Pennsylvania

"NMR Determination of Magnetic Susceptibility"

Dear Dr. Bothner-By:

This note presents the results of a rapid method for determining magnetic susceptibility, for the purpose of making susceptibility correction to the measured NMR shift, when an external reference is used. A brief outline of the method has been described[1,2]; however, no detail and no estimate of the probable accuracy has been given.

(1) C. A. Reilly, H. M. McConnell and R. C. Meisenheimer, Phys. Rev., 98, 264A (1955).
(2) N. C. Li, L. Johnson, and J. N. Shoolery, J. Phys. Chem., 65, 1902 (1961).

In our NMR experiments with amino acids and peptides in D_2O, we use the Wilmad Glass Company coaxial precision bore glass tubes, with benzene in the annulus as external reference and the sample in the inner cylindrical space. Immediately after the NMR spectrum is taken, with the Varian A-60 spectrometer, we stop the spinning of the concentric cell and use the same assembly for making susceptibility measurements. The resonance from benzene in the annulus displays two maxima (see the NMR trace in Fig. 1, in which water is placed in the inner cylinder space) whose separation (n c.p.s.) is a linear function of the volume susceptibility of the liquid in the inner cell. This is because of the following equation[1]

$$n = 4\pi \nu_o \left((k_1 - k_2)\ (a/r)^2 + (k_2 - k_3)\ (b/r)^2\right) \qquad (1)$$

where ν_o is the fixed radiofrequency, in this case 60mc, a and b are the internal and external radii respectively of the inner glass tube, r is the mean radius of the annulus, k_1, k_2, and k_3 are the volume magnetic susceptibilities of (1) solution contained in the inner glass tube, (2) glass, and (3) the annular liquid, in our case benzene. The coaxial precision bore glass tubes that we use are apparently sufficiently uniform so that the values of a, b, and r are essentially constant. A linear plot of n vs. the known volume magnetic susceptibilities of four liquids is shown in Fig. 1. For our cells, the equation of the line is

$$k = \frac{n + 198.7}{414.5} \qquad (2)$$

The magnetic susceptibility of a sample is therefore calculated from the equation, after n is obtained.

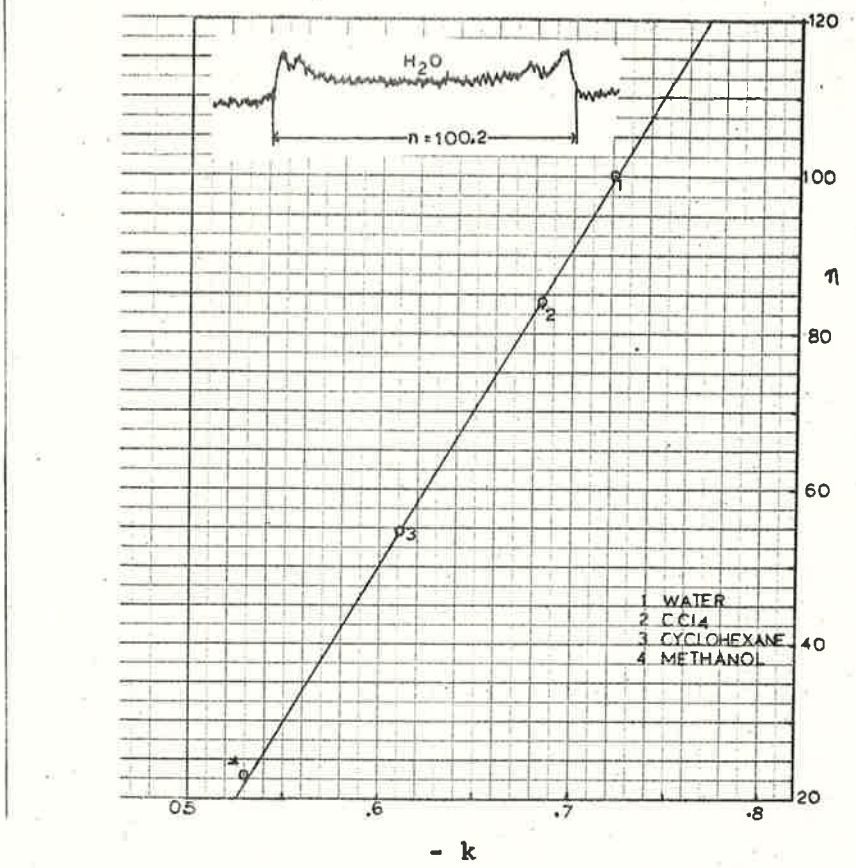


Figure 1. Plot of n c.p.s. vs. volume magnetic susceptibility, x 10^{-6} (cgs units)

We have found that at different settings of the concentric cell, different shapes and positions of the maxima may be obtained, and this is probably due to imperfections in the glass. However, if we make measurements in the same manner (in our case, we set n to be the distance in c.p.s. between two ends of the NMR trace at points which are 5 mm higher than the base line, see the insert in Fig. 1) the values of n become quite reproducible. The uncertainty in our volume susceptibility values is about 0.004 x 10^{-6} (cgs units).

When an external reference is used in NMR studies, the susceptibility correction is

$$\delta_{corr} = \delta_{obsd.} + 2\pi/3\ (k - k_{ref}) \qquad (3)$$

With an A-60 NMR spectrometer, therefore, an uncertainty of 0.004 in k produces an uncertainty of 0.5 c.p.s. in the chemical shift. The accuracy of our chemical shift is of the same order, so that the NMR determination of magnetic susceptibility is certainly adequate for the

purpose of measuring the extent of susceptibility corrections. The method possesses the advantage over the conventional Gouy method in that the former is much more rapid and no transferring of solution is necessary between the NMR and susceptibility measurements. Furthermore, the sample size necessary for the Gouy method is about ten times larger than for the NMR method.

Table I gives an example of the application of making susceptibility corrections to chemical shifts, using benzene as an external reference.

TABLE I

Proton Chemical Shifts due to the Presence of Metal Ions on Solutions Containing 0.4M N-acetylglycinate (AG^-), 0.1M N-acetylglycine in D_2O

$CdCl_2$,M	Volume susceptibility, $-k \times 10^6$	$-\nu_{CH_2}$ (values in parentheses corrected to k for AG^-)	$-\nu_{CH_3}$, c.p.s.
0.	0.716	163.0 (163.0)	266.0 (266.0)
0.20	.727	158.0 (159.4)	264.6 (266.0)
.40	.736	155.3 (157.8)	262.8 (265.3)
.60	.754	152.9 (157.7)	261.1 (265.9)
.80	.758	151.2 (156.5)	260.0 (265.3)
1.00	.766	149.1 (155.4)	257.8 (264.1)

In the cadmium complex of N-acetylglycinate, the coordination sites in the ligand are probably the nitrogen atom and the carboxylate anion. Since the CH_2 group is situated between the two coördination sites while the CH_3 group is at a distance away from the coördination sites, one might expect that the addition of $CdCl_2$ to N-acetylglycinate would be to shift the CH_2 proton frequency downfield, and leave the CH_3 proton frequency relatively unchanged. This prediction is borne out by the data of Table I. Without making the susceptibility corrections, however, the CH_3 frequency decreases from 266 to 257.8 c.p.s. in going from no metal to 1.0M Cd, and it is only after applying the corrections that the total change becomes 1.9 c.p.s. This small effect of the cadmium ion on the CH_3 frequency illustrates the

necessity of applying susceptibility corrections to chemical shifts and the adequacy of using the NMR method for determining magnetic susceptibilities.

Sincerely yours,

Robert L. Scruggs

Robert L. Scruggs
Research Assistant

Norman C. Li

Norman C. Li
Visiting Scientist, NIH
Professor of Chemistry,
Duquesne University

THE UNIVERSITY OF BIRMINGHAM

TELEPHONE: SELLY OAK 1301

Department of Chemistry,

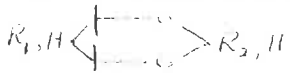
BIRMINGHAM, 15.

15th June, 1962.

Dr.A.A.Bothner-By,
Editor, Mellonmr,
Mellon Institute,
4400 Fifth Avenue,
Pittsburgh 13, Pa.,
U.S.A.

Dear Dr.Bothner-By,

We were interested in Dr. Muller's report (Mellonmr 43) on the coalescence of ring proton signals in cis-1-methyl-4-t-butyl cyclohexane which is presumably frozen in one conformation. In collaboration with Dr.A.B.Foster, whose team provided the compounds, Mr.Homer and I have examined related ring systems in order to assess the efficiency as 'anchors' of bulky groups other than t-butyl. All the compounds were 2,5 di-substituted 1,3-dioxans.



In one series briefly reported in Chem. and Ind. 1961, 106, R_2 = phenyl and R_1 ranged in size from hydroxy- up to benzoyloxy-. The trans isomers were, as expected, all 'frozen' with an analyzable spectrum arising from the axial and equatorial protons on C_4 and C_6. The cis isomers, however, all showed a single, fairly broad peak for the C_4, C_6 protons and a consistent shift to lower field of the sharp C_2 proton signal, which strongly suggest that inversion is taking place and that the phenyl group does not lock the ring irrespective of whether the other substituent is fairly small or equally bulky.

We have also looked at the series where R_1 = benzolyloxy- and R_2 = H, methyl, ethyl and iso-propyl. The trans isomers of the last three were again locked but their cis isomers and the first compound again appeared to be inverting. It would seem likely, therefore, that the benzoyloxy group is sufficiently long and flexible to allow this inversion to take place no matter what group is placed at R_2, provided that steric considerations permit the latter to occupy an axial position. We hope to examine the t-butyl analogues soon and expect a significant difference with the cis isomer in this case.

In continued appreciation of Mellonmr,

Yours sincerely,

L.F.Thomas

MELLON INSTITUTE
4400 FIFTH AVENUE
PITTSBURGH 13, PA.

STERIC EFFECTS ON C^{13} NUCLEAR MAGNETIC RESONANCE SPECTRA OF SUBSTITUTED BENZENES

Studies of steric effects on the C^{13} NMR spectra of various substituted benzenes are in progress in this laboratory, and papers on three series, methyl substituted iodobenzenes, anilines and N,N-dimethylanilines, and nitrobenzenes have been submitted for publication. The conclusions reached are outlined briefly below, and preprints, in limited supply, will be available soon.

Methyl-substituted iodobenzenes were studied in order to see what effect would be produced by introducing a methyl group ortho to a large substituent whose interactions with the ring could not be changed by rotation. Other substituents, such as -C≡N, $-CMe_3$, $-CCl_3$, etc., might have been included, but their necessary methyl derivatives were not available. The average methyl effects in six iodobenzenes, corrected for the normal methyl-substitution effects, are shown in Figure 9 below.

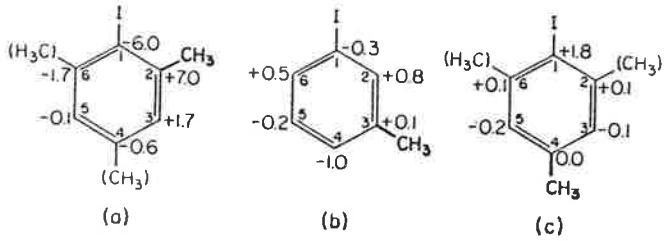


Figure 9. Corrected average methyl effects (in p.p.m.) on ring carbon shieldings in iodobenzenes. (a) ortho substitution, (b) meta substitution, (c) para substitution

The methyl symbols in parentheses indicates that a methyl group was present at that position in some of the compounds included in the average. It will be noticed that the additivity of methyl and iodo effects breaks down badly at the carbon bearing

the iodine when a methyl group is introduced ortho to it, as well as at the carbon acquiring the methyl group. Smaller effects are found ortho to the methyl group and iodine atom, and no effects outside the experimental uncertainty at the other two positions.

Methyl substitution effects in anilines are small and very similar to those in phenols, but ortho methyl substitution in N,N-dimethylanilines produces the large effects expected from the known steric inhibition of conjugation in such compounds. Figure 20 summarizes the effects in eight sets

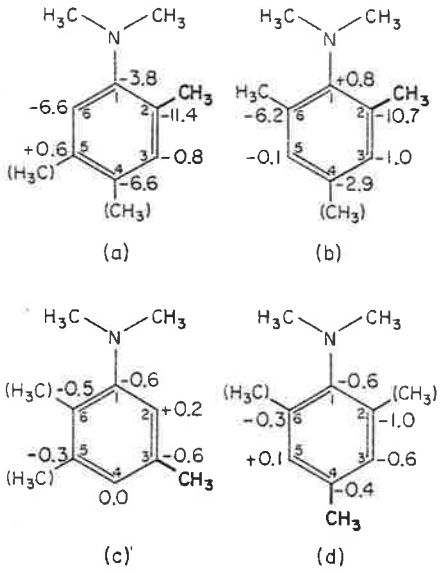


Figure 20. Average methyl effects (in p.p.m.) on ring carbon shieldings in N,N-dimethylanilines minus the corresponding effects in anilines. (a) ortho substitution, (b) ortho substitution with one ortho methyl group already present, (c) meta substitution, (d) para substitution

of compounds, and Figure 22 shows a comparison with other measures of the inhibition.

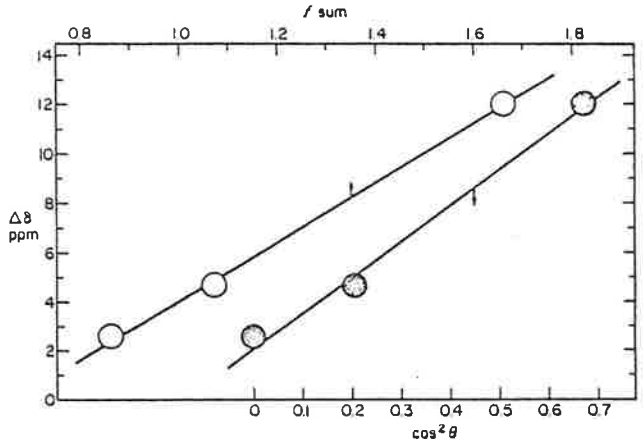


Figure 22. Para carbon shieldings (relative to benzene) vs. $\overline{\cos^2\theta}$ values and f sums for N,N-dimethylaniline N,N-dimethyl-o-toluidine and N,N,2,6-tetramethylaniline

Very similar results have been obtained for nitrobenzenes, except, of course, that the inhibition of conjugation increases the electron density, and hence the shielding, at the para position. The methyl effects are summarized in Figure 12 and some correlations displayed in Figure 14.

Steric effects on the conjugation of other groups, such as acetyl and methoxy, with aromatic rings are also being studied. It is likely that the C^{13} spectra can provide information on such interactions in other classes of compounds, including some to which other methods cannot be easily applied.

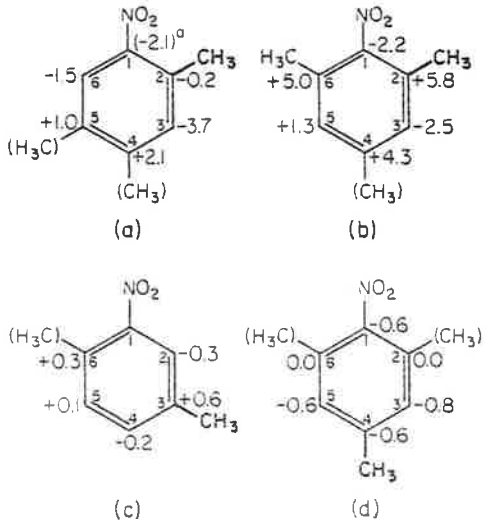


Figure 12. Average methyl effects (in p.p.m.) on ring carbon shieldings in nitrobenzenes minus the corresponding normal average effects given in Table IV. (a) ortho substitution, (b) ortho substitution with one ortho methyl group already present, (c) meta substitution, (d) para substitution

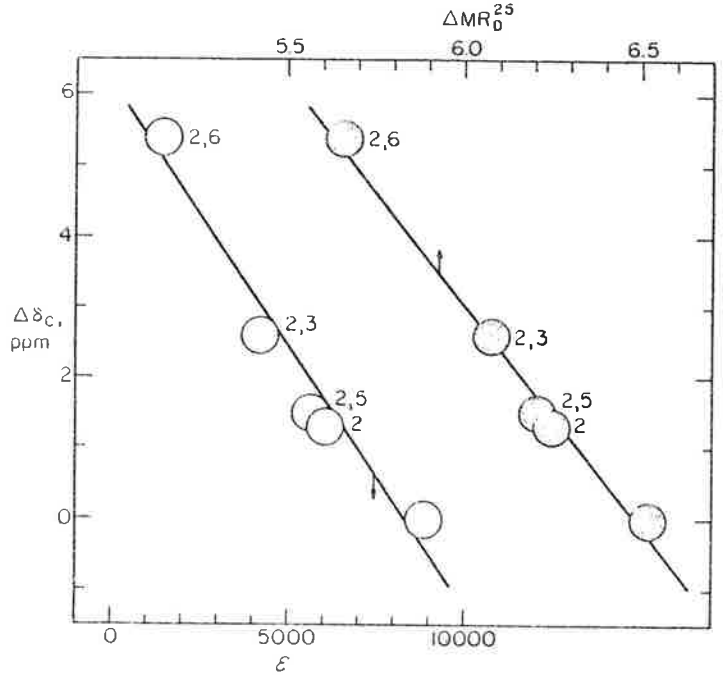


Figure 14. Para carbon shieldings (relative to nitrobenzene) vs. molar refraction differences (ΔMR_D^{25}) and extinction coefficients of the band near 250 mμ (ε)

Although the para effects are easily interpreted as outlined above, those at other positions are usually puzzling. It is by no means certain that the π-charge effects, which appear to dominate para to a substituent, are the most important factors at ortho positions, and I have been unable to reduce any other ideas to even semi-quantitative form. Any suggestions?

Paul C. Lauterbur

Duke University
DURHAM
NORTH CAROLINA

DEPARTMENT OF CHEMISTRY

June 25, 1962

Dr. A.A.Bothner-By
Mellon Institute
144 West Fifth Avenue
Pittsburg 13, Pennsylvania

Dear Dr. Bothner-By:

At an early date we found, as no doubt others have, that the pens on the Varian G-10 recorder are very fragile items. Rather than obtain new pen-reservoir assemblies from Varian, however, it has proved quicker and less expensive to replace the Leroy lettering pen in the Varian reservior using a few simple tools.

The tools we use consist of three drivers and a brass block having three holes drilled in it to accomodate the pen-reservoir assembly either upside down or right side up. These are sketched below. Drivers #1 and #2 are used to drive the old pen out. Driver #3 fits the inside of the new pen and is used to drive it in place. The new pen is drilled a little above the middle on its barrel with a #54 drill. The hole in the pen is lined up with the supply hole in the reservior by eye and the pen is driven in far enough to line up these two holes. This position can be detected by blowing through the reservoir or by measuring the distance the pen has been driven.

We hope that this might be of use to some of your readers.

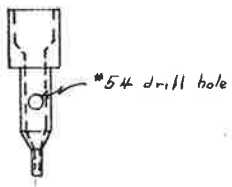
Sincerely yours,

John E. Baxter

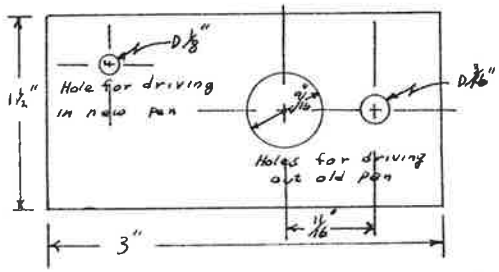
John E. Baxter

Duke University
DURHAM
NORTH CAROLINA

DEPARTMENT OF CHEMISTRY

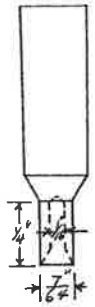


#3233-00
Leroy Lettering Pen

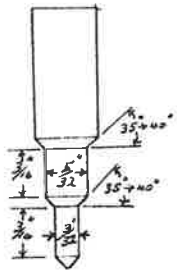


Brass Driving Block (¾" Thick)

Driver #1



Driver #2



Driver #3

NATIONAL RESEARCH COUNCIL
CANADA

DIVISION OF APPLIED CHEMISTRY

CABLE ADDRESS "RESEARCH"

IN YOUR REPLY PLEASE QUOTE

FILE No.

OTTAWA 2.

June 26th, 1962.

Dr. A. A. Bothner-By,
Mellon Institute,
4400 Fifth Avenue,
Pittsburgh 13, Penn.,
U. S. A.

Dear Dr. Bothner-By,

This letter will primarily be a collection of negative results. Perhaps it is permissible to include this category in contributions for MELLONMR. The unifying theme, if any, is the absence of hindered rotation in situations where one might hope to observe it. Enclosed are spectra of o-nitroaniline and N,N-dideutero-o-nitroaniline. It is apparent that the resonance absorption of the hydrogens bonded to nitrogen lies under that for protons A, B and C. This peak is also unusually broad. Since the spectra were obtained in a dilute acetone solution at room temperature it is unlikely that broadening is due to intermolecular hydrogen exchange. Perhaps the two protons are non-equivalent due to hindered rotation about the C-N bond caused by hydrogen bonding of one of them to the nitro group. This would give rise to an AB spectrum whose lines might be broadened by partial motional averaging or quadrupolar broadening of the N-H spin coupling. Solubility considerations severely limit low temperature work but perhaps one of your readers who is set up for N^{14}-H double resonance might be interested in this system. The chemical shifts, in ppm to low field of acetone, and spin couplings are listed below. They were obtained by a second order perturbation treatment. Since these chemical shifts are rather solvent dependant τ values seem inappropriate.

δ_A	= 4.90	J_{AB}	= 8.5	J_{AC}	= 1.6
δ_B	= 5.23	J_{BC}	= 8.0	J_{BX}	= 1.3
δ_C	= 4.48	J_{CX}	= 8.6	J_{AX}	= 0
δ_X	= 5.91				

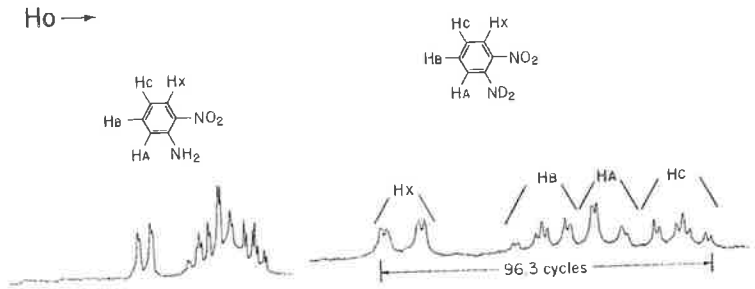
It was hoped that hindered rotation about the carbon nitrogen bond might be observed in ortho substituted dimethylanilines. However, down to 173°K no change was detected in the peaks due to the N-methyl protons in ortho methyl, bromo or nitro substituted N,N-dimethylanilines. Non-equivalent N-methyl groups in o-methyl-N-trimethylanilinium iodide have recently been reported. (Chem. and Ind. 818, 1962). However a single peak is observed by us for the N-trimethyl group of the o-methyl and o-bromo substituted compounds. Since the original report involved half times of at least a few hours something is unusual. Either the chemical shifts of the supposedly non-equivalent methyls are identical, which seems unlikely, or else there must be some other explanation for the radiochemical results.

Switching to carbon-carbon bonds, it has been reported that there is hindered rotation in $CH_3OCH_2CH_2HgI$, from an examination of its infra-red spectrum. However the proton resonance spectrum of this compound and many similar ones which we have studied would be hard to explain unless there is free rotation about the central carbon-carbon bond. Another example when infra-red evidence is interpreted as evidence of hindered rotation is CF_3CHO, with a reported energy barrier of 9.8 k. cal/mole. However down to 162°K there is no N.M.R. evidence of hindered rotation. The fluorine spectrum is a doublet and the proton spectrum a quartet with a fluorine-proton coupling constant of 2.8 cycles/sec. This is essentially the same as the proton-proton spin coupling constant in acetaldehyde.

Yours truly,

S. Brownstein.

SB:GG



EL PASO NATURAL GAS PRODUCTS COMPANY
POST OFFICE BOX 1161, EL PASO, TEXAS

June 27, 1962

Dr. Barry Shapiro
Mellon Institute
Pittsburgh, Pennsylvania

Dear Dr. Shapiro:

I would like very much to be placed on the mailing list for Mellonmr and, if possible, receive any back issues which may be available. I understand that to receive this news letter it is necessary to contribute an item about nuclear magnetic resonance at least once every six months. My initial contribution is as follows.

Recently I purchased an A60 instrument and, following Varian's suggestion, bought a Buffalow air-to-water heat exchanger. This heat exchanger is a closed system which recirculates distilled water from the A60 magnet to air-cooled coils and back to the magnet. The cooling system can deliver distilled water to the magnet which is approximately 5° F. higher than air temperature. Our air conditioning system gives laboratory air in the 73-74° F. range. However, when the heat exchanger was installed in the same room as the A60, the heat given off by the heat exchanger ran the air temperature to around 85° F. Eventually, the water became too hot and shut off the A60. We found it necessary to cut a hole in the wall and pump cold air through a duct to the heat exchanger outside. The system seems to work satisfactorily, and we have had no difficulty during the last week in which the temperature has been at least 100° F. outside.

The other problem which we had with the Buffalow heat exchanger was that either the fan was running backwards or the water in the coils was circulating in the wrong direction. We decided to reverse the water flow, and the instrument worked much better after this. Buffalow was informed of this, and I hope that this will not happen to other purchasers of this device. Even though I have had a lot of trouble with this system, I still feel that it offers a fairly simple method of providing distilled water for cooling the A60.

Very truly yours,

M. C. Harvey, Ph.D.
Senior Research Chemist

MCH.m

DEPARTMENT OF CHEMISTRY

EDMONTON, ALBERTA
CANADA

July 11, 1962.

Dr. A.A. Bothner-By,
Mellon Institute,
PITTSBURGH, Pa.,
U.S.A.

Dear Dr. Bothner-By:

In our laboratory, we have been interested recently in NMR measurements on hydrogen bonding and on proton exchange.

We have noticed that there is a good correlation between the hydrogen bond shift of $CHCl_3$ or $CHBr_3$ in an ether as solvent, relative to the $CHCl_3$ or $CHBr_3$ signal in C_6H_{12}, and the pK of the ether. When plotted, the $CHCl_3$ results and the $CHBr_3$ results form parallel lines. There also appears to be a linear relationship between the $CHCl_3$ NMR hydrogen bond shift in monobasic ethers and the corresponding $CDCl_3$ IR band intensity in dilute solution.

In our exchange work, we have set up some equations to describe the exchange broadening of spin-spin triplets, using McConnell's method. We use the equations for the case of the partially collapsed triplet in which the three peaks are still observable. From a measurement of T_2 and the peak separation, the exchange time τ is evaluated graphically. We find, for example, that in ethanol-water mixtures, the rate constant for the reaction $EtOH^* + HOH \rightarrow EtOH + HOH^*$ is approximately 3 l mole^{-1} sec^{-1} at 40°C. We are currently examining other alcohol systems in order to evaluate other similar rate constants.

The spectra of some p-substituted phenols have also been examined, and a qualitative correlation exists between the intramolecular ring shift and (a) Hammett's substituent constants, or (b) the calculated contribution to the shift from the substituent electric field effect of Buckingham.

Yours sincerely,

W.G. Paterson.

WGP:at

46-12

EMORY UNIVERSITY
ATLANTA 22, GEORGIA

June 28, 1962

DEPARTMENT OF CHEMISTRY

Dr. A. A. Bothner-by
Mellon-M-R
Mellon Institute
4400 Fifth Avenue
Pittsburg 13, Pennsylvania

Dear Aksel:

We have recently analyzed the spectrum of acridine:

The observed and calculated spectra are shown on page 2. The former was taken at 60 Mc/sec. in a 10.2% solution in $DCCl_3$ against an internal TMS reference. The calculated spectrum was obtained by first treating each ring independently as an ABCD system after which the small effects produced by H_9 were included as a first-order perturbation. The splitting diagram shown on page 2 represents strictly the results of the ABCD calculation upon which was superposed the H_9 splittings by first-order treatment. The agreement obtained was < 0.05 cps in all cases.

The parameters obtained by this treatment are tabulated below:

ν_1	-408.3 cps	J_{12}	8.4 cps	J_{34}	9.0
ν_2	-443.5 cps	J_{13}	1.4 cps	J_{19}	0.4
ν_3	-400.5 cps	J_{14}	0.6 cps	J_{29}	0.0
ν_4	-492.7 cps	J_{23}	6.6 cps	J_{39}	0.0
ν_9	-511.6 cps	J_{24}	1.2 cps	J_{49}	0.9

An interesting feature of this spectrum is the coupling of H_9 with only H_1 and H_4 of ring A (or H_5 and H_8) of ring C. Only the ortho and meta coupling constants within rings A and C are similar to those in naphthalene.[1] The very low chemical shift of H_9 is in accord with the high degree of reactivity at this position.

Further work on this problem presently in progress includes computation of magnetic anisotropy effects due to ring currents, dilution studies, and substituent effects.

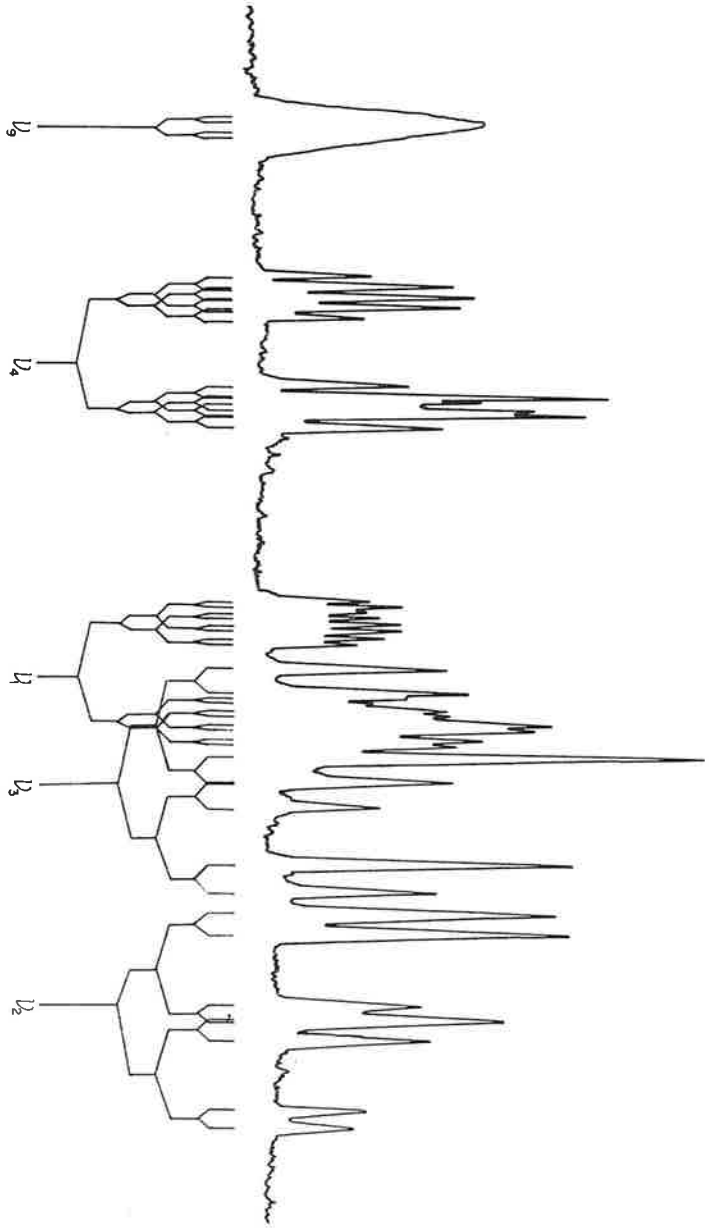
Sincerely yours,

J. H. Goldstein

J. P. Kokko

J. P. Kokko

1. Pople, J. A., Schneider, W. G., & Bernstein, H. J., Can. J. Chem., 35, 1060 (1957).



IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY
(UNIVERSITY OF LONDON)

DEPARTMENT OF CHEMISTRY

ROYAL COLLEGE OF SCIENCE
IMPERIAL INSTITUTE ROAD,
LONDON - - S.W.7
Telephone: KENSINGTON 5111

29th June, 1962.

Dear Dr. Bothner-By,

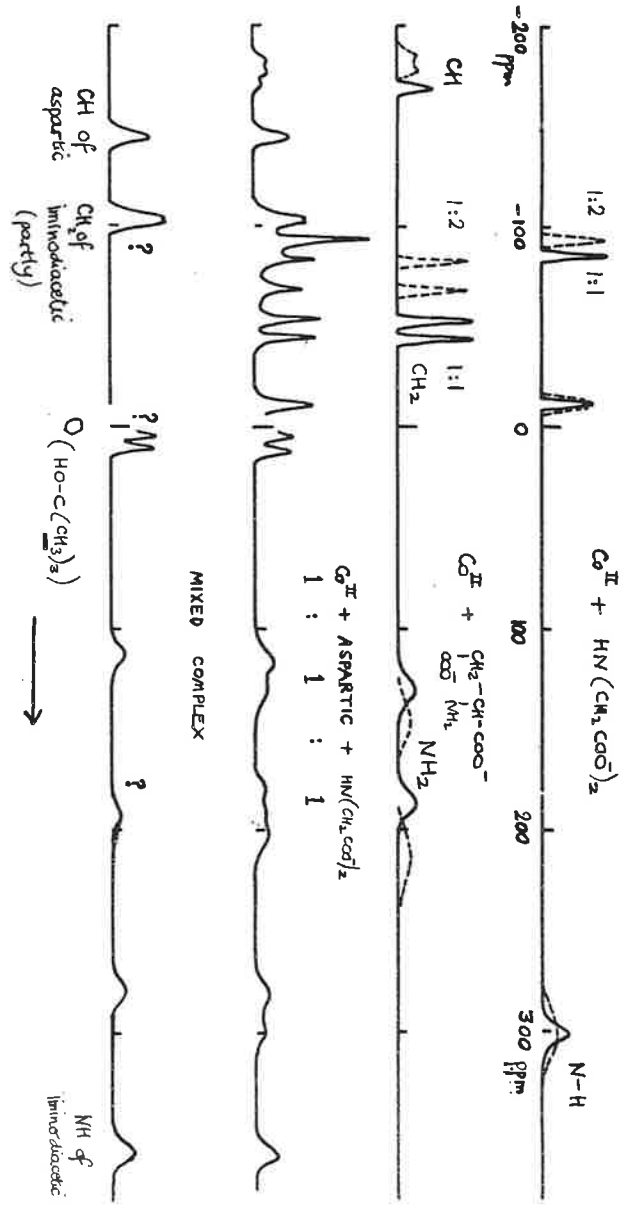
One of the things we have noticed with cobalt^{II} complexes is that the proton resonance spectra of solutions containing two sorts of ligand sometimes show lines which are not present in the solutions with either ligand separately. The new lines presumably come from mixed ligand complexes; in the example shown this would be $[Co^{II}(\text{iminodiacetic acid})(\text{aspartic acid})]^{=}$. A rough idea of the spectrum of the mixed complex can be got by subtracting from the observed spectrum the lines which represent the "unmixed" complexes which are also present, although it is difficult to be certain that some lines are not hidden. However, at least some of the protons in the mixed complex are shifted considerably, possibly because steric interactions between the ligands make them take up conformations which differ from those they have in the unmixed ones. The shifts in aliphatic ligands do seem to depend partly on the bond angles and distances, as the spin-spin coupling and (in free radicals) the electron-nuclear spin coupling are found to do. Smaller changes are found with bidentate ligands, especially in the complexes with only two ligands on the metal, presumably because they can keep out of each other's way in a trans arrangement.

Yours sincerely,

L. Pratt

L. Pratt.

Dr. A. A. Bothner-By,
Mellon Institute,
4400 Fifth Avenue,
Pittsburgh 13, Pa.



INFLUENCE OF SAMPLE GEOMETRY ON N M R PEAK HEIGHT

Neal L. McNiven and Thomas A. Wittstruck

The Worcester Foundation for Experimental Biology

Shrewsbury, Massachusetts

In running the N M R spectra of compounds isolated from biological sources it is often necessary to use minimum amounts of sample. For example in our work at The Worcester Foundation we are frequently requested to obtain spectra on 1 to 2 milligrams of steroids.

Other workers have reported methods of running small samples. For example workers at Varian Corp. in Mello N. M. R. (No 42) report the use of inserts to produce a spherical sample compartment in a standard N M R sample tube. Primas, (Mello N M R No. 33 and 44) by certain circuit modifications of a 25 Mc spectrometer has reported that N M R spectra can be produced using 85 micrograms of a steroid. The 60 Mc spectrometer apparently cannot be modified as described.

While we have not achieved spectra on samples as small as 85 micrograms we believe we have come up with a relatively simple method for running small samples using a Varian 60 Mc spectrometer without circuit modifications.

Fig. 1. shows a sketch of the sample tube used.

The cell is a precision bore Pyrex tube which will fit inside the probe insert. To prevent a vortex from forming in the spinning sample a close fitting inner Pyrex tube is pushed down into the sample tube until its flat bottom just touches the sample solution. The inner tube is held in position by a rubber sleeve at the top as shown.

Since the tube was set at different vertical positions in the probe insert it was necessary to center it to prevent it from wobbling during spinning. This was done by pushing on a 1 cm. length of Teflon tubing tightly over each tube. This Teflon bearing was placed approximately 3 cm. from the botton of the tube. Its wall thickness was chosen so that the bearing allowed the tube assembly to spin freely in the probe insert. The 4.5 mm. I. D. tube fitted the probe insert so closely that no bearing was necessary to prevent it from wobbling.

The experiments described below were done using the above sample assembly with the following N M R equipment:

Varian H R model V4300 Spectrometer operated at 60 Mc.

The water temperature in the magnet was kept constant to 0.2° C and the room temperature was maintained at 25° C $\pm$ 0.5° C. The sample tubes were spun at 1800 rpm as determined by stroboscopic methods. A constant spinning rate was achieved by the use of a Moore flow controller on the air supply. A Varian Field homogeneity Control unit, Model V-4365 was used.

Spectra were obtained on a Sargent M R recorder set at 50 mV full scale and 4 in./min. chart speed. Scanning speed was about 4 cps/sec. For each series only the Field Homogeneity Control was adjusted to obtain the maximum peak height.

Studies with Chloroform

The proton peak given by fixed amounts of chloroform in carbon tetrachloride solution was measured.

It was first shown that maximum peak heights were obtained when the sample was equally distributed above and below the center of the receiver coil. That is when a = b in the diagram (Fig. 1).

With this geometric arrangement the effect of different solution volumes and tube diameters was studied. Figure 2 shows the results obtained. The following conclusions can be drawn from these experiments:

(a) The optimum sample tube inner diameter is 4.0 mm.

(b) The optimum sample height is 20 mm. For the 4.0 mm. i.d. tube this corresponds to 0.25 ml.

Smaller quantities of chloroform were studied using the above optimum conditions. It was found that a 0.75 mg. sample of chloroform produced a peak with a signal to noise ratio of 10/1. This corresponds to a proton weight of 6 micrograms.

Studies with Steroids.

A similar study was made on 4.0 mg. of cortisone acetate. It was found that the optimum sample height again lies at 20 mm. and somewhat higher peaks are obtained with the 4 mm. I. D. tube.

This method of optimum sample geometry has been in routine use in this laboratory for over a year. Using it we can obtain good spectra routinely with 2 to 3 mg. of steroids. When necessary we have been able to obtain spectra on steroid samples as low as 0.5 mg. as shown in Fig. 3. It is seen that the C-4 proton is just detectable with this sample size.

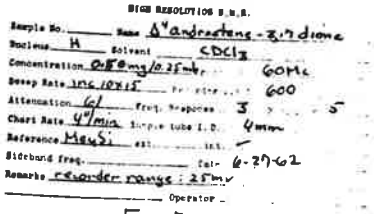


Fig. 3

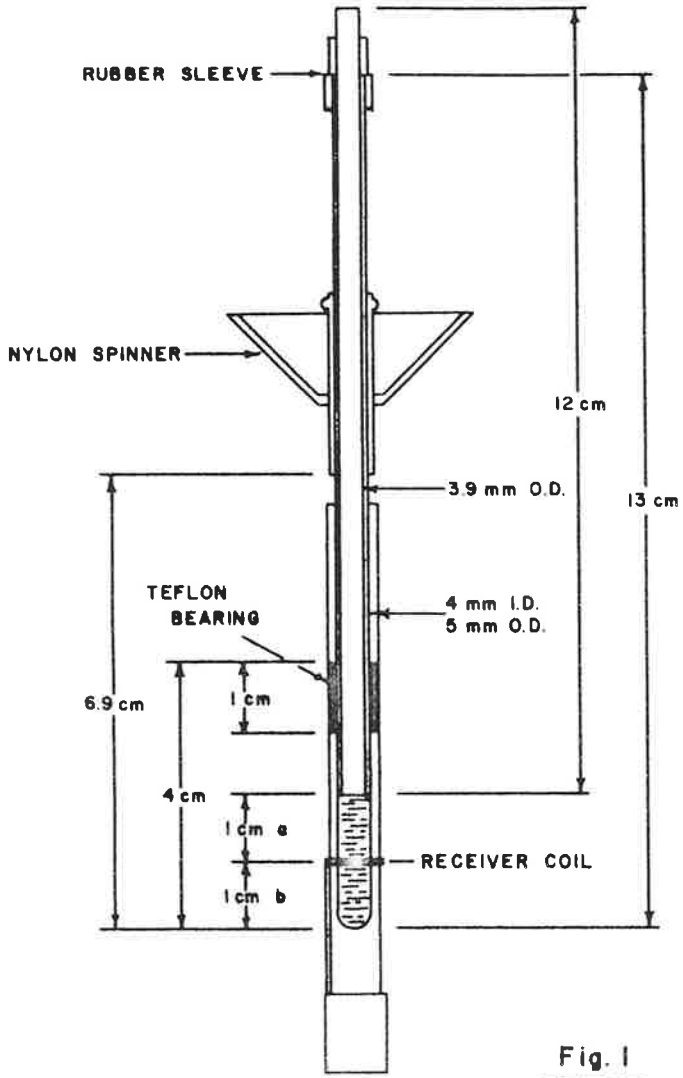
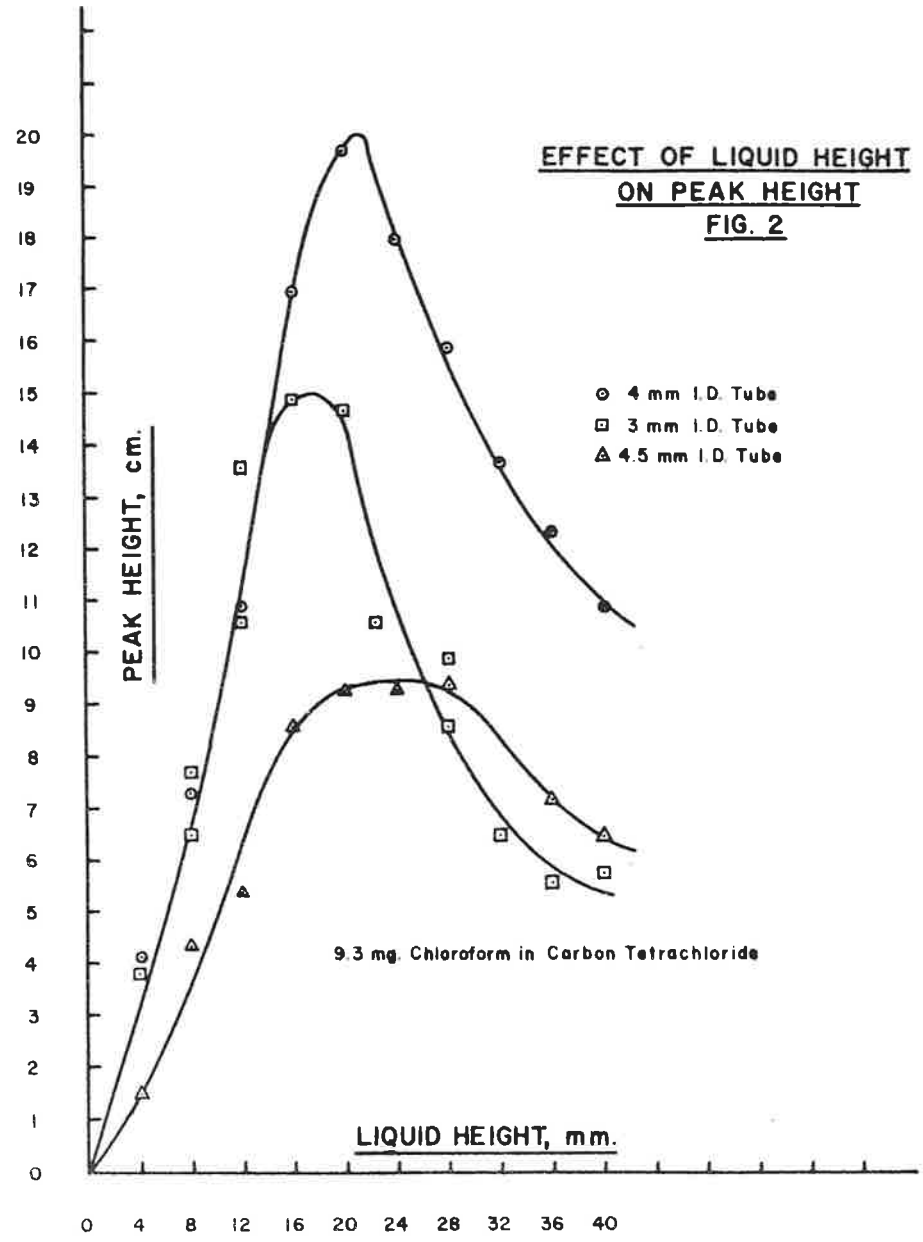

RUBBER SLEEVE
NYLON SPINNER
12 cm
13 cm
3.9 mm O.D.
4 mm I.D.
5 mm O.D.
TEFLON
BEARING
6.9 cm
1 cm
4 cm
1 cm a
1 cm b
RECEIVER COIL

Fig. 1


EFFECT OF LIQUID HEIGHT
ON PEAK HEIGHT
FIG. 2
4 mm I.D. Tube
3 mm I.D. Tube
4.5 mm I.D. Tube
9.3 mg. Chloroform in Carbon Tetrachloride
PEAK HEIGHT, cm.
LIQUID HEIGHT, mm.
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
0 4 8 12 16 20 24 28 32 36 40

DEPARTMENT OF CHEMISTRY
FACULTY OF SCIENCE
THE UNIVERSITY OF TOKYO
BUNKYO-KU, TOKYO

July 18, 1962

Dr. Aksel A. Bothner-By
Mellon Institute
4400 Fifth Avenue
Pittsburgh 13, Pennsylvania
U. S. A.

Dear Dr. Bothner-By:

Usually the electron coupled nuclear spin-spin interactions seems to be too small to become an important mechanism for the relaxation of nuclear magnetism. However, it is well-known that the exchange interaction such as $J(t)\mathbf{I}\cdot\mathbf{S}$ are one of the important mechanisms in HF molecule in liquid state. In addition, in the following part of this communication, I would like to show that the contribution from the spin-spin interactions where the interacting nuclei do not exchange is not always negligible.

Anisotropic part of spin-spin interaction will be responsible to this contribution. It may be assumed that the magnitude of the largest element of the traceless part of the spin-coupling tensor is comparable order as that of the time-independent part of the tensor. Though this time-independent part is, in general, small for the proton-proton interactions, it becomes larger as the number of the electrons belonging to the interacting nuclei increases. For example, the values of 1400 and 2000 cps have been reported for J_{PP} in PF_3 and for J_{PSb} in $NaSbF_6$, respectively. The magnitudes of these interactions are comparable with those of the dipolar interaction between two nuclear moments of one nuclear magneton, being apart about 2.5 Å.

Relaxation times contributed from such an anisotropic coupling may be calculated as follows. In the molecular system $O_{x'y'z'}$ the traceless part may be diagonalized as

$$J_{x'} = -\tfrac{1}{2}J_{z'}(1-\eta),\ J_{y'} = -\tfrac{1}{2}J_{z'}(1+\eta),\ \text{and}\ J_{z'},$$

where $J_{x'}$, $J_{y'}$, and $J_{z'}$ are the principal values of the tensor, and the relations

$$J_{z'} \geq J_{x'} \geq J_{y'} \quad \text{and} \quad \eta = (J_{x'} - J_{y'})/J_{z'},$$

are assumed without loss of generality. The corresponding Hamiltonian may be written in any coordinates as

$$\hbar H = 2\pi\hbar\mathbf{I}\cdot\underline{\mathbf{J}}\cdot\mathbf{I}' = \hbar\sum_q F^{(q)}S^{(q)}$$

with the spin operators

$$S^{(0)} = 3I_{z}I'_{z} - \mathbf{I}\cdot\mathbf{I}'$$
$$S^{(\pm1)} = \tfrac{1}{2}\sqrt{6}(I_{z}I'_{\pm} - I_{\pm}I'_{z})$$
$$S^{(\pm2)} = \tfrac{1}{2}\sqrt{6}I_{\pm}I'_{\pm},$$

where the functions $F^{(q)}$ transform according to the irreducible representation of the rotational group of degree two. Let the Euler's

which express the rotation from the molecular coordinate denote as $\boldsymbol{\Omega}$. Thus the functions $F^{(q)}(\boldsymbol{\Omega})$ at an arbitrary rotation are linearly related with the function in the molecular frame, $F^{(q')}(\boldsymbol{\Omega}')$, as

$$F^{(q)}(\boldsymbol{\Omega}) = \sum_{q'} A_{qq'}(\boldsymbol{\Omega})F^{(q')}(\boldsymbol{\Omega}'),$$

where

$$F^{(0)}(\boldsymbol{\Omega}') = \pi J_{z'},\ F^{(\pm1)}(\boldsymbol{\Omega}') = 0,\ \text{and}\ F^{(\pm2)}(\boldsymbol{\Omega}') = \pi\tfrac{1}{\sqrt{6}}\eta J_{z'},$$

and the transformation coefficients $A_{qq'}$ have a random character owing to the rotational Brownian motion of the molecule.

Using the probability density function for the rotational Brownian motion, the correlation function is given by

$$G^{(q)}(\tau) = \sum_{q'q''}\iint F^{(q')}(\boldsymbol{\Omega}')F^{(q'')*}(\boldsymbol{\Omega}')A_{qq'}(\boldsymbol{\Omega}_0)A_{qq''}(\boldsymbol{\Omega})^* \times g(\boldsymbol{\Omega}, \boldsymbol{\Omega}_0, |\tau|)d\boldsymbol{\Omega}_0 d\boldsymbol{\Omega}$$
$$= \frac{\pi^2}{5}J_{z'}^2(1 + \eta^2/3)e^{-\tau/\tau_c},$$

from which the spectral density is given by

$$J(\omega) = \frac{2}{5}\pi^2 J_{z'}^2 (1 + \eta^2/3)\frac{\tau_c}{1 + \omega^2\tau_c^2}$$

The relaxation times T_1 and T_2 will be obtained from this spectral density. For the details of further calculations, you can refer to Abragam's book, Principles of Nuclear Magnetism, p. 314.

The contribution from the above-mentioned mechanism will be important for the nuclei of $I=\frac{1}{2}$ in weak external magnetic field, since the spectral densities from the anisotropic shielding are proportional to the square of magnitude of the external field, which is weak in such a case.

Yours sincerely

Hiroshi Shimizu

Hiroshi Shimizu

THE FLORIDA STATE UNIVERSITY
TALLAHASSEE

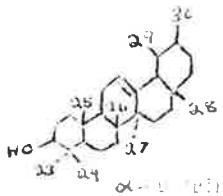
DEPARTMENT OF CHEMISTRY

July 9, 1962

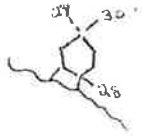
Dr. A. A. Bothner-By
Mellon Institute
Pittsburg, Pa.

Dear Art:

Some time ago Maurice Shamma, Raph Hurma, and I published a preliminary note on the NMR spectra of pentacyclic triterpenes. We are publishing the full paper (J. Org. Chem.), but will not include some preliminary methyl groups assignments for these compounds. As they might be of interest to some of your readers, I am including the assignments for publication in Mello-H-N-R." The structures and numbering systems are:



α-Amyrin



β-Amyrin

I would be glad to discuss my reasons for these assignments with any of your interested readers.

Yours truly yours,

R. E. Click

REC/ah

TABLE I

TRITERPENES STUDIED

Ursane Group

α-Amyrin Benzoate (19)
Uvaol Diacetate (17)
Ursolic Acid Methyl Ester Acetate (10)
Asiatic Acid Methyl Ester Triacetate (33)

Oleanane Group

β-Amyrin Benzoate (18)
Erythrodiol Diacetate (16)
Longispinogenin Triacetate (11)
Soyasapogenol-B Triacetate (26)
Chichipegenin Tetraacetate (20)
Δ¹²-Barrigenol Pentaacetate (37)
Phillyrapegenol Hexaacetate (32)
11-Keto-Δ¹²-Barrigenol Pentaacetate (39)
Hemsitorigenin Diacetate (22)
Oleanolic Acid Methyl Ester Acetate (9)
Cochalic Acid Methyl Ester (12)
Arjunolic Acid Methyl Ester
Echinocystic Acid Methyl Ester Diacetate (25)
β-Boswellic Acid Methyl Ester Acetate (23)
11-Keto-β-Boswellic Acid Methyl Ester Acetate (27)
Glycyrrhetic Acid Methyl Ester Acetate (28)
Morolic Acid Methyl Ester Acetate (30)

Lupane Group

Lupanol (8)
Betulin Diacetate (13)
Melaleucic Acid Methyl Ester (29)
Thurberogenin Acetate (21)

Other Triterpenes

Friedelin (31)
Phillyrigenin Diacetate (35)

TABLE II

PROTON NMR

C-METHYL ABSORPTION FOR VARIOUS PENTACYCLIC TRITERPENES
(τ VALUES)

C-me / CMPD	C_{23}	C_{24}	C_{25}	C_{26}	C_{27}	C_{28}	C_{29}	C_{30}
9	0.900	0.900	0.850	0.725	1.125	CO_2Me	0.850	0.850
11	a	a	0.875	0.875	1.275	CH_2OAc	0.825	0.825
12	b	b	0.90	0.725	1.125	CO_2CH_3	0.90	0.90
14	b	b	0.925	0.725	1.125	CO_2CH_3	0.925	0.925
16	0.975	0.975	0.875	0.900	1.175	CH_2OAc	0.875	0.875
18	1.025	1.025	0.925	0.925	1.225	1.00	0.900	0.900
20	0.950	0.950	0.850	0.950	1.275	CH_2OAc	0.850	0.850
22	0.975	0.975	1.025	1.025	1.175	CO_2 -	0.850	0.850
23	1.175	CO_2Me	0.825	0.775	1.175	1.00	0.875	0.875
24	1.275	CO_2Me	0.850	0.775	1.175	1.00	0.875	0.875
25	0.925	0.925	0.875	0.725	1.225	CO_2Me	0.825	0.825
26	1.00	CH_2OAc	0.825	0.875	1.125	0.900	1.00	1.00
27	1.10	CO_2Me	1.10	0.875	1.10	0.925	0.875	0.875
28	0.850	0.850	0.800	1.125	1.125	0.850	1.125	CO_2Me
34	CH_2OAc	1.025	0.825	0.875	1.05	CO_2Me	0.825	0.825
37	0.875	0.875	0.775	0.775	CH_2OAc	CH_2OAc	0.875	0.875
39	0.975	0.975	1.10	1.10	CH_2OAc	CH_2OAc	0.850	0.800

[a]Absorption at 1.00: and 0.950 T.

C-Me / CMPD	C_{23}	C_{24}	C_{25}	C_{26}	C_{27}	C_{28}	C_{29}	C_{30}
8	0.975	0.800	0.800	0.800	0.875	0.875	1.100	1.100
13	0.100	1.000	0.850	0.850	0.850	CH_2OAc	x	x
21	0.975	0.975	0.800	0.800	0.800	CO_2-	x	x
29	0.975	0.725	0.875	CO_2CH_3	0.900	CO_2CH_3	x	x

C-Me / CMPD	C_{23}	C_{24}	C_{25}	C_{26}	C_{27}	C_{28}	C_{29}	C_{30}
10	0.975	0.975	0.850	0.725	1.05	CO_2CH_3	0.850	0.850
15	b	b	0.950	0.950	1.075	CO_2CH_3	0.950	0.950
17	0.950	0.950	0.850	0.850	1.075	CH_2OAc	0.850	0.850
19	1.075	1.075	0.975	0.975	1.150	0.975	0.875	0.875
33	$AcOCH_2$	1.075	0.900	0.750	1.075	CO_2CH_3	0.900	0.900

TEXAS CHRISTIAN UNIVERSITY
FORT WORTH, TEXAS

DEPARTMENT OF CHEMISTRY

July 19, 1962

Dr. B. L. Shapiro
Mellon Institute
4400 Fifth Avenue
Pittsburgh, Pennsylvania

Dear Dr. Shapiro:

As an organic chemist whose graduate students seem to produce a rather constant stream of new compounds, I recently became interested in utilizing our A-60 for hydrogen analysis in order to save the time and expense of sending samples off to a commercial analytical firm. However, I have failed to find any detailed instructions on how to accomplish this although the rudiments and the necessary equation have been given by R. B. Williams[1]; the pertinent equation being:

$$a = k H C V$$

where a is the value of the total area under the n.m.r. curve as taken from the integral curve; k is a proportionality constant; H is the percent hydrogen; C is the weight of sample per unit volume; and V is the effective volume of the solution.

A standard solution of n-octane (0.2040 g/ml) was made up in carbon tetrachloride. A standard volume (0.525 ml) was introduced into each of two n.m.r. tubes, and one was sealed off as a standard sample. A volume calibration mark was made on the sample tube. The integrated absorption was the same for both sample and standard indicating the tubes to be of equal diameter. The value of k was determined for this standard and was redetermined on each occasion when a period of time elapsed between working periods.

To determine the percent hydrogen an amount of the unknown compound was weighted directly into the sample tube, and the sample was made up to the volume mark with carbon tetrachloride. The n.m.r. spectra was then run and integrated. From the value of the integral curve and the above equation the value of % H was then calculated.

For rapidity I chose sample amounts such that the integral amplitude adjustment was the same for both standard and sample. Of course, this was for convenience sake only and proper calibrations of the integral amplitude setting should allow one to operate with a variety of concentrations for the sample. While the results reported below involved the use of ca. 100 mg. samples, no doubt much smaller samples could be used.

Once set up, the average time for an analysis was around twenty minutes from start to finish - including all weighting and computation. The results appear to be at least as good as the usual combustion analysis and certainly were much easier to come by. Typical results are as follows:

Knowns	% H Calc'd	% H Found
cyclohexanone	10.29	9.90, 10.29,
1,5-Dibromopentane	4.17	4.30
new compounds		
2,2-Dimethyl-3-pentyl acetate	11.36	11.19
2,2-Dimethyl-3-pentyl methyl ether	13.93	13.71
2,3-Dimethyl-2-pentyl methyl ether	13.93	13.79

Yours sincerely,

William B. Smith

William B. Smith

WBS/dc

1. R. B. Williams, "Conference on Molecular Spectroscopy", London, 1958, Pergamon Press, New York, p. 43.

P. S. For those of your readers who may be interested, I would like to record the observation that dimethylfulvene gives only two sharp absorptions corresponding to the methyl groups and the ring-H's. The splitting among the latter in the pure liquid or in carbon tetrachloride solution is apparently very small or zero.

Protonation of Amides

The proton resonance spectra of solutions of acetamide, N,N-dimethylacetamide, formamide and N,N-dimethylformamide in fluorosulphuric acid have been studied at temperatures between 25° and -98°. At low temperatures a new peak appears in the spectra of all four compounds which is not present at room temperature and which, from peak areas, and other considerations, may be assigned with certainty to the $C=\overset{+}{O}H$ group. It is thereby unambiguously established that these amides protonate on the carbonyl oxygen and not on the nitrogen atom. The table lists the chemical shifts and coupling constants for the protonated forms of these amides and the spectra obtained at low temperature are given in the figure.

Acetamide. At -92° the spectrum consists of three peaks in addition to the solvent and reference (external TMS) peaks. Their relative areas were found to be A:B:C::1.07:2.10:3.00 and they are assigned to the OH, NH_2 and CH_3 groups respectively. The peak A merges with the solvent peak as the temperature is raised due to exchange of this proton with the solvent. The NH_2 resonance B is a doublet due to the non-equivalence of these two protons.

N,N-Dimethylacetamide. At -79° the spectrum consists of three peaks of relative areas A:B:C::0.96:5.91:3.00. They are assigned to the OH, $N(CH_3)_2$ and $C.CH_3$ groups respectively.

Formamide. At -98° two of the expected three peaks, B and C due to the NH_2 and CH protons, lie on top of each other. The relative peak areas are A:B+C::1.00:3.03 in agreement with their assignment to the $C=\overset{+}{O}H$ and NH_2+CH groups respectively.

N,N-Dimethylformamide. At -80° the spectrum contains three peaks of

relative areas A:B.C::1.04:0.96:6.00 which are assigned to the OH, CH and $N(CH_3)_2$ groups respectively. The OH and CH peaks are both doublets due to mutual spin-spin coupling, $J_{CH,OH}$ = 4.7 c/s.

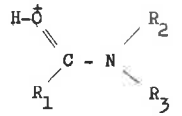
In all cases the A peak due to the proton captured by the carbonyl oxygen merges with the solvent on raising the temperature and is not visible at room temperature.

At room temperature the NH_2 signal changes from a broad single peak for pure formamide to a triplet due to N-H coupling in solution in fluorosulphuric acid. Evidently quadrupole relaxation is less effective in the latter solution but the reason for this is not clear. Protonation on oxygen must surely increase the double-bond character of the central C-N bond and thereby increase the electrical asymmetry around the nitrogen nucleus which would be expected to lead to more effective rather than less effective quadrupole relaxation.

TABLE

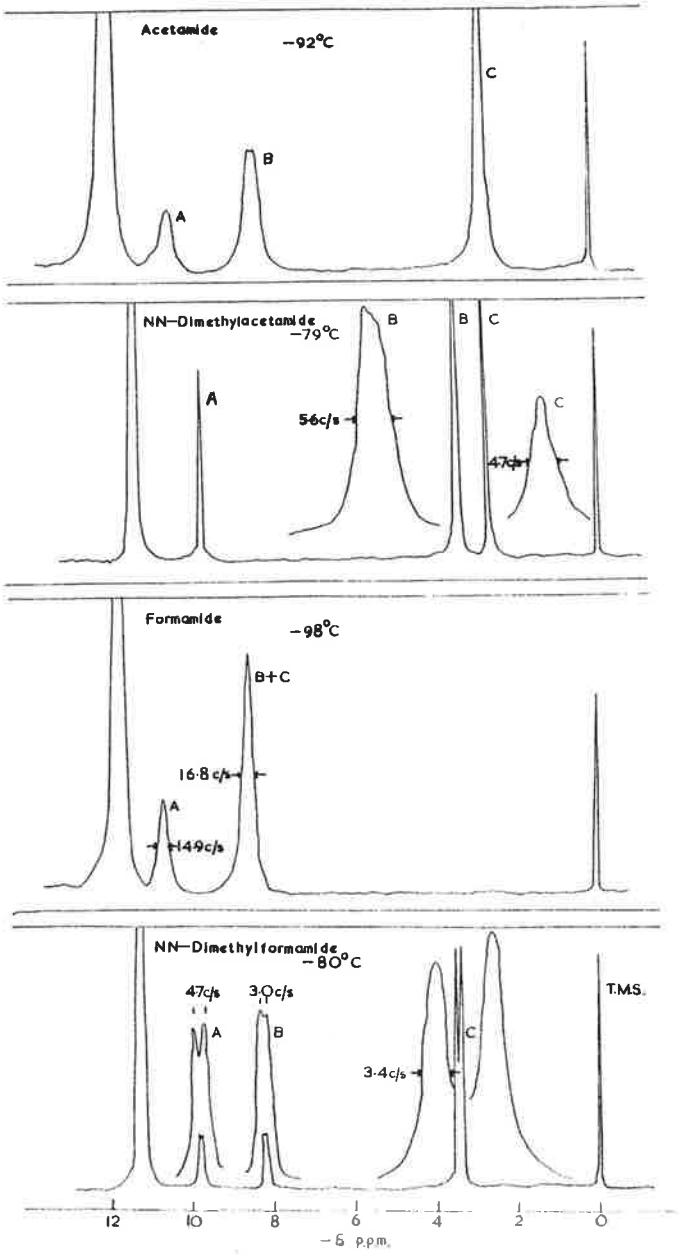
Amide	Temp. °C	$-\delta$ ppm from Ext. TMS OH	CR_1	NR_2	NR_3
Acetamide	+25	-	2.76	8.28	8.28
	-92	10.40	2.67	8.26	8.36
N,N-Dimethyl	+25	-	2.73	3.55	3.55
Acetamide	-79	9.80	2.64	3.45	3.45
Formamide	+25	-	8.55	8.68	8.68
	-98	10.69	8.60	8.60	8.60
N,N-Dimethyl	+25	-	8.38	3.49	3.59
Formamide	-80	9.98	8.38	3.43	3.53

J



$J_{N,R_{23}}$	62±5 c/s
J_{R_1,R_3}	8.5 c/s
J_{R_1,R_3}	1.1 c/s
J_{R_1,R_2}	0.7 c/s
$J_{R_1,OH}$	4.7 c/s

R. J. Gillespie and T. Birchall
Department of Chemistry, McMaster University, Hamilton, Ontario.



On the Relative Signs of CH and HH Coupling Constants. II.

Three Membered Rings

The double resonance experiments described in MELLON-M-R No. 45, p. 17 have been extended to ethylene oxide, and the result, along with recent experiments in other laboratories, throws some light on the anomalous HH couplings in three-membered rings.

The diagrammatic spectra in the figure below illustrate the experiment. Irradiation of the high field (low frequency) component of the carbon triplet (black) will affect the high field components of the inner multiplets if the sum of the vicinal HH coupling constants is positive. Because of the small value of J_{CCH}, only one component of each multiplet is not obscured by the peak from the C^{12}-C^{12} molecules, but the effect may be seen with just these components. The sum of the vicinal couplings was found to be of the same sign as the CH coupling, and hence may be presumed to be positive. Since the geminal and both vicinal coupling constants have been found to be of the same sign[1], it follows that the geminal coupling is also positive.

This would appear to contradict the epichlorhydrin analysis of Reilly and Swalen[1c], which seemed to show that the $-CH_2Cl$ geminal coupling was of the same sign as the ring geminal coupling. Since the former coupling is of normal magnitude, both couplings would have to be negative, in contradiction to the present results. However, a better fit of the epichlorhydrin spectrum has now been obtained with the two geminal coupling constants of opposite sign[2], removing the disagreement.

The "fine kettle of fish" remarked upon by Musher and Szöke[3] now appears to contain the following specimens. Vicinal couplings in three membered rings

where X is C[3,4], N[5], O[1a,5b,6] and S[5b,7] are all of similar magnitude and may now be considered to be positive. The geminal couplings, however, run as follows, if we assume all vicinal couplings to be positive.

X	J_{gem}
C	−4.3 cps
N	+2.0
O	+5.5
S	~ 0

The J_{gem}, taken from the references cited above, are for various substituted cyclics, and their sizes may depend in part on substituent effects. A very strong dependence upon X is unmistakable, however, and for the three first-row elements it might be roughly correlated with electronegativity. The

change of about 10 cps caused by the substitution of O for C is certainly surprising, and suggests that J correlations be made with extreme caution in unusual molecules.

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References:

(1) (a) H. S. Gutowsky, M. Karplus and D. M. Grant, J. Chem. Phys. 31, 1278 (1959);
(b) C. A. Reilly and J. D. Swalen, J. Chem. Phys. 32, 1378 (1960); 34, 980 (1961); (c) 35, 1522 (1961).

(2) J. D. Swalen, Symposium on High Resolution NMR Spectroscopy, Boulder, Colorado, July 2-4, 1962.

(3) MELLONMR No. 45, p. 12.

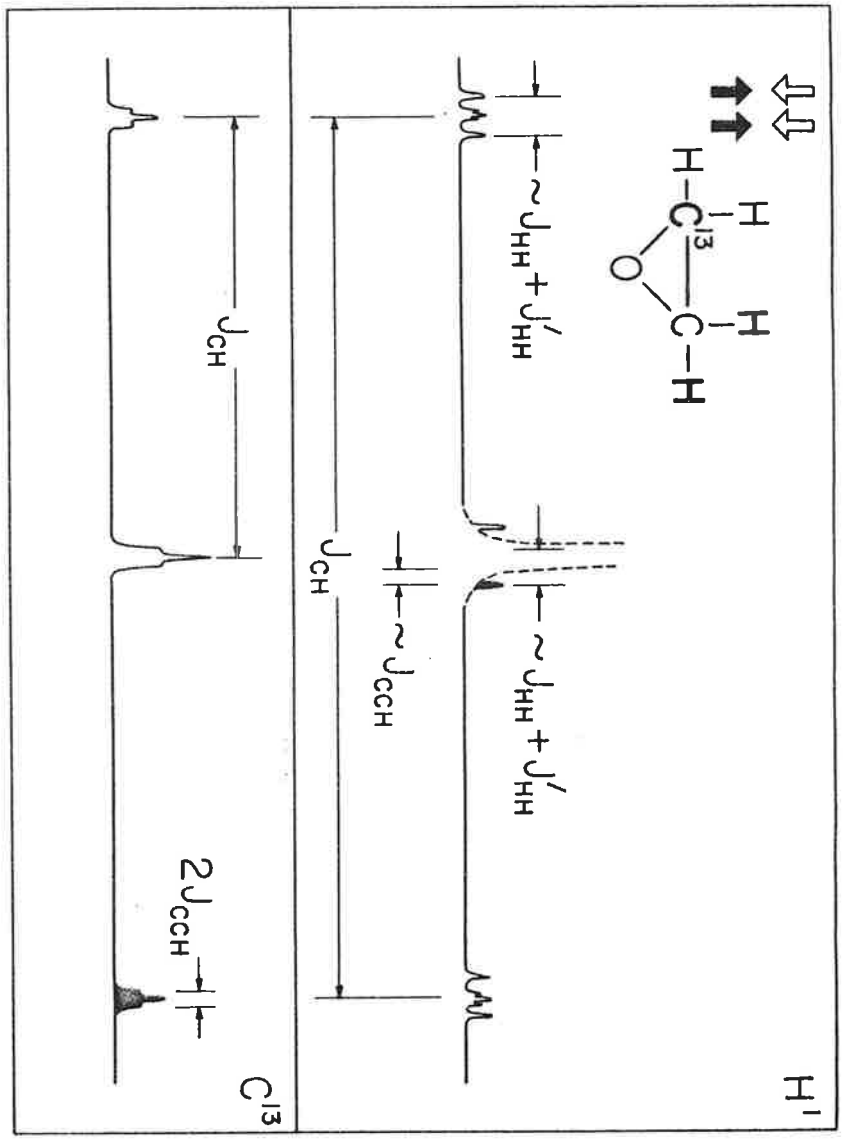
(4) (a) K. B. Wiberg, MELLONMR No. 38, p. 3.
(b) H. M. Hutton and T. Schaefer, Can. J. Chem. 40, 875 (1962).

(5) (a) Ref. (1a), quoted from J. P. Heeschen, Ph.D. thesis, University of Illinois, 1959.
(b) F. S. Mortimer, Mol. Spectroscopy 5, 199 (1960).

(6) N. Sheppard and J. J. Turner, Proc. Royal Soc. A 252, 506 (1959).

(7) J. I. Musher and R. G. Gordon, J. Chem. Phys. 36, 3097 (1962).

DIAGRAMMATIC SPECTRA



THE LILLY RESEARCH LABORATORIES

ELI LILLY AND COMPANY
INDIANAPOLIS 6, IND., U. S. A.

July 23, 1962

Dr. Bernard L. Shapiro
Mellon Institute
4400 Fifth Avenue
Pittsburgh 13, Pennsylvania

Dear Dr. Shapiro:

Perhaps by now you have received a flood of mail on spin decoupling, but here is our successful application of the technique described by L. F. Johnson in a recent issue of MELONMR.

Since the modification of the modulator output of the HR60 integrator involves only a capacitor in series with one side of the output, the capacitor and a SPDT switch were put in a 1-1/2" x 2" x 3" aluminum box which was mounted on the front of the console.

Ethanol, of course, was the first to be decoupled with results comparable to those of Johnson's. The next sample was that of Vindoline[1] which is a Vinca alkaloid with molecular weight 456.

[1] M. Gorman, et al, J. Am. Chem. Soc., 84 1058 (1962)

Figure 1 is a portion of the NMR spectrum of Vindoline with the decoupled spectrum directly above each multiplet. Above each decoupled group is the frequency of the auxiliary audio generator. Our integrator audio frequency is fairly stable at 2020 c/s. The difference between the two audio frequencies gave the position of the band responsible for the coupling. In this spectrum the olefinic proton at A which has a large coupling to B is coupled to a proton at D and one of two protons at C. It is interesting to note that C and D are almost the same distance apart as A and B since both C and D are decoupled with the same difference frequency.

It is our experience that bands closer than about 70 c/s give poor decoupling spectra with oscillations which appear to be a beat between the two audio frequencies.

Very sincerely yours,

ELI LILLY AND COMPANY

Paul W. Landis

Paul W. Landis
Physicochemical Research
Division

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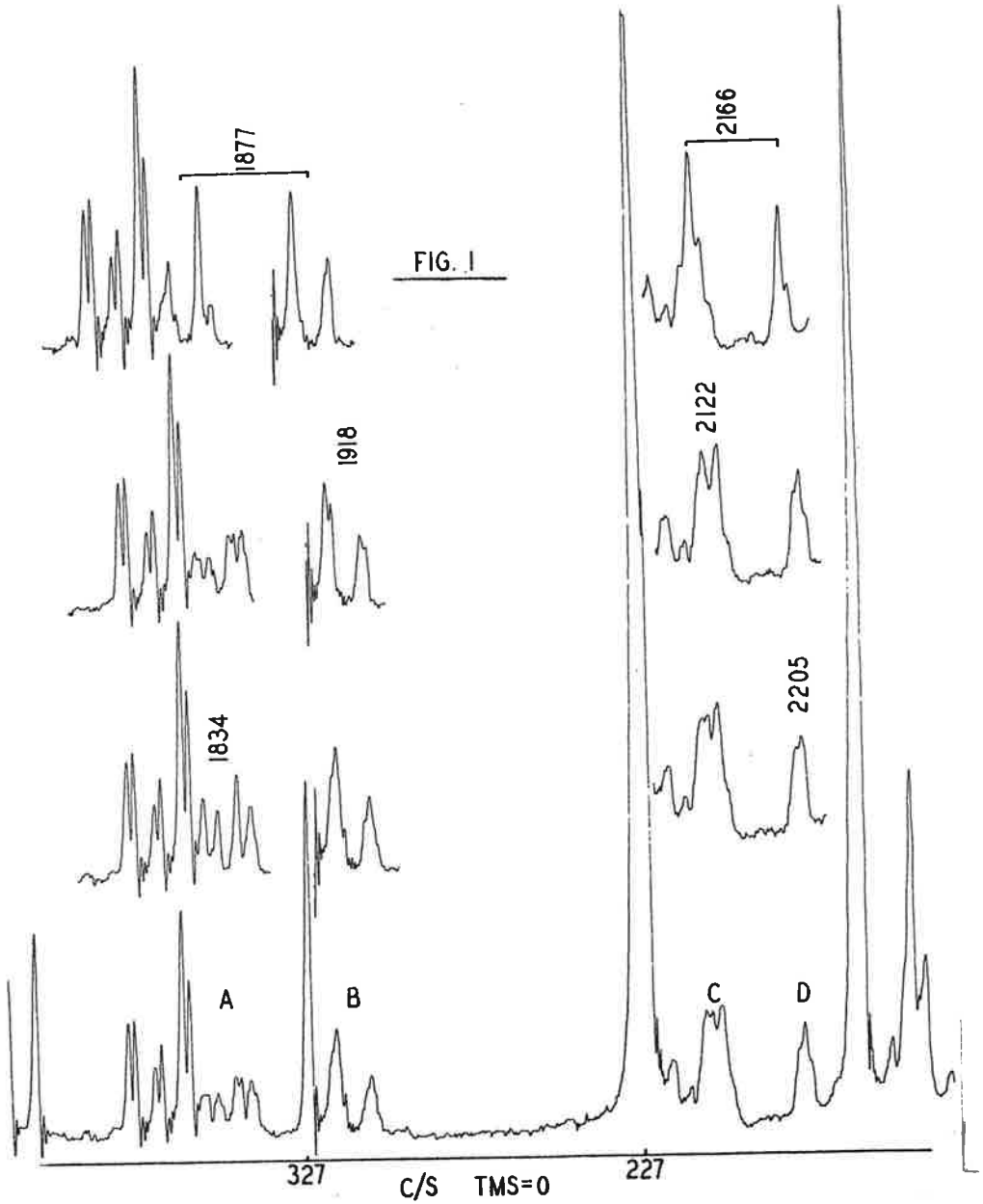

FIG. 1

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