REACTION OF DITHIOCARBAMIC ACID SALTS WITH 4-SUBSTITUTED 2-THIOLENE- AND 3,4-DISUBSTITUTED THIOLANE 1,1-DIOXIDES. STRUCTURAL STUDIES OF N-PHENYLTHIOLANO[3,4-d]THIAZOLIDINE-2-THIONE 5,5-DIOXIDE

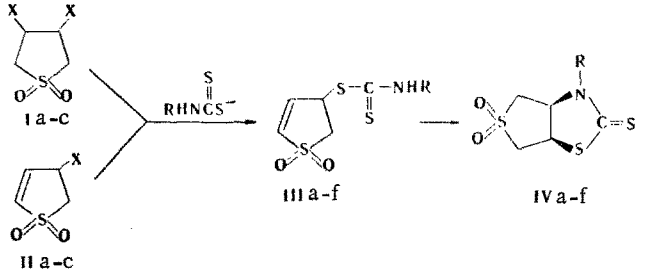
T. É. Bezmenova, G. I. Khaskin, V. I. Slutskii, P. G. Dul'nev, L. N. Zakharov, V. I. Kulishov, and Yu. T. Struchkov

UDC 547.732'733'789.6

The reaction of monoalkyl(aryl)dithiocarbamic acid salts with 4-substituted 2-thiolene and 3,4-disubstituted thiolane 1,1-dioxides gave N-alkyl(aryl)thiolano-[3,4-d]thiazolidine-2-thione 5,5-dioxides, the structure of which was proved by x-ray diffraction studies. 1,1-Dioxothiol-3-en-3-yl esters were obtained with salts of dialkyl(heteryl)dithiocarbamic acids.

Methods for the synthesis of cis-thiolano[3,4-d]imidazolidin-2-one 5,5-dioxide, the starting material for the preparation of biotin and its analogs from accessible derivatives of thiolane and thiolene 1,1-dioxides, were recently proposed [1-3]. In developing these studies we investigated the possibility of the preparation from them of new two-ring compounds with potential biologically active properties.

We found that salts of monoalkyl and aryldithiocarbamic acids react at 10-20°C with 3,4-disubstituted thiolane and 4-substituted 2-thiolene 1,1-dioxides (I, II) in a mixture of tetrahydrofuran (THF) (or dioxane) with water (2:1) to give the previously undescribed two-ring IV systems (Table 1):

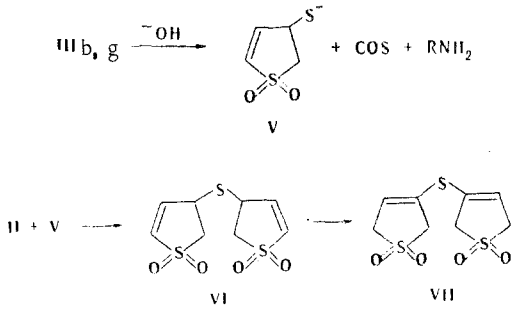


I, II a X=Cl; b X=Br; c X=OTs; III, IV a R=C_4H_9; b R=C_3H_7-*i*; c R=C_6H_5; d R=*p*-CH_3—C_6H_4; e R=*p*-Cl—C_6H_4; f R=$C_6H_5CH_2$

The formation of thioesters III precedes cyclization. In cases in which intramolecular addition is sterically hindered, as, for example, in the case of IIIb, we isolated two-ring system IVb and the known [4] bis(1,1-dioxothiol-3-en-3-yl) sulfide (VII), whereas in the reaction of sulfones Ia with o-$ClC_6H_4NHCSSNa$ we isolated only VII. We explain its formation by cleavage of esters IIIb, g (R = iso-C_3H_7 and o-ClC_6H_4) to 1,1-dioxothiolan-2-yl thiolate (V), which reacts with the starting 4-substituted 2-thiolene 1,1-dioxide to give bis(1,1-dioxothiol-2-en-4-yl) sulfide (VI). The latter undergoes isomerization to VII [4]:

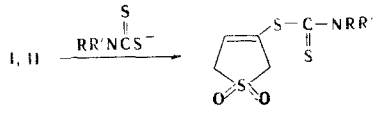
Petrochemical Sector of the Institute of Physical Organic Chemistry and Coal Chemistry, Academy of Sciences of the Ukrainian SSR, Kiev 252160. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 907-912, July, 1981. Original article submitted July 9, 1980.

 0009-3122/81/1707-0668$07.50



Sulfide VII was detected by thin-layer chromatography (TLC) in small amounts in the products of the reactions of sulfones I and II with other salts of monosubstituted dithiocarbamic acids, and this indicates the competitiveness of intramolecular addition and cleavage of thioesters IIIa-f.

Thioesters VIII (Table 2) were isolated in the reaction of I and II with hetaryl and disubstituted salts of dithiocarbamic acids:



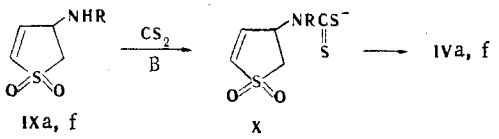
VIII a-d

VIII a $R=R'=NC_4H_8O$; b $R=R'=NC_5H_{10}$; c $R=R'=C_2H_5$; d $R=CH_3$, $R'=C_4H_7SO_2$.

The position of the double bond in esters VIII was established by means of PMR spectroscopy.

The PMR spectrum (at 80 MHz and 20°C) of the ring protons of VIIIc consists of three groups of signals with integral intensities of 2H, 2H, and 1H. The protons in the 5 position give a complex multiplet at 4.05 ppm. The signal of the C_4 proton in pyridine is superimposed on the signal of the solvent; however, in acetone it gives a multiplet at 6.44 ppm. The character of the splitting of the α protons of the ring of VIIIc in pyridine and in acetone is identical, and this proves the absence of migration of the C=C bond under the influence of pyridine.

Two-ring systems IVa, f were also obtained by the action of carbon disulfide on 4-amino-2-thiolene 1,1-dioxides (IX) in the presence of alkalis or tertiary amines.



IXa, f X

IX a $R=C_4H_9$; f $R=C_6H_5CH_2$

The absence of a melting-point depression for a mixture of the substances obtained from I, II, and IX makes it possible to conclude that intramolecular addition in both cases leads to two-ring compounds with identical ring fusion. To determine their three-dimensional structure we made an x-ray diffraction study of N-phenylthiolano[3,4-d]thiazolidene-2-thione 5,5-dioxide.

We found that it crystallizes in a monoclinic system with four molecules in the unit cell with P21/n symmetry with the parameters a = 17.958(4), b = 12.592(2), and c = 52.710(5) Å and α = 90.0, β = 94.49, and γ = 90.0°. The geometry of the molecule is presented in Fig. 1. The thiazolidine fragment is planar, while the thiolane fragment has an envelope configuration. The S_1 atom is removed from the plane formed by the $C_1C_2C_3C_4$ atoms by 0.74 Å, and the angle between this plane and the plane formed by the $C_1S_1C_4$ atoms is 37.4°. Tetrahydrofuran [5], tetrahydroselenophene [6], thiolane [7], and 3,4-epoxythiolane 1,1-dioxide [8] have nonpolar structures; the first compound, like cyclopentane [9], has the property of free pseudorotation, while the other three have a half-chair structure with C_2 symmetry. The envelope conformation observed in our case for the thiolane ring is probably the result of the effect of the thiazolidine ring. The angle between the plane formed by the C_1, C_2, C_3, and C_4 atoms and the plane of the thiazolidine ring is 58.3°. The S_1—C_1 and S_1—C_4 bond

TABLE 1. N-Alkyl(aryl)thiolano[3,4-d]thiazolidine-2-thione 5,5-Dioxides

Compound	Starting substance	mp, °C	IR spectrum, cm^{-1}	Found, %				Empirical formula	Calc., %				Yield, %
				C	H	N	S		C	H	N	S	
IVa	Ic	178	2970 w 2935 w, 2855 w, 1600 m, 1510 m, 1370 s, 1350 s, 1180 s, 1160 s, 1090 s			5,3	36,3	$C_9H_{15}NO_2S_3$			5,3	36,2	89
IVa	IIc												83
IVa	IXa												88
IVb	Ib	165—166	2990 w, 1930 w, 1440 s., 1320 s, 1285 m, 1190 m, 1140 s, 1080 m			5,8	38,0	$C_8H_{13}NO_2S_3$			5,6	38,2	52
IVc	Ia	292—294	2930 w, 1420 s, 1320 s., 1260 s, 1250 s., 1160 s, 1060 s, 900 m, 760 m, 690 m	46,4	4,4		33,7	$C_{11}H_{11}NO_2S_3$	46,4	4,3		33,8	80
IVc	Ib												55
IVc	IIa												69
IVc	IIb												70
IVc	IIc												95
IVd	Ia	270—272	3010 w, 2960 w, 2930 w, 1630 w, 1430 s 1390 m, 1290 s, 1270 s, 1250 s, 1170 m, 1105 m, 1060 m	47,9	4,5		32,4	$C_{12}H_{13}NO_2S_3$	48,2	4,4		32,2	93
IVe	Ia	277—278	3020 w., 2970 w., 1640 w, 1500 m, 1440 s, 1320 s, 1330 s., 1300 s, 1275 s., 1260 s., 1110 s., 1070 m, 925 m, 905 m	41,5	3,3		30,5	$C_{11}H_{10}ClNO_2S_3$	41,3	3,1		30,2	90
IVf	Ia	219—220	3010 w., 2920 w, 1630 w, 1460 m, 1320 s, 1280 s, 1245 m., 1140 s., 1105 m., 700 w	48,4	4,3	4,5	32,2	$C_{12}H_{13}NO_2S_3$	48,2	4,4	4,7	32,2	80

TABLE 2. 1,1-Dioxothiol-3-en-3-yl Esters of Dithiocarbamic Acids

Compound	Starting substance	mp, °C	IR spectrum, cm^{-1}	Found, %			Empirical formula	Calc., %			Yield, %
				C	H	S		C	H	S	
VIIIa	IIc	169—170	2980 w, 2930 w, 2870 w, 1485 m, 1310 s 1240 s, 1230 s., 1140 s, 1115 s, 990 s, 800 m, 600 s, 540 m	39,2	4,5		$C_9H_{13}NO_3S_3$	38,8	4,7		93
VIIIb	Ia	148—149	3000 w, 2950 m, 2870 w, 1485 m, 1310 s, 1240 s, 1230 s, 1120 s 1005 m, 970 m, 850 m, 765 m, 600 m	43,6	5,2	34,9	$C_{10}H_{15}NO_2S_3$	43,4	5,4	34,7	95
VIIIc	Ia	147—148	2980 w, 2950 w, 1500 m, 1420 m, 1310 s, 1215 s, 1200 m, 1125 s, 600 m	40,9	6,1	36,5	$C_9H_{15}NO_2S_3$	40,7	6,0	36,2	95
VIIId	IIc	177—178	3075 w, 3010 w, 2970 w, 2930 w, 1605 w, 1485 w., 1410 s, 1315 s, 1260 s, 1190 s, 1150 vs 930 s, 775 m, 615 m	35,3	4,5	37,5	$C_{10}H_{15}NO_4S_4$	35,2	4,4	37,6	91

TABLE 3. Bond Lengths and Bond Angles in IVc

Bond designation	Bond length, Å	Bond designation	Bond length, Å	Angle designation	Angle, deg	Angle designation	Angle, deg
1	1,769 (11)	11	1,419 (8)	1,2	105,82 (72)	8,13	121,69 (85)
2	1,501 (15)	12	1,448 (8)	2,3	110,10 (84)	9,3	108,32 (84)
3	1,554 (15)	13	1,459 (14)	2,6	111,68 (71)	9,13	119,28 (83)
4	1,525 (14)	14	1,400 (17)	3,4	109,87 (86)	10,7	119,86 (59)
5	1,780 (11)	15	1,334 (17)	4,5	104,46 (71)	10,8	128,56 (78)
6	1,826 (10)	16	1,381 (17)	4,9	112,24 (86)	11,1	112,60 (50)
7	1,735 (10)	17	1,415 (18)	5,1	93,66 (49)	11,5	112,29 (49)
8	1,347 (12)	18	1,313 (16)	6,3	106,40 (69)	11,12	118,25 (48)
9	1,479 (15)	19	1,390 (14)	6,7	95,09 (47)	12,1	108,24 (48)
10	1,650 (10)			7,8	111,54 (72)	12,5	109,01 (48)
				8,9	118,62 (85)		

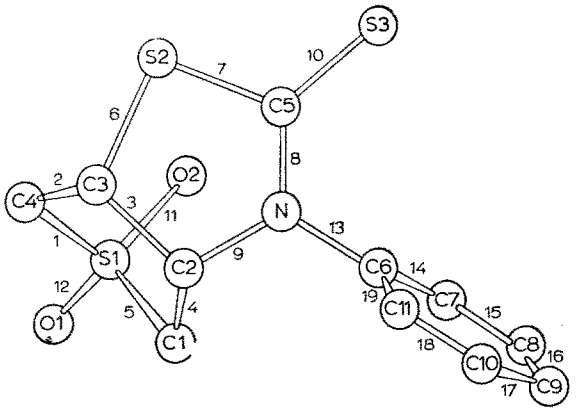


Fig. 1. Geometry of the N-phenyl-thiolano[3,4-d]thiazolidine-2-thione 5,5-dioxide molecule.

lengths (Table 3) are close to those we found (1.78 and 1.76 Å) in the 3-phenyl-2-thiolene 1,1-dioxide molecule [10] and in 3,4-epoxythiolane 1,1-dioxide (1.797 and 1.793 Å). The S—C bonds in the thiazolidine ring are nonequivalent. The length of the S_2—C_3 bond is close to the length of the S—C single bond (1.817 Å) [11], while the S_2—C_5 bond is substantially shorter, and its length is close to that found (1.740 Å) in 3,4-diisopropyl-5-methyl-4-thiazoline-2-thione [12]. The exocyclic S_3—C_5 bond is shortened considerably as compared with the endocyclic bond, and its length is close to that of the thione bond (1.688 Å) in similar compounds [12]. The C—N bonds in the same ring are nonequivalent. The length of one of them, viz., C_2—N, coincides with the standard value for a single bond (1.47 Å), while the length of the C_5—N bond occupies an intermediate position between that of a single bond and that of a double bond (1.255 Å) [13].

The S_1—O bond lengths also are not identical. The S_1—O_1 bond is similar to the S—O bond in 3-thiolene 1,1-dioxide (1.440 Å) [14] and in 3,4-epoxythiolane 1,1-dioxide (1.441 and 1.445 Å) [10], while the S_1—O_2 bond is shorter.

The results of x-ray diffraction analysis show that the sterically unhindered thioesters III and dithiocarbamic acid salts X form thiolano[3,4-d]thiazolidine-2-thione 5,5-dioxides with cis-fused rings by cyclization in the presence of bases.

EXPERIMENTAL

The x-ray diffraction study was made with a Syntex P2 automatic x-ray diffractometer. The structure was calculated by means of the Multan program. The final value of confidence factor R was 7.7%.

The PMR spectra were recorded with a Tesla BS-487B spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard. The IR spectra of KBr pellets of the compounds were obtained with a UR-20 spectrometer. Thin-layer chromatography (TLC) was carried out on Silufol UV-254 in diethyl ether—ethyl acetate systems.

1,1-Dioxothiol-3-en-3-yl N,N-Diethyldithiocarbamate (VIIIc). A solution of 1.2 ml (0.02 mole) of CS_2 in 10 ml of tetrahydrofuran (THF) was added at 15-20°C to a solution of 1.46 g (0.02 mole) of diethylamine and 1.6 g (0.04 mole) of NaOH in 20 ml of water, after which the mixture was allowed to stand for 2 h. It was then added dropwise at 20°C to a suspension of 3.8 g (0.02 mole) of 3,4-dichlorothiolane 1,1-dioxide, and the mixture was stirred at room temperature for 3 h. It was then evaporated to half its original volume, and the resulting precipitate was removed by filtration and crystallized from 30% aqueous methanol. Compounds VIIIa-d (Table 2) were similarly obtained.

N-Butylthiolano[3,4-d]thiazolidine-2-thione 5,5-Dioxide (IVa). A 1.2-g (0.02 mole) sample of CS_2 in 10 ml of THF was added at 15-20°C to a solution of 1.46 g (0.02 mole) of butylamine and 1.1 g (0.02 mole) of KOH in 20 ml of water, after which the mixture was allowed to stand for 3 h. It was then added dropwise at 20°C to a suspension of 5.5 g (0.02 mole) of 1,1-dioxothiol-2-en-4-yl tosylate in 20 ml of 50% aqueous dioxane, and the mixture was stirred for 4 h. It was then neutralized with 0.1 N HCl and evaporated to half its original volume. The resulting precipitate was removed by filtration and crystallized from 50% aqueous THF. Compounds IVb-f were similarly obtained (Table 1).

Reaction of 3,4-Dibromothiolane 1,1-Dioxide with Sodium N-(o-Chlorophenyl)dithiocarbamate. Bis(1,1-dioxothiol-3-en-3-yl) Sulfide. A solution of 0.02 mole of sodium N-(o-chlorophenyl)dithiocarbamate and 0.02 mmole of NaOH in 40 ml of a mixture of dioxane with water was added dropwise to a suspension of 5.56 g (0.02 mole) of 3,4-dibromothiolane 1,1-dioxide in 100 ml of water, and the mixture was stirred for 3 h. It was then evaporated, and the residue was crystallized twice from ethanol with charcoal to give 1.8 g (68%) of a product with mp 161°C. IR spectrum: 1305 and 1125 cm^{-1} (SO_2). PMR spectrum (in DMSO): 6.03 (unsymmetrical singlet) and 3.73 ppm (multiplet) in agreement with the data in [4].

LITERATURE CITED

1. H. Kotake, K. Inomata, I. Murata, N. Kinoshita, and M. Katsuragawa, Chem. Lett., No. 11, 1073 (1976).
2. F. Ellis and P. G. Sammes, J. Chem. Soc., Perkin Trans. I, No. 22, 2866 (1972).
3. P. I. Parkhomenko, T. A. Ovcharenko, S. M. Lukashov, and T. É. Bezmenova, Summaries of Papers Presented at the 13th Scientific Session on the Chemistry and Technology of Organic Sulfur Compounds and Sulfurous Petroleum Oils [in Russian], Riga (1974), p. 238.
4. S. N. Lewis and W. D. Emmons, J. Org. Chem., 31, 3572 (1966).
5. A. Almenningen, H. M. Seip, and T. Willadsen, Acta Chem. Scand., 23, 2748 (1969).
6. Z. Nahlovska, B. Nahlovsky, and H. M. Seip, Acta Chem. Scand., 27, 1903 (1970).
7. Z. Nahlovska, B. Nahlovsky, and H. M. Seip, Acta Chem. Scand., 23, 3534 (1969).
8. D. E. Sands, Acta Crystallogr., 28, 2465 (1972).
9. W. J. Adams, H. J. Geise, and L. S. Bartell, J. Am. Chem. Soc., 92, 5013 (1970).
10. T. É. Bezmenova, G. V. Klimushina, V. I. Kulishov, S. M. Lukashov, G. G. Rodé, G. M. Soroka, and V. I. Tantsyura, Khim. Geterotsikl. Soedin., No. 8, 1056 (1977).
11. G. Pepe and M. Pierrot, Acta Crystallogr., 15, 737 (1962).
12. P. Gerard and P. Marcel, Acta Crystallogr., 32, 1321 (1976).
13. E. Boyer and G. Hafelinger, Chem. Ber., 99, 1689 (1966).
14. D. E. Sands and V. N. Day, Z. Chem., 124, 220 (1967).