110. *Dithiols. Part IV. The Reaction of Toluene-*p*-sulphonates and Methanesulphonates with Potassium Thiolacetate: A New Method for the Preparation of Thiols.*

By J. H. Chapman and L. N. Owen.

The reaction of primary toluene-*p*-sulphonates, ROTs, with potassium thiolacetate, in ethanol or acetone, provides a useful method for the preparation of thiolacetates, RSAc, and thence, by hydrolysis, of thiols.

Secondary toluene-*p*-sulphonates show wide differences in behaviour. The simple compounds, *e.g.*, the *iso*propyl ester, and certain vicinal ditoluene-*p*-sulphonates where the adjacent group is primary, *e.g.*, the ditoluene-*p*-sulphonyl derivative of propane-1 : 2-diol, react normally, though the replacement of the secondary group requires conditions more vigorous than those necessary for reaction of the primary group. In more complex substances, *e.g.*, the 3-toluene-*p*-sulphonate of 1 : 2-5 : 6-di*iso*propylidene glucose, the reaction does not occur. *cyclo*Hexyl toluene-*p*-sulphonate gives mainly *cyclo*hexene; phenyl toluene-*p*-sulphonate is non-reactive.

Several methanesulphonates have been examined and, with one exception, their reactions follow the same course as with the corresponding toluene-*p*-sulphonates, but the yields are inferior.

The difference in reactivity between primary and secondary toluene-*p*-sulphonates in the exchange reaction has been used to establish the structure of the *2-toluene-*p*-sulphonate 1-benzoate* of propane-1 : 2-diol (*2-toluene-*p*-sulphonyloxypropyl 1-benzoate.*)

In connection with the preparation of dithiols with potential antiarsenical pharmacological properties (cf. Part III; Evans, Fraser, and Owen, *J.*, 1949, 248) it occurred to us that the well-known reactivity of toluene-*p*-sulphonates might be applied to the formation of thiolacetates by carrying out an exchange reaction with potassium thiolacetate:

$$\text{ROTs} + \text{AcSK} \longrightarrow \text{RSAc} + \text{TsOK} \ (\text{Ts} = \text{toluene-}p\text{-sulphonyl})$$

Some encouragement for this supposition was afforded by the earlier observations of Gilman and Beaber (*J. Amer. Chem. Soc.*, 1925, **47**, 1449) and of Raymond (*J. Biol. Chem.*, 1934, **107**, 85), who had shown that toluene-*p*-sulphonates react with the alkali-metal derivatives of aliphatic and aromatic thiols to give sulphides. Furthermore, the preparation of carbohydrate thiocyanates, by reaction of the toluene-*p*-sulphonates with potassium thiocyanate, had been recorded by Müller and Wilhelms (*Ber.*, 1941, **74**, 698) and by Carson and Maclay (*J. Amer. Chem. Soc.*, 1948, **70**, 2220).

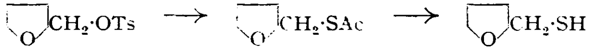
Such a reaction, if successful, would provide a useful method for the conversion of a hydroxyl group into a thiol group by the sequence ROH ⟶ ROTs ⟶ RSAc ⟶ RSH, and might be of particular value for the preparation of certain polyhydroxy-thiols where the corresponding halogen derivatives (necessary for the older method involving R·Hal ⟶ RSAc) are not easily accessible. In the carbohydrate field, for example, relatively few halogen derivatives are known, whereas a large number of toluene-*p*-sulphonates are readily available.

Since the reactivity of sulphonyl esters is markedly affected by the nature of the esterifying group, particularly by its primary or secondary character (cf. Clarke and Owen, *J.*, 1949, 315; Owen and Robins, *ibid.*, pp. 320, 326; and references there cited), it was necessary to study the reaction with potassium thiolacetate by the use of several types of compounds. The majority of these were toluene-*p*-sulphonates, but in view of the increasing interest in methanesulphonyl derivatives some of the latter were also investigated. Many of the starting materials were previously known compounds, and were prepared by standard methods; some, however, were new or exhibited some points of interest. *2-Methoxyethyl methanesulphonate, propylene* 1 : *2-dimethanesulphonate*, and *propylene* 1 : *2-ditoluene-*p*-sulphonate* were prepared by treatment of the corresponding hydroxy-compounds with the appropriate sulphonyl chloride in pyridine. *3-Acetoxypropylene* 1 : *2-ditoluene-*p*-sulphonate* was obtained by reaction of 2 : 3-dibromopropyl acetate with silver toluene-*p*-sulphonate. In an attempt to prepare a monotoluene-*p*-sulphonate of propane-1 : 2-diol, propylene oxide was treated with toluene-*p*-sulphonic acid in dry ether; an oily product was obtained, which by benzoylation gave a solid, separable by fractional crystallisation into two substances, m. p.s 105° and *ca.* 79°. The latter was eventually shown, by reaction with potassium thiolacetate, to be a mixture of the isomeric compounds (I) (identical with the substance of m. p. 105°) and (II), which could not readily be separated by further fractional crystallisation.

Preliminary experiments showed that the toluene-*p*-sulphonyloxy- and the methanesulphonyloxy-residues, particularly when primary, were readily replaceable by the acetylthio-group. Benzyl toluene-*p*-sulphonate showed exceptional reactivity; when it was dissolved in cold alcoholic potassium thiolacetate a precipitate of potassium toluene-*p*-sulphonate began to form almost immediately, and the reaction was complete within 15 minutes at room temperature. In general, however, the replacement was carried out by heating the reaction mixture in ethanol or acetone under reflux, using about twice the theoretical quantity of potassium thiolacetate; in many cases this excess is unnecessary for general preparative purposes, but was used in the present experiments in order that the yields of thiolacetates could be determined, under comparable conditions, for all the substances used. Potassium thiolacetate is readily soluble in ethanol, and the solid precipitated during the reactions in this solvent was almost pure potassium toluene-*p*-sulphonate. The reagent, however, is only sparingly soluble in acetone, and, since it was found to be unnecessary to use the large amount of solvent which would have been required to give complete solution, the solid remaining after completion of the reactions in acetone was a mixture of potassium toluene-*p*-sulphonate and unchanged potassium thiolacetate. All the primary compounds, and some secondary, gave the corresponding thiolacetates under these conditions, usually in good yield. With the primary compounds the reaction mixture became only slightly discoloured during the heating, but a deep red colour developed when secondary compounds were used. Hydrolysis of the thiolacetates afforded the free thiols.

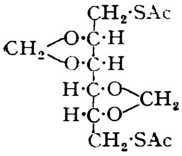
$$\underset{\text{(I.)}}{CH_3{\cdot}CH(OTs){\cdot}CH_2{\cdot}O{\cdot}COPh} \longrightarrow \underset{\text{(XIV.)}}{CH_3{\cdot}CH(SAc){\cdot}CH_2{\cdot}O{\cdot}COPh}$$

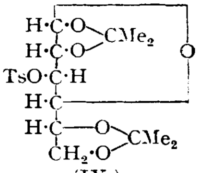
$$\underset{\text{(II.)}}{CH_3{\cdot}CH(O{\cdot}COPh){\cdot}CH_2{\cdot}OTs} \longrightarrow \underset{\text{(XV.)}}{CH_3{\cdot}CH(O{\cdot}COPh){\cdot}CH_2{\cdot}SAc}$$

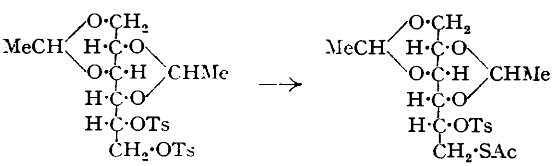

(III.) (IV.) (V.)

$$\underset{\text{(VI.)}}{CH_2(OR){\cdot}CH_2{\cdot}OTs} \longrightarrow \underset{\text{(VII.)}}{CH_2(OR){\cdot}CH_2{\cdot}SAc}$$

$$\underset{\text{(X.)}}{CH_2(OTs){\cdot}CH(OTs){\cdot}CH_2{\cdot}OAc} \longrightarrow \underset{\text{(XI.)}}{CH_2(SAc){\cdot}CH(SAc){\cdot}CH_2{\cdot}OAc}$$


(VIII.)


(IX.)


(XII.) (XIII.)

Tetrahydrofurfuryl toluene-*p*-sulphonate (III), in contrast to benzyl toluene-*p*-sulphonate, reacted only slowly at room temperature, but in the boiling solvent (acetone or ethanol) it gave a good yield of tetrahydrofurfuryl thiolacetate (IV). Alkaline hydrolysis of the latter readily gave *2-mercaptomethyltetrahydrofuran* (*tetrahydrofurylmethanethiol*) (V), though acid hydrolysis furnished only a small yield of the thiol, probably owing to simultaneous ring-fission. Tetrahydrofurfuryl methanesulphonate reacted much less readily than the toluene-*p*-sulphonate, and a longer period of heating was necessary. This observation is of interest in that a reverse order of reactivity is shown by these sulphonates in their reactions with potassium cyanide (Zief, Fletcher, and Kirshen, *J. Amer. Chem. Soc.*, 1946, **68**, 2743); furthermore, earlier investigators have usually reported a greater reactivity for the methansulphonates in reactions with, *e.g.*, sodium iodide (*inter al.*, Helferich and Gnüchtel, *Ber.*, 1938, **71**, 712).

n-Propyl toluene-*p*-sulphonate gave a better yield of *n*-propyl thiolacetate when acetone, rather than ethanol, was used, and it is probable that with the simple sulphonates of low molecular weight the competitive etherification reaction $ROTs + EtOH \longrightarrow ROEt$, when ethanol is used as a solvent, results in a diminished yield of thiolacetate; this was particularly apparent in the reaction with *iso*propyl toluene-*p*-sulphonate (see below).

Trimethylene ditoluene-*p*-sulphonate gave an excellent yield of the bisthiolacetate, and thence, by hydrolysis, 1 : 3-dimercaptopropane was obtained.

The possible effect of a neighbouring ether group was investigated by reactions using

2-methoxyethyl toluene-*p*-sulphonate (VI; R = Me) and methanesulphonate; *2-methoxyethyl thiolacetate* (VII; R = Me) was obtained in each case, but again the methanesulphonate was the less reactive. Hydrolysis of the product gave *2-methoxyethanethiol.* Similarly, 2-phenoxyethyl toluene-*p*-sulphonate (VI; R = Ph) gave an almost quantitative yield of *2-phenoxyethyl thiolacetate* (VII; R = Ph), and thence a high yield of *2-phenoxyethanethiol.* 2-Benzoyloxyethyl toluene-*p*-sulphonate (VI; R = COPh) afforded an example of a substance with a neighbouring ester group; it gave *2-benzoyloxyethyl thiolacetate* (VII; R = COPh), hydrolysed to 2-hydroxyethanethiol (2-mercaptoethanol). 1 : 6-Ditoluene-*p*-sulphonyl 2 : 3-4 : 5-dimethylene mannitol yielded 1 : 6-diacetyl 2 : 3-4 : 5-dimethylene 1 : 6-dithiomannitol [VIII; position of methylene residues not finally established (compare Haworth and Wiggins, *J.*, 1944, 61)].

Of the secondary toluene-*p*-sulphonates, the *iso*propyl ester reacted readily in boiling ethanol but, although potassium toluene-*p*-sulphonate was formed to the extent of 80% of the theoretical in 30 minutes, the yield of propane-2-thiol was only 6%; no propylene could be detected, and the main product was probably ethyl *iso*propyl ether, since a much better yield of thiolacetate was obtained in acetone solution. With *cyclo*hexyl toluene-*p*-sulphonate, on the contrary, poor yields of *cyclo*hexyl thiolacetate were obtained both in ethanol and in acetone, *cyclo*hexene being formed in each case; this elimination reaction is not unexpected, in view of similar results which have been observed when secondary alicyclic toluene-*p*-sulphonates are treated with a variety of reagents (Hückel, Neunhoeffer, Gercke, and Frank, *Annalen*, 1930, **477**, 143; Clarke and Owen, *loc. cit.*; Owen and Robins, *locc. cit.*). 3-Toluene-*p*-sulphonyl 1 : 2-5 : 6-di*iso*propylidene glucose (IX) failed to react with potassium thiolacetate in acetone at 110°.

The ditoluene-*p*-sulphonates of propane-1 : 2-diol and of 2 : 3-dihydroxypropyl acetate (X) provided examples of compounds containing vicinal primary and secondary sulphonyloxy-groups. In acetone solution, the primary and the secondary groups in both compounds were replaced, to give moderate yields of 1 : 2-bisacetylthiopropane and 2 : 3-bisacetylthiopropyl acetate (" BAL " triacetate) (XI), respectively. The dimethanesulphonate of propane-1 : 2-diol was somewhat less reactive than the corresponding ditoluene-*p*-sulphonate, but gave the same product as the latter. In striking contrast was the behaviour of the 5 : 6-ditoluene-*p*-sulphonate of 1 : 3-2 : 4-diethylidene sorbitol (XII) in which, even after vigorous treatment, only the primary group could be replaced, to give *6-acetyl 5-toluene-*p*-sulphonyl 1 : 3-2 : 4-diethylidene 6-thiosorbitol* (XIII). The corresponding 5 : 6-dimethanesulphonate appeared to undergo some reaction, but gave no recognisable product.

The only aryl compound studied, phenyl toluene-*p*-sulphonate, failed to react with potassium thiolacetate.

The results are summarised in the table, in which the yields refer to distilled or crystalline thiolacetates. It is clear from these experiments that the reaction of primary toluene-*p*-sulphonates with potassium thiolacetate provides a good method for the preparation of primary thiolacetates, and thence of the corresponding thiols, but that the behaviour of a secondary toluene-*p*-sulphonyloxy-group is capable of wide variation, ranging from non-reactivity to comparatively smooth replacement, with the possibility also of the occurrence of an elimination reaction and formation of an unsaturated product. The course taken in any particular case depends on the molecular environment, and the structural factors concerned merit further study, particularly since comparable variations are already known to occur in the reactions of secondary toluene-*p*-sulphonates with other reagents, *e.g.*, potassium acetate, sodium iodide. An interesting example of a carbohydrate derivative possessing two reactive secondary methanesulphonyl groups is discussed in Part V (following paper).

These experiments demonstrated a marked difference in reactivity between primary and secondary sulphonyloxy-groups, and thus provided a novel means of investigating the structures of the toluene-*p*-sulphonate–benzoates of propane-1 : 2-diol, m. p.s 105° and 79°, to which reference was made above. When the lower-melting material was boiled with potassium thiolacetate in acetone for an hour, a mixture was obtained, consisting of a liquid thiolacetate–benzoate, together with the crystalline toluene-*p*-sulphonate–benzoate, m. p. 105°. The latter was recovered almost quantitatively after further treatment under the same conditions, but under more vigorous conditions it reacted slowly to give a different thiolacetate–benzoate. It follows from these differences in reactivity that the compound of m. p. 105° contains a secondary toluene-*p*-sulphonyl group, and must therefore be the *2-toluene-*p*-sulphonate 1-benzoate* (I); the material of m. p. 79° is evidently a mixture of (I) with the isomeric 1-toluene-*p*-sulphonate 2-benzoate (II). During the short period of reaction the latter is converted into the *2-benzoate*

1-*thiolacetate* (XV), whilst (I) is unaffected; more drastic treatment subsequently converts (I) into the 1-*benzoate* 2-*thiolacetate* (XIV). Independent confirmation of the structure of (I) has been provided by Mr. G. A. Haggis (unpublished work), who has shown that on reaction with sodium iodide, followed by hydrogenation, it gives *n*-propyl benzoate.

The reaction of sulphonic esters with potassium thiolacetate.

(Ts = toluene-*p*-sulphonate; Ms = methanesulphonate.)

Ester.	Solvent.	Time at b. p., hrs.	Yield of thiolacetate, %.
Benzyl Ts	EtOH	1	79
Tetrahydrofurfuryl Ts	EtOH	1	71
	Me_2CO	1	69
Tetrahydrofurfuryl Ms	Me_2CO	1	20
	Me_2CO	6	60
n-Propyl Ts	EtOH	0·5	55
	Me_2CO	0·5	72
Propane-1 : 3-diol di-Ts	EtOH	1	88
2-Methoxyethyl Ts	EtOH	1	67
	Me_2CO	1	69
2-Methoxyethyl Ms	Me_2CO	1	56
2-Phenoxyethyl Ts	EtOH	1	92
2-Benzoyloxyethyl Ts	EtOH	1	70
2 : 3 : 4 : 5-Dimethylene mannitol 1 : 6-di-Ts	Me_2CO	6	89
*iso*Propyl Ts	EtOH	0·5	6
	Me_2CO	2	49
	Me_2CO	6	71
*cyclo*Hexyl Ts	EtOH	0·25	19
1 : 2-5 : 6-Di*iso*propylidene glucose 3-Ts	Me_2CO	18 *	0
Propane-1 : 2-diol di-Ts	Me_2CO	6	50
	Me_2CO	8	60
	Me_2CO	12	58
Propane-1 : 2-diol di-Ms	Me_2CO	4	38
	Me_2CO	6	43
Propane-1 : 2-diol 1-benzoate 2-Ts	Me_2CO	15 *	56
2 : 3-Dihydroxypropyl acetate di-Ts	Me_2CO	8	68
1 : 3-2 : 4-Diethylidene sorbitol 5 : 6-di-Ts	Me_2CO	6	87 †
1 : 3-2 : 4-Diethylidene sorbitol 5 : 6-di-Ms	Me_2CO	6	0
1 : 3-2 : 4-Diethylidene sorbitol 6-thiolacetate 5-Ts	Me_2CO	15 *	0
Phenyl Ts	Me_2CO	18 *	0

* Reaction at 110°.

† Primary group only.

EXPERIMENTAL.

(M. p.s were determined on the Koefler block, and are corrected.)

Preparation of the Sulphonic Esters.—The following were made by published methods: benzyl toluene-*p*-sulphonate, m. p. 58° (Tipson, *J. Org. Chem.*, 1944, **9**, 235); tetrahydrofurfuryl toluene-*p*-sulphonate, m. p. 37—38°, after distillation at 110° (bath)/0·0001 mm. (Barger, Robinson, and Urushibara, *J.*, 1937, 714; also obtained by the general method of Tipson, *loc. cit.*); tetrahydrofurfuryl methanesulphonate, b. p. 116°/1 mm., n_D^{18} 1·4613 (Zief, Fletcher, and Kirshen, *loc. cit.*); 2-methoxyethyl toluene-*p*-sulphonate, b. p. 120—130°/0·1 mm. (Tipson, *loc. cit.*); 2-phenoxyethyl toluene-*p*-sulphonate, m. p. 81° (Tipson, *loc. cit.*); 2 : 3 : 4 : 5-dimethylene mannitol 1 : 6-ditoluene-*p*-sulphonate, m. p. 164° (Haworth and Wiggins, *J.*, 1944, 61); *cyclo*hexyl toluene-*p*-sulphonate, m. p. 43° (Hückel, Neunhoeffer, Gercke, and Frank, *loc. cit.*); 1 : 2-5 : 6-di*iso*propylidene glucose 3-toluene-*p*-sulphonate, m. p. 120° (Freudenberg and Ivers, *Ber.*, 1922, **55**, 929); phenyl toluene-*p*-sulphonate, m. p. 95° (Reverdin and Crépieux, *Ber.*, 1902, **35**, 1443).

n-Propyl toluene-*p*-sulphonate was prepared by treatment of *n*-propanol (30 g.) in pyridine (250 c.c.) with toluene-*p*-sulphonyl chloride (105 g.) at −5° until all the chloride had dissolved, followed by 4 hours at 0°. The solution was then poured into ice-cold 5N-sulphuric acid (750 c.c.), and the oil was taken up in chloroform; the extract was washed with 2N-sulphuric acid and with sodium hydrogen carbonate solution, dried (K_2CO_3), and evaporated to an oil. The product (88 g., 82%) distilled at b. p. 134°/0·4 mm., n_D^{20} 1·5069.

The propylene 1 : 3-ditoluene-*p*-sulphonate was obtained from the diol (8 g.), toluene-*p*-sulphonyl chloride (44 g.), and pyridine (175 c.c.). After 1 hour at 0°, addition of 5N-sulphuric acid precipitated the ester as a solid, which formed plates, m. p. 92°, from methanol; yield, 27 g. (70%) (Found: C, 53·4; H, 5·2. Calc. for $C_{17}H_{20}O_6S_2$: C, 53·1; H, 5·25%) (cf. King, *J.*, 1928, 2426).

2-Benzoyloxyethyl toluene-*p*-sulphonate was prepared from 2-benzoyloxyethanol (Cretcher and Pittenger, *J. Amer. Chem. Soc.*, 1925, **47**, 2560) by a modification of the method of Butler *et al.* (*ibid.*, 1935, **57**, 575). The alcohol (20 g.), toluene-*p*-sulphonyl chloride (11·5 g.), and pyridine (100 c.c.), after being mixed at 0°, were kept at room temperature for 4 hours, and gave 23·6 g. (61%) of the ester (Butler *et al.*, *loc. cit.*, using less pyridine, recorded a yield of 26%).

Treatment of 2-methoxyethanol (10 g.) in pyridine (100 c.c.) with methanesulphonyl chloride

(16·6 g.), below −5° and then 12 hours at *ca.* 15°, dilution with water, and extraction of the product with chloroform, gave 2-*methoxyethyl methanesulphonate* (14·6 g., 72%), b. p. 80°/0·4 mm., n_D^{20} 1·4314 (Found: C, 31·1; H, 6·5. $C_4H_{10}O_4S$ requires C, 31·15; H, 6·55%).

*iso*Propyl toluene-*p*-sulphonate, n_D^{20} 1·5040, was prepared in the same way as the *n*-propyl ester.

Treatment of propane-1 : 2-diol (5 g.) in pyridine (150 c.c.) with toluene-*p*-sulphonyl chloride (28 g.) at 0° for 1 hour and at room temperature overnight gave, on pouring of the mixture into dilute sulphuric acid, a precipitate of the *ditoluene*-p-*sulphonate,* which crystallised from benzene–light petroleum (b. p. 60—80°) in colourless prisms, m. p. 68—69° (Found: C, 53·0; H, 4·95. $C_{17}H_{20}O_6S_2$ requires C, 53·1; H, 5·25%). The *dimethanesulphonate,* prepared in a similar way, crystallised from the same solvent in rectangular tablets, m. p. 53° (Found: C, 25·85; H, 5·25. $C_5H_{12}O_6S_2$ requires C, 25·85; H, 5·2%).

2 : 3-*Ditoluene*-p-*sulphonyloxypropyl acetate* was obtained by heating under reflux a solution of 2 : 3-dibromopropyl acetate (10 g., b. p. 130°/32 mm.; n_D^{21} 1·5060) in benzene (100 c.c.) with silver toluene-*p*-sulphonate (25 g.) for 15 hours. The filtered solution was then washed with aqueous sodium hydrogen carbonate, and evaporated to an oil, which crystallised on addition of light petroleum and formed needles (5·45 g., 32%), m. p. 100°, from benzene–light petroleum (b. p. 60—80°) (Found: C, 51·5; H, 5·1. $C_{19}H_{22}O_8S_2$ requires C, 51·55; H, 5·0%).

The dimethane sulphonate of 1 : 3-2 : 4-diethylidene sorbitol was obtained by the method described in Part VII. The corresponding ditoluene-*p*-sulphonate was prepared by addition of toluene-*p*-sulphonyl chloride (8·95 g.) to a solution of 1 : 3-2 : 4-diethylidene sorbitol (5 g.) in pyridine (20 c.c.) at 0°. After 12 hours at *ca.* 5°, addition of water gave the solid derivative (7·9 g.), m. p. 173°, $[\alpha]_D^{20}$ − 11·2° (*c*, 1 in chloroform), after recrystallisation from methanol (cf. Sullivan, *J. Amer. Chem. Soc.*, 1945, **67**, 837; Wiggins, *J.*, 1946, 388).

Reaction of Propylene Oxide with Toluene-p-*sulphonic Acid.*—To a solution of the oxide (9 g.) in dry ether (150 c.c.), dry toluene-*p*-sulphonic acid (27 g., 1 mol.) was added in small portions, and the solution was then kept overnight. During this time a lower oily layer was formed. The solvent was removed under reduced pressure, and the residual oil was dissolved in chloroform, washed with water and with sodium hydrogen carbonate solution, and dried. Evaporation of the solvent then gave a pale yellow viscous oil (33 g.). This was dissolved in pyridine (150 c.c.) and treated with benzoyl chloride (25 g.), with cooling. After 1 hour at 15°, water was added, and the precipitated oil was taken up in chloroform and washed with dilute sulphuric acid, sodium hydrogen carbonate, and finally with water. The dried solution was then evaporated, and gave a semi-solid residue. One recrystallisation from benzene–light petroleum (b. p. 60—80°) gave 35 g. of material, m. p. *ca.* 70—75°, from which, by several recrystallisations from methanol, 2-*toluene*-p-*sulphonyloxypropyl* 1-*benzoate* was obtained; it formed needles or plates, m. p. 105° (Found: C, 61·4; H, 5·7. $C_{17}H_{18}O_5S$ requires C, 61·05; H, 5·4%). The main portion of the reaction product, recovered from the mother-liquors, was a mixture of the structural isomers; after repeated crystallisations from benzene–light petroleum or from methanol it gave colourless needles, m. p. *ca.* 79° (Found: C, 60·8; H, 5·6%).

Reaction of Sulphonic Esters with Potassium Thiolacetate.—The conditions for each experiment are given individually below, and the yields of thiolacetates are summarised in the table. Except where otherwise stated, reaction products were worked up by the following procedure. The cooled mixture was filtered, and the salts were washed with cold solvent. The ethanol or acetone filtrate and washings were concentrated to small bulk and then diluted with water. The product, if solid, was collected, washed, and recrystallised; if liquid, it was extracted with ether, the extracts were washed with water, then dried and evaporated, and the residual oil was purified by distillation.

Hydrolysis of Thiolacetates to Thiols.—(*a*) *Alkaline hydrolysis.* The thiolacetate was dissolved in cold 5% methanolic potassium hydroxide (2·1 mols. of KOH per acetylthio-group) and left overnight, under nitrogen, at room temperature. A slight excess of hydrochloric acid was then added, with cooling, and after removal of methanol under reduced pressure the thiol was isolated by ether-extraction.

(*b*) *Acid hydrolysis.* The thiolacetate was dissolved in ten times its weight of N-methanolic hydrogen chloride and boiled under reflux for 4 hours under nitrogen. The cooled solution was then diluted with water, concentrated under reduced pressure to remove methanol, and extracted with ether to obtain the thiol.

The yields of thiol, recorded below in the individual cases, are based on thiolacetates, and are not overall yields.

Quantitative Determination of Thiol Values.—The method described in Part II (Evans and Owen, *J.*, 1949, 244) was used, except that with non-water-soluble thiols sufficient methanol was added to effect dissolution in the hydrochloric acid before titration with iodine.

Benzyl Thiolacetate.—(*a*) Benzyl toluene-*p*-sulphonate (1 g.) and potassium thiolacetate (1 g.) were separately dissolved in the minimum amount of ethanol. On mixing of the cold solutions, a copious white precipitate was formed within a few minutes. After 10 minutes, the potassium toluene-*p*-sulphonate (0·6 g., 75%) was filtered off and washed with cold ethanol.

(*b*) The toluene-*p*-sulphonate (5 g.) and potassium thiolacetate (5 g.) were heated in ethanol (250 c.c.) under reflux, and gave benzyl thiolacetate (2·5 g.), b. p. 54°/0·05 mm., n_D^{20} 1·5578, which on acid hydrolysis furnished toluene-ω-thiol, b. p. 100°/22 mm. (Found: thiol S, 25·4. Calc. for C_7H_8S: S, 25·8%).

Tetrahydrofurfuryl Thiolacetate.—The toluene-*p*-sulphonate reacted only slowly with potassium thiolacetate in ethanol at room temperature, replacement being incomplete after 10 days. The toluene-*p*-sulphonate (14 g.) or the methanesulphonate (6 g.), with potassium thiolacetate (12·5 g. or 7·5 g. respectively), on being heated under reflux, in acetone or ethanol (100 c.c.), gave the *thiolacetate,* b. p. 107°/16 mm., n_D^{20} 1·4941 (Found: C, 52·4; H, 7·65. $C_7H_{12}OS$ requires C, 52·5; H, 7·55%). Light absorption: max. 2300 A., ε 4800. Alkaline hydrolysis then gave 2-*mercaptomethyltetrahydrofuran* (55%), b. p. 113°/145 mm., n_D^{20} 1·4910 (Found: C, 50·5; H, 8·8; thiol S, 26·7. $C_5H_{10}OS$ requires C, 50·8; H, 9·1; S, 27·1%). The *phenylurethane,* prepared by treatment of the thiol with a slight excess of phenyl *iso*cyanate for 4 days at room temperature, crystallised from light petroleum (b. p. 60—80°) in needles, m. p. 99° (Found: N, 6·1. $C_{12}H_{15}O_2NS$ requires N, 5·9%).

n-*Propyl Thiolacetate.*—The toluene-*p*-sulphonate (10 g.), potassium thiolacetate (11 g.), and acetone (100 c.c.) were heated under reflux, and gave the thiolacetate (4 g.), b. p. 141°, n_D^{20} 1·4590 (Wallach and Bleibtreu, *Ber.*, 1879, **12**, 1062, give b. p. 135—137°).

1 : 3-*Bisacetylthiopropane.*—The ditoluene-*p*-sulphonate of propane-1 : 3-diol (9 g.) and potassium thiolacetate (10·5 g.) were heated under reflux in ethanol (200 c.c.), and gave the bisthiolacetate (4 g.), b. p. 152°/24 mm., n_D^{24} 1·5209, which on acid hydrolysis furnished propane-1 : 3-dithiol (57%), b. p. 110°/120 mm., n_D^{21} 1·5380 (Found : thiol S, 59·1. Calc. for $C_3H_8S_2$: S, 59·3%).

2-*Methoxyethyl Thiolacetate.*—The toluene-*p*-sulphonate (10 g.) or the methanesulphonate (8·4 g.) was treated with potassium thiolacetate (10 g. or 13·5 g., respectively) in the boiling solvent (100 c.c.). The *thiolacetate* had b. p. 110°/110 mm., n_D^{18} 1·4645 (Found : C, 44·7; H, 7·45. $C_5H_{10}O_2S$ requires C, 44·8; H, 7·55%). Light absorption : max. 2280 A., ε 2600.

Hydrolysis of the thiolacetate (8 g.) under acid conditions gave, on evaporation of the solvent, no thiol; owing to its volatility in methanol it was present in the distillate, which was therefore made alkaline by the addition of 10% methanolic potassium hydroxide (70 c.c.) and evaporated to dryness under nitrogen. The residue was acidified with concentrated hydrochloric acid and extracted with ether. The dried extract was evaporated, the ether being removed through a 10″ Vigreux column, and the residue on distillation gave 2-*methoxyethanethiol* (3 g., 55%), b. p. 112°, n_D^{23} 1·4488 (Found : C, 39·75; H, 9·0; thiol S, 34·1. C_3H_8OS requires C, 39·1; H, 8·75; S, 34·8%).

Treatment of the thiol (42 mg.) with 1-chloro-2 : 4-dinitrobenzene (100 mg.) and 2% aqueous sodium hydroxide (1·0 c.c.) in boiling ethanol (10 c.c.) for 10 minutes, followed by addition of water, gave 2 : 4-*dinitrophenyl 2-methoxyethyl sulphide* (95 mg.), which crystallised from ethanol in bright yellow plates, m. p. 90° (Found : N, 10·95. $C_9H_{10}O_5N_2S$ requires N, 10·85%).

2-*Phenoxyethyl Thiolacetate.*—The toluene-*p*-sulphonate (10 g.) and potassium thiolacetate (8 g.) in boiling ethanol (150 c.c.) gave the *thiolacetate*, which crystallised from methanol in plates, m. p. 48° (Found : C, 61·4; H, 6·4. $C_{10}H_{12}O_2S$ requires C, 61·4; H, 6·2%). On acid hydrolysis it gave 2-phenoxyethanethiol (90%), b. p. 134°/29 mm., n_D^{23} 1·5597 (Found : C, 62·3; H, 6·4; thiol S, 20·6. $C_8H_{10}OS$ requires C, 62·3; H, 6·5; S, 20·8%); the *phenylurethane* of this thiol formed needles, m. p. 113°, from light petroleum (b. p. 60—80°) (Found : N, 5·3. $C_{15}H_{15}O_2NS$ requires N, 5·15%).

2-*Benzoyloxyethyl Thiolacetate.*—The toluene-*p*-sulphonate (10 g.) and potassium thiolacetate (7 g.) were heated under reflux in ethanol (150 c.c.). The thiolacetate (4·7 g.) had b. p. 117°/0·1 mm., n_D^{20} 1·5446 (Found : C, 58·5; H, 5·4. $C_{11}H_{12}O_3S$ requires C, 58·9; H, 5·4%). On acid hydrolysis, 2-hydroxyethanethiol (52%), b. p. 65°/17 mm., was obtained, and was characterised as the bisphenylurethane, m. p. and mixed m. p. with an authentic sample, 146°.

1 : 6-*Diacetyl* 2 : 3-4 : 5-*Dimethylene* 1 : 6-*Dithiomannitol.*—The ditoluene-*p*-sulphonate (1 g.) was treated with potassium thiolacetate (0·9 g.) in boiling acetone (25 c.c.). The solid product, recrystallised from aqueous ethanol, furnished colourless needles of the *bisthiolacetate*, m. p. 109°, $[\alpha]_D^{20}$ +187° (*c*, 1·2 in chloroform) (Found : C, 44·8; H, 5·6; S, 19·8. $C_{12}H_{18}O_6S_2$ requires C, 44·7; H, 5·6; S, 19·9%). Light absorption : max. 2290 A., ε 11,000.

iso*Propyl Thiolacetate.*—The toluene-*p*-sulphonate (10 g.), in boiling ethanol or acetone (100 c.c.), was treated with potassium thiolacetate (11 g.), and gave *iso*propyl thiolacetate, b. p. 123°, n_D^{20} 1·4528 (Wallach and Bleibtreu, *loc. cit.*, give b. p. 124—127°).

cyclo*Hexyl Thiolacetate.*—When *cyclo*hexyl toluene-*p*-sulphonate (10 g.) and potassium thiolacetate (9 g.) were heated under reflux in ethanol (50 c.c.), a rapid reaction occurred and the mixture became deep red; after being heated for 15 minutes, it was worked up and gave 8·15 g. (98%) of potassium toluene-*p*-sulphonate. The solvent was removed through a 12″ Vigreux column, and the first runnings contained much *cyclo*hexene, identified by its characteristic odour and unsaturation towards bromine. The small residue, on distillation, gave *cyclo*hexyl thiolacetate (1·2 g.), b. p. 130°/110 mm., n_D^{20} 1·5091 (Cunneen, *J.*, 1947, 134, gives b. p. 90°/14 mm.).

1 : 2-*Bisacetylthiopropane.*—The ditoluene-*p*-sulphonate or dimethanesulphonate of propane-1 : 2-diol (10 g.) was heated with potassium thiolacetate (6 g. or 10 g., respectively) in acetone (100 c.c.), and gave the bisthiolacetate, b. p. 93°/1 mm., n_D^{21} 1·5197 (Found : C, 43·45; H, 6·25. $C_7H_{12}O_2S_2$ requires C, 43·7; H, 6·3%).

2 : 3-*Bisacetylthiopropyl Acetate.*—The toluene-*p*-sulphonate (5 g.) and potassium thiolacetate (6·5 g.) were heated under reflux in acetone (100 c.c.), and gave the triacetate of 2 : 3-dimercaptopropanol (1·9 g.), b. p. 120°/0·05 mm., n_D^{23} 1·5105 (Evans and Owen, *loc. cit.*, found n_D^{20} 1·5140); on acid hydrolysis, 2 : 3-dimercaptopropanol was obtained, b. p. 81°/1 mm., n_D^{21} 1·5710 (Found : thiol S, 49·8. Calc. for $C_3H_8OS_2$: S, 51·6%).

Non-interaction of Potassium Thiolacetate and 3-*Toluene*-p-*sulphonyl* 1 : 2-5 : 6-*Di*iso*propylidene Glucose.*—The toluene-*p*-sulphonate (1 g.), potassium thiolacetate (0·55 g.), and acetone (50 c.c.) were heated at 110° in a sealed tube for 18 hours. Unchanged toluene-*p*-sulphonate (0·9 g.) was recovered, m. p. and mixed m. p. 120°, after recrystallisation from acetone.

Action of Potassium Thiolacetate on 5 : 6-*Ditoluene*-p-*sulphonyl* 1 : 3-2 : 4-*Diethylidene Sorbitol.*—The ditoluene-*p*-sulphonate (5 g.) and potassium thiolacetate (4·5 g.) in acetone (100 c.c.) were heated under reflux for 6 hours. On addition of water to the filtered and concentrated solution, a solid (3·5 g.; m. p. 125°) was deposited. Recrystallisation from methanol gave needles of 5-*toluene*-p-*sulphonyl* 6-*acetyl* 1 : 3-2 : 4-*diethylidene* 6-*thiosorbitol*, m. p. 128°, $[\alpha]_D^{21}$ −23·2° (*c*, 2 in chloroform) (Found : C, 50·9; H, 5·6. $C_{19}H_{26}O_8S_2$ requires C, 51·1; H, 5·85%). Light absorption : max. 2260 A., ε 21,000. This compound (1 g.) was recovered unchanged, m. p. and mixed m. p. 128°, after being heated with potassium thiolacetate (0·5 g.) in acetone (25 c.c.) at 110° for 15 hours.

Action of Potassium Thiolacetate on 5 : 6-*Dimethanesulphonyl* 1 : 3-2 : 4-*Diethylidene Sorbitol.*—The dimethanesulphonate (1 g.) and potassium thiolacetate (1·2 g.) in acetone (25 c.c.) were heated under reflux for 6 hours. Only 0·05 g. of a dark water-insoluble product was obtained. With a shorter time of reaction (1 hour) a dark oil (0·7 g.) was isolated, but it appeared to contain much unchanged starting material.

Non-interaction of Potassium Thiolacetate and Phenyl Toluene-p-*sulphonate.*—The toluene-*p*-

sulphonate (1 g.), potassium thiolacetate (0·9 g.), and acetone (50 c.c.) were heated at 110° for 18 hours. Unchanged starting material (0·9 g.) was obtained, having m. p. 93°, raised to 95° on recrystallisation from ethanol.

*Action of Potassium Thiolacetate on the Isomeric Toluene-*p*-sulphonate–Benzoates of Propane-*1 : 2-*diol.*—(i) The material of m. p. 79° (5 g.) and potassium thiolacetate (3·5 g.) in acetone (50 c.c.) were heated under reflux for 1 hour; a quantity of potassium toluene-*p*-sulphonate was formed during this time. The cooled mixture was filtered, and the filtrate was concentrated to 10 c.c. and diluted with water, whereupon a semi-solid product was precipitated. This was collected, and on recrystallisation from methanol it gave the 2-toluene-*p*-sulphonate 1-benzoate of propane-1 : 2-diol, identical (m. p. and mixed m. p. 105°) with that described above. Evaporation of the mother-liquors from the crystallisation gave an oil, which on distillation furnished 2-*benzoyloxypropyl* 1-*thiolacetate* (1·2 g.), b. p. 122°/1 mm., n_D^{20} 1·5328 (Found: C, 60·8; H, 6·2. $C_{12}H_{14}O_3S$ requires C, 60·45; H, 5·9%); a small non-volatile residue consisted mainly of the compound, m. p. 105°. Treatment of the thiolacetate (0·1 g.) in ethanol (10 c.c.) with 1-chloro-2 : 4-dinitrobenzene (0·085 g., 1 mol.) and 10% aqueous sodium hydroxide (0·35 c.c., 2 mol.) under reflux for 10 minutes, followed by dilution with water, gave a precipitate of 2 : 4-*dinitrophenyl* 2-*benzoyloxypropyl sulphide*, which formed yellow needles (0·1 g.), m. p. 139°, from ethanol (Found: N, 7·75. $C_{16}H_{14}O_6N_2S$ requires N, 7·75%); the same product was obtained when the amount of sodium hydroxide was increased to 3 mols., indicating the resistance of the secondary benzoyl group towards hydrolysis under these conditions (compare the primary isomer, below).

(ii) The compound, m. p. 105° (3 g.), was recovered unchanged (2·9 g.) after being heated with potassium thiolacetate (2·1 g.) and acetone (50 c.c.) under reflux for 1 hour. The same mixture was therefore heated in a sealed tube at 110° for 15 hours, and gave 1-*benzoyloxypropyl* 2-*thiolacetate* (1·2 g.), b. p. 118°/1 mm., n_D^{20} 1·5248 (Found: C, 60·8; H, 6·05. $C_{12}H_{14}O_3S$ requires C, 60·45; H, 5·9%). When this compound (0·1 g.) was heated under reflux for 10 minutes in ethanol (10 c.c.) with 1-chloro-2 : 4-dinitrobenzene (0·085 g.) and 10% aqueous sodium hydroxide (0·53 c.c., 3 mols.), the subsequent addition of water gave 2 : 4-*dinitrophenyl* 2-*hydroxy*iso*propyl sulphide*, which crystallised from aqueous ethanol as pale yellow needles, m. p. 87° (Found: N, 10·9. $C_9H_{10}O_5N_2S$ requires N, 10·85%).

Light-absorption data were kindly determined by Dr. E. A. Braude.

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