M onthly

   E cumenical

      L etters from

        L aboratories

         O f

           N - M - R

           No. 32

Author Index

NUCLEAR MAGNETIC RELAXATION IN POLYMER MELTS AND SOLUTIONS

by

David W. McCall, Dean C. Douglass and Ernest W. Anderson
Bell Telephone Laboratories, Incorporated
Murray Hill, New Jersey

ABSTRACT

Nuclear magnetic relaxation times have been studied in
some polymer liquids and solutions. The nonexponential decay
of the transverse magnetization has been ascribed to the dis-
tribution of molecular weights. The use of such measurements
as a means of determining average molecular weights and distri-
butions is discussed. A preliminary application of this use is
made for polyethylene. The implications of nuclear magnetic
relaxation measurements are discussed in terms of molecular
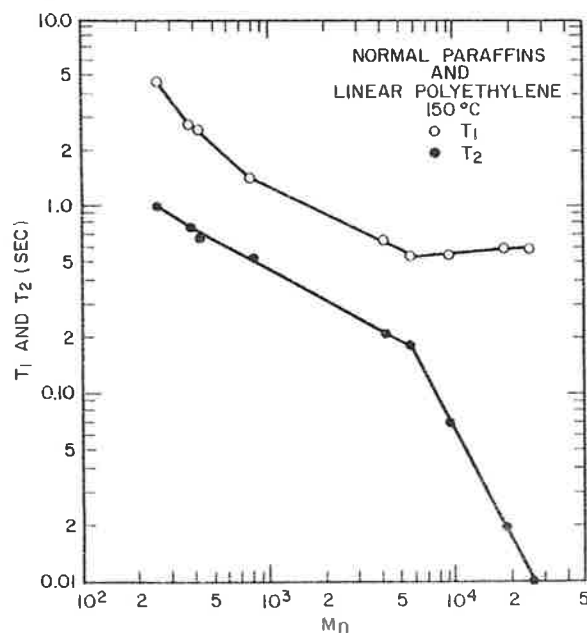motional processes of the polymer chains.

Fig. 2 - Dependence of T_1 and T_2 on the number average molecular
weight for linear polydimethylsiloxanes at 22°C.
The points marked with the "flags" refer to pure
substances.

Fig. 1 - Dependence of T_1 and T_2 on the number average molecular
weight for linear polyethylenes and n-paraffins at
150°C.

Fig. 3 - Relaxation curves for a solution of polyisobutylene
in cyclohexane (59% by weight). The T_2-curve is the
result of a 90° - 180° experiment and the ordinate
is the echo amplitude. The T_1-curve is the result
of a 180° - 90° experiment and the ordinate is a
function of the tail height defined in Reference 1.
The data was taken at 23°C.

32-1

Fig. 7 - Schematic relaxation time diagrams illustrating the various behaviors possible in a system possessing two relaxation mechanisms. The fast process has been given the greater activation energy and the slow process has been b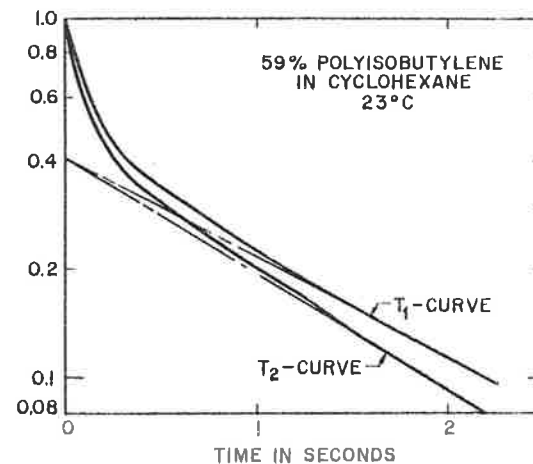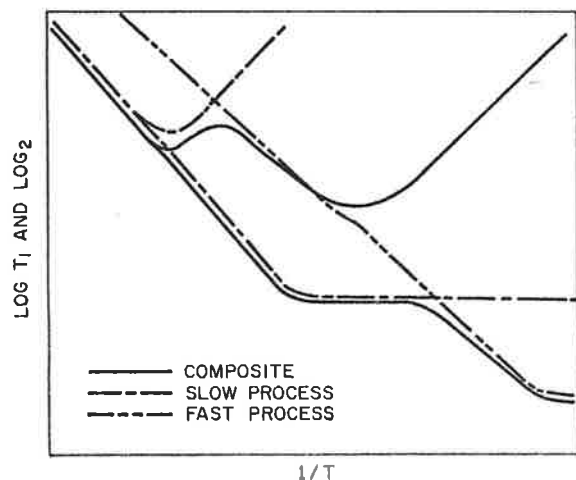roadened by a distribution of correlation times as indicated by the minimum in the T_1 dependence. These factors were introduced for purposes of illustration only and are not necessarily related to actual systems.
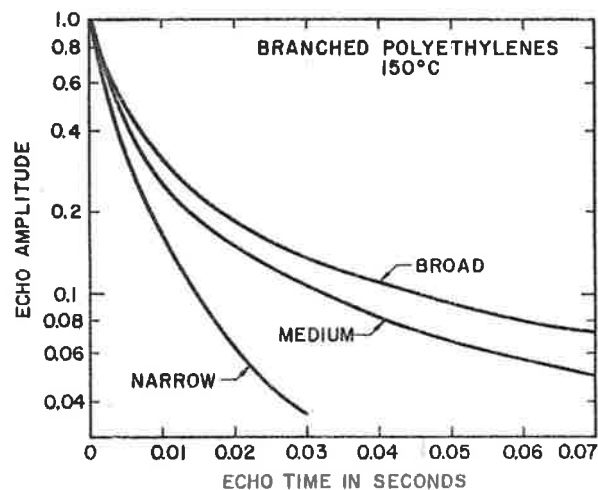

Fig. 8 - T_2-curves for unfractionated branched polyethylenes with varying widths of molecular weight distribution, 150°C.

May 10, 1961

Dr. Askel A. Bothner-By
Director of Research and
    Editor of MelloN-M-R
Mellon Institute
4400 5th Avenue
Pittsburgh, Pennsylvania

Dear A_2B_2:

I suppose one has to be pretty crusty to complain about free service, but let's chalk it up instead to the Growing Degeneracy of Our Modern American Culture, shall we?

Yes, MelloN-M-R is great, BUT........

It would, of course, be grossly unfair for me even to mention the quality of the humor in recent issues, so I won't. (A cartoon every few pages depicting a little of the poignant fun and laughter of N-M-R spectroscopy would liven things up a bit, but that is neither here nor there.) ....Your Circulation Manager, it is true, often seems a little gruff when demanding payment of his unorthodox subscription fee --- but most any broadminded reader can in time forgive this eccentricity.......This is also not the place to discuss the undeniable bias of many of your editorials, or even the questionable taste of your advertising copy.......And I shall defend to the death your right to arrange the Bibliography in any wild way you see fit.

No, my criticism is more basic. I keep my back copies of MelloN-M-R in a 3-ring notebook, and the holes you punch in the left margin of each issue just won't fit my notebook. Almost, but not quite. Enclosed is a sheet of ordinary, commercial 3-ring notebook paper for comparison with your production. Now, I ask you, is there any hope at all for standardizing High-Resolution N-M-R Spectra when we can't even standardize 3-ring notebook paper punching?

Yours for standardization,

Crusty Charlie

Charles W. Wilson, III

CWW:bh

P. S. All right, all right, I expect to have another contribution for MelloN-M-R --- perhaps even more valuable than this one --- within the next few days.

(We have sent C.W.W. one of our special non-standard binders -
This is not to be construed as a precedent, however, since it is
only with considerable difficulty and insistence that we
manage to remain non-conformist in these days of mass-production.
Other readers will have to arrive at their own standardization
methods -

Ye crusty editor)

3.2.2

School of Chemistry,

The University,

LEEDS, 2.

13th April, 1961.

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

Dear Dr. Bothner-By,

I wonder if your readers would be interested in some recent adjustments that we have been making on a permanent magnet intended for high-resolution nuclear magnetic resonance. The aim of the investigations was to develop a method by which the homogeneity of a new magnet could be conveniently and easily adjusted in the laboratory to high-resolution standards. The work was done in collaboration with Dr. A.F. McCann, Mr. F. Smith, Jr., and Mr. J.D. Thwaites.

The spectrometer was a twin-T r.f. bridge apparatus similar in many respects to previous instruments (e.g. Leane, Richards, and Schaefer, J. Sci. Instr., 1959, $\underline{36}$, 230). The oscillator had a day-to-day stability of $\pm$ 1 part in 10^8. The coil consisted of 2 closely-wound turns of 36 s.w.g. varnished copper wire wound on a glass tube of o.d. 6.5 mm., and the samples were contained in glass tubes of o.d. 4 mm. and i.d. 2.5 mm.

The permanent magnet was built by Swift Levick of Sheffield, England, and its essential features are illustrated in fig. 1 (diagrammatic only). The permanent magnetic material was "Columax" and after magnetization a field of 9,500 gauss was obtained in a pole gap of 1.37". In use, the magnet was thermostatted near 27.8°C by an air-circulation system with a stability of $\pm$ 0.04°.

The various stages in our attainment of high-homogeneity are outlined below.

(1). Before assembly, the soft-iron pole caps (diameter 16" tapering to 10") were ground optically flat (to at least $\pm$ ½ λ) to within ½" of the edge of the surface.

(2). After assembly and magnetization, the pole faces were parallel to within $\pm$1 thou. However, the parallelism of one of the pole caps (the right-hand one in fig. 1) was capable of being altered by at least twice this amount by means of three vanadium-steel wedges placed round the circumference of the pole-cap support, one of which is shown in fig. 1. These wedges helped to hold the pole cap against the pull of the permanent magnetic material across a small air-gap of about 40 thou. They were of such dimensions that one turn of the wheel which moved the wedge displaced the edge of the pole-cap surface at that point by ½ thou. Using these wedges and special gauges, we were able to align the pole surfaces to be parallel within 0.2 thou.

(3). We then carried out a field plot near the centre of the gap, and adjusted the wedges on the basis of this plot in an attempt to gain circular symmetry. The effect of the wedges on the field contours in the median plane is illustrated in fig. 2, in which the left-hand plot is transformed into the right-hand one by a $\frac{1}{6}$ th thou displacement of the bottom right-hand wedge in such a direction as to decrease the gap at that point. In fact, full circular symmetry was never achieved, although the homogeneity (without spinning or any form of current shim) was now quite reasonable (about 6 c/s).

(4). Having achieved as flat a distribution of field contours near the centre as we could, we inserted a sample of acetalde-hyde and watched the methyl-group signal on an oscilloscope while adjusting the three wedges by small amounts. By this means, we achieved a homogeneity of about 1.4 c/s, sufficient to resolve the methyl doublet, again without spinning or any form of homogeneity coils. A record of the methyl signal taken after a set of such adjustments is shown in fig. 3. Spinning (fig. 4) now removes the broad base and sharpens the lines to a width at half-height of 0.7 c/s. The ultimate resolution (at present) is thus no better than the majority of high-resolution instruments, but the adjustments required

to attain it are reasonably straightforward and once attained, little further correction is required.

We hope to send you shortly an account of some high-resolution spectra which we are recording on this instrument.

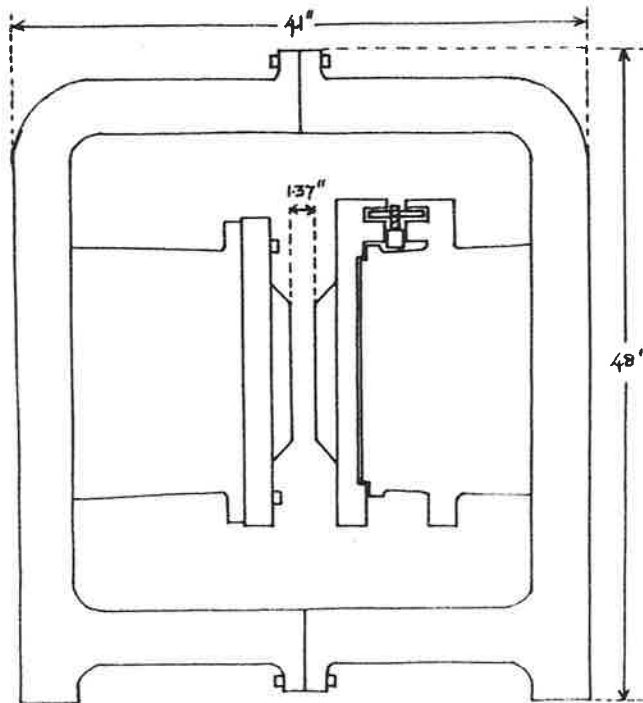Yours sincerely,
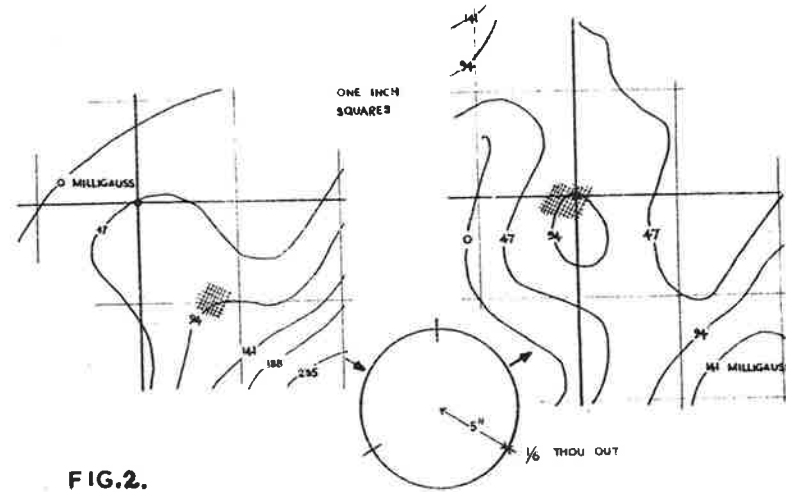
John. A. S. Smith
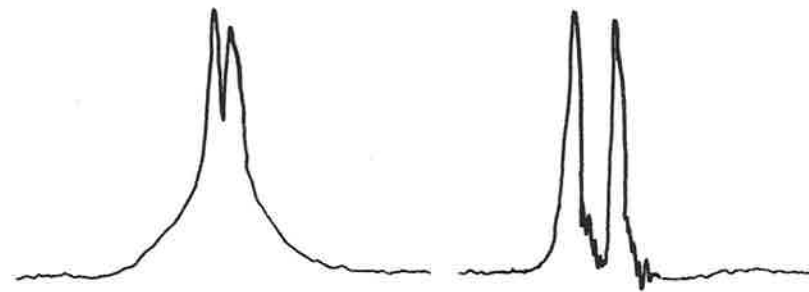
John A.S. Smith.

FIG.2.

FIG.1. MAGNET.

FIG.3. Without spinning.

FIG.4. With spinning.

FAIRCHILD

May 9, 1961

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

Dear Aksel:

We, Bill LeNobel, Asa Leifer and I, have been examining the evidence for hydrogen bonding as an explanation of the anomalous acid strength of butyric and o-toluic acids. As part of this program, we have had occasion to examine the strength of the hydrogen bond between the proton in chloroform and the oxygen in nitrosobenzene, nitrobenzene and pyridine oxide. Utilizing the sideband technique, we measured frequency separation between the chloroform proton and tetramethylsilane protons over a reasonable range of concentrations of the three oxygen containing compounds. All measurements were made at sixty megacycles. The frequency of the oscillator was monitored by a frequency counter and the sideband separations read from the frequency counter rather than from the oscillator. Chloroform was the solvent for all measurements. The data are summarized in Table I and Figure 1. The effect is just as one would predict.

Sincerely yours,

James E. LuValle

James E. LuValle
Director of Basic Research

JEL:mls

TABLE I

CHEMICAL SHIFT

Compound	Mole Fraction	$\Delta(\delta)$ c.p.s.	$\Delta\tau \times 10^2$
Nitrosobenzine	0.00	0.0	0.0
	0.09	-1	1.7
	0.16	1	-1.7
	0.34	-1	1.7
	0.54	-1	1.7
Nitrobenzene	0.00	0.0	0.0
	0.15	-11	18.4
	0.18	-1	1.7
	0.19	-8	13.0
	0.42	-6	10.0
	0.65	-11	18.4
Pyridine Oxide	0.00	0.0	0.0
	0.09	-12	20
	0.27	-17	28
	0.35	-45	75
	0.54	-66	110
	0.74	-84	140

$$\Delta(\delta) = \Delta_N - \Delta_0 = \left(\xi_{sample} - \xi_{ref}\right)_N - \left(\xi_{sample} - \xi_{ref}\right)_{N=0}$$

where N = mole fraction.

$$\Delta\tau = -\frac{\Delta\delta}{60}$$

Δτ

1.4

1.2

1.0

0.8

0.6

0.4

0.2

PYRIDINE OXIDE

NITROBENZENE

NITROSOBENZENE

0.2   0.4   0.6   0.8   1.0

MOLE FRACTION ARYL COMPOUND
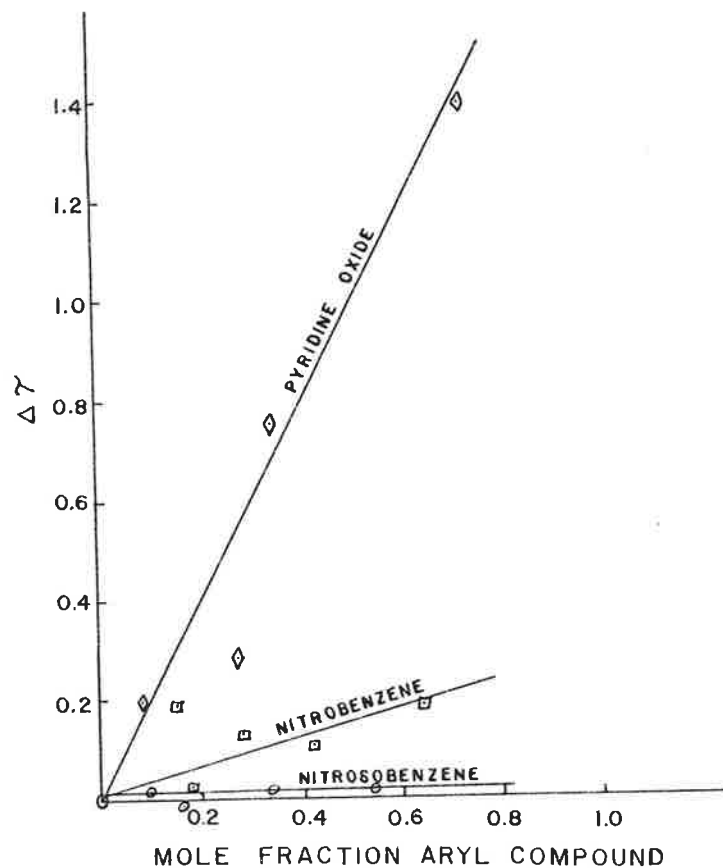
PRINCETON UNIVERSITY

DEPARTMENT OF CHEMISTRY

PRINCETON, NEW JERSEY

Frick Chemical Laboratory

May 9, 1961

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

Dear Aksel:

In the course of routine measurements of the chemical shift of the hydrogens in t-butyl isonitrile, we observed splitting of the proton resonance. The triplet of approximately 1:1:1 intensity cannot result from proton-proton coupling. We believe that this represents the first case of resolvable "long-range" $N^{14}-H^1$ interaction.

Several other isonitriles have been examined and similar results have been obtained (Table 1). Figure 1 shows the CH_3NC triplet, Figure 2 the CH of $(CH_3)_2CHNC$ and Figure 3 the CH_3 resonance of the same compound.

Table 1

Summary of the NMR Spectra of Isonitriles

Compound	$\tau \pm 0.02$	Multiplicity	J_{NH} cps ± 0.2	J_{HH} cps ± 0.2
$(CH_3)_3CNC^a$	8.56	triplet	3.5	
CH_3NC^a	7.15	triplet	2.7	
$\emptyset CH_2NC$	5.72	triplet	1.3	
$(CH_3)_2CHNC$				
$\quad CH_3$	8.55	2 triplets	2.6	7.0
$\quad CH$	6.13	tripled heptet	1.8	7.0
$CH_3(CH_2)_3NC$				
$\quad \alpha\text{-}CH_2$	6.70	tripled triplet	2.0	6.7
$\quad \beta\text{-}CH_2$		shows splitting		
Cyclohexyl-NC	6.42	broad peak		

a) CCl_4 solution; the other compounds were run neat.

---

1. For line broadening due to $N^{14} - H^1$ coupling, see MELLONMR 51-17.

The interpretation of these results is straightforward. Symmetrical electronic distribution about the N^{14} nucleus in these compounds greatly reduces the possibility of spin relaxation by nuclear-quadropole interactions, thus permitting spin coupling. In other nitrogen compounds, relaxation is sufficiently rapid to effectively decouple the N^{14} from hydrogens not directly bonded to nitrogen.[2]

The NMR spectrum of isopropyl isonitrile is of particular interest. There, as in $Pb(C_2H_5)_4$,[3] β-coupling is stronger than α-coupling. This effect has been discussed more recently by Narasimhan and Rogers for magnetic nuclei with higher atomic numbers.[4] The observed behavior of N^{14} corresponds with their treatment.

A brief survey of other nitrogen containing molecules has been made to determine the extent of this long-range coupling. Data on amines, nitroalkanes and heterocyclic compounds has been available for some time. These materials, of course, do not show such N^{14} splitting. Examination of nitriles, N-oxides and azides failed to reveal further examples of this splitting.

Spectra were run on a Varian 4300-B spectrometer at 40 mcps. TMS was used as an internal standard. Tau values and coupling constants were measured using the side band technique.
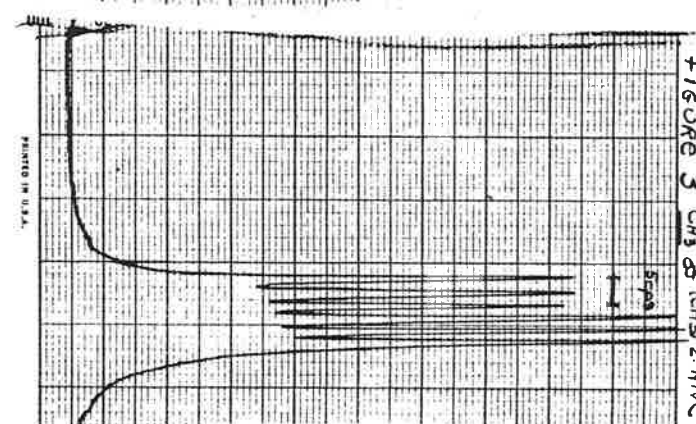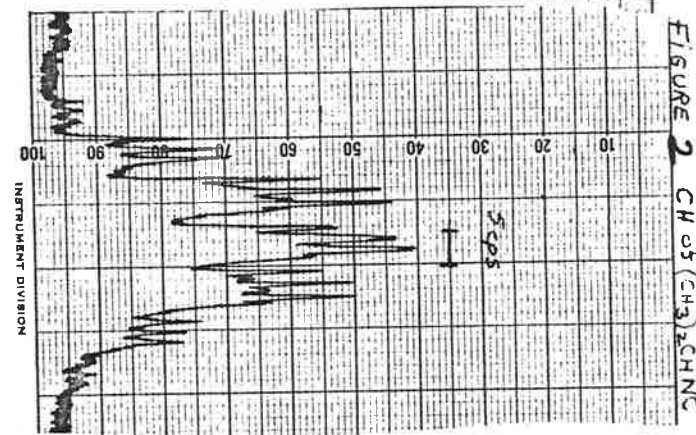
Sincerely yours,

I.D. Kuntz Jr.
I.D. Kuntz, Jr.

Paul Schleyer
Paul Schleyer

Adam Allerhand
Adam Allerhand

2. R.A. Ogg and J.D. Ray, J. Chem. Phys., 26, 1339 (1957); J.A. Pople, W.C. Schneider and H.J. Bernstein, "High-resolution Nuclear Magnetic Resonance", McGraw-Hill, New York, N.Y., pp. 215, 227. We are indebted to David Grant and James Schoolery for suggestions.
3. E.B. Baker, J. Chem. Phys., 26, 960 (1957).
4. P.T. Narasimhan and M.T. Rogers, ibid., 31, 1431 (1959); 34, 1049 (1961).

FIGURE 1 $(CH_3)_2CHNC$

FIGURE 2 CH of $(CH_3)_2CHNC$

FIGURE 3 CH_3 of $(CH_3)_2CHNC$
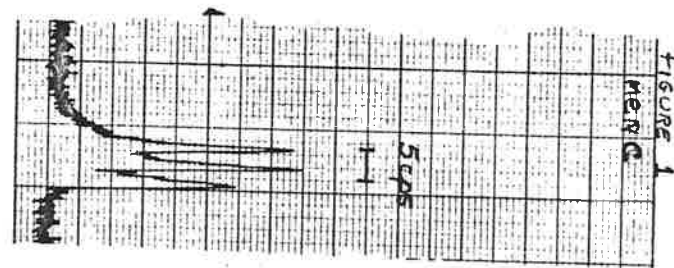
UNIVERSITY OF WASHINGTON
DEPARTMENT OF CHEMISTRY
SEATTLE 5

KENNETH B. WIBERG

May 15, 1961

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

Dear Aksel:

My letter of May 3 was not intended for MELLONMR, but was just for your information. I have written similar letters to those who asked for a listing of our version of the program.

We have recently decided to try to do something about organizing our n.m.r. data, and I wonder if others would care to join our effort. We have made up some coding sheets (see enclosure) on which we place our data - and then these data are key punched on IBM cards. By suitable sorting and listing, we can prepare tables of the data in a number of different formats.

Two questions arise - one of nomenclature and the other of how to designate the type of proton. If only a list in order of increasing τ value were wanted, the nomenclature problem would largely disappear. However, we should like to have an alphabetical listing also. We propose to name the compounds in Chem. Abstracts format, using the nomenclature for deuterium labeled compounds except that a $ sign will be used for the proton in question instead of the d which is used for deuterium replacement. Some examples are

BENZALDEHYDE-$

BENZALDEHYDE-$-4-NITRO

METHYL-$ FORMATE

METHYL FORMATE-$

ETHYL-1-$ ACETATE

ETHYL-2-$ ACETATE

ETHYL ACETATE-$

NITROBENZENE-2-$

CHLOROBENZENE-3-$-4-NITRO

Dr. A. A. Bothner-By   -2-   May 15, 1961

As far as the designation of the type of proton is concerned, our ideas are still vague. One possibility is to have a two-number system in which the first number indicated the type and the second the environment. For the first number, a possible arrangement would be

primary	1	olefinic	4	amino, amide	7
secondary	2	aromatic	5	aldehyde	8
tertiary	3	hydroxy	6	acid	9

and for the environment

H or alkyl on same carbon and adjacent carbons	1
H or alkyl on same carbon and elect with drawing on adjacent carbons	2
Electron withdrawing substituent on same carbon	3
Aromatic ring on same carbon	4
etc.	

If any of the readers of MELLONMR might be interested in this project, we would be happy to supply them with coding sheets. If they would send them to us, we would have the data key punched, and the cards sorted. The listing could be done on DITTO masters, duplicated and sent to those who contributed data. If there could be agreement on our nomenclature scheme, the data could be gathered while the type of proton designation were being considered, and then entered just prior to key punching.

I hope we may receive some comments concerning this idea.

Sincerely,

KBW:jp

THE UNIVERSITY OF BRITISH COLUMBIA

VANCOUVER 8, CANADA

DEPARTMENT OF CHEMISTRY

May 18, 1961

Dr. Aksel A. Bothner-By,
Director of Research,
Mellon Institute,
4400 Fifth Avenue,
Pittsburgh 13, Pa.

Dear Aksel,

The issues of Mellon-M-R. have proved useful many times in improving our instrument and keeping up with current work from this location. I should like to make a small contribution at present and perhaps in the next month or so mention some other work which is being written up.

In the course of attempting to make strong hydrogen bonded complexes in solution and measure the chemical shift of the hydrogen bonded proton, solutions of substituted acetic acids in N Methyl and NN dimethyl formamide were studied. The behaviour of acetic acid has been noted in a series of solvents. In CCl_4 the high field shift due to dissociation of hydrogen bonds occurs below 10 mole % acid and in more polar solvents such as acetone it occurs at higher concentrations.

The figure shows three dilution chemical shift curves. Curve 7 refers to CF_3COOH in N methyl formamide, curve 8 to CF_3COOH in N.N dimethyl formamide and Curve 9 to $CH_3CO.OH$ in NN. dimethyl formamide. The large unshielding of the CF_3COOH acid proton in the two solvents around 50.50 mole mixtures is surprising but the large changes in chemical shifts on further dilution to high field is exceptional even in hydrogen bonding systems.

The explanation I have for the shape of the curves is the complete protonation of the amides in CF_3COOH but little protonation with CH_3COOH. The 50.50 mole mixture in CF_3COOH is composed of ion pairs held together by a very strong hydrogen bond. This hydrogen bond in NN dimethyl formamide $-CF_3CO.OH$ (15 p.p.m. from $C \cdot C_6H_{12}$) is almost symmetrical. The symmetrical hydrogen bonds lie some 18 p.p.m. to low field from this same reference. The very large chemical shift to high field on further dilution is probably due

- 2 -

to isolation of the conjugate acid and base in the system by
breaking up ion pairs. The proton on the amide cation with no
hydrogen bond would be expected to show proton resonance at
relatively high field. We are continuing with protonation studies
in a range of systems and perhaps we can get more precise infor-
mation on the role of the hydrogen bond in protonation.

Yours sincerely,
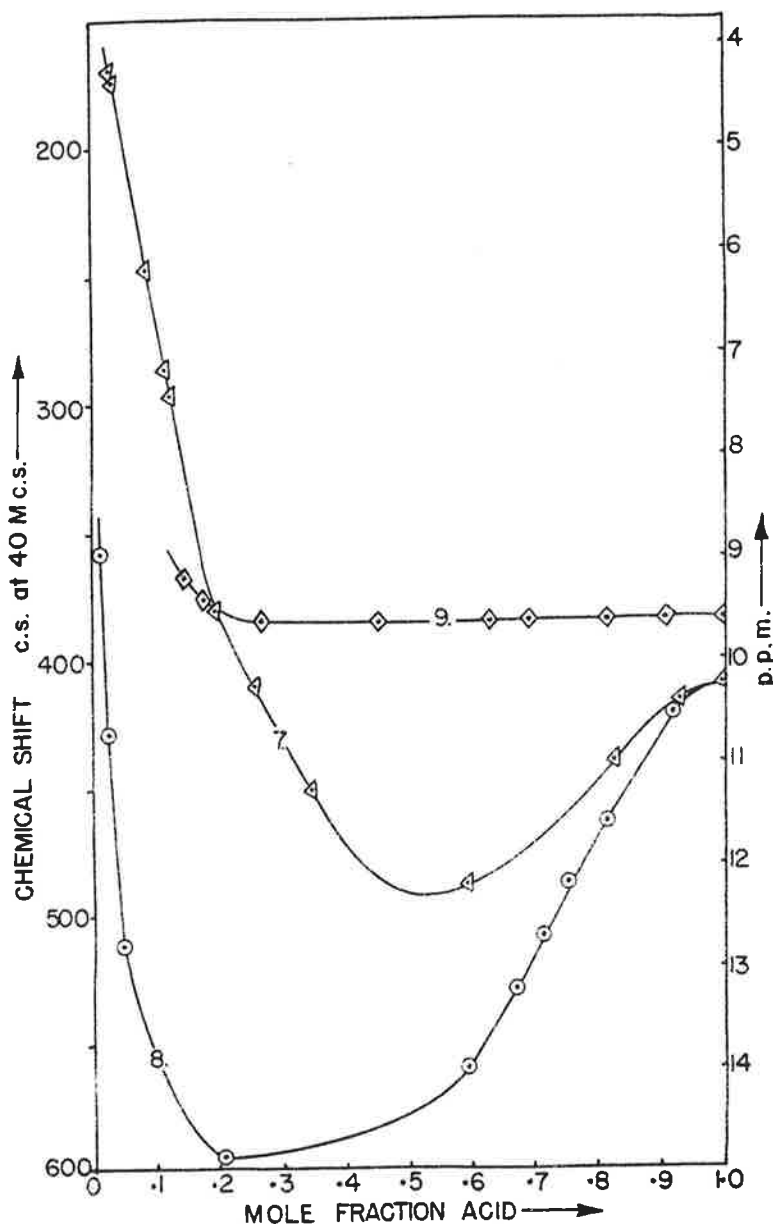
Leonard W. Reeves

LWR:aja

May 19, 1961

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

Dear Dr. Bothner-By:

I'm sorry it took your recent reminder to prod me into
sending along my subscription to your excellent Newsletter.
I am finding it immensely valuable and shall try to be more
prompt in the future. At any rate, here are some items
which may be of interest to some of your readers.

In several of the early issues of the Newsletter there were
comments in regard to impurities in TMS. Since no one has
mentioned the subject recently, perhaps it has completely
ceased to be a problem. But in case anyone is still going
to the trouble of purifying it, I thought it would be
worthwhile to mention that we have never been able to detect
any impurities in the TMS obtained from K & K Laboratories,
Jamaica, New York.*

Issue 18 of M.E.L.L.O.N.M.R. contained a sample of a plastic
plug which Lauterbur found convenient for capping conventional
5 mm. O.D. sample tubes. Unfortunately, this size will not
fit Varian thin-wall tubes which we are now using in all of
our work because of their greater "active" volume and excellent
spinning characteristics. Luckily, we found that the K-5 plug,
made by the same company, fits reasonably snugly over 5.0 mm.
O.D. tubes. I wish that I also could provide samples for your
readers, but I have found the manufacturer very generous in
providing samples of the various sizes that are available.

We are most pleased with the operation of our homogeneity
control unit. Since we are often forced to use one of the
more extreme solvents, which are all loaded with hydrogen, to
get even a suggestion of a spectrum, the absence of spinning
sidebands is a most welcome change. Often our problem is
compounded by the limited amount of sample available. We

have found Martin's small volume technique (Issue No. 12)
very useful though we have not been able to go much below
0.2 ml. without a major loss of resolution. With a
combination of Varian-type nylon inserts, Martin's bushing
and a good deal more adjusting, we have been able to get
good resolution from samples as small as 0.1 ml. In either
case a really major improvement in resolution can always be
obtained, after the sample has been properly positioned, by
readjustment of the curvature control of the homogeneity
control unit.

In cooperation with Harold Bright and Lloyd Ingraham of
the University of California, I have recently obtained the
proton spectra of a number of N- and O-acetyl five-membered-
ring anhydrides. The object of this study was to determine
the configuration of enzymaticly formed β-methyl aspartic
acid, hopefully by using the Karplus equation to determine
the dihedral angle formed by the α- and β-carbon protons in
the anhydride where there would be no doubt as to the
carboxyl configuration. Table 1 gives τ and J values for
the N-acetyl anhydrides of the two β-methyl aspartic isomers
(BMAA) together with the structures that we now believe are
correct. To show the effect of various changes in structure
on these values, I've also included data for the acetyl
anhydrides of aspartic and $3-d_1$ aspartic acids.

Table 1. Some N-Acetyl Aspartic Anhydrides

enzyme active BMAA $R_T = CH_3$, $R_c = H$ (4, 3')

enzyme inactive BMAA $R_T = H$, $R_c = CH_3$ (3, 4)

aspartic (AA) $R_T = H$, $R_c = H$ (3, 3')

$3d_1$ - aspartic ($3d_1$ -AA) $R_T = H$, $R_c = D$ (3)
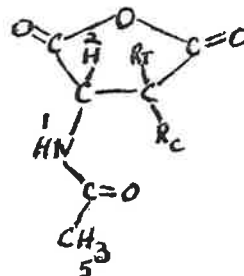
τ' (in d_6 - acetone)

Position	Active BMAA	Inactive BMAA	AA	3-d_1 AA
1	1.80	1.76	1.80	1.80
2	5.42	5.29	5.23	5.24
3	---	6.54	6.70	6.70
3'	6.58	---	6.95	---
4	8.61	---	---	---
4'	---	8.83	---	---
5	8.02	7.99	8.04	8.04

Interaction	Coupling (cps)			
J_{12}	7.4	7.3	7.2	6.8
J_{23}	-	10.2	9.9	10.2
$J_{23'}$	8.1	-	6.1	-
$J_{33'}$	-	-	18.0	-
J_{34} or $J_{3'4}$	7.1	7.3	-	-

Since neither isomer produces the very small coupling predicted by the equation for a 108° angle (about 0.6 cps), we had to resort to a model compound, though we might have based an assignment on the small change in peak position of the α-carbon proton which is discussed below. Fortunately, an excellent model was available, enzyme-formed 3-d_1 malic acid, (MDMA) the configuration of which had recently been established by two different groups. Its structure is shown in Table 2 together with its PMR data.

Table 2. O - Acetyl Malic Anhydride
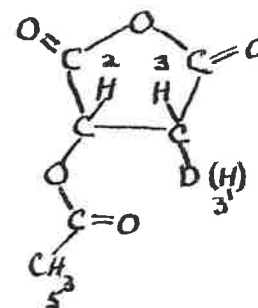
Position	τ' (in d_6 - acetone)	
	3-d_1	3-h_2
2	4.28	4.24
3	6.55	6.55
3'	-	6.75
5	7.88	7.86

Interaction	Coupling (cps)	
	3-d_1	3-h_2
$J_{23'}$ (trans)	-	6.6
J_{23} (cis)	9.6	8.9
J_{3D}	2.7	-
$J_{33'}$	-	19.0

I've also included in Table 2 the shielding and J values for undeuterated malic anhydride which were assigned on the basis of the deuterated data.

The good agreement of J_{23} for inactive BMAA with the coupling value of NDMA, which we know arises from a cis interaction, shows that the configuration of the active BMAA is threo (protons trans). While the variation of J with $\emptyset$ is in the direction predicted by theory, the lack of better agreement is not surprising since a five-membered ring anhydride is a rather strained ethane-like structure.

Having established the configuration of the BMA isomers, it is rather interesting to see to what extent current knowledge of long-range shielding effects confirms this assignment. The most obvious configurational effect is the greater shielding of a β-carbon proton when it is cis, rather than trans to an N- or O- acetyl group. The β-carbon protons in malic and aspartic anhydride, and the β-methyl protons in BMAA show approximately the same increase of 0.2 ppm. The β-carbon proton in active BMAA, however, shows an upfield shift of only 0.04. Since the same change is observed with an O-acetyl as with an N-acetyl, one is tempted to assign this effect to the shielding region of the acetyl carbonyl, which looks reasonable on the basis of models that were made of these structures. But until more is known of the anisotropy of the carbon-nitrogen and carbon-oxygen bonds, this can only be an educated guess, and I would certainly hesitate to base an assignment of configuration on it. On the other hand, the 0.13 upfield shift of the α-carbon proton in active BMAA where it is cis to the β-methyl is, at least qualitatively, what one would expect from the anisotropy of the β-carbon-to-methyl carbon bond, and an assignment of configuration could reasonably be made, I think, on this basis.

Yours sincerely,

R. E. Lundin

R. E. Lundin, Chemist
Fiber Physics Investigations
Wool and Mohair Laboratory

Dr. B.L. Shapiro
M.E.L.L.O.N.M.R.
Mellon Institute
4400 Fifth Avenue
Pittsburgh 13, Pennsylvania

May 23, 1961

Dear Dr. Shapiro:

We have recently found that selective broadening of absorption lines in the high resolution NMR spectra of molecules with a m.w. up to 600 can be used to determine the chemical groups preferentially stabilized by the formation of specific molecular complexes in solution. The line width at half height $2\Delta\nu_{1/2} = \frac{1}{\pi T_2}$ of the absorption peak attributable to a group of chemically equivalent protons in a solution free of paramagnetic species (including oxygen) is determined by the equation:

$$(1) \quad \left(\frac{1}{T_2}\right) = \left(\frac{1}{T_1}\right) = \left(\frac{1}{T_1}\right)_\rho + \left(\frac{1}{T_1}\right)_D + \left(\frac{1}{T_1}\right)_\sigma$$

where

$$(2a) \quad \left(\frac{1}{T_1}\right)_\rho = h^2\gamma_p^2\left(\frac{3}{2}\gamma_p^2 \sum_j r_{ij}^{-6}\tau_{\rho ij} + \gamma_f^{2*} \sum_f r_{if}^{-6}\tau_{\rho if}\right)$$

$$(2b) \quad \left(\frac{1}{T_1}\right)_D = h^2\gamma_p^2\left(\frac{3}{2}\gamma_p^2 \sum_K r_{iK}^{-6}\tau_{DiK} + \gamma_f^{2*} \sum_f r_{if}^{-6}\tau_{Df}\right)$$

$$(2c) \quad \left(\frac{1}{T_1}\right)_\sigma = \frac{2}{15}\gamma_i^2 H_0^2 (\Delta\sigma)^2 \tau_{\rho i}$$

All symbols having their usual significance (1), the subscripts ρ, D and σ referring to the rotational, translational, shielding anisotropy [and ~~paramagnetic~~] contributions to the relaxation rate, respectively.

Equations (2a) and (2b) are essentially similar to those of Gutowsky and Woessner (1,2), except that the correlation times are assumed to be different for different pairs of protons. Order of magnitude calculations show, that in the case of any proton which has a proton neighbor within 2-3Å (which is usual) (a) the linear relationship between $\left(\frac{1}{T}\right)$ and τ will hold as long as a high resolution spectrum is visible and (b) only the protons within this distance will make significant contributions to the relaxation rate. An additional term, representing quadrupolar relaxation (and the possibility of $T_1 \neq T_2$) is of importance only for protons in the immediate vicinity of an N^{14} atom. Its contribution to the relaxation rate can however be eliminated by a double resonance experiment. $\left(\frac{1}{T_1}\right)_\sigma$ can be evaluated from measurements at two field strengths H_0; eliminating solvent contributions to $\left(\frac{1}{T_1}\right)_D$ by using

deuterated (or other hydrogen-free) solvents and extrapolating $\frac{1}{\pi T_2}$ to infinite dilution to correct for intermolecular solute effects, it is possible to obtain a value for the intramolecular relaxation rate $\left(\frac{1}{T_1}\right)_\rho$. The evaluation of the rotational correlation times from (2a) is considerably simplified whenever, as is usually the case, a single correlation time governs the relaxation of each chemical group although not of the whole molecule. If in addition the interproton distances to nearest neighbors are not changed by complex formation, a selective increase in the relaxation rate of one group as compared to another can be directly interpreted in terms of a preferential stabilization of this group. Thus for two groups A and B

$$\left(\frac{1}{T_1}\right)_{\rho A} = K_A \tau_A \qquad\qquad \left(\frac{1}{T_1}\right)_{\rho B} = K_B \tau_B$$

$$\left(\frac{1}{T_1}\right)_{\rho A} = K_A \tau_A' \qquad\qquad \left(\frac{1}{T_1}\right)_{\rho B} = K_B \tau_B'$$

where K_A and K_B are numerical factors including the sum of interproton distances for the two groups, the primed values referring to measurements on the complex and unprimed to measurements on the free compound. The increase in line width is then directly proportional to the increase in the correlation times, so that if A is preferentially stabilized

$$\frac{\tau_A'}{\tau_A} \cdot \frac{\tau_B}{\tau_B'} > 1, \text{ and } \frac{T_{1A}}{T_{1A}'} \cdot \frac{T_{1B}'}{T_{1B}} > 1$$

In cases in which more than one correlation time or a change of interproton distances must be considered, a selective increase in the correlation time of a particular group can be determined from line width (or relaxation time) measurements on a series of deuterium-substituted analogs, using Eq (2), since the contribution of a deuteron to the relaxation rate is approximately 2% of that of a proton at an equivalent distance and with an equal correlation time.

The method outlined above was used to study the chemical groups involved in the binding of penicillin, streptomycin and oxytetracycline to serum albumen, and the complexing of epinephrine with different nucleotides. The case of epinephrine and adenosine triphosphate (ATP) is illustrated in Fig. (1).

$\left(\frac{1}{T_1}\right)_\rho$ of the CH_2-doublet and CH-triplet on the epinephrine side chain is increased by a factor of 4 as a result of complex formation, while $\left(\frac{1}{T_1}\right)_\rho$ of of the other lines increase by factors of not more than 1.5~2. The possibility of the broadening being a reflection of a change in N^{14}- quadrupolc relaxation was excluded by a double resonance experiment performed by Dr. J. Baldenschwieler. The selective broadening is not markedly pH dependent, but decreases with

increasing temperature with a transition temperature around $55^\circ C$. Since the proton spectrum of ATP is not affected, it appears likely that the complex formed has a structure of the type illustrated in Fig. (2).

Sincerely,

Oleg Jardetzky

OJ:jef

Ref. (1) J.A. Pople, W.G. Schneider and H.J. Bernstein, "High Resolution Nuclear Magnetic Resonance", McGraw-Hill, N.Y., 1959.

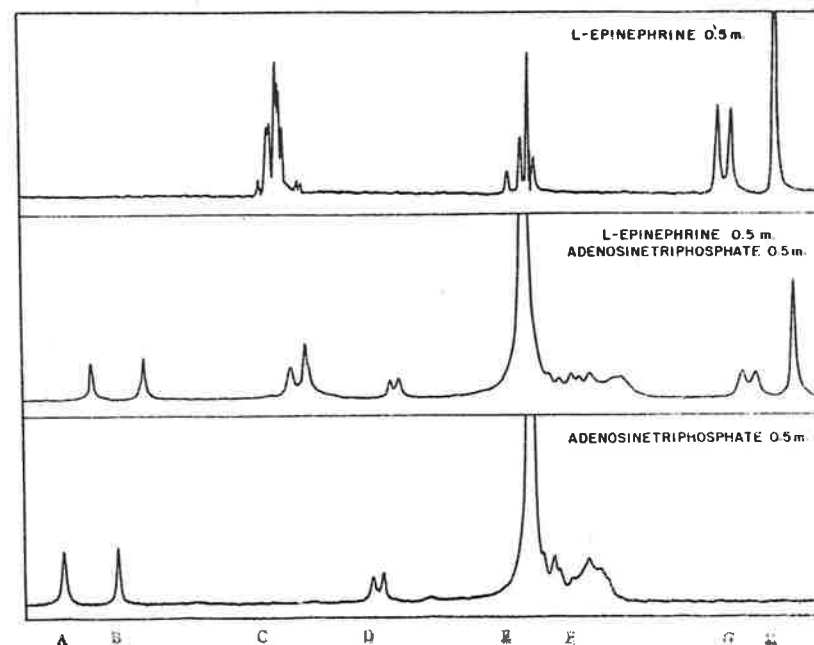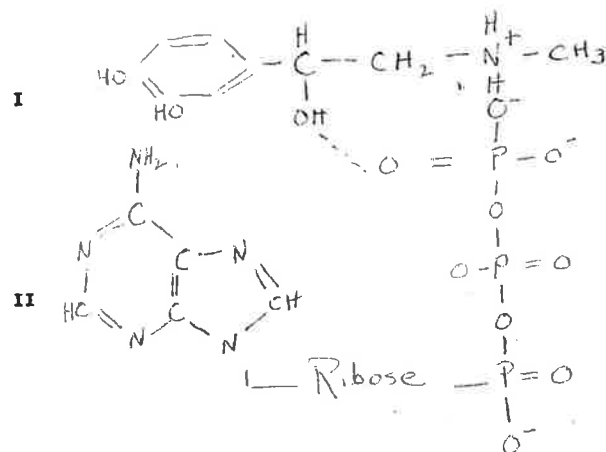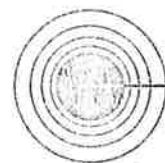(2) Gutowsky, H.S. and Woessner, D.H., Phys.Rev., 104:843 (1956).

Fig. 1 Peaks (H increasing from left to right) : A and B C_2 and C_8 of ATP purine, C epinephrine aromatic H, D C_1' of ATP ribose, E epinephrine CH triplet (and residual water peak), F $C_2' - C_5'$ of ATP ribose, G epinephrine CH_2 doublet, H epinephrine $N-CH_3$.

Fig. (2)

I

II

Epinephrine (I) – Adenosinetriphosphate (II) complex.

April 27, 1961

Dr. Bothner-By
Director of Research
Mellon Institute
4400 Fifth Avenue
Pittsburgh 13, Pa.
USA

Dear Dr. Bothner-By,

Back from a trip to England, I found the last 10 issues
of MELLON MR which you were so kind to send to our
laboratories. Since the literature on the NMR applications
is now undergoing a remarkable boom, it is a must for
every one concerned with it to be in possession of a
regular mean of communication like your MELLON MR letters.
I personally would be very glad to see it appear as an
official mean for quick publication in analogy to Tetra-
hedron letters in the field of organic chemistry and I
am persuaded that this possibility has been already taken
in consideration by you.

Meanwhile I would thus be very happy to be included in
the mailing list of MELLON MR and I am already working
on a little contribution from our laboratories.

Sincerely yours,

Attilio Melera
Research Chemist
VARIAN AG.

am:sj

UNIVERSITY OF CALIFORNIA

Bio-organic Chemistry Group
LAWRENCE RADIATION LABORATORY
BERKELEY 4, CALIFORNIA
1557 Life Sciences Building

May 24, 1961

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

Dear Dr. Bothner-By,

We are continuing work on the barrier heights to internal conversion, and the pathways open to such conversions in molecules of the type   where $x = O, S, Si$. To make the NMR spectra more

amenable to the usual rate analysis these molecules have been synthesized with methyl groups in the 3,3 and 6,6 positions. The methyl groups take axial and equatorial positions, and at low temperatures give a simple two line spectrum with a splitting of approximately 12 c/s.

The following table gives some of the numbers we have obtained so far:

	T_c	$\Delta E^\ddagger$	ν_0	$\Delta S^\ddagger$	$\Delta F^\ddagger$
	$^\circ K$	$\frac{Kcal}{mole}$	$sec.^{-1}$	e.u.	$\frac{Kcal}{mole}$
S-S	271	16.1	2.1×10^{14}	6.7	13.8
O-O	289	18.5	4.0×10^{16}	14.4	14.6

T_c is the temperature at which the axial and equatorial methyl peaks coalesce into one as the rate of interconversion becomes rapid. The other values come

from the usual equations: $k = \nu_0 \exp \frac{-\Delta E^\ddagger}{RT}$; $\nu_0 = K \frac{RT}{Nh} \exp \frac{+\Delta S^\ddagger}{R}$; the transmission coefficient, K, has been taken as one for the 1,2-dithiane, and as 1/2 for the 1,2-dioxane. The values of ν_0 and $\Delta S^\ddagger$ are, surprisingly, quite different for the two molecules. The difference can be explained qualitatively on the basis of two different interconversion pathways, I and II. As estimated from methylene
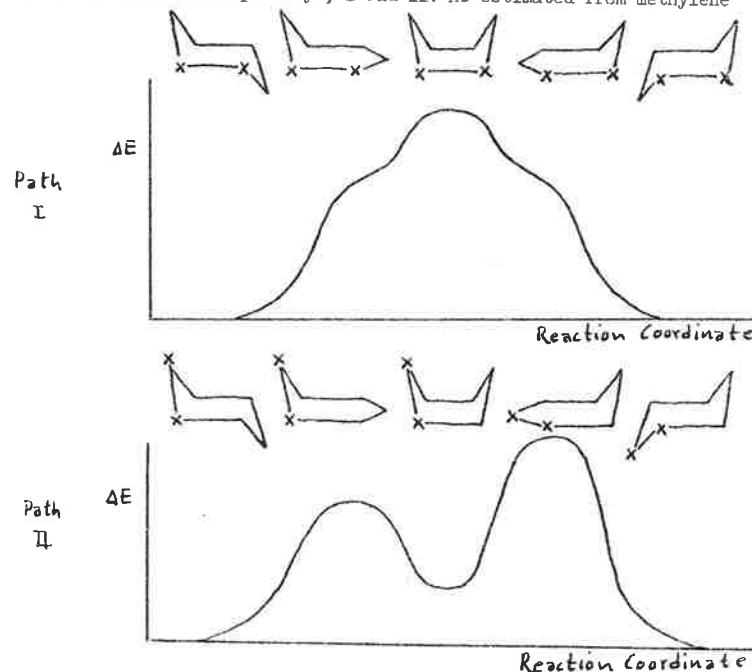
oppositions, and changes in both the ring-valence and the hetero-atom-dihedral angles, the maximum barrier height is greater in path II than in path I.

Molecular models indicate that if $x = S$, then both pathways are possible interconversion routes. Path I, with the lower barrier, is the more probable route.

If $x = O$, then the boat form of path I cannot be formed due to the interference of the methylene groups. Thus, the dioxane probably follows Path II. The models also indicate that the boat form of path II is highly flexible for the dioxane. This may account for the large $\Delta S^\ddagger$ term for this molecule.

We continue to find the newsletter stimulating.

Yours truly,

Gaylord Androes

Gaylord Androes

PURDUE UNIVERSITY
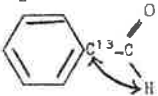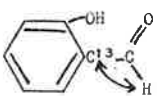DEPARTMENT OF CHEMISTRY
LAFAYETTE, INDIANA

May 15, 1961

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

Dear Aksel:

Thank you for your letter and for the monthly gift of M.E.L.L.O.N.M.R. Perhaps some of the readers of the newsletter will want to try to interpret some data which ought to be significant but which at the moment appears merely puzzling.

As can be seen from Jim Shoolery's contribution in M.E.L.L.O.N.M.R. number 11, p. 8, it is sometimes possible to observe coupling between a C^{13} nucleus and a proton in the group $C^{13}-C^{12}-H$. Shoolery's results for methyl-acetylene are included in our table below. In order to test whether the J-values could be correlated with either the C-C-H bond angle or the C-C bond order, we have attempted to measure analogous couplings in the proton spectra of other compounds containing C^{13} in natural abundance.

We found the following:

Molecule	$J_{C^{13}-C^{12}-H}$	
$H-C\equiv C^{13}-CH_3$	10.6 c/sec	(Shoolery)
$N\equiv C^{13}-CH_3$	27 c/sec	
$H-C\equiv C^{13}-CH_3$	50.8 c/sec	(Shoolery)
$H-C\equiv C^{13}-C_6H_5$	50 c/sec	
$\begin{matrix} H_2C \\ | \quad C^{13}-H_2 \\ H_2C \end{matrix}$	16 c/sec	
phenyl $C^{13}-C$(=O)H	24 c/sec	
(OH)phenyl $C^{13}-C$(=O)H	22 c/sec	
$Cl_3\ C^{13}-C$(=O)H	46 c/sec	

Because of the intense signal from the normal isotopic species, we can only see "distant C^{13} sidebands" when J is larger than perhaps 15 c/sec. Among the compounds for which we would not find $C^{13}-C^{12}-H$ couplings because J is apparently too small were acetone, acetic acid, ethylene, tetramethyl ethylene and neopentane.

We hope to get more related data, but these few values seem already to rule out most of the simple "explanations" which might appear plausible.

Several of the measurements were made by Don Pritchard when he was here. It is with deep regret that I must add that Don died last September, just a few months after completing his graduate work here.

With best regards,

Norbert Muller

NM:lb