Cytotoxic Compounds. Part XII.[1] Some 3-Arylthiopropane-1,2-diols and 2-Arylthiopropane-1,3-diols. Rearrangement of the 1,3-Dimethanesulphonates to the 1,2-Isomers

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Syntheses of the title diols, their acetates, and their methyl ethers are described, where the aryl group is *p*-chloro-, *p*-methoxy-, *p*-methylthio-, and 2,4-dinitro-phenyl. Rearrangement through an episulphonium ion-pair occurs in the preparation of a dimethanesulphonate from 2-(*p*-methoxyphenylthio)propane-1,3-diol, the product being the derivative of the isomeric 1,2-diol. Unrearranged dimethanesulphonates were obtained from all the other diols, but the 1,3-dimethanesulphonates where the aryl group is phenyl, *p*-chlorophenyl, and *p*-methylthiophenyl undergo rearrangement to the 1,2-isomers in boiling acetone. In methanol, solvolysis of the 1,3-dimethanesulphonates occurs much more rapidly than with the 1,2 isomers.

The two geometrical isomers of the *O*-toluene-*p*-sulphonate of 1,3-*O*-benzylideneglycerol have been separated and identified. Some of the aryl sulphides, obtained by displacement reactions on this sulphonate with aryl thiols, have also been obtained as individual stereoisomers.

The ^{1}H n.m.r. spectra of the diols and of their derivatives are tabulated.

In Part IX,[2] the reactions of the dimethanesulphonates (6) and (16) towards different types of nucleophiles were described, in which rearrangements, through a common intermediate episulphonium ion (21), often occurred. To obtain further information on the factors influencing the course of such reactions, analogues have now been prepared in which the aromatic ring carries a variety of substituents, and the present Paper is concerned mainly with the synthetical aspects of this programme.

Hutchison and Smiles [3] prepared 3-phenylthiopropane-1,2-diol (1) by reaction of phenyl sodium sulphide with 3-chloropropane-1,2-diol. By use of the appropriate

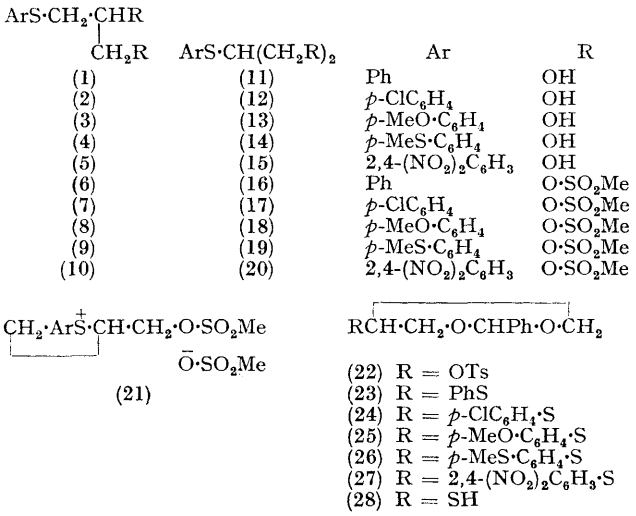
[1] Part XI, L. N. Owen and R. Sridhar, *J. Chem. Soc.* (*C*), 1970, 564.

[2] M. V. A. Baig and L. N. Owen, *J. Chem. Soc.* (*C*), 1967, 1400.

[3] C. G. Hutchison and S. Smiles, *Ber.*, 1914, **47**, 805; *cf.* H. L. Yale, E. J. Pribyl, W. Braker, F. H. Bergeim, and W. A. Lott, *J. Amer. Chem. Soc.*, 1950, **72**, 3710.

thiophenol this reaction provided a convenient source of the 3-arylthiopropane-1,2-diols (2)—(5). To serve as authentic reference compounds for later studies, the corresponding diacetates were prepared under conditions precluding rearrangement (pyridine–acetic anhydride). Methylation in tetrahydrofuran, with dimethyl sulphate and powdered sodium hydroxide,[4] converted the diols (2)—(4) into the dimethyl ethers, but because of the susceptibility of dinitrophenyl sulphides towards fission by strong base (see the succeeding Paper) the dimethyl ether of the dinitro-diol (5) was obtained by methylation with diazomethane in the presence of fluoroboric acid.[5] The dimethanesulphonates (7)—(10) were prepared by reaction of the diols with methanesulphonyl chloride in pyridine. The ^{1}H n.m.r. spectra of the 4 new diols and of their 12 derivatives (Table 1) were consistent with their structures.

Baig and Owen [2] synthesised 2-phenylthiopropane-1,3-diol (11) by reaction of 1,3-benzylidenedioxy-2-toluene-*p*-sulphonyloxypropane (22) with phenyl sodium sulphide to give the product (23), followed by acid



hydrolysis to remove the benzylidene group. The method was now used to prepare the *p*-chloro-, *p*-methoxy-, and *p*-methylthio-compounds (24)—(26) and thence the 1,3-diols (12)—(14), but 2,4-dinitrophenyl sodium sulphide failed to react with the toluene-*p*-sulphonate (22) and an indirect method had to be devised. The toluene-*p*-sulphonyloxy-group in (22) was displaced by thioacetate or thiobenzoate, and the product on de-esterification gave the thiol (28) from which the 2,4-dinitrophenyl derivative (27) was obtained by reaction with 1-chloro-2,4-dinitrobenzene. Acid hydrolysis then afforded the diol (15).

The geometrical isomers of 1,3-*O*-benzylideneglycerol and of several derivatives are well known,[6,7] but those of the toluene-*p*-sulphonate (22) have not been described. The melting point quoted for this compound [8] is 125°, but in our experience ranged from *ca.* 85° to *ca.* 122° with various batches. The ^{1}H n.m.r. spectra showed that all were mixtures of stereoisomers, two resonances (τ 4·58 and 4·50) appearing for the benzylic proton. By chromatography the two forms (m.p. 95° and m.p. 127°) were separable, each then showing a characteristic individual spectrum. Foster and his co-workers [7] have show that in compounds of this type the signal for the benzylic proton is at lower field for the *cis* than for the *trans*-isomer, and also that, for conformational reasons, the pattern given by the other ring-protons is simple for the *cis* but complex for the *trans*-compound. The two forms of the toluene-*p*-sulphonate (22) show precisely the same distinctions and consequently that of m.p. 127° has the *cis* and that of m.p. 95° the *trans*-configuration. The pure *cis*-isomer was also obtained by fractional crystallisation of the mixture from methanol.

Because the configuration was of no consequence as far as the synthetical scheme was concerned, the toluene-*p*-sulphonate used for reaction with the various thiols was usually a stereoisomeric mixture. When it was treated with potassium thioacetate or potassium thiobenzoate the crude product contained some unchanged toluene-*p*-sulphonate which was entirely the *cis*-isomer; the *trans*-form, having a diequatorial conformation for the phenyl and the toluene-*p*-sulphonate groups, is evidently more reactive than the conformationally less stable *cis*-isomer with the axial-equatorial arrangement.

All four 2-arylthio-1,3-benzylidenedioxypropanes (24)—(27) were obtained as mixtures of stereoisomers from which the *cis*- and the *trans*-form of the *p*-chloro- (24) and of the *p*-methylthio-compound (26) were isolated by chromatography; the configurations were again evident from the characteristic ^{1}H n.m.r. spectra. Only the *trans*-form of the *p*-methoxy-compound (25) could be separated in this way and isolation of either stereoisomer of the dinitro-compound (27) was precluded by its low solubility in common solvents.

When the pure *cis*-form of the toluene-*p*-sulphonate (22) was treated with *p*-chlorophenyl sodium sulphide the product was the pure *trans*-form of (24), in accordance with an S_N2 displacement.

The 1,3-diacetates and the 1,3-dimethyl ethers were prepared from the diols (12)—(15) by the methods used for the 1,2-isomers, as were the three 1,3-dimethanesulphonates (17), (19), and (20). The ^{1}H n.m.r. spectra of these 11 derivatives (Table 1) were quite distinct from those of the 1,2-series, and were in accord with unrearranged structures. However, the dimethanesulphonate obtained from the *p*-methoxy-diol (13) was identical to the 1,2-derivative (8), and the result was the same when methanesulphonic anhydride was used instead of the acid chloride; conditions could not be found

[4] E. L. Falconer and G. A. Adams, *Canad. J. Chem.*, 1956, **34**, 338.
[5] M. C. Caserio, J. D. Roberts, M. Neeman, and W. S. Johnson, *J. Amer. Chem. Soc.*, 1958, **80**, 2584.
[6] P. E. Verkade and J. D. van Roon, *Rec. Trav. chim.*, 1942, **61**, 831; B. Dobinson and A. B. Foster, *J. Chem. Soc.*, 1961, 2338.
[7] N. Baggett, B. Dobinson, A. B. Foster, J. Homer, and L. F. Thomas, *Chem. and Ind.*, 1961, 106; N. Baggett, K. W. Buck, A. B. Foster, M. H. Randall, and J. M. Webber, *J. Chem. Soc.*, 1965, 3394.
[8] N. K. Matheson and S. J. Angyal, *J. Chem. Soc.*, 1952, 1133.

for the preparation of the unrearranged dimethanesulphonate (18). Moreover, in one preparation of the *p*-chloro-compound (17), when there was inadequate cooling, the product contained an appreciable amount of the 1,2-isomer (7). With the dinitro-diol (15), on the other hand, temperature control was unimportant, and even at 20° no 1,2-isomer was formed. This variation in sensitivity towards rearrangement agrees with the effect which the ring substituent would be expected to have on participation by sulphur in the formation of the episulphonium ion-pair (21), collapse of which can then lead to the thermodynamically more stable derivative.

Several groups of workers [9] have studied rearrangements of primary to secondary sulphonate esters, through ion-pairs, but usually in nucleophilic solvents, so that solvolysis also occurred. This complication can be avoided by the use of dry acetone. In the boiling solvent the isomerisations of the three 1,3-dimethanesulphonates (17), (19), and (20) were compared by ^{1}H n.m.r. spectroscopy, and the results are shown in Table 2. The

TABLE 1

Chemical shifts (τ values) in $CDCl_3$

(i) Compounds $ArS{\cdot}CH_2{\cdot}CHR{\cdot}CH_2R$

Ar	R	CHR	CH_2R	$S{\cdot}CH_2$	CH_3 in R	
Ph (ref. 2)	OH		6·3m	6·98d		
p-ClC_6H_4	OH		6·4m	7·02d		
p-$MeO{\cdot}C_6H_4$	OH		6·4m	7·10d		
p-$MeS{\cdot}C_6H_4$	OH *		6·1m	6·88d		
2,4-$(NO_2)_2C_6H_3$	OH ‡		5·8—6·4m	6·8m		
Ph (ref. 2)	OAc †	5·0m	5·8m	6·95d	8·02s	8·08s
p-ClC_6H_4	OAc	4·9m	5·8m	6·72d	8·00s	8·05s
p-$MeO{\cdot}C_6H_4$	OAc	4·9m	5·8m	6·97d	7·95s	7·98s
p-$MeS{\cdot}C_6H_4$	OAc	4·8m	5·7m	6·89d	7·97s	8·02s
2,4-$(NO_2)_2C_6H_3$	OAc	4·8m	5·7m	6·67d	7·90s	
Ph (ref. 2)	OMe †	6·3m	6·6m	7·0m	6·67s	6·72s
p-ClC_6H_4	OMe		6·5m	6·92d	6·62s	6·68s
p-$MeO{\cdot}C_6H_4$	OMe		6·5m	7·0m	6·65s	6·75s
p-$MeS{\cdot}C_6H_4$	OMe		6·5m	6·9m	6·58s	6·60s
2,4-$(NO_2)_2C_6H_3$	OMe		6·4m	6·70d	6·53s	6·58s
Ph (ref. 2)	$O{\cdot}SO_2Me$	5·1m	5·55m	6·75m	6·98s	
p-ClC_6H_4	$O{\cdot}SO_2Me$	5·2m	5·6m	6·78m	6·98s	
p-$MeO{\cdot}C_6H_4$	$O{\cdot}SO_2Me$	5·2m	5·6m	6·9m	7·02s	
p-$MeS{\cdot}C_6H_4$	$O{\cdot}SO_2Me$	5·2m	5·5m	6·8m	6·96s	
2,4-$(NO_2)_2C_6H_3$	$O{\cdot}SO_2Me$ ‡	4·9m	5·4m	6·38d	6·77s	6·82s

(ii) Compounds $ArS{\cdot}CH(CH_2R)_2$

Ar	R	CH_2R	$S{\cdot}CH$	CH_3 in R
Ph (ref. 2)	OH	6·23d	6·75qn	
p-ClC_6H_4	OH	6·12d	6·66qn	
p-$MeO{\cdot}C_6H_4$	OH	6·23d	6·84qn	
p-$MeS{\cdot}C_6H_4$	OH	6·17d	6·73qn	
2,4-$(NO_2)_2C_6H_3$	OH §	6·02m		
Ph (ref. 2)	OAc †	5·82d	6·57qn	8·02s
p-ClC_6H_4	OAc	5·78d	6·52qn	8·00s
p-$MeO{\cdot}C_6H_4$	OAc	5·78d	6·68qn	7·98s
p-$MeS{\cdot}C_6H_4$	OAc	5·72d	6·53qn	7·97s
2,4-$(NO_2)_2C_6H_3$	OAc	5·6m		7·85s
Ph (ref. 2)	OMe †	6·50d	6·72qn	6·71s
p-ClC_6H_4	OMe	6·5m		6·68s
p-$MeO{\cdot}C_6H_4$	OMe	6·46d	6·7m	6·68s
p-$MeS{\cdot}C_6H_4$	OMe	6·5m		6·62s
2,4-$(NO_2)_2C_6H_3$	OMe	6·25s		6·58s
Ph (ref. 2)	$O{\cdot}SO_2Me$	5·57d	6·41qn	6·97s
p-ClC_6H_4	$O{\cdot}SO_2Me$	5·52d	6·38qn	6·93s
p-$MeS{\cdot}C_6H_4$	$O{\cdot}SO_2Me$	5·52d	6·42qn	6·91s
2,4-$(NO_2)_2C_6H_3$	$O{\cdot}SO_2Me$ ‡	5·4m		6·78s

* In $CDCl_3$–C_5D_5N. † In CCl_4. ‡ In $(CD_3)_2SO$. § In $(CD_3)_2CO$.

Resonances of *p*-methoxy (τ 6·23s), *p*-methylthio (τ 7·55s), aromatic, and hydroxy-protons are omitted. The high multiplicities of one or both of the methylene resonances in many compounds in section (i) is probably due to non-equivalence of the two protons. In most of the compounds in that section the methyl resonances are cleanly separated in the two differently situated R groups.

TABLE 2

Isomerisation of 1,3-dimethanesulphonates in boiling acetone

Ar	1,2-Dimethanesulphonate formed (%) 6 h	24 h
p-ClC_6H_4	34	80
Ph	66	100
p-$MeS{\cdot}C_6H_4$	84	100

[9] D. J. Cram, *J. Amer. Chem. Soc.*, 1952, **74**, 2129; S. Winstein and K. C. Schreiber, *ibid.*, p. 2171; S. Winstein and R. Heck, *ibid.*, 1956, **78**, 4801; D. B. Denney and B. Goldstein, *ibid.*, 1957, **79**, 4948; S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc. Special Publ.*, 1965, No. 19.

product from rearrangement of the *p*-methylthio-compound (19) was isolated; it was identical to the crystalline 1,2-isomer (9). One experiment was performed in which the 1,3-dimethanesulphonate (16) was heated in methanol until reaction was about 50% complete; the recovered crystalline dimethanesulphonate was the 1,2-isomer (6).

The rates of solvolysis of both types of dimethanesulphonate (except for the 2,4-dinitrophenyl derivatives, which were insufficiently soluble) were compared by heating them in methanol and titrating the methanesulphonic acid produced. Because successive reactions are involved, no simple kinetic picture emerged, and the times for 50% reaction were therefore measured from the curves obtained. These show (Table 3) the effect of

TABLE 3

Solvolysis of dimethanesulphonates in methanol at 50°

	Time for 50% reaction (min)	
Ar	1,2-series	1,3-series
p-ClC_6H_4	230	13
Ph	90	7
p-$MeS{\cdot}C_6H_4$	80	9
p-$MeO{\cdot}C_6H_4$	30	

substituents in the aromatic ring and also demonstrate that the 1,3-compounds are strikingly more reactive than their 1,2-counterparts. Since the initial stage in the solvolysis of both the 1,2- and the 1,3-compounds is the formation of the common episulphonium ion (21),[2] this must be the rate-determining stage, otherwise there would be no difference in rate between the isomers. Two factors can be considered to contribute to this difference. Firstly, in the 1,2-compound, bond-breaking, to release methanesulphonate anion from C-2, would be adversely affected by the neighbouring electron-attacting group at C-1; this does not apply to the 1,3-isomer. Secondly, in the 1,3-compound *both* groups are equally liable to displacement and consequently the conformational requirements for ring closure are less restrictive.

The ^1H n.m.r. spectra of the *p*-chloro-compounds showed an interesting feature, in that the four aromatic protons of the diol, the diacetate, the dimethyl ether, and the dimethanesulphonate in the 1,2-series appeared as a sharp singlet (τ *ca.* 2·75), whereas the corresponding signal was a doublet for the 1,3-isomers. This observation has been useful in current work to confirm the presence of a 1,3-component in a mixture of *p*-chloro-compounds consisting largely of 1,2-isomer.

EXPERIMENTAL

Unless stated otherwise, i.r. spectra were measured in chloroform. The ^1H n.m.r. spectra were recorded (by Mrs. A. I. Boston) on a Varian A-60 instrument. Petroleum refers to the fraction b.p. 40—60°.

3-(p-*Chlorophenylthio*)*propane*-1,2-*diol*.—When the reaction of sodium (1·2 g) with ethanol (80 ml) was complete, *p*-chlorothiophenol (7·0 g) and 3-chloropropane-1,2-diol (5·0 g) were added, and the mixture was boiled under reflux for 2 h under nitrogen, then cooled, filtered, and concentrated. The oily residue was extracted with benzene, and the extract was washed with 2N-NaOH, and with water, then dried and evaporated to a solid (7·5 g). Recrystallisation from carbon tetrachloride gave the *diol* (2), m.p. 60° (Found: C, 49·2; H, 5·3; S, 14·6. $C_9H_{11}ClO_2S$ requires C, 49·4; H, 5·1; S, 14·7%).

3-(p-*Methoxyphenylthio*)*propane*-1,2-*diol*.—Obtained in the same way from *p*-methoxythiophenol [10] (9·0 g), this *diol* (3) (12·2 g), when crystallised from benzene-petroleum, had m.p. 76° (Found: C, 56·0; H, 6·6; S, 14·7. $C_{10}H_{14}O_3S$ requires C, 56·0; H, 6·6; S, 15·0%).

3-(p-*Methylthiophenylthio*)*propane*-1,2-*diol*.—Similarly, *p*-(methylthio)thiophenol [11] (7·5 g) gave the *diol* (4) (10·0 g), m.p. 107° (from chloroform–petroleum) (Found: C, 52·4; H, 6·1; S, 27·6. $C_{10}H_{14}O_2S_2$ requires C, 52·1; H, 6·1; S, 27·85%).

3-(2,4-*Dinitrophenylthio*)*propane*-1,2-*diol*.—A mixture of 2,4-dinitrothiophenol [12] (6·0 g), 3-chloropropane-1,2-diol (4·0 g), and N-NaOH (37 ml) was stirred under nitrogen for 16 h. The solid was collected by filtration, washed with water, and recrystallised from aqueous ethanol to give the *diol* (5) (7·1 g), m.p. 144° (Found: C, 39·3; H, 3·6; N, 10·1; S, 11·7. $C_9H_{10}N_2O_6S$ requires C, 39·4; H, 3·7; N, 10·2; S, 11·7%).

1,2-*Diacetates*.—A solution of each of the preceding diols in pyridine (10—20 parts) and acetic anhydride (3—4 parts) was left at ambient temperature for *ca.* 20 h, then poured onto ice. Extraction with benzene followed by washing of the extract with dilute sulphuric acid and with water, gave, on evaporation of the dried solution, 1,2-*diacetoxy*-3-p-*chlorophenylthiopropane*, b.p. 136°/10^{-5} mmHg, n_D^{20} 1·5379, $\nu_{max.}$ 1740 cm^{-1} (Found: C, 51·6; H, 5·0; Cl, 11·8; S, 10·8. $C_{13}H_{15}ClO_4S$ requires C, 51·6; H, 5·0; Cl, 11·7; S, 10·6%); 1,2-*diacetoxy*-3-p-*methoxyphenylthiopropane*, b.p. 140°/10^{-5} mmHg, n_D^{22} 1·5280, $\nu_{max.}$ (in CCl_4) 1722 cm^{-1} (Found: C, 56·0; H, 6·35; S, 10·9. $C_{14}H_{18}O_5S$ requires C, 56·4; H, 6·1; S, 10·7%); 1,2-*diacetoxy*-3-p-*methylthiophenylthiopropane*, b.p. 160°/10^{-5} mmHg, n_D^{24} 1·5641, $\nu_{max.}$ (in CCl_4) 1730 cm^{-1} (Found: C, 53·7; H, 5·8; S, 20·5. $C_{14}H_{18}O_4S_2$ requires C, 53·5; H, 5·8; S, 20·4%); 1,2-*diacetoxy*-3-(2,4-*dinitrophenylthio*)*propane*, m.p. 115° (from benzene–petroleum), $\nu_{max.}$ 1740 cm^{-1} (Found: C, 43·7; H, 4·0; N, 7·9; S, 9·2. $C_{13}H_{14}N_2O_8S$ requires C, 43·6; H, 3·9; N, 7·8; S, 8·95%).

1,2-*Dimethyl Ethers*.—(i) A mixture of the 1,2-diol, dimethyl sulphate (2 parts), powdered sodium hydroxide (3 parts), and tetrahydrofuran (40 parts) was vigorously stirred under reflux at 45° for 20 h and then concentrated. The residue was extracted with benzene, and the extract was washed with water, then dried and distilled. Prepared in this way (yields *ca.* 80%) were 3-p-*chlorophenylthio*-1,2-*dimethoxypropane*, b.p. 96°/10^{-5} mmHg, n_D^{22} 1·5440 (Found: C, 53·5; H, 6·2; Cl, 14·4; S, 12·8. $C_{11}H_{15}ClO_2S$ requires C, 53·5; H, 6·1; Cl, 14·1; S, 13·0%); 1,2-*dimethoxy*-3-p-*methoxyphenylthiopropane*, b.p. 120°/10^{-3}

[10] C. M. Suter and H. L. Hansen, *J. Amer. Chem. Soc.*, 1932, **54**, 4100; *cf.* G. W. Perold and P. F. A. van Lingen, *Chem. Ber.*, 1959, **92**, 293.

[11] M. Protiva, M. Rajšner, E. Alderová, V. Seidlová, and J. Vejdělek, *Coll. Czech. Chem. Comm.*, 1964, **29**, 2161; *cf.* A. Burawoy, J. P. Critchley, and A. R. Thompson, *Tetrahedron*, 1958, **4**, 403.

[12] V. O. Lukashevich and M. M. Sergeeva, *Zhur. obshchei Khim.*, 1949, **19**, 1493.

mmHg, n_D^{23} 1·5346 (Found: C, 59·8; H, 7·75; S, 13·3. $C_{12}H_{18}O_3S$ requires C, 59·5; H, 7·5; S, 13·2%); 1,2-*dimethoxy*-3-p-*methylthiophenylthiopropane*, b.p. 134°/10^{-5} mmHg, n_D^{23} 1·5780 (Found: C, 56·0; H, 7·0; S, 25·0. $C_{12}H_{18}O_2S_2$ requires C, 55·8; H, 7·0; S, 24·8%).

(ii) To a solution of 3-(2,4-dinitrophenylthio)propane-1,2-diol (0·6 g) and fluoroboric acid (40%; 1 ml) in 1,2-dichloroethane (200 ml) was added an excess of ethereal diazomethane. After 20 h the solution was washed with 2N-NaOH and with water, then dried and evaporated to a residue which contained some diol. The required 3-(2,4-*dinitrophenylthio*)-1,2-*dimethoxypropane* (0·3 g) was extracted from this mixture with ether, and after recrystallisation from ether–petroleum had m.p. 80—81° (Found: C, 43·5; H, 4·6; N, 9·3; S, 10·8 $C_{11}H_{11}N_2O_6S$ requires C, 43·7; H, 4·7; N, 9·3; S, 10·6%).

1,2-*Dimethanesulphonates*.—Solutions of the 1,2-diol in pyridine (5—10 parts) and of methanesulphonyl chloride (20% excess) in pyridine (5 parts) were mixed at 0° and stored at 0° for 20 h. Crushed ice was then added, and the mixture was extracted with benzene. The extract was washed with dilute sulphuric acid and with water, then dried and evaporated. 3-p-*Chlorophenylthio*-1,2-*dimethanesulphonyloxypropane* had m.p. 65° (from ether–petroleum), $\nu_{max.}$ 1180—1220 and 1380 cm.$^{-1}$ (Found: C, 35·3; H, 4·1; S, 25·4. $C_{11}H_{15}ClO_6S_3$ requires C, 35·2; H, 4·0; S, 25·65%); 1,2-*dimethanesulphonyloxy*-3-p-*methoxyphenylthiopropane*, an oil, had $\nu_{max.}$ 1200 and 1380 cm^{-1} (Found: C, 38·7; H, 5·1; S, 25·8. $C_{12}H_{18}O_7S_3$ requires C, 38·9; H, 4·9; S, 26·0%); 1,2-*dimethanesulphonyloxy*-3-p-*methylthiophenylthiopropane* had m.p. 79° (from benzene–petroleum), $\nu_{max.}$ 1180—1200 and 1380 cm.$^{-1}$ (Found: C, 37·5; H, 4·8; S, 33·0. $C_{12}H_{18}O_6S_4$ requires C, 37·3; H, 4·7; S, 33·2%), 1,2-*dimethanesulphonyloxy*-3-(2,4-*dinitrophenylthio*)*propane* had m.p. 106—107° (from benzene–petroleum), $\nu_{max.}$ 1360—1380 cm.$^{-1}$ (Found: C, 30·9; H, 3·3; N, 6·4; S, 22·1. $C_{11}H_{14}N_2O_8S_3$ requires C, 30·7; H, 3·3; N, 6·5; S, 22·35%).

1,3-*Benzylidenedioxy*-2-*toluene*-p-*sulphonyloxypropane* (22).—The m.p. of different batches of this derivative, prepared [8] from 1,3-*O*-benzylideneglycerol, varied from *ca.* 85° to *ca.* 122°. A sample of the lowest-melting preparation was separated by t.l.c. (silica–ether) into two fractions, R_F 0·8 and 0·6. The former was the trans-*isomer*, m.p. 95° (from methanol), τ (in $CDCl_3$) 2·13 (2H, d, Ar), 2·60 (7H, m, Ar), 4·58 (1H, s, C*H*Ph), 5·2—6·6 (5H, m), 7·60 (3H, s, Me). The second fraction was the cis-*isomer*, m.p. 127° (from methanol), τ (in $CDCl_3$) 2·08 (2H, d, Ar), 2·62 (7H, m, Ar), 4·50 (1H, s, C*H*Ph), 5·53 (1H, m), 5·85 (4H, d), and 7·60 (3H, s, Me).

1,3-*Benzylidenedioxy*-2-p-*chlorophenylthiopropane* (24).—*p*-Chlorothiophenol (10 g) was added to a solution prepared from sodium (1·5 g) and dry ethanol (100 ml), and the solvent was then removed under reduced pressure. The solid residue, with the preceding toluene-*p*-sulphonate (15·0 g, mixed stereoisomers), was heated in dimethylformamide (60 ml) for 18 h at 96° under nitrogen. Dilution with water (300 ml) and extraction with benzene gave a solid, m.p. *ca.* 82°, which was separated by t.l.c. (silica–benzene) into two fractions. The first, R_F 0·6, m.p. 118° (from methanol), was the trans-*isomer*, τ (in $CDCl_3$) 2·68 (9H, d, Ar), 4·62 (1H, s, C*H*Ph), and 5·5—6·5 (5H, m) (Found: C, 62·2; H, 4·9; Cl, 11·5; S, 10·4. $C_{16}H_{15}ClO_2S$ requires C, 62·65; H, 4·9; Cl, 11·55; S, 10·45%). The second fraction, R_F 0·3, m.p. 106° (from methanol), was the cis-*isomer*, τ (in $CDCl_3$) 2·58 (9H, m, Ar), 4·43 (1H, s, C*H*Ph), 5·76 (4H, d), and 6·85 (1H, m) (Found: C, 62·5; H, 4·8; S, 10·3%). A mixture of the two isomers had m.p. 81—86°.

A similar experiment in which the *cis*-toluene-*p*-sulphonate was used gave a product, m.p. 115°, which furnished a ^{1}H n.m.r. spectrum identical to that of the pure *trans*-sulphide.

2-p-*Chlorophenylthiopropane*-1,3-*diol* (12).—A mixture of 1,3-benzylidenedioxy-2-*p*-chlorophenylthiopropane (12·0 g), N-H_2SO_4 (60 ml), and methanol (150 ml) was stirred at 55° for 3 h, then cooled, neutralised with aqueous ammonia, concentrated, and extracted with benzene. Evaporation of the washed and dried extract gave the *diol* (5·1 g), m.p. 79° (from carbon tetrachloride) (Found: C, 49·3; H, 5·1; Cl, 16·45; S, 14·8. $C_9H_{11}ClO_2S$ requires C, 49·4; H, 5·1; Cl, 16·2; S, 14·7%).

1,3-*Benzylidenedioxy*-2-p-*methoxyphenylthiopropane* (25).—Prepared from *p*-methoxythiophenol (13·0 g) as described for the *p*-chloro-compound, the product (12·5 g) had m.p. 87° (from methanol) (Found: C, 67·3; H, 6·2; S, 10·8. $C_{17}H_{18}O_3S$ requires C, 67·5; H, 6·0; S, 10·6%). The ^{1}H n.m.r. spectrum showed it to be a mixture of stereoisomers (τ 4·45 and 4·62); the trans-*form* was separated by t.l.c. (silica–benzene) and also had m.p. 87°, but τ (in $CDCl_3$) 2·62 (7H, m, Ar), 3·17 (2H, d, Ar), 4·62 (1H, s, C*H*Ph), 5·5—5·8 (2H, m), 6·0—6·9 (3H, m), and 6·31 (3H, s, OMe) (Found: C, 67·3; H, 6·2; S, 10·5%).

2-p-*Methoxyphenylthiopropane*-1,3-*diol* (13).—The preceding compound (13·6 g) on acid hydrolysis, as described above, gave the *diol* (7·3 g), m.p. 66° (from carbon tetrachloride) (Found: C, 55·8; H, 6·4; S, 14·7. $C_{10}H_{14}O_3S$ requires C, 56·0; H, 6·6; S, 15·0%).

1,3-*Benzylidenedioxy*-2-p-*methylthiophenylthiopropane* (26).—Prepared from *p*-(methylthio)thiophenol (8·0 g), the product (13·4 g) had m.p. *ca.* 67°, and was separated by t.l.c. (silica–benzene) into the trans-*isomer*, R_F 0·7, m.p. 95° (from methanol), τ (in $CDCl_3$) 2·58 (9H, m, Ar), 4·58 (1H, s, C*H*Ph), 5·45—5·75 (2H, m), 5·9—6·7 (3H, m), and 7·57 (3H, s, SMe) (Found: C, 63·8; H, 5·6; S, 20·1. $C_{17}H_{18}O_2S_2$ requires C, 64·1; H, 5·7; S, 20·1%); and the cis-*isomer*, R_F 0·4, m.p. 93° (from methanol), τ (in $CDCl_3$) 2·57 (9H, m, Ar), 4·42 (1H, s, C*H*Ph), 5·75 (4H, d), 6·87 (1H, m), and 7·56 (3H, s, SMe) (Found: C, 63·9; H, 5·8; S, 20·0%). A mixture of the two isomers had m.p. 70—72°.

2-p-*Methylthiophenylthiopropane*-1,3-*diol* (14).—Acid hydrolysis of the crude benzylidene compound (26) (15·0 g) gave the *diol* (7·0 g), m.p. 76° (from carbon tetrachloride) (Found: C, 52·4; H, 6·0; S, 27·8. $C_{10}H_{14}O_2S_2$ requires C, 52·1; H, 6·1; S, 27·85%).

2-*Acetylthio*-1,3-*benzylidenedioxypropane*.—Potassium thioacetate (6·0 g) and 1,3-benzylidenedioxy-2-toluene-*p*-sulphonyloxypropane (10·0 g, mixed stereoisomers) were heated in dimethylformamide (60 ml) at 100° for 20 h under nitrogen. The cooled mixture was then diluted with water (500 ml) and extracted with benzene. Evaporation of the washed and dried extract gave a dark red solid which was extracted with warm petroleum. The insoluble residue, when recrystallised from methanol, had m.p. 121° and gave a ^{1}H n.m.r. spectrum identical to that of the *cis*-isomer of the original toluene-*p*-sulphonate (22). Evaporation of the petroleum extract gave the *thioacetate* (2·8 g), m.p. 92° (from petroleum), $\nu_{max.}$ (in CCl_4) 1680 cm^{-1}, τ (in $CDCl_3$) 2·45 (5H, m, Ar), 4·33 and 4·42 (1H, 2s, C*H*Ph), 5·35—6·28 (5H, m), and 7·57 (3H, s, SAc) as a mixture of stereoisomers (Found: C, 60·4; H, 5·8; S, 13·4. $C_{12}H_{14}O_3S$ requires C, 60·5; H, 5·9; S, 13·45%).

1,3-*Benzylidenedioxy*-2-(2,4-*dinitrophenylthio*)*propane* (27).—Similar treatment of the toluene-*p*-sulphonate (22) (13·0 g) with potassium thiobenzoate (12·2 g) in dimethylformamide (50 ml) gave an oil which partly crystallised. The solid was collected and recrystallised from methanol; it then had m.p. 123° and was the *cis*-toluene-*p*-sulphonate (^{1}H n.m.r. spectrum). The residual oil (9·2 g) was dissolved in a solution prepared from sodium (1·8 g) and methanol (60 m), then boiled under reflux for 20 min and cooled. A solution of 1-chloro-2,4-dinitrobenzene (9·0 g) in methanol (60 ml) was added, whereupon a yellow solid (12·8 g) was precipitated. This was collected, washed with methanol, and recrystallised from benzene. The *sulphide* had m.p. 174°, τ (in C_5D_5N) 4·15 and 4·20 (1H, 2s, C*H*Ph) (Found: C, 52·9; H, 3·9; N, 7·5. $C_{16}H_{14}N_2O_4S$ requires C, 53·0; H, 3·9; N, 7·7%).

2-(2,4-*Dinitrophenylthio*)*propane*-1,3-*diol* (15).—The preceding benzylidene compound (27) (12·4 g), methanol (450 ml), and N-H_2SO_4 (60 ml) were stirred together at 60°. The mixture became homogeneous after 2 h and after a further 2 h it was cooled, neutralised with sodium hydrogen carbonate, filtered to remove sodium salts, and concentrated to *ca.* 100 ml. Dilution with water then precipitated the *diol* (4·3 g) which after recrystallisation from chloroform–petroleum had m.p. 128° (Found: C, 39·65; H, 3·9; N, 10·0; S, 11·9. $C_9H_{10}N_2O_6S$ requires C, 39·4; H, 3·7; N, 10·2; S, 11·7%).

1,3-*Diacetates*.—Prepared from the appropriate 1,3-diol, under the conditions described for the corresponding 1,2-compound, 1,3-*diacetoxy*-2-p-*chlorophenylthiopropane* had b.p. 130°/10^{-5} mmHg, n_D^{20} 1·5382, $\nu_{max.}$ 1735 cm^{-1} (Found: C, 51·5; H, 5·0; S, 10·8%); 1,3-*diacetoxy*-2-p-*methoxyphenylthiopropane*, b.p. 134°/10^{-5} mmHg, n_D^{23} 1·5323, $\nu_{max.}$ (in CCl_4) 1722 cm^{-1} (Found: C, 56·2; H, 5·9; S, 11·0%); 1,3-*diacetoxy*-2-p-*methylthiophenylthiopropane*, b.p. 158°/10^{-5} mmHg, n_D^{21} 1·5662, $\nu_{max.}$ (in CCl_4) 1730 cm^{-1} (Found: C, 53·5; H, 5·6; S, 20·7%); 1,3-*diacetoxy*-2-(2,4-*dinitrophenylthio*)*propane*, m.p. 76° (from carbon tetrachloride–petroleum), $\nu_{max.}$ 1730 cm^{-1} (Found: C, 43·7; H, 3·9; N, 7·8; S, 8·9%).

1,3-*Dimethyl Ethers*.—Methylation of each 1,3-diol was carried out under the conditions used for the 1,2-isomer. 1,3-*Dimethoxy*-2-p-*chlorophenylthiopropane* had b.p. 100°/10^{-5} mmHg, n_D^{20} 1·5438 (Found: C, 53·4; H, 6·1; S, 13·05%); 1,3-*dimethoxy*-2-p-*methoxyphenylthiopropane*, b.p. 106°/10^{-5} mmHg, n_D^{25} 1·5310 (Found: C, 59·2; H, 7·6; S, 13·1%); 1,3-*dimethoxy*-2-p-*methylthiophenylthiopropane*, b.p. 130°/10^{-5} mmHg, n_D^{21} 1·5790 (Found: C, 55·7; H, 6·9; S, 24·6%); 1,3-*dimethoxy*-2-(2,4-*dinitrophenylthio*)*propane*, m.p. 75° (from ether–petroleum) (Found: C, 43·8; H, 4·6; N, 9·5; S, 10·3%).

1,3-*Dimethanesulphonates*.—(i) 2-*p*-Chlorophenylthiopropane-1,3-diol (3·5 g) in pyridine (10 ml) was slowly added (30 min) to methanesulphonyl chloride (5·0 g) in pyridine (20 ml) at 0°. The solution was stored at 0° overnight, then worked up as previously described to give 2-p-*chlorophenylthio*-1,3-*dimethanesulphonyloxypropane* (17) (5·1 g), m.p. 60° (from ether–petroleum), $\nu_{max.}$ 1180—1220 and 1380 cm^{-1} (Found: C, 35·5; H, 4·2; S, 25·6%).

(ii) When methanesulphonyl chloride (5·0 g) was added *quickly* to the same diol (3·0 g) in pyridine (10 ml), initially at 0°, and the mixture was afterwards stored and worked up as before, the product (3·8 g), m.p. 50—51°, was a mixture of 1,2- and 1,3-dimethanesulphonate (^{1}H n.m.r. spectrum).

(iii) 2-*p*-Methylthiophenylthiopropane-1,3-diol (3·0 g), treated as in method (i), gave 1,3-*dimethanesulphonyloxy*-2-p-*methylthiophenylthiopropane* (19) (4·0 g) m.p. 100° (from benzene–petroleum), $\nu_{max.}$ 1180—1220 and 1380 cm^{-1} (Found: C, 37·5; H, 4·5; S, 33·05%).

(iv) 2-(2,4-Dinitrophenylthio)propane-1,3-diol (1·8 g) similarly gave 1,3-*dimethanesulphonyloxy*-2-(2,4-*dinitrophenylthio*)*propane* (20) (2·4 g), m.p. 119° (from chloroform), $\nu_{max.}$ 1380 cm^{-1} (Found: C, 30·4; H, 3·1; N, 6·3; S, 22·1%). The same product was obtained even when the mixture of reactants was stored at ambient temperature.

Dimethanesulphonate from 2-p-*Methoxyphenylthiopropane*-1,3-*diol*.—(i) Reaction of the 1,3-diol (2·6 g) with methanesulphonyl chloride, under the conditions specified in (i) above, gave an oil (3·0 g) which was the dimethanesulphonate (8) of the 1,2-diol (^{1}H n.m.r. spectrum).

(ii) A solution of the 1,3-diol (0·5 g) in benzene (5 ml) was slowly added (30 min) to methanesulphonic anhydride[13] (1·3 g) in benzene (30 ml) and pyridine (5 ml) at 0°. After storage at 0° overnight the mixture was worked up to give an oil (0·5 g), which again was the 1,2-dimethanesulphonate (^{1}H n.m.r. spectrum).

Rearrangement of 1,3-*Dimethanesulphonates to the* 1,2-*Isomers*.—(a) *In boiling acetone*. The 1,3-dimethanesulphonate (*ca.* 200 mg) in dry AnalaR acetone (*ca.* 30 ml) was boiled under reflux for 6 h or for 24 h. The solvent was then removed under reduced pressure, and the residue, taken up in benzene, was washed with water, then dried, and recovered by evaporation. The ^{1}H n.m.r. spectrum was recorded, and the extent of isomerisation (Table 2) calculated by comparison with the spectra of the authentic 1,3- and 1,2-dimethanesulphonates. The product from treatment (24 h) of the *p*-methylthio-compound (19) crystallised spontaneously; one recrystallisation from benzene–petroleum gave the 1,2-isomer (9), m.p. and mixed m.p. 77°.

(b) *In methanol*. A solution of 1,3-dimethanesulphonyloxy-2-phenylthiopropane [2] (0·34 g) in 1,2-dichloroethane (10 ml) and dry methanol (40 ml) was kept at 50°. The progress of the reaction was followed by periodic withdrawal of a sample, and titration with a 0·05N-NaOH. When the liberated acid reached 52% of the theoretical for complete displacement, the main reaction mixture was concentrated under reduced pressure and then taken up in benzene. This solution was washed with water, then dried and evaporated. The oily residue was extracted with cold petroleum to remove methanolysis products, whereupon it crystallised. Recrystallisation from chloroform–petroleum gave 1,2-dimethanesulphonyloxy-3-phenylthiopropane [2] m.p. and mixed m.p. 60°.

Rates of Solvolysis of Dimethanesulphonates.—A solution of the dimethanesulphonate (0·002 mol) in 1,2-dichloroethane (20 ml) was diluted with dry methanol to 100 ml. The mixture was maintained at 50°, and the progress of the solvolysis was followed as described above. Percentage reaction was plotted against time, and the time for 50% reaction obtained from the graphs. The results are shown in Table 3.

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[13] L. N. Owen and S. P. Whitelaw, *J. Chem. Soc.*, 1953, 3723.