## 533. *Antituberculous Sulphur Compounds. Part III.* Substituted Propylene Sulphides.*

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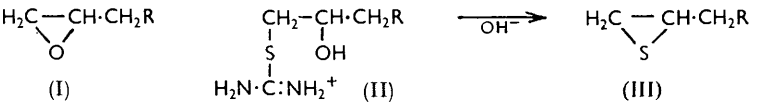
Some new 3-substituted propylene sulphides have been prepared from the corresponding oxides and thiourea. Alkaline hydrolysis of 3-chloropropylene sulphide has been shown to yield 2-hydroxytrimethylene sulphide, and not 3-hydroxypropylene sulphide as previously reported. Acylation of 3-mercaptopropylene sulphide by means of acid chlorides and both symmetrical and mixed anhydrides has afforded numerous 3-acylthiopropylene sulphides. Several examples of the thermal decomposition of 3-acylthiopropylene sulphides into 3-acylthiopropenes and sulphur are reported.

Since one of the most active antituberculosis agents encountered in this series was 3-mercaptopropylene sulphide, it was of interest to prepare other 3-substituted propylene sulphides. Four compounds of this type (III; R = SMe, SEt, OEt, and $NEt_2$) were prepared by the well-known method [1,2,3] of treating the corresponding oxides (I) with

* Part II, preceding paper.

[1] Dachlauer and Jackel, G.P. 636,708/1936.
[2] Culvenor, Davies, and Pausacker, *J.*, 1946, 1050.
[3] Bordwell and Andersen, *J. Amer. Chem. Soc.*, 1953, **75**, 4959.

thiourea. In the first two cases the intermediate thiouronium salts were also isolated; they were assigned structure (II) rather than the 1-hydroxy-2-propyl alternative by analogy with the proved structure of the intermediate in the preparation [3] of propylene sulphide itself.

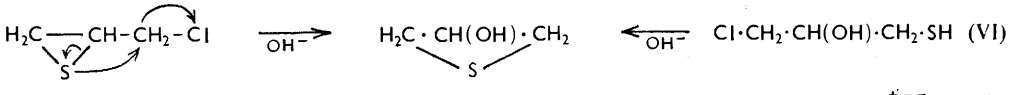


(I) (II) (III)

A bisthiouronium salt analogous to (II) was prepared by the action of thiourea on di-(2,3-epoxypropyl) disulphide, itself obtained by oxidation of 1-chloro-3-mercaptopropan-2-ol and treatment of the resulting bischlorohydrin with sodium hydroxide. The corresponding bisepisulphide, di(2,3-epithiopropyl) disulphide, was however more conveniently obtained by treating an ice-cold solution of 3-mercaptopropylene sulphide in chloroform with the calculated quantity of iodine.

Several attempts were made to reduce di-(2,3-epoxypropyl) disulphide to 3-mercaptopropylene oxide, which would be of interest as an oxygen analogue of the active antituberculosis agent, 3-mercaptopropylene sulphide. Aluminium amalgam appeared to effect reduction, but the product was too unstable to be purified. This is perhaps not surprising in view of the ease with which ethylene oxides react with thiols.

It was also desirable to examine the antituberculosis activity of the other oxygen analogue, namely 3-hydroxypropylene sulphide (III; R = OH). An earlier report [2] that this compound could not be prepared from glycidol and thiourea was confirmed. Culvenor and Davies [4] claimed to have prepared it by alkaline hydrolysis of 3-chloropropylene sulphide (IV), but this method is not structurally definitive. Displacement of chlorine in a β-chloro-sulphide by a nucleophilic reagent is generally considered to involve a cyclic sulphonium ion [5] and may lead to re-arrangement.[6] It was therefore not surprising to find that the compound which Culvenor and Davies regarded as 3-hydroxypropylene sulphide was actually 2-hydroxytrimethylene sulphide (V), identical with a specimen [7] prepared by cyclisation of 1-chloro-3-mercaptopropan-2-ol (VI). It seemed improbable that the chloro-thiol (VI) could also be an intermediate in the formation of 2-hydroxytrimethylene sulphide from chloropropylene sulphide, since even if rupture of the ring preceded displacement of halogen it would have been expected to give a secondary rather than a primary thiol. Alkaline hydrolysis of 3-chloropropylene sulphide more probably involves the electronic displacements indicated at (IV), as a result of which the hydroxyl group becomes attached at $C_{(2)}$ to give the less strained ring system (V).



(IV) (V) (VI) (VII)

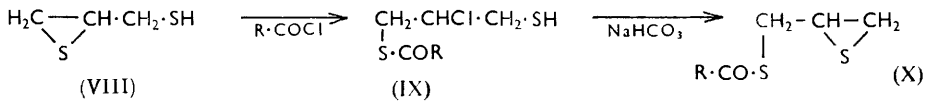
Physical evidence for the identity of the two specimens of 2-hydroxytrimethylene sulphide was supplemented by the following chemical considerations: (*a*) Both samples on desulphurisation with Raney nickel, followed by oxidation of the propanol with acidified potassium dichromate, yielded acetone, which was isolated as the 2,4-dinitrophenylhydrazone. The end-product expected from 3-hydroxypropylene sulphide would have been propionaldehyde. (*b*) Both specimens reacted with methyl iodide in excess to give 2-hydroxy-3-iodopropyldimethylsulphonium iodide (VII); this is characteristic

[4] Culvenor and Davies, *Austral. J. Sci. Res.*, 1948, **1**, *A*, 236.
[5] Gilman and Philips, *Science*, 1946, **103**, 409; Fuson, Price, and Burness, *J. Org. Chem.*, 1946, **11**, 475; Bartlett and Swain, *J. Amer. Chem. Soc.*, 1949, **71**, 1406.
[6] Marvel and Weil, *J. Amer. Chem. Soc.*, 1954, **76**, 61; Gundermann, *Annalen*, 1954, **588**, 167.
[7] Sjoberg, *Svensk Kem. Tidsk.*, 1938, **50**, 250; *Ber.*, 1941, **74**, 64.

of trimethylene sulphides,[8] whereas ethylene sulphides (including 3-chloropropylene sulphide) undergo more extensive disruption of the molecule and yield trimethylsulphonium iodide.[9]

Ring expansion also occurred when 3-chloropropylene sulphide was heated with potassium acetate in glacial acetic acid, the resulting 2-acetoxytrimethylene sulphide being indistinguishable from a sample prepared from 2-hydroxytrimethylene sulphide and acetic anhydride. The action of an excess of methyl iodide on 2-acetoxytrimethylene sulphide gave 2-hydroxy-3-iodopropyldimethylsulphonium iodide (VII), the acetyl group being lost in the reaction.

None of the new compounds described above had appreciable antituberculosis activity, so we turned to compounds more closely related to 3-mercaptopropylene sulphide. Although the acetyl derivative (III; R = SAc) is best prepared by distilling 2,3-diacetylthiopropyl acetate with aqueous sodium hydrogen carbonate solution at about 60°/150 mm.,[10] the method appears to be much less satisfactory for other acyl derivatives (cf. Part II of this series). We thus examined the acylation of 3-mercaptopropylene sulphide. Acetyl chloride, preferably in a diluent such as ether at 0°, gave a non-distillable oil which contained chlorine. Since acetyl chloride and propylene sulphide give 2-chloropropyl thiolacetate [11] the unstable compound was considered to have structure (IX; R = Me). From this, aqueous sodium hydrogen carbonate at room temperature eliminated hydrogen chloride, to give 3-acetylthiopropylene sulphide [10] (X; R = Me). There was no evidence of the presence of 2-acetylthiotrimethylene sulphide, which might have been formed by initial cleavage in the opposite sense.




This technique was used, with minor modifications, to bring about reaction of 3-mercaptopropylene sulphide with a large number of carboxylic acid chlorides and with several chloroformic esters. In a few cases the acyl derivative (X) was obtained even when no sodium hydrogen carbonate was used, but it is not known whether this was due to spontaneous loss of hydrogen chloride from the hypothetical intermediate (IX) or to direct reaction of the acid chloride with the thiol group of 3-mercaptopropylene sulphide rather than with the ethylene sulphide ring.

Acylation of 3-mercaptopropylene sulphide by means of acid anhydrides was next examined. Treatment with acetic anhydride in the presence of a little pyridine gave a 85% yield of 3-acetylthiopropylene sulphide after seven days at room temperature. At the b. p. the yield was considerably reduced and if excess of anhydride was used the ethylene sulphide ring appeared to be opened (as might be expected by analogy with Davies and Savige's observations [11]). Heating 3-mercaptopropylene sulphide for a few minutes with succinic anhydride and a trace of pyridine gave the crystalline acid (X; R = $CH_2$·$CH_2$·$CO_2H$), but phenylsuccinic anhydride, glutaric anhydride, and phthalic anhydride failed to react under conditions which the somewhat labile 3-mercaptopropylene sulphide would withstand.

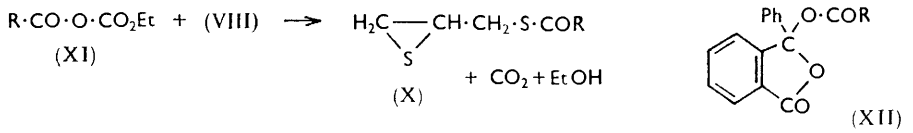
The more reactive mixed anhydrides of type (XI), which are conveniently prepared from ethyl chloroformate and the triethylamine salt of the appropriate acid in an inert solvent and used *in situ*,[12] with 3-mercaptopropylene sulphide at or near room temperature, occasionally

[8] Bennett and Hock, *J.*, 1927, 2496.
[9] Culvenor, Davies, and Heath, *J.*, 1949, 282.
[10] Miles and Owen, *J.*, 1952, 815.
[11] Davies and Savige, *J.*, 1950, 317.
[12] Vaughan and Osato, *J. Amer. Chem. Soc.*, 1952, **74**, 676; cf. Boissonnas, *Helv. Chim. Acta*, 1951, **34**, 874; Wieland and Bernhard, *Annalen*, 1951, **572**, 190.

in the presence of a catalytic quantity of pyridine, readily afforded the 3-acylthiopropylene sulphides; the anhydrides were of such various acids as *N*-benzyloxycarbonylglycine, hippuric acid, *N*-benzoyl-DL-phenylalanine, *NN*-dimethylglycine, and lævulic, terephthalic, *p*-acetamidobenzoic, and *p*-nitrobenzoic acid. However, certain other anhydrides underwent preferential decomposition; in some such instances typical decomposition products [13,14] of the mixed anhydride were isolated, such as the symmetrical anhydride or the ethyl ester of the appropriate acid.

The ethoxyformic anhydride of *p*-dimethylaminobenzoic acid also failed to react with 3-mercaptopropylene sulphide under the usual conditions, but in this instance the ethoxyformic anhydride itself proved to be rather stable and was isolated and recrystallised without difficulty. The first stable crystalline ethoxyformic anhydrides have only recently been reported,[14] although two methoxyformic anhydrides with similar properties have long been known.[15] *o*-Benzoylbenzoic acid also gave with ethyl chloroformate a stable derivative which did not react with 3-mercaptopropylene sulphide. In this case, however, comparison of the ultraviolet absorption spectrum of the derivative with the spectra of other derivatives [16] of *o*-benzoylbenzoic acid showed that the " anhydride " had the " pseudo "-structure (XII; R = OEt).

Crude 3-dimethylaminoacetylthiopropylene sulphide (X; R = $CH_2$·$NMe_2$) with one equivalent of methyl iodide gave a poor yield of the water-soluble quaternary ammonium salt (X; R = $CH_2$·$NMe_3^+I^-$), of interest since the ethylene sulphide ring is disrupted by an excess of methyl iodide.[9]




The yields of 3-acylthiopropylene sulphide were generally highest when this product could be isolated by crystallisation or by distillation at a relatively low temperature. In distillations at higher temperature there was doubtless some polymerisation, but another factor was also involved. In several cases elemental sulphur was observed and the main distillate was a yellow or orange oil of unexpectedly low boiling point which, after further purification, afforded analytical results indicating that they were 3-acylthiopropenes; these were sometimes the only isolable products; when the crystalline 3-*p*-chlorophenylacetylthiopropylene sulphide was distilled, even at 0·01 mm., sulphur was eliminated and the liquid distillate was identified as 3-*p*-chlorophenylacetylthiopropene.

Guss and Chamberlain [17] noted a similar decomposition, of styrene sulphide which, when distilled at 87—88°/4 mm., occasionally decomposed into styrene and sulphur. Tarbell and Harnish [18] have summarised a few earlier reports of similar decomposition of di- and poly-arylethylene sulphides; they consider the driving force to be the tendency to form a completely conjugated system, but this cannot apply to our examples or to the recently postulated [19] formation of octene from octylene sulphide. Actually the conversion into olefins and sulphur is but one example of a type of reaction peculiar to ethylene sulphides as a class. All the common three-membered heterocyclic systems (*i.e.*, imines, oxides, and sulphides) readily undergo many reactions in which one of the bonds linking the heteroatom to carbon is ruptured, but only in the ethylene sulphides may both such bonds be

[13] Einhorn, *Ber.*, 1909, **42**, 2773; Windholz, *J. Org. Chem.*, 1958, **23**, 2044.
[14] Tarbell and Leister, *J. Org. Chem.*, 1958, **23**, 1149.
[15] Fischer and Strauss, *Ber.*, 1914, **47**, 319; Auwers and Wolter, *Ber.*, 1930, **63**, 479.
[16] Schmid, Hochweber, and Halban, *Helv. Chim. Acta*, 1948, **31**, 354.
[17] Guss and Chamberlain, *J. Amer. Chem. Soc.*, 1952, **74**, 1342.
[18] Tarbell and Harnish, *Chem. Rev.*, 1951, **49**, 1.
[19] Moore and Porter, *J.*, 1958, 2062.

broken. This second type of reaction is brought about under mild conditions by, for instance, methyl iodide,[9] tervalent phosphorus compounds,[9,20] and organometallic compounds.[21]

Most of the 3-acyl- and 3-alkoxycarbonyl-thiopropylene sulphides described in this paper were active against experimental human tuberculosis (H37Rv) in mice. These results will be reported separately, by Mr. D. M. Brown and his colleagues.

## Experimental

*3-Methylthiopropylene Sulphide.*—3-Methylthiopropylene oxide (42 g.) was added to a stirred solution of thiourea (31 g.) in 3·6N-sulphuric acid (100 ml.) at 0—5°. After 2 hr. the white solid was collected and crystallised from ethanol, to give needles of S-2-*hydroxy*-3-*methylthiopropylthiouronium sulphate*, m. p. 154° (decomp.) (Found: C, 26·1; H, 5·3; N, 12·3; S, 35·2. $C_{10}H_{26}O_6N_4S_5$ requires C, 26·2; H, 5·7; N, 12·2; S, 35·0%). A solution of the sulphate (13 g.) in water (70 ml.) was covered with light petroleum (75 ml.; b. p. 40—60°) and stirred at 10—15° whilst 20% sodium carbonate solution (30 ml.) was added during 7 min. After a further 5 min. the organic layer was separated and the aqueous phase was stirred for 30 min. each time with two further 50 ml. portions of light petroleum. The combined petroleum extracts were washed, dried, and distilled, to give 3-*methylthiopropylene sulphide* (1·8 g.) as a pale yellow mobile liquid, b. p. 98—99°/35 mm., $n_D^{20}$ 1·5600 (Found: C, 40·3; H, 6·7; S, 53·3. $C_4H_8S_2$ requires C, 40·0; H, 6·7; S, 53·3%).

*3-Ethylthiopropylene Sulphide.*—A similar experiment with 3-ethylthiopropylene oxide (29 g.) gave S-3-*ethylthio*-2-*hydroxypropylthiouronium sulphate* (37 g.), m. p. 135—137° (decomp.) (from ethanol) (Found: C, 29·5; H, 6·2; N, 11·6. $C_{12}H_{30}O_6N_4S_5$ requires C, 29·6; H, 6·2; N, 11·5%). Treatment of the salt with sodium carbonate solution gave 3-*ethylthiopropylene sulphide*, b. p. 85°/13 mm., $n_D^{20}$ 1·5450, in 60% overall yield from the oxide (Found: C, 44·3; H, 7·2; S, 48·2. $C_5H_{10}S_2$ requires C, 44·7; H, 7·4; S, 47·8%).

*3-Ethoxypropylene Sulphide.*—3-Ethoxypropylene oxide (10·2 g.) in dioxan (50 ml.) and water (15 ml.) was treated with thiourea (7·6 g.), warmed at 55—60° for 1 hr., then poured on ice (*ca.* 150 g.). The mixture was extracted with ether (3 × 100 ml.), and the extracts were washed, dried, and distilled to give 3-ethoxypropylene sulphide (5·5 g.), b. p. 79°/65 mm., $n_D^{20}$ 1·4734 (Found: C, 51·1; H, 8·5. Calc. for $C_5H_{10}OS$: C, 50·9; H, 8·5%). Ohta and Ohta [22] report b. p. 66—67°/27 mm., $n_D^{15}$ 1·4731.

*3-Diethylaminopropylene Sulphide.*—This *compound*, b. p. 72°/14 mm., $n_D^{20}$ 1·4857, was prepared in 29% yield from 3-diethylaminopropylene oxide by the method described for the ethoxy-analogue (Found: C, 57·3; H, 10·3. $C_7H_{15}NS$ requires C, 57·8; H, 10·4%).

*Di-(3-chloro-2-hydroxypropyl) Disulphide.*—An ice-cold solution of 1-chloro-3-mercaptopropan-2-ol [7] (19 g.) and sodium hydrogen carbonate (20 g.) in water (200 ml.) was stirred whilst iodine (30 g.) was added in small portions during 30 min. After being stirred for a further 45 min. at room temperature, the colourless mixture was filtered and the solid was dried and recrystallised from benzene, to give needles (12·1 g.) of the *disulphide*, m. p. 80° (Found: C, 28·7; H, 4·8; Cl, 28·2. $C_6H_{12}O_2Cl_2S_2$ requires C, 28·9; H, 4·9; Cl, 27·9%).

*Di-(2,3-epoxypropyl) Disulphide.*—Di-(3-chloro-2-hydroxypropyl) disulphide (12 g.), dissolved in ether (200 ml.), was stirred with 40% aqueous sodium hydroxide (30 ml.) for 4½ hr., then diluted with water to dissolve the sodium chloride. The ether solution was separated, washed with water, dried, and evaporated, finally under reduced pressure, to leave the impure, oily diepoxide (7 g.) which could not be distilled (Found: C, 38·0; H, 5·4; S, 36·1. Calc. for $C_6H_{10}O_2S_2$: C, 40·4; H, 5·6; S, 35·9%). When shaken with sodium thiosulphate solution the compound gave a strongly alkaline reaction characteristic of ethylene oxides.[23]

*Sulphate of Di-(3-amidinothio-2-hydroxypropyl) Disulphide.*—A slurry of thiourea (10·4 g.) and 20% sulphuric acid (33 ml.) was kept at 0—5° whilst the diepoxide (preceding paragraph) (12 g.) was added with stirring during 30 min. The mixture was kept overnight at room temperature and the *dithiouronium sulphate* (17 g.) was collected. A further crop (5·6 g.) was

[20] Davis, *J. Org. Chem.*, 1958, **23**, 1767; Schuetz and Jacob, *ibid.*, p. 1799; Boskin and Denney, *Chem. and Ind.*, 1959, 330.
[21] Bordwell, Andersen, and Pitt, *J. Amer. Chem. Soc.*, 1954, **76**, 1082.
[22] Ohta and Ohta, *Nippon Kagaku Zasshi*, 1956, **77**, 198 (*Chem. Abs.*, 1958, **52**, 253).
[23] Culvenor, Davies, and Heath, *J.*, 1949, 278.

obtained by evaporation of the filtrate *in vacuo* and trituration of the residue with acetone. Recrystallisation from aqueous acetone gave the pure salt, decomp. 174—176° (Found: C, 22·5; H, 4·6; S, 37·3. $C_8H_{20}O_6N_4S_5$ requires C, 22·4; H, 4·7; S, 37·4%). In a similar experiment hydrochloric acid gave the very deliquescent *dihydrochloride*, m. p. 147—148° (decomp.) (from alcohol–acetone) (Found: C, 23·6; H, 5·0; N, 13·3; Cl, 17·8. $C_8H_{20}O_2N_4Cl_2$ requires C, 23·8; H, 5·0; N, 13·8; Cl, 17·6%).

*Di-(2,3-epithiopropyl) Disulphide* (With E. R. Stove).—A solution of iodine (6·35 g.) and potassium iodide (10 g.) in water (20 ml.) was added with stirring to a strongly cooled solution of 3-mercaptopropylene sulphide (5·3 g.) in chloroform (100 ml.). When decolorisation was complete the chloroform layer was separated, washed, and dried ($MgSO_4$). Removal of solvent, finally at 0·05 mm., left the impure diepisulphide as a viscous oil (4·6 g.) which retained chloroform tenaciously and could not be distilled without decomposition (Found: C, 32·1; H, 4·8; S, 57·1. Calc. for $C_6H_{10}S_4$: C, 34·2; H, 4·8; S, 61·0%).

*2-Hydroxytrimethylene Sulphide.*—(a) 1-Chloro-3-mercaptopropan-2-ol [7] (5 g.) and 10% aqueous sodium hydrogen carbonate (50 ml.) were warmed for 3 hr. at 60° with occasional shaking, cooled, and continuously extracted with ether for 24 hr. Evaporation of the dried extracts gave 2-hydroxytrimethylene sulphide (3-hydroxythietan) (3·2 g., 90%), b. p. 86°/16 mm., $n_D^{20}$ 1·5398 (Found: C, 39·3; H, 6·7; S, 34·7. Calc. for $C_3H_6OS$: C, 40·0; H, 6·6; S, 35·5%).

(b) 3-Chloropropylene sulphide [2] (92 g.) in ethanol (500 ml.) was stirred for 30 hr. at room temperature with 2N-aqueous sodium carbonate (1 l.), then the mixture was continuously extracted with ether for 16 hr. Distillation of the dried extracts gave 2-hydroxytrimethylene sulphide (32 g., 45%), b. p. 86°/16 mm., $n_D^{20}$ 1·5393 (Found: C, 40·0; H, 6·4; S, 35·3%). The infrared absorption spectrum was indistinguishable from that of the specimen prepared by method (a).

*Desulphurisation of 2-Hydroxytrimethylene Sulphide.*—The sulphide (1 g.; either preparation) was warmed under reflux for 3 hr. with Raney nickel (5 g.) in water (25 ml.). After filtration, the mixture was distilled and about 20 ml. of aqueous distillate collected. This distillate was treated with potassium dichromate (1 g.) and 10% sulphuric acid (20 ml.), and again distilled. Treatment of the second distillate with 2,4-dinitrophenylhydrazine in ethanol containing a little hydrochloric acid gave a yellow precipitate which, after crystallisation from ethanol, gave acetone 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 126°.

*2-Hydroxy-3-iodopropyldimethylsulphonium Iodide.*—2-Hydroxytrimethylene sulphide (either preparation) was kept for several days with an excess of methyl iodide in acetone, to give a white solid. Crystallisation from ethanol gave *2-hydroxy-3-iodopropyldimethylsulphonium iodide* as needles, m. p. 114° (Found: C, 16·1; H, 3·2; S, 8·5; I, 67·7. $C_5H_{12}OI_2S$ requires C, 16·1; H, 3·2; S, 8·5; I, 68·1%).

*2-Acetoxytrimethylene Sulphide.*—(*a*) A mixture of 2-hydroxytrimethylene sulphide (9 g.), acetic anhydride (5·2 g.), and fused sodium acetate (8·2 g.) was heated for 6 hr. on the steam-bath, cooled, poured into water, and extracted with ether. After being washed with sodium hydrogen carbonate solution, the extracts were dried and distilled to give *2-acetoxytrimethylene sulphide* (6 g.), b. p. 80°/17 mm., $n_D^{20}$ 1·4904 (Found: C, 45·1; H, 6·1; S, 24·6. $C_5H_8O_2S$ requires C, 45·4; H, 6·1; S, 24·3%).

(*b*) 3-Chloropropylene sulphide (10·8 g.), potassium acetate (9·8 g.), and glacial acetic acid (25 ml.) were heated for 20 hr. on the steam-bath, cooled, poured into water, neutralised with sodium carbonate, and extracted with ether. The extracts were washed, dried, and distilled, to give 2-acetoxytrimethylene sulphide (4·2 g.), b. p. 82°/20 mm., $n_D^{20}$ 1·4898, which with an excess of methyl iodide in acetone gave 2-hydroxy-3-iodopropyldimethylsulphonium iodide (needles from ethanol), m. p. and mixed m. p. 114°.

*3-Acetylthiopropylene Sulphide.*—(*a*) Acetyl chloride (7·1 ml.) was added dropwise to a stirred solution of 3-mercaptopropylene sulphide (10·6 g.) in dry ether (50 ml.) at 0—4° and, after 24 hr. at room temperature, the solvent was removed *in vacuo*. Attempts to distil the residual oil (probably IX; R = Me) under reduced pressure led to loss of hydrogen chloride and gave no pure product. The crude oil was stirred with sodium hydrogen carbonate (10 g.) in water (120 ml.) for 6 hr. and the resulting episulphide was extracted into ether, washed, and dried. Distillation gave 3-acetylthiopropylene sulphide (9 g.), b. p. 45—48°/0·05 mm. After redistillation, both it and authentic 3-acetylthiopropylene sulphide [10] had b. p. 46°/0·1 mm., $n_D^{25}$ 1·5530, and the infrared absorption spectra were identical (the peak at 9·55 μ is particularly

significant in confirming the presence of the three-membered ring since the spectra of ethylene sulphide [24] and propylene sulphide also show maxima in this region, but that of trimethylene sulphide does not) (Found: C, 40·2; H, 5·5; S, 43·5. Calc. for $C_5H_8OS_2$: C, 40·5; H, 5·4; S, 43·5%).

(*b*) A mixture of 3-mercaptopropylene sulphide (7 g.), acetic anhydride (7 g.), and pyridine (1 g.) was set aside for 7 days, then distilled to give 3-acetylthiopropylene sulphide (8 g.), b. p. 42—44°/0·08 mm., $n_D^{22}$ 1·5540 (Found: C, 40·6; H, 5·4; S, 43·5%).

3-β-*Carboxypropionylthiopropylene Sulphide.*—3-Mercaptopropylene sulphide (1 g.), succinic anhydride (0·95 g.), and pyridine (2 drops) were heated on the steam-bath for 3 min. Cooling gave 3-β-*carboxypropionylthiopropylene sulphide*, m. p. 78—80° (from aqueous alcohol) (Found: C, 40·6; H, 4·4; S, 30·8. $C_7H_{10}O_3S_2$ requires C, 40·8; H, 4·8; S, 31·1%).

*Other Acyl and Alkoxycarbonyl Derivatives of 3-Mercaptopropylene Sulphide.*—The episulphides listed in the Table are new except 3-butyrylthiopropylene sulphide (cf. preceding paper). Apart from 3-*p*-phenylazobenzoylthiopropylene sulphide, which was orange-red, they were colourless or nearly so. When the same solid episulphide was prepared by two methods identity was established by mixed m. p. The following general preparative methods were employed:

(*a*) The carboxylic acid chloride or chloroformic ester (0·1 mole) was slowly added to 3-mercaptopropylene sulphide (0·1 mole) in dry ether (50 ml.) at 0—4° and the mixture was set aside at room temperature for 16 hr., then refluxed for 1—2 hr. The cooled solution was stirred with sodium hydrogen carbonate (10 g.) in water (120 ml.) for 16 hr., then the ether layer was separated, washed, dried, and evaporated *in vacuo*. If the residual crude episulphide was solid, or if it solidified when triturated with methanol, light petroleum, or ether, it was recrystallised. Liquid episulphides were distilled under reduced pressure: the less volatile ones (especially the benzoyl, phenylacetyl, and furoyl compounds) had to be distilled with great care owing to the ease with which they eliminated sulphur.

(*b*) The acid chloride (0·1 mole) was added dropwise to a gently refluxing solution of 3-mercaptopropylene sulphide (0·1 mole) in dry ether (50 ml.), and the mixture was refluxed for 4 hr., cooled, stirred with sodium hydrogen carbonate solution, and worked up as in (*a*).

(*c*) As method (*b*), but the initial reaction was carried out in boiling benzene.

(*d*) A solution or suspension of the carboxylic acid (0·1 mole) in dry toluene (200 ml.) was treated with triethylamine (0·1 mole) and cooled to 0°. Ethyl chloroformate (0·1 mole) was added slowly with stirring, whereupon triethylamine hydrochloride rapidly separated. After 10 minutes' stirring, 3-mercaptopropylene sulphide (0·1 mole) was added dropwise, followed by pyridine (2 drops), and the mixture was stirred for 1 hr. more at 0°, set aside at the same temperature overnight, and next warmed gently for 30 min. It was then cooled, washed with water, and dried ($MgSO_4$). Toluene was removed *in vacuo* and the residual 3-acylthiopropylene sulphide was purified by distillation or crystallisation.

(*e*) The ethoxyformic anhydride was formed as in (*d*), but the pyridine catalyst was omitted and the mixture was stirred for several hours after addition of 3-mercaptopropylene sulphide, then refluxed for 2 hr. The cooled toluene solution was washed successively with water, sodium hydrogen carbonate solution, and water again, then dried and worked up as before. In the experiments with terephthalic acid the proportions of the reactants were adjusted so as to give the bis-derivative.

3-*Dimethylaminoacetylthiopropylene Sulphide Methiodide* (X; R = $CH_2{\cdot}NMe_3^+I^-$).—Ethyl chloroformate (5·4 g.) was added dropwise at 0° to a stirred solution prepared from *NN*-dimethylglycine hydrochloride (7 g.) and triethylamine (10·1 g.) in dry chloroform (50 ml.). After 10 min. 3-mercaptopropylene sulphide (5·3 g.) was added and the solution was set aside overnight, then refluxed for 45 min. The solution was next cooled, washed with water, dried, and evaporated *in vacuo*. The resulting oil (7·3 g.) was dissolved in ether (50 ml.) and stirred whilst methyl iodide (5·4 g.) was added dropwise. Next morning the crude *methiodide* (2 g.) was collected and recrystallised from methanol. The product, m. p. 143°, was soluble in cold water (Found: S, 19·4; I, 38·2. $C_8H_{16}ONS_2I$ requires S, 19·2; I, 38·1%).

p-*Dimethylaminobenzoic Ethoxyformic Anhydride.*—A suspension of *p*-dimethylaminobenzoic acid (4·1 g.) in dry ether (100 ml.) was treated with triethylamine (2·52 g.), cooled to 0°, and stirred whilst ethyl chloroformate (2·71 g.) was added dropwise. The mixture was stirred for a further 1 hr. at 0° and then for 2 hr. at room temperature. After removal of solid

[24] Guthrie, Scott, and Waddington, *J. Amer. Chem. Soc.*, 1952, **74**, 2795.

**3-*Acyl-* and 3-*alkoxycarbonyl-thiopropylene sulphides* (X).**

| R | Yield (%) and method | M. p.* or b. p./mm. | $n_D^{20}$ | Found (%) C | H | S | Cl (or N) | Formula | Required (%) C | H | S | Cl (or N) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $Pr^n$ | 35 *a* | 61—65°/0·15 | 1·5365 | 47·4 | 6·9 | 36·4 | — | $C_7H_{12}OS_2$ | 47·7 | 6·9 | 36·4 | — |
| $[CH_2]_{14}$·Me | 81 *a* | 59—60° (A) | — | 66·5 | 9·9 | 18·8 | — | $C_{19}H_{36}OS_2$ | 66·2 | 10·5 | 18·6 | — |
| $CH<[CH_2]_5$ | 53 *a* | 89°/0·05 | 1·5476 | 56·1 | 7·4 | — | — | $C_{10}H_{16}OS_2$ | 55·5 | 7·5 | — | — |
| $CH_2Cl$ | 49 *a* | 88°/0·2 | 1·5836 | 33·2 | 3·6 | 34·9 | — | $C_5H_7OS_2Cl$ | 32·9 | 3·9 | 35·1 | — |
| $CHCl_2$ | 29 *a* | 86°/0·1 | 1·5858 | 28·0 | 3·0 | 29·2 | 32·3 | $C_5H_6OS_2Cl_2$ | 27·7 | 2·8 | 29·5 | 32·7 |
| $CCl_3$ | 40 *a* | 111°/0·4 | 1·5830 | 23·9 | 2·2 | 25·1 | 42·5 | $C_5H_5OS_2Cl_3$ | 23·9 | 2·0 | 25·5 | 42·3 |
| $CH_2$·$CH_2Cl$ | 41 *a* | 98°/0·2 | 1·5645 | 36·4 | 4·5 | 32·2 | 17·6 | $C_6H_9OS_2Cl$ | 36·6 | 4·6 | 32·6 | 18·0 |
| $CH_2$·SEt | 9 *a* | 112°/0·025 | 1·5810 | 40·0 | 5·7 | 46·0 | — | $C_7H_{12}OS_3$ | 40·3 | 5·8 | 46·2 | — |
| $CH_2$·$CH_2$·SMe | 5 *a* | 122°/0·01 | 1·5789 | 40·5 | 6·0 | 46·5 | — | $C_7H_{12}OS_3$ | 40·3 | 5·8 | 46·2 | — |
| $CH_2$·$CH_2$·COMe | 63 *d* | 106°/0·01 | 1·5440 | 47·2 | 5·9 | 31·5 | — | $C_8H_{12}O_2S_2$ | 47·0 | 5·9 | 31·4 | — |
| $CH_2$·$CO_2Et$ | 45 *a* | 110—111°/0·15 | 1·5286 | 43·8 | 5·5 | 28·0 | — | $C_8H_{12}O_3S_2$ | 43·6 | 5·5 | 29·1 | — |
| $CH_2$·$CH_2$·$CO_2Me$ | 39 *a* | 120—124°/0·1 | 1·5382 | 43·6 | 5·7 | 28·8 | — | $C_8H_{12}O_3S_2$ | 43·6 | 5·5 | 29·1 | — |
| $CO_2Et$ | 13 *a* | 116—118°/0·3 | 1·5407 | 41·1 | 4·9 | 31·1 | — | $C_7H_{10}O_3S_2$ | 40·8 | 4·8 | 31·1 | — |
| OMe | 67 *a* | 65°/0·25 | 1·5432 | 36·7 | 5·0 | 39·4 | — | $C_5H_8O_2S_2$ | 36·6 | 4·9 | 39·0 | — |
| OEt | 50 *a* | 60°/0·01 | 1·5296 | 40·2 | 5·6 | 36·0 | — | $C_6H_{10}O_2S_2$ | 40·4 | 5·7 | 36·0 | — |
| $OBu^n$ | 19 *a* | 103°/0·01 | 1·5164 | 45·8 | 6·7 | 30·4 | — | $C_8H_{14}O_2S_2$ | 46·6 | 6·8 | 31·1 | — |
| O·$CH_2Ph$ | 20 *a* | 140°/0·05 | 1·5828 | 54·9 | 5·1 | 26·8 | — | $C_{11}H_{12}O_2S_2$ | 55·0 | 5·0 | 26·7 | — |
| Ph | 22 *b* | 130°/0·01 | 1·6242 | 56·7 | 4·7 | 29·6 | — | $C_{10}H_{10}OS_2$ | 57·1 | 4·8 | 30·5 | — |
| $C_6H_4$·Cl-*p* | 99 *b* | 74° (G) | | 48·9 | 3·8 | 26·4 | 14·1 | $C_{10}H_9OS_2Cl$ | 49·1 | 3·7 | 26·2 | 14·5 |
| $C_6H_4$·$NO_2$-*p* | 84 *b* (59 *d*) | 62° (G) | | 46·7 | 3·7 | 25·7 | (5·5) | $C_{10}H_9O_3NS_2$ | 47·0 | 3·6 | 25·1 | (5·5) |
| $C_6H_4$·NHAc-*p* | 54 *e* | 163° (E) | | 53·8 | 5·5 | — | (5·5) | $C_{12}H_{13}O_2NS_2$ | 53·9 | 4·9 | — | (5·2) |
| $C_6H_4$·$NMe_2$-*p* | 13 *c* | 78—81° (A) | | 56·9 | 6·2 | — | (6·0) | $C_{12}H_{15}ONS_2$ | 56·9 | 6·0 | — | (5·5) |
| $C_6H_4$·N:NPh-*p* | 83 *b* | 81—82° (A) | | 61·5 | 4·2 | 19·5 | (9·2) | $C_{16}H_{14}ON_2S_2$ | 61·1 | 4·5 | 20·4 | (8·9) |
| $C_6H_4$(1,4-bis) | 50 *e* | 112—113° (D) | | 49·5 | 4·6 | 37·7 | — | $C_{14}H_{14}O_2S_4$ | 49·1 | 4·1 | 37·4 | — |
| $CH_2Ph$ | 38 *a* | 137—138°/0·3 | 1·5981 | 58·4 | 5·5 | 28·1 | — | $C_{11}H_{12}OS_2$ | 58·9 | 5·4 | 28·6 | — |
| $CHPh_2$ | 65 *b* | 63° (D) | | 67·4 | 5·5 | 20·9 | — | $C_{17}H_{16}OS_2$ | 67·9 | 5·4 | 21·3 | — |
| CHClPh | 2 *a* | 69—71° (A) | | 50·4 | 4·9 | 24·7 | — | $C_{11}H_{11}OS_2Cl$ | 51·0 | 4·3 | 24·8 | — |
| $CH_2$·$C_6H_4Cl$-*p* | 77 *a* | 32—34° (C) | | 51·1 | 4·9 | 24·7 | — | $C_{11}H_{11}OS_2Cl$ | 51·0 | 4·3 | 24·8 | — |
| $CH_2$·O·$C_6H_4Cl$-*p* | 34 *a* | 42—42·5° (F) | | 48·4 | 4·5 | 23·1 | 12·0 | $C_{11}H_{11}O_2S_2Cl$ | 48·1 | 4·0 | 23·3 | 12·9 |
| $CH_2$·NH·CO·O·$CH_2Ph$ | 46 *d* | 69° (E) | | 52·8 | 5·3 | 21·5 | (4·8) | $C_{13}H_{15}O_3NS_2$ | 52·5 | 5·1 | 21·6 | (4·7) |
| $CH_2$·NH·COPh | 21 *c* (30 *e*) | 121° (G) | | 54·0 | 5·1 | 23·8 | (5·3) | $C_{12}H_{13}O_2NS_2$ | 53·9 | 4·9 | 24·0 | (5·2) |
| CH(NHBz)·$CH_2Ph$ † | 29 *d* | 130° (B) | | 64·3 | 5·7 | 17·9 | (4·3) | $C_{19}H_{19}O_2NS_2$ | 63·8 | 5·4 | 17·9 | (3·9) |
| Phthalimidomethyl | 74 *c* | 102° (D) | | 53·5 | 4·4 | 21·9 | (5·0) | $C_{13}H_{11}O_3NS_2$ | 53·2 | 3·8 | 21·9 | (4·8) |
| 2-Furyl | 56 *a* | 120°/0·1 | 1·6180 | 47·6 | 4·2 | — | — | $C_8H_8O_2S_2$ | 48·0 | 4·0 | — | — |

* Recrystallised from (A) light petrolum, (B) benzene, (C) methanol, (D) ethanol, (E) benzene–light petroleum, (F) ether–light petroleum, (G) aqueous ethanol.

† From *N*-benzoyl-DL-phenylalanine.

triethylamine hydrochloride, the ether was evaporated *in vacuo* and the residue was washed with light petroleum to leave p-*dimethylaminobenzoic ethoxyformic anhydride* (5·7 g.), m. p. 58° unchanged by recrystallisation from ether–light petroleum (Found: C, 60·1; H, 6·3. $C_{12}H_{15}O_4N$ requires C, 60·7; H, 6·4%). This anhydride, whether isolated or freshly prepared *in situ*, was recovered unchanged after attempted reaction with 3-mercaptopropylene sulphide in boiling ether containing a trace of pyridine.

*Ethyl 3-Phenyl-3-phthalidyl Carbonate* (XII; R = OEt).—In an attempt to prepare 3-(*o*-benzoylbenzoylthio)propylene sulphide, *o*-benzoylbenzoic acid (8·5 g.) and triethylamine (3·8 g.) in dry toluene (125 ml.) were treated at 0° with ethyl chloroformate (4·1 g.). After 15 min. 3-mercaptopropylene sulphide (4 g.) was added and the mixture was stirred at 0° for 20 min., set aside in the refrigerator overnight, filtered (to remove triethylamine hydrochloride), and evaporated *in vacuo*. The residue, on trituration with light petroleum, gave a white solid which contained no sulphur. Crystallisation from ether gave the *product*, m. p. 106° (Found: C, 68·6; H, 5·0. $C_{17}H_{14}O_5$ requires C, 68·5; H, 4·7%). The ultraviolet absorption spectrum (determined by Dr. H. D. C. Rapson) was virtually identical with that for 3-acetoxy-3-phenylphthalide [16] (XII; R = Me) [$\lambda_{max.}$ 217 mμ (ε 16,020), 280 mμ (ε 1430)]. The compound was unchanged by treatment with 3-mercaptopropylene sulphide in boiling benzene containing a trace of pyridine (4 hr.).

*Thermal Decomposition of 3-Acylthiopropylene Sulphides.*—Crystalline 3-*p*-chlorophenylacetylthiopropylene sulphide (10 g.) was melted and distilled under reduced pressure to give a main fraction (4·1 g.) of yellow oil, b. p. 120—132°/0·01—0·05 mm. Redistillation gave 3-p-*chlorophenylacetylthiopropene*, b. p. 102°/0·01 mm., $n_D^{23}$ 1·5720 (Found: C, 58·0; H, 5·0; S, 14·5; Cl, 15·5. $C_{11}H_{11}OSCl$ requires C, 58·3; H, 4·9; S, 14·1; Cl, 15·6%), hydrolysed by hot dilute hydrochloric acid to *p*-chlorophenylacetic acid, m. p. and mixed m. p. 106°, and a volatile thiol.

Although 3-benzoylthiopropylene sulphide could be distilled (see Table), occasional batches decomposed to a yellow oil which, on redistillation, gave 3-*benzoylthiopropene*, b. p. 64°/0·1 mm., $n_D^{20}$ 1·5846 (Found: C, 67·3; H, 5·7. $C_{10}H_{10}OS$ requires C, 67·4; H, 5·7%). Some batches of 3-phenylacetyl- and 3-2′-furoyl-thiopropylene sulphide decomposed on distillation to, respectively, 3-*phenylacetyl-*, b. p. 96—100°/0·1 mm. (Found: S, 16·7. $C_{11}H_{12}OS$ requires S, 16·7%), and 3-2′-*furoyl-thiopropene*, b. p. 70—74°/0·1 mm., $n_D^{18}$ 1·5701 (Found: C, 56·7; H, 4·7; S, 18·8. $C_8H_8O_2S$ requires C, 57·1; H, 4·8; S, 19·0%).

The products obtained by the action of both *p*-methoxyphenylacetyl and β-phenylpropionyl chloride on 3-mercaptopropylene sulphide (method *a* above), followed by treatment with sodium hydrogen carbonate solution in the usual way, decomposed with elimination of sulphur upon distillation. No episulphides were obtained, the only pure products being 3-p-*methoxyphenylacetyl-*, b. p. 108—119°/0·01 mm., $n_D^{20}$ 1·5663 (Found: C, 64·5; H, 6·6. $C_{12}H_{14}O_2S$ requires C, 64·8; H, 6·4%), and 3-β-*phenylpropionyl-thiopropene*, b. p. 93°/0·02 mm., $n_D^{22}$ 1·5530 (Found: C, 69·4; H, 7·0; S, 15·2. $C_{12}H_{14}OS$ requires C, 69·8; H, 6·8; S, 15·5%).

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