Some Applications of a Benzenoid Proton Chemical Shift Rule

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Proton magnetic resonance spectra of $1,3\text{-}C_6H_4(NO_2)Br$, $1,3\text{-}C_6H_4(NH_2)Cl$, $1,4\text{-}C_6H_4(NH_2)Cl$, $1,2,4,6\text{-}C_2H_2(NH_2)DFD$, and $1,2,4\text{-}C_6H_3(NH_2)DF$ have been recorded on a Varian A60 spectrometer (resonance frequency 60 Mc/s). It is shown how the use of an empirical rule on benzenoid proton chemical shifts helps considerably in an inspectional assignment which may be sufficient in itself, or may be desirable in connection with a rigorous mathematical analysis.

Since precalculation of proton chemical shifts, δ, relative to some chosen standard is practically impossible, the existence of empirical rules, such as Shoolery's rule[1] for CH_2-protons, is of importance. Rules for *benzenoid protons* have also been suggested. Recently, Diehl[2] has reviewed the pertinent literature, and he also contributed by fresh experiments. As stressed by Diehl, observation of benzenoid proton chemical shifts must be carried out on dilute solutions in a magnetically inert solvent such as cyclohexane (in contrast to aromatic solvents), if regularities are to be disclosed.

The law for benzenoid protons[2] may be exemplified as follows.

Suppose that precalculated values for the protons in the compound $1,3\text{-}C_6H_4XY$ are wanted. Suppose that we know the δ's for *ortho*, *meta*, and *para* protons in C_6H_5X and C_6H_5Y. Then the desired precalculation takes place following the scheme indicated in Fig. 1.

In order for the rule to be valid, no pair of substituents may be *ortho* to one another. The rule is, therefore, applicable only to *meta* and *para* di-substituted benzenes, and to 1,3,5 trisubstituted benzenes.
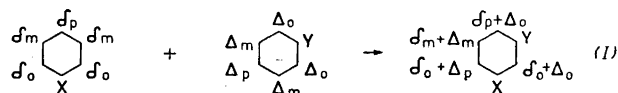

$$ \text{(1)} $$

Fig. 1. Calculation of proton chemical shifts in poly-substituted benzenes from data for mono-substituted benzenes.

Table 1. Proton chemical shifts (δ_o, δ_m, δ_p) of compounds C_6H_5X (5 mole % solution in cyclohexane) in c/s relative to the protons of benzene (5 mole % solution in cyclohexane) as found Spiesecke and Schneider [4], and by Diehl [2].

| | Spiesecke and Schneider | | | Diehl | | |
X	δ_o	δ_m	δ_p	δ_o	δ_m	δ_p
F	18.5	1.4	13.0	15.0	0.6	—
Cl	− 1.2	1.5	7.0	− 3.0	3.6	7.8
Br	−13.4	5.1	1.8	−13.2	6.6	3.6
I	−24.0	15.0	2.0	−24.6	13.2	—
OCH_3	26.0	2.4	22.0	25.2	6.0	19.8
NH_2	45.3	12.2	37.5	40.8	13.2	—
$N(CH_3)_2$	36.0	6.0	36.9	—	—	—
CHO	−34.8	−12.8	−16.5	—	—	—
NO_2	−56.9	−12.5	−20.0	−58.8	−12.6	—

Diehl [2] found the δ's by an indirect procedure, studying *meta* and *para* benzene derivatives. The δ's are, of course, also accessible through a direct investigation of C_6H_5X-compounds, but since most benzenoid protons absorb within a 1.5—2.0 p.p.m. range (or 100 c/s at 14 100 Ørsted) the spin-spin coupling constants ($J_{o.o} \sim 10$; $J_{o,m} \sim 3$; $J_{o,p} \sim 1$ c/s) may often be of the order of the δ-differences. When this happens, a complicated pattern arises which is hard to analyze. An *experimental* solution of this difficulty is the use of deuterated species [3,4] since the deuteron-proton spin-spin coupling is only about 1/6 of a corresponding proton-proton coupling. Spiesecke and Schneider [4] have applied this technique. In Table 1 their "direct" results are being compared with Diehl's indirectly derived δ's.

The discrepanices probably reflect the approximate validity of rule (I). We shall demonstrate by means of examples how useful the data of Table 1 are when analysing NMR-spectra of aromatic compounds of the types 1,3-C_6H_4XY, 1,4-C_6H_4XY (X may equal Y), and 1,3,5-C_6H_3XYZ (X, Y and Z may be identical).

EXPERIMENTAL

The instrument applied was a Varian A60 instrument. All solutions investigated were 5 mole % solutions in cyclohexane with an added amount of 5 % tetramethylsilane (TMS). All resonance frequencies of this paper are given in c/s, as measured relative to the internal TMS-standard. The benzene protons absorb at 432 c/s. The δ-value given for a certain type of proton, absorbing at x c/s, is the number $432 - x$.

In order to check our experimental procedure against Diehl's we ran samples of 1,4-difluorobenzene, 1,4-dichlorobenzene, and 1,4-dibromobenzene. No interpretational difficulties exist for these spectra. We found, respectively, $\delta = 19.0$ (Spiesecke and Schneider's data; rule (I) 19.9); $\delta = 3.0$ (0.3); $\delta = −2.0$ (−8.3). We are unable to explain the discrepancies, which, however, for the present purpose are less important.

1,3-$C_6H_4(NO_2)Br$

' The NMR-spectrum of 1,3-$C_6H_4(NO_2)Br$ is representative of a *simple* type of 1,3-C_6H_4XY spectrum. It has lines at 430.0 (4) *, 438.1 (12) *, 446.2 (9) *, 458.1 (6), 459.4 (8), 459.9 (8), 461.2 (7), 466.0 (3), 467.4 (4), 467.9 (5), 469.3 (4), 479.8 (5), 481.2 (5), 482.0 (7), 483.3 (6), 488.0 (3), 489.2 (4), 490.1 (6), 491.5

Table 2. Calculated and experimental proton chemical shifts of 1,3-$C_6H_4(NO_2)$Br (5 mole % in cyclohexane) in c/s relative to benzene. Resonance frequency 60 Mc/s. Spin-spin couplings in c/s.

	δ_2	δ_4	δ_5	δ_6
Calculated from rule (I) *	−70.3	−33.4	−7.4	−55.1
Found in this investigation	−66.4	−31.6	−6.0	−53.6
Deviations (numerical)	3.9	1.8	1.4	1.5

$J_{45} = 8.0-8.1$; $J_{56} = 8.1$; $J_{24} = 1.85-2.15$; $J_{26} = 2.15$; $J_{46} = 1.3-1.4$; $J_{25} \sim 0.3$.

* Using Spiesecke and Schneider's δ's.

(5), 496.4 (8) *, 498.4 (12) *, and 500.7 (6) *. The number in parenthesis following the frequency is the peak intensity on an arbitrary scale. Lines marked with * are doublets with a doublet separation of about 0.3 c/s.

Table 2 gives the data resulting almost by inspection of the spectrum.

1,3-$C_6H_4(NH_2)$Cl

The NMR-spectrum of 1,3-$C_6H_4(NH_2)$Cl is representative of a more complex type of 1,3-C_6H_4XY spectrum. From rule (I), with Spiesecke and Schneider's data, one calculates $\delta_2 = 44.1$; $\delta_4 = 36.3$; $\delta_5 = 13.7$; $\delta_6 = 52.3$. No calculated δ-difference is, therefore, smaller than 8 c/s. Using the estimate $J_{o,o} \sim 10$ c/s we get that $J_{45}/(\delta_5-\delta_4) = 10/22$, $J_{56}/(\delta_6-\delta_5) = 10/38$. Since the occurring J's are all smaller than the occurring δ-differences there is a hope that a reasonable estimate of the J's and the δ's may be made by inspection.

The observed spectrum has lines at 374.2 (3), 375.8 (5), 376.2 (6), 377.9 (5.5), 381.9 (3.5), 383.2 (4.5), 384.1 (7), 385.5 (7.5), 388.0 (5), 388.6 (6), 389.9 (9), 390.5 (10.5), 391.0 (9.5), 392.0 (9.5), 392.9 (11), 399.2 (8), 400.7 (8), 401.2 (8), 402.6 (5.5), 408.5 (8), 409.0 (8), 416.2 (8), 416.9 (8.5), 424.0 (2.5), 424.6 (2.5).

Since the predicted δ_6 equals 52.3, the H(6)-lines are grouped around 432−52 = 380 c/s. This suggests that the octet 374.2−385.5 are "H(6)"-lines. The 8 observed lines are very symmetrically spaced around 379.9 c/s. This would mean $\delta_6 = 52.1$ as compared to 52.3 from rule (I). H(6) couples strongly to H(5), weaker to H(4), and H(2). Thus $J_{65} > J_{64}$ and J_{62}, while $J_{64} \gtrless J_{62}$. This interpretation means that $J_{65} = 7.7$; $J_{64} = 2.15$; $J_{62} = 1.5$, where the values for J_{64} and J_{62} may be interchanged.

As $\delta_5 \sim 14$ (from rule (I)), the H(5) resonances must be located around 418 c/s. The lines could be doublets due to *para* coupling to H(2). Indeed, the three observed doublets at 408.5−409.0; 416.2−416.9; 424.0−424.6 fit this description. The H(4) and H(6) protons cannot exibit such doubling, their *para* positions being occupied by NH_2 and Cl.

From its measured position the doublet at 400.7−401.2 must then be the remaining 2 lines of the expected H(5)-octet. Since $J_{65} = J_{56}$ we get a check on the magnitude of J_{65} from the assigned H(5)-lines mentioned. One finds

$J_{56} = 7.8$ in good agreement with $J_{65} = 7.7$ above. Then, J_{54} must equal 15.5 c/s. Finally, $\delta_5 = 19.4$, as compared to 13.7 from rule (I). This discrepancy is not alarming in view of the somewhat over-simplified procedure applied as evidenced by the intensity difference between, for example, the 424.0 (2.5)—424.6 (2.5) doublet, and the 416.2 (8)—416.9 (8.5) doublet. Obviously, the coupling constant $J_{25} \sim 0.5$ c/s.

According to rule (I), the H(4) resonances should be located around $432-36 = 396$, the H(2) resonances around $432-44 = 388$ c/s. Hence, their resonances must merge. The H(2) proton couples only weakly to H(4) and H(6), giving rise to an octet (since we already know that $J_{25} \sim 0.5$ c/s) or a quartet if either J_{24} or J_{26} is negligible. Since no octet is observed in the spectrum we may conclude that $J_{24} \sim 0$, since $J_{26} = J_{62}$ is known to differ from zero. Considering the intensities, we must assign the lines at 389.9 (9), 390.5 (10.5), 392.0 (9.5), and 392.9 (11) as the quartet looked for. This means $\delta_2 = 40.6$ as compared to 44.1 from rule (I). Also, $J_{26} = 2.20 = J_{62}$ which, by way of exclusion (see above), lets $J_{46} = 1.5$.

Since there is no proton *para* to H(4), the H(4) resonances form a quartet. As $J_{45} = J_{54} = 15.5$ we must look for well-separated lines. This leaves us with no other possibility than the lines at 385.5, 388.6, 399.2, and 402.6. It follows that $\delta_4 = 38$ c/s as compared to 36.3 from rule (I). Also $J_{45} = 13.9$ and $J_{46} = 3.4$. Both values are at variance with $J_{54} = 15.5$ and $J_{64} = 1.5$ found above, but it is to be expected that the estimates involving the very centrally situated H(4)-pattern will be less reliable. The results are summarized in Table 3.

$1,4\text{-}C_6H_4(NH_2)F$

The NMR-spectrum of the compound $1,4\text{-}C_6H_4(NH_2)F$ is by no means simple. 15 lines were observed at 376.8 (8), 379.6 (6), 381.7 (11), 383.6 (8), 386.4 (24), 388.5 (8), 391.0 (23), 395.7 (23), 398.5 (7), 401.1 (5), 402.6 (6), 404.3 (23), 406.5 (5), 409.6 (3), 412.5 (10). This spectrum proved identical with the subsequently investigated spectrum of $1,4\text{-}C_6H_4(ND_2)F$ (except for the missing NH_2-absorption at 195 c/s). We may, therefore, ignore the NH_2-protons. By rule (I), $\delta_2 = \delta_6 = 46.7$, and $\delta_3 = \delta_5 = 30.7$. Hence $\delta_2 - \delta_3 > J_{23}$. First, we shall try to interpret the dominant lines of the spectrum by simple inspection. Afterwards, we shall check the estimates by means of data for deuterated derivatives.

Table 3. Calculated and experimental proton chemical shifts of $1,3\text{-}C_6H_4(NH_2)Cl$ (5 mole % in cyclohexane) in c/s relative to benzene. Resonance frequency 60 Mc/s. Spin-spin couplings in c/s.

	δ_2	δ_4	δ_5	δ_6
Calculated from rule (I) *	44.1	36.3	13.7	52.3
Found in this investigation	40.6	38.0	19.4	52.1
Deviations (numerical)	3.5	1.7	5.7	0.2

$J_{45} = 13.9-15.5$; $J_{56} = 7.7-7.8$; $J_{24} \sim 0$; $J_{26} = 2.2$; $J_{46} = 1.5-3.4$; $J_{25} \sim 0.5$.

* Using Spiesecke and Schneider's δ's.

Table 4. Calculated and experimental proton chemical shifts of 1,4-$C_6H_4(NH_2)F$ (5 mole % in cyclohexane) in c/s relative to benzene. Resonance frequency 60Mc/s. Spin-spin couplings in c/s.

	δ_2	δ_3	δ_5	δ_6
Calculated from rule (I) *	46.7	30.7	30.7	46.7
Found in this investigation	49.0	30.0	30.0	49.0
Deviations (numerical)	2.3	0.7	0.7	2.3

$J_{FH(3)} = J_{FH(5)} = 8.5$; $J_{23} = J_{65} = 9.6$; $J_{FH(2)} = J_{FH(6)} = 4.7$; $J_{35} = 3.0$.

* Using Spiesecke and Schneider's δ's.

The H(3), H(5) resonances are expected to occur in the vicinity of $432 - 31 = 401$. They would represent a doublet if only influenced by fluorine, but the interaction with the H(2), H(6) protons will produce a sextet which, dependent upon $J_{FH(3)}$ and J_{32}, may degenerate into a quintet (if $J_{FH(3)} = 2 J_{32}$) or into a quartet (if $J_{FH(3)} = J_{32}$).

In all 3 cases it seems clear that the difference $412.5 (10) - 404.3 (23) = 8.2$ represents $J_{FH(3)}$. This excludes the possibility of assigning a sextet. If a *quintet* is assigned, it is centred around 395.7 (23). If a *quartet* is assigned it is centred around 400, very close to the precalculated position. Since the centre of the H(2), H(6) pattern must be placed somewhere near the strong line at 391.0 (23), we may abandon any further attempt to an analysis by inspection if H(2), H(3) occur as a *quintet*, since in this case $\delta_2 - \delta_3 \sim 5$ while $J_{23} = 8.2 > \delta_2 - \delta_3$. If, however, a H(2), H(3) *quartet* is observed, then $J_{FH(3)} = J_{32} = 8.2$; $\delta_5 = \delta_3 = 32$. This suggest the existence of a H(2), H(6) sextet centred between 391.0 and 386.4 (average value 388.7; calculated from (I): 385.3). In this case $\delta_6 = \delta_2 = 43.3$, $J_{23} = 7.2$, $J_{FH(2)} = 4.6 - 4.7$. However, $J_{23}/(\delta_2 - \delta_3) \sim 7/11$ so that the simple analysis presented may be incorrect. Signs of its possible invalidity are seen in the intensity irregularities, and in the presence of unassigned, although weak, lines. This was why deuteration was applied.

1,2,4,6-$C_6H_2(NH_2)DFD$ and 1,2,4-$C_6H_3(NH_2)DF$

A 2:1 mixture of 1,2,4,6-$C_6H_2(NH_2)DFD$ and 1,2,4-$C_6H_3(NH_2)DF$ was prepared by two times repeated exchange of 1,4-$C_6H_4(NH_2)F$ in acid D_2O at 110°C, followed by shaking with H_2O at room temperature ($ND_2 \rightarrow NH_2$). Its spectrum has lines at 375.8 (4), 380.5 (4), 385.5 (9), 390.0 (9) 392.5 (5), 395.5 (11 on the "shoulder" of the following line), 397.7 (17), 400.5 (6), 403.5 (11 on the "shoulder" of the following line), 406.2 (17), and 410.5 (4). By its strong lines at 397.7 and 406.2, this spectrum at once discloses that $J_{FH(3)} = J_{FH(5)} = 8.5$ c/s and that $\delta_3 = \delta_5 = 432 - 402 = 30$ as compared to 30.7 from rule (I).

The lines at $375.8 - 390.0$ must stem from H(6) in 1,2,4-$C_6H_3(NH_2)DF$. H(6) is coupled strongly to H(5) and more weakly to fluorine. Hence $J_{65} = J_{23} = 9.6$ c/s while $J_{FH(2)} = J_{FH(6)} = 4.7$ c/s. Finally, $\delta_2 = \delta_6 = 432 - 383 = 49$, as compared to 46.7 from rule (I).

H(5) of 1,2,4-$C_6H_3(NH_2)DF$ couples, therefore, almost equally strongly to fluorine and to H(6). The expected quartet degenerates, therefore, into a triplet with its central line at the "unperturbed" H(5) position 402. However, on top of this a *meta* coupling to H(3) should make itself felt. This accounts for the two lines found at 400.5 and 403.5, symmetrically displaced with respect to 402. The assignment means that $J_{35} = 3.0$ c/s. J_{35}, of course, also occurs as the difference $395.5 - 392.5$.

Table 4 summarizes the results.

It is seen that the more laborious analysis by means of spectra of deuterated species confirms the main features found by "inspection" analysis of the spectrum of the parent molecule, relying on rule (I).

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