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NMR Spectrum of 2-Methylamino-4-phenylbenzothiazole*

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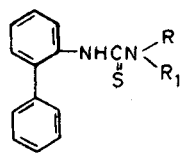
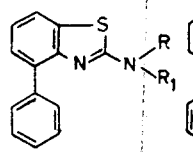
The abnormal chemical shift of the methyl group in the NMR spectrum of 2-methylamino-4-phenylbenzothiazole (V) in concentrated $CDCl_3$ solution (12%, wt/vol.) is attributed to its existence, in part, as the hydrogen bonded dimer (XIV). Further support is provided by the fact that the shift is solvent dependent. In a nonpolar solvent like CS_2, V largely exists as a dimer. The marked high field shifts for V in benzene may be a composite of collision complex and self-association effects. In polar solvent like dioxane and DMSO-d_6 the dimerization by self-association is suppressed due to competition from the solvent molecules, resulting in the almost normal values of methyl shifts. On the above analogy, compounds 2-amino-4-phenylbenzothiazole (IV), 2-methylaminobenzothiazole (X) and 2-aminobenzothiazole (XI) have the possibility of dimeric association by hydrogen bonding, but the absence of methyl in IV, phenyl in X and both in XI makes it impossible to detect the phenomenon in these cases by NMR spectroscopy. The NMR spectra of mixtures of V and X at different concentrations also show shifts in methyl group, thereby indicating that X effectively takes part in hydrogen bonding with V to produce hetero dimer XV.

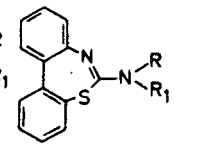
WE wish to report interesting observations concerning the marked concentration and solvent dependence of the chemical shift of the methyl group in the NMR spectrum of 2-methylamino-4-phenylbenzothiazole (V), due to strong intermolecular hydrogen bonding. Compound V and its 2-amino (IV) and 2-dimethylamino (VI) analogues were made by bromine oxidation of the thioureas II, I and III respectively. Alternative structural possibilities VII-IX for the oxidation products were ruled out by a study of their NMR spectra. Thus, the 60 MHz NMR spectrum† of the oxidation product of II (12%, wt/vol. in $CDCl_3$)‡ exhibited a triplet centred at 425 cps, with a spacing of ~7·5 cps, characteristic of the proton at C-6 in 4-substituted benzothiazoles. An one proton triplet is not to be expected of structures VII-IX.



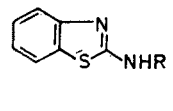
I R=R$_1$=H
II R=H; R$_1$=CH$_3$
III R=R$_1$=CH$_3$



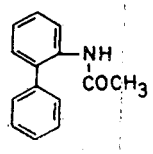
IV R=R$_1$=H
V R=H; R$_1$=CH$_3$
VI R=R$_1$=CH$_3$



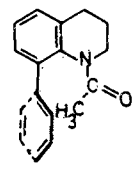
VII R=R$_1$=H
VIII R=H; R$_1$=CH$_3$
IX R=R$_1$=CH$_3$



X R = CH$_3$
XI R = H



XII



XIII

Unexpectedly, the methyl group of V appeared as a singlet at 139 cps, 45 cps higher field than its position in the spectrum ($CDCl_3$) of 2-methylaminobenzothiazole (X)[1]. However, as the concentration was decreased (see Table 1), the methyl signal shifted progressively downfield, and at 0·5%, its position was only slightly upfield from that in X. One possible explanation appeared to be that this might be the manifestation of a stacking effect due to a general type of loose intermolecular association, such as the ones encountered for dimethylformamide[2] and for anthracene-9- and phenanthrene-9-carboxaldehydes[3]. In these cases, collision complexes[4a] may be considered to have been formed among several solute molecules rather than between a solute and a solvent molecule. These effects were, however, small. Further, model compounds

TABLE 1 — SOLVENT AND CONCENTRATION DEPENDENCE OF METHYL SHIFTS (cps) IN 2-METHYLAMINO-4-PHENYLBENZOTHIAZOLE (V)

(Values in cps)

Solvent	Chemical shifts (cps) at conc. (% wt/vol.)						
	12	8	6	4	2	1	0·5
$CDCl_3$	139	146	—	154	162	172	180
$CDCl_3$+D_2O	144	—	—	—	—	—	—
DMSO-d_6	177	—	176	—	—	—	—
Dioxane	171	—	174	—	—	—	—
CS_2	—	—	—	125·5	129·5	134	—
Benzene	—	—	122·5	123·5	127·5	130	—

*Contribution No. 197 from CIBA Research Centre, Bombay.

†All spectra were run on a Varian A60 spectrometer. Chemical shifts are quoted in cps downfield from TMS internal standard; probe temperature was 40°C.

‡All percentages are quoted as wt/vol.

TABLE 2 — SOLVENT AND CONCENTRATION DEPENDENCE OF METHYL GROUP IN BENZOTHIAZOLES VI AND X AND DIPHENYL DERIVATIVES II, XII AND XIII

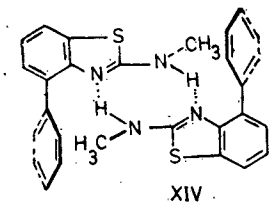
Compound	Solvent	Chemical shift of methyl group in cps (% of solution)
II	$CDCl_3$	178((10%), 180 (5%), 181 (2·5%)
VI	$CDCl_3$	185 (12%), 188 (8%), 190 (2%)
	CS_2	186 (8%)
X	$CDCl_3$	184 (10%), 184 (5%), 187 (1%)
	Benzene	153 (15%)
XII	$CDCl_3$	116 (20%), 117 (10%), 118 (5%)
XIII	$CDCl_3$	86 (20%), 86 (10%), 86 (5%)
	Benzene	86 (10%)
	Dioxane	78 (10%)

II, X and XII which had one or more of the structural features of V had normal chemical shifts for the methyl groups in the NMR spectrum (see Table 2).

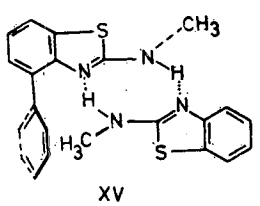
A better explanation for the observations on V would be that it existed, to varying degrees, as the dimer XIV wherein two molecules are held together by hydrogen bonding to nitrogen atoms. The phenyl group at C-4 must be twisted out of the plane of the benzothiazole ring to the extent of having the methyl group in a shielded position. Such a dimeric species must be in a fast equilibrium with the monomer (and perhaps polymers) and the protons on the nitrogen atom must also be exchanging its environment fast[4b]. This would explain the concentration dependence of the chemical shift of the methyl group and its singlet structure. A temperature dependence may likewise be predicted. Molecular weight determination by the osmometric method, carried out on a 1·5% solution of V in $CDCl_3$ at 30°, gave a value of 285. This was not inconsistent with the postulate that V existed partially as the dimer XIV in solution.

A 12% solution of V in chloroform showed in the IR spectrum two bands of medium intensity at 3430 and 3460 cm^{-1} for non-bonded N-H stretching and three strong bands at 3170, 3180 and 3220 cm^{-1} for intermolecularly bonded NH. As the concentration was decreased, the intensity of the bands due to the non-bonded species increased at the expense of the lower frequency bands and at 1% concentration, the intensity of the latter was almost negligible. The UV absorption spectrum of V in 95% EtOH had maxima at 255 (log ϵ 4·43), 278 (log ϵ 4·24) and 308 (inflex) (log ϵ 3·70) and minimum at 265 nm (log ϵ 4·21). The spectrum was similar to that of X[1], but all the maxima had undergone bathochromic shifts. It would thus appear that the phenyl group in V was not quite orthogonal to the benzothiazole plane and was conjugating to a limited extent.

As expected, the chemical shift of the methyl group in V was also solvent dependent (see Table 1).



XIV



XV

TABLE 3 — CHEMICAL SHIFTS OF THE METHYL GROUP IN V AND X IN VARIOUS MIXTURES IN $CDCl_3$

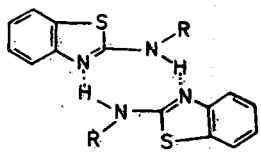
Composition of mixture	Chemical shifts of methyl groups (cps)
V (4%) + VI (12%)	150 (V), 185 (VI)
V (1%) + VI (12%)	166 (V), 185 (VI)
V (4%) + X (10%)	169 (V), 173 (X)
V (12%) + X (1%)	142 (V), 154 (X)
V (8%) + XII (14%)	150 (V), 115 (XII)
X (1%) + XII (20%)	182 (X), 115 (XII)

In the relatively nonpolar solvent CS_2, even in dilute solution, V was largely dimeric. In benzene, likewise, there was a marked high field shift of the methyl group (122·5 cps for 6% and 130 cps for 1% solutions). In the case of 2-methylamino-benzothiazole (X), going from $CDCl_3$ to benzene solution, the methyl group was shifted upfield by 30 cps[1]. This was attributed to the formation of solute-solvent collision complex[4a]. The observed shifts for V in benzene may be a composite of collision complex and self-association effects. In polar solvents like dioxane and DMSO-d_6, dimerization by self-association was suppressed due to competition from the solvent molecules. As a result, the methyl shifts were not only nearer the normal values but were also insignificantly dependent on concentration. A point of minor interest in the DMSO-d_6 spectrum was the fact that in this solvent alone, the proton on the nitrogen was residing long enough on it to allow coupling with the methyl group (J = 5 cps). When a 12% solution of V in $CDCl_3$ was kept in contact with D_2O for 18 hr, the methyl signal moved 5 cps downfield, which would have been expected from the weaker nature of the N-D bond, resulting in monomeric V being preferred to dimer XIV in the equilibrium. The dimethylamino derivative VI does not have the possibility of dimeric association by hydrogen bonding and, accordingly, the chemical shift of its methyl group was negligibly dependent upon concentration or solvent (Table 2).

Additional evidence for the postulate that XIV was present in concentrated solutions of V was obtained by studying the shift of the methyl groups in mixtures of V with IV, VI, X and XII. V cannot form dimers of type XIV with VI and XII. Accordingly, when dilute $CDCl_3$ solutions of V were mixed with relatively concentrated solutions of VI or XII, the methyl group of V suffered only a slight upfield shift in the NMR spectrum. Likewise, the methyl groups in VI and XII were only negligibly affected (see Table 3). Due to the poor solubility of IV in $CDCl_3$, the mixture experiment could be run only in DMSO-d_6 in which very little of V existed as a dimer. Hence, no change in the methyl shift was expected and none was seen.

The situation was dramatically altered when the NMR spectra of $CDCl_3$ solution of mixtures of V and X were run. In the spectrum of a mixture of 4% of V and 10% of X, the methyl group of V was shifted downfield by 15 cps and that of X by 11 cps. On the other hand, in the spectrum of a mixture of 12% of V and 1% of X, the methyl

group of the former moved downfield by 3 cps, while that of X went up by 33 cps. In contrast the NMR spectrum of a mixture of 1% of X and 20% of XII showed only a 5 cps upfield shift for the methyl group of the former and 1 cps downfield shift for that of the latter. It was thus obvious that X effectively took part in hydrogen bonding with V to produce the hetero dimer XV. The observed shifts of the methyl groups in these mixtures would depend upon the equilibria among the monomers V and X, the homo dimers XIV and XVI and the hetero dimer XV. It can also be inferred that besides V, IV, X and XI also exist as dimers to varying degrees in solution. But the absence of the methyl group in IV, the phenyl group in X and both in XI makes it impossible to detect the phenomenon in these cases by NMR spectroscopy.



XVI

The marked solvent and concentration dependence of the chemical shift of the methyl group in V prompted us to re-examine the NMR spectrum of 1-acetyl-8-phenyl-1,2,3,4-tetrahydroquinoline (XIII) more thoroughly. On the basis of data from the NMR spectra of XIII in $CDCl_3$, we had postulated[5] earlier a twisted diphenyl structure with the acetyl group oriented as shown, to explain the low chemical shift of the methyl group. We have now confirmed this further by noting that this shift is concentration independent in $CDCl_3$ and practically unchanged in other solvents (see Table 2).

Experimental Procedure

2-Amino-4-phenylbenzothiazole (IV) — A suspension of N-*o*-biphenylylthiourea[6] (I, 8·5 g; 0·037 mole) in dry $CHCl_3$ (150 ml) was treated with bromine (5·92 g; 0·037 mole). The mixture was refluxed under exclusion of moisture for 3 hr. The solvent was removed *in vacuo*. The residue was treated with ammonia and the crystalline base filtered (8 g). It was recrystallized from ethanol; yield 5·8 g; m.p. 205-6° (Found : C, 69·29; H, 4·65; N, 12·12. $C_{13}H_{10}N_2S$ requires C, 69·01; H, 4·46; N, 12·38%).

2-Methylamino-4-phenylbenzothiazole (V) — Bromine oxidation of N-*o*-biphenylyl-N′-methylthiourea[7] (II) afforded V in 91% yield; m.p. 160-61° (Found: C, 69·88; H, 4·92; N, 11·54. $C_{14}H_{12}N_2S$ requires C, 69·99; H, 5·03; N, 11·66%).

2-Dimethylamino-4-phenylbenzothiazole (VI) — N-*o*-Biphenylyl-N′-dimethylthiourea (III) was prepared from 2-biphenylylisothiocyanate[8] and dimethylamine in ethanol; m.p. 140-42° (Found: C, 70·67; H, 6·40; N, 10·70. $C_{15}H_{16}N_2S$ requires C, 70·29; H, 6·29; N, 10·93%. Bromine oxidation gave VI in 83% yield; m.p. 85-86° (Found: C, 70·67; H, 5·45; N, 10·84. $C_{15}H_{14}N_2S$ requires C, 70·85; H, 5·55; N, 11·02%).

Acknowledgement

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