The authors thank É. B. Lifshits under whose supervision the A values were determined (see Table 1).

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STRUCTURE AND TAUTOMERISM OF SUBSTITUTED 2-AMINO-4H-1,3-THIAZINES

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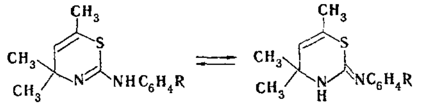
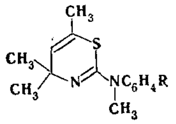
UDC 547.869.543.422.4.6.25

It is shown by means of the IR, UV, and PMR spectra of substituted 2-amino-4H-1,3-thiazines that they exist primarily in the amino form in the crystalline state and in solution.

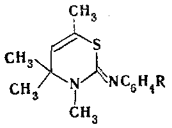
In a previous communication [1] it was shown that an amino structure is characteristic for 4,4,6-trimethyl-2-alkylamino-4H-1,3-thiazine. It might have been assumed that the presence of an electronegative substituent attached to the exocyclic nitrogen atom would promote a shift in the tautomeric equilibrium to favor the imino form [2]. In this connection, in the present research we studied the structure and tautomerism of 4,4,6-trimethyl-2-arylamino-4H-1,3-thiazines (I) [3].



IA IB



II



III

There are two distinct bands of approximately equal intensity associated with the stretching vibrations of the NH bond in the high-frequency region of the IR spectra of all of the investigated compounds (I) in the crystalline state (3105-3200 cm^{-1}) and in solution (3370-3430 cm^{-1}). The intensity of the low-frequency band at ~3380 cm^{-1} in the spectra of very dilute solutions (0.02% in CCl_4) is considerably reduced as compared

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with the band at 3437 cm^{-1}, although it does not completely vanish. This is evidently associated with the presence of rather strong intermolecular hydrogen bonds.

The bands of stretching vibrations of the ring C=C bonds in $CHCl_3$ solution are similar for I (1660-1666 cm^{-1}) and amino models II (1658-1661 cm^{-1}) and differ somewhat from the corresponding bands of imino models III (1668-1670 cm^{-1}). These frequencies of the C=C bonds of the thiazine ring were assigned on the basis of a comparison with the spectra of tetrahydropyrimidine-2-thiones [3] and acyclic S-methylisothioureas, which have only one band of C=C and C=N double bonds, respectively, in this region.

The $\nu_{C=N}$ frequencies* of Ia-f, which are capable of tautomerism, in the crystalline state (1575-1623 cm^{-1}) and in solution (1578-1606 cm^{-1} in $CHCl_3$) are extremely close to the analogous bands in the spectra of N-methylaminothiazines with fixed amino structure IIa-f (1583-1615 cm^{-1} in $CHCl_3$) and are shifted to the high-frequency region as compared with the corresponding C=N band in the spectra of imino models III (1566-1580 cm^{-1}) (see Table 1). A similar difference in the C=N frequencies was previously observed for alkyl [4] and acyl [5] derivatives of thiazoline and alkyl-substituted 1,3-thiazines [1].

These results constitute evidence for the amino structure of the aminothiazines both in the crystalline state and in solution.

Three bands, rather than the two bands observed in the case of the model compounds, are observed in the IR spectra of crystalline p-nitrophenylaminothiazine Ig and of chloroform and dioxane solutions of Ig, for which a shift in the equilibrium to favor the imino form is most likely, in the region of stretching vibrations of double bonds at 1560-1620 cm^{-1}. It may be assumed that this is associated with the presence of a small amount of the imino form in the nitro derivative.

In connection with the different position of the C=N bond in the amine and imine forms one should observe a difference in the anisotropic effect of this bond on the chemical shifts of the ortho protons of the phenyl ring and the protons of the two 4-CH_3 groups. It follows from the PMR spectra that the chemical shifts of the ortho protons of the phenyl ring of the amino models (7.0 ppm, IIb) are shifted to weak field as compared with the imino models (6.75 ppm, IIIb). In addition, the resonance signals of the ortho protons in the spectra of I (7.12 ppm, Ib) are found at even weaker field, and in some cases the difference between the chemical shifts of the ortho protons of tautomeric Ig and amino models IIg ($\Delta\delta$ 0.44 ppm) proves to be greater than the difference in the chemical shifts of these protons in the spectra of models IIg and IIIg ($\Delta\delta$ 0.35).

The chemical shift of the ortho protons of the phenyl ring in the investigated compounds is apparently determined not only by the amino or imino structure of the molecule but also depends on other factors. The latter may include the difference in the character of the association of the molecules of the dissolved substance and the solvent for the model and tautomeric compounds, the different angles of rotation of the phenyl ring for the tautomeric compounds and the more sterically hindered N-methyl derivatives, etc. In this connection, the chemical shift of the ortho protons of the phenyl ring cannot be used to make a reliable choice between the amino and imino structures.

The situation is considerably better when the chemical shifts of the signals of the protons of the 4-CH_3 gem-dimethyl groups are compared. The signals of the protons of these methyl groups (1.27-1.32 ppm) in the PMR spectra of the model compounds of amine structure are shifted to strong field as compared with the imino models (1.39-1.43 ppm) and coincide with the corresponding signals of I (1.29-1.31 ppm). These PMR spectral data are in agreement with the IR spectral data. The results show that it was not possible to shift the tautomeric equilibrium to favor the imino form by introduction of substituted phenyl residues. The possibility of a certain amount of the imino form is not excluded only in the case of the nitro derivative, for which additional bands appear in the IR spectra in the double-bond region.

In the UV spectra one's attention should be directed to the fact that the N-methyl model compounds with fixed amine and imine structures have less distinctly expressed absorption maxima than I, and the intensities of these maxima are considerably lower (see Fig. 1).

As has been observed for 2-alkylamino-4H-1,3-thiazines [1] and in a number of other cases [2, 4, 5], the spectra of the potentially tautomeric compounds and the N-methyl derivatives of analogous structure are usually close. The observed anomaly in the spectra of the N-methyl derivatives as compared with I is evidently associated with steric hindrance arising because of the presence of a methyl group, owing to which the phenyl ring is partially removed from conjugation with the amidine system of bonds. A similar phenomenon was observed

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*The bands of the phenyl ring also lie in the same region (1600 cm^{-1}). In a number of cases it is difficult to clearly distinguish these bands from the frequencies.

TABLE 1. IR and UV Spectra of I-III

Compound	R	IR spectra, ν, cm^{-1}						UV spectra (in dioxane)	
		in the crystalline state			in chloroform				
		phenyl ring C = N and C = C	thiazine ring C = C	NH	phenyl ring C = N and C = C	thiazine ring C = C	NH	λ_{max}, nm	ε
Ia–g	*p*-OC$_2$H$_5$	1614 s 1600 sh	1675 m	3200 m 3130 m, br	1600 vs, br	1663 m	3428 m 3377 m	267	16760
	p-OCH$_3$	1613 s 1601 s	1668 m	3196 m 3140 s	1600 vs, br	1664 m	3430 m 3377 m	265	13640
	p-CH$_3$	1623 s 1606 s	1668 m	3210 m 3133 m, br	1598 vs, br	1663 m	3423 m 3375 m	265	16600
	H	1614 s 1585 s	1676 m	3198 m 3136 m 3108 m	1604—1588 s s	1663 m	3426 m 3373 m	263	17400
	p-Br	1606 s 1575 s	1668 m	3200 m 3140 m	1596 s 1578 s	1660 m	3421 w 3370 w	269	22500
	m-Cl	1614 s 1579 s	1674 m	3200 w 3120 m	1606—1583 s s	1665 m	3422 w 3375 w	265	7600
	p-NO$_2$	1613 s 1595 m 1578 s, br	1668 m	3190 m 3156 m 3105 m	1607 s 1592 s 1578 s	1666 m	3420 w 3379 w	347	19200
IIa–g	*p*-OC$_2$H$_5$	1623 s 1600 sh	1667 m		1615 s 1595 s	1659 m		252 sh 222 sh	8900 18040
	p-OCH$_3$	1613 s 1600 sh	1663 m		1615 s	1658 m		257 sh 222 sh	9000 19240
	p-CH$_3$	1601 vs, br	1658 m		1600 s, br 1620 sh	1660 m		259	8880
	H	1605—1585 s s	1657 m		1612—1590 m s	1661 m		264	7100
	p-Br	1617 s 1587 m	1663 m		1608 s, br 1583 s	1658 m		274	8600
	m-Cl	1617—1592 s s	1664 m		1612—1585 m s	1658 m		273	7400
	p-NO$_2$	1617 s 1587 s	1663 m		1615 m 1590 s	1659 m		355	12100
IIIa–g	*p*-OC$_2$H$_5$	1583 vs, br	1680 m		1578 s, br	1668 w		247 290 sh	16600 6100
	p-OCH$_3$	1584 vs, br	1666 m		1580 vs, br	1669 w		246 290 sh	17400 6800
	—H	1570 vs, br	1662 m		1578 vs, br	1668 w		236 280 sh	14400 6500
	p-Br	1564 vs, br	1675 m		1577 vs, br	1669 w		252 286 sh	16940 8800
	m-Cl	1573 vs, br	1667 m		1577 vs, br	1670 w		240 w, sh 284 w, sh	14060 7200
	p-NO$_2$	1567 vs, br 1597 m	1676 w		1566 vs, br 1598 m	1670 w		340 248 w, sh	14260 9100

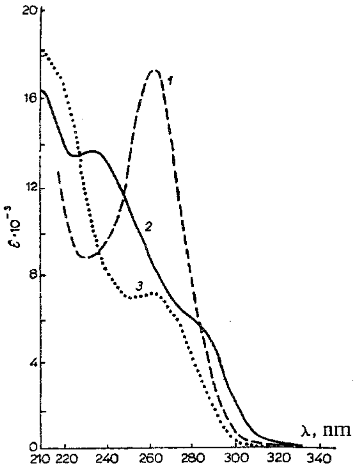


Fig. 1. UV spectra in dioxane: 1) 4,4,6-trimethyl-2-phenylamino-4H-1,3-thiazine (Id); 2) 3,4,4,6-tetramethyl-2-phenylimino-2,3-dihydro-4H-1,3-thiazine (IIId); 3) 4,4,6-trimethyl-2-methylphenylamino-4H-1,3-thiazine (IId).

in the UV spectra of 2-phenylamino-4-oxazolidone [6] and its amino model, as well as in several other cases [7]. In addition, if one considers the positions of the absorption maxima rather than their intensities, the spectra of tautomeric I are close to those of their amino models (II) with respect to this parameter and differ from those of imino models III (see Table 1). This also provides evidence in favor of the amino structure of arylaminothiazines I.

The anomalous effect of the methyl group in the N-methyl models is also in agreement with data on the basicities of these compounds. Thus, proceeding from the spectral data on the shift of the tautomeric equilibrium to favor the amino form, one might have expected that the basicities of amino models II would be close to the basicities of tautomeric compounds I and lower than the basicities of the corresponding imino models (III), as in the case of alkylaminothiazines [1]. In fact, different relationships in the basicities are observed (for example, pK_a 5.88 for IId, 5.10 for Id, and 4.42 for IIId in CH_3OH).

The decrease in the basic properties of III as compared with I and II is due to the existence of a p-π interaction of the proton-acceptor center – the exocyclic nitrogen atom – with the phenyl ring. Derivative IId has the maximum basicity, apparently due to the steric interaction of the CH_3 group with the phenyl ring, as a result of which the latter is removed from conjugation with the amidine system of bonds. This sort of steric effect is absent in I that have a hydrogen attached to the exocyclic nitrogen atom, and the conjugation of the phenyl ring with the amidine system of bonds reduces the basicity somewhat.

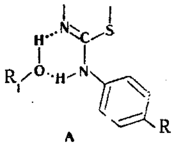
In the UV spectra of I one's attentions should also be directed to the systematic decrease in the intensities of the maxima (and, in some cases, to the change in the form of the absorption bands) on passing from nonpolar solvents (hexane and dioxane) to alcohol and aqueous alcohol mixtures.* A sharp change in the spectra of all of the compounds is observed in mixtures with a high percentage of water (95%), and they become similar to the spectra in 0.1 N HCl.

These changes in the UV spectra of I may be due to several reasons: a) ionization (protonation) of the molecules to give the corresponding cations; b) a shift in the tautomeric equilibrium to favor the imino form on passing to hydroxyl-containing solvents; c) solvation of I molecules with the formation of intermolecular hydrogen bonds with water molecules.

On the basis of the identical character of the spectra of I in alkaline and aqueous alcohol mixtures containing up to 50% water, protonation is practically excluded (for If even in 75% aqueous alcohol). However, it may be one of the reasons for the observed phenomena in solutions with a high water content (~95%), inasmuch as the character of the spectra in such media approaches the character of the spectra obtained from 0.1 N HCl solutions.

Insofar as tautomerism is considered as the reason for the changes in the spectra, it is extremely difficult to arrive at an unambiguous conclusion from UV spectral data here (see above). However, as we have shown above, according to the IR and PMR spectral data, compounds I exist in the amino form, and the indicated changes in the UV spectra apparently cannot be associated with tautomerism.

Thus one is left with the assumption that the principal reason for the changes in the spectra is specific solvation of the molecules due to the formation of intermolecular hydrogen bonds of the A type with hydroxyl-containing solvents.



A

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* Changes are also observed in the spectra of N-methyl derivatives II and III, but they are considerably weaker and less distinct than in the case of I.

The character of the conjugation of the phenyl ring with the amidine system of bonds changes in this sort of solvated molecule, and this may lead to a decrease in the intensities in the maxima in the UV spectra [8, 9]. The formation of the indicated hydrogen bonds can be considered to be a process that precedes complete protonation.

EXPERIMENTAL

The IR spectra of mineral oil pastes and solutions ($CHCl_3$, CCl_4, dioxane, and C_2H_5OD) of the compounds were recorded with a Perkin–Elmer recording spectrometer. The UV spectra of solutions of the compounds in dioxane, hexane, 95% hexane + 5% dioxane, alcohol, aqueous alcohol mixtures, and aqueous and alcoholic 0.1 N HCl and 0.1 N NaOH were obtained with an EPS-3 spectrophotometer. The PMR spectra of CD_3OD solutions were recorded with a JNM-C-60HL spectrometer with tetramethylsilane as the internal standard.

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BENZOXAZINES AND RELATED COMPOUNDS

V.* SYNTHESIS OF 2,4,4-TRISUBSTITUTED 4H-1,3-BENZOTHIAZINES

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UDC 547.869.1+547.895

The reaction of 2-mercapto(and benzylthio)-α,α-dialkylbenzyl alcohols with nitriles under the influence of acids serves as a method for the synthesis of 2,4,4-trisubstituted 4H-1,3-benzothiazines.

It has been shown that the reaction of 2-hydroxy-α,α-dialkylbenzyl alcohols with nitriles in the presence of acids leads to substituted 4H-1,3-benzoxazines [1, 2].

We have found that replacement of the 2-hydroxy group by a 2-mercapto(and benzylthio) grouping (alcohols IIa-d) leads to the previously unknown 2-substituted 4,4-dialkyl-4H-1,3-benzothiazines (IIIa-e) under similar conditions.

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*See [11] for communication IV.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, pp. 1620–1624, December, 1975. Original article submitted January 3, 1975.