STRUCTURE OF 2-ARYLAMINO-5,6-DIHYDRO-4H-1,3-THIAZINES

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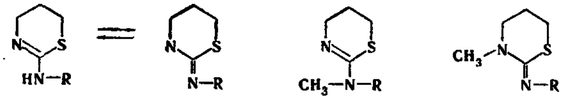
It follows from the data from the PMR, IR, and UV spectra of 2-arylamino-5,6-dihydro-4H-1,3-thiazines and model derivatives with amine and imine structures that they have amine structures.

2-phenylamino derivatives of 4,4,6-trimethyl-4H-1,3-thiazines have amine structures [1, 2]. At the same time, contradictory data regarding the structure of similar 1,3-thiazine derivatives (Ia) have been presented.



I II III

I-III a R = Ar; b R = CH_3

Thus, on the basis of the IR and UV spectra, Tisler [3] concluded that they have an imine structure. Convincing proof in favor of the amino form was subsequently presented with the aid of the same spectra [4] and also the pK_a values of the S- and O-containing analogs [5]. An imine structure for derivatives Ia was later again assumed from an examination of the PMR and IR spectral data [6-8]. It must be noted that a number of inaccuracies, which, in our opinion, could lead to erroneous conclusions, were allowed in these studies. For example, such inaccuracies include the unfortunate choice of the amine model [6, 7], disregard of the closeness of the chemical shifts of the signals of the methylene groups of the heteroring of aryl and alkyl derivatives of 1,3-thiazine [6], and the insufficient reliability of the spectral data for solutions of Ia in trifluoroacetic acid (TFA) (compare [6] and [7]). In addition, the frequency of the absorption of the exocyclic double bond of the imino model at 1610 cm^{-1} is cited [8] from [3] without allowance for the correction in [4], in accordance with which this frequency must be ascribed to the endocyclic C = N bond of the amine model. The indicated contradictions and the data for 4,4,6-trimethyl-substituted 1,3-thiazines [1, 2] have made it necessary to investigate the structure of aminothiazines in the case of Ia and Ib.

The $\nu_{C=H}$ and λ_{max} values of tautomeric derivatives Ia and model compounds with amine structure IIa coincide and differ from the corresponding values for imine models IIIa (Table 1). This indicates the amine structure of aminothiazines Ia and is in agreement with the results in [4].

The imine structure of aryl derivatives Ia in [6-8] was assumed on the basis of the closeness of the chemical shifts of the signals in the PMR spectra for the 4-methylene groups of the tautomers and imine models in deuterochloroform solutions. At the same time, the position of this signal for Ia depends substantially on the temperature, changing by 0.3 ppm in nonpolar solvents from −80° (CS_2,$CDCl_3$) to +115° (tetrachloroethylene); at low temperatures the absorption of the 4-methylene group of the tautomeric compound is found in the region of the signal of the imine model, whereas at high temperatures it approaches the signal of the amine model. In analogy with thiazines [2, 9], this is due to the formation of cyclic dimeric structures of Ia, in contrast to IIa and IIIa, the signals of which remain practially unchanged as the temperature changes. It is evident that it is incorrect to determine the tautomeric state of Ia in nonpolar solvents from the signals of the 4-methylene groups.

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TABLE 1. Data from the IR and UV Spectra of I-IIIa

Compound	R	IR spectra, cm^{-1}, $\nu_{C=N}$, $\nu_{C=C}$		UV spectra, λ_{max}, nm (dioxane)
		crystals	chloroform	
Ia	p-$CH_3OC_6H_4$	1620 s, br, 1573 w, (1600 w, sh)	1607—1597 s, br (1618 sh	266
IIa	p-$CH_3OC_6H_4$	1610 s, br, 1578 m	1610 s, 1597 sh	260
IIIa	p-$CH_3OC_6H_4$	1579 s, br, (1602 sh)	1580 vs, br	244 280 sh, br
Ia	C_6H_5	1610 s, 1577 s	1603 s, 1588 s (1620 sh)	265
IIa	C_6H_5	1613 s, 1589 s	1610 s, 1588 s	268
IIIa	C_6H_5	1570 vs, br	1577 s, (1597 sh)	240 270 sh, br
Ia	o-$CH_3OC_6H_4$	1609 s, br, 1582 s	1641 s (m), 1597 s (1583 sh)	265 285
IIIa	o-$CH_3OC_6H_4$	1568 s, br, 1591 s	1575 s, br, 1593 s	240 sh 286

TABLE 2. Data from the PMR Spectra of I-III

Compound	R	$\delta_{(CH_2)}$, ppm			δ_{NH}, ppm	$\Delta\delta_{(CH_2)}$, ppm			Solvent
		4-CH_2	5-CH_2	6-CH_2		4-CH_2	5-CH_2	6-CH_2	
Ia	p-$CH_3OC_6H_4$	3.37	1.65	2,92	7,53				DMSO
Ia	p-$CH_3OC_6H_4$	3,67	2,32	3,30	8,63 and 7.85	0.30	0,67	0,38	TFA
IIa	p-$CH_3OC_6H_4$	3,43	1,60	2.82	—				DMSO
IIa	p-$CH_3OC_6H_4$	3.66	2.25	3,25	—	0.23	0.65	0,43	TFA
IIIa	p-$CH_3OC_6H_4$	3.22	1.95	2.83	—				DMSO
IIIa	p-$CH_3OC_6H_4$	3.73	2,32	3.23	8.38	0,51	0.37	0.40	TFA
Ia	C_6H_5	3,38	1.65	2,93	7,73				DMSO
Ia	C_6H_5	3.65	2.30	3.25	8.82 and 7.93	0,27	0.65	0.32	TFA
IIa	C_6H_5	3.42	1.60	2,82	—				DMSO
IIa	C_6H_5	3,65	2.25	3.23	—	0.23	0.65	0.41	TFA
IIIa	C_6H_5	3,25	1.97	2.83	—				DMSO
IIIa	C_6H_5	3.75	2.30	3.20	8,48	0.50	0.36	0.37	TFA
Ia	o-$CH_3OC_6H_4$	3.32	1.70	2.92	—				DMSO
Ia	o-$CH_3OC_6H_4$	3.63	2.30	3.27	8.32 and 7.88	0.31	0.60	0.35	TFA
IIIa	o-$CH_3OC_6H_4$	3.25	1.95	2.80	—				DMSO
IIIa	o-$CH_3OC_6H_4$	3,75	2.30	3 21	8,25	0.50	0.35	0,41	TFA
Ib	CH_3	3.35	1.60	2,90	—				DMSO
Ib	CH_3	3.62	2.30	3.27	7.70 and 7.17	0.27	0.70	0,37	TFA
IIb	CH_3	3.38	1.58	2.93	—				DMSO
IIb	CH_3	3.56	2.28	3.27	7,38	0.28	0.70	0,34	TFA
IIIb	CH_3	3.15	1.97	2.90	—				DMSO
IIIb	CH_3	3.67	2.32	3,25	6,93	0 52	0.35	0,35	TFA

Information regarding the structures of derivatives Ia and Ib can be obtained from the change in the form and position of the signal of the NH group as a function of the temperature. Slowing down of exchange of the NH protons is observed in the PMR spectra of solutions of these compounds in deuteroacetone at −90°, and the NH signals appear in the form of a quartet (1 : 3 : 3 : 1) (Ib) and a singlet (Ia) at 9.0 ppm. This form of the signals of the NH protons and the retention of the triplet character of the signals of the 4-methylene groups at low temperatures constitute evidence in favor of the amine structures of alkyl and aryl derivatives Ia and Ib. In the case of Ib, the amine structure also follows from the closeness of the chemical shifts of the signals of the methylene groups of these compounds and the corresponding amine models.

Complete coincidence of the chemical shifts of the signals of all of the methylene groups (see [6]) of the heteroring is observed for Ia and Ib in a polar solvent (DMSO), in which dimers are not formed (Table 2). However, in the case of the aryl derivatives the signals of the 4-methylene groups of tautomeric Ia and amine model IIa do not coincide even in this solvent. This is evidently due to a change in the character of the delocalization of the electron density in the amidine system of the model compounds (as compared with the tautomeric derivatives) due to rotation of the phenyl ring caused by the rather bulky methyl group. A comparison of the chemical shifts of the signals of the 4-methylene protons in order to determine the structure of tautomer Ia therefore proved to be ineffective here.

A comparison of the chemical shift of the 5-methylene groups, which, like the 4-methyl groups of 4,4,6-trimethyl-substituted 1,3-thiazines, are removed from the ring nitrogen atom by one carbon atom and therefore depend to a lesser extent on the character of the hybridization of the ring nitrogen atom, can be considered to be more expedient. The coincidence of δ (5-CH_2) in the PMR spectra of tautomeric Ia and model derivatives IIa (Table 2) indicates the amine structure of 2-arylamino-5,6-dihydro-4H-1,3-thiazines Ia.

It follows from the PMR spectra of TFA solutions of I-III that bases I-III are protonated at the nitrogen atom attached to the C=N double bond, but the positive charge is delocalized over the amidine system. The coincidence of the chemical shifts of the signals of all of the methylene groups of I-III (Table 2) indicates an identical structure for the resulting cations. At the same time, on passing from the bases to the cations the weak-field shifts of the signals of these groups ($\Delta\delta_{CH_2}$) of amine models II and substituted I are found to be close and differ markedly from the corresponding values of models of imine structure III, and the differences between the $\Delta\delta_{CH_2}$ values of the latter (III) and the $\Delta\delta_{CH_2}$ values of tautomeric derivatives I are close to the differences in the chemical shifts of the methylene groups of bases II and III (Table 2). This once again indicates that aryl- and alkylaminothiazines Ia and Ib exist in the amine form.

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SYNTHESIS OF 2-HYDRAZINO- AND 2-AMINO-1,3,4-THIADIAZINES CONTAINING POLYHYDRIC PHENOL RESIDUES IN THE 5 POSITION

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2-Hydrazino-1,3,4-thiadiazines containing polyhydric phenol residues in the 5 position were obtained by reaction of 3,4-dihydroxy-, 2,5-dihydroxy-, and 2,3,4-trihydroxyphenacyl ω-halides with thiocarbohydrazide. 2-Amino-1,3,4-thiadiazines were obtained by reaction of 3,4-dihydroxy- and 2,5-dihydroxyphenacyl ω-halides with thiosemicarbazide in acidic and alcoholic media. In contrast to the dihydroxy derivatives, 2,3,4-trihydroxyphenacyl halide forms a 2-amino derivative only in strongly acidic media, whereas the isomeric thiazole compound with a hydrazine group in the 2 position of the thiazole ring is formed in alcoholic media.

In order to obtain new inhibitor-antioxidants we synthesized a series of 2-hydrazino- and 2-amino-1,3,4-thiadiazines containing polyhydric phenol (pyrocatechol, hydroquinone, and pyrogallol) residues in the 5 position.

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