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SYNTHESIS AND REACTIONS OF 3-AMINOTHIAZOLIDINE-2-THION-4-ONE DERIVATIVES.

3.* REACTION OF 3-[N-(α-METHYLTHIO)ETHYLIDENE] AMINOTHIAZOLIDINE-2-THION-4-ONE WITH AMINES

E. K. Mikitenko, N. N. Romanov,
and I. S. Shpileva

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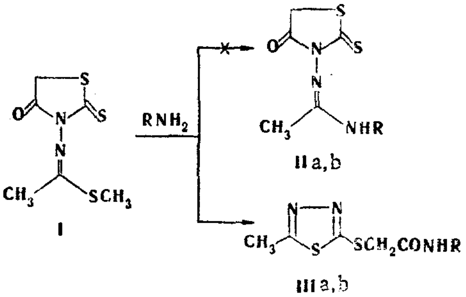
It is shown that recyclization leading to the formation of 1,3,4-thiadiazole derivatives occurs in the reaction of 3-[N-(α-methylthio)ethylidene]aminothiazolidine-2-thion-4-one with amines. The structures of the compounds obtained were established by spectral methods and were confirmed by alternative synthesis.

Continuing our research on the reactions of 3-aminothiazolidine-2-thion-4-one derivatives [1] we have studied the reaction of 3-[N-(α-methylthio)ethylidine]aminothiazolidine-2-thion-4-one (I) with ammonia and aniline; the formation of diverse products is possible in this case, since there are three electrophilic centers in the starting compound. Since rhodanine I can be regarded as a substituted thioimino ester from which amidines are formed by the action of amines [2], in our case one might have expected the production of derivatives of the II type or their transformation products.



a R=H; b R=C$_6$H$_5$

In fact, we found from the results of elementary analysis that the methylthio group is replaced by an amine residue in the compounds obtained. The same conclusion also follows from the PMR spectra, in which singlets of C-methyl and methylene groups (2.67 and ~4.0 ppm), as well as signals of protons of amino or phenylamino groups, are observed (see the experimental section).

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*See [1] for Communication 2.

Institute of Organic Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252660. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 3, pp. 339-342, March, 1981. Original article submitted June 26, 1980.

TABLE 1. Mass Spectra of the Products of the Reaction of Rhodanine I with Ammonia and Aniline*

Compund	m/e values (relative intensities in percent)
III a (I+NH_3)	40 (8,6), 41 (23,6), 42 (39,0), 43 (2,9), 44 (39,1), 45 (23,3), 46 (75,2), 47 (13,6), 48 (3,6), 56 (6,2), 57 (2,3), 58 (13,9), 59 (40,7), 60 (11,4), 61 (2,3), 64 (2,1), 69 (5,8), 72 (8,7), 73 (6,5), 74 (2,0), 75 (2,3), 76 (2,2), 78 (6,5), 88 (5,5), 90 (2,5), 99 (8,2), 101 (5,4), 105 (18,1), 113 (3,6), 117 (2,4), 144 (3,2), 145 (11,6), 146 (100), 147 (8,2), 148 (9,3), 172 (11,7), 189 (11,6)
III b (I+$C_6H_5NH_2$)	38 (3,7), 39 (29,2), 40 (5,9), 41 (17,8), 42 (29,7), 43 (5,5), 45 (15,3), 46 (48,2), 47 (5,1), 48 (2,2), 50 (2,4), 51 (15,5), 52 (4,2), 55 (2,3), 56 (6,3), 57 (2,1), 58 (6,8), 59 (30,0), 60 (7,7), 63 (5,9), 64 (8,3), 65 (45,2), 66 (9,8), 69 (50,4), 70 (2,1), 72 (6,0), 73 (2,3), 75 (2,7), 77 (37,1), 78 (5,2), 79 (6,5), 80 (2,1), 88 (4,4), 91 (8,2), 92 (14,9), 93 (58,4), 94 (4,7), 97 (16,1), 99 (7,3), 101 (5,6), 104 (4,2), 105 (21,2), 106 (20,5), 113 (4,6), 119 (4,4), 120 (3,5), 124 (7,4), 132 (3,0), 133 (8,3), 142 (3,6), 145 (14,0), 146 (65,7), 147 (5,7), 148 (5,9), 172 (42,0), 173 (100), 174 (16,6), 175 (14,5), 265 (14,0), 266 (2,6)

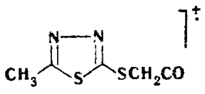
*The peaks of ions with intensities ≥ 2% are presented.

However, the chemical properties of the synthesized products did not correspond to the II structure. Thus, in contrast to ordinary 3-substituted rhodanines [3], these compounds do not react with p-dimethylaminobenzaldehyde but do react readily with it after prior heating with dimethyl sulfate.

On the basis of the UV spectra it may be concluded that the products of the reaction of thiazolidine I with amines do not contain a rhodanine ring, since the absorption maxima of their solutions (265 and 250 nm) are considerably higher than in the case of solutions of the starting rhodanine [1] or 3-aminorhodanine (295 nm) [4]. Absorption bands of an amide carbonyl group at 1690 cm^{-1} and of an N–H bond (3080-3360 cm^{-1}), as well as bands characteristic for a substituted thiadiazole ring [5] (1250, 1390, and 1505 cm^{-1}), are observed in the IR spectrum of the compound obtained by the action of aniline on rhodanine I, and this indicates the possibility of the formation of thiadiazoles IIIa,b.

The mass-spectral data (Table 1) also are in good agreement with the assumption of a thiadiazole structure for the reaction products. The results of a study of the effect of electron impact on 2-ureido-1,3,4-thiadiazoles [6] were taken into account in the interpretation of these spectra.

Fragment ions formed by cleavage of the amide bond or by cleavage of the exocyclic C–C bond, which proceeds both with transfer of a hydrogen atom to the charged fragment and without it, are clearly recorded in the spectra:



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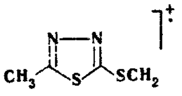

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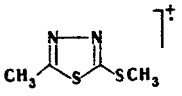

146

The charge in the molecular ions may also be localized on the part of the molecule that includes the amino group. Then, for example, in the case of IIIb, $C_6H_5NH^+$, $C_6H_5NH_2^{+\cdot}$, $C_6H_5NCO^+$, and $C_6H_5NHCO^+$ ions (92, 93, 119, and 120, respectively) are formed as a result of the bonds indicated above. The elementary compositions of the ions with m/e 119 and 120 were confirmed by precise measurements of their masses (Table 2), and their formation serves as absolute proof that the investigated product cannot have rhodanine structure IIb. Evidence for this is also provided by the absence in the examined spectra of ion peaks with masses M–28 and M–72, which could arise in the case of successive ejection of CO and CS molecules from the rhodanine ring.

Other ions that are common to the reaction products (99, 132, 105, and 106) evidently have the following structures:

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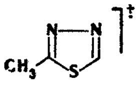
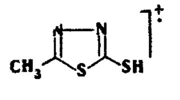
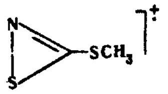
*Here and subsequently, the numbers that characterize the ions are the mass-to-charge ratios.

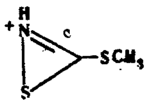
TABLE 2. Precise Masses of the Ions in the High-Resolution Mass Spectrum of IIIb

m/e	Determined	Empirical formula	Calc.
265	265,0369	$C_{11}H_{11}N_3OS_2$	265,0343
173	172,9860	$C_5H_5N_2OS_2$	172,9843
146	145,9997	$C_4H_6N_2S_2$	145,9972
145	144,9954	$C_4H_5N_2S_2$	144,9894
120	120,0423	C_7H_6NO	120,0449
119	119,0378	C_7H_5NO	119,0371
105	104,9716	$C_2H_3NS_2$	104,9706
93	93,0606	C_6H_7N	93,0578

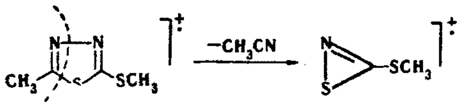

99


132


105

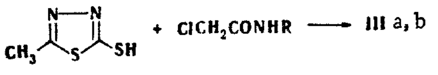

106

The ions with m/e 105 and 106 are probably formed as a result of contraction of the thiadiazole ring, as, for example, via the schemes



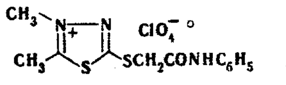
The high-resolution mass spectrum, which completely confirmed the compositions of the molecular and principal fragment ions, was measured for product IIIb (Table 2).

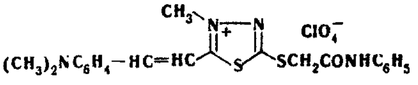
The structures of the products of the reaction of rhodanine I with amines were proved definitively by alternative synthesis, which was accomplished from 2-methyl-5-mercapto-1,3,4-thiadiazole (IV) and the corresponding chloroacetic acid derivatives Va,b via the scheme



IV. Va,b R = H, C_6H_5

A mixture of two quaternary salts, the ratio of which is 2:3 according to the data from the PMR spectrum, is formed in the quaternization of IIIb. The chemical shifts of their C-methyl and methylene groups are, respectively, 2.65, 4.05 and 2.40, 4.20 ppm. Crystallization of the reaction mixture yielded an isomer, which is formed in smaller amounts and for which the signal of the C-methyl group is found at weaker field and the signal of the methylene group is found at stronger field. The latter fact and the formation of a compound in smaller amounts are due to the different nucleophilicities of the nitrogen atoms of the thiadiazole ring [7], and this makes it possible to assign structure VI to the isolated isomer.


VI


VII

This is also confirmed by its ability to react with the corresponding intermediates for the synthesis of dyes (for example, styryl VII was obtained with p-dimethylaminobenzaldehyde).

EXPERIMENTAL

The PMR spectra were recorded with a Tesla BS-467 spectrometer at 60 MHz on the δ scale with hexamethyldisiloxane as the internal standard. The UV spectra of solutions of the compounds in CH_3OH were recorded with an SF-8 spectrophotometer. The IR spectra of KBr pellets were recorded with a UR-10 spectrometer. The mass spectra were obtained with a Varian MAT-311A spectrometer under conditions of direct introduction of the samples in the ion source and under standard operating conditions for the spectrometer; the ionizing-electron energy was 70 eV, and the cathode emission current was 300 μA. The high-resolution mass spectrum

TABLE 3. Characteristics of the Synthesized Compounds

Compound	mp, °C (from alcohol)	Found, %		Empirical formula	Calc., %		Yield, %
		N	S		N	S	
IIIa*	164—165	22,3	33,7	$C_5H_7N_3OS_2$	22,2	33,9	44
IIIb	152—153	15,9	24,1	$C_{11}H_{11}N_3OS_2$	15,8	24,2	61
VI	213—214	10,9	17,1	$C_{12}H_{14}ClN_3O_5S_2$	11,0	16,9	40
VII	248—249	10,9	12,7	$C_{21}H_{23}ClN_4O_5S_2$	11,0	12,5	51

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*Compounds IIIa and IIIb were also obtained by alternative synthesis in 60 and 77% yields.

was recorded under the same conditions with a resolution of $M/\Delta M \sim 10{,}000$ and the use of perfluorinated kerosene as the internal standard.

2-Methyl-5-carbamoylmethylthio-1,3,4-thiadiazole (IIIa). A 0.8-ml sample of saturated ammonium hydroxide was added to a mixture of 0.44 g (2 mmole) of rhodanine I and 2 ml of alcohol. The reaction product was removed by filtration (Table 3). PMR spectrum (in CF_3COOH): 2.67 (3H), 3.87 (2H), and 7.17 ppm (2H).

2-Methyl-5-phenylcarbamoylmethylthio-1,3,4-thiadiazole (IIIb). A mixture of 0.22 g (1 mmole) of rhodanine I and 0.1 g (1 mmole) of aniline was heated at 80°C for 2 h, after which the melt was triturated with acetone to give 0.2 g of product. PMR spectrum (in $CDCl_3$): 2.67 (3H), 4.00 (2H), 7.0-7.5 (5H), and 9.50 (1H); (in CF_3COOH): 2.67 (3H), 4.00 (2H), 7.15 (5H), and 8.75 ppm (1H).

Compounds IIIa,b. These compounds were obtained by alternative synthesis by the following general method. A mixture of 1.3 g (10 mmole) of thiadiazole IV, 0.56 g (10 mmole) of potassium hydroxide, 10 mmole of the corresponding chloroacetamide Va,b, and 10 ml of alcohol was heated at 80°C for 5 min, after which it was filtered, and the filtrate was evaporated to a small volume. The reaction product was removed by filtration.

2,3-Dimethyl-5-phenylcarbamoylmethylthio-1,3,4-thiadiazolium Perchlorate (VI). This compound was obtained by heating equimolar amounts of thiadiazole IIIb and methyl p-toluenesulfonate or dimethyl sulfate at 115°C for 1 h. The product was converted to the perchlorate and crystallized from alcohol. PMR spectrum (in CF_3COOH): 2.65 (3H), 3.88 (3H), 4.05 (2H), 7.05 (5H), and 8.78 ppm (1H).

3-Methyl-2-(p-dimethylamino)styryl-5-phenylcarbamoylmethyl-thio-1,3,4-thiadiazolium Perchlorate (VII). A mixture of 0.76 g (2 mmole) of salt VI, 0.3 g (2 mmole) of p-dimethylaminobenzaldehyde, and 4 ml of acetic anhydride was refluxed for 30 min, after which 0.5 g product was removed by filtration. UV spectrum, λ_{max}: 518 nm.

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