Dithiols. Part XIV. The Alkaline Hydrolysis of Acetylated Non-vicinal Hydroxy-thiols.*

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Quantitative alkaline hydrolyses of partly and of fully acetylated derivatives of (i) 3 : 4-dimercaptobutanol, (ii) 4-mercaptobutanol, (iii) 3-mercaptobutanol, (iv) 3-mercaptopropanol, have shown that cyclisation occurs only with (i); the presence of a dithiol grouping is therefore necessary for the formation of the larger-ring sulphides (compare the formation of ethylene sulphides, preceding paper), and possible reasons for the enhanced reactivity of the dithiol are discussed. Acetyl migration occurs with the *S*-acetyl derivatives of (i), (iii), and (iv), but not (ii); a $C_{(3)} \longrightarrow C_{(1)}$ transference, involving a six-membered orthoacetate intermediate, thus represents the limiting condition for this isomerisation.

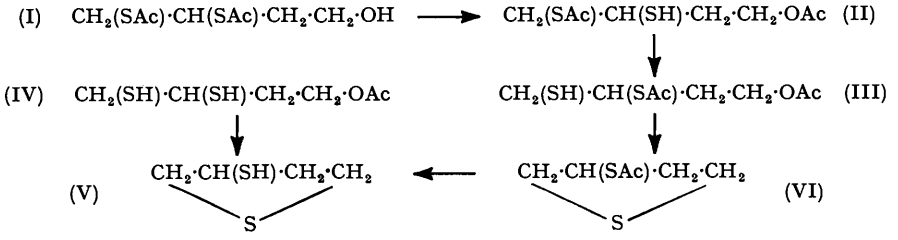
2-Acetoxyethyl 2 : 3-bisacetylthiopropyl ether, and *trans*-2-acetoxy-*cyclo*hexyl 2 : 3-bisacetylthiopropyl ether have been synthesised. These are simple analogues of acetylated 2 : 3-dimercaptopropyl-polyol ethers and 2 : 3-dimercaptopropyl glucoside, and their quantitative alkaline hydrolysis has thrown some light on abnormalities in the deacetylation of the more complex compounds.

THE formation of ethylene sulphides by alkaline deacetylation of acetylated vicinal hydroxy-thiols has been discussed in the preceding paper. Miles and Owen (*J.*, 1952, 817) found that similar treatment of the acetyl derivatives of 3 : 4-dimercaptobutanol gave 3-mercaptothiophan (V), but it was not established whether this was a special case (owing to the presence of the dithiol grouping) or whether the reaction was general for the preparation of larger-ring sulphides. The behaviour of these and simpler non-vicinal compounds has therefore been studied by the quantitative method described in Part XIII.

The di-*S*-acetyl (I), *O*-acetyl (IV), and triacetyl derivatives of 3 : 4-dimercaptobutanol gave final thiol values of 1·5, 1·7, and 1·5 groups, corresponding to 50, 30, and 50% cyclisation, respectively (Fig. 1). Under similar conditions the acetyl derivatives of 2 : 3-dimercaptopropanol are hydrolysed about twice as rapidly and undergo a greater degree

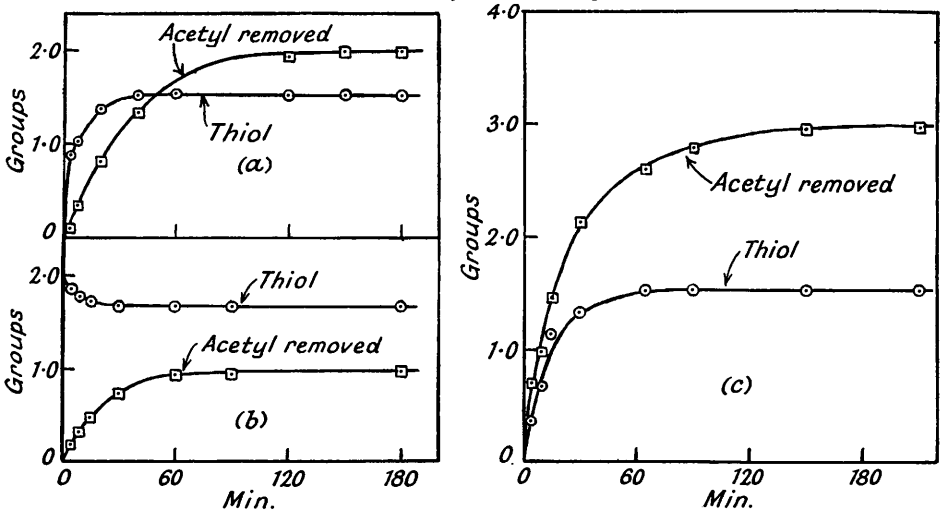
* Part XIII, preceding paper.

of cyclisation (see preceding paper); the interposition of the extra methylene group in 3 : 4-dimercaptobutanol thus considerably reduces the reactivity of the system. In the



early stages of the hydrolysis of (I) the liberation of thiol was more rapid than that of acetyl, indicating the occurrence of acetyl migration. From observations on the hydrolysis of 3- and 4-acetylthiobutanol (see below) this probably affects the secondary group, leading

FIG. 1. *Derivatives of* 3 : 4-*dimercaptobutanol.*



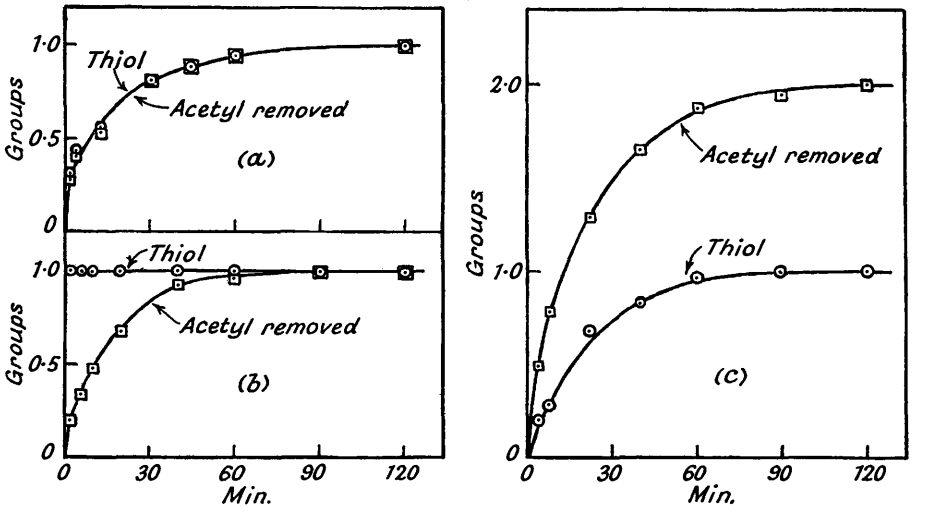
(*a*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot CH_2\cdot OH$, 0·0036M. (*b*) $CH_2(SH)\cdot CH(SH)\cdot CH_2\cdot CH_2\cdot OAc$, 0·0074M. (*c*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot CH_2\cdot OAc$, 0·0030M

to (II), but once this has occurred it is of course possible for the acetyl group on $C_{(4)}$ to migrate to $C_{(3)}$; in this product (III) the thiol group at $C_{(4)}$ is free to attack $C_{(1)}$ by a mechanism analogous to that outlined in the preceding paper, and this would lead *via* 3-acetylthiothiophan (VI) to (V). That the degree of cyclisation is higher with (I) than with (IV) supports such a reaction scheme because it indicates that an intermediate other than (IV) must be involved; the only one possible is (III), and this may cyclise more readily than (IV) for the reason suggested (previous paper) to account for the greater amount of cyclisation with 2 : 3-bisacetylthiopropanol than with 2 : 3-dimercaptopropyl acetate.

The next step was to investigate the acetyl derivatives of 4-mercaptobutanol, from which thiophan would be obtained if cyclisation occurred. 4-Acetylthiobutyl acetate (VII) was prepared by reaction of 4-bromobutyl acetate with potassium thiolacetate. Hydrolysis with aqueous sodium hydroxide gave 4-mercaptobutanol (X) with no thiophan, and the absence of cyclisation was confirmed quantitatively, when the theoretical thiol value for complete normal hydrolysis was attained (Fig. 2*c*). The *S*-acetyl (VIII) and the *O*-acetyl derivative (IX) were obtained by monoacetylation of the hydroxy-thiol under alkaline and acid conditions respectively (cf. Miles and Owen, *loc. cit.*), and they also behaved normally, there being no acetyl migration or cyclisation (Fig. 2*a*, *b*); both compounds were hydrolysed at about the same rate, in conformity with the usual behaviour

of simple acetates and thiolacetates (for references, see preceding paper). Furthermore, since there is no migration, the absence of a discontinuity in the changing slope of the acetyl curve in Fig. 2*c* shows that there is also no large difference between the rates of hydrolysis of the *S*- and the *O*-acetyl group in the diacetyl compound; this is also indicated by the slope of the thiol curve, which is about half that of the acetyl curve at any time. It follows that the two groups in (VII) are behaving independently and that the hydrolysis proceeds through both (VIII) and (IX).

FIG. 2. *Derivatives of 4-mercaptobutanol.*



(*a*) AcS·$[CH_2]_4$·OH, 0·0062M. (*b*) HS·$[CH_2]_4$·OAc, 0·0068M. (*c*) AcS·$[CH_2]_4$·OAc, 0·0054M.

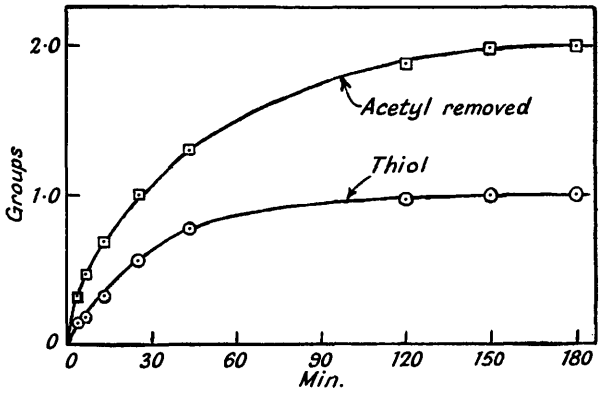
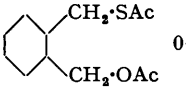


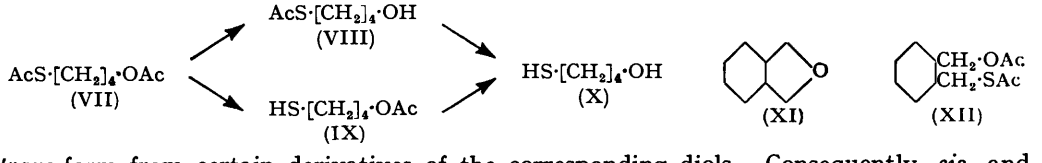
FIG. 3. *Derivative of* cis-2-*mercaptomethyl*cyclo*hexylmethanol.*



0·0053M.

(The *trans* isomer gave almost identical results.)

If the conformation of the carbon chain in 4-mercaptobutanol could be fixed in a favourable position, ring-formation might occur more readily. Haggis and Owen (*J.*, 1953, 389) have shown that the cyclic oxide (XI) can be obtained in both the *cis*- and the

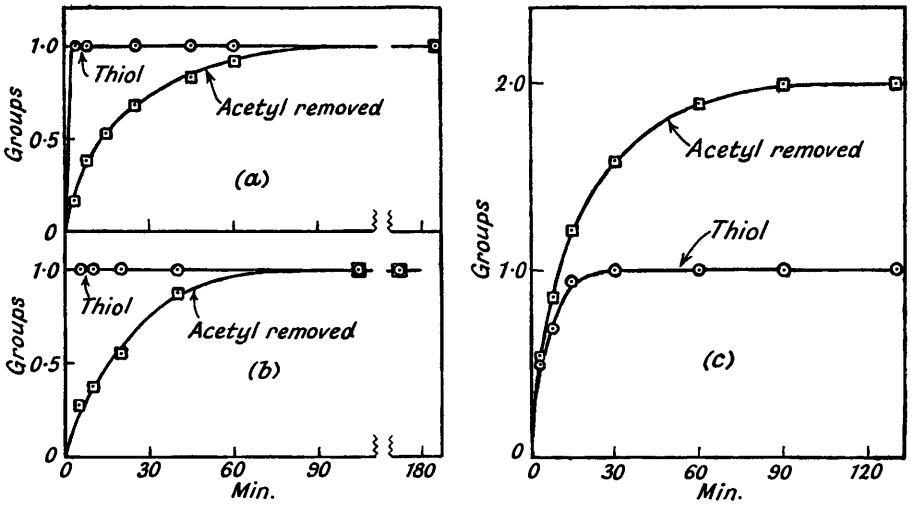


trans-form from certain derivatives of the corresponding diols. Consequently, *cis*- and *trans*-2-(acetylthiomethyl)*cyclo*hexylmethyl acetate (XII), also described by these authors (*ibid.*, p. 408), were examined, but quantitative hydrolysis proceeded normally (Fig. 3)

and showed no migration or cyclisation; *trans*-2-mercaptomethyl*cyclo*hexylmethanol was isolated in good yield by hydrolysis of *trans*-(XII) with aqueous sodium hydroxide.

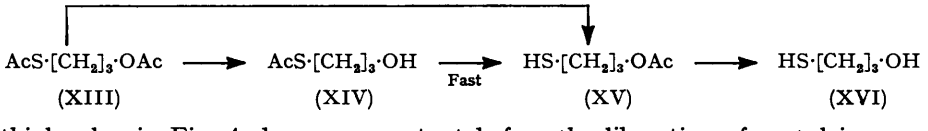
As a typical 1 : 3-hydroxy-thiol, 3-mercaptopropanol was chosen for examination. Addition of thiolacetic acid to allyl alcohol in the presence of ascaridole (Brown, Jones, and Pinder, *J.*, 1951, 2123) gave 3-acetylthiopropanol (XIV) from which 3-acetylthiopropyl acetate (XIII) was obtained by acetylation, and 3-mercaptopropanol (XVI) by hydrolysis with aqueous alkali, no cyclic sulphide being detected. The *O*-acetate (XV) was obtained by monoacetylation of the hydroxy-thiol under acid conditions, and also by rearrangement of (XIV) by heating it in the presence of acetic acid. The latter observation showed that acetyl migration was possible, and when the three derivatives were quantitatively hydrolysed (Fig. 4) the *S*-acetyl compound underwent very rapid isomerization, almost complete liberation of the thiol group having occurred in 3 minutes; the acetyl curve in Fig 4*a* should therefore be practically identical with that of the *O*-acetate, and comparison with Fig. 4*b* shows it to be so. In no case did any cyclisation take place, the final thiol values

FIG. 4. *Derivatives of 3-mercaptopropanol.*



(*a*) AcS·$[CH_2]_3$·OH, 0·0118M. (*b*) HS·$[CH_2]_3$·OAc, 0·0064M. (*c*) AcS·$[CH_2]_3$·OAc, 0·0085M.

being the theoretical for complete normal hydrolysis. In the hydrolysis of the diacetyl compound (XIII), deacetylation to the *O*-acetate (XV) can occur by direct loss of the *S*-acetyl group and also by loss of the *O*-acetyl group to give (XIV) followed by rearrangement, but the two routes are indistinguishable experimentally because the migration is so fast. It follows that the final stage in the hydrolysis involves only the reaction (XV) ⟶ (XVI), *i.e.*, liberation of acetyl group with no change in thiol value, which explains why

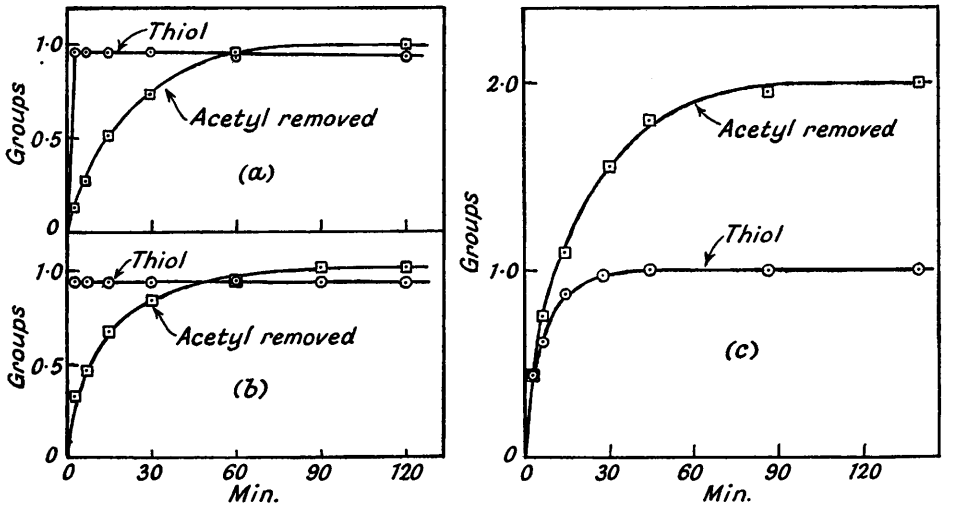


the thiol value in Fig. 4*c* becomes constant before the liberation of acetyl is complete. This is in contrast to the results with 4-acetylthiobutyl acetate (Fig. 2*c*), where, because no acetyl migration occurs, the hydroxy-thiol is formed by two routes (VIII) ⟶ (X) and (IX) ⟶ (X); consequently the thiol and the acetyl value become constant at the same time.

The occurrence of migration in the *S*-acetyl derivative of 3-mercaptopropanol and not in that of 4-mercaptobutanol suggested that the migration observed in 3 : 4-bisacetylthiobutanol involved the 3- and not the 4-*S*-acetyl group, but a more valid comparison required a study of the derivatives of 3-mercaptobutanol. Selective acetylation of the primary

hydroxyl in butane-1 : 3-diol gave 3-hydroxybutyl acetate, which was converted into the crystalline toluene-*p*-sulphonate (XVII). Replacement of a secondary toluene-*p*-sulphonyloxy-group by acetylthio does not always proceed smoothly (cf. Chapman and Owen, *J.*, 1950, 579), but (XVII) readily gave 3-acetylthiobutyl acetate (XVIII), the structure of which was proved by desulphurisation in aqueous alkali by Raney nickel alloy to give *n*-butanol. Alkaline hydrolysis of (XVIII) gave 3-mercaptobutanol, from which 3-mercaptobutyl acetate (XX) and 3-acetylthiobutanol (XIX) were prepared by mono-acetylation under the appropriate conditions, though some difficulty was experienced in the isolation of (XIX) owing to its ease of isomerisation. Brown, Jones, and Pinder (*loc. cit.*) claimed to have obtained it, amongst other products, by addition of thiolacetic acid to crotyl alcohol, but the physical properties of their material correspond more nearly to those of the *O*-acetate (XX); they reported a correct sulphur analysis, but did not record any thiol value. In our hands, repetition of their procedure gave very variable results, and no pure *O*- or *S*-acetyl compound was obtained; from several experiments a considerable quantity of crotyl acetate was isolated, thus providing a further example of

FIG. 5. *Derivatives of 3-mercaptobutanol.*



(*a*) $CH_3 \cdot CH(SAc) \cdot CH_2 \cdot CH_2 \cdot OH$, 0·0082M. (*b*) $CH_3 \cdot CH(SH) \cdot CH_2 \cdot CH_2 \cdot OAc$, 0·0067M.
(*c*) $CH_3 \cdot CH(SAc) \cdot CH_2 \cdot CH_2 \cdot OAc$, 0·0065M.

the acetylating action of thiolacetic acid on alcohols (cf. Stewart and McKinney, *J. Amer. Chem. Soc.*, 1931, **53**, 1482). Brown, Jones, and Pinder suggested crotyl acetate as an intermediate in their reaction scheme, but did not confirm its formation.

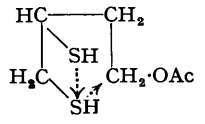
The behaviour of (XIX), (XX), and (XVIII) on quantitative hydrolysis (Figs. 5*a*, *b*, *c*) was very similar to that of the 3-mercaptopropanol derivatives, acetyl migration from the *S*-acetyl group being almost instantaneous; again, no cyclisation took place. With the diacetyl derivative the thiol value became constant before the liberation of acetyl was complete (Fig. 5*c*); the explanation for this is clearly similar to that outlined above for the hydrolysis of 3-acetylthiopropyl acetate.

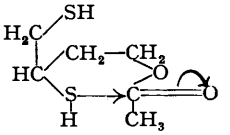
The cyclisation which occurs with the derivatives of 3 : 4-dimercaptobutanol, but not with those of 4-mercaptobutanol, must depend upon the presence of the extra thiol group, which is itself not directly involved in the reaction. In the preceding paper two possible explanations were given for the high degree of cyclisation obtained with the derivatives of 2 : 3-dimercaptopropanol, and both of these are applicable to the present problem. First, the cyclisation, which involves electron-accession to $C_{(1)}$ from the thiol group on $C_{(4)}$, would be facilitated by the reinforcing electron-donating power of the sulphur atom on $C_{(3)}$, as shown in (XXI*a*); an alternative cyclisation between $C_{(1)}$ and the thiol group on $C_{(3)}$, reinforced by the sulphur on $C_{(4)}$, is also theoretically possible, but formation of a five-

rather than a four-membered ring would undoubtedly be favoured. Secondly, as suggested by Dr. L. M. Jackman, cyclisation may be due to the occurrence of chelation between the sulphur on $C_{(3)}$ and the carbonyl-carbon atom in the acetoxy-group, to give (XXI*b*) in which, with a suitable ring conformation, the thiol group on $C_{(4)}$ might more readily take up a position for rear attack on $C_{(1)}$.

(XVII) $CH_3{\cdot}CH(OTs){\cdot}CH_2{\cdot}CH_2{\cdot}OAc \longrightarrow CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$ (XVIII)

(XIX) $CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}CH_2{\cdot}OH \longrightarrow CH_3{\cdot}CH(SH){\cdot}CH_2{\cdot}CH_2{\cdot}OAc$ (XX)

(XXI*a*) 

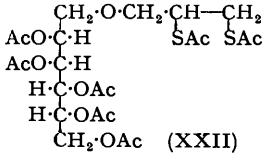


(XXI*b*)

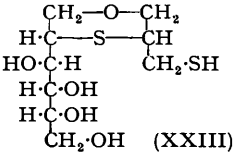
(Ts = p-$C_6H_4Me{\cdot}SO_2{\cdot}$)

Acetyl migration in the *S*-acetyl derivatives has been observed with all the 2- and the 3-hydroxy-thiols studied in this and the preceding paper, and presumably occurs through an intermediate five- or six-membered cyclic orthoacetate. The absence of migration with 4-acetylthiobutanol is significant, and must be attributed to the improbability of formation of a seven-membered cyclic orthoacetate.

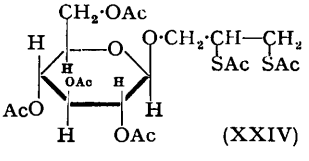
The examples of abnormal alkaline deacetylation recorded in some earlier papers in this series concerned the acetylated glucosides and hexitol ethers of 2 : 3-dimercaptopropanol. Cyclisation in such compounds would probably give a 4-oxathian structure, the six-membered ring being more likely than a larger one, and on the assumption that inversion occurs at $C_{(2)}$ in the hexitol or sugar portion when the acetyl at that position is displaced, the acetylated mannitol ether (XXII) (Bladon and Owen, *J.*, 1950, 591) and the acetylated β-glucoside (XXIV) (Fraser, Owen, and Shaw, *Biochem. J.*, 1947, **41**, 325) would give (XXIII) and (XXV) respectively.* The simple analogues (XXVI) and (XXVII) have now been synthesised in order to detect quantitatively any cyclisation in structures of those types.



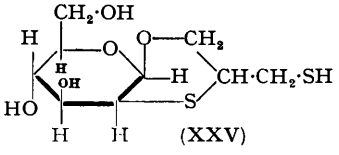
(XXII)



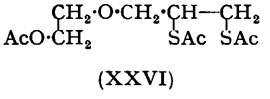
(XXIII)



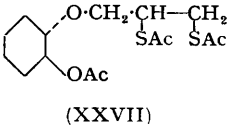
(XXIV)



(XXV)



(XXVI)



(XXVII)

Reaction of ethylene chlorohydrin with sodium allyl oxide gave allyl 2-hydroxyethyl ether, the acetate of which, with bromine, furnished 2-acetoxyethyl 2 : 3-dibromopropyl ether; reaction with potassium thiolacetate then gave 2-acetoxyethyl 2 : 3-bisacetylthiopropyl ether (XXVI). On quantitative alkaline hydrolysis under the standard conditions, the thiol value reached a maximum of 1·9 groups when deacetylation was complete, corresponding to 10% of cyclisation (Fig. 6) On a preparative scale, alkaline deacetylation gave the crude hydroxy-dithiol (crystalline trisphenylurethane), but attempts to isolate the cyclic product were unsuccessful.

Alkoxide-catalysed ring fission of *cyclo*hexene oxide with allyl alcohol gave allyl *trans*-2-hydroxy*cyclo*hexyl ether. Acetylation, addition of bromine, and reaction of the dibromide with potassium thiolacetate gave *trans*-2-acetoxy*cyclo*hexyl 2 : 3-bisacetylthiopropyl ether (XXVII). On quantitative alkaline hydrolysis the thiol value rose to a constant maximum of 1·6 groups when deacetylation was complete (Fig. 6), indicating 40% of cyclisation.

* No abnormality was observed in the deacetylation of the tetra-*O*-methyl analogue of (XXIV), in which such cyclisation cannot occur (Miles and Owen, *J.*, 1950, 2934).

In the deacetylation products from (XXII) and similar hexitol derivatives, the thiol content was usually 85—95% of the total sulphur (Bladon and Owen, *loc. cit.*), *i.e.*, the degree of cyclisation was small; from the glucoside (XXIV), however, the thiol-sulphur in the product was only 60—70% of the total. The behaviour of (XXVI) and (XXVII), thus parallels that of their more complex analogues.

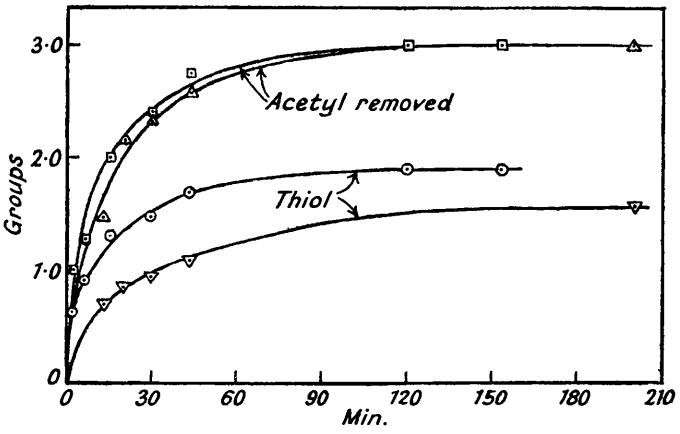
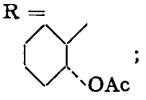


FIG. 6. *Acetylated ethers of 2 : 3-dimercaptopropanol.*
$CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OR$
⊡ ⊙ R = $AcO\cdot[CH_2]_2$—; 0·0042M.
△ ▽ R = 

; 0·0025M.

EXPERIMENTAL

3 : 4-Dimercaptobutyl acetate, b. p. 85°/0·002 mm., n_D^{21} 1·5154; 3 : 4-bisacetylthiobutanol, $\lambda_{max.}$ 2280 Å; ε 7800; and 3 : 4-bisacetylthiobutyl acetate, b. p. 137°/0·01 mm., n_D^{21} 1·5137, were prepared by the method of Miles and Owen (*J.*, 1952, 817).

cis-2-(Acetylthiomethyl)*cyclo*hexylmethyl acetate, b. p. 118°/0·2 mm., n_D^{20} 1·4990, was prepared according to Haggis and Owen (*J.*, 1953, 408).

4-*Bromobutyl Acetate.*—To tetrahydropyran (24 g.) containing zinc chloride (10 mg.; anhyd.), acetyl bromide (45 g.) was slowly added at 0°. When the reaction had subsided the mixture was heated under reflux for 1½ hr., then cooled, diluted with chloroform (150 c.c.), and washed with aqueous sodium hydrogen carbonate and with water. Evaporation of the dried (Na_2SO_4) solution gave impure 4-bromobutyl acetate (56·4 g.), b. p. 89—91°/11 mm., n_D^{24} 1·4628 (Found : Br, 44·2. Calc. for $C_6H_{11}O_2Br$: Br, 41·0%). Cloke and Pilgrim (*J. Amer. Chem. Soc.*, 1939, **61**, 2667) obtained a product b. p. 87—93°/15 mm., n_D^{20} 1·4680 (Br, 46·6%), and failed to obtain any material with a lower bromine content.

4-*Acetylthiobutyl Acetate.*—Crude 4-bromobutyl acetate (30 g.), potassium thiolacetate (18·5 g.), and thiolacetic acid (0·5 g.) in ethanol (200 c.c.) were boiled under reflux for 2 hr. The filtered solution was concentrated under reduced pressure, and then diluted with water and extracted with chloroform, to give 4-*acetylthiobutyl acetate* (20 g.) as a pale yellow oil, b. p. 84—86°/0·3 mm., n_D^{20} 1·4724 (Found : C, 50·3; H, 7·6; S, 17·2. $C_8H_{14}O_3S$ requires C, 50·5; H, 7·4; S, 16·8%). Light absorption in EtOH : max., 2270 Å; ε 4600.

4-*Mercaptobutanol.*—The diacetyl compound (9·5 g.) was stirred with 2N-sodium hydroxide (60 c.c.) at room temperature for 3 hr. under nitrogen. Acidification with hydrochloric acid and extraction with chloroform gave 4-mercaptobutanol (4·0 g.) as a colourless liquid, b. p. 102—103°/20 mm., n_D^{19} 1·4870 (Found : C, 45·5; H, 9·5; S, 29·9. Calc. for $C_4H_{10}OS$: C, 45·3; H, 9·5; S, 30·2%). Szarvasi (*Bull. Soc. chim.*, 1950, 463) records b. p. 99—100°/16 mm., n_D^6 1·491. With phenyl *iso*cyanate it gave the *bisphenylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 128° (Found : C, 62·9; H, 6·1; N, 8·2. $C_{18}H_{20}O_3N_2S$ requires C, 62·8; H, 5·9; N, 8·1%).

4-*Mercaptobutyl Acetate.*—The hydroxy-thiol (1·6 g.), acetic anhydride (1·45 g.) and 10% sulphuric acid in acetic acid (0·1 c.c.) were mixed at 0°, then heated at 60° for an hour, and kept at room temperature for 24 hr. Dilution with water (15 c.c.) and extraction with ether gave 4-mercaptobutyl acetate (1·05 g.), b. p. 125—127°/20 mm., n_D^{18} 1·4634 (Found : thiol-S, 21·2. Calc. for $C_6H_{12}O_2S$: S, 21·6%). Szarvasi (*loc. cit.*) records b. p. 96—98°/15 mm., n_D^{16} 1·467. Treatment with α-naphthyl *iso*cyanate for an hour at 100° gave the *α-naphthylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 76° (Found : C, 64·4; H, 6·3; N, 4·6. $C_{17}H_{19}O_3NS$ requires C, 64·3; H, 6·0; N, 4·4%).

4-*Acetylthiobutanol*.—Acetic anhydride (3 c.c.) was added to 4-mercaptobutanol (3·35 g.) in a solution of sodium hydroxide (1·3 g.) in water (10 c.c.) at 0°. The mixture was stirred for 10 min. and extracted with benzene, to give 4-*acetylthiobutanol* (1·8 g.), b. p. 124°/10 mm., n_D^{13} 1·4905 (Found: C, 48·4; H, 8·4; S, 21·2; thiol-S, 0. $C_6H_{12}O_2S$ requires C, 48·6; H, 8·2; S, 21·6%). Light absorption in EtOH: max., 2280 Å; ε 3600. With phenyl *iso*cyanate for 1 hr. at 100° it gave the *phenylurethane*, m. p. 64° (from light petroleum, b. p. 40—60°) (Found: C, 58·4; H, 6·4; N, 5·6. $C_{13}H_{17}O_3NS$ requires C, 58·4; H, 6·4; N, 5·25%).

trans-2-(*Acetylthiomethyl*)cyclo*hexylmethyl Acetate*.—*trans*-2-Bromomethyl*cyclo*hexylmethyl acetate (Haggis and Owen, *J.*, 1953, 389) (22 g.) was heated under reflux for 3 hr. with potassium thiolacetate (10 g.) in ethanol (100 c.c.). Filtration, concentration under reduced pressure, dilution with water, and extraction with chloroform gave *trans*-2-(acetylthiomethyl)*cyclo*hexylmethyl acetate (18·3 g.), b. p. 108°/0·002 mm., n_D^{16} 1·4990 (Found: C, 59·1; H, 8·3; S, 13·0. Calc. for $C_{12}H_{20}O_3S$: C, 59·0; H, 8·25; S, 13·1%). This material was purer than that obtained by Haggis and Owen (*loc. cit.*).

trans-2-*Mercaptomethyl*cyclo*hexylmethanol*.—The above acetate-thiolacetate (14·7 g.) was stirred at room temperature with N-sodium hydroxide (150 c.c.) for 6 hr. under nitrogen. The solution was then acidified with dilute sulphuric acid and extracted with ether, to give the *hydroxy-thiol* (7·6 g.), b. p. 97°/0·2 mm., n_D^9 1·5241 (Found: C, 59·6; H, 10·2; S, 19·8; thiol-S, 19·8. $C_8H_{16}OS$ requires C, 60·0; H, 10·1; S, 20·0%). Treatment with excess of phenyl *iso*cyanate at 100° for 2 hr. gave the *bisphenylurethane* (0·3 g.), which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 127° (Found: C, 66·1; H, 6·7; N, 7·1. $C_{22}H_{26}O_3N_2S$ requires C, 66·3; H, 6·6; N, 7·0%).

3-*Acetylthiopropanol*.—Thiolacetic acid (18 g.) was slowly added, with shaking and cooling, to allyl alcohol (18 g.) containing ascaridole (0·5 c.c.), at 0°. The mixture was kept at room temperature for 2 days and then for 2 hr. at 60°. Distillation gave 3-acetylthiopropanol (23·2 g.), b. p. 57°/0·3 mm., n_D^{18} 1·4938 (Found: C, 44·4; H, 7·7; S, 23·4; thiol-S, 0. Calc. for $C_5H_{10}O_2S$: C, 44·8; H, 7·5; S, 23·85%). Light absorption in EtOH: max., 2320 Å; ε 4300. [Brown, Jones, and Pinder (*J.*, 1951, 2123) record n_D^{20} 1·4827; their product probably contained some *O*-acetyl isomer.] The *phenylurethane* after recrystallisation from light petroleum (b. p. 60—80°) had m. p. 53° (Found: C, 56·5; H, 6·2; N, 5·6. $C_{12}H_{15}O_3NS$ requires C, 56·9; H, 6·0; N, 5·5%).

With excess of acetic anhydride, containing 1% of sulphuric acid, 3-acetylthiopropanol gave 3-acetylthiopropyl acetate, b. p. 120—121°/19 mm., n_D^{23} 1·4720. Light absorption in EtOH: max., 2300 Å; ε 4400. Brown, Jones, and Pinder (*loc. cit.*) give n_D^{20} 1·4720.

3-*Mercaptopropyl Acetate*.—(i) 3-Acetylthiopropanol (15 g.) was stirred at room temperature with 10% aqueous sodium hydroxide (250 c.c.) under nitrogen until the mixture was homogeneous (4 hr.). The solution was acidified with hydrochloric acid and extracted with ether to give 3-mercaptopropanol (5·3 g.), b. p. 87°/14 mm., n_D^{22} 1·4918 (Found: thiol-S, 35·0. Calc. for C_3H_8OS: S, 34·8%). Rojahn and Lemme (*Arch. Pharm.*, 1925, **263**, 612) give b. p. 85—90°/15 mm. A mixture of the hydroxy-thiol (2·85 g.), acetic anhydride (2·9 c.c.), and 10% sulphuric acid in acetic acid (0·1 c.c.) was kept at room temperature overnight, and then diluted with water (15 c.c.) and extracted with ether, to give 3-*mercaptopropyl acetate* (2·25 g.), b. p. 87°/20 mm., n_D^{22} 1·4618 (Found: C, 44·9; H, 7·7; thiol-S, 23·9. $C_5H_{10}O_2S$ requires C, 44·8; H, 7·5; S, 23·85%). Treatment with α-naphthyl *iso*cyanate at 100° for 2 hr. gave the α-*naphthylurethane*, which after recrystallisation from light petroleum (b. p. 60—80°) had m. p. 75° (Found: C, 63·4; H, 5·7; N, 4·5. $C_{16}H_{17}O_3NS$ requires C, 63·4; H, 5·65; N, 4·6%).

(ii) 3-Acetylthiopropanol (3 g.) was heated at 100° with acetic acid (0·1 c.c.) for 48 hr. Dilution with water (5 c.c.) and extraction with ether gave 3-mercaptopropyl acetate (1·8 g.), b. p. 97—99°/30 mm., n_D^{18} 1·4638 (Found: thiol-S, 23·4%).

3-*Hydroxybutyl Acetate*.—A solution of acetic anhydride (51 g.) in pyridine (75 c.c.) was added dropwise during 4 hr. to a stirred solution of butane-1:3-diol (45 g.) in chloroform (100 c.c.) and pyridine (75 c.c.), cooled to 0°. After being left at room temperature overnight, the bulk of the solvent was removed under reduced pressure at 40°; the residue was cautiously mixed with concentrated hydrochloric acid (100 c.c.), with cooling, and then extracted four times with chloroform. The extracts were washed with aqueous sodium hydrogen carbonate, dried ($MgSO_4$), and evaporated to an oil, distillation of which afforded 3-hydroxybutyl acetate (42 g.), b. p. 102°/18 mm., n_D^{20} 1·4235. Kulpinski and Nord (*J. Org. Chem.*, 1943, **8**, 256) give b. p. 87—89°/13 mm., n_D^{25} 1·4182, for a product assumed to have this structure, obtained by a different method.

3-*Acetylthiobutyl Acetate*.—A solution of 3-hydroxybutyl acetate (30 g.) and toluene-*p*-

sulphonyl chloride (48 g.) in pyridine (150 c.c.) was prepared at 0°, kept thereat overnight, and then concentrated under reduced pressure at 30°. Gradual addition of crushed ice to the residue precipitated an oil, which soon solidified. Recrystallisation of the crude solid (48 g.) from benzene–light petroleum (b. p. 40—60°) gave *3-toluene-p-sulphonyloxybutyl acetate* (38 g.), m. p. 62—63° (Found: C, 54·7; H, 6·5; S, 11·4. $C_{13}H_{18}O_5S$ requires C, 54·5; H, 6·3; S, 11·2%).

This product (20 g.) was boiled under reflux with potassium thiolacetate (10 g.) in ethanol (100 c.c.) for 5 hr., then concentrated under reduced pressure, diluted with water, and extracted with chloroform, to give 3-acetylthiobutyl acetate (8·6 g.), b. p. 52—53°/0·1 mm., n_D^{22} 1·4690 (Found: C, 50·4; H, 7·6; S, 16·85. Calc. for $C_8H_{14}O_3S$: C, 50·5; H, 7·4; S, 16·8%). Light absorption: max., 2320 Å; ε 4200. Brown, Jones, and Pinder (*loc. cit.*) give b. p. 110°/11 mm., n_D^{20} 1·4674, for the product obtained by interaction of thiolacetic acid and crotyl acetate.

Desulphurisation. 3-Acetylthiobutyl acetate (1 g.) and 2N-aqueous sodium hydroxide (20 c.c.) were boiled under reflux until a clear solution was obtained (10 min.). Raney nickel alloy (5 g.) was then added in small portions at a rate sufficient to keep the mixture boiling without the application of heat (15 min.); a filtered test portion then gave no thiol reaction with nitroprusside. Distillation at ordinary pressure gave a first fraction (1·5 c.c.) containing *n*-butanol in suspension; this was characterised as the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 64°.

3-Mercaptobutanol.—(i) A solution of 3-acetylthiobutyl acetate (20 g.) in 1% methanolic hydrogen chloride (100 c.c.) was boiled under reflux for 6 hr., then cooled, diluted with chloroform (200 c.c.), washed with water, dried (Na_2SO_4), and evaporated to an oil, distillation of which gave a main fraction (4·8 g.), b. p. 80—90°/16 mm., n_D^{17} 1·4800. Redistillation gave *3-mercaptobutanol* (3·8 g.), b. p. 90—91°/20 mm., n_D^{16} 1·4816 (Found: C, 44·9; H, 9·7; thiol-S, 30·1. $C_4H_{10}OS$ requires C, 45·2; H, 9·5; S, 30·2%). The *bisphenylurethane*, fine needles from light petroleum (b. p. 100—120°), had m. p. 106° (Found: C, 63·0; H, 5·9; N, 8·3. $C_{18}H_{20}O_3N_2S$ requires C, 62·8; H, 5·9; N, 8·3%).

(ii) 3-Acetylthiobutyl acetate (11 g.) was stirred with 2N-sodium hydroxide (100 c.c.) at room temperature under nitrogen until the mixture became homogeneous (3 hr.). Acidification with dilute sulphuric acid and extraction with chloroform then gave 3-mercaptobutanol (4·2 g.), b. p. 108—109°/25 mm., n_D^{18} 1·4768 (Found: thiol-S, 30·2%).

3-Mercaptobutyl Acetate.—A mixture of 3-mercaptobutanol (1·35 g.), acetic anhydride (1·2 g.), and 10% sulphuric acid–acetic acid (0·1 c.c.) was set aside overnight, then diluted with water (10 c.c.) and extracted with ether, to give *3-mercaptobutyl acetate* (1·1 g.), b. p. 93°/25 mm., n_D^{18} 1·4560 (Found: C, 48·3; H, 8·3; thiol-S, 21·5. $C_6H_{12}O_2S$ requires C, 48·6; H, 8·2; S, 21·6%).

3-Acetylthiobutanol.—(i) Acetic anhydride (1·7 g.) was added in one portion to a stirred solution of 3-mercaptobutanol (1·7 g.) and sodium hydroxide (0·7 g.) in water (10 c.c.) at 0°. After 10 min. the solution was extracted with benzene (15 c.c.). Evaporation of the dried extract and distillation of the residual oil gave a main fraction (0·9 g.), b. p. 70—71°/0·5 mm., n_D^{16} 1·4850, consisting essentially of the *S*-acetyl derivative (Found: thiol-S, 1·0; Ac, 29·2. Calc. for $C_6H_{12}O_2S$: Ac, 29·05%). A lower-boiling fraction (0·2 g.), b. p. 45—65°/0·5 mm., n_D^{16} 1·4580, was probably mainly *O*-acetate.

(ii) Thiolacetic acid (9·5 g.) was added to crotyl alcohol (9 g.) containing ascaridole (50 mg.), and the mixture was kept at room temperature for 3 days. Low-boiling material was removed at 40—50°/25 mm., and the residue was then distilled to give: (*a*) 4·75 g., b. p. 50—65°/0·2 mm., which contained much free thiol; and (*b*) 5·5 g., b. p. 70—72°/0·2 mm., n_D^{20} 1·4849, probably a mixture of mono- and di-acetyl derivatives (Found: S, 18·3; thiol-S, 1·0; Ac, 32·4. Calc. for $C_6H_{12}O_2S$: S, 21·6; Ac, 29·05%. Calc. for $C_8H_{14}O_3S$: S, 16·8; Ac, 45·3%). The results could not be reproduced, later experiments giving very much smaller yields of the higher-boiling fractions.

(iii) A mixture of crotyl alcohol (10 g.), thiolacetic acid (12 g.), and ascaridole (0·1 g.) was heated on the steam-bath under reflux for 12 hr. and then distilled, to give mainly low-boiling material (10 g.), b. p. 50—70°/50 mm., redistillation of which furnished crotyl acetate (7 g.), b. p. 130—131°/765 mm., n_D^{20} 1·4150 (Found: sap. equiv., 113. Calc. for $C_6H_{10}O_2$: equiv., 114). The high-boiling residue on distillation gave a main fraction (1·2 g.), b. p. 65—66°/0·5 mm., n_D^{20} 1·4875—1·4955 (Found: S, 19·5; Ac, 47·5%), from which no homogeneous product could be obtained.

2-Acetoxyethyl Allyl Ether.—Ethylene chlorohydrin (60 g.) in allyl alcohol (50 c.c.) was added slowly to a boiling solution of sodium (18 g.) in allyl alcohol (200 c.c.), under reflux.

When the addition was complete the mixture was boiled for a further 90 min. and then cooled, neutralised with carbon dioxide, filtered, and evaporated to an oil, distillation of which gave allyl 2-hydroxyethyl ether (42 g.), b. p. 165—170°, n_D^{17} 1·4367. Hurd and Pollack (*J. Amer. Chem. Soc.*, 1938, **60**, 1905) record b. p. 63—64°/18 mm., n_D^{20} 1·4356, for the product obtained by interaction of allyl bromide, ethylene glycol, and sodium.

Treatment of this ether (40 g.) with acetic anhydride (40 c.c.) and a trace of sulphuric acid for 24 hr. at room temperature, followed by dilution with water and extraction with ether, gave *2-acetoxyethyl allyl ether* (41 g.), b. p. 175—177°, n_D^{21} 1·4255 (Found: C, 58·4; H, 8·5. $C_7H_{12}O_3$ requires C, 58·3; H, 8·4%).

2-Acetoxyethyl 2 : 3-Dibromopropyl Ether.—Bromine (50 g.) in carbon tetrachloride (100 c.c.) was added during 2 hr. to a stirred solution of the acetoxy-ether (41 g.) in carbon tetrachloride (100 c.c.) at 0°. Distillation then gave 62 g., b. p. 130—145°/1 mm., n_D^{25} 1·5050—1·4990; redistillation of a middle fraction furnished *2-acetoxyethyl 2 : 3-dibromopropyl ether*, b. p. 93°/0·05 mm., n_D^{19} 1·5055 (Found: C, 27·95; H, 4·2; Br, 51·8. $C_7H_{12}O_3Br_2$ requires C, 27·65; H, 4·0; Br, 52·6%).

2-Acetoxyethyl 2 : 3-Bisacetylthiopropyl Ether.—The dibromo-compound (40 g.) was boiled under reflux with potassium thiolacetate (37 g.) and thiolacetic acid (0·5 g.) in ethanol (200 c.c.) for 3 hr. Isolation in the usual way gave an oil which was fractionally distilled, 32·1 g. being collected at b. p. 165—168°/0·002 mm. (n_D^{21} 1·5090—1·5137). Redistillation of the middle fraction (13·9 g.) gave *2-acetoxyethyl 2 : 3-bisacetylthiopropyl ether*, b. p. 134°/0·0001 mm., n_D^{18} 1·5097 (Found: C, 44·8; H, 6·4; S, 21·5. $C_{11}H_{18}O_5S_2$ requires C, 44·9; H, 6·2; S, 21·8%). Light absorption in EtOH: max., 2290 Å; ε 8800.

2 : 3-Dimercaptopropyl 2-Hydroxyethyl Ether.—The triacetyl compound (12 g.) was stirred at room temperature with 2N-sodium hydroxide (200 c.c.) under nitrogen for 2 hr., and then extracted with light petroleum (b. p. 100—120°) to remove unchanged material. The aqueous solution was acidified with hydrochloric acid and extracted with ether to give, on evaporation, crude 2 : 3-dimercaptopropyl 2-hydroxyethyl ether (2·3 g.). This could not be completely purified; the distilled material, b. p. 85—87°/0·0003 mm., n_D^{18} 1·5402, was cloudy, probably because of slight decomposition (Found: S, 35·5; thiol-S, 34·6. Calc. for $C_5H_{12}O_2S_2$: S, 38·1%), but treatment with excess of phenyl *iso*cyanate at 100° for 6 hr. yielded the *trisphenylurethane*, which after recrystallisation from light petroleum (b. p. 100—120°) had m. p. 148° (Found: C, 59·6; H, 5·6; N, 7·9. $C_{26}H_{27}O_5N_3S_2$ requires C, 59·4; H, 5·2; N, 8·0%).

*2-Acetoxy*cyclo*hexyl Allyl Ether.*—*cyclo*Hexene oxide (56 g.) and a solution of sodium (2 g.) in allyl alcohol (120 c.c.) were boiled together under reflux for 30 hr. The solution was cooled, neutralised with carbon dioxide, diluted with water, and extracted with ether, to give *allyl 2-hydroxy*cyclo*hexyl ether* (67 g.), b. p. 59°/0·05 mm., n_D^{20} 1·4711 (Found: C, 69·2; H, 10·5. $C_9H_{16}O_2$ requires C, 69·2; H, 10·3%). The 3 : 5-*dinitrobenzoate*, after recrystallisation from benzene–light petroleum (b. p. 100—120°), had m. p. 84° (Found: C, 55·0; H, 5·4; N, 8·1. $C_{16}H_{18}O_7N_2$ requires C, 54·85; H, 5·2; N, 8·0%). Acetylation of the hydroxy-compound (60 g.) with acetic anhydride (70 c.c.) and a trace of sulphuric acid gave *2-acetoxy*cyclo*hexyl allyl ether* (68 g.), b. p. 63°/0·3 mm., n_D^{19} 1·4557 (Found: C, 66·6; H, 9·2. $C_{11}H_{18}O_3$ requires C, 66·6; H, 9·15%).

*2-Acetoxy*cyclo*hexyl 2 : 3-Dibromopropyl Ether.*—The above acetoxy-ether (68 g.) in carbon tetrachloride (100 c.c.) was treated with bromine (55 g.) in carbon tetrachloride (100 c.c.) for 2 hr. at 0°, and gave the *dibromide* (98 g.), b. p. 135°/0·0004 mm., n_D^{16} 1·5117 (Found: C, 37·4; H, 5·3; Br, 43·3. $C_{11}H_{18}O_3Br_2$ requires C, 36·9; H, 5·1; Br, 44·6%).

*2-Acetoxy*cyclo*hexyl 2 : 3-Bisacetylthiopropyl Ether.*—The dibromide (50 g.) was boiled under reflux with potassium thiolacetate (35 g.) in ethanol (300 c.c.) for 10 hr. Isolation by the usual procedure gave a crude bisthiolacetate (42 g.) which could not be distilled in quantity, owing to decomposition. Distillation of a small sample gave *2-acetox*y cyclo*hexyl 2 : 3-bisacetylthiopropyl ether*, b. p. 200° (bath)/0·0001 mm., n_D^{14} 1·5151 (Found: C, 51·5; H, 7·0; S, 18·0. $C_{15}H_{24}O_5S_2$ requires C, 51·7; H, 6·9; S, 18·4%). Light absorption in EtOH: max., 2280 Å; ε 7300.

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