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INTRAMOLECULAR HYDROGEN BONDING IN 2'-SUBSTITUTED ANILIDES

by

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In our recent proton magnetic resonance study of aromatic amines and their derivatives[1] we proposed that certain ortho-substituted acetanilides exhibit intramolecular hydrogen bonding between the amide proton and the ortho-substituent in deuterochloroform solutions. In such a case the amide group and the aromatic ring are coplanar and the aromatic proton adjacent to the amide group is strongly deshielded. Several other authors have described the unusual chemical shifts of such protons,[2] although intramolecular hydrogen bonding was not always invoked as a causative factor.[3]

Results of studies in more-polar solvents were consistent with the proposed effects of hydrogen bonding[4] and we now present further examples for deuterochloroform solutions which enable us to rank substituents according to their hydrogen bonding ability. This ranking is broadly consistent with evidence derived from other sources and strongly supports our published proposals.

We believe that the particularly large downfield shift of an aromatic proton such as H-6' (Fig 1) which accompanies the N-acylation of the amide (acylation shift) is indicative of (a) the Z-configuration[5] about the C-N partial double bond, and (b) intramolecular hydrogen bonding, as depicted in Fig. 1. Furthermore, the extent to which such an acylation shift exceeds that in the absence of an ortho-substituent is advanced as a measure of the strength of the hydrogen bonding interaction. As we intimated earlier, acylation shifts for aromatic protons <u>meta</u> and <u>para</u> to the nitrogen atom are approximately 0.2 ppm and 0.4 ppm.

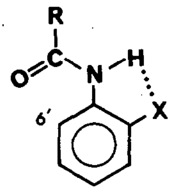

Fig. 1.

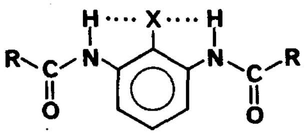

Fig. 2.

Table I

Acylation shifts of H-6' in 2-substituted acetanilides[6,8]

Substituent X	Acylation Shift (ppm)	Substituent X	Acylation Shift (ppm)
-COOMe	2.07-2.10[7]	-Oalkyl	1.77-1.78[7]
$-NO_2$	1.90-2.20[7]	-CN	1.62
$-CF_3$	1.91	-F	1.69
$\mathrm{-\underset{\underset{O}{\vert}}{S}-Me}$	1.82	-Cl	1.70[7]
		-Br	1.52[7]
-SMe	1.81	-I	1.35
		$-NMe_2$	1.55
$\mathrm{-\overset{\overset{O}{\vert}}{\underset{\underset{O}{\vert}}{S}}-Me}$	1.76	-Me	0.75-1.02[7]
		-H	0.88-1.05[7]

In the amides derived from 2-substituted-1,3-phenylene diamines (Fig. 2), certain hydrogen bonding groups can function in a dual role, i.e. so as to simultaneously bond to two amide protons with undiminished ability. This information is derived from the symmetrical nature of the aromatic proton resonances and the acylation shifts of H-4'

(H-6'), which almost equal the arithmetic sum of one ortho and one para acylation shift. Examination of the corresponding mono-amides (not reported in the table) confirms the ability of some substituents to accept a second hydrogen bond.

Table II

Acylation shifts for 2-substituted 1, 3-diamido benzenes[8]

Substituent	Acylation Shifts (ppm)		
X	H-4	H-5	
$-NO_2$	2.26	0.62	(pivalamide)
-NMe	1.88	0.31	(acetamide)
-Cl	1.87	0.38	(pivalamide)
-OMe	1.85	0.36	(pivalamide)
-p-tolyl	1.78	0.25	(acetamide)
$-CH_3$	1.40	0.20	(pivalamide)
-H	1.27	0.37	(pivalamide)

Detailed discussion of these results will be attempted in the full publication, but at this stage we wish to draw attention to the potentialities of this method in which the aromatic ring serves as a framework, and its hydrogens as a probe, for the hydrogen bonding interaction.

By making use of the orienting power of a suitably placed hydrogen bonding site a number of cumulative and/or competitive effects may be obtained. For instance the acylation shifts of the aromatic protons (0.26, 3.28 ppm) in Fig. 3.

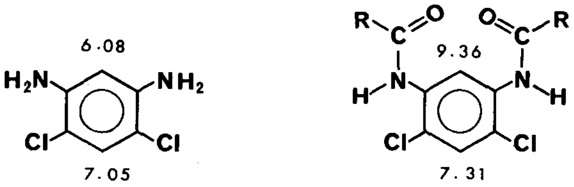

Fig. 3. Chemical Shifts in ppm from TMS[8]

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2.(a) J.R. Bartels-Keith and R.F.H. Cieciuch, Can.J.Chem., **46**, 2593 (1968)

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6. In most cases a third substituent was present at C-4 or C-5 in order to simplify spectral interpretations. Spectra were recorded for approx. 7% solutions on Varian A-60 or HA-100 spectrometers at ambident temps. In the ortho-F case a pivalanilide was used in place of the acetanilide for solubility reasons. It has been found that replacement of the acetamido group by a pivalamido group does not affect the acylation shift (1).

7. These data are taken from Ref. 1.

8. A number of new compounds were prepared, for which satisfactory combustion analyses have been obtained. The details will be reported in a full publication.