LITERATURE CITED

1. T. N. Sidorenko, G. A. Terent'eva, V. S. Raida, O. S. Andrienko, Yu. V. Savinykh, and V. S. Aksenov, Khim. Geterotsikl. Soedin., No. 12, 1618 (1982).
2. T. N. Sidorenko, G. A. Terent'eva, O. S. Andrienko, Yu. V. Savinykh, and V. S. Aksenov, Khim. Geterotsikl. Soedin., No. 2, 192 (1983).
3. T. N. Sidorenko, G. A. Terent'eva, and V. S. Aksenov, Khim. Geterotsikl. Soedin., No. 2, 197 (1983).
4. N. K. Lyapina, M. A. Parfenova, T. S. Nikitina, E. S. Brodskii, and A. D. Ulendeeva, Neftekhimiya, 20, 619 (1980).
5. H. Moussa and S. Abdel-Meguid, J. Heterocycl. Chem., 18, 1519 (1981).
6. K. Oka and S. Hara, Tetrahedron Lett., 2939 (1977).
7. M. S. Neumann and P. K. Sujecth, J. Org. Chem., 43, 4367 (1978).

SULFUR-CONTAINING DERIVATIVES OF FIVE-MEMBERED CYCLIC SULFONES.

1. SYNTHESIS OF SALTS OF ISOTHIOUREIDOTHIOLENE 1,1-DIOXIDES

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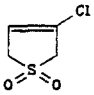
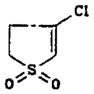
Salts of isothioureidothiolene 1,1-dioxides with different positions of the ring double bond were obtained by the reaction of thiourea with halo derivatives of thiolene 1,1-dioxides.

Sulfur-containing derivatives of five-membered cyclic sulfones are of considerably practical interest: light stabilizers for polymers [1], antioxidants [2], and emulsifiers [3] have been detected among them, and the use of these compounds as biologically active substances has been patented [4-6]. Substituted 3-thiolene 1,1-dioxides are also used to obtain difficult-to-obtain functionally substituted dienes that are used in syntheses of heterocyclic analogs of anthracyclines [7].

We have previously reported the preparation of 3-methyl-5-isothioureido-2-thiolene 1,1-dioxide hydrobromide [8]; however, other salts of isothioureidothiolene 1,1-dioxides were unknown. We studied the possibility of obtaining such salts by the reaction of halo derivatives of thiolene 1,1-dioxides I-V with thiourea.


I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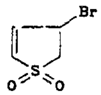
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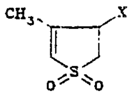
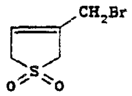

IVa, b


V

IV a X=Br; b X=Cl

It was established that 3-chloro-3-thiolene 1,1-dioxide (I) does not undergo this reaction; this can be explained by the low activity of the vinyl halogen atom in nucleophilic substitution reactions and the impossibility of isomerization of the double bond from the 3 position to the 2 position of the thiolene 1,1-dioxide ring under the influence of the weakly basic thiourea. In contrast to sulfone I, the presence of an electron-acceptor SO_2 group in the α position with respect to the double bond in 3-chloro-2-thiolene 1,1-dioxide (II) increases the activity of the vinyl chlorine atom, as a result of which sulfone II gives 2-isothioureido-2-thiolene 1,1-dioxide hydrochloride (VI) when it is heated with thiourea

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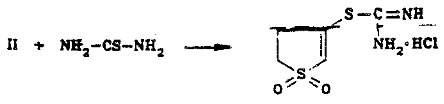
TABLE 1. Characteristics of the Synthesized Compounds

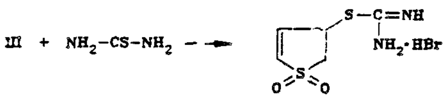
Compound	mp, °C	Found, %			Empirical formula	Calc., %			Yield, %
		Hal	N	S		Hal	N	S	
VI	119—120	15,6	12,4	28,1	$C_5H_8N_2O_2S_2\cdot HCl$	15,5	12,3	28,0	87
VII	232—234	28,9	10,6	23,4	$C_5H_8N_2O_2S_2\cdot HBr$	29,3	10,3	23,5	81
IX	206—207	28,2	9,9	22,6	$C_6H_{10}N_2O_2S_2\cdot HBr$	27,8	9,8	22,3	66
IX	199—201	14,5	11,8	26,0	$C_6H_{10}N_2O_2S_2\cdot HCl$	14,6	11,5	26,4	84
X	161—162	28,0	9,8	22,6	$C_6H_{10}N_2O_2S_2\cdot HBr$	27,9	9,8	22,3	85

in isopropyl alcohol at 80°C for 2 h.



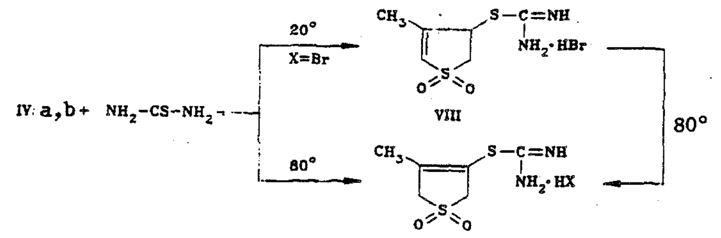
VI

Halo derivatives III-V react readily with thiourea in isopropyl alcohol to give salts VII-X; this is explained by the increased activity of the allyl halogen atom in nucleophilic substitution reactions. Thus sulfone III forms salt VII in the reaction at 20°C for 24 h.



VII

Sulfone IVa under similar conditions gives salt VIII, which we previously described in [8]. However, if this reaction is carried out at 80°C, 3-methyl-4-isothioureido-3-thiolene 1,1-dioxide hydrobromide (IXa), the formation of which can be explained by thermal isomerization of the initially formed salt VIII under the reaction conditions, is obtained in 66% yield after 10 h. In fact, salt IXa is formed in 83% yield when VIII is heated in isopropyl alcohol at 80°C for 8 h.

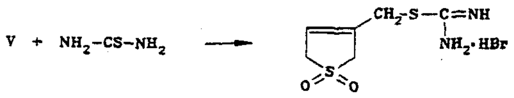


IXaX=Br;bX=Cl IXa,b

Sulfone IVb reacts with thiourea only at 80°C to give 3-methyl-4-isothioureido-3-thiolene 1,1-dioxide hydrochloride (IXb).

It is known that the SO_2 group, not having the ability to undergo conjugation, by means of its negative inductive effect destabilizes the double bond in the 2 position of the thiolene 1,1-dioxide ring and promotes its migration to the 3 position [9]. In the case of the formation of salts of isothioureidothiolene 1,1-dioxides from halo derivatives IVa, b this isomerization takes place at elevated temperatures.

Sulfone V gives 3-methyleneisothioureido-3-thiolene 1,1-dioxide hydrobromide (X) upon reaction with thiourea for 5 h at 80°C.



X

The synthesized compounds were characterized by the results of elemental analysis (Table 1) and IR and ^{13}C NMR spectroscopic data (Table 2). Absorption bands that are characteristic for stretching vibrations of SO_2 (1120-1140, 1280-1310 cm^{-1}), C=N (1640-1670 cm^{-1}), =N—H (3300-3400 cm^{-1}), and $\overset{+}{N}H_3$ (3050-3220 cm^{-1}) groups and absorption bands of deformation

TABLE 2. Spectral Characteristics of the Synthesized Compounds

Compound	IR spectrum, cm^{-1}					^{13}C NMR, δ, ppm				
	ν_{SO_2}	$\nu_{C=N}$	$\nu_{=N-H}$	$\nu_{\overset{+}{N}H_3}$	$\delta_{=N-H}$	$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$ (rт)	Difference in the signals
VI	1130, 1280	1640	3400	3220	1480	128,4d	146,7s	32,7t	51,0	18,3
VII	1130, 1300	1670	3300	3100	1540	134,2d	138,8d	42,9d	54,3	—
IX^a	1120, 1310	1660	3310	3080	1540	60,9t	112,4s	152,5s	59,1	1,8
IX^b	1120, 1310	1660	3310	3080	1540	60,9t	112,4s	152,5s	59,1	1,8
X	1140, 1310	1660	3400	3050	1540	55,4t	130,6s	122,6d	56,3	0,9

vibrations of the =N—H group (1480-1540 cm^{-1}) are present in the IR spectra of salts VI, VII, IX, and X. The assignment of the signals in the ^{13}C NMR spectra of these compounds was made on the basis of a comparison of the spectra recorded without decoupling of the protons and under conditions of complete decoupling of the protons. The presence in the spectrum of VII of one triplet and three doublets indicates the presence in the thiolene 1,1-dioxide ring of only one CH_2 group and three CH groups; this is possible only in the case of the 4-substituted 2-thiolene 1,1-dioxide structure. The presence in the spectra of IXa, b of two triplets and two singlets, which we assigned to signals of the carbon atoms of thiolene 1,1-dioxide rings, confirms the 3,4-disubstituted 3-thiolene 1,1-dioxide structure proposed for these compounds. The presence of one singlet, one doublet, and two triplets of carbon atoms of the thiolene 1,1-dioxide ring in the spectrum of X and the small difference in the chemical shifts of the signals of the carbon atoms of the CH_2 groups (0.9 ppm) as compared with the analogous difference for IXa, b (1.8 ppm) constitute evidence in favor of the 3-substituted 3-thiolene 1,1-dioxide structure. One singlet, one doublet, and two triplets of carbon atoms of the thiolene 1,1-dioxide ring are also present in the spectrum of VI. However, the difference in the chemical shifts of the signals of the carbon atoms of the CH_2 groups in the spectrum of this compounds (18.3 ppm) is considerably greater than the corresponding differences for salts IXa, b and X, which have a 3,4-disubstituted (3-substituted) 3-thiolene 1,1-dioxide structure. This indicates the presence of a 2-thiolene 1,1-dioxide ring in the molecule and, consequently, confirms the 3-substituted 2-thiolene 1,1-dioxide structure for salt VI.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-20 spectrometer. The ^{13}C NMR spectra of solutions in water were recorded with a Bruker CXP-200 spectrometer (50 MHz). The resonance conditions were stabilized with respect to the D nuclei of deuteroacetone, which was used as the internal standard. The signal of the CD_3 group was taken as 29.2 ppm. All of the shifts are presented on the tetramethylsilane (TMS) scale. The error in the measurement of the ^{13}C chemical shifts was ±0.1 ppm.

Halo derivatives of thiolene 1,1-dioxides I-V were obtained by the method in [9]. The characteristics of VI, VII, IXa, b, and X are presented in Tables 1 and 2.

3-Isothioureido-2-thiolene 1,1-Dioxide Hydrochloride (VI). A mixture of 0.76 g (0.01 mole) of thiourea, 1.53 g (0.01 mole) of sulfone II, and 25 ml of isopropyl alcohol was heated at 80°C for 2 h, after which it was cooled to 5°C, and the resulting precipitate was removed by filtration, recrystallized from ethanol, and air dried to give 2.0 g of salt VI.

4-Isothioureido-2-thiolene 1,1-Dioxide Hydrobromide (VII). A mixture of 0.76 g (0.01 mole) of thiourea, 1.97 g (0.01 mole) of sulfone III, and 40 ml of isopropyl alcohol was stirred at 20°C for 24 h, after which the precipitate was removed by filtration, crystallized from concentrated HCl, and air dried to give 2.2 g of VII.

3-Methyl-4-isothioureido-3-thiolene 1,1-Dioxide Hydrobromide (IXa). A) A mixture of 0.76 g (0.01 mole) of thiourea, 2.11 g (0.01 mole) of sulfone IVa, and 30 ml of isopropyl alcohol was heated at 80°C for 10 h, after which it was cooled to 20°C, and the resulting precipitate was removed by filtration, crystallized from ethanol, and air dried to give 1.89 g of IXa.

B) A mixture of 2.87 g (0.01 mole) of salt VIII and 30 ml of isopropyl alcohol was heated at 80°C for 8 h, after which it was cooled to 20°C, and the resulting precipitate of salt IXa was removed by filtration and air dried to give 2.38 g of IXa.

3-Methyl-4-isothioureido-3-thiolene 1,1-Dioxide Hydrochloride (IXb). A mixture of 0.76 g (0.01 mole) of thiourea, 1.67 g (0.01 mole) of sulfone IVb, and 40 ml of isopropyl alcohol was heated at 80°C for 16 h, after which it was cooled to 20°C. The resulting precipitate of salt IXb was removed by filtration, crystallized from water, and air dried to give 2.04 g of IXb.

3-Methyleneisothioureido-3-thiolene 1,1-Dioxide Hydrobromide (X). A mixture of 0.76 g (0.01 mole) of thiourea, 2.11 g (0.01 mole) of sulfone V, and 20 ml of isopropyl alcohol was heated at 80°C for 5 h, after which it was cooled, and the resulting precipitate of salt X was removed by filtration, crystallized from ethanol, and air dried to give 2.43 g of X.

LITERATURE CITED

1. J. R. Garson, US Patent No. 3444209; Chem. Abstr., 71, 13012 (1969).
2. M. E. Chiddix, D. J. Tracy, and V. Shah, US Patent No. 3407140; Chem. Abstr., 70, 12295 (1969).
3. A. V. Golubev, V. F. Kovaleva, V. I. Stadnik, G. S. Maslyuk, B. I. Kurlyuchenko, and K. I. Matkovskii, USSR Inventor's Certificate No. 765305; Byull. Izobret., No. 35, 152 (1980).
4. S. B. Greenbaum, US Patent No. 3288671; Chem. Abstr., 66, 45785 (1967).
5. P. E. Newallis, US Patent No. 3234084; Chem. Abstr., 64, 11177 (1966).
6. D. I. Relyea, R. J. Sperley, and R. B. Ames, US Patent No. 3563725; Chem Abstr., 75, 20178 (1971).
7. P. J. Proteau and P. B. Horkins, J. Org. Chem., 50, 141 (1985).
8. G. I. Khaskin, Yu. V. Bezuglyi, A. B. Rozhenko, A. A. Tukhar', and T. É. Bezmenova, in: Summaries of Papers Presented at the 16th All-Union Conference on the Chemistry and Technology of Organic Sulfur Compounds and Sulfurous Petroleum Oils [in Russian], Riga (1984), p. 218.
9. T. É. Bezmenova, The Chemistry of Thiolene 1,1-Dioxides [in Russian], Naukova Dumka, Kiev (1981).

BROMINATION OF 1,3,5-TRIMETHYL-4-CHLOROPYRAZOLE

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The bromination of 1,3,5-trimethyl-4-chloropyrazole with N-bromosuccinimide (NBS) in the presence of benzoyl peroxide leads to 5-bromomethyl-1,3-dimethyl-4-chloropyrazole, whereas 3,5-bis(bromomethyl)-1-methyl-4-chloropyrazole predominates in the case of a twofold excess of NBS. Products of subsequent substitution in the 3- and 5-bromomethyl groups of the 3,5-bis(bromomethyl) compound in a ratio of 3:1 were detected in small amounts; this is evidently associated with the syn orientation of the bromine atom in the 5-bromomethyl group, which hinders attack by the bromine radical.

We have previously studied the peculiarities of the bromination of 1,3- and 1,5-dimethyl-4-chloropyrazoles with N-bromosuccinimide (NBS) in the presence of benzoyl peroxide [1]. In the present research we carried out the radical bromination of 1,3,5-trimethyl-4-chloropyrazole (I) to determine the relative reactivities of the methyl groups in the 3 and 5 positions of the pyrazole ring. In the case of an equimolar ratio of chloropyrazole I and NBS the principal reaction product is bromomethyl-substituted II, which was obtained in individual form after distillation in 60% yield based on the converted chloropyrazole I. Signals of protons of a 1-CH_3 group and of CH_3 and $BrCH_2$ groups in the 3 and 5 positions were identified

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