531. *Antituberculous Sulphur Compounds. Part I. New Mercapto-derivatives of Alkanols, Sulphides, and Hydroxy-sulphides.*

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Three general methods have been used to prepare eight new dimercapto-alkanols and also 1,3,4-trimercaptobutan-2-ol and α-hydroxy-β-mercapto-α-mercaptomethylpropionic acid. A number of mercapto-derivatives of aliphatic sulphides and hydroxy-sulphides have been prepared by the action of suitably substituted thiols on propylene sulphide or 3-mercaptopropylene sulphide. The compounds have been tested for antituberculosis activity.

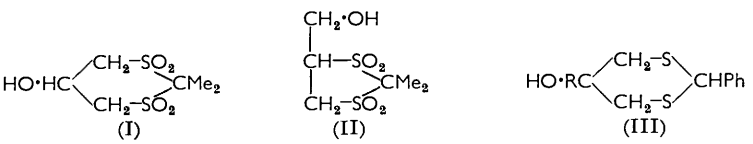
An investigation in these laboratories some years ago showed that 2,3-dimercaptopropan-1-ol (BAL) had slight but significant antituberculosis activity in mice. This had in fact been noted earlier from tests [1] *in vitro* and was also subsequently confirmed *in vivo*.[2] We also found that the known isomer, 1,3-dimercaptopropan-2-ol was too toxic to be tested in mice whilst the known 3-mercaptopropane-1,2-diol and 1,2,3-trimercaptopropane had little or no activity. Many simple thiols, dithiols, and hydroxy-thiols were similarly tested, but appreciable activity was found only in ethanethiol and closely related compounds, a group of antituberculosis agents that is now well-known.[2,3] In an attempt to find compounds more active than BAL itself we have now prepared a series of dimercapto-alkanols, the only other representatives of this class to have been prepared hitherto being 1,3-dimercaptopropan-2-ol, 3,4-dimercaptobutan-1-ol,[4,5] and 4,5-dimercaptopentan-1-ol.[6]

BAL is most conveniently prepared by the reaction of 2,3-dibromopropan-1-ol with alcoholic sodium hydrogen sulphide,[7] and similar treatment of 3,4-dibromobutan-2-ol gave 3,4-dimercaptobutan-2-ol in good yield. However, we confirmed an earlier report [4] that 2,3-dimercaptobutan-1-ol could not be prepared from 2,3-dibromobutan-1-ol by this method, and we were likewise unable to obtain any dithiol from 2,3-dibromo-2-methylpropan-1-ol and alcoholic sodium hydrogen sulphide under a variety of conditions. The only pure product isolated from 1,4-dibromobutan-2-ol and alcoholic sodium hydrogen sulphide was 3-hydroxythiophan, characterised as the α-naphthylurethane, but this was not entirely unexpected since Hall and Reid [8] obtained only a poor yield of dithiol from tetramethylene dibromide owing to thiophan formation. The preparation of 3-hydroxythiophan from 1,4-dichlorobutan-2-ol and sodium sulphide has since been reported.[9]

We further found that certain dimercaptoalkanols can be prepared more conveniently from halogenoalkylene oxides than from dibromo-alcohols. Thus, 1,3-dimercaptopropan-2-ol was obtained in 60% yield when epichlorohydrin was kept overnight with alcoholic sodium hydrogen sulphide at room temperature, whereas a similar preparation [7] from 1,3-dibromopropan-2-ol required a reaction period of four days. 1,3-Dimercaptopropan-2-ol was characterised as a crystalline triacetyl derivative and a liquid isopropylidene derivative. Oxidation of the latter with hydrogen peroxide in acetic acid gave the crystalline cyclic disulphone (I), which differed from the oxidation product (II) of the

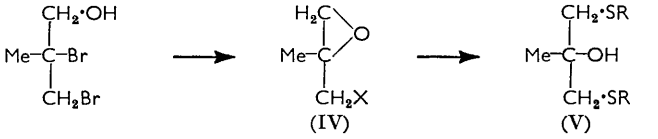
[1] Anderson and Chin, *Science*, 1947, **106**, 643.
[2] Kushner, Dalalian, Bach, Centola, Sanjurjo, and Williams, *J. Amer. Chem. Soc.*, 1955, **77**, 1152.
[3] Brown, Matzuk, Becker, Conbene, Constantin, Solotorovsky, Winsten, Ironson, and Quastel, *J. Amer. Chem. Soc.*, 1954, **76**, 3860; Davies, Driver, Hoggarth, Martin, Paige, Rose, and Wilson, *Brit. J. Pharmacol.*, 1956, **11**, 351.
[4] Pavlic, Lazier, and Signaigo, *J. Org. Chem.*, 1949, **14**, 59.
[5] Miles and Owen, *J.*, 1952, 817.
[6] Fitt and Owen, *J.*, 1957, 2240.
[7] Stocken, *J.*, 1947, 592.
[8] Hall and Reid, *J. Amer. Chem. Soc.*, 1943, **65**, 1466.
[9] Arbuzov and Ovchinnikov, *Doklady Akad. Nauk S.S.S.R.*, 1957, **117**, 813; *Chem. Abs.*, 1958, **52**, 8120.

corresponding derivative of 2,3-dimercaptopropanol. The formation of 1,3-dimercaptopropan-2-ol rather than 2,3-dimercaptopropan-1-ol from epichlorohydrin represents the normal fission of unsymmetrical alkylene oxides under neutral or alkaline conditions.[10] By analogy, a product from the oxide (IV; X = Br) was formulated as (V; R = H).



The solid benzylidene derivatives (III; R = H and Me), like that of 2,3-dimercaptopropan-1-ol,[11,12] were obtained as mixtures of geometrical isomers. The two forms of compound (III; R = H) were fairly readily separated by crystallisation, only the less soluble form having been reported hitherto,[7] but separation of the homologue (III; R = Me) proved more difficult and only one constituent was obtained pure.

In view of the limitations of the sodium hydrogen sulphide route the possibility of preparing dimercaptoalkanols *via* their *SS*-dibenzyl derivatives was next examined. Although 2,3-dibromo-2-methylpropan-1-ol had failed to react satisfactorily with sodium hydrogen sulphide, it readily gave a dibenzylthio-compound on treatment with the sodium derivative of toluene-ω-thiol in alcohol at room temperature. The product, however, was the t-butanol derivative (V; R = CH_2Ph) since on reduction with sodium and ethanol in liquid ammonia it gave the corresponding dithiol, characterised as the benzylidene derivative (III; R = Me) which was identified by mixed melting point with the single isomer described above. Also, the dithiol gave no evidence of the presence of vicinal mercapto-groups in the manganous acetate colour reaction.[13] The rearrangement, like the previously reported formation of 1,3-dibenzylthiopropan-2-ol from 2,3-dibromopropan-1-ol,[14,15] doubtless proceeds *via* an epoxide (IV; X = Br or S·CH_2Ph). In agreement with this view, substitution of the oxide (IV; X = Br) for 2,3-dibromo-2-methylpropan-1-ol in the reaction with the sodium derivative of toluene-ω-thiol gave the same product.

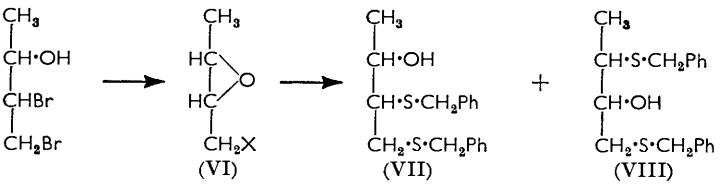


The rearrangement to give non-vicinal dibenzylthio-compounds appears to be complete or very nearly so, as would be expected on the assumption that the intermediate epoxides undergo " normal " ring-opening. The reaction of 3,4-dibromobutan-2-ol with the sodium derivative of toluene-ω-thiol, proceeding through the intermediate (VI; X = Br or S·CH_2Ph) with alkyl substituents on both carbon atoms of the oxide ring, appeared to give the two dibenzylthiobutanols (VII and VIII). The product was clearly not pure 3,4-dibenzylthiobutan-2-ol (VII) since, unlike an authentic specimen prepared by benzylation of the dithiol, it failed to give a crystalline α-naphthylurethane. Debenzylation yielded a mixture of 1,3- and 3,4-dimercaptobutan-2-ol, the comparatively weak green colour developed with manganous acetate suggesting that the vicinal dithiol was probably only a minor constituent.

In the reactions of 1,4-dibromobutan-2-ol and 1,6-dichlorohexan-2-ol with the sodium

[10] Winstein and Henderson in " Heterocyclic Compounds," Vol. 1, Chapter 1, ed. Elderfield, Wiley, New York, 1950.
[11] Miles and Owen, *J.*, 1950, 2938.
[12] Roberts and Cheng, *J. Org. Chem.*, 1958, **23**, 983.
[13] Rosenblatt and Jean, *Analyt. Chem.*, 1955, **27**, 951.
[14] Johary and Owen, *J.*, 1955, 1302.
[15] Doyle and Nayler, *Chem. and Ind.*, 1955, 714.

derivative of toluene-ω-thiol rearrangement appeared improbable since it would involve " abnormal " opening of the hypothetical epoxide intermediates, and the resulting dibenzylthio- and dimercapto-compounds were formulated accordingly. The same



applies to the trithiol prepared from 1,3,4-trichlorobutan-2-ol and the dibenzylthio-compound obtained from β-chloro-α-chloromethyl-α-hydroxypropionic acid. α-Hydroxy-β-mercapto-α-mercaptomethylpropionic acid was obtained in moderate yield by treating the dibenzyl compound with sodium in liquid ammonia, although the conditions were critical. Hydrogenolysis of the dibenzylthio-ester offered no advantage since the ester group suffered hydrolysis under the conditions of the reaction. Crystalline acetyl derivatives of both 1,3,4-trimercaptobutan-2-ol and the dimercapto-acid have been prepared.

Treatment of 2,3-dibromobutan-1-ol with the sodium derivative of toluene-ω-thiol in ethanol at room temperature gave sodium bromide, dibenzyl disulphide, and unidentified products. Thompson [16] has previously reported the formation of disulphides and olefins from mercaptans and vicinal secondary dibromides.

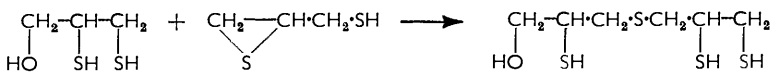
Synthesis of dimercapto-alkanols by reduction of suitable carboxylic acid derivatives was next investigated. Claeson's method [17] for the preparation of methyl αγ-di(acetylthio)butyrate from the corresponding dibromo-ester was extended to ethyl αδ-dibromovalerate and, with slight modification, to methyl 2,11-dibromoundecanoate. On treatment with lithium aluminium hydride the three αω-diacetylthio-esters gave good yields of 2,4-dimercaptobutan-1-ol, 2,5-dimercaptopentan-1-ol, and 2,11-dimercaptoundecan-1-ol. Application of similar methods to the preparation of hydroxy-dithiols containing vicinal mercapto-groups was limited by difficulties in the preparation of the dimercapto-carboxylic acid derivatives. Thus heating ethyl αβ-dibromobutyrate with potassium thioacetate in ethanol gave a little ethyl β-(acetylthio)butyrate but no pure αβ-di(acetylthio)-butyrate. In a similar reaction methyl αβ-dibromo-α-methylpropionate gave only a low yield of β-acetylthio-ester. The same two dibromo-esters, treated at room temperature with the sodium derivative of toluene-ω-thiol in ethanol, gave only the β-benzylthio-esters, accompanied by dibenzyl disulphide. All four reactions may be pictured, at least formally, as involving the elimination of bromine from the dibromide, addition of part of the thiolating agent to the hypothetical unsaturated intermediate, and probably oxidation of the remainder of the thiolating agent by the bromine. Analogy (cf. Hurd and Gershbein [18]) suggests that addition of thiolating agent has been assumed to proceed in the anti-Markownikoff sense; in agreement, methyl αβ-dibromopropionate and the sodium derivative of toluene-ω-thiol gave some methyl αβ-di(benzylthio)propionate but more methyl β-(benzylthio)propionate (which was rigorously characterised) and much dibenzyl disulphide.

Ethyl αβ-di(acetylthio)butyrate was eventually obtained by a route similar to Pavlic's synthesis of methyl αβ-di(acetylthio)propionate,[19] although more vigorous conditions were required. Ethyl α-bromocrotonate was heated with thioacetic acid to give ethyl β-acetylthio-α-bromobutyrate, which with a further quantity of thioacetic acid

[16] Thompson, U.S.P., 2,553,797.
[17] Claeson, *Acta Chem. Scand.*, 1955, **9**, 178.
[18] Hurd and Gershbein, *J. Amer. Chem. Soc.*, 1947, **69**, 2328.
[19] Pavlic, U.S.P., 2,408,094.

in pyridine gave the diacetylthio-compound. Reduction with lithium aluminium hydride then gave 2,3-dimercaptobutan-1-ol.

An interesting hydroxy-trithiol, in which the alkyl chain is interrupted by a sulphur atom, was obtained by Miles and Owen [5] by the action of cold aqueous sodium hydroxide on 2,3-diacetylthiopropyl acetate. It apparently arose by interaction of 2,3-dimercaptopropan-1-ol, which was also isolated, with another primary reaction product (IX or its



(IX) (X)

acetate), and was therefore formulated as (X). It was tacitly assumed that the episulphide ring had been attacked by the primary rather than the secondary thiol group of 2,3-dimercaptopropan-1-ol and that ring-opening occurred in the " normal " manner,[20] the episulphide sulphur retaining its link with $C_{(2)}$. An apparently similar product has now been obtained, together with polymeric material, by direct addition of 2,3-dimercaptopropanol to 3-mercaptopropylene sulphide (IX) in the presence of aqueous sodium hydroxide. In agreement with structure (X) the compound gave a positive result in the manganous acetate test [13] for vicinal dithiols, whereas the branched structure which would have resulted from " abnormal " ring-opening would contain only non-vicinal thiol groups.

In order to prepare simpler analogues, we examined the addition of four hydroxythiols, two dithiols, and 1,2,3-trimercaptopropane to propylene sulphide in the presence of a base. Structures analogous to (X) were assigned to the products, but in addition the dithiols and the trithiol gave compounds derived from reaction with two molecules of episulphide. As in similar reactions with propylene oxide and cyclohexene oxide [21] the mono- and the di-adducts were separable by fractional distillation. We also prepared 2,3-dimercaptopropyl 3-mercaptopropyl sulphide, from 3-mercaptopropylene sulphide and 1,3-dimercaptopropane. Interaction of propylene oxide and 1,2,3-trimercaptopropane gave 2,3-dimercaptopropyl 2-hydroxypropyl sulphide which, like the corresponding product from cyclohexene oxide,[21] could not be distilled without decomposition and was isolated as its triacetyl derivative.

Finally, 2,3-dimercaptopropyl *p*-tolyl sulphide was prepared by a method similar to that used by Hach [22] for the *p*-tolyl ether. The sodium derivative of thio-*p*-cresol was allowed to react with 2,3-benzylidenedithiopropyl chloride, and the protecting benzylidene group was cleaved from the product by means of silver nitrate.

The compounds described in this paper were tested against experimental human-type (H37Rv) tuberculosis in mice, but only 2,3-dimercaptopropyl 3-mercaptopropyl, 2-mercaptoethyl 2-mercaptopropyl, and 3-hydroxy-2-mercaptopropyl 2-mercaptopropyl sulphide showed significant activity. Details of the biological results will be reported by Mr. D. M. Brown and his colleagues.

Experimental

1,6-*Dichlorohexan*-2-*ol*.—Reppe's method [23] for converting butane-1,2,4-triol into 1,4-dichlorobutan-2-ol was applied to hexane-1,2,6-triol. Dry hydrogen chloride was passed into a stirred mixture of hexane-1,2,6-triol (134 g.) and acetic acid (3 ml.) at 110—120° for 7 hr., the increase in weight amounting to 43·5 g. The mixture was distilled and the fraction of b. p. 116—140°/12 mm. collected. Refractionation gave moderately pure 1,6-*dichlorohexan*-2-*ol* (61 g., 36%), b. p. 64—74°/0·1 mm. A specimen, distilled once more, had b. p. 68—70°/0·05 mm., n_D^{16} 1·4821 (Found: C, 42·0; H, 6·9. $C_6H_{12}OCl_2$ requires C, 42·1; H, 7·1%).

3-*Bromo*-2-*methylpropylene Oxide*.—A stirred mixture of 2,3-dibromo-2-methylpropan-1-ol

[20] Cf. Davies and Savige, *J.*, 1950, 317.
[21] Owen and Smith, *J.*, 1951, 2973.
[22] Hach, *Chem. Listy*, 1953, **47**, 227.
[23] Reppe, *Annalen*, 1955, **596**, 140, 141.

(116 g.) and water (100 ml.) was treated with calcium hydroxide (45 g.) and distilled as in the preparation [24] of epibromohydrin from 1,3-dibromopropan-2-ol. After the aqueous phase of the distillate had been recycled the organic material was separated by ether-extraction, washed, dried, and distilled, to give the crude product (41·6 g.), b. p. 35—51°/20 mm., together with 5·7 g. of unchanged 2,3-dibromo-alcohol, b. p. 90—100°/20 mm. The redistilled *oxide* had b. p. 41°/23 mm., n_D^{24} 1·4687 (Found: C, 31·3; H, 4·6; Br, 53·0. C_4H_7OBr requires C, 31·8; H, 4·7; Br, 52·9%).

Methyl 2,11-Dibromoundecanoate.—Thionyl chloride (130 ml.) and 11-bromoundecanoic acid [25] (185 g.) were refluxed for 6 hr., then the excess of thionyl chloride was removed *in vacuo*. The residual crude acid chloride was heated on the steam-bath under reflux whilst bromine (40 ml.) was added with stirring during 3 hr. and then for 4 hr. more. The resulting crude 2,11-dibromoundecanoyl chloride was cooled in ice-water whilst dry methanol (90 ml.) was added during 30 min. The mixture was stirred for 3 hr., then diluted with ether and washed with sodium hydrogen carbonate solution and then with water. The dried ether solution was evaporated and the residue distilled to give *methyl 2,11-dibromoundecanoate* (192 g.), b. p. 154—158°/0·4 mm. A redistilled specimen, b. p. 125—130°/0·05 mm., n_D^{20} 1·4922, was analysed (Found: C, 40·1; H, 6·5. $C_{12}H_{22}O_2Br_2$ requires C, 40·2; H, 6·2%).

Reactions of Alcoholic Sodium Hydrogen Sulphide.—(a) *With 3,4-dibromobutan-2-ol.* A solution of sodium hydroxide (50 g.) in methanol (1 l.) was saturated with hydrogen sulphide at 0°, treated with 3,4-dibromobutan-2-ol (46·4 g.), and set aside in a sealed vessel at room temperature for 10 days. The cooled and stirred mixture was then brought to pH 4—5 by means of hydrochloric acid, filtered, and concentrated *in vacuo*. Water was added and the product extracted into chloroform, washed, and dried. A little ammonium acetate was added as a stabiliser,[26] the chloroform was removed *in vacuo*, and the residual oil distilled to give 3,4-dimercaptobutan-2-ol (20 g.), b. p. 65—66°/0·1 mm., n_D^{24} 1·5519 (Found: C, 35·1; H, 6·8; S, 46·2. $C_4H_{10}OS_2$ requires C, 34·7; H, 7·3; S, 46·4%).

(b) *With 1,4-dibromobutan-2-ol.* Methanolic sodium hydrogen sulphide [1 l. prepared as in (a)] and 1,4-dibromobutan-2-ol (46·4 g.) were allowed to react in a sealed vessel at room temperature for 11 days. The main product (10·1 g.), isolated as in (a), had b. p. 57—58°/0·35 mm. Redistillation gave 3-hydroxythiophan, b. p. 51—52°/0·12 mm., n_D^{18} 1·5433 (lit.,[9] b. p. 84—85°/7 mm., n_D^{20} 1·5427) (Found: C, 45·8; H, 7·9; S, 30·7. Calc. for C_4H_8OS: C, 46·1; H, 7·7; S, 30·8%). The *α-naphthylurethane*, prepared in toluene (5 hours' refluxing), crystallised from methanol in needles, m. p. 114—115° (Found: N, 5·2; S, 11·8. $C_{15}H_{15}O_2NS$ requires N, 5·1; S, 11·7%).

(c) *With epichlorohydrin.* The sodium hydrogen sulphide solution (1 l.) and epichlorohydrin (18·5 g.) were kept for 16 hr. in a sealed vessel at room temperature, then the mixture was worked up as above to give 1,3-dimercaptopropan-2-ol (15 g.), b. p. 52—54°/0·15 mm.

(d) *With 3-bromo-2-methylpropylene oxide.* The sodium hydrogen sulphide solution (1 l.) and oxide (26 g.) were kept for 10 days in a sealed vessel at room temperature. Working up in the usual way gave *1,3-dimercapto-2-methylpropan-2-ol* (5·46 g.), b. p. 54°/0·13 mm. (Found: C, 34·7; H, 7·1; S, 46·2. $C_4H_{10}OS_2$ requires C, 34·7; H, 7·3; S, 46·4%).

2-Acetylthio-1-(acetylthiomethyl)ethyl Acetate.—A mixture of 1,3-dimercaptopropan-2-ol (6 g.), acetic anhydride (30 ml.), and anhydrous sodium acetate (7·5 g.) was refluxed for 6 hr., cooled, and diluted with ether. Sodium acetate was removed with water, and the ether solution was dried and distilled. The oily product, b. p. 106—110°/0·03 mm., solidified under light petroleum to give the acetate (9·8 g.), which crystallised from light petroleum containing a little benzene in prismatic needles, m. p. 44—45° (Found: C, 43·1; H, 5·8. Calc. for $C_9H_{14}O_4S_2$: C, 43·2; H, 5·6%). Johary and Owen [14] give m. p. 46—48°.

1,3-Isopropylidenedithiopropan-2-ol (*5-Hydroxy-2,2-dimethyl-1,3-dithian*).—1,3-Dimercaptopropan-2-ol (24·8 g.) and acetone (15 ml.) in benzene (40 ml.) were treated with concentrated hydrochloric acid (4 drops), refluxed for 24 hr., and evaporated *in vacuo*. The residual oil was taken up in ether, washed with sodium hydroxide solution and then with water, dried, and distilled to give a straw-coloured oil (11·4 g.), b. p. 115—120°/11 mm. Redistillation gave colourless *1,3-isopropylidenedithiopropan-2-ol*, b. p. 117—118°/11 mm., n_D^{17} 1·5635 (Found: C, 43·3; H, 7·8. $C_6H_{12}OS_2$ requires C, 43·9; H, 7·4%).

[24] *Org. Synth.*, Coll. Vol. II, p. 256.
[25] Jones, *J. Amer. Chem. Soc.*, 1947, **69**, 2352.
[26] Cf. Rigby, U.S.P., 2,423,344.

This product (5 g.) in acetic acid (15 ml.) was treated with 30% hydrogen peroxide (15 ml.) and cooled to moderate the exothermic reaction. After 30 min. further peroxide (5 ml.) was added and the solution was heated on the steam-bath for 1 hr. The *disulphone* (5·23 g.) separated on cooling and crystallised from water in needles, m. p. 258—260° (Found: C, 31·1; H, 5·1. $C_6H_{12}O_5S_2$ requires C, 31·6; H, 5·3%).

2,3-Isopropylidenedisulphonylpropan-1-ol (*4-Hydroxymethyl-2,2-dimethyl-1,3-dithiolan 1,1,3,3-Tetroxide*).—Oxidation of 2,3-isopropylidenedithiopropanol [7] as described above gave the *disulphone*, m. p. 103—105° (from water) (Found: C, 31·3; H, 5·0. $C_6H_{12}O_5S_2$ requires C, 31·6; H, 5·3%).

1,3-Benzylidenedithiopropan-2-ol (*5-Hydroxy-2-phenyl-1,3-dithian*).—1,3-Dimercaptopropan-2-ol (24 g.) and benzaldehyde (21 ml.) in benzene (60 ml.) were treated with concentrated hydrochloric acid (1 ml.) and set aside for 24 hr. The mixture was evaporated *in vacuo* and the residue triturated with benzene (30 ml.) to yield the known isomer of 1,3-benzylidenedithiopropan-2-ol (9·24 g.), needles, m. p. 141—142° (from benzene) (Stocken [7] gives m. p. 142—143°) (Found: C, 56·9; H, 5·8. Calc. for $C_{10}H_{12}OS_2$: C, 56·6; H, 5·7%). The syrup obtained by evaporating the original benzene filtrate was triturated with light petroleum and the resulting solid was collected and freed from gum by admixture with light petroleum (75 ml.) and benzene (25 ml.). This material (22·8 g.; m. p. 64—76°) was extracted with boiling light petroleum (4 × 100 ml.; b. p. 60—80°), and the extracts were cooled to give needles (5·27 g.), m. p. 92—96°. Repeated crystallisation from benzene–light petroleum and then from methanol gave the second *isomer* as flat needles, m. p. 103—104° depressed on admixture with the other form (Found: C, 56·8; H, 5·7; S, 30·5. $C_{10}H_{12}OS_2$ requires C, 56·6; H, 5·7; S, 30·2%). Neither product contained a free thiol group. 1,3-Dimercaptopropan-2-ol, prepared by the action of sodium and ethanol in liquid ammonia on pure crystalline 1,3-dibenzylthiopropan-2-ol,[15] gave the same two benzylidene derivatives.

1,3-Benzylidenedithio-2-methylpropan-2-ol (*5-Hydroxy-5-methyl-2-phenyl-1,3-dithian*).—1,3-Dimercapto-2-methylpropan-2-ol (0·94 g.) and benzaldehyde (0·8 ml.) in benzene (5 ml.) were treated with a drop of concentrated hydrochloric acid and set aside for 3 days. Evaporation *in vacuo*, followed by trituration with a little ether, yielded a solid (0·60 g.), m. p. 121—134°, which on repeated recrystallisation from benzene–light petroleum gave one geometrical isomer of the *dithian* as needles, m. p. 145—146° (Found: C, 58·2; H, 5·8; S, 28·1. $C_{11}H_{14}OS_2$ requires C, 58·4; H, 6·2; S, 28·3%). Material from a second crop, m. p. 112—115°, also afforded a satisfactory analysis (Found: C, 58·3; H, 6·1%) and presumably consisted of a mixture of the geometrical isomers. Repeated recrystallisation of this material changed the m. p. only slightly, but there was no depression on admixture with the specimen of m. p. 145—146°.

3,4-Dibenzylthiobutan-2-ol.—3,4-Dimercaptobutan-2-ol (2·78 g.) in liquid ammonia (150 ml.) was converted into the disodium derivative by means of sodium (0·93 g.). Benzyl chloride (5·1 g.) was added with stirring during 10 min. and, after the mixture had been stirred for a further 2 hr., the ammonia was allowed to evaporate. Water was added and the product was extracted into ether, washed, dried, and distilled (b. p. 155—163°/0·1 mm.; 3·26 g.). Redistillation gave *3,4-dibenzylthiobutan-2-ol*, b. p. 165—167°/0·1 mm., n_D^{20} 1·6042 (Found: C, 67·9; H, 7·1; S, 20·0. $C_{18}H_{22}OS_2$ requires C, 67·9; H, 7·0; S, 20·1%). The *α-naphthylurethane*, prepared in toluene (8 hours' refluxing), crystallised from light petroleum in needles, m. p. 84—85° (Found: C, 71·5; H, 5·9; S, 13·1. $C_{29}H_{29}O_2NS_2$ requires C, 71·4; H, 6·0; S, 13·1%).

Preparation of Hydroxy-thiols via *S-Benzyl Derivatives*.—(a) *1,3-Dimercapto-2-methylpropan-2-ol*. A solution prepared from ethanol (400 ml.) and sodium (11·5 g.) was treated with toluene-ω-thiol (59 ml.) and cooled to 0°, then 2,3-dibromo-2-methylpropan-1-ol (58 g.) was added with stirring during 20 min. After the mixture had been kept at room temperature overnight, sodium bromide was removed and the filtrate evaporated *in vacuo* to an oil, which was dissolved in ether, washed, and dried. The crude *1,3-dibenzylthio-compound* which remained after removal of the ether was suitable for reduction to the dithiol, but a distilled specimen had b. p. 172—174°/0·1 mm., n_D^{15} 1·6047 (Found: C, 68·2; H, 7·0. $C_{18}H_{22}OS_2$ requires C, 67·9; H, 7·0%). The crude dibenzyl compound in dry ether (150 ml.) containing ethanol (20 ml.) was stirred with liquid ammonia (800 ml.), and sodium (23 g.) was added portionwise until a permanent blue colour resulted. The colour was discharged with ammonium chloride and the ammonia allowed to evaporate, then the strongly cooled residue was treated with water and the layers were separated. The aqueous phase was extracted with ether and the combined organic layers were washed twice with sodium hydroxide solution, the washings being added to

the original aqueous solution. The ether solution was then discarded: it contained bibenzyl which, unless removed in this way, contaminated the final product and could not be separated from it by distillation. Finally the aqueous solution was cooled strongly and acidified with hydrochloric acid to liberate the dithiol, which was extracted into ether. Distillation of the washed and dried extracts gave the dithiol (17·6 g., 51% from the dibromide) as a yellow liquid, b. p. 49—59°/0·15 mm. A redistilled specimen had b. p. 50—52°/0·1 mm., n_D^{23} 1·5584 (Found: C, 35·0; H, 7·1; S, 46·7. Calc. for $C_4H_{10}OS_2$: C, 34·7; H, 7·3; S, 46·4%).

Condensation of the dithiol with benzaldehyde as previously described gave the mixed isomers of the benzylidene derivatives, m. p. 117—133°. Repeated recrystallisation from benzene–light petroleum raised the m. p. to 145—146°, not depressed on admixture with the previous specimen.

The same dithiol, characterised as the benzylidene derivative, was prepared in 62% yield from 3-bromo-2-methylpropylene oxide *via* the dibenzyl compound, which was not isolated.

(b) 1,3- *and* 3,4-*Dimercaptobutan-2-ol.* 3,4-Dibromobutan-2-ol (23·2 g.) was allowed to react with the calculated quantity of the sodium derivative of toluene-ω-thiol in ethanol as described under (a), to give a yellow oil (22·1 g.), b. p. 173—183°/0·1 mm. A redistilled specimen had b. p. 172—174°/0·06 mm. (Found: C, 67·7; H, 6·9. Calc. for $C_{18}H_{22}OS_2$: C, 67·9; H, 7·0%). No crystalline product was isolated from the reaction of this mixture of 1,3- and 3,4-dibenzylthiobutan-2-ol with α-naphthyl isocyanate.

The distilled dibenzyl compound (9·5 g.) was reduced by sodium and ethanol in liquid ammonia as above to a mixture of 1,3- and 3,4-dimercaptobutan-2-ol (4·18 g.), b. p. 48—52°/0·1 mm. Two further distillations gave a colourless product, b. p. 53—54°/0·1 mm. (Found: C, 34·6; H, 7·6. Calc. for $C_4H_{10}OS_2$: C, 34·7; H, 7·3%). Comparison of the colours which this sample and authentic 3,4-dimercaptobutan-2-ol gave with the manganous acetate reagent [13] indicated that the present mixture probably contained not more than 15% of the vicinal dithiol.

(c) 1,4-*Dimercaptobutan-2-ol.* 1,4-Dibromobutan-2-ol (12·7 g.) was allowed to react in the usual way with the sodium derivative of toluene-ω-thiol to give a liquid (11·9 g.), b. p. 175—195°/0·03 mm. Redistilled 1,4-*dibenzylthiobutan-2-ol* had b. p. 195—197°/0·05 mm., n_D^{22} 1·6030 (Found: C, 68·0; H, 6·9; S, 20·3. $C_{18}H_{22}OS_2$ requires C, 67·9; H, 7·0; S, 20·1%). The *α-naphthylurethane* crystallised from benzene–light petroleum in needles, m. p. 83—84° (Found: C, 71·6; H, 6·1; S, 12·9 $C_{29}H_{29}O_2NS_2$ requires C, 71·4; H, 6·0; S, 13·1%).

The reaction was repeated with 69·6 g. of 1,4-dibromobutan-2-ol but, instead of distilling the 1,4-dibenzylthiobutan-2-ol, the crude intermediate was dissolved in dry ether (150 ml.) containing ethanol (15 ml.) and reduced with sodium (26·1 g.) in liquid ammonia. The product (25·0 g.), b. p. 67—71°/0·05 mm., was redistilled to give 1,4-*dimercaptobutan-2-ol*, b. p. 68—69°/0·02 mm., n_D^{20} 1·5580 (Found: C, 34·8; H, 7·1; S, 46·5. $C_4H_{10}OS_2$ requires C, 34·7; H, 7·3; S, 46·4%).

(d) 1,6-*Dimercaptohexan-2-ol.* A solution of 1,6-dichlorohexan-2-ol (61 g.) in ethanol (150 ml.) was added to a solution of the sodium derivative of toluene-ω-thiol prepared from ethanol (325 ml.), sodium (16·4 g.) and toluene-ω-thiol (84 ml.), and the mixture was refluxed for 5 hr., cooled, and filtered. Evaporation of the filtrate *in vacuo* left crude 1,6-*dibenzylthiohexan-2-ol* (127 g.) which solidified. A specimen, recrystallised with some difficulty from butan-1-ol–light petroleum, had m. p. 30—35° (Found: C, 69·1; H, 7·6; S, 18·2. $C_{20}H_{26}OS_2$ requires C, 69·3; H, 7·6; S, 18·5%).

The crude dibenzyl compound (127 g.) in dry ether (200 ml.) containing ethanol (25 ml.) was reduced with sodium (32·8 g.) in liquid ammonia. The product (37·2 g.), b. p. 92—101°/0·3 mm., was redistilled to give 1,6-*dimercaptohexan-2-ol*, b. p. 97°/0·005 mm., n_D^{19} 1·5365 (Found: C, 43·2; H, 8·5; S, 38·0. $C_6H_{14}OS_2$ requires C, 43·3; H, 8·5; S, 38·6%).

(e) 1,3,4-*Trimercaptobutan-2-ol.* A solution of 1,3,4-trichlorobutan-2-ol [23] (16·8 g.) in ethanol (20 ml.) was added dropwise with stirring to a solution prepared from ethanol (60 ml.), sodium (6·9 g.), and toluene-ω-thiol (35 ml.), the mixture becoming warm. After 30 min. the reaction was completed under reflux (45 min.). The cooled mixture was filtered and the filtrate evaporated *in vacuo*. Water was added and the crude 1,3,4-tribenzylthiobutan-2-ol was extracted into ether, washed, and dried. The ether solution (100 ml.) was added to liquid ammonia (500 ml.) containing ethanol (15 ml.), reduced with sodium, and worked up in the usual way to give 1,3,4-*trimercaptobutan-2-ol* (10·1 g.), b. p. 96—100°/0·0005 mm., n_D^{22} 1·6131 (Found: C, 28·7; H, 6·0; S, 55·6. $C_4H_{10}OS_3$ requires C, 28·2; H, 5·9; S, 56·5%).

The trithiol (5 g.), acetic anhydride (25 ml.), and anhydrous sodium acetate (6 g.) were refluxed for 4 hr., cooled, and poured on to ice. The pale yellow solid was collected and crystallised from aqueous alcohol to give the *tetra-acetate* (9·9 g.), m. p. 76° (Found: C, 42·7; H, 5·5; S, 28·0. $C_{12}H_{18}O_5S_3$ requires C, 42·6; H, 5·4; S, 28·4%).

(f) *α-Hydroxy-β-mercapto-α-mercaptomethylpropionic acid.* Separate ethanolic solutions, one of β-chloro-α-chloromethyl-α-hydroxypropionic acid [27] (86·5 g.) and the other of sodium ethoxide (from 11·5 g. of sodium), were added simultaneously during 20 min. to a solution prepared from ethanol (400 ml.), sodium (23 g.), and toluene-ω-thiol (118 ml.). During the reaction much solid separated and very vigorous stirring was required. After 6 hours' stirring the mixture was set aside for 2 days and then acidified with concentrated hydrochloric acid, whereupon most of the solid redissolved. The bulk of the ethanol was removed *in vacuo* and the residue was diluted with water and extracted with ether. Evaporation of the dried extracts left *β-benzylthio-α-benzylthiomethyl-α-hydroxypropionic acid* (170 g., 98%) which crystallised from benzene in needles, m. p. 111—112° (Found: C, 61·8; H, 5·9; S, 18·4. $C_{18}H_{20}O_3S_2$ requires C, 62·0; H, 5·8; S, 18·4%). The *ethyl ester*, prepared by 4N-ethanolic hydrogen chloride, crystallised from methanol–water in needles, m. p. 38—40° (Found: C, 63·3; H, 6·3; S, 16·9. $C_{20}H_{24}O_3S_2$ requires C, 63·8; H, 6·4; S, 17·0%).

The preceding acid (48 g.) in liquid ammonia (550 ml.) was stirred and treated portionwise with sodium (12·8 g., 4 equivs.; this quantity of sodium was insufficient to produce a permanent blue colour, but when more was used, or when ethanol was included, the yield of dithiol was reduced). When the ammonia had evaporated, the residue was dissolved in water (cooling) and extracted with ether. After being washed with dilute sodium hydroxide, the ether solution was discarded. The combined aqueous solutions were acidified (pH 1) with hydrochloric acid, and the product was extracted into ether, washed, and dried. Removal of the ether left a crude oil (22·5 g.) which was best purified by crystallisation from xylene, although the need to reject much sparingly soluble gum made this tedious. (Similar difficulty has been reported [28] in purifying the hydrogenolysis product from β-benzylthio-α-benzylthiomethylpropionic acid.) The yield of moderately pure *α-hydroxy-acid*, m. p. 70—74°, was 9·07 g. (39%). Further crystallisation from benzene gave needles, m. p. 74—77° (Found: C, 28·9; H, 4·5; S, 37·6. $C_4H_8O_3S_2$ requires C, 28·6; H, 4·8; S, 38·1%). The acid was readily soluble in water and most organic solvents.

This acid (11·1 g.), acetic anhydride (55 ml.), and anhydrous sodium acetate (14 g.) were refluxed for 4 hr., then poured into water (250 ml.) and set aside over the week-end. The mixture was brought to pH 1 by hydrochloric acid and extracted with ether. The extracts were washed, dried, and evaporated to a red oil (13·7 g.) which crystallised. Recrystallisation from water gave colourless platelets of *triacetyl derivative*, m. p. 113—114° (Found: C, 40·9; H, 4·6; S, 21·3. $C_{10}H_{14}O_6S_2$ requires C, 40·8; H, 4·8; S, 21·8%). Treatment with diazomethane in ether gave the *methyl ester* quantitatively, m. p. 59—60° (from aqueous alcohol) (Found: C, 43·3; H, 5·3; S, 20·8. $C_{11}H_{16}O_6S_2$ requires C, 42·8; H, 5·2; S, 20·8%).

Ethyl αδ-Di(acetylthio)valerate.—A solution prepared from potassium hydroxide (44·6 g.) and thioacetic acid (60·5 g.) in methanol (150 ml.) was added with stirring and mild cooling during 30 mins. to ethyl αδ-dibromovalerate [29] (101 g.). The mixture was stirred for 2 hr., set aside for 2 days, and filtered. The filtrate was evaporated *in vacuo* and the residual oil dissolved in ether, washed with water, dried, and distilled. An amber liquid (62·7 g.), b. p. 137—143°/0·15 mm., was collected and redistilled to give pure *ethyl αδ-di(acetylthio)valerate*, b. p. 140—141°/0·4 mm., n_D^{21} 1·5091 (Found: C, 47·6; H, 6·5; S, 22·8. $C_{11}H_{18}O_4S_2$ requires C, 47·5; H, 6·5; S, 23·0%).

Methyl 2,11-*Di(acetylthio)undecanoate.*—Methyl 2,11-dibromoundecanoate (47 g.) was added dropwise to a stirred solution of thioacetic acid (30·4 g.) in dry pyridine (70 ml.). After being stirred overnight, the mixture was cooled in ice and an excess of 5N-hydrochloric acid was added. The oily product was extracted into ether, washed, dried, and distilled twice to give *methyl* 2,11-*di(acetylthio)undecanoate* (31·2 g.), b. p. 166—176°/0·02 mm., n_D^{21} 1·4986 (Found: S, 18·1. $C_{16}H_{28}O_4S_2$ requires S, 18·4%).

2,4-*Dimercaptobutan*-1-*ol.*—Lithium aluminium hydride (12 g.) in dry ether (450 ml.) was stirred under nitrogen whilst a solution of methyl αγ-di(acetylthio)butyrate [17] (36·6 g.) in ether

[27] Fourneau, *Bull. Soc. chim. France*, 1921, **29**, 413.
[28] Corse and Jansen, *J. Amer. Chem. Soc.*, 1955, **77**, 6632.
[29] Merchant, Wickert, and Marvel, *J. Amer. Chem. Soc.*, 1927, **49**, 1828.

(150 ml.) was added at such a rate as to maintain gentle refluxing. Then the mixture was stirred for 1 hr., treated with water (50 ml.), and poured into ice-cold 6% sulphuric acid (600 ml.). The layers were separated and the aqueous phase was thoroughly extracted with ether. The combined ether solutions were washed, dried, and distilled in the presence of a little ammonium acetate [26] to yield pale yellow *2,4-dimercaptobutan-1-ol* (15·2 g.), b. p. 75—79°/0·05 mm. (Found: C, 34·7; H, 7·1; S, 46·4. $C_4H_{10}OS_2$ requires C, 34·7; H, 7·3; S, 46·4%).

2,5-Dimercaptopentan-1-ol.—Ethyl αδ-di(acetylthio)valerate (24·6 g.) was reduced with lithium aluminium hydride (7·1 g.) as described for methyl αγ-di(acetylthio)butyrate to give *2,5-dimercaptopentan-1-ol* (10·8 g.), b. p. 83—94°/0·1 mm. A redistilled specimen had b. p. 93—95°/0·3 mm., n_D^{20} 1·5492 (Found: C, 39·7; H, 7·7; S, 41·6. $C_5H_{12}OS_2$ requires C, 39·5; H, 8·0; S, 42·1%).

2,11-Dimercaptoundecan-1-ol.—Reduction of methyl 2,11-di(acetylthio)undecanoate (45 g.) with lithium aluminium hydride gave *2,11-dimercaptoundecanol* (20·7 g.), b. p. 140°/0·005 mm., n_D^{21} 1·5096 (Found: C, 55·6; H, 10·5; S, 26·9. $C_{11}H_{24}OS_2$ requires C, 55·9; H, 10·2; S, 27·1%).

Reactions with Vicinal Dibromo-esters.—A mixture of ethyl αβ-dibromobutyrate (26 g.) and potassium thioacetate (34·2 g.) in dry ethanol (250 ml.) was refluxed with stirring for 6 hr., becoming red and finally almost black. Potassium bromide was removed, the filtrate evaporated *in vacuo*, and the residue treated with water. The mixture was extracted with ether (an insoluble tar being discarded), and the extracts were washed, dried, and distilled. The principal fractions were a mobile yellow liquid (2·5 g.), b. p. 56—61°/0·03 mm., and a red oil (6·0 g.), b. p. 97—120°/0·05 mm. Redistillation of the first fraction gave *ethyl β-(acetylthio)-butyrate*, b. p. 53°/0·05 mm., n_D^{19} 1·4730 (Found: C, 50·2; H, 7·8; S, 17·5. $C_8H_{14}O_3S$ requires C, 50·5; H, 7·4; S, 16·9%). The second fraction was not identified, but it was not the desired ethyl αβ-di(acetylthio)butyrate.

The reaction of methyl α-bromo-α-bromomethylpropionate (26 g.) with potassium thioacetate (34·2 g.) similarly gave, as only identifiable product, *methyl β-acetylthio-α-methylpropionate* (3·14 g.), b. p. 42—46°/0·2 mm., n_D^{17} 1·4758 (Found: C, 47·7; H, 7·1; S, 18·4. $C_7H_{12}O_2S$ requires C, 47·7; H, 6·9; S, 18·2%).

Ethyl αβ-dibromobutyrate (27·4 g.) was added during 15 min. to a stirred solution prepared from ethanol (400 ml.), sodium (4·6 g.), and toluene-ω-thiol (24·8 g.). Next morning sodium bromide was removed and the filtrate evaporated *in vacuo*. The residue was taken up in ether, washed, dried, and distilled to give an amber liquid (10·9 g.), b. p. 95—110°/0·1 mm., and a pink oil, b. p. 120—150°/0·1 mm. Redistillation of the first fraction gave *ethyl β-(benzylthio)-butyrate* as a yellow liquid, b. p. 99—102°/0·03 mm., n_D^{23} 1·5301 (Found: C, 65·4; H, 7·6; S, 13·7. $C_{13}H_{18}O_2S$ requires C, 65·5; H, 7·6; S, 13·5%). The second fraction afforded dibenzyl disulphide, identified by mixed m. p., when rubbed with methanol.

Methyl α-bromo-α-bromomethylpropionate (26 g., 0·1 mole) was added in 15 min. with stirring and water-cooling to the sodium derivative of toluene-ω-thiol (0·2 mole) in methanol (150 ml.), whereupon crystals rapidly separated. Next morning the solid was collected and washed with methanol and water, to leave dibenzyl disulphide (16·6 g.), m. p. and mixed m. p. 68—70°. The methanol filtrate was evaporated *in vacuo* and the residue dissolved in ether, washed, dried, and distilled to give a liquid (10·8 g.), b. p. 88—98°/0·01 mm. Redistillation gave pale yellow methyl β-benzylthio-α-methylpropionate, b. p. 81°/0·01 mm., n_D^{21} 1·5340 (Found: C, 64·0; H, 7·3; S, 14·4. Calc. for $C_{12}H_{16}O_2S$: C, 64·3; H, 7·3; S, 14·3%). Hurd and Gershbein [18] obtained this ester with b. p. 169·5°/13 mm., n_D^{20} 1·5323.

Methyl αβ-dibromopropionate (123 g., 0·5 mole) was added in 1 hr. with stirring and water-cooling to the sodium derivative of toluene-ω-thiol (1 mole) in methanol (500 ml.). Next morning the mixture was diluted with an equal volume of water to dissolve the sodium bromide which had separated, and concentrated under reduced pressure to remove methanol. The oil was extracted into ether, and the extracts were washed, dried, and distilled. The two main fractions were a pale yellow mobile liquid (47·0 g.), b. p. 98—108°/0·1 mm., and a light red oil (42·5 g.), b. p. 163—180°/0·2 mm. There was also a considerable quantity of material of intermediate b. p., which crystallised when rubbed with methanol, yielding dibenzyl disulphide (26·5 g.). Redistillation of the low-boiling fraction gave methyl β-(benzylthio)propionate, b. p. 98—102°/0·1 mm., n_D^{17} 1·5492 (Found: C, 62·8; H, 6·5; S, 15·5. Calc. for $C_{11}H_{14}O_2S$: C, 62·8; H, 6·7; S, 15·2%) (Hurd and Gershbein [18] give b. p. 173°/14 mm., n_D^{20} 1·5414). Redistillation of the high-boiling fraction gave *methyl αβ-di(benzylthio)propionate*, b. p.

166—169°/0·15 mm. (Found: C, 64·7; H, 5·8; S, 20·1. $C_{18}H_{20}O_2S_2$ requires C, 65·0; H, 6·1; S, 19·3%).

The structure of the methyl β-(benzylthio)propionate was established by acid hydrolysis [30] to β-(benzylthio)propionic acid which, after crystallisation from benzene–light petroleum and then from aqueous methanol, had m. p. and mixed m. p. 79—81°. Admixture with α-(benzylthio)-propionic acid [31] led to a large m. p. depression. Also, oxidation of the ester with hydrogen peroxide in acetic acid [18] gave methyl β-benzylsulphonylpropionate, m. p. and mixed m. p. 99—100°.

Ethyl β-Acetylthio-α-bromobutyrate.—Ethyl α-bromocrotonate (57·9 g.) and thioacetic acid (33·1 g.) were refluxed for 18 hr., then distilled under reduced pressure. After a considerable forerun, a yellow liquid (63·1 g.), b. p. 130—150°/17 mm., was collected. Redistillation gave *ethyl β-acetylthio-α-bromobutyrate*, b. p. 142—146°/14 mm. (Found: C, 35·7; H, 4·8; S, 11·9. $C_8H_{13}O_3SBr$ requires C, 35·7; H, 4·9; S, 11·9%).

Ethyl αβ-Di(acetylthio)butyrate.—Ethyl β-acetylthio-α-bromobutyrate (42·4 g.) was added during 1 hr. to a stirred solution of thioacetic acid (16 g.) in pyridine (80 ml.) at 0—5°. The solution was then stirred at room temperature for 21 hr. and next heated on the steam-bath for 90 min. It was then cooled strongly, acidified with 5N-hydrochloric acid, and extracted with ether. The extracts were washed, dried, and distilled to give a pale yellow liquid (35·2 g.), b. p. 102—116°/0·1 mm. Redistilled *ethyl αβ-diacetylthiobutyrate* had b. p. 108—110°/0·02 mm., n_D^{22} 1·5065 (Found: C, 45·2; H, 5·9; S, 24·0. $C_{10}H_{16}O_4S_2$ requires C, 45·4; H, 6·1; S, 24·3%).

2,3-Dimercaptobutan-1-ol.—Ethyl αβ-di(acetylthio)butyrate (19·6 g.) was reduced with lithium aluminium hydride (6·5 g.) as described for methyl αγ-di(acetylthio)butyrate to give *2,3-dimercaptobutan-1-ol* as a yellow liquid (5·05 g.), b. p. 69—76°/0·01 mm. After two further distillations the product was colourless and had b. p. 67—69°/0·01 mm., n_D^{18} 1·5540 (Found: C, 35·0; H, 7·6; S, 46·2. $C_4H_{10}OS_2$ requires C, 34·7; H, 7·3; S, 46·4%).

2,3-Dimercaptopropyl 3-Hydroxy-2-mercaptopropyl Sulphide.—3-Mercaptopropylene sulphide (5·3 g.) and 2,3-dimercaptopropan-1-ol (6·2 g.) were shaken for 16 hr. with 10% sodium hydroxide solution (2 ml.). The mixture, which contained a considerable quantity of polymer, was diluted with ether, washed with water, dried, and distilled. The main fractions were unchanged 2,3-dimercaptopropan-1-ol (3 g.) and the sulphide (3 g.), b. p. 141—145°/0·0003 mm. (lit.,[5] b. p. 150—160°/0·001 mm.) (Found: C, 31·8; H, 5·7; S, 56·0. Calc. for $C_6H_{14}OS_4$: C, 31·3; H, 6·1; S, 55·7%).

Reaction of Propylene Sulphide with Thiols.—In all experiments propylene sulphide (3·7 g., 0·05 mole) was added to a cooled solution of the thiol (0·05 mole) in ethanol (50 ml.) containing a little sodium ethoxide (from *ca.* 50 mg. of sodium). Next morning, water (1 ml.) was added, the mixture was saturated with carbon dioxide and filtered, and the filtrate evaporated *in vacuo*. Fractionation of the residual viscous oil gave the following products:

(a) 2-Mercaptoethanol gave *2-hydroxyethyl 2-mercaptopropyl sulphide* (3·8 g.), b. p. 74°/0·05 mm., n_D^{32} 1·5369 (Found: C, 38·5; H, 8·0; S, 41·6. $C_5H_{12}OS_2$ requires C, 39·4; H, 8·0; S, 42·1%).

(b) 3-Mercaptopropan-1-ol gave *3-hydroxypropyl 2-mercaptopropyl sulphide* (1·0 g.), b. p. 92—96°/0·15 mm., n_D^{24} 1·5324 (Found: C, 42·6; H, 8·2; S, 38·7. $C_6H_{14}OS_2$ requires C, 43·3; H, 8·5; S, 38·6%).

(c) 2,3-Dimercaptopropan-1-ol gave *3-hydroxy-2-mercaptopropyl 2-mercaptopropyl sulphide* (1·8 g.), b. p. 132—136°/0·005 mm., n_D^{20} 1·5783 (Found: C, 35·6; H, 6·8; S, 48·2. $C_6H_{14}OS_3$ requires C, 36·3; H, 7·1; S, 48·5%). Refluxing for 3 hr. with acetic anhydride and anhydrous potassium acetate gave the *triacetyl derivative*, b. p. 140—149°/0·00005 mm., n_D^{20} 1·5338 (Found: C, 44·8; H, 6·3; S, 29·0. $C_{12}H_{20}O_4S_3$ requires C, 44·4; H, 6·2; S, 29·6%).

(d) 1,3-Dimercaptopropan-2-ol gave *2-hydroxy-3-mercaptopropyl 2-mercaptopropyl sulphide* (1·2 g.), b. p. 115°/0·0005 mm., n_D^{26} 1·5604 (Found: C, 36·8; H, 7·2; S, 48·7. $C_6H_{14}OS_3$ requires C, 36·3; H, 7·1; S, 48·5%), and *1,3-di-(2-mercaptopropylthio)propan-2-ol* (1·2 g.), b. p. 172°/0·0002 mm., n_D^{26} 1·5726 (Found: S, 46·9. $C_9H_{20}OS_4$ requires S, 47·1%).

(e) 1,2-Dimercaptoethane gave *2-mercaptoethyl 2-mercaptopropyl sulphide* (2·8 g.), b. p. 70—75°/0·07 mm., n_D^{23} 1·5728 (Found: C, 36·1; H, 7·3; S, 58·1. $C_5H_{12}S_3$ requires C, 35·7; H, 7·2; S, 57·1%), and *1,2-di-(2-mercaptopropylthio)ethane* (2·5 g.), b. p. 90°/0·07 mm., n_D^{23} 1·5762 (Found: C, 39·3; H, 7·5. $C_8H_{18}S_4$ requires C, 39·6; H, 7·5%).

[30] Szabo and Stiller, *J. Amer. Chem. Soc.*, 1948, **70**, 3667.
[31] Owen and Sultanbawa, *J.*, 1949, 3109.

(f) 1,3-Dimercaptopropane gave 2-*mercaptopropyl* 3-*mercaptopropyl sulphide* (1·8 g.), b. p. 79°/0·05 mm., n_D^{23} 1·5600 (Found: S, 53·5. $C_6H_{14}S_3$ requires S, 52·7%), and 1,3-*di*-(2-*mercaptopropylthio*)*propane* (1·6 g.), b. p. 100°/0·0001 mm., n_D^{23} 1·5660 (Found: C, 41·6; H, 7·6. $C_9H_{20}S_4$ requires C, 42·1; H, 7·9%).

(g) 1,2,3-Trimercaptopropane gave 2,3-*dimercaptopropyl* 2-*mercaptopropyl sulphide* (3·1 g.), b. p. 99—102°/0·00003 mm., n_D^{20} 1·6018 (Found: C, 33·5; H, 6·6; S, 59·7. $C_6H_{14}S_4$ requires C, 33·6; H, 6·6; S, 59·8%), and 2-*mercapto*-1,3-*di*-(2-*mercaptopropylthio*)*propane* (1·4 g.), b. p. 142—146°/0·0001 mm., n_D^{22} 1·5991 (Found: C, 36·8; H, 6·8; S, 55·8. $C_9H_{20}S_5$ requires C, 37·4; H, 7·0; S, 55·5%).

2,3-*Dimercaptopropyl* 1-*Mercaptopropyl Sulphide.*—Interaction of 3-mercaptopropylene sulphide and 1,3-dimercaptopropane as in similar experiments with propylene sulphide gave a small yield of the *trimercapto-sulphide*, b. p. 124°/0·004 mm., n_D^{24} 1·6229 (Found: C, 34·3; H, 6·2; S, 60·0. $C_6H_{14}S_4$ requires C, 33·6; H, 6·6; S, 59·8%).

2-*Acetoxypropyl* 2,3-*Diacetylthiopropyl Sulphide.*—1,2,3-Trimercaptopropane (7 g.) was added to ethanol (40 ml.) in which a trace of sodium had been dissolved. Propylene oxide (2·9 g.) was added with cooling and the mixture was set aside for 24 hr., then concentrated *in vacuo*. The oily residue was refluxed with acetic anhydride (50 ml.) and anhydrous sodium acetate (6 g.) for 8 hr., cooled, and diluted with ether. Sodium acetate was removed with water, and the organic layer was dried and distilled, to give the *triacetyl derivative* (4·1 g.), b. p. 133—136°/0·00002 mm., n_D^{21} 1·5289 (Found: C, 44·5; H, 6·2. $C_{12}H_{20}O_4S_3$ requires C, 44·4; H, 6·2%).

2,3-*Benzylidenedithiopropyl* p-*Tolyl Sulphide.*—2,3-Benzylidenedithiopropyl chloride [7] (30 g.) in benzene (160 ml.) was added to a solution prepared from ethanol (200 ml.), sodium (3 g.), and thio-*p*-cresol (17 g.). The mixture was refluxed with stirring for 6 hr., cooled, and filtered. The filtrate was concentrated under reduced pressure to about 120 ml. whereupon a bulky precipitate separated. The cooled mixture was filtered and the crude tacky solid was crystallised from alcohol (charcoal) to yield moderately pure 2,3-*benzylidenedithiopropyl* p-*tolyl sulphide* (24·6 g.), m. p. 60—63°. Recrystallisation gave needles, m. p. 68—70° (Found: C, 64·2; H, 6·1. $C_{17}H_{18}S_3$ requires C, 64·2; H, 5·7%).

2,3-*Dimercaptopropyl* p-*Tolyl Sulphide.*—The preceding benzylidene derivative (14 g.) was suspended in ethanol (160 ml.) and stirred at 60—65° whilst silver nitrate (17 g.) in water (80 ml.) was added during 30 min. The mixture was stirred at the same temperature for 3 hr. more, then cooled and filtered. The silver derivative was washed successively with alcohol, boiling water, alcohol, and ether, a yellow powder (23 g.) remaining. This was suspended in methanol (150 ml.) and stirred vigorously whilst hydrogen sulphide was passed in for 3 hr. Silver sulphide was removed and the pale yellow filtrate and methanol washings were evaporated *in vacuo* under nitrogen. The residual oil was dissolved in ether, washed with sodium hydrogen carbonate solution and then with water, and dried. The solvent was removed and the product distilled to give 2,3-*dimercaptopropyl* p-*tolyl sulphide* as a pale yellow liquid (3·48 g.), b. p. 120—124°/0·1 mm., n_D^{18} 1·6217 (Found: C, 52·5; H, 6·4. $C_{10}H_{14}S_3$ requires C, 52·1; H, 6·1%).

We thank Mr. J. B. Blackman and Mr. B. Hatt for experimental assistance.

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[*Received, November 24th,* 1959.]