Binuclear Crown-Ethers (XV-XVII). Solutions of 0.01 mole aza-15-crown-5 and 0.005 mole of the corresponding polyoxyethylene diisothiocyanate in 5 ml methanol were mixed with stirring. The reaction mixture was warmed to 40-45°C. After stirring for 15 min, the methanol was extracted under reduced pressure. The product was obtained in the form of an oil which did not require further purification.

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BASICITY AND MECHANISM OF TRANSMISSION OF ELECTRONIC EFFECTS OF SUBSTITUENTS IN THE SERIES OF 2-AMINO-5-ARYL-1,3,4-THIADIAZOLES

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UDC 547.794.3.04:548.422.6

The basicity of 2-amino-5-aryl-1,3,4-thiadiazoles was studied. A correlation was obtained between the pK_{BH+} values of the compounds and the σ constants of the substituents. It was shown that the electronic effects of the substituents in the phenyl ring are transmitted both on account of conjugation and by an induction mechanism.

2-Amino-5-aryl-1,3,4-thiadiazoles (I) are potential biologically active substances [1]. In order to predict the behavior in acid-catalyzed reactions and to assess the transmission of the effects of the substituents through the thiadiazole ring we investigated their basicity. For this purpose we studied the IR spectra of compounds (I) in aqueous solutions with various acidities.

The electronic spectra of aqueous solutions of compounds (I) are characterized by an absorption maximum in the region of 275-300 nm [with the exception of (Ih)].
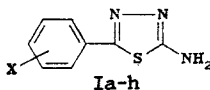
I a X=H; b X=p-OCH$_3$; c X=m-Br; d X=p-Br; e X=p-Cl; f X=p-F; g X=m-NO$_2$; h X=p-NO$_2$

TABLE 1. The UV Spectra and Ionization Constants of the Compounds

Compound	UV spectrum, λ_{max}, nm ($\varepsilon \cdot 10^{-4}$, liter/mole·cm)		pK_{BH^+}*	λ_{anal}, nm
	B (pH=7,5)	BH$^+$ (0,2N. H$_2$SO$_4$)		
Ia	282 (1,28)	267 (1,42)	2,47	285
Ib	297 (1,59)	292 (1,75)	2,56	285
Ic	297 (3,64)	277 (4,35)	2,22	300
Id	300 (2,64)	283 (3,20)	2,33	285
Ie	298 (1,61)	282 (1,95)	2,34	290
If	291 (2,51)	277 (2,91)	2,39	300
Ig	275 (2,75)	260 (3,59)	2,01	265
Ih	337 (2,69)	303 (3,11)	1,87	345

*With a correction for the ionic strength of the solution $\mu = 0.01$, error ± 0.05.

On the basis of the position and intensity this band can be assigned to the $\pi-\pi^*$ transition of the conjugated aminophenylthiadiazole chromophore. With change in the pH value from 4 to 1 there is a hypsochromic shift of the absorption band by approximately 15 nm. We attributed the changes in the UV spectra to the protonation of compounds (I), which reduces the extent of the chromophore. Both the nitrogen atom in the amino group and the heteroatoms of the ring can act as nucleophilic centers in aminoazoles [2]. For the series of 5(3)-substituted 3(5)-amino-1,2,4-triazoles and 5(3)-substituted 1,2,4-triazoles (with and without the amino group respectively) the basicity changes little, and there is common correlation between the pK_{BH^+} values and the sum of the σ constants of the substituents. This made it possible to show unambiguously that the point of protonation is the nitrogen atom of the ring [3]. The 3- and 5-aminoisoxazoles are protonated at this nitrogen atom, situated in the ring, while 4-amino-isoxazole is protonated at the exocyclic nitrogen atom [2].

The position of protonation at the exocyclic nitrogen atom was demonstrated by comparison of the IR spectra of (Ia) and its hydrochloride. In the IR spectra of (Ia) in the high-frequency region there are absorption bands at 3300 and 3100 (NH) and 1650 cm^{-1} (C=N), belonging to the stretching vibrations, and there is also a band due to the deformation vibrations of the NH$_2$ group (1635 cm^{-1}). In the IR spectra of the hydrochloride of (Ia) there are bands at 3260 and 3025 cm^{-1}, while the bands corresponding to the C=N stretching vibrations lie at 1650 cm^{-1}; the vibrations of the C=NH group [4] are absent. The band for the deformation vibrations of the amino group in the hydrochloride of (Ia) is shifted toward the low-frequency region compared with the corresponding band of the free amine (1630 cm^{-1}). Thus, the IR spectra of (Ia) and its hydrochloride indicate that the proton adds to (Ia) at the exocyclic nitrogen atom.

Protonation can take place at different centers in the solid sample and in solution. Therefore, in addition to the UV spectra of the amines, we investigated the protonation of the model 2-chloro-5-p-chlorophenyl-1,3,4-thiadiazole (II). In the thiadiazoles (I), as in the 1,2,5-oxadiazoles [5], substitution of the amino group by the halogen gave rise to a considerable reduction in basicity, which indicates a change in the point of protonation. The changes in the UV spectra of solutions of (IIh) and, accordingly, protonation at the ring nitrogen atom only begin when the sulfuric acid concentration is increased above 15%. The difference in the basicity of the amino group and the thiadiazole ring in compounds (I) thus amounts to more than three orders of magnitude, which makes it possible to neglect the second protonation constant at pH values between 1 and 4 and to calculate the protonation constant of the amino group in compounds (I) by the method in [6].

The spectral characteristics of the amines (I) in the neutral and protonated forms and also the ionization constants of the respective conjugate acids are given in Table 1.

The obtained results agree satisfactorily with the pK_{BH^+} value of the amine (Ia) (2.9) [7]. The difference of 0.43 units is probably explained by the fact that the UV spectrum assigned to the nonprotonated compound was recorded in water [7], which has a small buffer capacity.

The pK_{BH^+} values of the investigated aminothiodiazoles (I) correlate satisfactorily with the σ^0 constants of the substituents in the phenyl ring.

$$pK_{BH^+} = (2.50 \pm 0.02) - (0.65 \pm 0.03)\sigma^0$$

$$(r = 0.99, \ S = 0.03, \ n = 8). \tag{1}$$

In this case the thiadiazole ring acts as a conducting unit between the substituted benzene ring and the amino group. From comparison with the analogous correlation for anilines in which the ρ_A value amounts to 2.889 [8] or 2.54 (with the exclusion of phenols with electron-withdrawing substituents at the para position from the series), we determined the transmission factor [9] for the thiadiazole ring. The value of $\pi' = \rho/\rho_A$ lies between 0.65/2.889 and 0.65/2.54, which is 0.22 to 0.26, i.e., the thiadiazole ring is comparable in its conductivity with the para-phenylene bridge ($\pi' = 0.27$) [9]. For the investigated compounds in contrast to anilines, for example, there is no direct polar conjugation between the amino group and the substituents in the phenyl ring. This is demonstrated by the agreement, within the experimental error limits, between the calculated and experimental pK_{BH^+} values for the para-halogeno and para-nitrophenyl derivatives (Id-f, h). Judged from the intense yellow color of the nitro derivative (Ih) and of its solutions and the position of the absorption band in the UV spectrum ($\lambda_{max} = 337$ nm), which is shifted appreciably toward the long-wave region, compound (I) would have to be assigned a structure with intramolecular charge transfer from the amino group of the thiadiazole to the para-nitro group in the phenyl ring. However, direct polar conjugation is evidently realized only in the excited state, since the pK_{BH^+} values correlate satisfactorily with the σ^0 constants of the substituents.

In order to determine the mechanism of the transmission of the effect of the substituents in the phenyl ring in the investigated compounds we undertook a two-parameter correlation between the pK_{BH^+} values and the σ_I and σ_R constants:

$$pK_{BH^+} = 2.47 - 0.71 \cdot \sigma_I - 0.62 \cdot \sigma_R \tag{2}$$

$$(n = 8, \ r_{multiple} = 0.98, \ r_I = 0.94, \ r_R = 0.95).$$

The analogous equation for the series of anilines with the same substituents has the following form:

$$pK_{BH^+} = 4.56 - 3.57 \cdot \sigma_I - 4.08 \cdot \sigma_R \tag{3}$$

$$(r_{multiple} = 0.96, \ r_I = 0.92, \ r_R = 0.89).$$

In spite of the low correlation coefficient of the relationship for the anilines [Eq. (3)], which is due to the neglect of direct polar conjugation, it is seen from comparison of Eqs. (2) and (3) that the role of the resonance effect in the phenylthiadiazole system (I) compared with the phenyl system is somewhat smaller. Accordingly, the transmission coefficients amount to $\pi'_I = 0.20$ and $\pi'_R = 0.15$. Thus, for the investigated series of 2-amino-5-aryl-1,3,4-thiadiazoles (I) variation of the substituent in the phenyl ring has an appreciable effect on the basicity of the amino group. The electronic effects of the substituents are transmitted both through conjugation and by an induction mechanism, and in contrast to anilines with the same substituents the induction mechanism predominates; direct polar conjugation between the R substituents and the amino group is not realized. The basicity of compounds (I) can be calculated from the σ^0 constants of the substituents.

EXPERIMENTAL

Compounds (I) were obtained by the method in [10], (II) by the method in [11], and the hydrochloride of (Ia) by the method in [12]. The IR spectra were recorded on an IKS-29 spectrometer for films and for tablets with potassium bromide. The UV spectra of the aqueous and buffer solutions were recorded on a Perkin-Elmer 402 spectrophotometer in a 1-cm cuvette at 25°C. The spectra of the limiting forms of the investigated compounds (protonated and neutral) were recorded in solutions having pH values in the range of $pK_{BH^+} \pm 2$ pH units. The equilibrium forms of the compounds were obtained in buffer solutions with an ionic strength of 0.01 based on chloroacetic acid [13]. The accurate pH values of the buffer solutions were checked by means of a pH-121 millivoltmeter with an ESL-43-07 glass electrode.

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REACTION OF 1,2,4-TRIAZOLE-3-THIONES WITH
# 1-CHLORO-2,3-EPOXYPROPANE

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UDC 547.431.2'792'864:543.422

Addition of 1-chloro-2,3-epoxypropane to 1,2,4-triazole-3-thiones depending on the ratio of the reactants leads to the formation of 3-(1-chloro-2-hydroxypropyl)-3-(1-chloro-2-hydroxypropylthio)-1,2,4-triazoles. 3-Hydroxy-1,2,4-triazolo[2,3-b] tetrahydro-1,3-triazines have been synthesized by intramolecular cyclization of the monoadducts.

When five-membered nitrogen-containing heterocyclic compounds are interacted with 1-chloro-2,3-epoxypropane (I), two reaction pathways occur depending on the conditions. Base catalyzed alkylation leads to the formation of glycidyl-substituted azoles [1-3] or opening of the epoxide ring gives 1-chloro-2-hydroxypropyl-substituted azoles [4-7].

In the present work the reaction of 1,2,4-triazole-3-thione and its derivatives (IIa-c) with epoxypropane I has been studied. In the presence of organic bases the process occurs with opening of the epoxide ring to give 3-(1-chloro-2-hydroxypropylthio)-5-R-1,2,4-triazoles (IIIa-c).
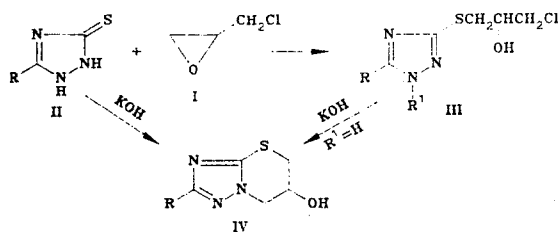
II, IV ·a R=H, b R=CH₃, c R=C₆H₅; III a,d R=H, b,e R=CH₃, c,f R=C₆H₅;
a—c R'=H, d—f R'=CH₂CHOHCH₂Cl