432. *Dithiols. Part XIX.* Further Studies on the Deacetylation of Acetylated Dithiols.*

By Peter S. Fitt and L. N. Owen.

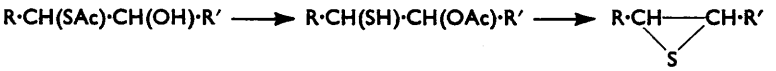
4 : 5-Dimercaptopentanol and its triacetyl, di-*S*-acetyl, and *O*-acetyl derivatives have been synthesised; alkaline hydrolysis of these acetates, unlike that of the 3 : 4-dimercaptobutanol derivatives, proceeds without cyclisation, though there is evidence of acetyl migration in the bisthiolacetate. Attempts to prepare 3 : 4-bisacetylthiopentyl acetate, by addition of thiolacetic acid to pent-3-yn-1-yl acetate, gave only the mono-adduct, 3-acetylthiopent-3-en-1-yl acetate, the light absorption of which is anomalous.

Toluene-*p*-sulphonyl derivatives of mono-*O*-*iso*propylidenepentaerythritol show very low reactivity in substitution reactions, probably because of the *neo*pentyl type of structure.

The two stereoisomeric forms of 2 : 3-dimercaptobutane-1 : 4-diol, and several derivatives, have now been synthesised; alkaline deacetylation of the acetyl derivatives is accompanied by cyclisation.

Unlike 2 : 3-bisacetylthiopropyl acetate, which on mild alkaline hydrolysis readily gives 3-acetylthiopropylene sulphide, 2-acetoxy-1 : 3-bisacetylthiopropane undergoes little or no cyclisation. The absence of cyclisation in the alkaline hydrolysis of a series of $\alpha\omega$-bisthiolacetates shows that there is no tendency for alkyl–sulphur fission in the thiolacetate group.

Previous investigations [1,2] have revealed that alkaline hydrolysis of certain acetylated vicinal hydroxy-thiols gives the episulphide in addition to the free hydroxy-thiol, and that similar results are obtained with the partly acetylated derivatives. The *S*-acetyl compound also underwent preliminary isomerisation into the *O*-acetate, the latter being the actual precursor of the episulphide :



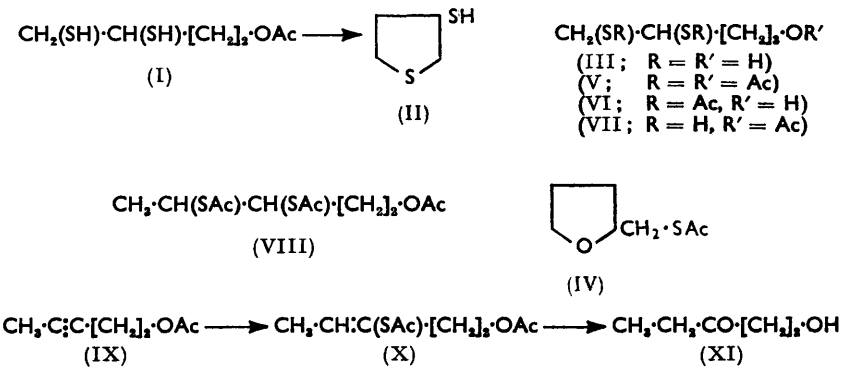
Similar treatment of the mono- or the di-acetyl derivatives of 3-mercaptopropanol, 3-mercaptobutanol, and 4-mercaptobutanol showed [3] that in these non-vicinal structures cyclisation to four- or five-membered ring sulphides did not occur; acetyl migration was observed, however, with the *S*-acetyl derivative of 3-mercaptopropanol and of 3-mercaptobutanol, but not with that of 4-mercaptobutanol, which indicated that a six-membered ortho-acetate ring intermediate represented the limiting size for this isomerisation. The absence of cyclisation was interesting in view of the fact that alkaline hydrolysis of the fully or partly acetylated derivatives of 3 : 4-dimercaptobutanol [*e.g.*, (I)] had been shown [1,2] to give 3-mercaptothiophan (II), and it was therefore clear that cyclisation in the latter instance was facilitated by the presence of the additional thiol group. Two possible reasons were suggested, one involving direct activation of one thiol group by its neighbour, and the other the formation of a chelate ring. If the first suggestion were correct, the acetyl derivatives (or at least the *O*-acetate) of 4 : 5-dimercaptopentanol (III) should also be capable of undergoing cyclisation to give either 2-mercaptomethylthiophan or tetrahydro-3-mercaptothiopyran, and the synthesis of the pentanol (III) was therefore investigated.

Reaction of 4 : 5-dibromopentanol with potassium thiolacetate failed to give any pure 4 : 5-bisthiolacetate, the main identifiable product being tetrahydrofurfuryl thiolacetate

* Part XVIII, Johary and Owen, *J.*, 1955, 1307.

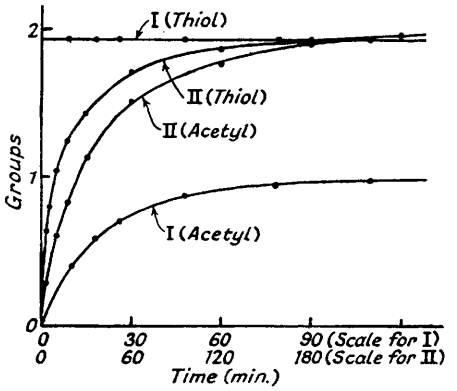
[1] Miles and Owen, *J.*, 1952, 817.
[2] Harding and Owen, *J.*, 1954, 1528.
[3] *Idem, ibid.*, p. 1536.

(IV), evidently formed by intramolecular elimination of hydrogen bromide from the secondary position. To obviate this difficulty, 4 : 5-dibromopentyl acetate was used instead of the dibromo-alcohol, and 4 : 5-bisacetylthiopentyl acetate (V) was obtained in good yield. Quantitative alkaline hydrolysis of this showed that no cyclisation occurred,



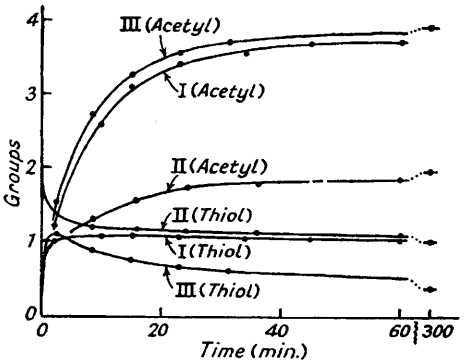
the final thiol value corresponding to that for completely normal hydrolysis, but this result was not conclusive because it was conceivable that the *O*-acetyl group was undergoing preferential hydrolysis to give the di-*S*-acetyl compound (VI); since cyclisation involves attack by a free thiol group (as anion) on the *O*-acetate, this clearly could not take place unless preceded by acyl migration, which, from analogy with the behaviour of

FIG. 1. *Derivatives of* 4 : 5-*Dimercaptopentanol.*



I : $CH_2(SH)\cdot CH(SH)\cdot [CH_2]_3\cdot OAc$.
II : $CH_2(SAc)\cdot CH(SAc)\cdot [CH_2]_3\cdot OH$.

FIG. 2. *Derivatives of* 2 : 3-*Dimercaptobutane*-1 : 4-*diol.*

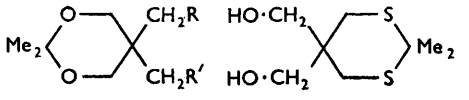


I : $CH_2(OAc)\cdot CH(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, m. p. 118—119°.
II : $CH_2(OAc)\cdot CH(SH)\cdot CH(SH)\cdot CH_2\cdot OAc$, m. p. 58—59°
III : $CH_2(OAc)\cdot CH(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, m. p. 72—73°.

4-acetylthiobutanol, was thought to be unlikely. The triacetyl compound was therefore hydrolysed to 4 : 5-dimercaptopentanol, from which the *O*-acetyl (VII) and the di-*S*-acetyl derivative (VI) were prepared by selective acetylation under acidic and basic conditions, respectively. Quantitative alkaline hydrolysis of the *O*-acetate proceeded without indication of cyclisation (see Fig. 1), thus providing conclusive evidence that it does not occur in the system under investigation; this seems to dispose of the possibility of increased nucleophilic activity of one thiol group due to the presence of a neighbouring one, but

does not, of course, prove that cyclisation in the 3 : 4-dimercaptobutanol derivatives is necessarily due to chelation. An unexpected observation, however, was the occurrence of acetyl migration on alkaline treatment of the di-*S*-acetyl derivative (VI), the liberation of thiol groups in the early stages of the hydrolysis (Fig. 1) being more rapid than the removal of acetyl groups; the additional thiol group must in some way assist the formation of the intermediate cyclic orthoacetate, which in this instance would contain a seven- or eight-membered ring.

3 : 4-Bisacetylthiopentyl acetate (VIII) would be of interest for cyclisation studies as a compound analogous to the triacetyl derivative of 3 : 4-dimercaptobutanol, but with both groups secondary. It is unlikely that the required compound could be prepared from 3 : 4-dibromopentyl acetate, because attempts to replace a vicinal pair of secondary bromine atoms by mercapto- or acetylthio-groups have usually resulted only in debromination, and formation of the corresponding olefin.[4, 5] We therefore attempted to synthesise it by the addition of thiolacetic acid to pent-3-yn-1-yl acetate (IX), following the procedure which had been successful [6] with alk-1-ynes and also [7] with acetylenedicarboxylic acid. Pent-3-yn-1-ol has previously been prepared [8] in several stages from tetrahydrofuran, but the recently improved preparation [9] of propyne rendered feasible

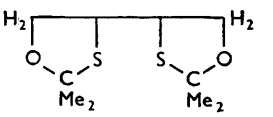


(XVIII)

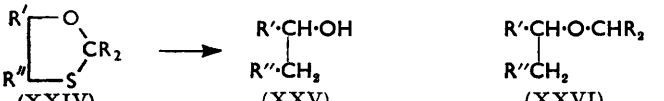
(XII; R = SAc, R′ = OAc)
(XIII; R = OTs, R′ = OTs)
(XIV; R = SAc, R′ = OTs)
(XV; R = SAc, R′ = SAc)
(XVI; R = OTs, R′ = OH)
(XVII; R = OTs, R′ = OAc)

$MeO_2C{\cdot}CH(SAc){\cdot}CH(SAc){\cdot}CO_2Me$
(XIX)

$CH_2(OR'){\cdot}CH(SR){\cdot}CH(SR){\cdot}CH_2{\cdot}OR'$
(XX; R = R′ = H)
(XXI; R = R′ = Ac)
(XXII; R = H; R′ = Ac)



(XXIII)



(XXIV) (XXV) (XXVI)

the direct formation of the acetylenic alcohol by interaction of propyne (made *in situ*) with ethylene oxide in liquid ammonia. Acetylation of the product gave the required acetate (IX) which was then heated for several hours at 100° with an excess of thiolacetic acid in the presence of ascaridole. The product was almost entirely a mono-adduct, for which two structures are possible depending on the direction of addition. On treatment with 2 : 4-dinitrophenylhydrazine in ethanolic sulphuric acid it gave an essentially homogeneous 2 : 4-dinitrophenylhydrazone of a hydroxypentanone. This was shown by direct comparison not to be that of 5-hydroxypentan-2-one, and must therefore be the derivative of 1-hydroxypentan-3-one (XI), derived from 3-acetylthiopent-3-en-1-yl acetate (X). Prolongation of the reaction, or re-treatment of the mono-adduct, failed to yield any appreciable amount of di-adduct. The ultraviolet light absorption of the mono-adduct (max. 2260 Å, ε 4250) is anomalous, in that it corresponds quite closely to that of a saturated monothiolacetate; all the compounds reported by Bader *et al.*,[6] containing the

[4] Rosenheim and Stadler, *Ber.*, 1905, **38**, 2687.
[5] Evans, Fraser, and Owen, *J.*, 1949, 248.
[6] Bader, Cross, Heilbron, and Jones, *J.*, 1949, 619; Bader, *J.*, 1956, 116.
[7] Owen and Sultanbawa, *J.*, 1949, 3109.
[8] Crombie and Harper, *J.*, 1950, 873.
[9] Allan, Jones, and Whiting, *J.*, 1955, 1862.

chromophore ·CH:CH·SAc, showed maxima at *ca.* 2510 Å (ε *ca.* 8000), and it is surprising that increased substitution on the ethylenic carbon atom should nullify the conjugative effect of the double bond.

Although the acetyl derivatives of 3-mercaptopropanol do not cyclise on alkaline hydrolysis, such a reaction might occur more readily in a ββ-disubstituted system, and attempts were therefore made to synthesise the derivative (XII) of thiopentaerythritol. Bladon and Owen [10] found that the ditoluene-*p*-sulphonate (XIII) of *O-iso*propylidenepentaerythritol reacted with potassium thiolacetate to give the thiolacetate toluene-*p*-sulphonate (XIV), which on prolonged further treatment gave the bisthiolacetate (XV). Two routes therefore appeared to be available: (i) replacement of the toluene-*p*-sulphonyloxy-group in the derivative (XIV) by acetoxy; and (ii) replacement of one group in the diester (XIII) by acetoxy, followed by replacement of the other by acetylthio. All attempts to introduce the acetoxy-group, however, using potassium acetate, sodium acetate, or silver acetate with the esters (XIII) or (XIV), were unsuccessful, as were experiments in which the dimethanesulphonate was used instead of the ditoluene-*p*-sulphonate; the starting materials were largely recovered. This remarkable lack of reactivity in a primary toluene-*p*-sulphonate must be attributed to the *neo*pentyl type of structure,[11] and the fact that replacement does occur (though only slowly) when the entering group is acetylthio is evidently a reflection of the much greater nucleophilic reactivity shown by the acetylthio than by the acetoxy-ion. A third route was then investigated: partial esterification of mono-*O-iso*propylidenepentaerythritol with toluene-*p*-sulphonyl chloride gave a crystalline monotoluene-*p*-sulphonate (XVI), acetylation of which furnished the acetate toluene-*p*-sulphonate (XVII); although this compound slowly reacted with potassium thiolacetate, no pure product could be isolated. The possibility of effecting replacement of a toluene-*p*-sulphonyloxy-group by solvolysis was considered, but in a trial experiment the ditoluene-*p*-sulphonate (XIII) was unchanged after 12 hours' treatment with boiling thiolacetic acid.

In the course of the above investigations, we re-examined the hydrolysis of di-*S*-acetyl-*O-iso*propylidenedithiopentaerythritol (XV) under both acid and alkaline conditions. Acid hydrolysis was accompanied by migration of the *iso*propylidene group and gave *S-iso*propylidenedithiopentaerythritol (XVIII), in agreement with the earlier work; [10] none of this material could be detected, however, in the product obtained under alkaline conditions, and it seems probable that in the original experiment, in which migration was claimed to occur, the product was allowed to become acid at some stage in the working-up process.

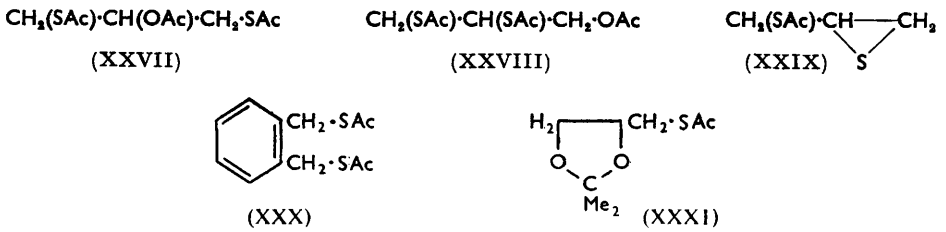
For reasons mentioned above, aliphatic vicinal disecondary thiols are not readily accessible, and an earlier attempt [5] to prepare the tetra-acetyl derivative of 2 : 3-dimercaptobutane-1 : 4-diol, by reaction of *meso*-1 : 4-diacetoxy-2 : 3-dibromobutane with potassium thiolacetate, gave only 1 : 4-diacetoxybut-2-ene. The required product would be readily accessible if it were possible to add two mols. of thiolacetic acid to 1 : 4-diacetoxybut-2-yne, but although some reaction occurred no pure material could be isolated. Owen and Sultanbawa,[7] however, condensed methyl acetylenedicarboxylate with an excess of thiolacetic acid and obtained two stereoisomeric forms of methyl αα′-bisacetylthiosuccinate (XIX). By reduction of each of these with lithium aluminium hydride we have now obtained the corresponding forms of 2 : 3-dimercaptobutane-1 : 4-diol (XX). The higher-melting ester gave an oil which could not be distilled without decomposition, but which furnished a crystalline tetra-acetyl derivative (XXI) whilst partial acetylation under acid conditions gave 1 : 4-diacetoxy-2 : 3-dimercaptobutane (XXII). Condensation of the oil with acetone gave a di*iso*propylidene derivative for which the most likely structure is (XXIII); on desulphurisation with Raney nickel it gave butane-1 : 4-diol, in agreement with the reports [12] that hemithioketals (XXIV) usually yield the free alcohol (XXV)

[10] Bladon and Owen, *J.*, 1950, 585.
[11] Dostrovsky, Hughes, and Ingold, *J.*, 1946, 187.

rather than the expected ether (XXVI). Reduction of the lower-melting bisacetylthiosuccinate with lithium aluminium hydride showed that this ester was not stereochemically pure, since it gave a partly crystalline product the liquid portion of which gave a tetra-acetyl and a di*iso*propylidene derivative identical with those described above; the major part was the solid stereoisomeric dihydroxy-dithiol, which gave a tetra-acetyl derivative and a di*iso*propylidene derivative. Quantitative alkaline hydrolysis of the various acetyl derivatives showed that they cyclised readily, the tetra-acetyl derivative and the di-*O*-acetate of the liquid dihydroxy-dithiol to the extent of about 50%, and the tetra-acetyl derivative of the solid isomer to the extent of about 75% (see Fig. 2).

The favourable effect on cyclisation of the presence of a vicinal dithiol grouping is again evident in both the above stereoisomers, as it is in 2 : 3-dimercaptopropanol,[2] since the acetyl derivatives of 2-mercaptoethanol cyclise only to the extent of about 30%. It was thus of interest to examine the behaviour of 2-acetoxy-1 : 3-bisacetylthiopropane (XXVII) in comparison with 2 : 3-bisacetylthiopropyl acetate (XXVIII), since although the former contains no vicinal dithiol system the acetoxy-group is liable to attack from both sides. Surprisingly, quantitative alkaline hydrolysis proceeded normally, without any appreciable cyclisation. Even on treatment with boiling aqueous sodium carbonate it gave only a very small amount of 3-acetylthiopropylene sulphide (XXIX), which with this reagent is obtained [1] in good yield from the 2 : 3-isomer. The lack of reactivity is remarkable, as some cyclisation would be expected from analogy with the behaviour of 2-acetylthioethyl acetate.

The cyclisation which occurs in the hydrolysis of acetylated hydroxy-thiols involves displacement of the acetoxy-group (alkyl–oxygen fission) by a thiol anion.[2] If the oxygen functions are present as methyl ethers, instead of acetates, alkaline hydrolysis proceeds normally. Thus no difficulty was experienced [13] in the isolation of polymethoxy-dithiols by alkaline hydrolysis of their di-*S*-acetyl derivatives. These observations indicate



(XXVII) (XXVIII) (XXIX) (XXX) (XXXI)

that there is no tendency for cyclisation to occur by displacement of an acetylthio-group (alkyl–sulphur fission) by a thiol anion, but in order to obtain more definite evidence on this point the αω-bisthiolacetates AcS·[CH_2]$_n$·SAc (n = 2—5) and *o*-di(acetylthiomethyl)-benzene (XXX) have now been prepared from the corresponding dibromides, and subjected to quantitative alkaline hydrolysis. All of them behaved normally, the attainment of the full thiol values on completion of the hydrolysis indicating the absence of any cyclisation.

It was incidentally observed that the acetyl groups in (XV) were unusually susceptible to acid hydrolysis, free thiol being steadily produced in N-aqueous hydrochloric acid, containing 25% dioxan, at room temperature (continuous uptake of iodine, with no stable end-point); under these conditions all the other thiolacetates studied have been relatively stable. For comparison, the *iso*propylidene derivative (XXXI) of 3-acetylthiopropane-1 : 2-diol was prepared by interaction of *O*-*iso*propylideneglycerol toluene-*p*-sulphonate with potassium thiolacetate; this also showed similar acid lability.

[12] Romo, Rozenkranz, and Djerassi, *J. Amer. Chem. Soc.*, 1951, **73**, 4961; Djerassi, Gorman, and Henry, *ibid.*, 1955, **77**, 4647.
[13] Miles and Owen, *J.*, 1950, 2934.

Experimental

Reaction of 4 : 5-*Dibromopentanol with Potassium Thiolacetate.*—Crude 4 : 5-dibromopentanol [14] (31 g.), potassium thiolacetate (31 g.), and ethanol (250 c.c.) were stirred and heated under reflux for 6 hr. under nitrogen. The solution was filtered, concentrated under reduced pressure, and diluted with water. The oil which separated was isolated by extraction with ether and distilled to give (i) 4·9 g., b. p. 70—75°/0·5 mm., and (ii) 16·2 g., b. p. 150—165°/8 × 10^{-3} mm. Extensive decomposition took place during the distillation. The higher-boiling product was redistilled, but no pure 4 : 5-bisacetylthiopentanol could be obtained. The lower-boiling material was redistilled to give tetrahydrofurfuryl thiolacetate (4·6 g.), b. p. 54—59°/0·3 mm., n_D^{22} 1·494—1·497. Chapman and Owen [15] give b. p. 107°/16 mm., n_D^{20} 1·4941.

A solution of this thiolacetate (4·4 g.) in methanol (25 c.c.) containing concentrated hydrochloric acid (2·5 c.c.) was boiled under reflux for 5 hr. Water was added and the mixture was extracted with ether to give tetrahydro-2-mercaptomethylfuran (3·0 g.), b. p. 76°/50 mm., n_D^{24} 1·4882, characterised as the phenylurethane, m. p. and mixed m. p. 98—99°. Chapman and Owen [15] obtained only a small yield by acid hydrolysis, possibly owing to losses in working-up, as the thiol co-distils with methanol.

4 : 5-*Dibromopentyl Acetate.*—A solution of pent-4-en-1-ol [16] (30 g.) in acetic anhydride (48 g.) was heated on a steam-bath for 16 hr., then cooled and poured into water. The oil which separated was isolated by extraction with ether and distilled to give the acetate (32 g.), b. p. 149—154°. Paul,[17] who used a zinc chloride catalyst, gives b. p. 150—151°. Reaction in the usual way with the calculated amount of bromine in carbon tetrachloride gave 4 : 5-dibromopentyl acetate, b. p. 92—93°/0·2 mm., n_D^{18} 1·507. Paul [17] gives b. p. 156—157°/23 mm.

4 : 5-*Bisacetylthiopentyl Acetate.*—4 : 5-Dibromopentyl acetate (25 g.), potassium thiolacetate (25 g.), thiolacetic acid (0·1 c.c.), and ethanol (250 c.c.) were stirred and heated under reflux in an atmosphere of nitrogen for 10 hr. The cooled mixture was filtered, and concentrated under reduced pressure. Water was added, and the insoluble oil was isolated by extraction with chloroform and distilled to give 4 : 5-*bisacetylthiopentyl acetate* (18·6 g.), b. p. 116°/4 × 10^{-4} mm., n_D^{18} 1·5140 (Found: C, 47·3; H, 6·6; S, 23·2. $C_{11}H_{18}O_4S_2$ requires C, 47·5; H, 6·5; S, 23·0%).

4 : 5-*Dimercaptopentanol.*—4 : 5-Bisacetylthiopentyl acetate (14·5 g.) was dissolved in methanol (95 c.c.) containing concentrated hydrochloric acid (10 c.c.), and the solution was refluxed for 3 hr. under nitrogen, then set aside overnight at room temperature, and concentrated under reduced pressure. Water was added to the residue, and the mixture was extracted with ether. The ether extracts were washed with water, dried (Na_2SO_4), and concentrated to an oil, which on distillation gave 4 : 5-*dimercaptopentanol* (4·3 g.), b. p. 102—103°/0·5 mm., n_D^{19} 1·5491 (Found: C, 39·1; H, 8·0; S, 41·6; thiol-S, 40·2. $C_5H_{12}OS_2$ requires C, 39·4; H, 7·9; S, 42·1%). There was a large viscous undistilled residue.

4 : 5-*Dimercaptopentyl Acetate.*—4 : 5-Dimercaptopentanol (0·9 g.), acetic anhydride (0·65 g.), and 10% sulphuric acid in acetic acid (0·1 c.c.) were mixed at 0° and kept at 0° for 1 hr. and at room temperature for 4 days. Water (10 c.c.) was added, and the oil which separated was isolated with ether and distilled to give 4 : 5-*dimercaptopentyl acetate* (0·7 g.), b. p. 100—101°/0·1 mm., n_D^{20} 1·5109 (Found: C, 43·1; H, 7·1; S, 32·5; thiol-S, 30·5. $C_7H_{14}O_2S_2$ requires C, 43·3; H, 7·3; S, 33·0%).

4 : 5-*Bisacetylthiopentanol.*—4 : 5-Dimercaptopentanol (3·04 g.) was dissolved in water (14 c.c.) containing sodium hydroxide (1·83 g.). Acetic anhydride (4·10 g.) was added to the solution at 0°, and the mixture was stirred at 0° for 15 min. The mixture was extracted with ether, the dried (Na_2SO_4) extract was evaporated under reduced pressure, and the residue distilled to give 4 - 5-*bisacetylthiopentanol* (3·09 g.), b. p. 150—154°/0·01 mm., n_D^{20} 1·5299 (Found: C, 45·8; H, 6·7; S, 26·8; thiol-S, 0·05. $C_9H_{16}O_3S_2$ requires C, 45·7; H, 6·8; S, 27·1%). Light absorption in ethanol: max. 2320 Å, ε 7800.

Pent-3-yn-1-ol.—A solution of sodamide in liquid ammonia (*ca.* 750 c.c.), prepared in the

[14] Paul, *Compt. rend.*, 1931, **192**, 1574.
[15] Chapman and Owen, *J.*, 1950, 579.
[16] *Org. Synth.*, Coll. Vol. III, 698.
[17] Paul, *Ann. Chim.*, 1932, **18**, 303.

usual way from sodium (75·5 g.), was stirred during the dropwise addition of 1 : 2-dichloropropane (114 g.), and for a further 3 hr. Ethylene oxide (50 g.) in dry ether (50 c.c.) was then added, and the stirring was continued overnight to assist the evaporation of ammonia. Dry ether was added to the residue followed by ammonium chloride (50 g.) and water. The ether layer was separated, and the aqueous layer was extracted several times with ether. The dried (Na_2SO_4) extracts were concentrated, and the residue was distilled to give pent-3-yn-1-ol (20 g.), b. p. 153—158°, n_D^{16} 1·4569. Crombie and Harper [8] give b. p. 154—157°, n_D^{20} 1·4554.

Pent-3-yn-1-yl Acetate.—Pent-3-yn-1-ol (10 g.), acetic anhydride (20 c.c.), and a few drops of pyridine were mixed, and the solution was heated on a steam-bath for 6 hr., then set aside overnight, and poured into water (100 c.c.). The mixture was occasionally stirred during 30 min., and the oily upper layer was then separated and washed twice with water. The combined aqueous layer and washings were extracted once with ether, and the ethereal extract was added to the oil. The ethereal solution was dried ($CaCl_2$) and distilled to give *pent-3-yn-1-yl acetate* (13·3 g.), b. p. 65—67°/15 mm., n_D^{18} 1·4391, n_D^{22} 1·4372 (Found : C, 66·25; H, 8·15%; ≡ by hydrogenation, 1·07. $C_7H_{10}O_2$ requires C, 66·6; H, 8·0%; ≡ 1·0).

Addition of Thiolacetic Acid to Pent-3-yn-1-yl Acetate.—Pent-3-yn-1-yl acetate (3·2 g.) and thiolacetic acid (6·5 g.) were mixed, 2 drops of ascaridole were added, and the mixture was heated on the steam-bath for 4 hr. Excess of thiolacetic acid and unchanged pentynyl acetate were removed under reduced pressure, and the residue was dissolved in ether. The ethereal solution was washed once with water, once with saturated aqueous sodium hydrogen carbonate solution, and twice with water; it was then dried ($CaSO_4$) and evaporated to an oil, which after two distillations gave 3-*acetylthiopent-3-en-1-yl acetate* (2·4 g.), b. p. 96°/0·1 mm., n_D^{20} 1·4905 (Found : C, 53·3; H, 7·0; S, 16·2. $C_9H_{14}O_3S$ requires C, 53·4; H, 7·0; S, 15·9%). Light absorption in ethanol : max. 2260 Å, ε 4250.

Reaction of 3-Acetylthiopent-3-en-1-yl Acetate with 2 : 4-Dinitrophenylhydrazine.—A solution of the mono-adduct (1·19 g.) in ethanol (10 c.c.) was added to 2 : 4-dinitrophenylhydrazine (2 g.) in sulphuric acid (2 c.c.) and ethanol (15 c.c.), and the mixture was set aside overnight at room temperature. Hydrogen sulphide and ethyl acetate were produced, and an orange solid was precipitated; this was collected and dried. Chromatography of small portions on alumina and on bentonite–kieselguhr showed that the compound was probably homogeneous. The bulk of it was chromatographed on alumina, benzene being used as solvent and eluant, and evaporation of the eluate under reduced pressure gave a solid, m. p. 158—160°, which on recrystallisation from chloroform–ethanol gave 1-*hydroxypentan-3-one* 2 : 4-*dinitrophenylhydrazone*, m. p. 186° (Found : C, 46·9; H, 4·8; N, 19·8. $C_{11}H_{14}O_5N_4$ requires C, 46·8; H, 5·0; N, 19·85%). 5-Hydroxypentan-2-one was prepared by Bennett and Phillips's method [18] and converted into its 2 : 4-dinitrophenylhydrazone, m. p. 150° (lit.,[19] 150°). The m. p. of a mixture with the above isomer was 140—142°.

O-iso*Propylidene*-O-*toluene*-p-*sulphonylpentaerythritol.*—To a solution of *O-iso*propylidenepentaerythritol [10] (17·6 g.) in dry pyridine (100 c.c.) at 0°, toluene-*p*-sulphonyl chloride (20·0 g.) in dry pyridine (100 c.c.) was added slowly with stirring during 5 hr. The solution was set aside at 0° overnight, and the bulk of the pyridine was then removed under reduced pressure. Chloroform was added to the residue, and the chloroform solution was washed with dilute acid, then dried ($MgSO_4$), and concentrated under reduced pressure. The semi-solid residue (30·6 g.) was dissolved in hot methanol and cooled to give O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol* (16 g.), m. p. 94° (from methanol) (Found : C, 54·2; H, 6·9; S, 9·6. $C_{15}H_{22}O_6S$ requires C, 54·5; H, 6·7; S, 9·7%). The mother liquors gave a second crop of crude product (2·1 g.).

O-*Acetyl*-O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol.*—The above monotoluene-*p*-sulphonate (20·5 g.) was dissolved in dry pyridine (50 c.c.), and acetic anhydride (35 c.c.) was added. The solution was heated on a steam-bath for 10 hr., then cooled and poured into a large volume of water. The precipitate was crystallised from methanol to give O-*acetyl*-O-iso*propylidene*-O-*toluene*-p-*sulphonylpentaerythritol* (16·5 g.), m. p. 69—70° (Found : C, 54·5; H, 6·5; S, 8·9. $C_{17}H_{24}O_7S$ requires C, 54·8; H, 6·5; S, 8·6%).

Attempted Replacements of Toluene-p-sulphonyloxy-groups in Derivatives of Pentaerythritol.—(i) *O-iso*Propylidenepentaerythritol ditoluene-*p*-sulphonate [10] (9·6 g.), silver acetate (3·6 g.), and acetic anhydride (100 c.c.) were boiled under reflux for 30 min. The cooled mixture was

[18] Bennett and Phillips, *J.*, 1928, 1937.
[19] Paul and Tchelitcheff, *Compt. rend.*, 1950, **230**, 1872.

filtered, then diluted with water, stirred for 1 hr., and extracted with chloroform. Concentration of the dried (Na_2SO_4) extracts gave unchanged material (8·3 g.), m. p. and mixed m. p. 152°.

(ii) The ditoluene-*p*-sulphonate (4·9 g.), fused sodium acetate (0·9 g.), and ethanol (50 c.c.) were stirred and boiled under reflux for 20 hr. Most of the ethanol was then removed under reduced pressure and the residue worked up with water and chloroform to give unchanged material (3·5 g.).

(iii) In an experiment as (ii), but with potassium acetate, refluxed for 52 hr., unchanged material (90%) was recovered. A similar result was obtained with the dimethanesulphonate (recovery, 93%).

(iv) A solution of the ditoluene-*p*-sulphonate (0·50 g.) in thiolacetic acid (1·5 c.c.) was boiled under reflux for 12 hr. Removal of the acid under reduced pressure gave a solid which was dissolved in chloroform and washed with aqueous sodium hydrogen carbonate. Removal of the solvent gave unchanged material (0·46 g.).

(v) The toluene-*p*-sulphonate [10] of *S*-acetyl-*O*-*iso*propylidenemonothiopentaerythritol (3·9 g.), fused potassium acetate (3 g.), and acetone (40 c.c.) were stirred and boiled under reflux for 30 hr. Working up as in (ii) gave unchanged material, m. p. and mixed m. p. 93°.

(vi) The toluene-*p*-sulphonate of *O*-acetyl-*O*-*iso*propylidenepentaerythritol (16·5 g.), potassium thiolacetate (8 g.), and acetone (250 c.c.) were stirred and boiled under reflux for 4 hr. The mixture was then cooled and filtered, and the salts were washed with acetone. Concentration of the filtrate and washings gave a semi-solid residue, which was dissolved in the minimum amount of hot methanol. The cooled solution deposited unchanged material (10 g.); evaporation of the mother liquors gave an oil which on distillation gave fractions (1·5 g.), b. p. 120—130° (bath)/3 × 10^{-4} mm., n_D^{20} 1·4810—1·4780, all of which contained free thiol (Found on a middle fraction: thiol-S, 4·8%).

Alkaline Hydrolysis of Di-S-*acetyl*-O-iso*propylidenepentaerythritol*.—The compound (2·0 g.) was treated exactly as previously described.[10] Distillation of the product gave partly crystalline material (1·06 g.), which on crystallisation from methanol furnished O-iso*propylidene*-4 : 4-*bishydroxymethyl*-1 : 2-*dithiolan* (the cyclic disulphide derived from *O-iso*propylidenedithiopentaerythritol) (0·1 g.), m. p. 59—60° (Found: C, 46·1; H, 6·6; S, 30·8. $C_8H_{14}O_2S_2$ requires C, 46·6; H, 6·8; S, 31·1%). Light absorption in ethanol: max. 3280 Å, ε 132; min. 2800 Å, ε 25. No other crystalline product could be isolated.

1 : 4-*Diacetoxybut*-2-*yne*.—But-2-yne-1 : 4-diol (60 g.) was added to acetic anhydride (180 g.) containing a few drops of pyridine. After the initial reaction had subsided, the mixture was heated on the steam-bath for 2 hr., then cooled and poured into an excess of saturated sodium hydrogen carbonate solution. Isolation of the product with ether gave the diacetate (61 g.), b. p. 138—140°/14 mm., n_D^{20} 1·4530, which solidified; recrystallisation from methanol gave thick needles, m. p. 25—27° (Found: C, 56·5; H, 6·0. Calc. for $C_8H_{10}O_4$: C, 56·5; H, 5·9%). Johnson,[20] who does not record the method used, reported the diacetate to be a liquid, b. p. 122—123°/10 mm., n_D^{20} 1·4611.

Reaction of 1 : 4-*Diacetoxybut*-2-*yne with Thiolacetic Acid*.—The diacetate (10 g.), thiolacetic acid (15 g.), and ascaridole (0·2 c.c.) were boiled under reflux for 4 hr., and then poured into water. The dark red oil was taken up in ether and washed with aqueous sodium hydrogen carbonate. Removal of solvent and distillation of the residue (5·5 g.) gave: (i) 2·7 g., b. p. 130—135°/10 mm., n_D^{20} 1·4562, mainly unchanged diacetate; and (ii) 1·5 g., b. p. 110—155°/1 mm., n_D^{20} 1·4700—1·5031. The higher-boiling fraction (Found: S, 17·4. Calc. for $C_{10}H_{14}O_5S$: S, 13·0. Calc. for $C_{12}H_{18}O_6S_2$: S, 19·9%) showed light-absorption max. in ethanol at 2300 Å (ε 4900).

Methyl αα′-Bisacetylthiosuccinate.—Prepared by Owen and Sultanbawa's method,[7] the two forms had m. p.s 118—120° and 69—70°; the latter was not stereochemically pure (see below). Owen and Sultanbawa recorded 119·5—120·5° and 71—72°, respectively.

2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) Lithium aluminium hydride (37 g.) was suspended in dry ether (750 c.c.) in a Soxhlet extraction apparatus, the thimble of which contained the higher-melting methyl αα′-bisacetylthiosuccinate (50 g.). Refluxing was continued for 6 hr. after disappearance of the ester, and the cooled mixture was then cautiously treated with water to decompose the excess of hydride and poured into dilute sulphuric acid. The ether layer was removed, and the aqueous portion was extracted continuously with ether overnight.

[20] Johnson, *J.*, 1946, 1009.

The combined ethereal solutions were dried (Na_2SO_4) and evaporated to an oil (25 g.) (Found : thiol-S, 32·9. Calc. for $C_4H_{10}O_2S_2$: thiol-S, 41·6%), which could not be distilled without decomposition.

(ii) Similar reduction of the lower-melting ester (29 g.) with lithium aluminium hydride (25 g.) in dry ether (600 c.c.) gave a product (20·7 g.), m. p. 84—87°, which on crystallisation from ether furnished 2 : 3-*dimercaptobutane*-1 : 4-*diol* (6·75 g.), m. p. 90—92° (Found : C, 31·4; H, 6·8; O, 20·85; S, 41·2; thiol-S, 41·3. $C_4H_{10}O_2S_2$ requires C, 31·1; H, 6·5; O, 20·75; S, 41·6%). Concentration of the mother liquors gave a semi-solid residue (6·4 g.), from which the oil was drained off; this oil gave derivatives identical with those (see below) of the liquid thiol obtained in (i).

Derivatives of the Liquid 2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) The crude thiol (0·53 g.) was heated with acetic anhydride (4·9 g.) and a trace of sulphuric acid for 12 hr. at 100°. The solution was then concentrated under reduced pressure and the residue was treated with water and ether. Evaporation of the ethereal solution gave the *tetra-acetyl* derivative (0·9 g.), which formed prisms (from methanol), m. p. 118—119° (Found : C, 44·6; H, 6·0; S, 19·2. $C_{12}H_{18}O_6S_2$ requires C, 44·7; H, 5·6; S, 19·9%).

(ii) The crude thiol (3·1 g.), acetic anhydride (3·1 g.; 2 mol., based on thiol value), and sulphuric acid (10 mg.) were mixed at 0° and then heated at 50—70° for 6 hr. Dilution with water and extraction with ether gave an oil (3·0 g.) which partly crystallised. The solid was drained on porous tile and recrystallised from methanol to give the *di*-O-*acetyl* derivative (0·7 g.), m. p. 58—59° (Found : C, 40·15; H, 6·2; S, 26·4; thiol-S, 24·9. $C_8H_{14}O_4S_2$ requires C, 40·3; H, 5·9; S, 26·9%).

(iii) The crude thiol (5·0 g.) was dissolved in acetone (50 c.c.), concentrated hydrochloric acid (0·1 c.c.) was added, and the solution was set aside for a week. The crystals (4·0 g.) were removed, and the solution was diluted with water. The precipitate (1·1 g.) and the crystals were crystallised from methanol giving the 1 : 2-3 : 4-di*iso*propylidene derivative, m. p. 103—104° (Found : C, 51·2; H, 7·7; S, 27·7. $C_{10}H_{18}O_2S_2$ requires C, 51·2; H, 7·7; S, 27·4%).

Derivatives of the Solid 2 : 3-*Dimercaptobutane*-1 : 4-*diol*.—(i) The solid thiol (2·1 g.) was heated with acetic anhydride (25 c.c.) and fused sodium acetate (1 g.) for 15 hr. at 100°. The mixture was poured into water and stirred, and the precipitate (4·4 g.) crystallised from methanol, giving the *tetra-acetyl* derivative, m. p. 72—73° (Found : C, 44·45; H, 5·4; S, 19·7%).

(ii) A solution of the solid thiol (0·29 g.) in acetone (3 c.c.), containing a trace of sulphuric acid, was set aside for 3 weeks and then diluted with aqueous sodium hydrogen carbonate. The precipitate (0·4 g.) on recrystallisation from methanol gave the 1 : 2-3 : 4-di*iso*propylidene derivative, m. p. 92—93° (Found : C, 51·5; H, 8·0; S, 27·45%).

Desulphurisation of 1 : 2-3 : 4-*Di*-OS-iso*propylidene*-2 : 3-*dimercaptobutane*-1 : 4-*diol*.—A solution of the di*iso*propylidene derivative (1·2 g.), m. p. 103—104°, from the liquid thiol, in ethanol (20 c.c.) was stirred and boiled under reflux with Raney nickel (*ca.* 10 g.) for 3 hr. The filtered solution was evaporated at 35°/25 mm., to an oil (0·6 g.), which on distillation gave butane-1 : 4-diol, b. p. 105—115°/12 mm., n_D^{21} 1·4280—1·4380, characterised as the bis-α-naphthylurethane, m. p. and mixed m. p. 195—196° (lit.,[21] 198°).

Alkaline Hydrolysis of 2-*Acetoxy*-1 : 3-*bisacetylthiopropane*.—The triacetyl compound [22] (2 g.) was added to a warm solution of sodium hydrogen carbonate (3 g.) in water (30 c.c.). The mixture was heated at 70° (bath)/120 mm., but no cyclic sulphide distilled. When it was boiled at atmospheric pressure, however, a small amount of oil steam-distilled; this was isolated by extraction with light petroleum (b. p. 40—60°) and distilled to give 3-acetylthiopropylene sulphide (0·18 g., 15%), b. p. 130—134°/58 mm., n_D^{19} 1·5507. Light absorption in ethanol : max. 2300 Å, ε 4000. Miles and Owen [1] give b. p. 120°/35 mm., n_D^{23} 1·5500, $\lambda_{max.}$ 2290 Å (ε 3500).

In a control experiment, 2 : 3-bisacetylthiopropyl acetate [5] (2 g.) gave at atmospheric pressure the cyclic sulphide (0·9 g., 75%), b. p. 160°/80 mm., n_D^{18} 1·5503.

1 : 3-*Bisacetylthiopropane*.—1 : 3-Dibromopropane (20 g.), potassium thiolacetate (25 g.), and dry ethanol (140 c.c.) were stirred and boiled under reflux for 6 hr. under nitrogen. The cooled mixture was then poured into water, and the insoluble oil, isolated by chloroform, was distilled to give the bisthiolacetate (14 g.), b. p. 97—98°/0·5 mm., n_D^{21} 1·5220. Chapman and Owen [15] give b. p. 152°/24 mm., n_D^{24} 1·5209.

[21] Bennett and Heathcoat, *J.*, 1929, 271.
[22] Johary and Owen, *J.*, 1955, 1303.

1 : 4-*Bisacetylthiobutane*.—Prepared in a similar way from 1 : 4-dibromobutane [23] (20 g.), the *compound* (11·7 g.) had b. p. 126°/1 mm., n_D^{17} 1·5189 (Found : C, 46·9; H, 7·1; S, 30·6. $C_8H_{14}O_2S_2$ requires C, 46·6; H, 6·8; S, 31·1%).

1 : 5-*Bisacetylthiopentane*.—1 : 5-Dibromopentane [24] (9·1 g.) similarly gave the *compound* (4·6 g.), b. p. 184—187°/0·5 mm., n_D^{20} 1·5141 (Found : C, 49·3; H, 7·3; S, 28·7. $C_9H_{16}O_2S_2$ requires C, 49·1; H, 7·3; S, 29·1%).

o-*Di*(*acetylthiomethyl*)*benzene*.—*o*-Di(bromomethyl)benzene [25] (8·8 g.) and potassium thiolacetate (8·8 g.) were dissolved separately in the minimum volumes of cold ethanol and then mixed; reaction occurred rapidly, and was completed by heating under reflux for 15 min. The product, isolated as above, on distillation afforded the *bisthiolacetate* (7·3 g.), b. p. 140°/0·08 mm., n_D^{18} 1·5885 (Found : C, 56·5; H, 5·6; S, 25·4. $C_{12}H_{14}O_2S_2$ requires C, 56·7; H, 5·55; S, 25·2%).

3-*Acetylthio*-1 : 2-O-iso*propylidenepropane*-1 : 2-*diol*.—1 : 2-*O*-*iso*Propylidene-3-*O*-toluene-*p*-sulphonylglycerol [26] (18·5 g.), potassium thiolacetate (8 g.), and acetone (200 c.c.) were stirred and heated under reflux for 14 hr. Concentration of the filtered solution, dilution with water, and extraction with ether gave the *thiolacetate* (10·2 g.), b. p. 114°/15 mm., n_D^{22} 1·4740 (Found : C, 50·25; H, 7·6; S, 16·6. $C_6H_{14}O_3S$ requires C, 50·5; H, 7·4; S, 16·9%). Light absorption in ethanol : max. 2300 Å, ε 4560. When the compound (0·21 g.) was dissolved in methanol (10 c.c.) and diluted with 2N-hydrochloric acid, titration with 0·111N-iodine gave a rapidly fading end-point; in 2½ hr. at room temperature the uptake (5·18 c.c.) corresponded to 50% hydrolysis of the thiolacetate.

Quantitative Hydrolysis of Thiolacetates by 0·1N-*Sodium Hydroxide in* 50% *Aqueous Dioxan at* 0°.—Harding and Owen's method [2] was used, with slight modification for the derivatives of 2 : 3-dimercaptobutane-1 : 4-diol, which dissolved too slowly in the cold reaction medium for the standard procedure to be followed; for these compounds a solution of the solid in warm dioxan (50 c.c.) was added to 0·1N-sodium hydroxide in 50% aqueous dioxan (250 c.c.) at 0°, titrations then being carried out as before.

The figures following each compound below are the final constant values for the number of acetyl groups liberated, and the number of free thiol groups present, respectively; the attainment of the full thiol value (Calc. : 2·0 groups) indicates the absence of cyclisation. The slightly high values for 1 : 2-bisacetylthioethane, for which the normal method was used, are due to incomplete dissolution in the early stages of the hydrolysis.

4 : 5-Bisacetylthiopentyl acetate : 2·92, 1·98. 4 : 5-Dimercaptopentyl acetate : see Fig. 1. 4 : 5-Bisacetylthiopentanol : see Fig. 1. 2-Acetoxyl : 3-bisacetylthiopropane : 2·94, 1·98. 1 : 2-Bisacetylthioethane : [27] 2·12, 2·12. 1 : 3-Bisacetylthiopropane : 2·01, 1·96. 1 : 4-Bisacetylthiobutane : 2·00, 2·00. 1 : 5-Bisacetylthiopentane : 2·01, 2·02. *o*-Di(acetylthiomethyl)-benzene : 2·03. 2·03. Derivatives of 2 : 3-dimercaptobutane-1 : 4-diol : see Fig. 2.

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[24] *Org. Synth.*, Coll. Vol. III, 692.
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[27] Owen and Smith, *J.*, 1951, 2973.