LITERATURE CITED

1. K. Venkataraman (editor), The Chemistry of Synthetic Dyes, Vol. 3, Academic Press (1970-1972).
2. K. H. Drexhage, Topics in Applied Physics, 144 (1973).
3. D. M. Brown and G. A. R. Kon, J. Chem. Soc., 2147 (1948).
4. I. Ya. Postovskii, L. N. Pushkina, and S. A. Mazalov, Zh. Obshch. Khim., 32, 2617 (1962).
5. W. Ried and S. Hinsching, Ann., 600, 47 (1956).
6. F. A. Mikhailenko and A. N. Boguslavskaya, Ukr. Khim. Zh., 35, 943 (1969).
7. L. Bellamy, Infrared Spectra of Complex Molecules, Methuen (1958).
8. G. I. Kagan, V. A. Kosobutskii, V. K. Belyakov, and O. G. Rarakanov, Khim. Geterotsikl. Soedin., No. 2, 189 (1974).
9. G. V. Gobov, R. N. Nurmukhametov, and L. N. Pushkina, Zh. Fiz. Khim., 43, 57 (1969).

BASICITIES AND STRUCTURES OF 4,4,6-TRIMETHYL-2-ARYLAMINO-5,6-DIHYDRO-4H-1,3-THIAZINES AND 4,4,6-TRIMETHYL-2-ARYLAMINO-5,6-DIHYDRO-4H-1,3-OXAZINES

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UDC 547.867.869:541.623:543.257.1

The relative basicities of 4,4,6-trimethyl-2-arylamino-5,6-dihydro-4H-1,3-thiazines and 4,4,6-trimethyl-2-arylamino-5,6-dihydro-4H-1,3-oxazines, which are capable of amine–imine tautomerism, and of model compounds with fixed amine and imine structures were determined by potentiometric titration in methanol. Good correlation of the pK_a values with the Hammett σ constants in the investigated reaction series was found. The inapplicability of the use of the pK_a values of model compounds for the determination of the tautomeric equilibrium constants in the case of some N-heterocyclic amines of nonaromatic character with an aryl substituent attached to the exocyclic nitrogen atom of the amidine fragment of the molecule is demonstrated.

We have previously established that 4,4,6-trimethyl-2-arylamino-5,6-dihydro-4H-1,3-thiazines (I) and 4,4,6-trimethyl-2-arylamino-4,6-dihydro-4H-1,3-oxazines (II) exist in the crystalline state in the amine form (A), which also predominates in solvents with different polarities. This conclusion was drawn on the basis of a comparison of the spectral characteristics of tautomeric I and II and model compounds – 4,4,6-trimethyl-2-(N-methyl-N-aryl)amino-5,6-dihydro-4H-1,3-thiazines (III) and 4,4,6-trimethyl-2-(N-methyl-N-aryl)amino-5,6-dihydro-4H-1,3-oxazines (IV), which have a fixed amine structure, and 3,4,4,6-tetramethyl-2-aryliminotetrahydro-1,3-thiazines (V) and 3,4,4,6-tetramethyl-2-aryliminotetrahydro-1,3-oxazines (VI), which have a fixed imine structure. In addition, in [2] we demonstrated the inapplicability of the use of the ionization constants of model compounds for the determination of the tautomeric equilibrium constants (K_t) in the 4,4,6-trimethyl-2-arylamino-4H-1,3-thiazine (VII) series because of considerable steric-electronic differences in the models and the corresponding tautomeric compounds.

TABLE 1. Relative Basicities of Aminothiazines and Aminooxazines of Reaction Series I-VI

Reaction series	Hetero-atom Y	Basicity constant $pK_a \pm 0.04$						
		a X= $=p\text{-}OCH_3$	b X= $=p\text{-}C_2H_5$	c X= $=p\text{-}CH_3$	d X= $=m\text{-}CH_3$	e X=H	f X=p-Br	g X=p-Cl
Ia,c–g	S	7,56	—	7,31	7.07	6,88	6,29	5,90
IIa–g	O	8,80	8,74	8,53	8,39	8,30	7,65	7,42
IIIa,c–g	S	8,11	—	8,02	7,92	7,79	7,25	7,05
IVa–g	O	9,35	9,24	9,08	9,10	8,94	8,52	8,36
Va, c, e	S	6,96	—	6,65	—	6,25	—	—
VIb–g	O	—	8,49	8,28	8,14	7,97	7,22	7,00

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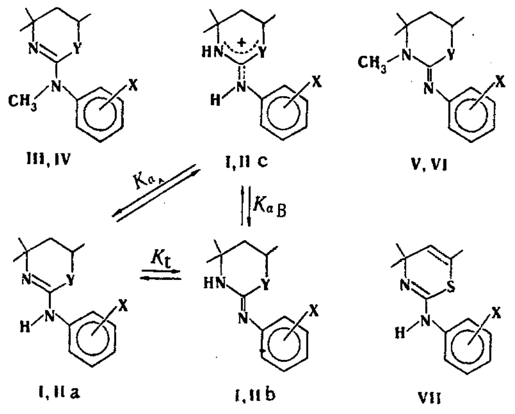
TABLE 2. Parameters of the Correlation of the pK_a Values of Compounds of Series I-IV and VI with the Hammett σ Constants

Series	pK_{a_0}	$-\rho$	r	s	s_ρ
I	6,88	2,54	0,997	0,03	0,09
III	7,66	1,77	0,989	0,07	0,13
II	8,22	2,18	0,987	0,10	0,16
IV	8,92	1,15	0,988	0,06	0,11
VI	7,91	2,53	0,994	0,08	0,15



Ia-c, III, V Y=S; IIa-c, IV, VI Y=O

In order to verify and correlate the results, the possibility of the determination of the K_t values for compounds of the thiazine and oxazine series (I and II) by means of data on the basicities of model compounds III, V and IV, VI is examined in the present research. Information regarding the basicities of amino derivatives of 1,3-thiazines and 1,3-oxazines is also of independent interest, since the ionization constants are one of the important quantitative characteristics of their reactivities.

The amine–imine tautomerism of the investigated compounds (IA⇌IB and IIA⇌IIB) is an acid–base protolytic equilibrium that is realized through a common mesomeric cation; this is confirmed by the identical character of the electronic spectra of aminothiazines I and aminooxazines II and the spectra of the corresponding model compounds II, V and IV, VI in 0.1 N hydrochloric acid and in a 0.1 N solution of HCl in methanol. This makes it possible to use the ionization constants of model compounds [3] to determine K_t.

The relative pK_a values of compounds of reaction series I-VI, determined by potentiometric titration in methanol, are presented in Table 1.

Analysis of the data on the basicities of compounds of series I-VI shows that replacement of the sulfur atom in the ring by an oxygen atom increases the basicities of the oxazines by 1-1.5 pK_a units; this is evidently explained by the higher degree of interaction of the 2p electrons of the oxygen atom in the oxazines with the 2π electrons of the C=N bond of the amidine fragment as compared with the analogous interaction of the 3p electrons of the sulfur atom in the thiazines, both in the bases and in the protonated forms [4, 5].

A similar relationship in the basicities of O- and S-heteroanalogs was previously established in the case of some similarly constructed N-heterocyclic amines of nonaromatic character [6]. At the same time, the opposite principle in the basicities of S- and O-analogs is observed in heterocyclic compounds in which the p electrons of the oxygen or sulfur atoms additionally interact with the π electrons of the C=C bond via a scheme of the mesomeric type to form an aromatic system of bonds (for example, in substituted 2-aminothiazoles, 2-aminooxazoles [7], 4,5-tetramethylene-2-aminothiazoles, and 4,5-tetramethylene-2-aminooxazoles [8]). In compounds of this type the effect of the heteroatom on the electron density of the protonation center of the amidine system is apparently due to the large contribution of the inductive component.

The pK_a values of compounds of reaction series I-IV and VI correlate well with the Hammett σ constants (Table 2). Only three compounds were studied in series V.

The linear dependence of the pK_a values on the Hammett σ constants in the series of tautomeric I and II provides evidence for a shift in the A⇌B tautomeric equilibrium to favor one of the tautomers [9], which, judging from the parameters of the IR and UV spectra, is amine form Ia and IIa.

Since in acid–base tautomeric systems the equilibrium is always shifted to favor the less basic tautomeric form [9], whereas transition from tautomeric compounds to their N-methyl-substituted models, as is supposed, changes the basicity only slightly (with allowance for the +I effect of the methyl group) [3], one might have expected lower basicities for amine models III and IV as compared with the basicities of imine models V and VI.

A comparison of the pK_a values of the amine and imine models shows that imine models V and VI are less basic, i.e., there is a "reversal" of the relative basicities of the models similar to that which we previously established [2] during a study of basicity and tautomerism in the 2-amino-4H-1,3-thiazine series (VII). The same relationships in the pK_a values of models has been noted [6] for some similarly constructed nonaromatic N-heterocyclic amines, for example, for the tautomerism-capable models 2-phenylamino-2-thiazoline, 2-phenylimino-5,6-dihydro-4H-1,3-thiazine, and 2-phenylamino-5,6-dihydro-4H-1,3-oxazine, although a shift in the equilibrium to favor the amine form has been established for tautomeric compounds by means of spectral data.

The reason for the observed anomaly in the basicities of the model structures for compounds of this type is evidently, as we have previously discussed in detail [2], the substantial difference in the conformations of the molecules of the tautomeric forms and the corresponding model compounds, which consists of a different mutual orientation of the aromatic ring of the arylamino group relative to the amidine fragment of the molecule. This three-dimensional difference results in a change in the character and degree of electronic interaction in the molecules of the model compounds, and, as a consequence, the amine models become more basic than the imine models. This circumstance does not justify the use of the ionization constants of model structures for determination of the tautomeric equilibrium constants in nonaromatic heterocyclic compounds of the I and II type with an aryl substituent attached to the exocyclic nitrogen atom.

The normal relationship of the pK_a values of the model compounds corresponding to that observed for the individual tautomers evidently holds only in the case of those N-aryl-N-heterocyclic amines in which the tautomeric equilibrium is shifted markedly ($K_t > 10^3$) to favor the form that has an aromatic system of bonds, for example, in substituted 2-arylaminooxadiazoles [10, 11]. In this case the absolute values of the ionization constants of the model compounds may change substantially as compared with the ionization constants of the tautomers because of conformational-electronic factors, but no "reversal" of them occurs.

In those cases where hydrogen atoms or an alkyl or aralkyl substituent are attached to the exocyclic nitrogen atom of the amidine fragment in place of an aryl group, which interacts directly with the amidine system, there is no substantial change in the character of the electronic interactions on passing from the tautomeric forms to their N-methyl-derivative models, and the basicities of the latter change only slightly; this is due primarily only to the inductive effect of the methyl group, and the ratios of the pK_a values of the models sufficiently accurately correspond to the ratios of the pK_a values of the tautomeric forms. As applied to such compounds, the method of determination of the K_t values by means of the ionization constants of model compounds is correct and gives good results, particularly for N-heteroaromatic tautomeric systems with a markedly shifted equilibrium [3, 8, 12-15].

EXPERIMENTAL

The compounds of series I-VI were synthesized previously in [16-18], and their purity was confirmed by TLC data and also by the results of potentiometric titration, the error in which did not exceed 2%. The ionization constants were determined by potentiometric titration with 0.1 N perchloric acid of $(5-7) \cdot 10^{-3}$ M solutions of the compounds in anhydrous methanol at 20° by means of an LPU-01 pH meter, an ÉSL-41G-04 glass electrode, and a small calomel electrode filled with a saturated solution of potassium chloride in methanol. The electrodes were calibrated with respect to a 0.05 N potassium biphthalate solution (pH 4.00), a phosphate buffer (pH 6.88), and 0.01 M sodium tetraborate solution (pH 9.22). The potentiometer was adjusted according to the method in [19]. The error in the determination of the pK_a values did not exceed 0.04 pK_a units. The correlation parameters were obtained by statistical treatment of the results by the method of least squares.

LITERATURE CITED

1. E. M. Peresleni, A. P. Engoyan, T. D. Zotova, Yu. N. Sheinker, L. A. Ignatova, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 3 (1977).
2. L. A. Ignatova, P. L. Ovechkin, A. E. Gekhman, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 6, 777 (1975).
3. A. Katritzky and J. Lagowski, Advances in Heterocyclic Chemistry, New York (1963).
4. B. A. Trofimov, É. I. Kositsyna, N. I. Shergina, S. T. Shevchenko, and E. P. Vyalykh, Izv. Akad. Nauk SSSR, Ser. Khim., 1581 (1971).

5. L. Wallmark, M. H. Krackov, Chu Shi-Hsi, and A. G. Mautnes, J. Am. Chem. Soc., 92, 4447 (1970).
6. H. Najer, J. Armand, J. Menin, and N. Voronin, Compt. Rend., 260, 4343 (1965).
7. U. Stauss, H. Harter, and O. Schindler, Chimia, 27, 99 (1973).
8. H. Najer, J. Giudicelli, and J. Menin, Bull. Soc. Chim. France, 2040 (1967).
9. M. I. Kabachnik, Zh. Veseoyuzn. Khim. Obshchestva, 263 (1962).
10. J. Giudicelli, J. Menin, and H. Najer, Bull. Soc. Chim. France, 870 (1969).
11. J. Giudicelli, J. Menin, and H. Najer, Bull. Soc. Chim. France, 874 (1969).
12. G. Bianchi, A. Boulton, L. Fletcher, and A. Katritzky, J. Chem. Soc., B, 2355 (1971).
13. J. Giudicelli, J. Menin, and H. Najer, Bull. Soc. Chim. France, 4568 (1968).
14. J. Pitha, J. Jones, J. Kovar, and K. Blaha, Coll. Czech. Chem. Commun., 26, 834 (1961).
15. P. L. Ovechkin, L. A. Ignatova, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 7, 946 (1971).
16. L. A. Ignatova, P. L. Ovechkin, M. Z. Branzburg, A. E. Gekhman, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 8, 1037 (1972).
17. P. L. Ovechkin, L. A. Ignatova, A. E. Gekhman, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 3, 357 (1973).
18. L. A. Ignatova, A. E. Gekhman, P. L. Ovechkin, and B. V. Unkovskii, Khim. Geterotsikl. Soedin., No. 3, 354 (1974).
19. A. Albert and E. Serjeant, Ionization Constants of Acids and Bases, Methuen (1962).

SYNTHESIS OF THE β ISOMERS OF 2,4,6-TRISUBSTITUTED 1,3,5-TRITHIANES

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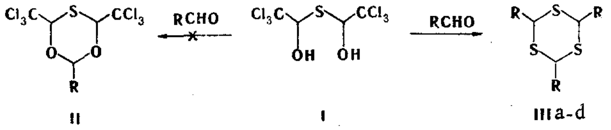
UDC 547.871.07:541.63

The condensation of bis(α-hydroxy-β,β,β-trichloroethyl) sulfide with aldehydes under acid catalysis conditions gives 2,4,6-trisubstituted 1,3,5-trithianes. The latter are realized only in the thermodynamically more favorable β forms.

It is known [1] that the addition of H_2S to carbonyl compounds frequently gives 1:2 adducts. When we carried out the condensation of the CCl_3CHO-H_2S adduct (I) with aldehydes we obtained derivatives of the 1,3,5-trithiane series (IIIa-d) instead of the expected 1,3,5-dioxathiane systems (II).



III a R=CH_3; b R = C_6H_5; c R=p-ClC_6H_4; d R=p-$NO_2C_6H_4$

A sufficiently large number of methods for the synthesis of 1,3,5-trithianes are presented in the literature, and the most widely used method is the reaction of H_2S with aldehydes [2]. The formation of polymeric impurities should be considered to be the only disadvantage of the "hydrogen sulfide" method. In accordance with our synthetic method, the yields of 1,3,5-trithianes in the case of aromatic aldehydes are close to quantitative, and practically pure substances are obtained. There is a reference in [3] that the introduction of a strong acceptor group in the aromatic ring does not promote the formation of thioaldehyde in the reaction of aldehydes with B_2S_3 and SiS_2. We were able to obtain trithiane IIId from sulfide I and p-nitrobenzaldehyde, but, because of its ex-

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