SULFUR-CONTAINING DERIVATIVES OF THIOLAN-1,1-DIOXIDE

3.* REACTIONS OF SALTS OF 2-(N,N-DIALKYL)IMINIO-5,5-DIOXOPERHYDROTHIENO[3,4-d]-1,3-DITHIOLANS WITH BASES

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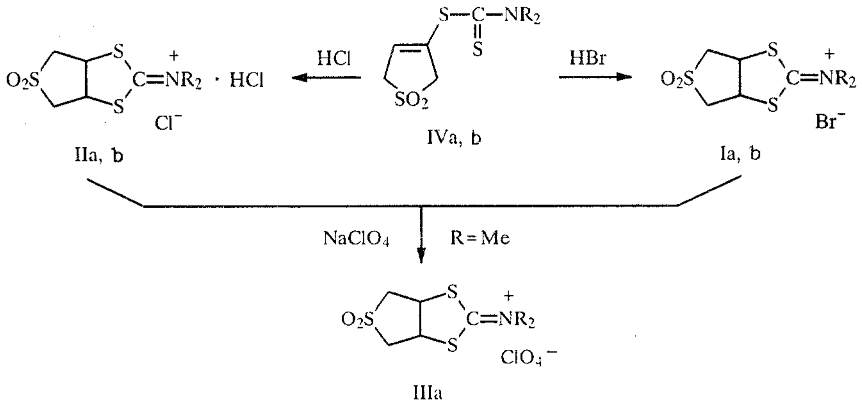
Salts of condensed 2-(N,N-dialkyl)iminio-1,3-dithiolan and 1,1-dioxothiolan rings are converted in alkaline media to 1,1-dioxothiolen esters of N,N-dialkyldithiocarbamic acids and into unsaturated bicyclic compounds. The latter are formed when the initial salts contain a bromine atom β to the sulfonyl group.

There are known to be two electrophilic centers in 2-(N,N-dialkyl)iminio-1,3-dithiolan salts: the carbon atoms $C_{(2)}$ and $C_{(4)}$ or $C_{(5)}$. Consequently these salts form two types of addition or substitution products with nucleophiles. However, if the nucleophile is strongly basic, it may abstract a proton from atoms $C_{(4)}$ or $C_{(5)}$. Subsequently the C-S bond to the neighboring carbon breaks to give a vinyl N,N-dialkyldithiocarbamate [2]. Similar concurrent substitution and elimination reactions have been observed in the alkaline hydrolysis of some derivatives of thiolan-1,1-dioxide [3]. It is of interest in this connection to investigate their behavior in the presence of basic salts in which the 2-(N,N-dialkyl)iminio-1,3-dithiolan ring is condensed to the 1,1-dioxothiolan ring.

Scheme 1



I-IV a R=Me, b R=Et

One of us previously reported the synthesis of compounds containing a bromine atom β to a sulfonyl group [4]. We have prepared the unsubstituted salts of 2-(N,N-dialkyl)iminio-5,5-dioxoperhydrothieno[3,4-d]-1,3-dithiolan (I, IIa, IIb, and IIIa) by condensation of the known [5] 1,1-dioxo-3-thiolen-3-yl esters of N,N-dialkyldithiocarbamic acid (IVa, IVb) with hydrogen chloride or hydrogen bromide (scheme 1). Double bonds in 3-thiolen-1,1-dioxide deactivated by the sulfonyl group are known to add bromine 100 times more slowly than normal olefinic double bonds and hydrogen halides do not add at all [6, 7]. We explain the successful cyclization of esters IVa and IVb with hydrogen halides by the facts that the reaction is intramolecular,

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*For Communication 2, see [1].

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TABLE 1. Characteristics of the Compounds Synthesized

Compound	Molecular formula	mp, °C	UV spectrum, λ_{max}, nm (log c_m)	IR spectrum, ν, cm^{-1}			Yield, %
				SO_2	C=N*	C=C	
Ia	$C_7H_{12}BrNO_2S_3$	260	247 (4,09)	1120, 1320	1610	—	86
I b	$C_9H_{16}BrNO_2S_3$	260	—	1128, 1296	1568	—	65
IIa	$C_7H_{12}ClNO_2S_3 \cdot HCl$	260	248 (4,04)	1145, 1310	1620	—	67
II b	$C_9H_{16}ClNO_2S_3 \cdot HCl$	220...222	250 (4,08)	1135, 1310	1580	—	83
IIIa	$C_7H_{12}ClNO_6S_3$	260	247 (4,07)	1132, 1300	1608	—	92
Va	$C_7H_{11}NO_2S_3$	130...133	220 (4,09)**, 244 (4,02), 278 (3,95)	1140, 1300	1510	1610	95
V b	$C_9H_{15}NO_2S_3$	68...72	222 (4,07), 248 (4,06), 280 (4,00)	1144, 1300	1496	1594	69
VIIIa	$C_7H_{10}ClNO_6S_3$	175...177	301 (3,98)	1150, 1328	1608	1565	36
VII b	$C_9H_{14}ClNO_6S_3$	165...166	306 (3,96)	1155, 1328	1592	1540	37
IX	$C_5N_4O_3S_3$	136...144	—	1150, 1312	1580	1624	30

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*For compounds Va and b — S-C=S; for compound IX — C=O

**The corresponding values for isomer IVa are 252 (3.99) and 279 (3.90)

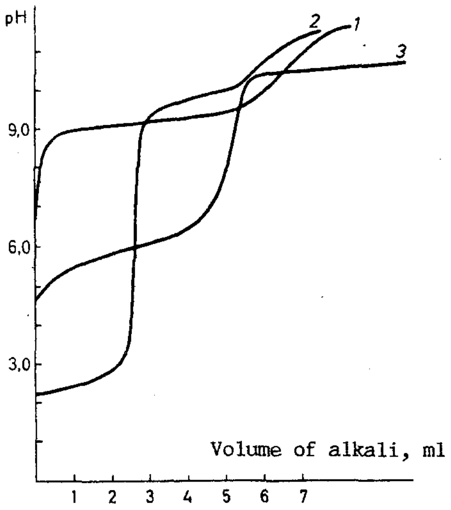

Fig. 1. Potentiometric titration curves with 0.103 N NaOH: 1) 0.2007 g (0.63 mmole) of salt Ia; 2) 0.1032 g (0.32 mmole) of compound IIa; 3) 0.1986 g (0.50 mmole) of salt VIa.

the geometry of the molecule is favorable for the formation of a five-membered ring, and the sulfur atom is more nucleophilic than the halide ion with respect to the protonated double bond. It is also possible that the substituent at the C=C bond in esters IVa and IVb increases its activity in electrophilic addition reactions as with methyl substituted sulfones [6, 7]. Both esters cyclize more readily with the stronger acid, which is in accord with an electrophilic mechanism in which the first step is protonation of the C=C double bond.

The spectroscopic characteristics of salts I, IIa, IIb, and IIIa are given in Tables 1 and 2. The positions of the UV absorption maximum and the molar extinction coefficients for the $C=N^+R_2$ groups in all compounds scarcely differ from the corresponding values for the monocyclic 2-(N,N-dialkyl)iminio-1,3-dithiolan salts [2, 8]. Within the limits of error of the observations they are independent of the nature of the anion and of the presence of a molecule of hydrogen chloride in com-

TABLE 2. ^{13}C NMR Spectra of Compounds I-IX

Compound	Solvent	Chemical shifts, δ, ppm						
		$C_{(2)}$	$C_{(3)}$	$C_{(4)}$	$C_{(5)}$,	C=X,	CH_2,	CH_3,
IVa	DMSO-D_6 + D_2O	58,1 t	126,5 s	135,8 d	58,1	190,9	—	44,8; 42,3
IVb	DMSO-D_6	58,18*t	126,24 s	135,89d	57,94*	189,68	48,91; 47,65	12,63; 11,32
Va	DMSO-D_6	134,2 d	138,9 d	48,1 d	54,3	191,8	—	45,63; 41,6
Xa	DMSO-D_6	62,45 t	126,52*s	126,15*s	60,02	188,80	—	44,72; 42,36
Xb	DMSO-D_6	62,44 t	126,71 s	126,71 s	60,12	187,1	48,91; 47,79	13,16; 11,17
		$C_{(4)}$, t	$C_{(3a)}$	$C_{(6a)}$	$C_{(6)}$, t			
Ia	Acetone-D_6+H_2O	53,73	54,68 d	54,68 d	53,73	192,9	—	48,25
IIa	Acetone-D_6 + H_2O	54,80	53,74 d	53,74 d	54,80	192,1	—	48,25
IIb	Acetone-D_6 +H_2O	54,03	53,68d	53,68 d	54,03	190,6	55,15	10,75
VIa	DMSO-D_6	62,63	71,50 s	66,17d	55,61	189,51	—	49,20 48,52
VIb	Acetone-D_6+H_2O	62,70	68,17 s	64,20 d	54,98	187,6	55,79; 54,98	10,77; 10,63
VIIa	DMSO-D_6	56,70	127,56 s	127,56 s	56,70	187,6	—	47,89
VIIb	DMSO-D_6	56,67	126,91s	126,91 s	56,67	186,6	54,20	10,35
VIIb	DMSO-D_6	56,28	126,87 s	126,87 s	56,28	186,64	54,10	10,18
IX	DMSO-D_6	55,38	121,92 s	121,92 s	55,38	192,38	—	—

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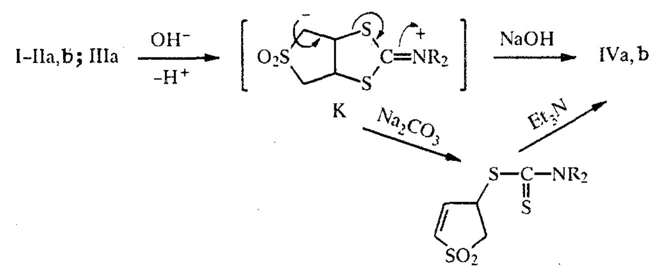
*Alternate assignments may be made for the marked atoms.

pounds IIa and IIb. However a small (about 10 nm) bathochromic shift of the absorption maximum is observed in the spectra of salts VIa and b, which contain bromine (Table 1 and [4]). In the ^{13}C NMR spectra of compounds Ia, IIa, and IIb, in which the sulfonyl group is symmetrically placed, pairs of carbon atoms are equivalent, which indicates unambiguously that all three compounds contain the 1,3-dithiolan ring and that the hydrogen chloride is not covalently bonded in the two latter compounds.

Chemical properties confirm these conclusions. The same perchlorate IIIa is obtained from salt Ia and compound IIa. In titration of compound IIa with NaOH solution (curve 2 in Fig. 1), the first portion of base is used to neutralize the hydrochloric acid. Reaction of hydroxide ions with the bicyclic cation begins under weakly basic conditions. This process corresponds to the horizontal part of the titration curves for sulfones Ia and IIa in the pH 9-10 region.

Scheme 2



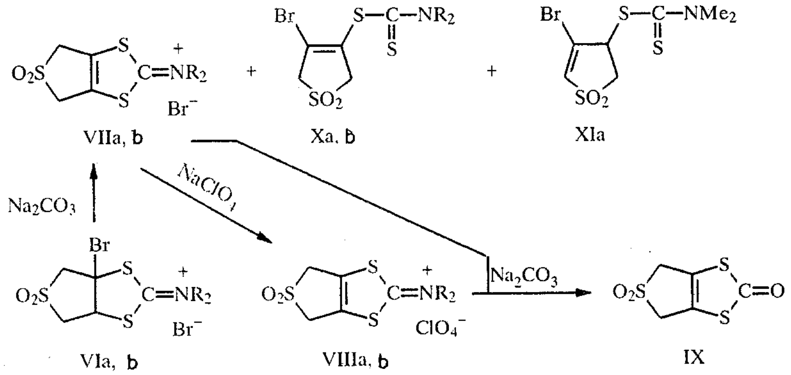
Va, b

I-V a R=Me, b R=Et

Figure 1 shows that equimolar amounts of alkali and the bicyclic salt react together. The only observed products are unsaturated esters of N,N-dialkyldithiocarbamic acid, IVa and b and Va and b (scheme 2). Derivatives of the 4-substituted 2-thiolen-1,1-dioxide, the esters Va and b, are formed on reaction with the weak base Na_2CO_3. The esters IVa and b, derivatives of 3-substituted 3-thiolen-1,1-dioxide, are formed in dilute solution and in the presence of excess NaOH. The latter are evidently formed by base catalyzed isomerization of Va and b, the initial reaction products. This isomerization was carried out on a preparative scale. Scission of salt Ia by Na_2CO_3 in D_2O gave the ester Va with no incorporation of deuterium according to IR and NMR spectroscopy. Consequently either no intermediate is formed in the opening of the 1,3-dithiolan ring (E2 mechanism) or the α-sulfonylcarbanion (K) (scheme 2) is formed more slowly than scission of the leaving S atom. The second route, i.e., sulfur elimination by an $E1cB_1$ mechanism [9], appears the more likely since base catalyzed elimination reactions of thiolan-1,1-dioxide derivatives go via the carbanion mechanism even with easily leaving groups [10].

The previously synthesized [4] salts VIa and b have two leaving groups so that they should undergo β-elimination concurrently. In fact, unlike salts Ia and b, two different types of compound are formed when aqueous solutions of salts VIa and b and Na_2CO_3 are mixed (scheme 3). The basic products (80-95% according to spectroscopic data) are salts of 2-(N,N-dialkyl)iminio-5,5-dioxo-4,6-dihydrothieno[3,4-d]-1,3-dithiolans (VIIa and b), which were isolated in moderate yield as the perchlorates VIIIa and b. A regular impurity is 2,5,5-trioxo-4,6-dihydrothieno[3,4-d]-1,3-dithiolan (IX) which is formed by base hydrolysis of the unsaturated salts VII and VIII (horizontal part of curve 3 in the basic region, Fig. 1). The structures of compounds VII-IX are confirmed by the spectroscopic results cited in Tables 1 and 2.

Scheme 3

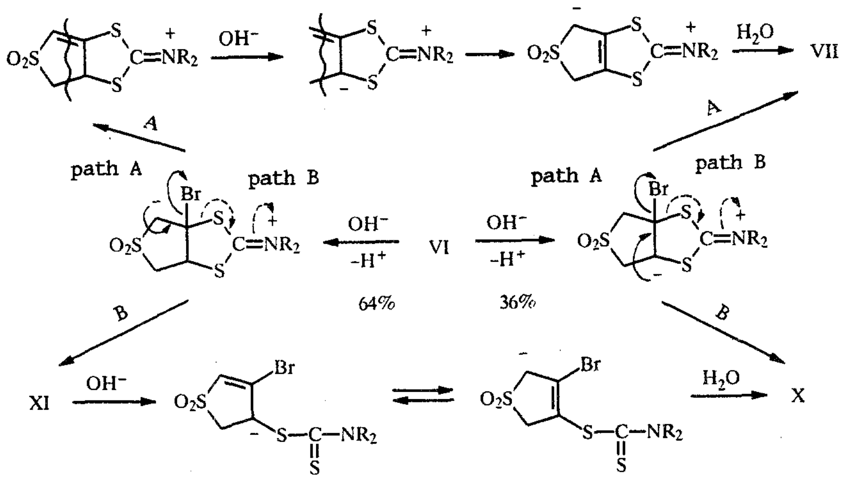


VI-VIII, X a R=Me, b R=Et

The minor, water insoluble products from the salt VIa are the 1,1-dioxo-3-bromo-3-thiolen-4-yl (Xa) and 1,1-dioxo-3-bromo-2-thiolen-4-yl (XIa) esters of N,N-dimethyldithiocarbamic acid. This conclusion is based on a comparison of the ^1H NMR spectra of salt Va and the precipitate (see experimental). We have assigned the singlets in the latter at 4.633 and 3.79 ppm to the protons of compound IX (0.16% from salt VIa) and water respectively, while the signals at 4.33 (2H, t, CH_2), 4.18 (2H, t, CH_2), 3.42 (3H, s, CH_3) and 3.39 ppm (3H, s, CH_3) are assigned to the protons of ester Xa (5% from salt VIa). The remaining signals at 7.47 (1H, dd, J = 2 and 1.4 Hz, HC=C), 5.72 (1H, m, J = 8, 2, 1.5 Hz, HC-S), 4.08 (1H, dd, J = 14 and 8 Hz, ½CH_2), 3.38-3.52 (m, ½CH_2), 3.50 (3H, s, CH_3), and 3.39 ppm (3H, s, CH_3) agree with the structure ester XIa (1.3% from salt VIa).

In the case of salt VIb similar products were separated as a water insoluble oil. It was concluded from analysis of the ^{13}C NMR spectrum that the principal product is 1,1-dioxo-3-thiolen-4-yl N,N-diethyldithiocarbamate (Xb): signals at 187.1, 126.1, 62.44, 60.12, 48.91, 47.79, 13.16, and 11.17 ppm (Table 2). The unsaturated salt VIIb was present as an impurity in the oil (signals at 186.4, 126.7, 56.3, 53.96, and 10.06 ppm) plus unidentified compounds (see Experimental). As in the case of salts Ia-c no hydroxyl-containing addition and substitution products nor 4,4-disubstituted derivatives of 2-thiolen-1,1-dioxide were observed among the reaction products from salts VIa and b with Na_2CO_3, which shows that, no matter what the leaving group, only protons β to bromine are removed (scheme 4).

Scheme 4



Evidently the ratio of mono- (X and XI) to bicyclic (VII) reaction products cited above reflects the relative ease of removing the leaving group from atom $C_{(3a)}$. As expected, the Br^- ion is removed much more readily than the sulfur function. In its turn, the ratio of the derivatives of 2- and 3-thiolen-1,1-dioxides should reflect the relative rate of removal of protons α and β to the sulfonyl group. However the initial isomer ratio may change as a result of isomerization as shown for esters IV and V in scheme 2. Therefore the scission of salts VIa and b was also carried out in D_2O and with different amounts of Na_2CO_3. Evidently one of the protons of the methylene group in derivatives of 3-thiolen-1,1-dioxide, obtained by isomerization of 2-thiolen-1,1-dioxides, should exchange with deuterium. Unfortunately salt VIIa exchanges protons for deuterium under the reaction conditions (1 mole Na_2CO_3 in D_2O). Hence the initial ratio of isomers is determined only from esters Xa and XIa.

When salt VIa was decomposed in D_2O (1 mole Na_2CO_3 per mole of VI) the mixture of esters obtained contained 73% isomer Xa (NMR data) and only this ester was deuterated. The degree of deuteration (hydrogens at $C_{(2)}$) was 25%, i.e., half the maximum value of 50%., which indicates that half the ester Xa was formed directly by decomposition of VIa. Hence the calculated initial ratio of the sulfones Xa:XIa is 36.5:63.5. The same ratio (36:64) was obtained directly from the decomposition of salt VIa in H_2O with a smaller amount of Na_2CO_3 (0.7 mole). Ester XIa isomerizes except when free H_2CO_3 is present in the reaction mixture. It follows from the isomer ratios obtained that the proton α to the sulfonyl group in the salt VIa is removed about twice as fast as the β-proton. It was shown above that only the α-proton is removed from salt Ia and at a considerably greater OH^- concentration than for VIa. Hence introduction of bromine in position 3a causes equalization and a general increase in acidity of the protons β to the substituent, i.e., at atoms $C_{(4)}$ and $C_{(6a)}$. Since the isomerization of the bromine containing sulfone XIa to 3-thiolen-1,1-dioxide derivatives occurs at a considerably lower OH^- concentration (Na_2CO_3 + $NaHCO_3$) than for Va, an analogous increase in acidity occurs for monocyclic esters of type XIa.

Thus, salts with condensed 2-(N,N-dialkyl)iminio-1,3-dithiolane and 1,1-dioxothiolan rings react with bases in aqueous solution to give β-elimination, but not addition, products. Bromine-containing salts eliminate HBr predominantly and are converted to unsaturated bicyclic compounds. In unsubstituted compounds only the proton α to the sulfonyl group is eliminated. With a bromine atom on the carbon atom β to the sulfonyl group, a levelling and a general increase in acidity of both protons β to bromine occurs in both mono- and bicyclic sulfones. It is proposed that the elimination occurs via a carbanion mechanism. The formation of products with replacement of the N,N-dialkyliminium group by the carbonyl group was noted for salts containing the unsaturated 1,1-dioxo-3-thiolene ring.

EXPERIMENTAL

NMR spectra were recorded on Bruker CXP-200 and Varian VXR-200 spectrometers at room temperature. Chemical shifts were measured relative to the signals of the solvent methyl group and calculated relative to TMS. IR spectra were recorded as KBr discs on a Specord M-80 spectrometer, and UV spectra of aqueous or ethanolic (IV and V) solutions were obtained with an SF-46 machine. Titration curves were obtained with a Radelkis OP-930/1 automatic burette with a titrant consumption of 0.6 ml/min.

Sulfur, halogen, and nitrogen analyses for new compounds agreed with calculated values.

2-(N,N-Dimethyl)iminio-5,5-dioxoperhydrothieno[3,4-d]-1,3-dithiolan Bromide (Ia). Gaseous HBr (obtained from KBr (1.5 g, 12 mmole and conc. H_2SO_4 (1.1 ml, 20 mmole)), freed from moisture with red phosphorus and dried over P_2O_5, was passed into a stirred suspension of ester IVa (2.37 g, 10 mmole) in methylene chloride (50 ml). After passage of HBr was completed, the precipitate was filtered off, washed with acetone, and dried to give salt Ia (2.75 g) as slightly yellowish crystals which were purified by recrystallization from water with charcoal.

2-(N,N-Diethyl)iminio-5,5-dioxoperhydrothieno[3,4-d]-1,3-dithiolan Bromide (Ib). Dry HBr (12 mmole), prepared as in the previous experiment, was passed into a solution of ester IVb (2.7 g, 10 mmole) in CH_2Cl_2 (25 ml). The solution containing a white precipitate was kept overnight and then treated as above to give salt Ib as a dirty white microcrystalline powder.

HCl Complexes of 2-(N,N-Dialkyl)iminio-5,5-dioxoperhydrothieno[3,4-d]-1,3-dithiolan Chlorides (IIa and b). A 2.5-4 fold excess of gaseous HCl (dried over H_2SO_4) was passed into a solution or suspension of esters IVa,b in CH_2Cl_2. The solution saturated with HCl was kept for 1-2 days and the crystals of IIa and b were treated as above. Compounds IIa and b lost HCl on storage or recrystallization.

2-(N,N-Dialkyl)iminio-5,5-dioxoperhydrothieno[3,4-d]-1,3-dithiolan Perchlorate (IIIa). A. Salt Ia (3.18 g, 10 mmole) was dissolved in water (50 ml) at 40° C and sodium perchlorate solution (4 N, 2.5 ml, 10 mmole) was added. The solution and precipitate were kept for 1 h, the residue was filtered off, washed with water and dried to give salt IIIa (3.12 g) as a white microcrystalline powder.

B. Compound IIa (2 g, 6.45 mmole) was dissolved in water (30 ml), a small quantity of insoluble material was filtered off, and $NaClO_4$ solution (4 N, 1.5 ml, 6 mmole) was added to the filtrate. The precipitate was treated as in the previous experiment to give a light powder identical with perchlorate IIIa prepared by method A (IR spectra, titration curves, elemental analyses).

1,1-Dioxo-2-thiolen-4-yl N,N-dimethyldithiocarbamate (Va). A solution of Na_2CO_3 (10%, 10 ml, 10 mmole) was added dropwise with constant stirring over 15 min to a solution of salt Ia (1.59 g, 5 mmole) in warm water (30 ml). The solution and precipitate were stirred for 5 min and then worked up in the normal way to give Va (1.12 g), m.p. 128.5-135° C, as a white powder which was purified by crystallization from ethanol.

1,1-Dioxo-2-thiolen-4-yl N,N-diethyldithiocarbamate (Vb). Unpurified bromide IIb (1.73 g, 5 mmole) was dissolved in water (30 ml), the insoluble residue was filtered off, and Na_2CO_3 (10%, 10 ml, 10 mmole) was added over 10 min. The solution was decanted from the viscous oil which was covered with water acidified with HCl and left for days to crystallize. The solid mass was pulverized, filtered off, washed with water, and dried in the air to give a light brown powder (0.92 g), m.p. 65.5-69° C. An analytically pure sample was obtained by crystallization from ethanol.

1,1-Dioxo-2-thiolen-3-yl N,N-dimethyldithiocarbamate (IVa). A. NaOH (0.25 N, 100 ml, 25 mmole) was added to a stirred solution of salt Ia (1.59 g, 5 mmole) in water (500 ml). The reaction mixture was kept for 1 h. After normal work up, fine acicular crystals were obtained (1.1 g, 93%), m.p. 175-176° C, which did not depress the melting point of an authentic sample of ester IVa.

B. Triethylamine (0.1 ml, 0.7 mmole) was added to a saturated solution of ester Va (1.1 g, 4.64 mmole) in boiling ethanol (12 ml). The reaction mixture was boiled for 3 min, cooled, and the precipitate filtered off to give a microcrystalline powder (0.97 g, 88%), m.p. 170-172° C, which did not depress the melting point of an authentic sample of ester IVa.

1,1-Dioxo-2-thiolen-3-yl N,N-diethyldithiocarbamate (IVb). A. NaOH (0.21 N, 95 ml, 20 mmole) was added to a stirred solution of IIb (1.39 g, 4.1 mmole) in water (350 ml), the mixture was stirred for 10 min and left overnight. The precipitate was worked up as usual to give a white powder (0.91 g, 84%), m.p. 143-146° C, which did not depress the melting point of an authentic sample of ester IVb.

B. Ester IVb (97%) was obtained by isomerization of ester Vb analogously to that described for ester Va.

Reactions of 2-(N,N-Dimethyl)- (VIa) and 2-(N,N-Diethyl)iminio-3a-bromo-5,5-dioxoperhydrothieno- [3,4-d]-1,3-dithiolan (VIb) Bromides with Sodium Carbonate. An equimolar amount of Na_2CO_3 (10% solution) was added dropwise to a saturated aqueous solution of one of the salts VIa and b. The reaction mixture and precipitate (VIa) or oil (VIb) was kept for 0.25-1 h, then acidified with HCl and the water soluble products separated by filtration or decantation. After addition of an excess of 4 N $NaClO_4$ and prolonged storage crystalline precipitates of the perchlorates VIIIa or VIIIb were obtained. The precipitate was washed with acetone to remove the 2,5,5-trioxo-4,6-dihydrothieno[3,4-d]-1,3-dithiolan impurity (IX; 1.6% based on VIa in the case of perchlorate VIIIa). The pure dithiocarbonate IX was obtained by treatment of perchlorate VIIIb with Na_2CO_3 solution with subsequent acidification.

^{1}H NMR spectrum of the precipitate (yellowish powder) from treatment of salt VIa with Na_2CO_3 (acetone-D_6, ppm): intense signals at 4.33 t, 4.18 t, 3.424 s, and 3.41 s; low-intensity signals at 7.47 m, 5.75-5.69 m, 4.63 s, 4.14-4.03 dd, 3.785 s, 3.497 s, 3.39 s, and 3.52-3.38 m.

^{13}C NMR spectrum of the oil obtained on treatment of salt VIb with Na_2CO_3 solution (H_2O + acetone-D_6, ppm): 187.1, 186.4, 126.71, 126.05, 62.44, 60.12, 56.30, 53.96, 48.91, 47.79, 41.93, 39.67, 13.16, 12.53, 11.17, and 10.06

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