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^{1}H AND ^{13}C NMR STUDIES OF SALICYLALANILINES

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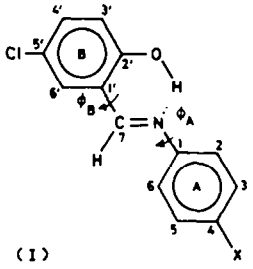
Abstract - Several substituted salicylanilines (I) are studied by ^{1}H (chemical shifts) and ^{13}C (chemical shifts and T_1 relaxation times) NMR in order to obtain information on molecular geometry changes and the transmission of the electronic effects due to substituents, as well as on the relative rates of the overall molecular tumbling and of the flipping of the phenyl rings. In particular, a good linear correlation of the OH proton shifts (affected by intramolecular hydrogen bonding) with Hammett's σ constants for p-substitution in the aniline moiety is found. Changes in rigidity of the rings expected as a result of the OH...N interaction and of p-substitution are reflected on the phenyl carbon relaxation times.

INTRODUCTION

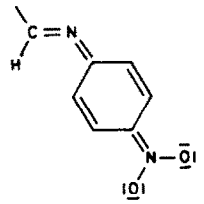
This paper reports a study by ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy of OH hydrogen bonding in substituted salicylalanilines (I) (the 5'-chloro derivatives were used in order to facilitate NMR signal assignements)



(I)

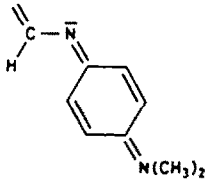
X:	NO_2	(Ia)
	Cl	(Ib)
	H	(Ic)
	CH_3	(Id)
	OCH_3	(Ie)
	$N(CH_3)_2$	(If)

as a function of substituent X, and of the effects such an intramolecular hydrogen bond has on the deviations from planarity of the ring planes with respect to the nuclear plane of the imine group (HC=N); this, in turn, affects the transmission of the electronic effect of X across the imine group to the B-ring. An electron withdrawing group such as $X=NO_2$ is expected to stabilize n-π conjugation with electron transfer between the N σ lone-pair and the A-ring



in a perpendicular arrangement of the HC=N nuclear plane and the plane of the A-ring. As a result, the intramolecular hydrogen bond weakens with respect to the compound having X=H. Also, due to the relative destabilization of the coplanar conformation, the electronic effect of the nitro group upon ring B should be small and about the same as in the absence of the OH group.

On the contrary, an electron donating group such as $X=N(CH_3)_2$ is expected to stabilize π-π conjugation with electron transfer from the A-ring into the imine group and the B-ring:

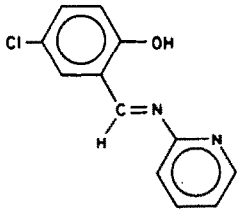


in a planar overall conformation. In this case, the OH...N hydrogen bond should be strengthened. Also, due to stabilization of the planar conformation, the electronic effect of the $-N(CH_3)_2$ group upon the imine group and on the B-ring (namely the 4' position) should be comparatively large.

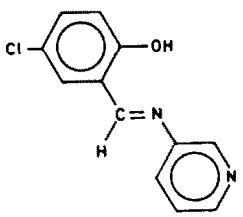
These predictions have been tested by means of the ^1H and ^{13}C chemical shifts. In this respect, the present work is an extension of a preliminary ^1H study of ours (1). This was preceeded by a conformational study of p-substituted N-benzyledeneanilines (benzalanilines) by ^1H NMR (2), which have subsequently also been studied by other authors using ^1H, ^{13}C and ^{15}N NMR (3-7).

In view specially of the presumed differences in mobility of the B-ring due to the hydrogen bond and in mobility of the A-ring associated to a variable stabilization of the planar relative to the perpendicular conformation, we have also obtained ^{13}C longitudinal relaxation times (T_1) for salicylalanilines as well as for some of the previously studied benzalanilines for comparison.

We have also extended the ^1H and ^{13}C study to the systems (IIa,b,c).



(II a)



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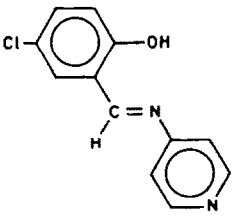


(II c)

EXPERIMENTAL

The salicylanilines were prepared by refluxing equimolar amounts of the corresponding anilines and aminopyridines and 5-chloro-salicylaldehyde in MeOH and recrystallizing from the same solvent.

Carbon and hydrogen analysis were performed for the series of compounds (I) and (II):

I a):	C, Anal. calc.	56.42	Found 56.57	H, Anal. calc.	3.27	Found 3.36
b)		58.64	58.66		3.38	3.42
c)		67.39	67.18		4.32	4.49
d)		68.43	68.22		4.88	5.10
e)		64.24	63.91		4.58	4.70
II a)		61.94	61.73		3.90	3.97
b)		61.94	61.80		3.90	4.02
c)		61.94	61.51		3.90	3.87

Solutions (0.1M-0.2M) for NMR measurements were prepared in chloroform-d ($CDCl_3$, Gold Label, Aldrich Co.). The solutions for ^{13}C T_1 measurements were nitrogen bubbled for 10-15 mins and sealed in 10 mm tubes.

Broad-band proton decoupled carbon-13 and proton NMR spectra were recorded at 50.3 MHz and 200 MHz, respectively, using a VARIAN XL-200 spectrometer operating in the pulsed Fourier-transform mode. The probe temperature was controlled to within 20±1°C. Spin-Lattice relaxation times (T_1) were measured by the usual 180°-τ-90° pulse sequence, with an appropriate delay time between sequences. Automatic three-parameter least-squares fitting of relaxation measurements was provided by the spectrometer. The accuracy of the T_1 measurements is estimated as better than 5%.

RESULTS AND DISCUSSION

A. CHEMICAL SHIFTS

Table 1 shows the proton chemical shifts of (I) with X=H, in $CDCl_3$, and the effects due to substituents X=NO_2, Cl, CH_3, OCH_3, $N(CH_3)_2$. Table 2 shows the corresponding carbon-13 chemical shifts. The proton and carbon δ - values for imines (IIa), (IIb) and (IIc) are given in Table 3.

TABLE 1. Proton chemical shifts of salicylalanilines (I), in $CDCl_3$[a]

X	2(6)	3(5)	4	7	3'	4'	6'	OH
NO_2	0.10	0.94	---	0.10	0.10	0.11	-0.01	-0.72
Cl	0.01	0.09	---	0.12	0.07	0.09	0.01	-0.17
H	7.19	7.30	7.16	8.40	6.83	7.18	7.34	13.20
CH_3	-0.03	-0.14	---	0.12	0.08	0.06	-0.05	0.18
OCH_3	0.02	-0.41	---	0.05	0.08	0.06	-0.07	0.20
$N(CH_3)_2$	0.08	-0.57	---	0.12	0.10	0.09	-0.04	0.50

(a) X=H, shifts relative to TMS (δ - values)
X≠H, " " " (I) with X=H

TABLE 2. Carbon chemical shifts of salicylalanilines (I), in $CDCl_3$[a]

X	1	2(6)	3(5)	4	7	1'	2'	3'	4'	5'	6'
NO_2	5.9	0.9	-4.1	19.1	3.1	-0.6	0.5	-0.3	1.4	0.6	0.6
Cl	-1.4	1.2	0.1	5.7	0.4	-0.1	0.1	-0.8	0.2	0.4	-0.1
H	147.7	121.0	129.3	127.2	161.0	119.7	159.3	119.4	132.7	123.4	131.1
CH_3	-2.6	-0.1	0.7	10.1	-0.8	0.2	0.2	-0.8	-0.2	0.0	-0.2
OCH_3	-7.5	1.3	-15.1	30.8	-2.3	-0.1	-0.9	-1.0	-0.7	-0.7	-0.6
$N(CH_3)_2$	-11.4	1.3	-12.6	22.6	-5.3	0.6	0.1	-0.8	-1.2	0.0	-0.9

(a) X=H, shifts relative to TMS (δ - values)
X≠H " " " (I) with X=H

TABLE 3. δ_H and δ_C values for the imines (II), in $CDCl_3$

	(IIa)		(IIb)		(IIc)	
	H	C	H	C	H	C
1	---	156.8	---	143.6	---	153.1
2	---	---	8.52	142.5	7.12	114.2
3	8.44	148.9	---	---	8.64	149.2
4	7.16	122.7	8.52	147.9	---	---
5	7.70	138.4	7.38	123.5	8.64	149.2
6	7.26	118.7	7.59	127.5	7.12	114.2
7	9.28	163.3	8.57	162.6	8.53	162.6
1'	---	119.5	---	119.2	---	117.2
2'	---	160.2	---	159.1	---	157.9
3'	6.90	120.7	6.98	118.6	6.94	117.5
4'	7.24	133.4	7.33	133.1	7.27	132.3
5'	---	123.5	---	123.5	---	122.2
6'	7.36	132.0	7.38	131.1	7.38	129.9
OH	13.42	---	12.77	---	12.55	---

The most striking feature among the proton data is the shift of the OH signal upon X substitution. As expected, electron-withdrawing substituents (NO_2, Cl) reduce the ability of the imine N atom to hydrogen bond to the OH group; accordingly, the OH signal moves to low frequency. The opposite occurs with electron-donor substituents (CH_3, OCH_3, $N(CH_3)_2$). Figure 1 shows a correlation between these shifts and Hammett's σ constants. A least-squares fit of the data gives

$$\Delta\delta(OH) = -0.880\sigma - 0.0067$$

with a standard deviation of 0.031.

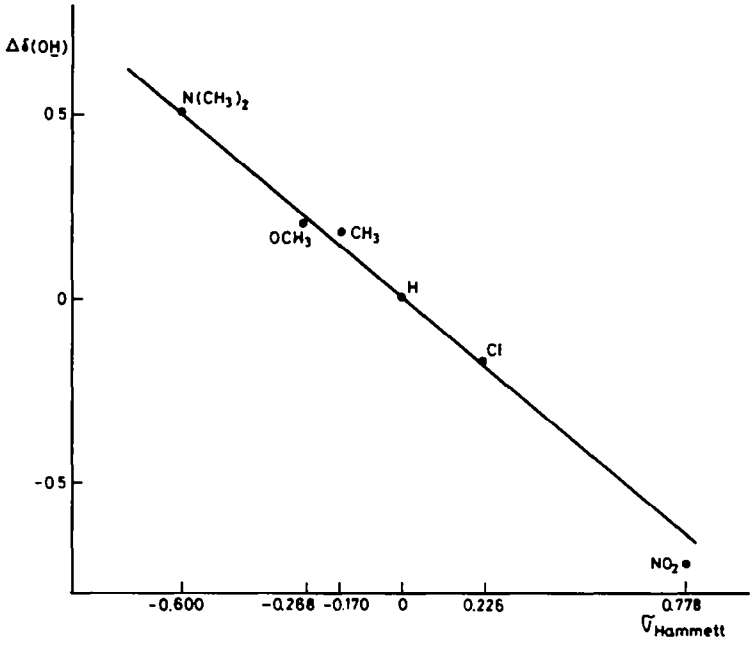
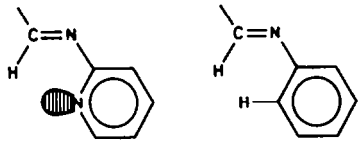


Fig. 1 - Proton OH shifts vs. Hammett's σ constants for imines (I), in $CDCl_3$.

Low-frequency shifts of OH are also observed for (IIb) and (IIc) with respect to (Ic); however, in the case of (IIa) a high-frequency shift occurs. We associate this high-frequency shift with that of proton 7 in (IIa) with respect to (IIb) and (IIc). They can both be explained as follows. The non-bonded interaction between C-H (7) and the N atom in position 2 of the A-ring is less repulsive than between C-H (7) and a C-H (2) group:



As a consequence, the average value for ϕ_A is smaller in (IIa) and this enhances the high-frequency effect of the A-ring current upon H (7) and OH. In addition, we have the electric field effect due to the local dipole associated with the nitrogen N (2) lone-pair, and the magnetic anisotropy effect due to this same atom. These effects have also been invoked to explain proton shifts in phenylazines (13) where similar geometrical arrangements occur.

Regarding the carbon chemical shifts, special attention is paid to C (7) in the imine group and to C (4') in the B-ring. Plots of such chemical shifts vs. Hammett's substituent parameters lead to the following expressions

$$\Delta\delta_{C(7)} = 5.74\ \sigma - 0.78 \qquad (SD = 0.78)$$
$$\Delta\delta_{C(4')} = 1.86\ \sigma - 0.073 \qquad (SD = 0.13)$$

We note that these substituent shifts are not significantly different from those obtained in N-benzylideneanilines substituted only in position 4, which are as follows:

X:	NO_2	Cl	CH_3	OCH_3	$N(CH_3)_2$
C(7)	(2.78)	0.6(0.39)	-0.6(-1.20)	-2.5(-2.06)	-4.0
C(4')	(1.32)	-0.1(0.33)	-0.6(-0.33)	-1.0(-0.20)	-1.1

(the values in brackets are taken from reference 3). This suggests that the inclusion of the OH group does not significantly changes the effective ϕ_B angle, (close to 0°) nor the effective ϕ_A angle, except, perhaps, for $X=N(CH_3)_2$. In this case, a stronger hydrogen bond may help to decrease ϕ_A (n-π conjugation which stabilizes a conformation with ϕ_A=90° is reduced) and thus explain the bigger effect of the dimethylamino group upon C(7) when the OH group is present (-5.3 vs. -4.0). Another possible contribution to this difference may come from an increase of the $n \rightarrow \pi^*$ (and $n-\sigma^*$) excitation energy due to the involvement of the N lone pair in hydrogen bonding; such an increase leads to a smaller paramagnetic term for the adjacent C atom (as well as for N itself, of course).

A more planar arrangement of the A-ring and of the imine nuclear plane in the case of electron-donating substituents may also be the reason why the shifts produced on H(7) are positive and similar to those of electron-withdrawing groups: a smaller effective ϕ_A angle means a bigger high-frequency effect of the A-ring current upon H(7).

B. RELAXATION TIMES

Carbon-13 spin-lattice relaxation times (T_1) are very useful in studying details of molecular motion in solution, especially when they are dominated by the dipolar interaction with the directly bonded protons (14-16). This is most probably the case for the compounds studied. In this case one can calculate effective correlation times, τ_c^{eff}, for the different CH carbons from

$$R_1^{dd} = (\mu_0/2\pi)^2 (\gamma_C \gamma_H \hbar\, r^{-3})^2 . \tau_c^{eff} \qquad (1)$$

where $R_1^{dd} \equiv (T_1^{dd})^{-1}$ are the dipolar (assumed to coincide with the total) ^{13}C spin-lattice relaxation rates, γ_C and γ_H are the magnetogyric ratios for ^{13}C and ^1H nuclei, respectively, and r is the relevant CH bond length.

The values of τ_C^{eff} of the imine CH carbon are a function of overall motion only, whereas the values for benzene ring CH carbons depend both on internal rotation of these rings and on the overall molecular motion. This later motion can be simply analysed by Woessner's equations using a diffusional model with spherical (17) or cylindrical (18) symmetry. The formalism has been extended to fully anisotropic overall motion, both in the analytical (10) and numerical forms (19). Internal motion of chemical groups in the presence of isotropic (17), cylindrical (18) and fully anisotropic (10,19) overall diffusion was also analysed. However, a fully anisotropic diffusion analysis requires the measurement of T_1 for many different carbons, as well as the knowledge of the principal axis of inertia and of diffusion, which may not coincide (10). Therefore, in this work we only undertake a qualitive comparative discussion of the T_1 values shown in Fig. 2 in terms of the two types of motions referred above. Only the values for typical compounds are given in this Figure.

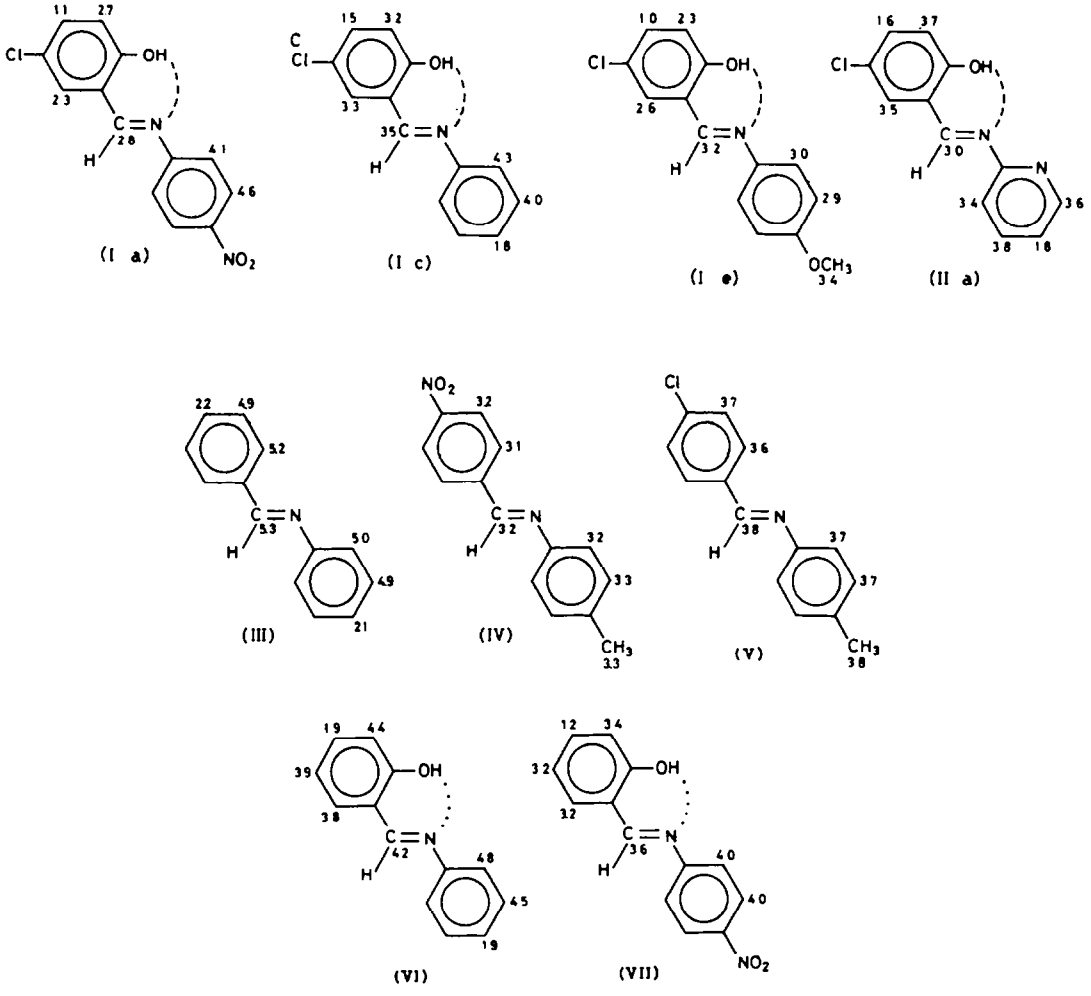
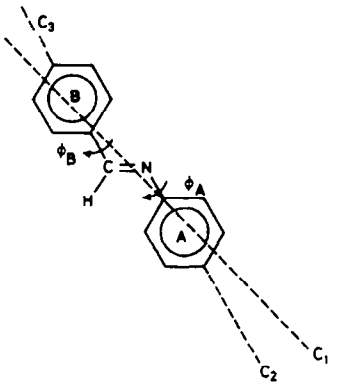


Fig. 2 - ^{13}C T_1 relaxation times (in seconds) for various aromatic imines, in $CDCl_3$

We first discuss the imine CH carbon T_1 values, as they depend only on the overall molecular motion. Assuming that this overall tumbling has axial symmetry

with a constant symmetry axis C_1 for all the compounds studied, represented approximately by the following scheme,



we conclude that their T_1 values (III>VI>V≥VII≥Ic>IV=Ie>IIa>Ia) are dominated by inertial effects due to the substituents the heavier molecules having shorter relaxation times. This is generally also the case for the phenyl CH carbons, although their T_1 values are also modulated by the independent flipping motions of the two phenyl rings A and B along the C_2 and C_3 axis, respectively.

By applying Woessner's equations (17,18) to internal rotations of phenyl groups it has been shown that these motions decrease the relaxation rates of the *ortho*-(o) and *meta*-(m) carbons, relative to the *para*-(p), and that the ratio $\alpha=(T_1^{dd}(p))^{-1}/(T_1^{dd}(o,m))^{-1}$ is a measure of the relative rates of internal motion and overall tumbling: complete rigidity gives $\alpha=1$, whereas very rapid internal rotation (or extreme anisotropy) gives $\alpha=64$(15). The experimental values $\alpha=2.1-2.8$ indicate that phenyl group flipping is only slightly faster than overall tumbling.

We have concluded from the chemical shift data that the OH group does not significantly alter the effective ϕ_B angle, but a reduction of the mobility of the B-ring due to intramolecular hydrogen bonding is likely to occur. This is consistent with the T_1 values for (III) and (VI): a general decrease of T_1 is observed on going from (III) to (VI), as expected from the increased size effect, but the decrease is larger for the B-ring.

A stabilization of a coplanar arrangement of the A-ring and the H-C=N nuclear planes with respect to a perpendicular conformation in the case of electron-donating X groups is expected to reduce the mobility of the A-ring. This is supported by the T_1 values of (Ia) and (Ie); in fact, the T_1 values for the A-ring of (Ie) are smaller than the corresponding ones for (Ia), in spite of (Ia) being heavier.

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