A study of the behaviour of some substituted 1,2,4-triazoline-3-thiones in different media

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The acid-base behaviour of 4-phenyl-5-(4-*R*-benzyl)-1,2,4-triazoline-3-thione (**1**(R = OH); **2**(R = OC$_2$H$_5$)) was studied in aqueous sulfuric acid and sodium hydroxide solutions. Three ionisation equilibria of compound **1** (p$K_{BH_3}{}^+$ = –4.64, pK_{BH_2} = 7.50, p$K_{BH}{}^-$ = 10.06) and two ionisation equilibria of compound **2** (p$K_{BH_2}{}^+$ = –4.82, pK_{BH} = 7.45) were found. The first equilibrium belongs to the protonation of 1,2,4-triazoline-3-thione, while the second belongs to the dissociation of the same part of the molecule. The third equilibrium represents the dissociation process of the phenolic OH group of compound **1**. The kinetics of hydrolysis of compounds **1** and **2** were studied in high concentrated sulfuric acid solutions. The hydrolysis follows an irreversible first-order consecutive reaction path.

Keywords: 1,2,4-triazoline-3-thione derivatives, electonic absorption spectra, dissociation constants, acid hydrolysis.

INTRODUCTION

1,2,4-Triazole and its derivatives have found wide use in the pharmaceutical and chemical industries.[1] Recent investigations of 1,2,4-triazoline-3-thiones are almost exclusively based on their biological activity[2–4] because of possibility of these compounds to act as drugs.

1,2,4-Triazole has pK values of 2.19 (as a base) and 10.26 (as an acid)[1] but there are no literature data about the ionisation of 1,2,4-triazoline-3-thiones. Triazolines and 1,2,4-triazoline-3-ones are readily hydrolyzed in acidic media[1] and it is to be expected that the 3-thione derivatives would show similar properties.

The aim of this work was to investigate the electronic absorption spectra and the behaviour of 4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-3-thione and 4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoline-3-thione in different organic solvents, as well as in the solutions of different acidity.

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EXPERIMENTAL

The compounds of the following structure were investigated in this work:

R—⟨◯⟩—CH₂—C(=N—NH)C=S (N—phenyl)   **1**: R = OH
                                      2: R = OC₂H₅
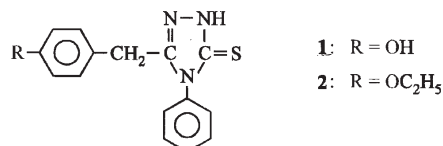
The synthesis of 4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-3-thione (**1**) and 4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoline-3-thione (**2**) has been reported elsewhere.[5] The synthesized compounds were characterized by their melting points and IR and NMR spectra, as well as by elemental analysis.

Stock solutions of the investigated compounds (2×10^{-3} mol dm^{-3}) were prepared by dissolving the required amounts of the substances in absolute ethanol (Zorka, Šabac). These solutions were stable for a long time; *i.e.*, during two months there were no changes in their absorption spectra.

The test solutions were prepared by adding the appropriate volume of the stock solution to a H_2SO_4 or NaOH solution of known concentration, immediately before the recording of spectra. The solutions of H_2SO_4 were prepared by diluting concentrated H_2SO_4 (Carlo Erba) and their concentrations were determined by density measurements.[6] The H_T[7] and X[8] acidity functions were used for the characterisation of the concentrated H_2SO_4 solutions. The alkaline solutions were prepared by dilution of a standard NaOH solution (0.1 mol dm^{-3} Titrival, Kemika). The pH values of the diluted aqueous solutions were measured on an Iskra MA-5704 pH-meter after recording the spectra. The ionic strength ($I = 0.1$ mol dm^{-3}) of the diluted aqueous solutions was adjusted with NaClO$_4$ (Kemika). All chemicals were of analytical grade (p.a.).

Triply distilled water was used for the preparation of the aqueous solutions. Allhough the investigated compounds are less soluble in nonpolar solvents, the compounds are soluble in chloroform, so CHCl$_3$ (Kemika) was used. However, chloroform is not UV transparent at wavelengts shorter than 240 nm.

The concentration of the test solutions of the investigated compounds was 2×10^{-5} mol dm^{-3}. The blanks had the same composition as the test solutions and the same volume of ethanol was added instead of stock solutions of the investigated compounds. The ethanol content in all of the test solutions and the blanks was 1 %.

The spectrophotometric measurements were carried out on a Varian Cary 219 spectrophotometer in 1 cm quartz cells, at 25 °C.

RESULTS AND DISCUSSION

Absorption spectra

The absorption spectra of the investigated compounds were recorded in solvents of various polarities. The relevant spectral data are presented in Table I.

Since the structures of the investigated compounds are similar, the absorption spectra of **1** and **2** are also similar, so only the spectra of compound **1** are shown in the figures. The absorption spectra of the investigated compounds have, in neutral aqueous solutions, absorption maxima at about 223 nm, 253 nm and 280 nm. The first band is ascribed to the excitation of π-electrons of the aromatic system, since the λ_{max} and ε_{max} of this band are little influenced by changing the polarity and protogenity of the solvent (Fig. 1, Table I). The second and the third absorption

maxima are characteristics of electron transitions in the 1,2,4-triazoline-3-thione ring.[4] A small blue shift of the second maximum, without a considerable change of ε_{max}, is observed on going from non-polar to polar solvents (Fig. 1).

TABLE I. The absorption spectral data of the investigated compounds

Compound **1**			Compound **2**		
Species (solvent)	λ_{max} nm	$\varepsilon_{max} \times 10^{-3}$ dm^3 cm^{-1} mol^{-1}	Species (solvent)	λ_{max} nm	$\varepsilon_{max} \times 10^{-3}$ dm^3 cm^{-1} mol^{-1}
BH$_2$ (chloroform) ($D = 4.81$)	267	12.90	BH (chloroform) ($D = 4.81$)	267.5	13.70
BH$_2$ (ethanol) ($D = 24.3$)	230 259 sh 280	14.25 12.25 5.08	BH (ethanol) ($D = 24.3$)	228.5 259.5	14.88 12.43
BH$_2$ (water) ($D = 81.7$)	223 253 sh 282	12.95 13.10 1.49	BH (water) ($D = 81.7$)	224 253.5	14.27 13.65
BH$_3^+$ (≈ 10 mol/dm^3 H$_2$SO$_4$)	220 267.5 282	13.11 1.07 0.55	BH$_2^+$ (≈ 10 mol/dm^3 H$_2$SO$_4$)	220 263.5	14.45 1.00
BH$^-$ (pH≈ 9)	223 277	15.70 1.30	B$^-$ (pH ≈ 9)	225 276	17.82 1.12
B^{2-} (pH≈ 12)	248 278 297	18.45 1.10 2.00	–	–	–

The spectra were unchanged in the weakly acidic media (pH $\approx$ 6 to $c_{H_2SO_4} \approx 1$ mol dm^{-3}), they were like those in the aqueous solutions. An increase of the solution acidity above an H$_2$SO$_4$ concentration of 1 to 10 mol dm^{-3} was accompanied by the disappearance of the absorption maximum at about 253 nm (Fig. 2) with an
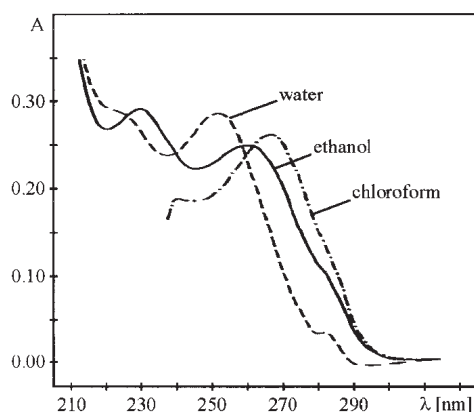

Fig. 1. Absorption spectra of 4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-3-thione in different solvents.
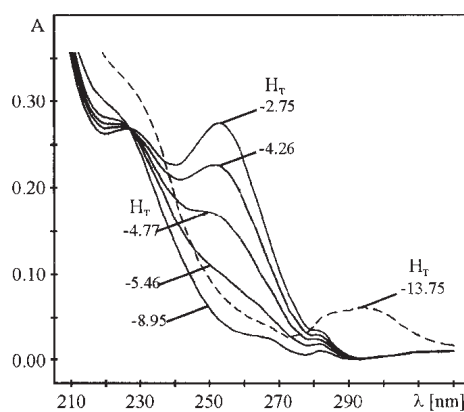
Fig. 2. Absorption spectra of 4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoline-3-thione in solutions of different concentration of H$_2$SO$_4$.
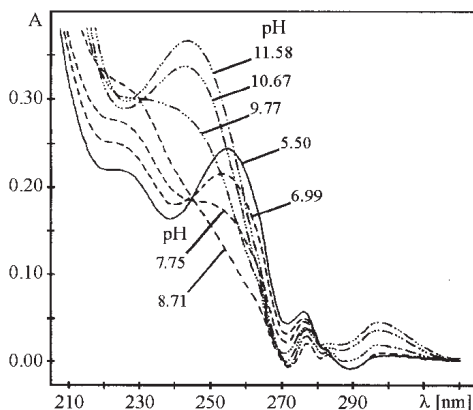
Fig. 3. Absorption spectra of
4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-
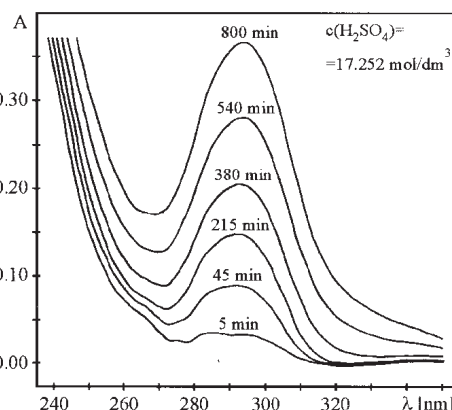3-thione in solutions of different pH.

Fig. 4. Absorption spectra of
4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoline-
3-thione in H_2SO_4 solution with respect to time.

isosbestic point at 227 nm. The absorbance decreases at 253 nm and slightly increases at 223 nm, forming an isosbestic point at 241 nm (Fig. 3), in going from very weakly acidic to basic media (pH 6 – 9). A new absorption maximum at about 245 nm, followed by two isosbestic points at 219 nm and 230 nm (Fig. 3), was formed in the spectra of 4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-3-thione recorded in more alkaline solutions (pH > 9).

In solutions containing more than 15 mol dm^{-3} H_2SO_4, a new absorption band at about 290 nm appeared. The absorbance intensity of this maximum continually increased during several hours (Fig. 4). These spectral changes confirmed that the investigated compounds were hydrolised under these conditions with the formation of a new compound.

The ionisation constants

Using the absorption spectra recorded in solutions of different concentration of H_2SO_4 or different pH (NaOH solutions), the protonation and dissociation processes of the 1,2,4-triazoline-3-thione derivatives were investigated.

The plots of absorbances on the chosen wavelengths against acidity functions and pH give sigmoid curves (Fig. 5) which confirm three ionisation processes for compound **1** and two for compound **2**.

The equilibrium constant of a weak organic base B, can be defined as the acid dissociation constant of the protonated form BH$^+$:

$$BH^+ \rightleftarrows B + H^+$$
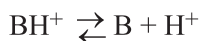
$$pK_{BH^+} = \log\left(\frac{c_{BH^+}}{c_B}\right) - \log c_{H^+} - \log\left(\frac{f_B \cdot f_{H^+}}{f_{BH^+}}\right) \tag{1}$$

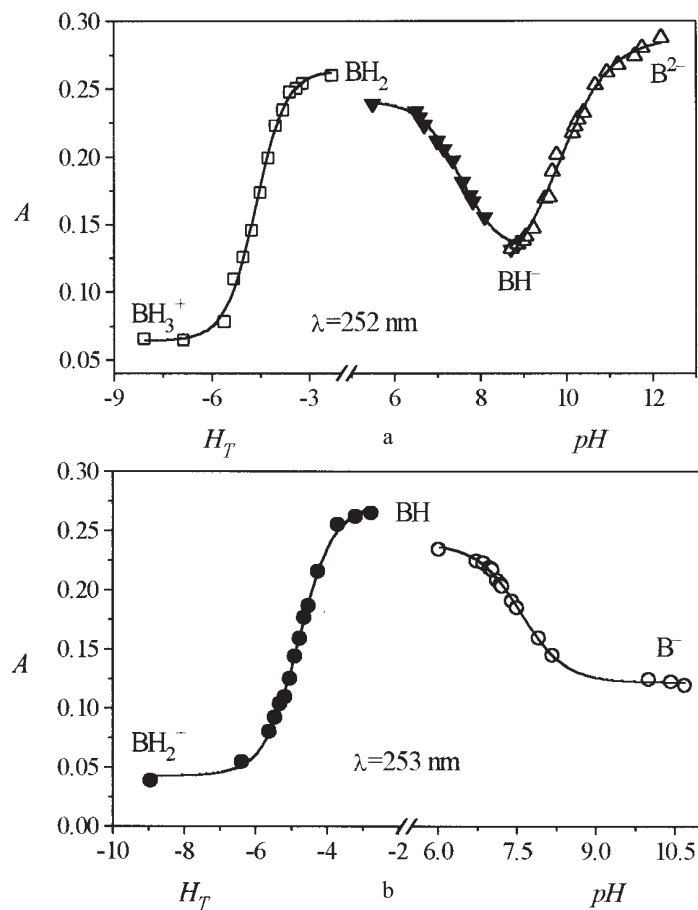where c is concentration and f is activity coefficient.

Fig. 5. The absorbance changes as a function of the acidity of the solutions: a) compound **1**; b) compound **2**.

The ionisation ratio $I = c_{BH^+}/c_B$ can be calculated on the basis of spectral changes under different acidity, from the relation:

$$I = \frac{A - A_B}{A_{BH^+} - A} \qquad (2)$$

where A_B is the absorbance of the unprotonated form, A_{BH^+} is the absorbance of the protonated form and A is the absorbance of the solution at the given acidity, at the same wavelength λ.

There are several methods of calculation of pK_{BH^+} values. In this work the pK_{BH^+} values were calculated using two methods:

1. Hammett acidity function method[9] (HAFM)

$$pK_{BH}^{+} = \log I + m \cdot H_X \qquad (3)$$
$$\text{(on condition that the slope parameter } m \approx 1)$$

where the $H_T^{[7]}$ acidity function was used for H_X (Table II, Fig. 5).

2. "Excess acidity" function method[8] (EAFM)

$$pK_{BH+} = (\log I - \log c_{H}^{+}) - m^{*} \cdot X \qquad (4)$$

where c_{H+} is the proton concentration and X the excess acidity, values which are available for the aqueous sulfuric acid system as a function of weight percent composition.[8] The slope parameter m^{*} expresses the hydrogen-bonding solvation of the protonated base (Table II, Fig. 5).

TABLE II. Experimental data for the calculation of the protonation constants

Compound **1**							
$c_{H_2SO_4}$	H_T	X	$\log c_{H}^{+}$	$A, \lambda = 252$ nm	$\log I$	$pK_{BH_2^+} (H_T)$	$pK_{BH_3^+} (X)$
3.552	−2.304	0.986	0.646	0.260			
5.328	−3.201	1.635	0.834	0.254			
5.683	−3.393	1.769	0.862	0.250			
6.038	−3.594	1.904	0.888	0.247			
6.394	−3.806	2.042	0.911	0.234	−0.820	−4.626	−4.684
6.749	−4.028	2.182	0.932	0.223	−0.636	−4.664	−4.724
7.104	−4.262	2.326	0.951	0.199	−0.346	−4.608	−4.660
7.459	−4.508	2.473	0.967	0.174	−0.101	−4.609	−4.644
7.814	−4.767	2.624	0.982	0.146	0.150	−4.617	−4.626
8.169	−5.037	2.779	0.995	0.126	0.343	−4.694	−4.671
8.525	−5.319	2.938	1.008	0.109			
8.880	−5.611	3.103	1.019	0.078			
15.274	−11.770	6.889	1.132	0.065			
15.629	−12.116	7.145	1.115	0.066			
($A_{BH_3^+} = 0.064$, $A_{BH_2} = 0.261$)							
Compound **2**							
$c_{H_2SO_4}$	H_T	X	$\log c_{H}^{+}$	$A, \lambda = 252$ nm	$\log I$	$pK_{BH_2^+} (H_T)$	$pK_{BH_3^+} (X)$
4.440	−2.749	1.306	0.749	0.265			
5.328	−3.201	1.635	0.834	0.262			
6.216	−3.699	1.973	0.900	0.255		,	
7.104	−4.262	2.326	0.951	0.2155	−0.550	−4.812	−4.956
7.459	−4.508	2.473	0.967	0.1865	−0.274	−4.782	−4.915
7.637	−4.636	2.548	0.975	0.1765	− 0.192	−4.828	−4.952
7.814	−4.767	2.624	0.982	0.1585	−0.052	−4.818	− 4.931
7.992	−4.900	2.701	0.989	0.1435	0.063	−4.837	−4.938
8.169	− 5.037	2.779	0.995	0.125	0.208	−4.829	−4.915
8.347	−5.176	2.858	1.002	0.1095	0.339	−4.837	−4.909
8.525	−5.319	2.938	1.008	0.1035			
8.702	−5.464	3.020	1.014	0.092			
8.880	−5.611	3.103	1.019	0.080			
9.768	−6.386	3.535	1.046	0.0545			
12.432	−8.948	5.020	1.120	0.0385			
($A_{BH_2^+} = 0.038$, $A_{BH} = 0.266$)							

The pK_{BH^+} values obtained using the methods presented above, are thermodynamic values, according to the definitions of the acidity functions H_X and X.[10,11]

The equilibrium constant of a weak organic acid BH, can be defined as follows:

$$BH \rightleftarrows B^- + H^+$$

The pK_{BH} can be calculated from equation (5):

$$pK_{BH} = \log I + m \cdot pH \quad \left(I = \frac{c_{BH}}{c_{B^-}} = \frac{A - A_{B^-}}{A_{BH} - A} \right) \tag{5}$$

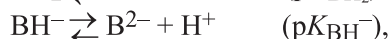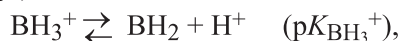(on condition that the slope parameter $m \approx 1$)

where A_{BH} is the absorbance of the neutral form, A_{B^-} is the absorbance of the dissociated form and A is the absorbance of the solution at the given pH, at the same wavelength λ (Table III, Fig. 5).

TABLE III. Experimental data for the calculation of the dissociation constants

Compound 1								Compound 2			
pH	$A\,\lambda{=}235$ nm	$\log I$	pK_{BH_2}	pH	$A\,\lambda{=}235$ nm	$\log I$	pK_{BH^-}	pH	$A\,\lambda{=}255$ nm	$\log I$	pK_{BH}
5.50	0.239			8.71	0.1315			6.02	0.2345		
6.50	0.2335			8.87	0.1355			6.74	0.2245		
6.58	0.229			8.99	0.138			6.87	0.223		
6.69	0.2235	0.762	7.452	9.05	0.141			6.99	0.2185		
6.99	0.2115	0.459	7.449	9.23	0.147	0.965	10.195	7.03	0.217		
7.15	0.206	0.350	7.500	9.50	0.169	0.509	10.009	7.12	0.2085	0.304	7.424
7.35	0.1975	0.199	7.549	9.59	0.170	0.494	10.084	7.20	0.2045	0.242	7.442
7.58	0.1815	−0.060	7.520	9.67	0.189	0.245	9.915	7.22	0.023	0.220	7.440
7.75	0.1715	−0.225	7.525	9.77	0.2015	0.102	9.872	7.41	0.1905	0.042	7.452
7.82	0.167	−0.304	7.516	10.14	0.2175	−0.074	10.066	7.50	0.185	−0.035	7.465
8.10	0.1555			10.20	0.2225	−0.130	10.070	7.92	0.1595	−0.419	7.501
8.71	0.1315			10.27	0.2275	−0.186	10.084	8.18	0.145	−0.720	7.459
8.87	0.1355			10.40	0.2325	−0.245	10.155	10.01	0.1245		
8.99	0.138			10.67	0.2525	−0.509	10.161	10.43	0.1225		
				10.94	0.262			10.70	0.1195		
				11.20	0.2675						
				11.58	0.274						
				11.75	0.280						
				12.20	0.2875						
($A_{BH_2} = 0.240$, $A_{BH^-} = 0.131$, $A_{B^{2-}} = 0.289$)								($A_{BH} = 0.240$, $A_{B^-} = 0.125$)			

Since the concentrations of the investigated compound were very small, it is not necessary to correct the activity coefficients. The ionic strength is constant because of the addition of salt to each sample, and the obtained pK_{BH} are thermodynamic values.[11]

According to Fig. 5, the ionisation equilibria of 4-phenyl-5-(4-hydroxy-benzyl)-1,2,4-triazoline-3-thione are:

$$BH_3^+ \rightleftarrows BH_2 + H^+ \qquad (pK_{BH_3^+}),$$
$$BH_2 \rightleftarrows BH^- + H^+ \qquad (pK_{BH_2}),$$
$$BH^- \rightleftarrows B^{2-} + H^+ \qquad (pK_{BH^-}),$$

and the ionisation equilibria of 4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoli-ne-3-thione are:

$$BH_2^+ \rightleftarrows BH + H^+ \qquad (pK_{BH_2^+}),$$
$$BH \rightleftarrows B^- + H^+ \qquad (pK_{BH}).$$
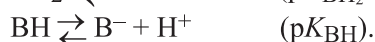
The mean pK values calculated using the equations (3), (4) and (5) are presented in Table IV.

TABLE IV. The values of the ionisation constants at 25 °C

Compound	Protonation constants						Dissociation constants			
	HAFM[*]		EAFM[**]							
	$pK_{BH_3^+}$	m	$pK_{BH_3^+}$	m^*	pK_{BH_2}	m	pK_{BH^-}	m		
1	−4.64 ±0.03	0.98 ±0.04	−4.68 ±0.04	1.45 ±0.05	7.50 ±0.03	0.93 ±0.03	10.06 ±0.09	0.94 ±0.08		
	$pK_{BH_2^+}$	m	$pK_{BH_2^+}$	m^*	pK_{BH}	m				
2	−4.82 ±0.02	0.96 ±0.02	−4.94 ±0.03	1.48 ±0.05	7.45 ±0.02	0.96 ±0.02	−	−		

[*]Hammett acidity function method (Eq.(3)); [**]"Excess acidity" function method (Eq. (4))

The protonation occurs on the thiourea fragment of the 1,2,4-triazoline-3-thi-one ring, since the values of the slopes m show that the protonation process "follows" the H_T acidity function which has been established for thiocarbonyl compounds. Protonation of the thiocarbonyl sulfur of 1,2,4-triazoline-3-thiones is indicated, too, by the fact that their protonation give the values m* which obey the criterion $m^* = 1.39 \pm 0.14$,[8] characteristic for the protonation of sulfur.

1,2,4-Triazoline-3-thione ring can exist in the thiol-form, as is the case with other heterocyclic thiones,[12,13] so the first dissociation equilibrium corresponds to the dissociation of –SH groups. The values of 7.50 and 7.45 are in good agreement with the literature data for the pK_{BH} values of the –SH group of the thiol-form of pyrimidine-thione.[13] The similarity of the absorption spectra of the monocation and the monoanion (Figs. 2 and 3, Table I) indicates the existence of the equilibrium shown in Scheme 1.
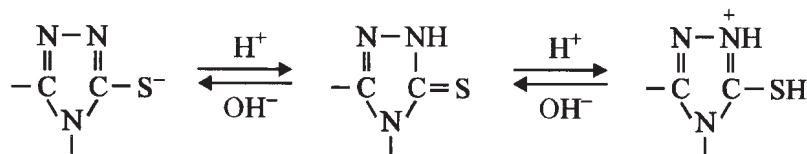
Scheme 1.

The second dissociation equilibrium of 4-phenyl-5-(4-hydroxyben-zyl)-1,2,4-triazoline-3-thione corresponds to the phenolic –OH group.[11]

The kinetics of acid hydrolysis

In highly concentrated H_2SO_4 solutions, the increase of the absorption intensity at the new apsorption maximum at 290 nm with time, clearly indicated that a new molecular species was being formed. The compounds studied in this work were synthesized by cyclization of 1-(4-*R*-phenylacetyl)-4-phenylthiosemicarbazide in NaOH solution.[5] With the aim of determining the hydrolysis products of the 4-phenyl-5-(4-*R*-benzyl)-1,2,4-triazoline-3-thiones, the spectra of 1-(4-*R*-phenylacetyl)-4-phenylthiosemicarbazide were recorded under the same conditions. It
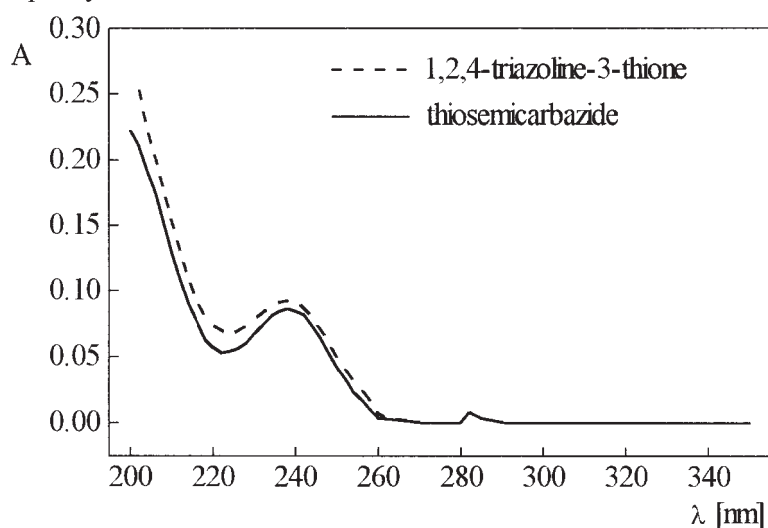

Fig. 6. Absorption spectra of the hydrolysis products.

was observed that a new absorption maximum occurs at 285 nm and that the intensity of this absorption increases with respect to time, which proves that thiosemicarbazides hydrolyse in H_2SO_4 solutions, too. The products of the hydrolysis of 1,2,4-triazoline-3-thione, as well as of thiosemicarbazide, were separated by extraction with ether. After the extraction, the ether was evaporated and the rest was dissolved in ethanol. The absorption spectra of the hydrolysis products were identical (Fig. 6). All of these facts, as well as the hydrolysis of 1,2,4-trazoline-3-ones,[1]
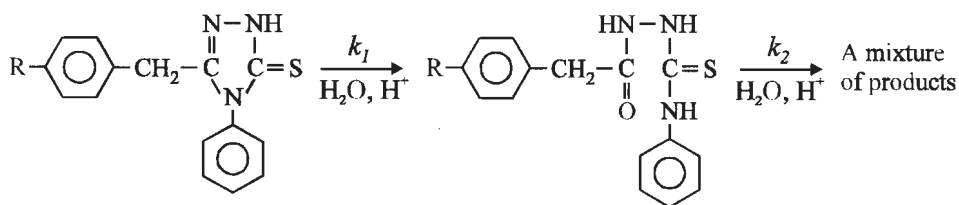
Scheme 2.

show that the hydrolysis of the investigated 1,2,4-triazoline-3-thiones follows an irreversible first-order consecutive reaction path (Scheme 2).

The kinetic data were found to fit the equation known from literature[14]

$$(A - A_0) = (A_\infty - A_0) \cdot \left[1 + \frac{1}{k_1 - k_2} \cdot (k_2 \cdot e^{-k_1 \cdot t} - k_1 \cdot e^{-k_2 \cdot t}) \right] \tag{6}$$

where A is the absorbance of the solution at time t, A_0 and A_a are the absorbances of solution before the beginning and after end of the reaction, k_1 and k_2 are the observed pseudo-first order rate constants. By substitution of a parameter ρ for k_2/k_1, one obtains

$$(A - A_0) = (A_\infty - A_0) \cdot \left[1 + \frac{1}{1-\rho} \cdot (\rho \cdot e^{-k_1 \cdot t} - e^{-\rho \cdot k_1 \cdot t}) \right] \tag{7}$$

Equation (7) was solved for k_1 by introducing various trial values of ρ using the Newton-Raphson method. The best possible value of ρ was obtained by selecting the trial value which gave the minimum value for the sum of the squares of the difference between the observed and calculated values. This fitting was performed using the computer program *Mathcad 7*. Tha value of k_2 was determined from the exact value of ρ and k_1. The results are shown in Table V.

TABLE V The observed pseudo-firs order rate constants obtained at different acid concentrations, at 25 ºC

Compound	c_{H2SO4} mol dm^{-3}	$k_1 \times 10^2$ min^{-1}	$\rho \times 10^3$	$k_2 \times 10^{4\ a)}$ min^{-1}	$k_2 \times 10^{4\ b)}$ min^{-1}
1	15.629	1.5	9.459	1.42	1.43
	16.162	3.0	9.92	2.98	3.05
	16.872	8.9	9.789	8.71	8.96
	17.405	15.0	10.0	15.0	15.49
2	15.981	1.9	9.232	1.75	1.78
	16.526	4.0	10.0	4.0	4.13
	17.252	10.1	9.875	9.78	9.89
	17.797	17.9	9.191	16.36	17.08

a) from Eq. (7); b) from Eq. (8)

As k_1 is much larger than k_2, Eq. (7) transforms into the simple equation of a first-order reaction rate

$$k_2 = \frac{1}{t} \cdot \ln \frac{A_\infty - A_0}{A - A_0} \tag{8}$$

The results obtained from Eq. (8) are presented in Table V. There are no significant differences between the values k_2 obtained using either Eq. (7) or (8).

The variation of k_1 and k_2 with H_2SO_4 concentration, *i.e.*, the "excess acidity" function, satisfies the equations

$\log k_1 = 0.755\,X - 7.209$ $(r = 0.993)$

$\log k_2 = 0.769\,X - 9.326$ $(r = 0.994)$

for 4-phenyl-5-(4-hydroxybenzyl)-1,2,4-triazoline-3-thione

and

$\log k_1 = 0.696\,X - 6.855$ $(r = 0.997)$

$\log k_2 = 0.690\,X - 8.826$ $(r = 0.990)$

for 4-phenyl-5-(4-ethoxybenzyl)-1,2,4-triazoline-3-thione.

As the acid hydrolysis of the investigated substituted 1,2,4-triazoline-3-thiones is a slow reaction even in concentrated sulfuric acid, it had no influence on the determination of the $pK_{BH_3}^+$ and $pK_{BH_2}^+$ values.

The obtained similar values of the ionisation constants, as well as of the reaction rate constants of the investigated compounds, are the result of the small difference in the structure of the molecules.

И З В О Д

ИСПИТИВАЊЕ ПОНАШАЊА НЕКИХ ДЕРИВАТА 1,2,4-ТРИАЗОЛИН-3-ТИОНА У
РАЗЛИЧИТИМ СРЕДИНАМА

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Испитиване су кисело-базне особине 4-фенил-5-(4-R-бензил)-1,2,4-триазолин--3-тиона (**1**(R = OH); **2**(R = OC$_2$H$_5$)) у воденим растворима сумпорне киселине и натријум-хидроксида. Доказано је постојање три јонизационе равнотеже једињења **1** (p$K_{BH_3}^+$ = − 4,64, pK_{BH_2} = 7,50, pK_{BH^-} = 10,06) и две јонизационе равнотеже једињења **2** (p$K_{BH_2}^+$ = − 4,82, pK_{BH} = 7,45). Прва равнотежа представља протонацију 1,2,4-триазолин-3-тиона, а друга дисоцијацију истог дела молекула. У једињењу **1**, трећа равнотежа представља дисоцијацију фенолне OH групе. У јако концентрованим растворима сумпорне киселине, испитивана је брзина реакције хидролизе једињења **1** и **2**. Закључено је да је киселином катализована хидролиза неповратна консекутивна реакција првог реда.

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