8-Hydroxy-7-phenylthio-2,3-trimethylene-4-oxo-3,4-dihydrobenzothieno[2,3-d]pyrimidine (VI). Pyrrolidone (0.94 g, 11 mmole) and phosphorus oxychloride (1 ml, 11 mmole) were added to a solution of IV (3.45 g, 10 mmole) in dry dichloroethane (30 ml) and the reaction mixture was heated for 1.5 h. It was cooled, saturated aqueous sodium acetate solution (30 ml) added, and refluxed for 20 min. After cooling, the organic layer was separated, washed with water, and the dichloroethane distilled off. The residue was treated with alcohol, heated to reflux, cooled, and the precipitate filtered off to give VI (2 g). Found: M^+ 366. Calculated: M 366.

8-Hydroxy-7-phenylthio-2,3-pentamethylene-4-oxo-3,4-dihydrobenzothieno[2,3-d]pyrimidine (VII) was prepared similarly to VI. Found: M^+ 394. Calculated: M 394.

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SYNTHESIS AND SOME REACTIONS OF 4-CARBOXY-2-THIAZOLYLHYDRAZONES

Z. A. Bredikhina, B. I. Buzykin, and Yu. P. Kitaev

UDC 547.556.9+547.789

The condensation of thiosemicarbazones with bromopyruvic acid gives thiazolylhydrazone hydrobromides, which were converted to the free bases. The question of the site of protonation was studied by PMR spectroscopy. The possibility of self-protonation in 4-carboxythiazolylhydrazone crystals is not excluded. The thiazolylhydrazones are brominated in the 5 position. Both cyclization to thiazolyltriazoles and the Chetteueya—Walker reaction are realized in the case of oxidation with lead tetraacetate.

The most thoroughly studied method for obtaining 2-thiazolylhydrazones is the Hantzsch reaction — the reaction of α-halo carbonyl compounds with thiosemicarbazones (TSC) [1, Part 1, pp. 66-80, 249-257; Part 2, pp. 17-20]. Changes in the structure of the α-halo carbonyl compound and the TSC, as well as in the pH of the medium, may lead not only to thiazole derivatives but also to other heterocycles such as thiadiazines [2].

In the present research we used bromopyruvic acid as the halo carbonyl compound for the first time. One might have assumed that the carboxy group of the halo carbonyl compound would first protonate the TSC and thereby change the centers of attack in its molecule. However, this assumption was not confirmed, and the reaction of acid Ia with acetone TSC and the TSC of a series (IIa-f) of aldehydes gave 4-carboxythiazolylhydrazone hydrobromides IIIa-f, which were converted to the corresponding thiazolylhydrazones IVa-e (Table 1). An analytically pure sample of salt IIIe was not isolated but was converted immediately to hydrazone IVe.

A. E. Arbuzov Institute of Organic and Physical Chemistry, Kazan Branch, Academy of Sciences of the USSR, Kazan 420083.

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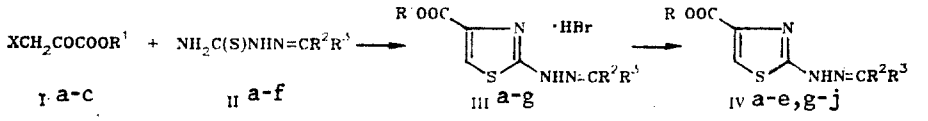
TABLE 1. Characteristics of III-VIII and XI

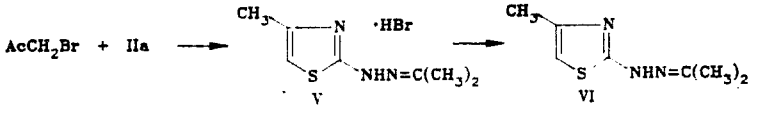
Compound	Empirical formula	mp, °C	Yield, %	Compound	Empirical formula	mp, °C	Yield, %
III a	$C_7H_9N_3O_2S \cdot HBr$	250 ... 251	74	IVi	$C_{14}H_{15}N_3O_3S$	210 ... 212	73
III b	$C_{11}H_9N_3O_2S \cdot HBr$	285 ... 287*	98	IVj	$C_{13}H_{13}BrN_3O_2S$	257 ... 260*	60
III c	$C_{12}H_{11}N_3O_3S \cdot HBr$	261 ... 264*	90	V	$C_7H_{11}N_3S \cdot HBr$	149 ... 151	76
III d	$C_{11}H_8BrN_3O_2S \cdot HBr$	267*	81	VI	$C_7H_{11}N_3S$	108 ... 110	60
III f	$C_{10}H_8N_4O_2S \cdot HBr$	360*	75	VII	$C_{13}H_{11}N_3O_2S$	155 ... 157	12÷34
IV c	$C_{12}H_{11}N_3O_3S$	255 ... 257*	87	VIIIa	$C_{15}H_{15}N_3O_4S$	125 ... 128	29
IV d	$C_{11}H_8BrN_3O_2S$	250*	85	VIIIb	$C_{16}H_{17}N_3O_5S$	193 ... 195	42
IV e	$C_{10}H_8N_4O_2S$	350*	67	XIa	$C_{11}H_8BrN_3O_2S$	225 ... 226	85
				XIb	$C_{13}H_{12}BrN_3O_2S$	171 ... 172	77

*With decomposition.



I a R^1=H, X=Br; b R^1=C_2H_5, X=Cl; c R^1=C_2H_5, X=Br; II—IV a R^1=H, R^2, R^3=CH_3; b R^1, R^3=H, R^2=C_6H_5; c R^1, R^3=H, R^2=4-$CH_3OC_6H_4$; d R^1, R^3=H, R^2=4-BrC_6H_4; e R^1, R^3=H, R^2=3-Py; g R^1=C_2H_5, R^2, R^3=CH_3; h R^1=C_2H_5, R^2=C_6H_5, R^3=H; i R^1=C_2H_5, R^2=4-$CH_3OC_6H_4$, R^3=H; j R^1=C_2H_5, R^2=4-BrC_6H_4, R^3=H

In view of the fact that 1,3,4-thiadiazine derivatives, 2-thiazolylhydrazones, or 2-amino-3-ylideneaminothiazoles could be formed in the investigated reaction and since tautomerism is possible for them, to solve the question of the structures of the products and the possibility of self-protonation of 4-carboxythiazolylhydrazones IVa-e and the structures of their cations (the protonation centers and the electron structures) we studied the spectral characteristics of the compounds obtained (Table 2) and synthesized model compounds: 4-carbethoxy-2-thiazolylhydrazones IVg-j by condensation of TSC IIa-d with ethyl chloropyruvate (Ib) and acetone 4-methyl-2-thiazolylhydrazone (VI) and its hydrobromide (V) by the reaction of bromoacetone with TSC IIa. Hydrazono ester IVg was previously obtained from ethyl bromopyruvate (Ic) [3,4]. Hydrazono acid IVb and hydrazono ester IVh were synthesized by condensation of the corresponding 4-R-2-thiazolylhydrazines with benzaldehyde [3], while hydrazono acid IVa was synthesized by saponification of hydrazono ester IVg [4].



Thiazolylhydrazone hydrochlorides cannot be isolated in the reaction of TSC IIb-d with ester Ib because of their low thermal stabilities (under the reaction conditions they are converted to hydrazones IVh-j).

The IR spectra of salts IIIa-d and free hydrazono acids IVa-d recorded in mineral oil are very similar (see Table 2). In addition to bands that are characteristic for the vibrations of thiazolyl, aryl, amino, and carbonyl groups, absorption bands at 2400-2800 cm^{-1} that are characteristic for salt structures with an HN+ fragment are observed in both cases; absorption bands of this sort are not observed in the spectra of hydrazono esters IVg-j and 4-methylthiazolylhydrazone VI, whereas they are present in the spectra of their salts. This makes it possible to assume that a betaine structure (as a consequence of self-protonation) or a structure with strong hydrogen bonds is realized in crystals of hydrazono acids IVa-d; this also may lead to the appearance of absorption bands at 2400-2800 cm^{-1} [5]..

As noted above, the basicities of thiazolylhydrazones IVa-e, g-j and VI are low and depend markedly on the nature of the substituents in both the ring 4 position and in the ylidene groups of the hydrazone fragment. The UV spectra of salts III in solutions could be recorded only for acetone hydrazone bromides IIIa,g and V in acetonitrile. In alcohol bromides III, including salts IIa,g, are hydrolyzed to free bases IV, as evidenced by the identical character of the UV spectra of such solutions and the spectra of hydrazones IVa-j (Table 3). A similar conclusion can also be drawn from a comparison of the PMR spectra of solutions in DMSO. The character of the UV spectra in ethanol and acetonitrile of hydrazono acids IVa-c and hydrazono esters IVg-i, which contain the same ylidene fragment, is similar, just as is the character of the PMR spectra of these compounds in DMSO; this makes it possible to conclude that the self-protonated forms observed for related systems even in the case of the less acidic phenol group [6] are absent in solutions of hydrazono acids IVa-e.

TABLE 2. Spectral Characteristics of Thiazolylhydrazones III and IV

Compound	IR spectrum,* cm^{-1}		PMR spectrum,*2 ppm					
			d 6 -DMSO*3			CF_3COOH*3		
	NH	C=O	5-H	N=CH	$=(CH_3)_2$	5-H	N=CH	$=(CH_3)_2$
III a	3120	1730, 1690	7,60	—	2,08; 2,02	7,88	—	2,30
III b	3120	1690, 1705	7,72	8,13	—	8,10	8,58	—
III c	3100	1725	7,68	8,13	—	7,85	8,30	—
III d	3110	1700	7,75	8,12	—	—	—	—
III g	3150 br.	1740 br	7,51	—	1,95; 1,92	7,70	—	2,28
IV a	3160 br.	1700 br	7,53	—	1,97; 1,93	7,75	—	2,25; 2,17
IV b	3140, 3200	1680, 1720	7,55	7,90	—	7,85	8,18	—
IV c	3140, 3190	1680, 1725	7,51	7,86	—	7,80	8,13	—
IV d	3140, 3180	1690, 1720	7,55	7,87	—	—	—	—
IV g	3120, 3150	1720	7,47	—	1,95; 1,90	7,67	—	2,23; 2,15
IV h	3130, 3190	1725	7,80	8,23	—	7,80	8,23	—
IV i	3160 br.	1725	7,67	7,92	—	7,75	8,15	—
IV j	3130, 3190	1725	—	—	—	7,77	8,10	—
V	3230	—	6,67*4	—	2,10; 2,13	6,57*4	—	2,43
VI	—	—	6,13*5	—	1,92; 1,88	6,40*5	—	2,23; 2,15

*The absorption of Ar, thiazole, and C=N is registered by several bands at 1600-1635, 1570-1590, and 1485-1520 cm^{-1}; for salts IIIa-g and hydrazono acids IVa-e there is intense absorption in the form of a broad band at 2400-2800 cm^{-1}.

*2Signals of aromatic protons are recorded at 7.2-7.6 ppm.

*3The PMR spectra of esters IVg-j contain signals of ethyl and Ar groups; in d_6-DMSO an NH signal is present at 9.5-10.5 ppm.

*4$\delta_{4\text{-}CH_3}$ (in d_6-DMSO) 2.25 ppm; in CF_3COOH 2.43 ppm.

*5$\delta_{4\text{-}CH_3}$ (in d_6-DMSO) 2.12 ppm; in CF_3COOH 2.37 ppm.

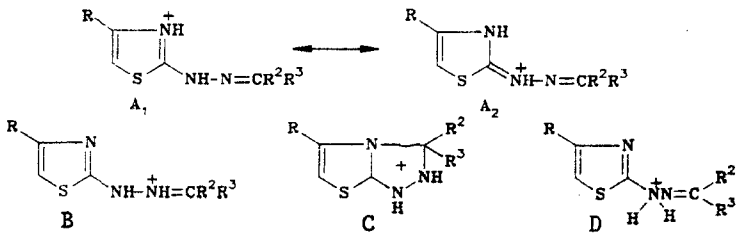
TABLE 3. UV Spectra of IIIa, g, IVa-c, g-i, V, and VI

Compound	UV spectrum, λ_{max}, nm (log ε)	
	in acetonitrile	in ethanol
III a	276	217, 263, 296*
III g	275 (4,23), 287 sh	220 (4,23), 262 (4,11), 300 (3,78)*
IV a	217, 258, 295	217, 263, 296
IV b	244, 312, 322, 333	237, 288, 337
IV c	217, 267, 290, 338	217, 267, 290, 339
IV g	220 (4,29), 260 (4,12), 300 (3,81)	220 (4,26), 262 (4,15), 300 (3,79)
IV h	233,286,333	234, 294, 337
IV i	—	220, 271, 194, 342
V	220 (3,89), 292 (4,19)	290 (4,13)
VI	285 (4,12)	287 (4,03)

*A consequence of hydrolysis to free hydrazones IV

All of the signals are shifted to weak field in the PMR spectra of solutions of hydrazones IVa-c, g-j in CF_3COOH (see Table 2). The magnitudes of the shifts attest to protonation and not only to an increase in the polarity of the solvent (for example, see the data for thiazole compounds in [1]). The protonation center in hydrazones may change, depending on the nature of substituents R^2 and R^3 in the ylidene fragment [7]. For protonated thiazolylhydrazones one also cannot exclude a priori the possibility of ring-chain tautomerism, which is observed for their analogs: thiosemicarbazones [8] or cyclic amidrazones such as phthalazinylhydrazones [9]. Thus for the cations formed from hydrazones IV one may assume one of the following structures (see scheme below).

It is known that 2-aminothiazoles are protonated primarily at the endocyclic nitrogen atom [1, 6, 10]. The solution of the problem regarding the site of protonation in 4-carboxythiazolylhydrazones proved to be more complex. As a result of the formation of cyclic cations in the protonation of acetone thiosemicarbazone [8] or N-methyl-N-phthalazinylhydrazones [9], in the PMR spectra one observes a 0.2 ppm shift of the signals of the methyl groups of



the isopropylidene fragment to strong field and their merging to a singlet. In contrast to this, in the spectrum of hydrobromide V in d_6-DMSO (see Table 2) two signals (2.13; 2.12 ppm), which are shifted to weak field as compared with those of base VI (1.92; 1.88 ppm), correspond to the $C(CH_3)_2$ protons, while the 4-CH_3 signal is shifted 0.15 ppm to weak field, and the 5-H signal is shifted 0.54 ppm. This makes it possible to assume that the ring nitrogen atom is protonated in this case and that the cation has a linear structure of the A_1 type. A bathochromic shift of the long-wave band ($\Delta\nu$ 360 cm^{-1} in ethanol, as compared with 840 cm^{-1} in acetonitrile) is observed in the UV spectrum on passing from hydrazone VI to its salt V; this is in agreement with the interpretation of the PMR spectroscopic data. Decomposition of salt V in solutions is not observed.

The picture changes substantially on passing to hydrazone IVg. In the PMR spectrum of hydrazono ester IVg the signals of the $C(CH_3)_2$ group are shifted 0.28 ppm to weak field as compared with the spectrum in d_6-DMSO, while the 5-H signal is shifted 0.2 ppm. In addition, the UV spectrum of hydrazone IVg in acetonitrile contains three bands, while the spectrum of salt IIIg contains two bands; a hypsochromic shift of the long-wave band ($\Delta\nu$ 1500 cm^{-1}) occurs. These data constitute evidence that protonation does not take place at the imino nitrogen in this case also. Protonation of acetone benzoyl- and acetylhydrazone at the imino nitrogen atom [7-9] leads to a 0.70-0.80 ppm shift of the $C(CH_3)_2$ signals to strong field. It may be assumed that protonation of hydrazone IVg takes place in the ring, but electron structure A_2 is realized, or cation D is formed. Similar results are obtained when hydrobromide IIIa and hydrazono acid IVa are examined.

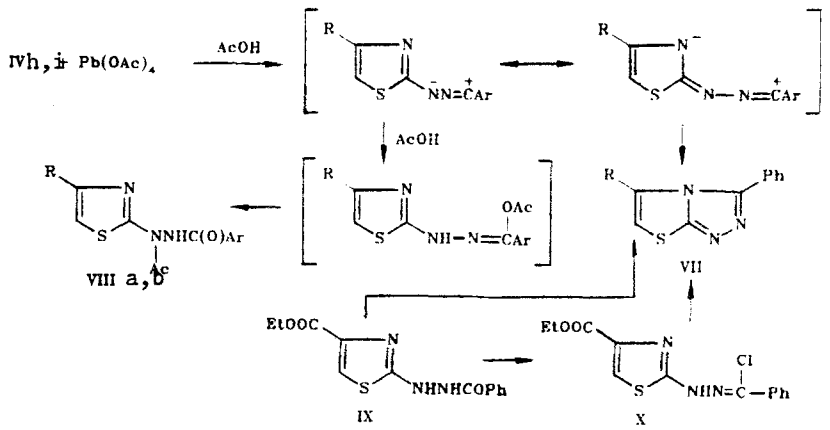
The basicity of the imino nitrogen atom of the hydrazone decreases naturally in aromatic aldehyde hydrazones IVb-d, h-j (see [7]). Protonation at the ring 3-N atom is evidently preferable for hydrazones IVb,d,h,j, while the equal probability of protonation at two centers (A ⇌ B) is not excluded for hydrazones IVc,i. Thus, as compared with 4-methylthiazolylhydrazone VI, which gives a stable salt structure, 4-carboxythiazolylhydrazones are weaker bases, and their protonation center is not so unambiguous.

The chemical properties of thiazolylhydrazones IV, particularly their transformations under the influence of lead tetraacetate (LTA) and bromine, were also studied. It is known that their analogs — benzothiazolylhydrazones — react with LTA to give primarily 1-aroyl-2-acetyl-2-benzothiazolylhydrazines but also undergo partial oxidative cyclization to 1,2,4-triazolo[3,4-b]benzothiazoles [11, 12]. Primarily 3-phenyl-5-carbethoxythiazolo[2,3-c]-1,2,4-triazole (VII) is formed in the reaction of hydrazone IVh with LTA in AcOH, and only a small amount of 1-benzoyl-2-acetyl-2-(4-carbethoxy-2-thiazolyl)hydrazine (VIIIa) is obtained. Carrying out the reaction in benzene leads to an increase in the yield of thiazolotriazole VII. Only diacylheterylhydrazine VIIIb was isolated in the oxidation of hydrazone IVi. It is considered to be an established fact that nitrilimines are intermediates in the action of LTA on α-azaheterylhydrazones [13]; the transformation of these intermediates (intramolecular cyclization or the competitive addition of AcOH via a 1,3-addition scheme with subsequent rearrangement of the acylhydrazonate via the Chetteueya—Walker scheme) is also responsible for the structures of the products formed (see the scheme).

Three bands at 1680-1740 cm^{-1}, which are related to the stretching vibrations of three C=O groups, and a band of NH stretching vibrations are observed in the IR spectra of VIII. The PMR spectra of hydrazines VIIIa,b contain a signal of protons of an acetoxy group. A broad composite band (λ 262 and 280 nm) is observed in the UV spectrum of thiazolotriazole VII in ethanol; the spectrum of a solution in acetonitrile contains two bands with λ 265 and 283 nm. The 5-methyl- and 5-phenylthiazolotriazoles, which are the closest analogs of VII, absorb at 262 and 271 nm, respectively (in methanol) [14]. The UV spectrum of VIIIb contains a band at 257 nm (for comparison, the long-wave band in the starting hydrazone IVi is found at 342 nm).

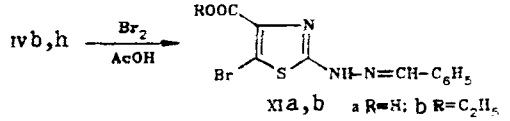
We obtained thiazolotriazole VII by intramolecular cyclization of 4-carbethoxy-2-(benzoylhydrazino)thiazole (IX) by the action of $POCl_3$, in analogy with [14, 15], and also by treatment of benzoyl chloride 4-carbethoxy-2-thiazolylhydrazone (X), which we obtained from hydrazide IX by the method in [16], with triethylamine.

It is known that bromine can also be used as an agent that causes cyclization of aldehyde azaheterylhydrazones to annelated 1,2,4-triazoloazaheterocycles [17], although the reaction is complicated by a number of side processes. For example, according to the data in [18], benzaldehyde (4-methyl-2-thiazolyl)-N-acetylhydrazone is brominated in the 5



VIII R=COOEt; a Ar=Ph; b Ar=$C_6H_4OCH_3$-4

position. Our studies showed that the bromination of benzaldehyde thiazolylhydrazones IVb,h with 1 mole of bromine in acetic acid also leads to benzaldehyde 4-carboxy- and 4-carbethoxy-5-bromothiazolylhydrazones XIa, b.



XIa,b a R=H; b R=C_2H_5

The PMR spectra of XIa,b contain a signal of a methylidyne proton at 8.2 ppm (in CF_3COOH), whereas the 5-H signal of starting hydrazone IVb (7.85 ppm) vanishes after bromination (for comparison, δ 5-H of chlorohydrazone X is 7.9 ppm). The introduction of bromine into the thiazole ring rather than at the methylidyne carbon atom is also confirmed by the fact that prolonged refluxing of hydrazones XIa,b in ethanol or benzene with triethylamine does not change them.

EXPERIMENTAL

The IR spectra of suspensions of the compounds in mineral oil were recorded with a UR-20 spectrometer. The UV spectra of solutions in ethanol and acetonitrile were obtained with a Specord UV-vis spectrophotometer. The PMR spectra were recorded with a Varian T-60 spectrometer (60 MHz) with tetramethylsilane (TMS) as the internal standard. The melting points were determined with a Boetius heating stage.

The authors thank N. E. Timofeeva for recording the IR and UV spectra.

4-Carboxy-2-thiazolylhydrazone Hydrobromides IIIa-d, f. A 20-mmole sample of bromopyruvic acid in 15 ml of dioxane was added to a solution of 20 mmole of the corresponding thiosemicarbazone IIa-f in 250 ml of dioxane, the solution was heated gradually with stirring to 65°C, and stirring at this temperature was continued for 30 min. The mixture was then cooled to 20°C, and the resulting precipitate was removed by filtration and washed with ether. This procedure gave hydrobromides IIIa-d, f; hydrobromide IIIe could not be obtained in analytically pure form. The IR spectra of salts IIIe, f were similar to the spectrum of salt IIIb.

Hydrobromide IIIg was obtained by the methods in [3, 4] and had mp 103-105°C.

4-Carboxy-2-thiazolylhydrazones IVa-e. A 10-mmole sample of the corresponding hydrobromide III was dissolved by heating in 600 ml of water, and the solution was neutralized with 10 mmole of KOH. The mixture was cooled, and the precipitate was removed by filtration to give the hydrazono acid IV. Hydrazone IVa had mp 265-267°C (dec.) (mp 260°C [4]) and was obtained in 70% yield. Hydrazone IVb had mp 273-275°C and was obtained in 87% yield.

4-Carbethoxy-2-thiazolylhydrazones IVg-j. A 15-mmole sample of ethyl chloropyruvate was added with stirring to a solution of 15 mmole of the corresponding thiosemicarbazone IIa-d in 100 ml of dioxane or ethanol, and the mixture was stirred for 30 min at 65°C. Half of the solvent was removed, and the precipitate was washed on the filter with 3% sodium carbonate solution and recrystallized from alcohol. This procedure gave hydrazono esters IVg-j. Hydrazone IVg had mp 134-136°C (mp 133°C [3]) and was obtained in 60% yield. Hydrazone IVh had mp 235-237°C (mp 276-279°C [3]) and was obtained in 85% yield.

Acetone 4-Methyl-2-thiazolylhydrazone Hydrobromide (V). A 4.11-g (30 mmole) sample of bromoacetone in 10 ml of methanol was added to 3.93 g (30 mmole) of acetone thiosemicarbazone in 40 ml of methanol, and the mixture was refluxed for 1 h. The methanol was removed in vacuo, and the precipitate was washed with ether to give salt V.

4-Methyl-2-thiazolylhydrazone VI. A 2.5-g sample of salt V was dissolved in 50 ml of water, and a solution of 10 mmole of KOH in 10 ml of water was added. The resulting precipitate was removed by filtration and recrystallized from acetone to give hydrazone VI.

3-Phenyl-5-carbethoxythiazolo[2,3-c]-1,2,4-triazole VII. A) A 2.2-g (5 mmole) sample of lead tetraacetate (LTA) was added to a suspension of 1.38 g (5 mmole) of hydrazone IVh in 10 ml of AcOH, and the reaction mixture was heated up to 38°C, during which hydrazone IVh dissolved completely, and the solution turned dark cherry-red. The mixture was poured into 100 ml of water, and the mixture was allowed to stand overnight. The crystals were removed by filtration and recrystallized from ethyl acetate to give thiazolotriazole VII. IR spectrum: 3080 (CH), 1735 (C=O), 1575 (rings, Ph), 1475 cm^{-1}. PMR spectrum (CF_3COOH): 8.50 (1H, s, 6-H), 7.62 (5H, s, Ph), 4.20 (2H, q, CH_2), 1.17 ppm (3H, t, CH_3).

The resinous precipitate that remained on the walls of the reaction flask was recrystallized from ethanol to give **1-benzoyl-2-acetyl-2-(4-carbethoxy-2-thiazolyl)hydrazine (VIIIa).** IR spectrum: 3275 (NH); 3100, 3070, 3040 (CH); 1740, 1720, 1700 (C=O); 1610, 1590, 1545, 1510 cm^{-1} (thiazole, Ph). PMR spectrum (CF_3COOH): 8.28 (1H, s, 5-H), 7.70 (5H, m, Ph), 4.55 (2H, q, CH_2), 3.73 (3H, s, CH_3), 1.47 ppm (3H, t, CH_3).

B. A 1.21-g (2.7 mmole) sample of LTA was added with stirring to 0.75 g (2.7 mmole) of hydrazone IVh in 30 ml of benzene. After 30 min, 40 ml of water was added, and the benzene was removed in vacuo. The precipitate was removed by filtration, washed with water, and recrystallized from ethyl acetate to give thiazolotriazole VII in 34% yield.

C. A mixture of 0.6 g of benzhydrazide IX, 0.6 ml of $POCl_3$, and 30 ml of xylene was refluxed for 8 h, after which petroleum ether was added, and a precipitate formed. The solution was decanted, water was added to the precipitate, and the aqueous mixture was extracted with chloroform. The extract was dried over Na_2SO_4, the solvent was removed, and the residue was recrystallized from ethyl acetate. Thiazolotriazole VII was obtained in 10% yield.

D. A 1-ml sample of triethylamine was added to a solution of 0.45 g of chlorohydrazone X in 5 ml of ethanol, and the mixture was refluxed for 30 min. The alcohol was partially removed, and the precipitate was removed by filtration to give thiazolotriazole VII in 20% yield.

1-(4-Methoxybenzoyl)-2-acetyl-2-(4-carbethoxy-2-thiazolyl)hydrazine (VIIIb). A 1.45-g (3.3 mmole) sample of LTA was added to a suspension of 1.0 g (3.3 mmole) of hydrazone IVi in 5 ml of AcOH, and the mixture was stirred for 30 min. Water (15 ml) was added, and the precipitate was removed by filtration and recrystallized from ethanol to give hydrazine VIIIb. IR spectrum: 3300, 3120 (NH); 1735, 1720, 1680 (C=O); 1625, 1580, 1500 (thiazole, Ph). PMR spectrum (CF_3COOH): 8.21 (1H, s, 5-H), 7.88 (2H, d), 7.22 (2H, d, $^3J_{HH}$ = 9 Hz, C_6H_4), 4.57 (2H, q, CH_2), 4.02 (3H, s, OCH_3), 2.62 (3H, s, CH_3), 1.48 ppm (3H, t, CH_3).

4-Carbethoxy-2-(benzoylhydrazino)thiazole (IX). A 4.8-g (24.6 mmole) sample of ester Ic was added to a solution of 4.8 g (24.6 mmole) of benzoylthiosemicarbazide in 100 ml of ethanol, and the mixture was refluxed for 30 min. It was then cooled and neutralized with ammonia, and the precipitate, which had mp 198-200°C, was removed by filtration. IR spectrum: 3280, 3180, 3130 (N–H); 1710, 1670 (C=O); 1570 cm^{-1} (thiazole, Ph). The yields was 68%.

Benzoyl Chloride 4-Carbethoxy-2-thiazolylhydrazone (X). A 0.193-ml sample of pyridine was added dropwise with cooling to 0.65 ml (7.2 mmole) of $POCl_3$, after which 0.7 g (2.4 mmole) of hydrazide IX was added in portions. The temperature was gradually raised to room temperature and then to 90°C, at which it was maintained for 2 h. The mixture was then cooled to room temperature and poured into water (200 ml), and the precipitate was removed by filtration to give 0.45 g of chlorohydrazone X with mp 150-152°C. IR spectrum: 3150 (NH); 3060 (=C–H); 1730 (C=O); 1628, 1580 cm^{-1} (C=N, thiazole). PMR spectrum (DMSO): 7.85 (1H, s, 5-H), 7.65 (5H, m, Ph), 4.28 ppm (2H, q, CH_2).

Benzaldehyde 4-Carboxy-5-bromo-2-thiazolylhydrazone (XIa). A 0.615-g (7.5 mmole) sample of AcONa was added to a mixture of 0.62 g (2.5 mmole) of hydrazone IVb in 25 ml of AcOH, and a solution of 0.4 g (2.5 mmole) of bromine in 5 ml of AcOH was added with stirring. Stirring was continued for 30 min, after which the mixture was poured into 100 ml of water, and the precipitate was recrystallized from dioxane to give XIa (Table 2).

Benzaldehyde 4-Carbethoxy-5-bromo-2-thiazolylhydrazone (XIb). This compound was obtained in the same way as hydrazone XIa.

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4- AND 5-HYDROXYLAMINOTHIAZOLIDINE-2-THIONES. REACTION WITH 4-NITROBENZALDEHYDE

T. I. Orlova, S. P. Épshtein, V. P. Tashchi, and Yu. G. Putsykin

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Stable nitrones are formed in the condensation of 5-hydroxylaminothiazolidine-2-thiones with 4-nitrobenzaldehyde. At the same time, nitrones obtained from the isomeric 4-hydroxylaminothiazolidine-2-thiones, as well as 4-hydroxylaminoimidazolidin-2-one, can undergo rearrangement to E- or Z-O-substituted 4-nitrobenzaldoximes, depending on the structure and the reaction conditions.

In a continuation of our research on the synthesis and study of the reactivities of hydroxylaminothia(imida)zolidine-2-thiones(ones) [1, 2] we examined their reaction with 4-nitrobenzaldehyde.

Thus, regardless of the structures of substituents R^1—R^4, 5-hydroxylaminothiazolidine-2-thiones I react with the aldehyde to give stable [N-(thiazolidine-2-thion-5-yl)-C-(4-nitrophenyl)]nitrones IIa,b [1] and IIc,d; it is best to carry out the reaction in the presence of 4-toluenesulfonic acid (TSA).

In the case of the isomeric 4-hydroxylaminothiazolidine-2-thiones III, however, the corresponding nitrones Va-e can be obtained only in the absence of TSA and when R^1 = H. Similar conditions are also necessary for the formation of nitrone VI from 4-hydroxylaminoimidazolidin-2-one IV.

A completely different situation arises when the reaction of 4-hydroxylamino derivatives III and IV with the aldehyde is carried out in the presence of TSA and, in the case of the sterically hindered hydroxylamines IIf,g (R^1 = CH_3), also without it. Although they do have the empirical formulas of the corresponding nitrones, the UV spectra (ethanol) of the resulting VIIa-g and VIII do not contain the absorption at 340-350 nm that is characteristic for nitrones [1], a 0.1-0.4 ppm shift of the signal of the azomethine proton to weaker field as compared with the PMR spectra of nitrones III is observed in their PMR spectra, and the IR spectra (KBr) do not contain bands of stretching vibrations of an N—O bond but do contain bands at 900-1000 cm^{-1}, which are more characteristic for the vibrations of an oxime group [3]. In addition, VII and VIII do not react with sodium borohydride [3].

An O-substituted 4-nitrobenzaldoxime structure can be assigned to VII and VIII on the basis of these data. The alternative synthesis of VIIc and VIII by the reaction of, respectively, 4-hydroxythiazolidine-2-thione IXa and 4-hydroxyimidazolidin-2-one IXc with E-4-nitrobenzaldoxime [2] makes it possible to conclude that the oxime group of derivatives VII and VIII has an E configuration.

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