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DESHIELDING OF THE ORTHO PROTON IN THE NMR SPECTRA OF N-(2-SUBSTITUTED-PHENYL)AMIDES

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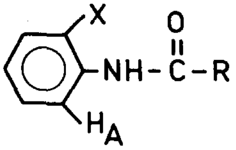
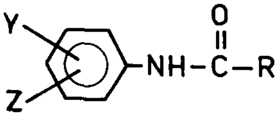
Although the NMR spectra of N-phenylamides have been studied by several authors (1,2,3) no reference appears to have been made to any anomalies in the aromatic region of the spectra. We now report a large low-field shift of the signal corresponding to the *ortho* proton (H_A) in a number of N-(2-substituted)-phenylamides of general structure



(I)

(where X= F,Cl, Br, I, and R = methyl, trichloromethyl, methoxy, dimethylamino, diethylamino, di-n-propylamino, di-iso-propylamino, di-n-butylamino).

Assignment of the low-field signal to H_A is based upon the fact that among all possible isomeric compounds of general formula

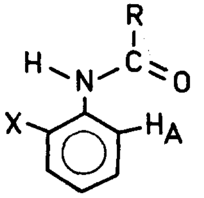


(II)

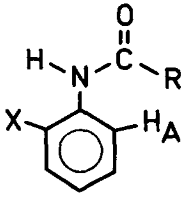
(where Y = Cl and Z = Cl, methyl) only those which simultaneously have one free and one occupied *ortho* position exhibit this effect.

Inspection of the Table shows that τ_A values range from 1.69 to 1.87 ppm, which represents a down-field shift of 0.86 to 1.04 ppm relative to benzene protons. In order to interpret the observed shift it seems convenient to separate both electronic and neighbouring effects. A correction for the contribution of X to the shift was first made by using $S_{\underline{meta}}$ values taken from ref. 4; the results (τ_A^*) are listed in the Table. To correct for the electronic effect alone of -NH-CO-R a reference should be chosen since the $S_{\underline{ortho}}$ value for this group also includes its neighbouring effect. In this connection, the _para_ hydrogen of acetanilide (τ 2.93 ppm) would appear to be a good reference. For whereas it can be considered to be affected to roughly the same extent than the _ortho_ hydrogen by the electronic influence of the acetamido group, it is virtually free from any neighbouring effects due to the latter. Taking the above into account the magnitude of the low-field shift for our series becomes $\Delta(\text{ppm}) = 2.93-\tau^* = 1.13$ to 1.30 ppm. These values, within a small range, are likely to represent minor variations due to the arbitrary choice of acetanilide ($R=CH_3$) as a common reference for all the compounds in this series.

In structure (I) substituent R-CO- may be assumed to lie in approximate coplanarity with the ring, provided it stays furthest from X. This well known situation arises in some substituted anilines (e.g. N-methyl-o-toluidine) (5). On the other hand there is ample evidence of hindered rotation about the C-N amide bond which gives rise to the existence of two conformational isomers. This means in our case that two structures, (Ia) and (Ib), are likely _a priori_. There is no evidence, as is the case in phenylformamides (1), for coexistence of the two isomers.



(Ia)



(Ib)

The large value obtained for Δ can, in our opinion, be best explained by assuming the greatest possible proximity between the carbonyl group and H_A , whence Ia represents the preferred configuration. This would seem reasonable on account of the larger bulk of R as compared to that of the

TABLE

Chemical Shifts (ppm) of the <u>Ortho</u> Protons (H_A)
in N-(2-Substituted-phenyl)amides
(60 MHz, 0.50 M Solutions in CCl_3D)

-X	-R	τ_A[a]	τ_A^*[b]	Δ[c]
-H	$-CH_3$	2.52	2.52	0.41
-F	$-CH_3$	1.75	1.74	1.19
-Cl	$-CH_3$	1.70	1.64	1.29
-Br	$-CH_3$	1.77	1.67	1.26
-I	$-CH_3$	1.87	1.65	1.28
-Cl	$-CCl_3$	1.69	1.63	1.30
-Cl	$-OCH_3$	1.86	1.80	1.13
-Cl	$-N(Me)_2$	1.76	1.70	1.23
-Cl	$-N(Et)_2$	1.74	1.68	1.25
-Cl	$-N(^nPr)_2$	1.72	1.66	1.27
-Cl	$-N(^iPr)_2$	1.73	1.67	1.26
-Cl	$-N(^nBu)_2$	1.72	1.66	1.27

[a] With reference to internal TMS (τ_{TMS} 10 ppm)

[b] After correcting for the contribution of X:

$$\tau_A^* = \tau_A - S_{\underline{meta}}\ (X)$$

[c] Shift to low field with reference to the chemical shift (τ 2.93) of the <u>para</u> proton in acetanilide
Δ(ppm) = 2.93 - τ_A^*

carbonyl oxygen atom.

On the assumption of a planar structure and using atomic distances derived from crystalline acetanilide (6), we obtain a value of 2.16 Å for the $H_A...O=C$ distance. Magnetic anisotropy of the C=O bond has been invoked in several instances (7) as an additional underlying cause of frequency shifts undergone by protons in its neighbourhood. To calculate any effect of the C=O anisotropy one should have the susceptibility components of this bond. Hooper and Kaiser (8) have calculated the three susceptibility components of the amide C=O bond from the internal chemical shifts of methyl groups in N,N'-dimethyl acetamide and of methylene groups in N-acetyl pirrolidine. They obtain two sets of components depending on the assignment of the methyl peaks, which amounts to accepting a shielding or a deshielding effect by the C=O throughout the bond plane. The views on this point are conflicting. Several empirical rules and theoretical studies (7,9) favour a deshielding effect, whereas experimental evidence drawn from coupling constants (10), aromatic dilution shifts (11), and contact shifts (12) supports the opposite. Accepting the planar structure discussed above, we arrived at the following values for the contribution of the magnetic anisotropy effect of the C=O bond upon H_A :

Deshielding set : 1.21 ppm downfield
Shielding set : 1.54 ppm upfield

As may be seen, the first set is that which accounts for the observed low field shift, which appears to be in disagreement with the conclusions arrived at by Hooper and Kaiser. We believe that the $H_A...O=C$ distance may be short enough for the induced magnetic dipole approximation to be no longer valid. An investigation of this possibility is currently under way.

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