SYNTHESIS OF 3-AMINO-4-HYDROXYLAMINOTHIAZOLIDINE-2-THIONES AND 2,3-DIMETHYL-4*a*,5-DIHYDRO-7-THIOXOTHIAZOLO[3,4-b]-1,2,4-TRIAZINES

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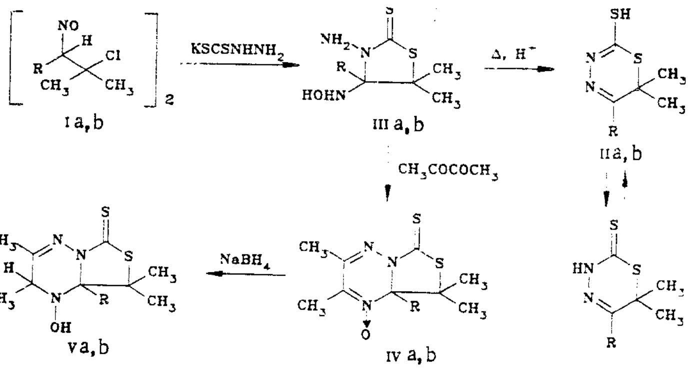
The reaction of dimeric nitroso chlorides of olefins with potassium dithiocarbazate was used to synthesize 3-amino-4-hydroxylaminothiazolidine-2-thiones, which undergo rearrangement to 2-mercapto-1,3,4-thiadiazines on heating and react with butane-2,3-dione to give 2,3-dimethyl-4*a*,5-dihydro-7-thioxothiazolo[3,4-b]-1,2,4-triazine 4-oxides. The latter are reduced by sodium borohydride to the corresponding 3,4,4*a*,5-tetrahydro-7-thioxo derivatives.

According to the data in [1], 2-mercapto-1,3,4-thiadiazines IIa, b, which are intermediates in the synthesis of biologically active compounds, are formed when dimeric nitroso chlorides Ia, b are heated in alcohol with potassium dithiocarbazate.

Considering the data in [2] regarding the synthesis of 4-hydroxylaminothiazolidine-2-thiones on the basis of dimeric nitroso chlorides Ia, b and dithiocarbamic acid salts, in the case under consideration [1] one might also expect the initial formation of a thiazolidine ring. In fact, in the course of the research it was established that the previously unknown 3-amino-4-hydroxylaminothiazolidine-3-thiones IIIa, b are formed under mild conditions in the reaction of dimeric nitroso chlorides Ia, b with a dithiocarbazic acid salt. For example, in addition to singlets of three methyl groups at 1.22, 1.37, and 1.44 ppm, a broad signal of an amino group at 5.2 ppm and doublets of protons at 6.0 (NH) and 7.24 (OH) with J = 3 Hz are observed in the PMR spectrum of IIIb. A number of broad absorption bands of NH groups at 3170-3400 cm^{-1} and a band of an OH group at 3590 cm^{-1} are present in the IR spectra of IIIa, b (CCl_4).



I–V a R=H; b R=CH_3

Heating IIIa, b in organic solvents or water leads to expansion of the five-membered ring with the formation of the known [1] 1,3,4-thiadiazines IIa, b. Broad signals of protons of NH and SH groups at 9.9 and 4.5-5.0 ppm, respectively, are noted in the PMR spectra (d_6-acetone) of thiadiazines IIa, b; this indicates the presence of thione–thiol tautomerism, although the absorption of a thiol group is absent in the IR spectra (CCl_4), and only an NH band at 3390 cm^{-1} is observed.

The presence of two nucleophilic groupings in the IIIa, b molecules is confirmed by condensation with butane-2,3-dione. The resulting N-oxides IVa, b are yellow crystalline sub-

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TABLE 1. Characteristics of the Compounds Obtained

Compound	mp, °C	Found, %			Empirical formula	Calculated, %			Yield, %
		C	H	N		C	H	N	
IIIa	127—128	31,3	5,6	22,1	$C_5H_{11}N_3S_2O$	31,1	5,7	21,7	72
IIIb	123—124	34,5	6,3	20,5	$C_6H_{13}N_3S_2O$	34,7	6,3	20,2	66
IVa	220	44,3	5,4	17,2	$C_9H_{13}N_3S_2O$	44,4	5,4	17,2	80
IVb	250	46,8	5,8	16,1	$C_{10}H_{15}N_3S_2O$	46,6	5,9	16,3	82
Va	190	43,9	6,1	17,0	$C_9H_{15}N_3S_2O$	43,9	6,1	17,0	60
Vb	216	46,2	6,4	16,1	$C_{10}H_{17}N_3S_2O$	46,3	6,6	16,2	50

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*Compounds IVa, b and Va, b melted with decomposition.

stances that are only slightly soluble in organic solvents. Reduction of the N-oxides with sodium borohydride leads to Va, b, the UV spectra of which do not contain the absorption that is characteristic for the conjugated nitrone grouping of N-oxides V [λ = 380 nm (ε = 7300)]. In addition to singlets of four methyl groups at 1.23 (4*a*-CH_3), 1.42, 1.46 [5-$C(CH_3)_2$], and 1.98 ppm (2-CH_3), a doublet and a broad quartet of a >$CHCH_3$ group at 1.27 and 3.28 ppm, with J = 6 Hz, as well as a signal of a hydroxy group at weak field at 8.88 ppm, are present in the PMR spectrum of Vb.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a Perkin—Elmer spectrometer. The UV spectra of solutions in ethanol were obtained with a Specord UV spectrophotometer. The PMR spectra of solutions of the compounds in d_6-DMSO were obtained with a Varian FT-80A spectrometer with tetramethylsilane (TMS) as the internal standard.

The characteristics of the synthesized compounds are presented in Table 1.

3-Amino-4-hydroxylamino-5,5-dimethylthiazolidine-2-thiones IIIa, b. A suspension of nitroso chloride I in 100 ml of alcohol was added to a suspension of 1 mmole of potassium dithiocarbazate in 50 ml of alcohol, after which the mixture was stirred at 20°C for 5 h, and the precipitate was removed by filtration and washed with hot acetonitrile. The mother liquors were combined and evaporated in vacuo without heating. The residue was recrystallized from acetonitrile. PMR spectrum of IIIa: 1.46, 1.50 [6H, s, $C(CH_3)_2$]; 4.46 (1H, s, CH); 5.32 (2H, broad s, NH_2); 6.41 (1H, broad s, NH); 7.3 ppm (1H, broad s, OH).

2-Mercapto-6,6-dimethyl-1,3,4-thiadiazines IIa, b. A suspension of 1 mmole of IIIa, b in 20 ml of 5% hydrochloric acid was heated until the solid dissolved, and the solution was neutralized to pH 7. It was then cooled, and the precipitate was removed by filtration, washed with water, and recyrstallized from alcohol. Compound IIa, with mp 122-123°C [1], was obtained in 76% yield. Compound IIb, with mp 150-151°C (mp 132-133°C [1]), was obtained in 84% yield. IR spectra of IIa, b: 1090-1100, 1300-1320, 1465-1490 cm^{-1} (NHCSS).

2,3-Dimethyl-4*a*,5-dihydro-7-thioxothiazolo[3,4-b]-1,2,4-triazine 4-Oxides IVa, b. A mixture of 1 mmole of III and 1 mmole of butane-2,3-dione was refluxed in acetonitrile for 5 min, after which the precipitate was removed by filtration to give yellow crystals that were virtually insoluble in water, acetone, and DMSO. IR spectra of IVa, b: 1595 w, 1515 (C=N), 1290 cm^{-1} (N—O). UV spectrum of IVa: λ_1 259 nm (ε 12200), λ_2 273 nm (ε 12900), λ_3 380 (ε 7300).

2,3-Dimethyl-3,4,4*a*,5-tetrahydro-4-hydroxy-7-thioxothiazolo[3,4-b]-1,2,4-triazines Va, b. A 1.5-mmole sample of sodium borohydride was added in portions to a suspension of 1 mmole of IV in 50 ml of methanol, and the mixture was stirred for 30 min. At the end of the reaction (disappearance of the solid) the alcohol was evaporated, and the precipitate was washed with water, dried, and recrystallized from benzene. PMR spectrum of Va: 1.53, 1.57 [6H, s, 5-$C(CH_3)_2$]; 1.96 (3H, s, 2-CH_3); 1.36 (3H, d, J = 6 Hz, 3-CH_3) and 3.37 (1H, m, 3-CH); 4.38 (1H, broad s, 4*a*-CH); 8.8 ppm (1H, broad s, OH). IR spectra of Va,b: 1625 (C=N); (CCl_4): 3580 cm^{-1} (OH). UV spectrum of Va: λ_1 278 nm (ε 16900), λ_2 303 nm (ε 18800).

LITERATURE CITED

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