Dithiols. Part XIII. The Alkaline Hydrolysis of Acetylated Vicinal Hydroxy-thiols.*

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[Reprint Order No. 4825.]

The rates of liberation of acetyl and of thiol groups have been determined during the alkaline hydrolysis of partly and fully acetylated derivatives of 2-mercaptoethanol, *trans*-2-mercapto*cyclo*hexanol, *trans*-2-mercapto*cyclo*pentanol, and 2 : 3-dimercaptopropanol. The degree of cyclisation to the corresponding 1 : 2-sulphide is measured by the deficiency in thiol value when deacetylation is complete, and varies from 25 to 90% of the total reaction; with *S*-acetyl derivatives cyclisation is always preceded by migration of acetyl from sulphur to oxygen. The formation of the cyclic sulphide probably occurs by intramolecular displacement of the acetoxy-group (alkyl–oxygen fission) by the neighbouring $-S^-$.

Attempts to synthesise *cis*-2-mercapto*cyclo*hexanol from *trans*-2-acetylthio*cyclo*hexyl toluene-*p*-sulphonate were unsuccessful.

IN Part XII* it was shown that the alkaline hydrolysis of certain partly or fully acetylated hydroxy-thiols gave not only the parent hydroxy-thiols but also cyclic sulphides, the latter often preponderating :

$$\text{R·CH(SH)·CH(OH)·R}' \longleftarrow \text{R·CH(SAc)·CH(OAc)·R}' \longrightarrow \text{R·CH}\overset{\text{S}}{\diagdown\diagup}\text{CH·R}'$$

It was not possible, from the evidence than presented, to prove the precise course of the overall reaction, but the observation that *cyclo*hexene sulphide, for example, was formed from both the *O*- and the *S*-monoacetyl derivative of *trans*-2-mercapto*cyclo*hexanol suggested that only one of these compounds was the true precursor of the sulphide, and that the other underwent preliminary isomerisation. The purpose of the work now to be described was to study the reaction quantitatively by measuring the rates of liberation of acetyl and thiol groups during the alkaline hydrolysis of various partly or fully acetylated vicinal hydroxy-thiols, and so detect any acetyl migration and determine the proportion of cyclisation for each compound. Non-vicinal compounds, which behave differently, are discussed in the succeeding paper.

The method involved treatment of the derivative with excess of 0·1N-standard alkali in aqueous dioxan at 0°, removal of samples, quenching of the reaction by immediate acidification with standard acid,† back-titration with alkali to determine the acetyl liberated, and finally reacidification and titration with iodine to determine the thiol content of the solution. The formation of a cyclic sulphide involves the disappearance of a thiol group which would otherwise be free; hence any deficiency in the final thiol value from that which would be attained by complete normal hydrolysis corresponds to the amount of cyclisation which has occurred. Apart from polymerisation of the ethylene sulphide, which would not affect the result, the only likely secondary reaction would be ring-fission by free thiol, which is known to occur under vigorous conditions with, *e.g.*, *cyclo*hexene sulphide (Miles and Owen, *loc. cit.*). Under the present conditions such fission probably does not occur to any appreciable extent, but even if it did the result would not be vitiated, because in the reaction

$$\text{R·SH} + \text{>C}\overset{\text{S}}{\diagdown\diagup}\text{C<} \longrightarrow \text{>C(SR)·C(SH)<}$$

there is no change in the number of thiol groups.

The results with 2-acetylthioethanol (II) are shown in Fig. 1*a*. The initial rise in thiol value occurs much more rapidly than the liberation of the acetyl group, and clearly indic-

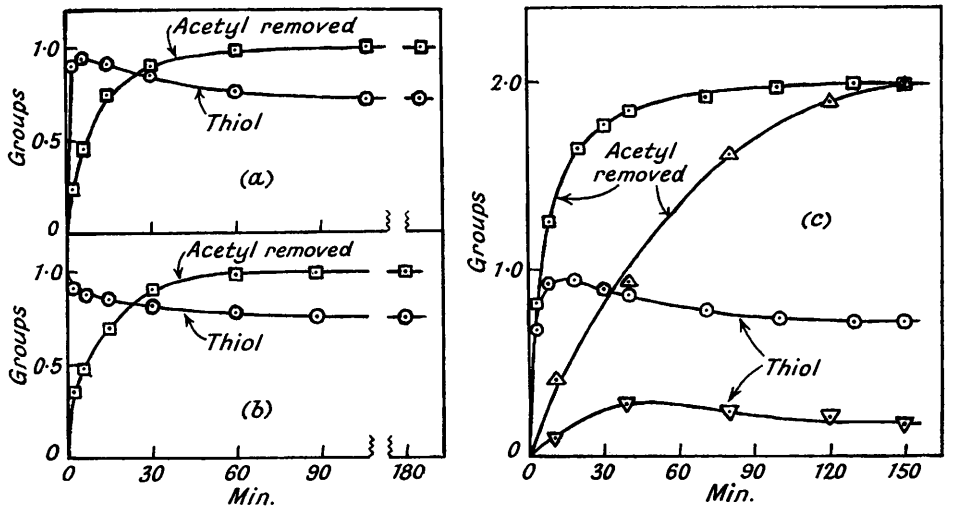
* Part XII, Miles and Owen, *J.*, 1952, 817.

† Acid-catalysed hydrolysis of simple acetates and thiolacetates is very slow compared with alkaline hydrolysis (Böhme and Schran, *Ber.*, 1949, **82**, 453; Schaefgen, *J. Amer. Chem. Soc.*, 1948, **70**, 1308; Rylander and Tarbell, *ibid.*, 1950, **72**, 3021; Noda, Kuby, and Lardy, *ibid.*, 1953, **75**, 913), and control experiments confirmed that no further hydrolysis or migration occurred after acidification.

ates a rearrangement to the *O*-acetate (III) which then undergoes normal hydrolysis (70%) to 2-mercaptoethanol accompanied by cyclisation (30%) to ethylene sulphide (IV); this result is similar, within experimental error, to that observed with 2-mercaptoethyl acetate itself (Fig. 1*b*). The acetyl migration was confirmed by brief treatment of (II) with cold aqueous sodium carbonate, (III) being then isolated in 50% yield. Such rearrangement under mild alkaline conditions has not previously been reported for thiolacetates, although the migration of an acetyl group from sulphur to oxygen has been observed when (II) and similar compounds are heated, especially in the presence of acids (Nylen and Olsen, *Svensk Kem. Tidskr.*, 1941, **53**, 274; Sjöberg, *Ber.*, 1941, **74**, 64; 1942, **75**, 13; Miles and Owen, *loc. cit.*).

With 2-acetylthioethyl acetate (I) rigid interpretation of the result (Fig. 1*c*) is difficult because of the number of possible reactions involved. The almost complete initial liberation of the thiol group suggests at first sight that the *S*-acetyl group is removed first, but taking into account the rapid migration observed with 2-acetylthioethanol the same result

FIG. 1. *Derivatives of 2-mercaptoethanol.*



(*a*) $CH_2(SAc)\cdot CH_2\cdot OH$, 0·0144M. (*b*) $CH_2(SH)\cdot CH_2\cdot OAc$, 0·0123M.
(*c*) $CH_2(SR)\cdot CH_2\cdot OR$ ⊡ ⊙ R = Ac; 0·0131M. △ ▽ R = Bz; 0·0070M.

would evidently arise from a preferential removal of the *O*-acetyl group to give (II), followed by rapid rearrangement to (III). Experimentally, it is impossible to distinguish between these alternatives, and it is probable that both are involved; for unifunctional compounds

$$\underset{\text{(I)}}{CH_2(SAc)\cdot CH_2\cdot OAc} \longrightarrow \underset{\text{(II)}}{CH_2(SAc)\cdot CH_2\cdot OH} \longrightarrow \underset{\text{(III)}}{CH_2(SH)\cdot CH_2\cdot OAc} \longrightarrow \underset{\text{(IV)}}{CH_2{-}CH_2 \atop \quad S}$$

the rate of alkaline hydrolysis of a thiolester is usually about the same as that of the corresponding *O*-ester (Böhme and Schran, *loc. cit.*; Schaefgen, *loc. cit.*; Rylander and Tarbell, *loc. cit.*), and although the presence of a neighbouring acetylthio-group probably facilitates the removal of an acetoxy-group by alkyl–oxygen fission (see discussion on mechanism, below) its effect on normal hydrolysis, which presumably takes place by acyl–oxygen fission, is likely to be less pronounced.

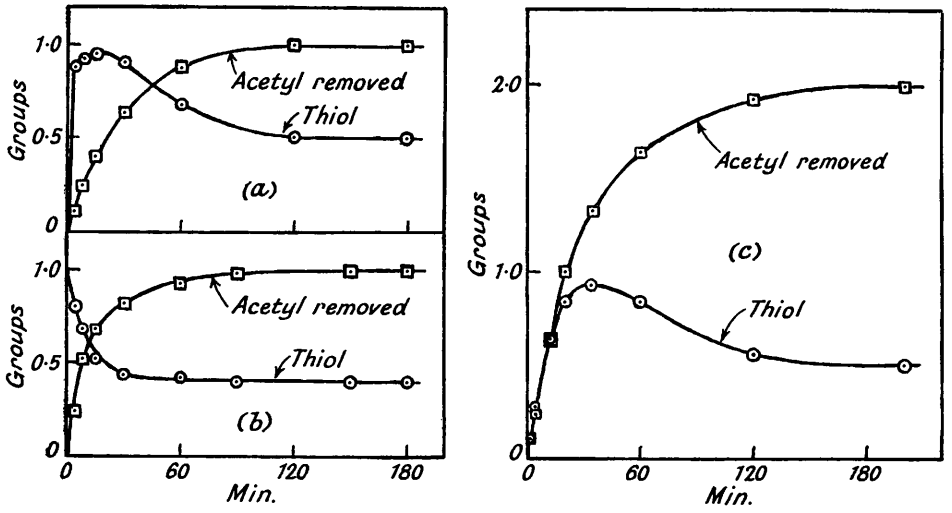
To obtain some preliminary evidence on the possible extension of the cyclisation reaction to other acyl derivatives the dibenzoyl derivative of 2-mercaptoethanol was examined. Under the same conditions as for the diacetyl analogue the rate was much slower, but the final thiol value indicated 85% of cyclisation (Fig. 1*c*). This enhanced degree of elimination is paralleled by the observation (Linstead, Owen, and Webb, *J.*, 1953, 1211) that

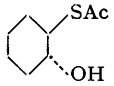
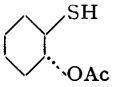
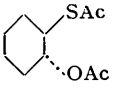
under alkaline conditions β-benzoyloxy-esters give a higher proportion of unsaturated acids than do the β-acetoxy-analogues. The di-*p*-nitrobenzoyl derivative was also prepared, but its low solubility precluded its examination under the standard conditions; qualitative tests showed that much ethylene sulphide was formed on treatment with alkali.

The hydrolyses of the *S*-acetyl, *O*-acetyl, and diacetyl derivatives of *trans*-2-mercapto-*cyclo*hexanol (Fig. 2) followed the same general pattern as those of the mercaptoethanol analogues, and though the acetyl migration (Fig. 2*a*) is slower than that observed with 2-acetylthioethanol (Fig. 1*a*), the degree of cyclisation with the *cyclo*hexane compounds, 50—60%, is considerably greater, probably because of more favourable steric factors.

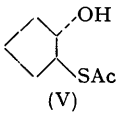
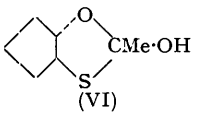
*cyclo*Pentane compounds often undergo substitution and elimination much more rapidly than their *cyclo*hexane analogues (see, *e.g.*, Owen and Smith, *J.*, 1952, 4026), and it was of interest to find whether this applied also to the cyclisation reaction being studied.

FIG. 2. *Derivatives of 2-mercapto*cyclo*hexanol.*



(a)  0·0056M. (b)  0·0074M. (c)  0·0079M.

trans-2-Acetylthio*cyclo*pentanol (V) was synthesised by ring-fission of *cyclo*pentene oxide with thiolacetic acid; on acetylation it gave the diacetyl compound, whilst deacetylation with cold methanolic hydrogen chloride yielded *trans*-2-mercapto*cyclo*pentanol and some *cyclo*pentene sulphide. Monoacetylation of the hydroxy-thiol under acid conditions gave *trans*-2-mercapto*cyclo*pentyl acetate (VII). *cyclo*Pentene sulphide was isolated in 20% yield after treatment of (V) with hot aqueous sodium carbonate, much polymer also being formed. Quantitative hydrolysis showed (Fig. 3) that deacetylation of the three acetyl derivatives was much faster than for the *cyclo*hexane analogues. The greater degree of cyclisation undergone by the *O*-acetyl compared with the *S*-acetyl compound agrees with the supposition that the former is the true precursor of the cyclic sulphide; that this


(V)

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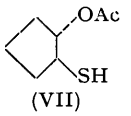
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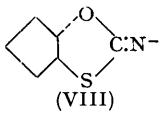
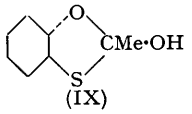
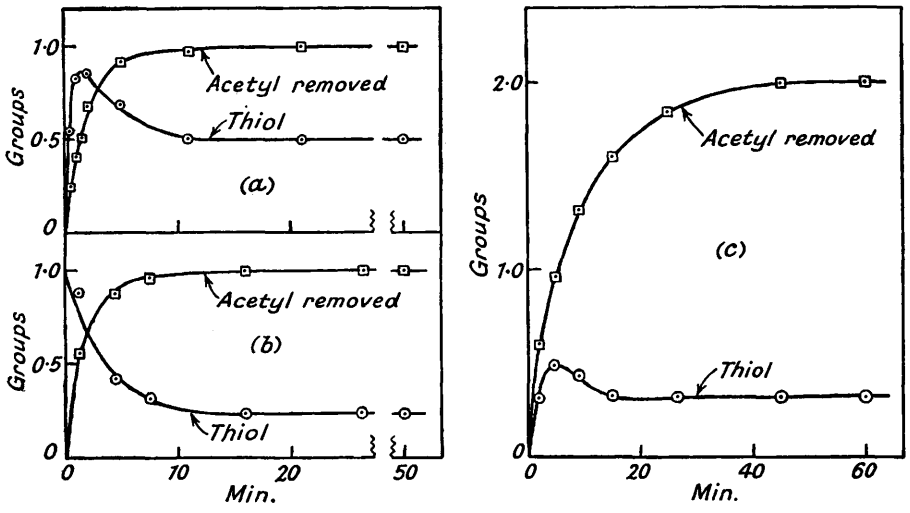

(VIII)

(IX)

differentiation was less marked in the *cyclo*hexane series, and not evident at all with the derivatives of 2-mercaptoethanol, indicates that in *trans*-2-acetylthio*cyclo*pentanol direct hydrolysis of the *S*-acetyl group competes with acetyl migration more effectively than in

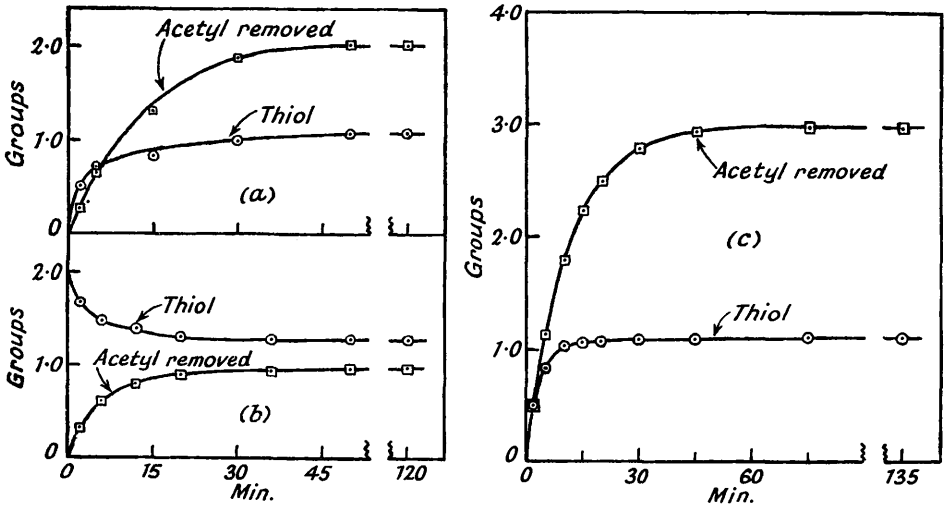
the series previously considered. The fact that migration takes place at all is perhaps surprising, because if it occurs through the usual orthoester intermediate it must involve the

FIG. 3. *Derivatives of 2-mercaptocyclopentanol.*



formation of the strained system (VI) containing two *trans*-fused five-membered rings, whereas in the *cyclo*hexane series a strainless intermediate (IX) is possible. However, although (VI) may be formed less readily than (IX) its highly strained nature probably

FIG. 4. *Derivatives of 2 : 3-dimercaptopropanol.*

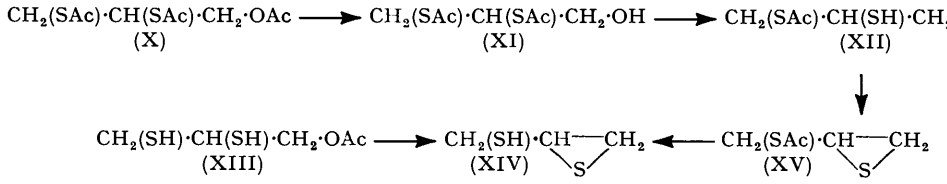


(*a*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OH$, 0·0103M. (*b*) $CH_2(SH)\cdot CH(SH)\cdot CH_2\cdot OAc$, 0·0110M.
(*c*) $CH_2(SAc)\cdot CH(SAc)\cdot CH_2\cdot OAc$, 0·0082M.

results in very rapid rearrangement to the *O*-acetate (VII), whereas the *cyclo*hexane compound (IX), being more stable, would rearrange more slowly; the overall result could well be the observed more rapid migration in the *cyclo*pentane series. In his investigations into the preparation of ethylene sulphides by reaction of ethylene oxides with potassium

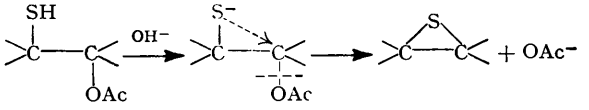
thiocyanate, van Tamelen (*J. Amer. Chem. Soc.*, 1951, **73**, 3444; compare Harding, Miles, and Owen, *Chem. and Ind.*, 1951, 887) postulated the intermediate existence of cyclic oxathiolans, the formation of which was later confirmed by Price and Kirk (*J. Amer. Chem. Soc.*, 1953, **75**, 2396). The failure of the reaction with *cyclo*pentene oxide was attributed by van Tamelen to non-formation of the strained intermediate (VIII), and the structural conditions necessary for the *trans*-fused bicyclic system are evidently critical. It seems likely that even (VI) is not formed in acid solution as attempts failed to isomerise (V) to (VII) by acid catalysis, a method which is successful with 2-acetylthio*cyclo*hexanol.

The hydrolyses of the di-*S*-acetyl, *O*-acetyl, and triacetyl derivatives of 2 : 3-dimercaptopropanol (BAL) are shown in Fig. 4. The relative positions of the curves in Fig. 4*a* prove the occurrence of acetyl migration in 2 : 3-bisacetylthiopropanol (XI), and since mild alkaline hydrolysis of this compound gives 3-acetylthiopropylene sulphide (XV) in high yield (Miles and Owen, *loc. cit.*) it follows that migration occurs from the secondary acetylthio-group, with formation of (XII), which then cyclises.* The triacetyl derivative (X) also gives (XV) under mild conditions, and the first stage in its hydrolysis is probably the removal of the *O*-acetyl group to give (XI); the behaviour of the three acetyl derivatives can thus be summarised as follows :



The lower degree of cyclisation (70%) observed with the *O*-acetate, compared with the di-*S*-acetyl compound (90%) is contrary to the result for the *cyclo*pentane derivatives discussed above, and is probably a consequence of the fact that with the BAL compounds two cyclisation reactions are involved. The *O*-acetate (XIII) contains two free thiol groups, each of which in alkaline solution will exist partly as an anion; the proportion of secondary thiol anion (which, on the basis of the mechanism proposed below, is necessary for cyclisation to occur) will therefore be less than in the alkaline solution of (XII), where the whole of the ionised thiol is in the form suitable for cyclisation.

The formation of the ethylene sulphide ring from acetylated vicinal hydroxy-thiols involves elimination of the acetoxy-group by alkyl–oxygen fission, which is very rare, particularly in alkaline solution (cf. Linstead, Owen, and Webb, *loc. cit.*). In general, this type of fission is facilitated by electron-donating groups in the " alkyl " portion (Balfe, Doughty, Kenyon, and Poplett, *J.*, 1942, 605), and since the transference of electrons in a direction other than that of its covalent bonds occurs much more readily with sulphur than with oxygen (Baddeley, *J.*, 1950, 663) this tendency could provide the necessary driving force for an intramolecular displacement :



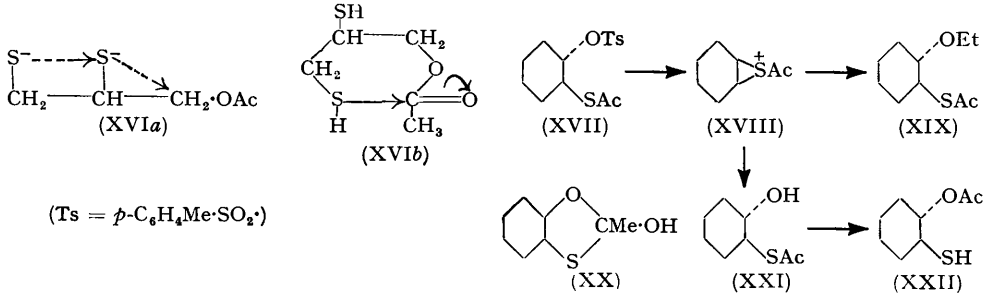
With a monoester of a 1 : 2-diol, epoxide formation only occurs when the ester is of the type which normally undergoes alkyl–oxygen fission (*e.g.*, toluene-*p*-sulphonate, halide); the driving force required is then less, and can be provided even by a neighbouring $-O^-$.

The electron-donating properties of sulphur may also be the cause of the unexpectedly high degree of cyclisation which occurs in the derivatives of 2 : 3-dimercaptopropanol compared with those of 2-mercaptoethanol, in that electron release towards $C_{(1)}$ from the attacking thiol group on $C_{(2)}$ would be reinforced in the dithiol by the similar properties

* Although acetyl migration could occur from the primary group in (XI) (compare 3-acetylthiopropanol, Part XIV, following paper) the derivation of (XII) by two successive migrations, 3 ⟶ 1, 2 ⟶ 3, although possible, appears unlikely.

of the thiol group on $C_{(3)}$, as shown in (XVI*a*). An alternative suggestion, by Dr. L. M. Jackman of this Department, is that in 2 : 3-dimercaptopropyl acetate the sulphur atom on $C_{(3)}$ can chelate with the carbonyl-carbon atom (carrying a fractional positive charge owing to the normal polarisation of the carbonyl group) to give (XVI*b*), in which the thiol group on $C_{(2)}$ may be held in a relatively favourable position for rear attack on $C_{(1)}$. Further evidence on the special reactivity of acetylated hydroxy-dithiols is presented in the succeeding paper.

Formation of the cyclic sulphides from the *trans-cyclo*pentane and *trans-cyclo*hexane derivatives involves an inversion of configuration at the carbon atom carrying the *O*-acetyl group, and it would therefore be of considerable interest to examine the corresponding *cis*-compounds. Winstein, Hess, and Buckles (*J. Amer. Chem. Soc.*, 1942, **64**, 2796) have shown that the monoacetate of *cis-cyclo*hexane-1 : 2-diol can be obtained by reaction of *trans*-2-acetoxy*cyclo*hexyl toluene-*p*-sulphonate with calcium carbonate in moist ethanol. *trans*-2-Acetylthio*cyclo*hexanol was therefore converted into the toluene-*p*-sulphonate (XVII) and treated with those reagents, but the product was 2-acetylthio*cyclo*hexyl ethyl ether (XIX), from which ethyl 2-mercapto*cyclo*hexyl ether was obtained by alkaline hydrolysis. Ether formation was not observed by Winstein, although Owen and Saharia (*J.*, 1953, 2582) obtained a mixture of *cis*-monoacetate and monoacetate-ethyl ether from a similar reaction with *trans*-2-acetoxy*cyclo*heptyl toluene-*p*-sulphonate. In an attempt to circumvent the difficulty, (XVII) was treated with calcium carbonate in moist dioxan, but it gave only *trans*-2-mercapto*cyclo*hexyl acetate (XXII). The different course taken by (XVII) in comparison with the oxygen analogue suggests that elimination of the toluene-*p*-sulphonyloxy-group leads to the sulphonium structure (XVIII) rather than the cyclic *cis*-orthoacetate (XX), which would be the expected intermediate for the formation of a *cis*-monoacetyl derivative; ring-fission of (XVIII) by OEt^- or OH^- would then give (XIX) or (XXI) respectively, and (XXI) would rapidly isomerise to (XXII).



Experimental

The following were prepared by the methods indicated: 2-Acetylthioethanol, b. p. 95°/15 mm., n_D^{20} 1·4720; and 2-mercaptoethyl acetate, b. p. 55°/13 mm., n_D^{17} 1·4658 (Nylen and Olsen, *Svensk Kem. Tidsk.*, 1941, **53**, 274).

2-Acetylthioethyl acetate, b. p. 104°/15 mm., by treatment of 2-mercaptoethanol with excess of acetic anhydride and a trace of sulphuric acid (cf. Rojahn and Lemme, *Arch. Pharm.*, 1925, **263**, 612).

trans-2-Acetylthio*cyclo*hexanol, b. p. 85°/0·002 mm., n_D^{18} 1·5204; and *trans*-2-mercapto-*cyclo*hexyl acetate, b. p. 110°/16 mm., n_D^{20} 1·4870 (Miles and Owen, *J.*, 1952, 817).

trans-2-Acetylthio*cyclo*hexyl acetate, b. p. 132°/10 mm., n_D^{20} 1·4800, in 80% yield from *trans*-2-mercapto*cyclo*hexyl acetate and acetic anhydride–sulphuric acid (cf. Culvenor, Davies, and Heath, *J.*, 1949, 282).

2 : 3-Bisacetylthiopropanol, $\lambda_{max.}$ 2800 Å, ε 7800 (Miles and Owen, *loc. cit.*).

2 : 3-Dimercaptopropyl acetate, b. p. 93—94°/0·8 mm., n_D^{15} 1·5245 (Pavlic, Lazier, and Signaigo, *J. Org. Chem.*, 1949, **14**, 59).

2 : 3-Bisacetylthiopropyl acetate, b. p. 124°/0·1 mm., n_D^{21} 1·5140 (Evans, Fraser, and Owen, *J.*, 1949, 248).

Isomerisation of 2-Acetylthioethanol with Aqueous Sodium Carbonate.—2-Acetylthioethanol (2 g.) was stirred at 0° for 8 min. with N-sodium carbonate (200 c.c.). The mixture was then poured into 2N-hydrochloric acid (90 c.c.) at −10°, and quickly extracted with ether (4 × 50 c.c.). Evaporation of the dried ($MgSO_4$) extracts, and distillation of the residue, gave 2-mercaptoethyl acetate (0·89 g.), b. p. 63°/12 mm., n_D^{19} 1·4614 (Found : thiol-S, 26·6. Calc. for $C_4H_8O_2S$: thiol-S, 26·7%). Miles and Owen (*loc. cit.*) record n_D^{20} 1·4612.

2-Benzoylthioethyl Benzoate.—To a solution of 2-mercaptoethanol (5 g.) in pyridine (20 c.c.) at 0° benzoyl chloride (20 g.) was slowly added. The mixture was kept at 0° for 5 hr. and then diluted with water and extracted with chloroform. The extracts were washed successively with 2N-sulphuric acid, water, aqueous sodium hydrogen carbonate, and water, and then dried (Na_2SO_4), and evaporated to an oil. Distillation gave a main fraction (6 g.) of the *dibenzoyl* derivative, b. p. 167—177°/0·001 mm., n_D^{18} 1·5965, which solidified, but had m. p. <30° and could not be recrystallised (Found : C, 66·9; H, 4·9; S, 11·0. $C_{16}H_{14}O_3S$ requires C, 67·1; H, 4·9; S, 11·2%). Light absorption in EtOH : max., 2270, 2360, 2640 Å; ε 20,800, 18,600, 8900.

2-p-*Nitrobenzoylthioethyl* p-*Nitrobenzoate.*—Similar treatment of 2-mercaptoethanol (2 g.) in pyridine (50 c.c.) at 0° with *p*-nitrobenzoyl chloride (10·5 g.) for 48 hr. gave a solid when the reaction mixture was diluted with water. Recrystallisation from benzene–light petroleum (b. p. 40—60°) gave the *di*-p-*nitrobenzoate*, flattened needles, m. p. 145° (Found : C, 51·1; H, 3·3; N, 7·6. $C_{16}H_{12}O_7N_2S$ requires C, 51·1; H, 3·2; N, 7·45%). Light absorption in ethanol : max., 2270, 2510, 2580—2660 Å; ε 10,000, 20,700, 24,100.

trans-2-*Acetylthio*cyclo*pentanol.*—A mixture of *cyclo*pentene oxide (Owen and Smith, *loc. cit.*) (10·3 g.) and thiolacetic acid (9·8 g.) was kept at room temperature for 4 davs and then distilled, to give trans-2-*acetylthio*cyclo*pentanol* (14·4 g.), b. p. 69°/0·001 mm., n_D^{17} 1·5133 (Found : C, 52·2; H, 7·6; S, 19·5; thiol-S, 0. $C_7H_{12}O_2S$ requires C, 52·5; H, 7·55; S, 20·0%). Light absorption in ethanol : max., 2350 Å; ε 4000. The α-*naphthylurethane*, after recrystallisation from light petroleum (b. p. 100—120°), had m. p. 118° (Found : C, 65·5; H, 6·0; N, 4·4. $C_{18}H_{19}O_3NS$ requires C, 65·6; H, 5·8; N, 4·25%).

Treatment of the thiolacetate with acetic anhydride–sulphuric acid gave trans-2-*acetylthio*-cyclo*pentyl acetate*, b. p. 90°/0·5 mm., n_D^{23} 1·4888 (Found : C, 53·1; H, 7·0; S, 15·7. $C_9H_{14}O_3S$ requires C, 53·45; H, 7·0; S, 15·8%). Light absorption in ethanol : max., 2350 Å; ε 4400.

*Attempted Isomerisation of 2-Acetylthio*cyclo*pentanol.*—(i) The compound (1 g.) was heated at 100° with acetic acid (0·1 c.c.) for 12 hr. Distillation gave only unchanged material (0·75 g.), b. p. 70°/0·01 mm., n_D^{16} 1·5131, which contained no free thiol.

(ii) No free thiol was present in the solution after treatment of the compound (0·7 g.) with ethereal 0·9N-hydrogen chloride (25 c.c.) for 18 hr. at room temperature.

(iii) The compound (1 g.) was shaken at room temperature with aqueous N-sodium carbonate (200 c.c.) for 5 min. under nitrogen. Acidification with hydrochloric acid and extraction with ether gave unchanged material (0·85 g.), b. p. 75—76°/0·2 mm., n_D^{23} 1·5129. Similar results were obtained by treatment for 25 min.

trans-2-*Mercapto*cyclo*pentyl Acetate.*—A solution of 2-acetylthio*cyclo*pentanol (12 g.) in methanolic 0·8% hydrogen chloride (40 c.c.) was kept at room temperature for 4 days. After removal of the solvent and hydrogen chloride under reduced pressure at room temperature, the residue was distilled, to give *cyclo*pentene sulphide (0·95 g.), b. p. 45°/15 mm., n_D^{17} 1·5262, and 2-mercapto*cyclo*pentanol (2·5 g.), b. p. 97°/15 mm., n_D^{17} 1·5180 (Found : thiol-S, 27·2. Calc. for $C_5H_{10}OS$: S, 27·1%). Van Tamelen (*loc. cit.*) records b. p. 69—70°/65 mm., n_D^{25} 1·5222, for *cyclo*pentene sulphide, and b. p. 92—94°/15 mm., n_D^{25} 1·5190, for the hydroxy-thiol.

Treatment of the hydroxy-thiol with phenyl *iso*cyanate gave the *bisphenylurethane*, which was difficult to purify; after several recrystallisations from light petroleum (b. p. 100—120°) it had m. p. 162° (Found : C, 64·5; H, 5·9; N, 8·3. $C_{19}H_{20}O_3N_2S$ requires C, 64·0; H, 5·7; N, 7·9%).

Selective monoacetylation of the hydroxy-thiol (2·1 g.) at room temperature with acetic anhydride (1·9 g.) and sulphuric acid catalyst in the usual way gave, after two distillations, trans-2-*mercapto*cyclo*pentyl acetate* (1·0 g.), b. p. 93—95°/15 mm., n_D^{14} 1·4845 (Found : thiol-S, 19·5; Ac, 27·0. $C_7H_{12}O_2S$ requires S, 20·0; Ac, 26·9%).

Formation of cyclo*Pentene Sulphide by Alkaline Deacetylation of* trans-2-*Acetylthio*cyclo-*pentanol.*—The thiolacetate (3·2 g.) was " steam-distilled " at 60° under reduced pressure with sodium hydrogen carbonate (3 g.) in water (30 c.c.). The solution rapidly became cloudy and oily drops appeared in the distillate. Extraction of the latter with ether, evaporation of the dried ($CaCl_2$) extracts, and distillation of the residue gave *cyclo*pentene sulphide (0·4 g., 20%),

b. p. 125—130°, n_D^{11} 1·5240; another fraction (0·2 g.), b. p. 130—170°, n_D^{11} 1·5115, probably contained some isomerised starting material. The cyclic sulphide was characterised by treatment of a portion (0·1 g.) with methyl iodide (1 g.) for 4 days at room temperature. The trimethylsulphonium iodide (0·1 g.) was collected, washed with acetone, and recrystallised from ethanol; it had m. p. 213°. Culvenor, Davies, and Heath (*loc. cit.*) give m. p. 215°.

Quantitative Deacetylations.—Phenolphthalein, the usual indicator for determination of acetyl values, is unsatisfactory for thiolacetates because of the acidity of the free thiol produced. Conductimetric experiments, in which standard hydrochloric acid containing appropriate amounts of sodium acetate and 2-mercaptoethanol was titrated with sodium hydroxide, showed that the true end-point would be given by an indicator changing colour in the region pH 6·0—7·5; bromocresol-purple was found to be satisfactory, its suitability being confirmed by control experiments in which it showed the same end-point in both the presence and the absence of thiol.

Distilled water was boiled, and cooled under nitrogen before use. Dioxan was purified by successive treatments with hydrochloric acid, potassium hydroxide, and sodium (Vogel, " Textbook of Practical Organic Chemistry," Longmans, 2nd edn., p. 175) and was finally distilled over sodium. The hydrolysing medium, *ca.* 0·1N-sodium hydroxide in aqueous dioxan (1 : 1 by volume), was made and stored under nitrogen, and for each run 250 c.c. of this solution were introduced into the 500-c.c. reaction flask, surrounded with a bath of ice and water, and fitted with a stirrer, thermometer, and nitrogen-inlet. Air was displaced with purified nitrogen, previously saturated with dioxan–water vapour by passage through some of the hydrolysing solution at 0° (neglect of this precaution resulted in appreciable errors caused by volatilisation of solvent from the reaction vessel), a steady stream of the gas being thereafter maintained throughout the run. Stirring was begun, and when the temperature of the solution became constant at 0° the acetyl derivative (0·001—0·003 mole), weighed in a shallow glass tube, was tipped in, followed by the tube itself. At intervals, 25-c.c. portions were withdrawn by pipette, immediately run into 25 c.c. of *ca.* 0·12N-hydrochloric acid and back-titrated with 0·1N-sodium hydroxide, with bromocresol-purple as internal indicator, the titration being carried to the full violet colour. The same solution was then immediately acidified with 2N-hydrochloric acid and titrated with 0·1N-iodine, with starch as internal indicator. Each run was continued until both the acetyl and the thiol value became constant. A blank experiment was performed under the same conditions in the absence of the acetyl compound. In the calculations no allowance was made for the temperature of the samples withdrawn, control experiments having shown that the weight of solution removed by the pipette at 0° differed by less than 0·2% from that removed at 20°.

Control Hydrolysis Under Acid Conditions.—2-Acetylthioethanol (0·08 g.) was dissolved in 2N-hydrochloric acid and titrated with 0·1N-iodine in the presence of starch. The blue colour disappeared after a few minutes, and was restored by further titration, the process being repeated at intervals. The rate of liberation of thiol group thus determined was: 0·05 (25 min.); 0·08 (50 min.); 0·25 (3·5 hr.); 0·61 (21·5 hr.). Thus, in the quantitative experiments in alkaline solution no appreciable migration or hydrolysis occurs after the samples are acidified.

trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate.*—*trans*-2-Acetylthio*cyclo*hexanol (34 g.) and toluene-*p*-sulphonyl chloride (41 g.) in pyridine (200 c.c.) were kept at 0° for 20 hr. On the addition of crushed ice (150 g.) a dark oil separated; this was taken up in chloroform (2 × 100 c.c.), and the extracts were washed in the usual way, dried (Na_2SO_4), and evaporated to an oil. This was dissolved in benzene (100 c.c.), and diluted with light petroleum (b. p. 40—60°) to incipient turbidity at room temperature; after storage at 0° for 3 days the deposited crystals of the *toluene*-p-*sulphonate* (40 g.) were collected. Recrystallisation from the same solvent gave needles, m. p. 58° (Found: C, 54·4; H, 6·4; S, 19·5. $C_{15}H_{20}O_4S_2$ requires C, 54·9; H, 6·1; S, 19·5%).

Reaction of trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate with Calcium Carbonate.*—(i) The toluene-*p*-sulphonate (34 g.) was heated under reflux with calcium carbonate (10 g.), ethanol (200 c.c.), and water (1 c.c.) in a atmosphere of nitrogen for 24 hr. The precipitated calcium toluene-*p*-sulphonate and unchanged calcium carbonate were removed by filtration and washed with ethanol. The combined filtrate and washings were concentrated under reduced pressure to 75 c.c., then diluted with water and extracted with chloroform, to give 2-*acetylthio*cyclo*hexyl ethyl ether* (18·6 g.), b. p. 67—70°/0·0001 mm., n_D^{16} 1·4924 (Found: S, 15·45; thiol-S, nil; thiol-S after alkaline hydrolysis, 15·4; Ac, 21·2. $C_{10}H_{18}O_2S$ requires S, 15·8; Ac, 21·3%).

Treatment of the product (4 g.) with 2N-sodium hydroxide (250 c.c.) at room temperature for 20 hr. under nitrogen, followed by acidification, and extraction with light petroleum (b. p.

40—60°) gave *ethyl* 2-*mercapto*cyclo*hexyl ether* (2·8 g.), b. p. 48—50°/0·5 mm., n_D^{18} 1·4820 (Found : C, 60·1; H, 10·1; S, 19·9; thiol-S, 20·6. $C_8H_{16}OS$ requires C, 60·0; H, 10·1; S, 20·0%).

(ii) The toluene-*p*-sulphonate (5 g.) was heated under reflux with calcium carbonate (1·5 g.), water (0·3 c.c.), and dioxan (25 c.c.) for 4 hr. After filtration, and dilution of the filtrate and washings with water (150 c.c.), extraction with chloroform gave *trans*-2-mercapto*cyclo*hexy acetate (1·4 g.), b. p. 70°/0·01 mm., n_D^{17} 1·4884, characterised as the *phenylurethane*, m. p. 122° (from light petroleum, b. p. 80—100°) (Found : C, 61·1; H, 6·6; N, 5·0. $C_{15}H_{19}O_3NS$ requires C, 61·4; H, 6·5; N, 4·8%), undepressed on admixture with the derivative prepared from authentic mercapto-ester.

cyclo*Hexene Sulphide from* trans-2-*Acetylthio*cyclo*hexyl Toluene*-p-*sulphonate*.—The toluene-*p*-sulphonate (3 g.) was boiled under reflux with sodium hydrogen carbonate (4 g.) and water (20 c.c.) for 3 hr. Steam-distillation, and extraction of the distillate with light petroleum (b. p. 60—80°), gave *cyclo*hexene sulphide (0·05 g.), b. p. 75°/25 mm. A large amount of involatile polymeric material remained after the steam-distillation.

We thank the Department of Scientific and Industrial Research for a maintenance grant (J. S. H.), and the Medical Research Council for defraying the cost of some materials. Absorption spectra were determined by Mrs. A. I. Boston, and the analyses were carried out in the Organic Microanalytical Laboratory by Mr. F. H. Oliver and his staff.

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South Kensington, London, S.W.7. [*Received, November 23rd*, 1953.]