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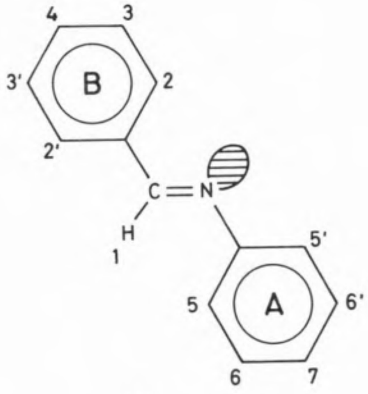
N.M.R. STUDIES OF NITROGEN CONTAINING MOLECULES

III. The conformation of salicylalanilines (1)

The proton resonance spectra of three substituted salicylalanilines in several solvents are studied in relation to their conformations. In particular, it is found that, in cyclohexane solution, a strong intramolecular OH......N hydrogen bond greatly stabilizes the quasi-planar arrangement of the C-phenyl ring plane and the H—C=N nuclear plane with respect to benzalanilines; there are indications that it also reduces the averaged effective dihedral angle between the H—C=N plane and the N-phenyl ring plane, because of a reduction of the n — π conjugation. The relative strength of the hydrogen bond, as measured by the OH proton chemical shift, is shown to depend appreciably on the nature of the substituent on the N-phenyl ring.

1 — *INTRODUCTION*

The conformation of the *trans* isomer of benzalaniline (I)



(I)

and its derivatives in solution has been the object of several papers in recent years (1-7). Various properties, especially electronic spectra, have been investigated and have led to the conclusion that, contrary to the traditionally accepted view, (I) is not planar. This is reasonable because, although π-electron delocalization would be maximum for a planar situation, steric considerations (involving H atoms 1 and 5, as in biphenyl) and the possibility of n-π conjugation (involving the N lone pair and the adjacent aromatic ring, as in aniline) would favour a perpendicular arrangement of the H—C=N nuclear plane and that of the N-phenyl ring. Values of 40°-60° (5) and about 90° (6) (perpendicular situation) have been proposed for the dihedral angle φ_A between those planes, based on interpretations of electronic spectra.

The authors have recently applied nuclear magnetic resonance spectroscopy to this problem (7). Proton chemical shifts for benzalaniline and some *p, p'*-derivatives in dilute solutions in cyclohexane (where specific solvent effects are minimized) were obtained and compared with those for the corresponding parent benzaldehydes and anilines. These chemical shifts clearly showed that there is rapid rotation of the phenyl rings about the CC and CN bonds at room temperature. Therefore, instead of fixed angles, one should consider, at most, weighted average dihedral angles. In fact, properties such

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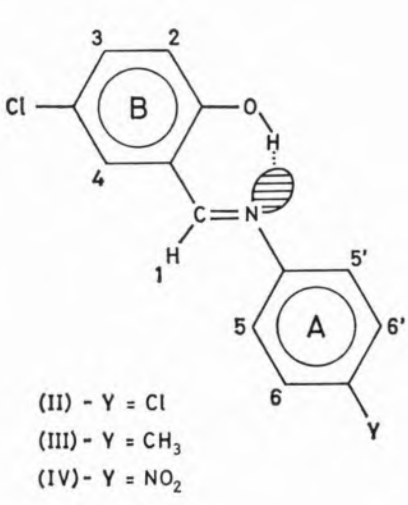
(1) Parts I and II, *Rev. Port. Quím.*, **11**, 214 e 219(1969).

as changes of molar extinctions or N.M.R. shifts of the A-ring protons due to π-π and n-π conjugation are not linear functions of the dihedral angle φ_A, but are approximately proportional to $\cos^2 \varphi_A$, in so far as they can be explained in terms of the resonance or overlap integrals for the «directly bonded» atomic orbitals, i.e. the N non-bonding orbital and the nearest p_π orbital of ring A. Thus, rigorously, what one may get from studying those properties is a weighted average of $\cos^2 \varphi_A$, which, for convenience, may be taken equal to the squared cosine of an effective $(\varphi_{A\ \text{eff.}})$ angle. The values found in the literature for the dihedral angle between the $H-C=N$ plane and the N-phenyl ring (5,6) of (I) should, in fact, be taken as approximate $(\varphi_A)_{\text{eff.}}$ values. Our previous work shows that the $(\varphi_A)_{\text{eff.}}$ value from N.M.R. data is appreciably larger than 0° but does not exceed 45°, in reasonable agreement with the conclusions of reference (5).

As far as the effective angle φ_B between the $H-C=N$ plane and the C-phenyl ring plane is concerned, this is expected to be small (5-7).

We have also briefly investigated solvent effects, especially the effect of protonation, on the N.M.R. spectra, but have been unable to unambiguously correlate such changes with alterations of $(\varphi)_{\text{eff.}}$. In particular, the protonation of the N lone pair would be expected to lead to a decrease of $(\varphi_A)_{\text{eff.}}$, as the electronic spectra seem to show (6).

In this paper we present further N.M.R. work of benzalanilines, namely, substituted salicylalanilines (II-IV), where



(II) - Y = Cl
(III) - Y = CH_3
(IV) - Y = NO_2

the possibility of a OH...N hydrogen bond is expected to further stabilize the quasi-planar arrangement of the B-ring and the $H-C=N$ planes, as well as make $(\varphi_A)_{\text{eff.}}$ smaller, because of a reduction of the n-π conjugation.

2. *EXPERIMENTAL AND RESULTS*

The three substituted salicylalanilines were prepared in the usual way by refluxing equimolar amounts of 5-chloro-salicylaldehyde and the corresponding anilines in methanol (7), and recrystallizing from the same solvent.

The N.M.R. spectra were obtained on a Varian HA-100 spectrometer. Dilute solutions containing 5 mg/ml for the parent compounds and 10 mg/ml for the salicylalanilines were used throughout, except for compounds (II) and (III) in cyclohexane, in which cases the concentration was less because of low solubility. The extremely low solubility of IV in C_6H_{12} did not allow the determination of the corresponding spectrum, even after an accumulation of 100 scans in a time averaging computer (CAT).

Table 1 shows τ-values for (II) and (III) in C_6H_{12}, as well as the differences Δ observed with respect to the corresponding parent compounds in similar conditions of solvent and concentration

Table 1

τ-Values for Salicylalanilines (II) and (III) (in C_6H_{12}) and differences Δ relative to the corresponding salicylaldehydes and anilines

Molecule	Proton	τ-values	Δ (p.p.m.)
II	1	1.61	1.32
	2	3.15	− 0.04
	3	2.86	0.16
	4	2.76	0.11
	5,5'	2.93	− 0.68
	6,6'	2.70	− 0.36
	OH	− 2.41	− 1.55
III	1	1.59	1.30
	2	3.18	− 0.01
	3	2.86	0.16
	4	2.80	0.15
	5,5'	2.90	− 0.73
	6,6'	2.90	− 0.31
	OH	− 2.71	− 1.85

(positive Δ-values correspond to shifts to high field). Table 2 shows the τ-values for (II), (III) and (IV) in acetone, d-chloroform and trifluoracetic (TFA) acid, and the differences Δ' observed with respect to the cyclohexane solutions. The spectra arising from the B-ring protons are of the ABX or AMX type; those corresponding to the A-ring are of the AA′BB′, type, except of course for (III) because of coupling with the CH_3 protons. The τ-values quoted are thought to be accurate to $\pm$ 0.01 p.p.m.

3. *DISCUSSION*

a) *Spectra in cyclohexane*

The Δ-value for protons 2,3 and 4 essentially reflect the smaller π inductive effect of N as compared with O; this reduction should cause an increase in the τ-values of 3 and 4 with respect to the salicylaldehyde and only a slight change in τ for the *meta* proton 2, as observed.

The Δ-values for the A-ring are much more pronounced. They result primarily from changes in the π-electron density at the *ortho* and *meta* carbon atoms, on going from the p-Y-aniline to the salicylalaniline. In turn, these changes arise essentially because of the π inductive effect of N (absent in the anilines) upon ring A, as well as alterations in the n-π conjugation due to variations in the angle φ_A distribution and to changes of the nature of the N lone-pair orbital. A detailed discussion of similar effects on some p, p′-substituted benzalanilines in connection with $(\varphi_A)_{eff.}$ values has already been given (7). From the Δ-values for those compounds and the presence of a comparatively strong electrodonating group in the B-ring (the OH group), less negative Δ-values than observed would be expected for protons 5,5′ and 6,6′ in II and III. This discrepancy can be explained by a reduction of the n-π conjugation due to the intramolecular hydrogen bond, as well as by a possible decrease of $(\varphi_A)_{eff.}$ (see reference 7).

The Δ-values for proton 1 of II and III are appreciably (0.3 p.p.m.) less than the corresponding values for the p,p′-derivatives of benzalaniline previously studied (7). Such a big difference can only be explained by an enhanced paramagnetic effect of the π-electron ring currents of A or B, or both. This, in turn, requires, respectively, a smaller $(\varphi_A)_{eff.}$ angle for II and III than it would be in the absence of OH...N hydrogen bonding, a decrease of $(\varphi_B)_{eff.}$ on going from salicylaldehyde to II and III, or both. In order to understand the former effect it should be noted that reduction of the n-π conjugation destabilizes especially the large φ_A conformations. The decrease of $(\varphi_B)_{eff.}$ would reflect a stronger hydrogen bond in salicylalanilines (OH....N) than in salicylaldehyde (OH.....O), which seems reasonable.

Finally, the Δ-values for the OH proton are quite large (negative in sign) and, surprisingly strongly dependent on the p-substituent group in the aniline ring. There are several factors that can lead to a shift of the OH proton signal to low field on going from salicylaldehyde to the imine: *a)* a ring-current effect due to the aniline fragment, *b)* differences between the electric field effect of $>C=O$ and $>C=N-$ groups, and *c)* differences between the magnetic anisotropy effects of those groups. Contribution *a)* is calculated (9) to be -0.4 p.p.m. at the maximum, corresponding to the extreme situation of the OH proton being in the nuclear plane of ring A. If we assume that *b)* and *c)* can be obtained by considering only the effect of a second lone-pair orbital in $>C=O$ as compared to a $N-C$ σ-bond in the imine, then approximate calculations similar to those previously done for pyridine (10) show that contribution *b)* to Δ is of the order of -0.3 p.p.m., whereas contribution *c)* is even smaller. These contributions are not, however, sufficient to explain the large magnitude of the Δ-values observed. This conclusion suggests again the existence of a stronger hydrogen bond in the imine compared to the aldehyde; a stronger hydrogen bond means a more marked lowfield shift, as observed.

The hypothesis that a large part of the Δ-value observed for the OH proton is due to a stronger hydrogen bond in the imine is consistent with the dependence of the corresponding τ-value upon the nature of the distant p- substituent group in the A-ring. Conjugation between these groups, (Cl in II, CH_3 in III) and the benzene ring increases the electron density on N to a different extent, this being greater for III than for II, as is shown by the τ-values of NH_2 in p-toluidine (6.87) and

Table 2

τ-Values for Salicylalanilines in various solvents and differences Δ′ with respect to solutions in C_6H_{12}

Molecule	Proton	Acetone		$CDCl_3$		TFA	
		τ	Δ′	τ	Δ′	τ	Δ′
II	1	1.11	− 0.50	1.49	− 0.12	1.03	− 0.58
	2	3.04	− 0.11	3.04	− 0.11	2.76	− 0.39
	3	2.66	− 0.20	2.70	− 0.16	2.26	− 0.60
	4	2.41	− 0.35	2.65	− 0.11	2.22	− 0.54
	5,5′	2.60	− 0.33	2.81	− 0.12	2.41	− 0.52
	6,6′	2.60	− 0.10	2.61	− 0.09	2.41	− 0.29
	OH	— (a)	—	− 2.96	− 0.55	— (b)	—
III	1	1.17	− 0.42	1.47	− 0.12	1.06	− 0.53
	2	3.10	− 0.08	3.05	− 0.13	2.87	− 0.31
	3	2.68	− 0.18	2.74	− 0.16	2.26	− 0.60
	4	2.47	− 0.33	2.69	− 0.11	2.19	− 0.61
	5,5′	2.76	− 0.14	2.81	− 0.09	2.51	− 0.39
	6,6′	2.76	− 0.14	2.81	− 0.09	2.51	− 0.39
	OH	— (a)	—	− 3.31	− 0.60	— (b)	—
IV	1	1.02	—	1.46	—	0.79	—
	2	3.00	—	3.00	—	2.67	—
	3	2.57	—	2.73	—	2.28	—
	4	2.33	—	2.61	—	2.12	—
	5,5′	2.37	—	2.66	—	2.03	—
	6,6′	1.68	—	1.71	—	1.49	—
	OH	— (a)		− 2.50		— (b)	

(a) Signal too broad to be observed.

(b) Signal not observed due to fast proton exchange with the solvent.

p-chloroaniline (6.69) (1). Therefore, the N...HO hydrogen bond will be stronger in III, thus leading to a more negative τ-value of OH. In compound IV, where the substituent is a nitro group, the hydrogen bond should be weaker than in II and III and, consequently, the corresponding τ_{OH} value should be larger; IV is not soluble in C_6H_{12}, but the τ-values for the three compounds in $CDCl_3$ (Table 2) corroborate this conclusion.

b) *Solvent effects*

Changing from cyclohexane to acetone and chloroform as solvents leads to low field shifts Δ′ in a manner similar to that found for the parent compounds, mainly as a result of solute-solvent hydrogen bonding and solvent reaction field effects. Larger shifts to low field are observed in TFA solution due to protonation, especially of the N atom, as previously observed for p, p′-derivatives of benzalaniline. However, the Δ′-values for proton 1 of II, III, and IV are appreciably smaller in magnitude than for those compounds (for which $\Delta' \simeq -0.9$ p.p.m.). This suggests that the low field shift of proton 1 due to nitrogen protonation is partially cancelled by a simultaneous high field effect that is absent, or is less important, in the mentioned benzalanilines. We propose that this effect results from an appreciable increase of $(\varphi_B)_{eff.}$ upon protonation, from a very small value in the neutral species to an appreciable value

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(1) Solvent C_6H_{12}, concentration 15 mg/ml.

because of steric hindrance involving OH and NH^+. In the absence of an OH group in an *ortho* position of ring B, not only is the neutral molecule less planar but also steric considerations for the protonated species are much less relevant; therefore changes in $(\varphi_B)_{eff.}$ upon protonation are, in such cases, much smaller.

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RESUMO

Estudam-se os espectros de ressonância protónica de três salicilalanilinas substituidas, em vários solventes, em relação com as respectivas conformações. Em particular, verifica-se que, em solução em ciclohexano, uma forte ligação-hidrogénio OH......N intramolecular estabiliza notòriamente o arranjo quase-planar do grupo fenilo-C com o plano nuclear $H-C=N$*, em comparação com o que sucede nas benzalanilinas; há também indicações de que aquela ligação reduz o ângulo diedro médio efectivo entre o plano* $H-C=N$ *e o anel fenilo-N, como resultado da redução da conjugação* $n-\pi$*. Mais se verifica que a força relativa da ligação-hidrogénio, medida pelo deslocamento químico do protão OH, depende apreciàvelmente da natureza do grupo substituinte no anel fenilo-N.*