Monthly
Ecumenical
Letters from
Laboratories
Of
N-M-R

No. 7

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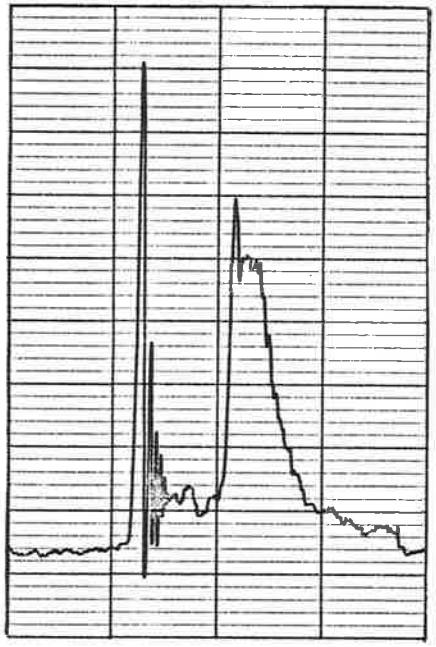
We would like to remind recipients of M.E.L.L.O.N.M.R. of the condition on public quotation of items appearing in the Newsletter as set forth in issue No. 1, viz.,

> " It is understood that appearance of material in this letter will be construed in no way to constitute official publication. Material appearing in this letter is to be solely for the readers' personal use, and quotation of results is to be made only by direct arrangement with the originators of the work."

Leon Mandell and Jake Goldstein of Emory University have informed us of a convenient purification of commercial tetramethylsilane (cf., Wiberg in M.E.L.L.O.N.M.R. No. 5, page 6). This consists in shaking the tetramethylsilane with concentrated sulfuric acid and then distilling from the mixture into an ice-cooled receiver. For the distillation, an all glass system and a warm water heating bath is used. The distillate shows no CH_3-CH_2-X lines in its 40 mc. spectrum.

AAB BLS



The above spectrum is that of the aromatic hydrogens in a degassed mixture of ~ 15% benzene and ~ 85% toluene obtained at 60 mc., with a sweep rate of 0.2 cps/sec. The sharp line on the left arises from benzene and the multiplet on the right from the toluene aromatic hydrogens. The structure and width of the toluene aromatic "line" was quite reproducible; Paul Lauterbur reports similar observations at 40 mc. In view of the asymmetric character and complicated nature of the toluene "line", it would seem mandatory to remove it from the list of acceptable reference signals.

AAB BLS

A Relationship Between Chemical Shifts and Substituent Constants

(An extended footnote to Figure 16 of "Some Applications of C^{13} Nuclear Magnetic Resonance Spectra to Organic Chemistry," Annals N. Y. Acad. Sci. 70 (4), 841 (1958).)

It has been brought to my attention that the above-mentioned figure is more mystifying than informative. This is true. In fact, it represents a good example of how not to introduce an idea into the literature. The missing justification is given below, pending its possible inclusion in a more detailed discussion of the C^{13} spectra of aromatic compounds.

First, a partial review of the situation is presented. It has been found that the ortho-shifts in the fluorobenzenes cannot be correlated by the Hammett σ parameter (1) or by the separated σ_I and σ_R parameters (2). The methyl C^{13} shifts are similarly anomalous. The implication is that in both series of compounds large proximity effects are present. The carbon and fluorine shifts are compared in Figure 1. They seem to be roughly proportional, but the relationship is not very good. It will be noted, however, that the points for groups which are electron-withdrawing by resonance interaction (positive σ_R) tend to lie in the upper left part of the graph, and those which are electron-releasing by resonance interaction (negative σ_R) tend to lie in the lower right portion. This suggests that the scatter of the points might be caused by the different susceptibilities of the methyl group and fluorine atom to resonance effects. In order to put this idea on a more quantitative basis, consider the following derivation.

Let us first assume that the shifts in these compounds can be separated into inductive, resonance, and "neighbor" contributions as shown in Equations (1) and (2).

$$(1) \qquad \delta_O^C = \delta_I^C + \delta_R^C + \delta_N^C$$

$$(2) \qquad \delta_O^F = \delta_I^F + \delta_R^F + \delta_N^F$$

Now, let us further assume that the δ_i^M can be represented as $m_i \sigma_i$, giving Equations (3) and (4).

$$(3) \qquad \delta_O^C = c_I\sigma_I + c_R\sigma_R + c_N\sigma_N$$

$$(4) \qquad \delta_O^F = f_I\sigma_I + f_R\sigma_R + f_N\sigma_N$$

The coefficients are those for ortho-interactions, and are not necessarily the same as those for meta- and para-interactions, but the additional subscript is omitted for simplicity. The σ_I and σ_R are Taft's separated substituent constants,

and σ_N is an analogous constant for the special effect of an ortho-substituent. We may now rearrange (4) into

$$\sigma_I = \frac{1}{f_I}\left(\delta_O^F - f_R\sigma_R - f_N\sigma_N\right) \qquad (5)$$

and then eliminate σ_I by substituting (5) into (3), giving

$$\delta_O^C = \frac{c_I}{f_I}\left(\delta_O^F - f_R\sigma_R - f_N\sigma_N\right) + c_R\sigma_R + c_N\sigma_N \qquad (6)$$

which can be rearranged to

$$\delta_O^C = \frac{c_I}{f_I}\left[\delta_O^F + \left(\frac{c_R f_I}{c_I} - f_R\right)\sigma_R\right] + \left(c_N - \frac{c_I f_N}{f_I}\right)\sigma_N \qquad (7)$$

This is the equation of a straight line of the form

$$\delta_O^C = m(\delta_O^F + a\sigma_R) + b \qquad (8)$$

if b is a constant. In order to test the validity of (8) we must have a value for "a". If we assume that "b" is a constant, we can calculate "a" by solution of the three simultaneous equations derived from (8) for any three substituents. The best value is found to be about 23. Figure 2 shows that all but two of the nine basic points fall on a straight line within experimental error. (This Figure is entirely equivalent to the original Figure 16, as can be seen by rearranging Eq. (8). The points are more evenly placed when the new form of the equation is used.) The exceptions are the hydrogen and iodine points. The latter falls somewhat low, possibly because of a much stronger steric effect on the methyl group. The point marked "I(m-CH_3)" is for 2,6-dimethyliodobenzene and appears to demonstrate a "buttressing" effect by the other methyl group on the iodine. The normal effect of a m-CH_3 can account for only about one-fifth of the shift difference.

The failure of the line to pass through the hydrogen point means that "b" is not zero, but has a small nearly constant value of about 2 ppm. This implies that the percentage variation in σ_N for different substituents is rather small. Since the scatter about the straight line is less than 1 ppm., this variation is less than 50%. The fact that the ortho-shifts themselves cannot be correlated at all well by an equation of the form

$$\delta_O = \alpha\sigma_I + \beta\sigma_R \qquad (9)$$

means that the additional effects, which have been lumped under σ_N, must be quite large. The small size of "a" then requires that the coefficient $\left(c_N - \frac{c_I f_N}{f_I}\right)$ be small. This seems reasonable, since it can be rearranged as follows.

$$c_N - \frac{c_I f_N}{f_I} = f_N\left(\frac{c_N}{f_N} - \frac{c_I}{f_I}\right) \qquad (10)$$

If the relative susceptibilities of methyl groups and fluorine atoms to inductive effects and neighbor effects are about the same, the term in the parentheses will be small. We may think of the inductive effect as a polarization of the atom or group in the direction of the ring, and of the neighbor effect as a similar polarization at about a 60° angle to that direction. The two effects might well be nearly proportional to one another for groups of similar symmetry, such as methyl and fluorine.

We can make our estimate of the sign and magnitude of "a" as follows. From (7) we see that the slope "m" is c_I/f_I. The coefficient of σ_R is, therefore, given by

$$a = \frac{c_R}{m} - f_R \qquad (11)$$

Taft gives a value of f_R for the para position of -18.8 (in our units). If we assume that the resonance interactions are about the same at ortho and para positions, and insert the value of m = (0.305) from our plot, we have

$$a \simeq 3.28\, c_R + 18.8 \qquad (12)$$

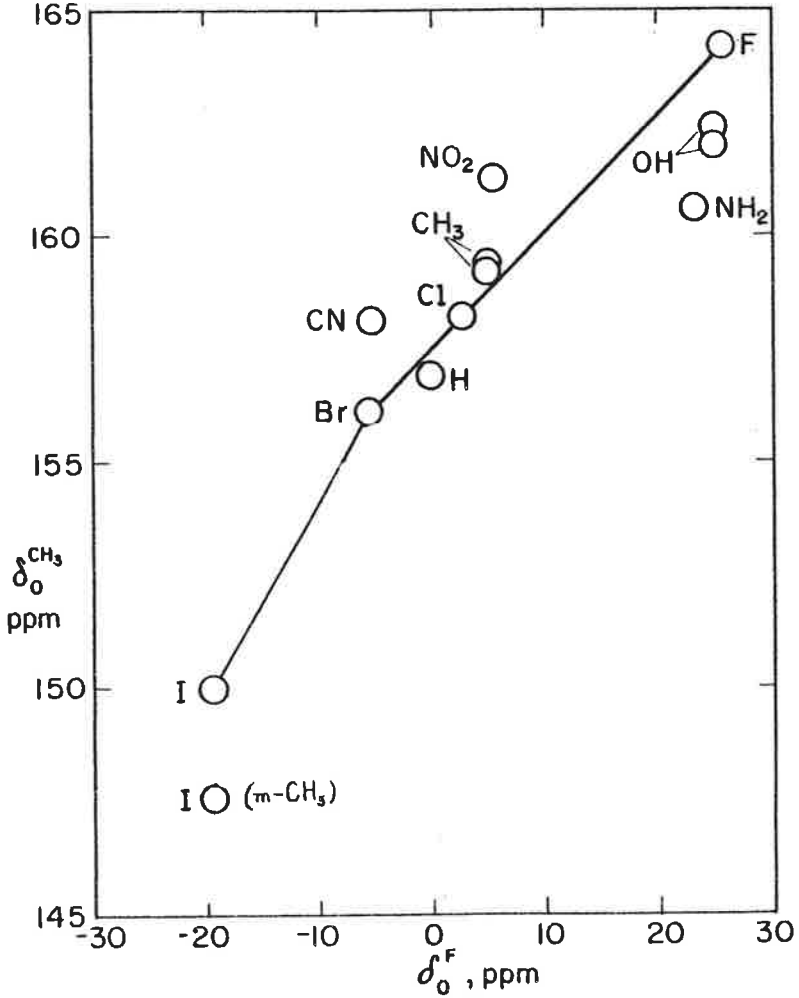
If c_R, the resonance coefficient for the methyl shifts, is small we have a value of about 18 for "a", compared with the experimental value of 23. The sign of the coefficient is correct and its size is about right.

The success of the treatment outlined above would seem to be further evidence for the usefulness of Taft's separation of the substituent constants, and suggests that proximity effects are rather well behaved in unreacting molecules.

(1) H. S. Gutowsky, D. W. McCall, B. R. McGowey and L. H. Mayer, J. Am. Chem. Soc. 74, 4809 (1952).

(2) R. W. Taft, Jr., J. Am. Chem. Soc. 79, 1045 (1957).

Paul C. Lauterbur
Mellon Institute



METHYL C^{13} SHIFTS IN ORTHO-SUBSTITUTED TOLUENES VS F^{19} SHIFTS IN ORTHO-SUBSTITUTED FLUOROBENZENES

Figure 1.

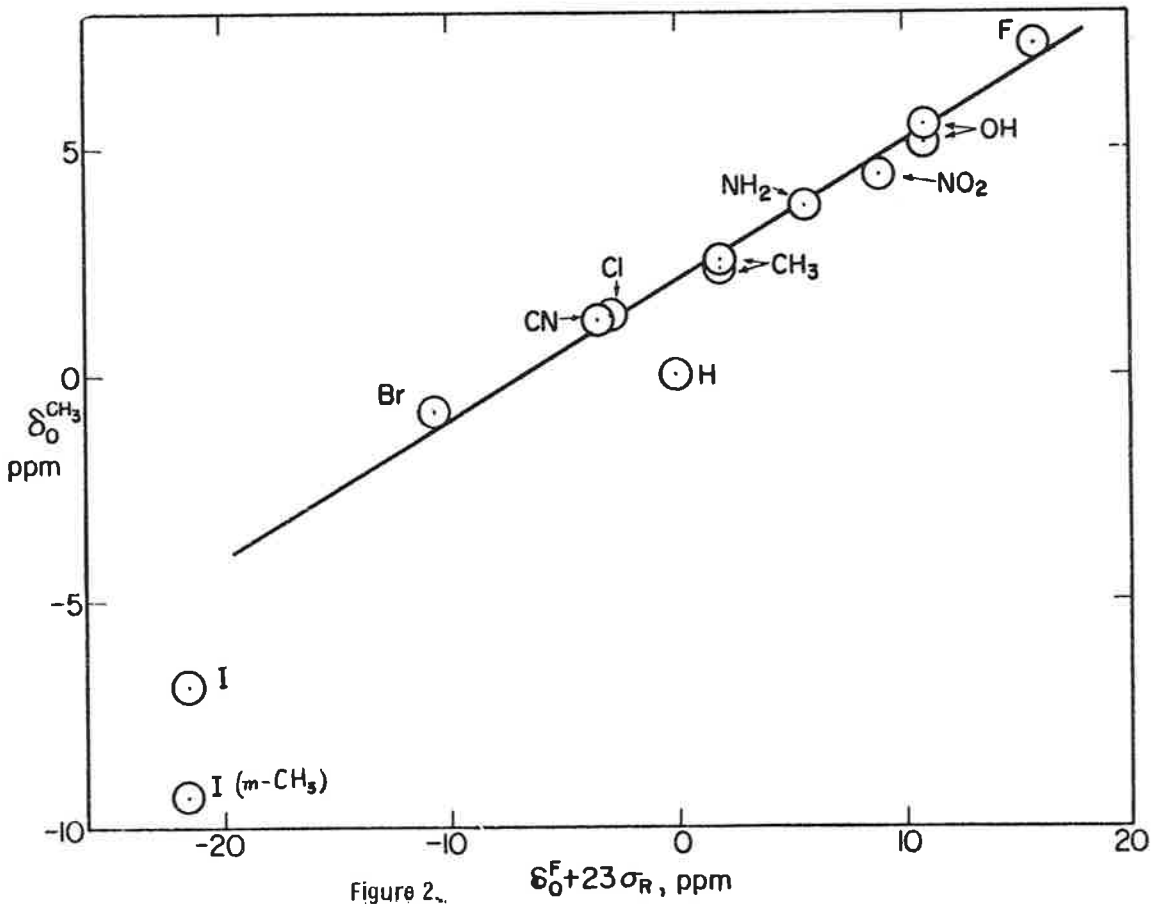


Figure 2.

METHYL C^{13} SHIFTS IN ORTHO-SUBSTITUTED TOLUENES VS. ADJUSTED F^{19} SHIFTS IN ORTHO-SUBSTITUTED FLUOROBENZENES

Laboratorium
für organische Chemie
Eidg. Technische Hochschule
Zürich

ZÜRICH, April 21st, 1959
Universitätstr. 6

Dr. A. Bothner-by,
Mellon Institute,
4400, Fifth Avenue,
Pittsburgh,
Pennsylvania,
U. S. A.

Dear Aksel,

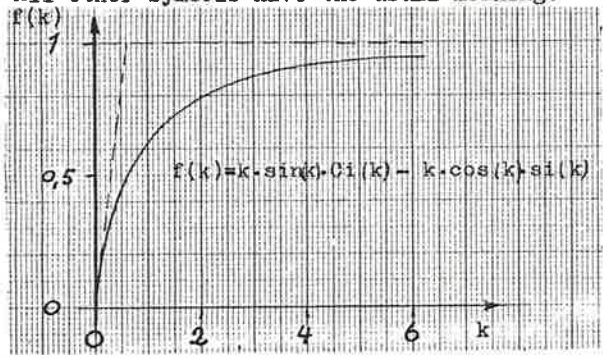
In his recent book J.D.Roberts mentions some difficulties with the integration of nmr spectra arising from very different relaxation times of the various nuclei in a molecule. If the relaxation time T_1 is very long (e.g. 30 sec.) than it will be of course somewhat difficult to perform a quasi-stationary experiment. But by no means it is necessary to work under quasi-stationary conditions to get very exact integral values. Supposing the correctness of the classical Bloch equations one can find the following expression for the integral of the absorption-mode v(t).

$$\int_{-\infty}^{\infty} v(t)dt = \tilde{x}\,\frac{|\gamma|\cdot B_1\, M_o}{a}\left\{1 - \frac{s}{2}\cdot f(k) + O(B_1{}^4)\right\} \quad (1)$$

B_1 = amplitude of the high frequency field
s = $(\gamma B_1)^2 T_1 T_2$ (adiabatic saturation parameter)
k = $2/aT_1T_2$
a = velocity of the linear sweep (B_o = const. + at)

$$f(k) = k\left\{\sin(k).Ci(k) - \cos(k).si(k)\right\} \quad (2)$$

All other symbols have the usual meaning.



Using a high sweep rate the integration error $\varepsilon = \frac{1}{2}\,s.f(k)$ becomes therefore asymptotically independent of the relaxation times T_1 and T_2.

$$\lim_{a\to\infty} \varepsilon = \frac{\tilde{x}}{2}(\gamma B_1)^2/a \quad (3)$$

Increasing the sweep rate a and holding all other parameters constant would not be the proper solution of course, since this would make worse the signal-to-noise ratic of the integrated spectrum. It is well known and can also be seen from eq. (3) that, if one increases the sweep rate over the quasi-stationary conditions ($aT_2{}^2 \ll 1$), one can also increase the strength of the rf-field B_1, Working out the expression for the signal-to-noise ratio, R, one gets

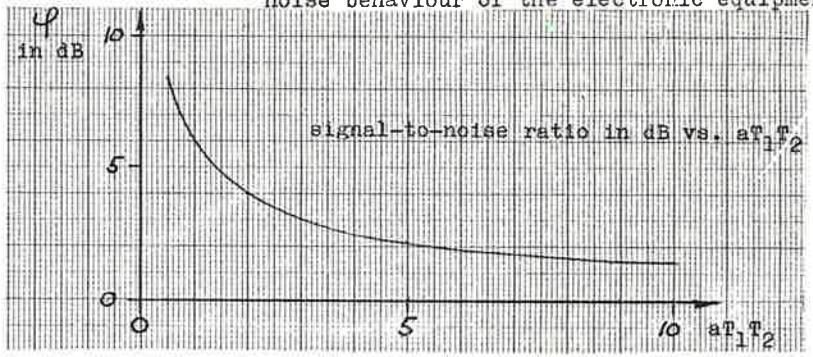
$$R = \text{const.}\ \frac{\varepsilon}{\Omega}\,\varphi(aT_1T_2) \quad \text{(power ratio)} \quad (4)$$

with

$$\int_{-\infty}^{\infty} v(t)dt = \frac{\tilde{x}|\gamma|B_1\, M_o}{a}(1-\varepsilon) \quad (5)$$

Ω = length of the whole spectrum in sec^{-1}

const. = only dependent on the probe and on the noise behaviour of the electronic equipment



Because of the limitation of the stability of the magnetic field it is often not recommendable to work with a sweep rate essentially slower than $aT_1T_2 = 1$. The loss of signal power by sweeping faster than quasi-stationarily is not very severe. Therefore, if you like the best possible integrated spectra, you have to proceed as follows:

1. Choose the required integration error ε (say 1 %).
2. Choose the slowest possible sweep rate on your spectrometer, so that the field fluctuations are in accordance with your integration error (a too rapid sweep rate spoils the signal-to-noise ratio and the resolution).
3. Choose the highest possible strength of the rf-field "without saturation". Halve the strength of the rf-field

and check whether the saturation is in accordance with the chosen integration error ε .

Supposing that the rest of the equipment is appropriate for integration (fine linearity of the electronic equipment; good zero stability of the output - preferably some modulation method - ; very pure absorption mode; preferably electronic integration), it should be possible to get very exact integral values in the nmr-spectroscopy of any substance.

As soon as we have a pure sample of cyclobutene we will send you an integrated spectrum. I am quite shure that the intensities will be exactly as 2 : 1 and not (as quoted in J.D. Roberts' book) 2,8 : 1.

Sincerely yours

Hans Primas

Hans Primas.

VARIAN associates

611 HANSEN WAY • PALO ALTO, CALIFORNIA • DAVENPORT 6-4000

April 7, 1959

Drs. A. A. Bothner-by and B. ~~X.~~ L. Shapiro
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Dear Aksel and Barry:

After lengthy consideration of the pros and cons of the matter, I have finally concluded that the ordinary δ symbol for chemical shift does not carry enough information to satisfy me and, rather reluctantly, I have experimented with some compound symbol notations. I thought that it might be worth describing this in MELLONMR in order to get some reactions to it.

One superscript and one subscript do not seem to me to be too unwieldy, in spite of George Tier's comments in MELLONMR No. 4 to the effect that some chemists will not take kindly to such notation. This is probably true; however, there are other chemists who do not enjoy being left in a confused state trying to figure what kind of δ is being referred to and perhaps these two groups will just about cancel out.

Although no "standard" state has been defined in NMR work, it seems to me that there is general willingness to accept a dilute CCl_4 solution (or better, an extrapolation to infinite dilution) as a satisfactory substitute. The standard state is usually designated with a superscript ^{o}; therefore, I would propose that measurements in sufficiently dilute CCl_4 solution be written as δ^o. Two other possibilities also exist; first, that the reference is added in small quantity to the neat sample. I would then propose δ^{int}. Finally, a capillary or concentric cell might be used, leading to the symbol δ^{ext}.

The subscript poses more of a problem. It is rather attractive to go mathematical and consider the sample as consisting of 1, 2, 3 ..... i sets of non-equivalent nuclei and to denote the chemical shift of the i^{th} set as δ_i^o in very dilute CCl_4. We are then left with describing the reference which we do by placing it in following parentheses, i.e., δ_i^o ($SiMe_4$). However, when we begin to use the symbol we find that the compact subscript i must often be replaced by some unwieldy description, e.g., "the CH_2 group next to the carbonyl in the 7-membered ring" unless we have had the foresight to number all of the carbon atoms and draw a nice little picture nearby (which might not be a bad idea).

An alternative scheme is to put the reference as subscript since it is always fairly easy to write and to save the description of the compound for parentheses where there is plenty of room. Then the shielding of the i^{th} nucleus relative to benzene in an annular cell would be written $\delta^{ext}_{C_6H_6}$ (i). Some people might prefer this.

I am bringing this matter up since I have found that in writing material for inclusion in a book on the subject it is rather frustrating to try to develop a system of notation without knowing whether or not it would be generally acceptable. I do not feel that a book is the place to advance such ideas but that instead it should adopt the most widely accepted system. But if we don't get some general agreement soon there will be no choice. I would appreciate any and all views on (a) the acceptability of such a compound symbol (b) which form is preferable (c) other better ideas.

It is perhaps worth mentioning two other points. First, in my humble opinion the term "chemical shift" is too good for either δ^{int} or δ^{ext} and ought to be reserved for δ^o, the others perhaps called "relative

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shielding". Measurements of δ^o seem to be about as close as we can come to just the intramolecular part of the shielding (allowing a constant effect due to the CCl_4 environment). The second point has to do with the sign of the shielding difference. I sense that the majority (but certainly not all) of workers prefer that this number increase as the applied sweep field increases (perhaps mainly through force of habit). This can be accomplished by defining

$$\delta_i^j = 10^6 \, (H_i^j - H_{ref}^j)/H_{ref}^j \quad \text{where} \quad j = o, \text{int, or ext}$$

and where the factor 10^6 has been chosen arbitrarily again to conform to what I believe is most generally used. It is interesting to note that we can then write

$$\tau_i = 10.00 + \delta_i^j \, (SiMe_4) \quad \text{with} \quad j = o \text{ or int.}$$

Whether or not a compound δ symbol is needed badly enough to justify its existence, and assuming it is, whether an additional symbol, τ, is needed in view of its simple relationship to δ_i^j are questions that only the mass of NMR spectroscopists can answer.

If this is too long for MELLONMR I apologize.

Sincerely yours,

J. N. Shoolery

JNS:mjr

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April 27, 1959

Open Reply to Letter from J. N. Shoolery

Dr. J. N. Shoolery
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Dear Jim:

Thank you very much for your thoughtful letter on symbols and referencing. We feel very much in agreement with the views you have expressed, and have arrived at a number of the same conclusions.

One of the difficulties we have experienced is keeping clearly in mind the operational definitions of our own measurements taken under a variety of conditions, let alone everyone else's. In attempting to develop a notation which would define clearly and unmistakeably exactly what was being measured, we have evolved the following scheme which we would like to present for discussion and criticism along with yours.

Firstly, we would like to point out the necessity for distinguishing between the experimental data, i.e., separations between the individual lines observed in a given spectrum, and the mathematical construct "chemical shift" which is an end result of the application of certain computational procedures to the raw data. It would seem to us highly desirable to have spectral reports include the observed line positions (in cps at a particular, designated R.F.) as well as assignments made from these data.*

We suggest a notation using the symbol ν for experimentally-measured separations given in cycles per second and δ for the calculated chemical shifts given in parts per million.

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* An analogous system is of course almost universally used when reporting infra-red spectra. In this case absorption maxima are reported as raw data, and any assignments as to group absorptions, force constants, and structure are reported separately.

In order to specify completely the referencing system it is necessary to state explicitly the following data:

1) The identity of the compound and of the group of nuclei giving rise to the signal observed.

2) The physical state of the sample.

3) The identity of the reference and of the group of nuclei therein giving rise to the reference signal, and

4) The physical state of the reference.

As a possible means of representing the measurements, we therefore define the symbol $\nu^{k}_{i(j)}$ as the separation (in cps) of a signal arising from the jth group of nuclei in compound i in a medium of composition k, from any arbitrary (not necessarily stated) external reference. Experimental separations are always represented as a difference between two such symbols. For example,

$$\nu^{C_6H_6}_{C_6H_6} - \nu^{CHCl_3}_{CHCl_3}$$

would represent the separation between signals from pure benzene and pure chloroform measured externally,

$$\nu^{CCl_4}_{C_6H_6} - \nu^{CCl_4}_{Me_4Si}$$

would represent the separation between benzene and tetramethylsilane both at infinite dilution in carbon tetrachloride* and

$$\nu^{C_6H_6,Me_4Si}_{C_6H_6} - \nu^{C_6H_6,Me_4Si}_{Me_4Si}$$

would represent the separation between the signals from benzene and tetramethylsilane used as an internal reference. In the latter case, the concentration of the internal reference should also be specified.

---

* Tiers has shown that if both sample and reference are in the same physical state (say infinite dilution in carbon tetrachloride) it does not make any difference if they are mixed or separated by concentric cell walls or capillary walls.

The same system of superscripts and subscripts can be applied to δ

Use of superscript "o" for standard state is fine, provided everybody agrees on a standard state. We would like to hope that it will eventually be possible to correct to δ_i^{gas} or δ_i^{vacuum} for all substances, in which case the latter might take over as δ_i^o standard state.

To use such a symbol pair routinely could be quite awkward and repetitive. The problem might be solved by defining a γ or a δ once in terms of these symbols, and then using that in the body of a paper or report. The sign convention must also be given; like most others we are now quite accustomed to having numbers increase with shielding, and suggest that that practice be followed both for γ and for δ.

Once again, thank you for your stimulating letter.

Sincerely yours,

Aksel A. Bothner-By

Paul C. Lauterbur

B. L. Shapiro