3-Heteraglutaraldehydes. Part II.[1] Tetrahydrothiophen-3,4-diol 1,1-Dioxides and the Chemistry of their Oxidation Product, 3-Thiaglutaraldehyde 3,3-Dioxide, and its Derivatives

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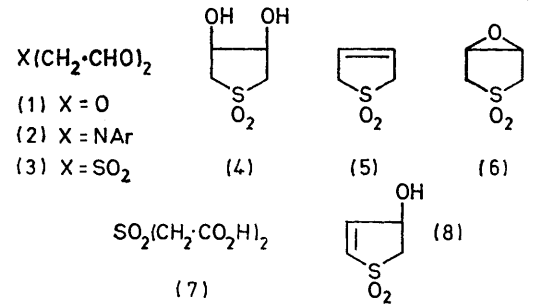
Reproducible methods are described for the preparation of 3,4-epoxytetrahydrothiophen 1,1-dioxide and *trans*-tetrahydrothiophen-3,4-diol 1,1-dioxide by acid-catalysed reactions of 2,5-dihydrothiophen 1,1-dioxide with hydrogen peroxide. Earlier confusing accounts of the effect of acetic and formic acids have been clarified. The *trans*- as well as the more reactive *cis*-diol was oxidised by periodate to 2,2'-sulphonyldiacetaldehyde. In reaction with nitrogen-, sulphur-, or oxygen-containing nucleophiles, the dialdehyde formed crystalline linear derivatives and the only cyclic compounds readily obtained were 2-acetoxy-6-phenylthio-1,4-oxathian 4,4-dioxide and 1,4-dithian-2,6-diol 4,4-dioxide. 2,2'-Sulphonyldi(acetaldehyde oxime) was dehydrated to sulphonyldiacetonitrile, also prepared by oxidation of the known thiodiacetonitrile. An alternative approach to the dialdehyde by addition of sulphuryl chloride to ethyl vinyl ether was unsuccessful.

We recently described [1] the preparation of the oxa- and aza-dialdehydes (1) and (2) and their reaction with thiosemicarbazides. When attention was turned to the sulphone (3),[2] the required precursor was tetrahydrothiophen-3,4-diol 1,1-dioxide (4), which was derived from 2,5-dihydrothiophen 1,1-dioxide (5). The relevant literature contains some errors which we have now corrected. We have also characterised the dialdehyde (3) through several crystalline derivatives. The bis-(4-methylthiosemicarbazone) shows some anti-tumour activity.[3]

The hydroxylation of the sulphone (5) was originally carried out by van Zuydewijn.[4] Oxidation with permanganate gave the *cis*- and with peracetic acid the *trans*-diol; in both cases yields were low and experimental procedures tedious. The *cis*-diol was later [5] prepared more conveniently with osmium tetroxide,



while Birch and McAllan [6] and Sorenson [7] claimed to have obtained, in 75—80% yield, the *trans*-diol by

[1] V. C. Barry, J. E. McCormick, and R. S. McElhinney, *Carbohydrate Res.*, 1968, **7**, 299 is considered to be Part I.
[2] D. Fornelli, Ital.P. 683,293 (*Chem. Abs.*, 1966, **64**, 9881).
[3] V. C. Barry, M. L. Conalty, J. E. McCormick, R. S. McElhinney, M. R. McInerney, and J. F. O'Sullivan, *J. Medicin. Chem.*, 1970, **13**, 421.
[4] E. de R. van Zuydewijn, *Rec. Trav. chim.*, 1938, **57**, 445.
[5] M. Procházka and V. Horák, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1509.
[6] S. F. Birch and D. T. McAllan, *J. Chem. Soc.*, 1951, 2556.
[7] W. R. Sorenson, *J. Org. Chem.*, 1959, **24**, 1796, *cf.* Houben-Weyl, 'Methoden der Organischen Chemie,' 1965, **6/3**, 392; J. A. Elvidge and M. A. Smith, *Mechanisms of Reactions of Sulphur Compounds*, 1968, **3**, 43.

treatment with an excess of peroxide in acetic acid for 24 h (instead of 1 month [4]) at room temperature. In both accounts, the solution was finally heated under reflux for 3 h to destroy the excess of peroxide. Attempts [5] to prepare the *trans*-diol from the dihydrothiophen dioxide (5) with peroxide and various heavy metal catalysts were abortive.

Sorenson [7] also found that the action on the sulphone (5) of peroxide in formic acid for 2—3 days at room temperature yielded the epoxide (6) (30%), which to his surprise was stable to boiling formic acid (even though the oxidation product from peracetic acid was apparently the diol). This epoxide has otherwise always been made indirectly, by the action of base on halogenohydrins.[8-10] The literature gives the impression that it is unusually difficult to hydrate, requiring lengthy treatment with dilute sulphuric acid [7] or superheated steam,[8] although halogen acids open the epoxide ring readily to give halogenohydrins.[8a] Dilute perchloric acid [5,10] has hitherto been the most convenient reagent for preparing the *trans*-diol.

We have now clarified the situation, as follows. An experiment similar to that of Birch and McAllan [6] (the amount of peroxide they used is not clear) confirmed formation of the *trans*-diol, but if the solution was quenched with disulphite (metabisulphite) after 24 h instead of being boiled, the sulphone (5) was almost quantitatively recovered. If formic acid is used under reflux, the diol is also formed, although in somewhat lower yield. Peroxide is consumed much faster in the stronger acid, but it is still necessary to heat the solution for a few hours longer (see Experimental section).

The epoxide (6) is indeed the product from 2,5-dihydrothiophen 1,1-dioxide (5) and peroxide and formic acid under mild conditions. Similar treatment with acetic acid instead gave the epoxide in comparable yield (40—50%).* In this case a longer reaction time was used, and even then some peroxide remained; this was destroyed by disulphite (metabisulphite). When we attempted to destroy the peroxide by boiling, the *trans*-diol was obtained in 30—50% yields, even though the epoxide was supposed to be very stable to acids. The reaction of the epoxide with various acids was accordingly reinvestigated.

Most of the epoxide was recovered when 65% acetic acid under reflux was used. However, with formic acid under similar conditions, the major product was the diol. This contrasts with Sorenson's results [7] with 98% formic acid. Mineral acids give the diol in better yields, boiling for a few hours with 0·2N-$HClO_4$ or 2N-H_2SO_4 being equally effective.

The yields of diol and epoxide isolated respectively when the acetic acid solution (after 7 days at 40°) is or is not heated under reflux are not sufficiently high to show that the diol is exclusively formed from the epoxide during boiling, but certainly this treatment greatly increases the amount of diol present and decreases that of epoxide. A significant factor may be the presence of the relatively strong acid (7) ($pK_1^{25°}$ 1·89 [11]). A small amount of the crystalline dimethyl ester [12] was isolated when methanol was used to help remove last traces of water during evaporation of solvent from the crude product in another experiment. Sodium hydrogen sulphate (originating from the disulphite) was present on this occasion, but it was absent on another and the dimethyl ester was still identified. When the epoxide was heated with an aqueous 10% solution of acid (7), some diol was indeed formed.

The rate of decomposition of peroxide in the presence of 2,5-dihydrothiophen 1,1-dioxide (5) in warm acid solution was found to vary, and is no doubt susceptible to obscure catalytic influences. These would also account for the difficulty in obtaining the pure diol from an older batch of commercial dioxide (5), which was otherwise apparently of normal purity. Two final complicating factors are that the epoxide (6) exists in two different crystalline modifications,[8b,10] and is moreover readily isomerised to the allylic alcohol (8) under mild basic conditions.[5] We found that some samples of methanol even contained sufficient catalyst to effect this isomerisation, as the epoxide was stable when a trace of acetic acid was added to such methanol. However, no great difficulty should henceforth be experienced in preparing the diol or the epoxide in reasonable yields as described in the Experimental section.

The *cis*- and *trans*-diols (4) were also prepared readily by oxidation of the corresponding tetrahydrothiophendiols [13] with peroxide in acetic acid. The diacetate of the *trans*-diol (4) has m.p. in agreement with the literature [10] value. A compound assumed in another report [8b] to be the *trans*-diacetate is probably the acetate of the unsaturated alcohol (8), as indicated by the m.p. and the manner of preparation; no sulphur analysis was recorded.

The *cis*-diol was rapidly oxidised by periodate to the dialdehyde (3), unlike the *trans*-diol, which required 24—48 h. The dialdehyde could be isolated as the bis-(2,4-dinitrophenylhydrazone), bis-(4-methylthiosemicarbazone) (14), or dioxime (31), and the yield of the two last derivatives from the *trans*-diol was not significantly greater after the longer period of oxidation. Like its sulphide analogue,[1] the sulphone (14) gives the exchange product with acidic 2,4-dinitrophenylhydrazine and no glyoxal derivative was obtained.

Evaporation of dialdehyde solutions yielded syrupy materials, although crystalline 2,6-dioxy-derivatives of

* This has been confirmed very recently (A. I. Meyers and T. Takaya, *Tetrahedron Letters*, 1971, 2609).

[8] (*a*) O. E. van Lohuizen and H. J. Backer, *Rec. Trav. chim.*, 1949, **68**, 1137; (*b*) B. Loev, *J. Org. Chem.*, 1961, **26**, 4394.

[9] H. E. Faith, M. P. Kautsky, and B. E. Abreu, *J. Org. Chem.*, 1962, **27**, 2889; J. D. McClure, *ibid.*, 1967, **32**, 3893.

[10] K. G. Mason, M. A. Smith, E. S. Stern, and J. A. Elvidge, *J. Chem. Soc.* (*C*), 1967, 2171.

[11] J. M. Lovén, *Z. phys. Chem.*, 1894, **13**, 557.

[12] H. J. Backer and W. Stevens, *Rec. Trav. chim.*, 1940, **59**, 444.

[13] J. E. McCormick and R. S. McElhinney, *Chem. Comm.*, 1969, 171.

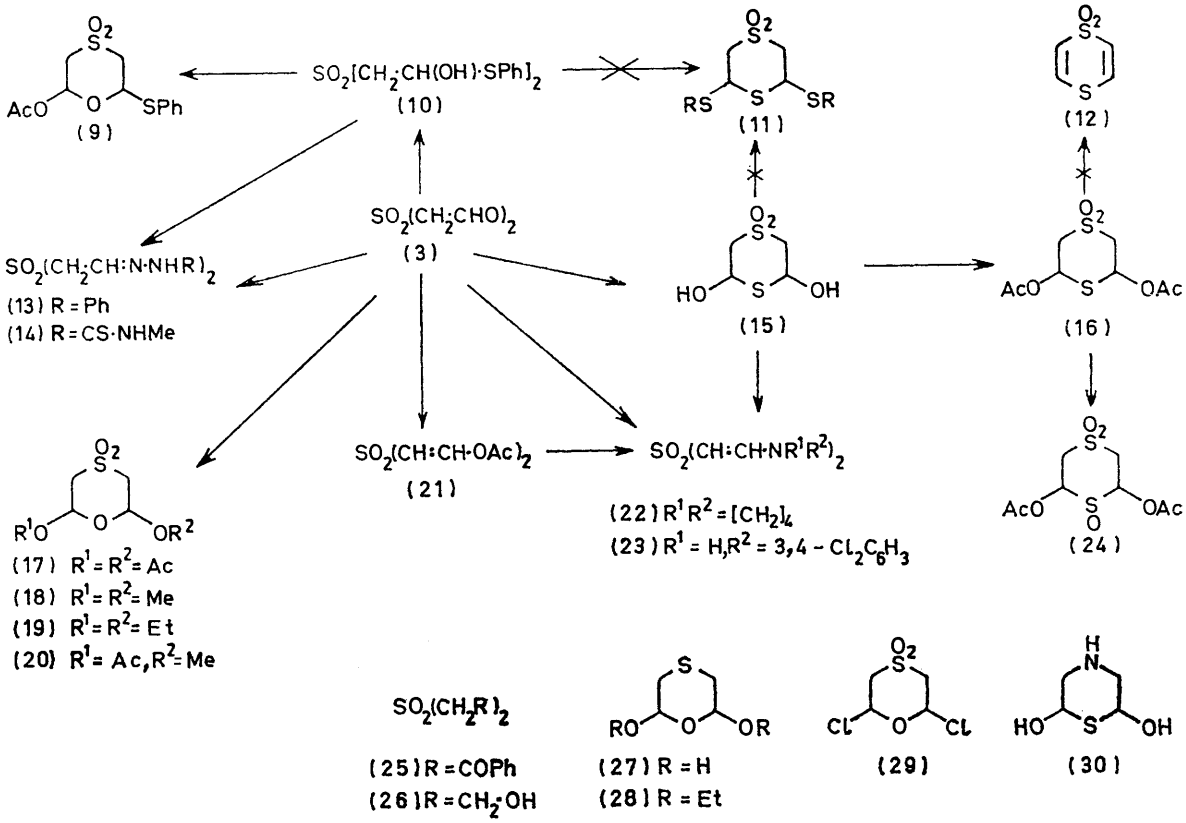
1,4-oxathian [*e.g.*, (27)] are readily prepared from 3-thiaglutaraldehyde [14] and even from some α-sulphonylmonoaldehydes. These last have been studied in some detail by Wanzlick,[15] but the only derivative of the dialdehyde known was the dichloride (29).[16]

When the dialdehyde (3) was extracted from inorganic material with acetone, acetylation with pyridine as catalyst yielded the enol acetate (21) and not the cyclic product (17). There is some i.r. evidence that a cyclic acetate is formed in the presence of boron trifluoride, but after work-up (with alcohols) only traces of crystalline compounds could occasionally be isolated. These were the mono-ester (20) and the ethers (18) and (19); the ethers may indeed have been formed from a cyclic acetate.

Treatment of the dialdehyde with methanol gave the ether (18) in only poor yield, although the analogous reaction with 2,2′-thiodiacetaldehyde yielded the ether (28) very readily.[14] The latter was also easily obtained from the linear bisacetal.[17] We prepared the linear sulphone acetal by oxidation with peroxide–acetic acid,[18] but when treated with hydrogen chloride as described in ref. 17 it was virtually unchanged. Clarke and Smiles emphasise the unreactive nature of the sulphur atom in compound (28):[17] for instance, it could not be oxidised in the same manner as the linear sulphide acetal. While a more vigorous oxidation was not attempted, it seems that this third approach to the cyclic sulphone (18) is not promising.

Treatment with benzenethiol yielded the monothioacetal (10) rather than a cyclic compound, although acetylation then gave the monoacetate (9) in good yield. The bis-(4-methylthiosemicarbazone) (14) was readily obtained from the monothioacetal (10) in aqueous acetic acid, but 2,4-dinitrophenylhydrazine in methanolic sulphuric acid gave a mixture of products.

Reaction of the enol acetate (21) with pyrrolidine yielded the enamine (22). Attempts to displace the acetoxy-groups in (21) by benzenethiol or by hydrogen sulphide failed, but hydrogen sulphide and a solution of the dialdehyde (3) in aqueous hydrochloric acid yielded the crystalline dithian-2,6-diol (15). An aza-analogue (30) has been previously described.[19] The diacetate (16) was obtained on acetolysis of (15) in pyridine. The comparatively simple n.m.r. spectrum of the diacetate indicates rapid interconversion of chair conformations.[20] Treatment of a methanolic solution with triethylamine



SCHEME

[14] R. D. Coghill, *J. Amer. Chem. Soc.*, 1937, **59**, 801.
[15] H.-W. Wanzlick and H. Ahrens, *Chem. Ber.*, 1966, **99**, 1580.
[16] H. Bluestone, B.P. 860,380 (*Chem. Abs.*, 1961, **55**, 14,486).
[17] H. T. Clarke and S. Smiles, *J. Chem. Soc.*, 1909, **95**, 992.
[18] F. W. Stacey, J. C. Sauer, and B. C. McCusick, *J. Amer. Chem. Soc.*, 1959, **81**, 987.
[19] L. Wolff and R. Marburg, *Annalen*, 1908, **363**, 169.
[20] *Cf.* W. A. Thaler and P. E. Butler, *J. Org. Chem.*, 1969, **34**, 3389; R. Rahman, S. Safe, and A. Taylor, *Quart. Rev.*, 1970, **24**, 223.

caused the immediate appearance of an intense band at 287 nm in the u.v. spectrum, but the dithiin (12) could not be isolated. The diol (15) also reacted vigorously with methanesulphonyl chloride and pyridine, but again no crystalline product was obtained. Parham *et al.*[21] prepared a dioxide formulated as (12) by partial oxidation of 1,4-dithiin, but its structure has not been established.

The diacetate (16) and an excess of peroxide in acetic acid yielded the sulphoxide (24). The presence of electron-attracting groups renders the oxidation of sulphides difficult (*q.v. post*); these conditions yielded sulphones from mono-acetoxy-sulphides.[22] The sulphoxide was not homogeneous; if one of the impurities was a second sulphoxide with the configuration at the sulphoxide group inverted, the sulphide (16) would have to be symmetrical, *i.e.* to have *cis*-acetoxy-groups. The sulphoxide reacted readily with hot acetic anhydride, but no crystalline Pummerer rearrangement product [13] was obtained after chromatography.

Repeated attempts to displace the hydroxy-groups of the diol (15) by mercaptans failed, nor could the sulphide (11, R = Ph) be prepared from the monothioacetal (10) and hydrogen sulphide.[23] Pyrrolidine reacted exothermally with the diol (15) to give the enamine (22).

The dialdehyde (3) gave no crystalline product with benzylamine and thus resembles diphenacyl sulphone (25) [24] rather than the dihydroxy-sulphone (26) and its congeners.[25] On the other hand, the enamine (23) was obtained by reaction of the dialdehyde with 3,4-dichloroaniline (even in 1 : 1 proportions). This structure rather than the Schiff base follows from the i.r. spectrum, and is moreover consistent with Wanzlick's findings.[15] The bisphenylhydrazone has the normal [26b] structure (13).

These experiments emphasise the difficulty of preparing cyclic derivatives of 2,2′-sulphonyldiacetaldehyde (3). Compounds (9) and (15) are the only ones readily obtained from acyclic precursors. The sulphone (3) resembles the sulphide [1] since even an excess of dialdehyde yields only the bis-compound (14), which moreover cannot be cyclised by heating with acid.

Another synthetic approach to the dialdehyde involved the reaction of sulphuryl chloride with ethyl vinyl ether. Various sulphur chlorides add to vinyl ethers to give aldehyde derivatives with sulphur-containing α-substituents.[26] However we found that, in the case of sulphuryl chloride, sulphur dioxide is eliminated and the product is mainly the chlorine adduct, αβ-dichloroethyl ethyl ether, which was identified by transformation into α-chloroacetaldehyde derivatives. This very convenient synthesis with sulphuryl chloride has apparently not been carried out before.[27]

Some reactions were carried out with the dioxime (31). Periodate was tested as an oxidant [28] for converting isonitroso- into nitro-groups,[29] and was either ineffective or too vigorous. Treatment of the dioxime with thionyl chloride readily afforded the dinitrile (32); acetic anhydride gave poor results. The dinitrile can be prepared more conveniently by oxidation of the sulphide (33).[30] The presence of α-cyano-groups greatly retards oxidation of the sulphur atom: methylthioacetonitrile can be oxidised with difficulty by peroxide in acetic acid,[31] but readily when this reagent is catalysed by sulphuric acid.[32] Even under these conditions the dicyano-compound (33) was oxidised quite slowly. The properties of the sulphone (32) will be described elsewhere.

$$\underset{(31)}{SO_2(CH_2{\cdot}CH{:}N{\cdot}OH)_2} \longrightarrow \underset{(32)}{SO_2(CH_2{\cdot}CN)_2} \longleftarrow \underset{(33)}{S(CH_2{\cdot}CN)_2}$$

EXPERIMENTAL

M.p.s are corrected. I.r. spectra were recorded for KBr discs, u.v. spectra for solutions in 95% ethanol except where otherwise stated, and n.m.r. spectra at 60 MHz. Evaporations were carried out at 40°. The hydrogen peroxide used throughout was a 30% w/v solution. Light petroleum had b.p. 40—60°. Purity of crystalline compounds was determined by t.l.c. on Silica Gel H (Merck)-coated microscope slides developed, except where specified, with benzene containing 10—20% methanol.

trans-*Tetrahydrothiophen*-3,4-*diol* 1,1-*Dioxide* (4).—(*a*) A solution of *trans*-tetrahydrothiophen-3,4-diol [33] (840 mg, 7 mmol) in acetic acid (3·7 ml) was treated with hydrogen peroxide (2·1 ml). After standing, the solution was heated under reflux for 3 h and evaporated *in vacuo* to give the sulphone (856 mg, 80%), m.p. 159—160·5° (from ethanol) (lit.,[4] 159—160°).

(*b*) (Experiment 1, Table 1). A solution of 2,5-dihydrothiophen 1,1-dioxide (59 g) and hydrogen peroxide (226 ml) in acetic acid (400 ml) was heated under reflux for 3 h. The remaining peroxide was destroyed by sodium disulphite (48·6 g $Na_2S_2O_5$) in water (80 ml), and the solution was evaporated *in vacuo*; 3 portions of methanol were added to assist this process. The residue was extracted (×4) with boiling benzene (250 ml in all). Evaporation gave fraction A (2·49 g).

The benzene-insoluble material was extracted with boiling

[21] W. E. Parham, H. Wynberg, and F. Ramp, *J. Amer. Chem. Soc.*, 1953, **75**, 2065; W. E. Parham, B. Gadsby, and R. A. Mikulec, *J. Org. Chem.*, 1959, **24**, 1819; W. E. Parham in 'Organic Sulfur Compounds,' ed. N. Kharasch, Pergamon Press, vol. 1, 1961, p. 249, *cf.* W. E. Parham, E. T. Harper, and R. S. Berger, *J. Amer. Chem. Soc.*, 1960, **82**, 4932.

[22] R. L. Whistler, T. van Es, and R. M. Rowell, *J. Org. Chem.*, 1965, **30**, 2719.

[23] L. Schutte, *Tetrahedron Letters*, 1971, 2321.

[24] C. R. Johnson and I. Sataty, *J. Medicin. Chem.*, 1967, **10**, 501.

[25] A. H. Ford-Moore, *J. Chem. Soc.*, 1949, 2433; E. Molenaar and J. Strating, *Rec. Trav. chim.*, 1967, **86**, 436.

[26] (*a*) E. Kobayashi and R. Sakata, *J. Pharm. Soc. Japan*, 1962, **82**, 455 (*Chem. Abs.*, 1963, **58**, 4552); (*b*) F. Effenberger and J. Daub, *Chem. Ber.*, 1969, **102**, 104.

[27] Houben-Weyl, 'Methoden der Organischen Chemie,' 1962, **5/3**, 874; *ibid.*, 1965, **6/3**, 130, 566.

[28] *Cf.* H. Tanabe, *J. Pharm. Soc. Japan*, 1956, **76**, 1023 (*Chem. Abs.*, 1957, **51**, 2598); R. J. Sundberg and P. A. Bukowick, *J. Org. Chem.*, 1968, **33**, 4098.

[29] For the corresponding nitro-compound, see R. L. Heath and A. Lambert, *J. Chem. Soc.*, 1947, 1477.

[30] N. von Zweigbergk, *Ber.*, 1913, **45**, 3337; W. Steinkopf, J. Herold, and J. Stöhr, *ibid.*, 1921, **53**, 1012, 1671; H. Böhme and A. Dick, *Arch. Pharm.* 1961, **294**, 475.

[31] S. Hünig and O. Boes, *Annalen*, 1953, **579**, 23.

[32] R. Dijkstra and H. J. Backer, *Rec. Trav. chim.*, 1954, **73**, 569.

[33] G. W. Kilmer, M. D. Armstrong, G. B. Brown, and V. du Vigneaud, *J. Biol. Chem.*, 1942, **145**, 495.

ethanol (3 × 150 ml). Concentration and cooling afforded fraction B (53·4 g, m.p. 145—155°). A sample (851 mg) in water (5 ml) required 0·1N-NaOH (4·95 ml) for neutralisation (Methyl Red). This would be equivalent to sulphonyldiacetic acid (45 mg).

Recrystallisation of fraction A from ethanol gave dimethyl sulphonyldiacetate (1·08 g), m.p. 113—115°. The analytical sample (from benzene–light petroleum) had m.p. 114—115° as reported [12] (Found: C, 34·5; H, 4·8; S, 15·3. Calc. for $C_6H_{10}O_6S$: C, 34·3; H, 4·8; S, 15·25%). The compound gave the appropriate thiazine (81%, m.p. 223°) with *p*-chlorobenzaldehyde and ammonium acetate as described (lit.,[34] m.p. 220—221°).

Recrystallisation of a portion (40·6 g) of fraction B from ethanol gave *trans*-tetrahydrothiophen-3,4-diol 1,1-dioxide (32·5 g, 56%), m.p. 159—161°, undepressed by material prepared as in (*a*).

3,4-*Epoxytetrahydrothiophen* 1,1-*Dioxide* (6).—(Experiment 6, Table 1). A solution of 2,5-dihydrothiophen 1,1-dioxide (5) (2·95 g) and hydrogen peroxide (11·3 ml) in formic acid (20 ml; 90%) was kept at 40°. Peroxide was consumed after 3 days. The solution was evaporated and reflux for 1·5 h with methanol (15 ml), evaporation left a syrup, which had a much smaller R_F value than the epoxide. Acetylation gave a crystalline product, m.p. 110—113° undepressed on admixture with 3-acetoxy-2,3-dihydrothiophen 1,1-dioxide (8; OAc for OH) (lit.,[5] 111·5—112°). With other methanol, or ethanol, the epoxide was unchanged.

Reaction of 3,4-*Epoxytetrahydrothiophen* 1,1-*Dioxide* (6) *with Acids.*—(*a*) The epoxide (268 mg, 2 mmol), when heated under reflux for 3 h with acetic acid (1·6 ml) and water (0·9 ml), was recovered unchanged (65%).

(*b*) If acetic acid in (*a*) was replaced by formic acid, crystals were obtained (162 mg), m.p. 152—157·5° (from ethanol) undepressed on admixture with the *trans*-diol. The i.r. spectrum was almost identical with that of *trans*-diol ($\nu_{max.}$ 3440 cm^{-1}); the main difference was the weak absorption at 1730 cm^{-1}, probably due to a trace of formate ester.

(*c*) Heating the epoxide (268 mg) with water (4 ml) and perchloric acid (0·2 ml; 72%) under reflux for 4 h, followed by evaporation gave *trans*-diol (246 mg), m.p. and mixed m.p. 154—157·5° (from ethanol).

TABLE 1

Expt.*	Time	Temperature	Peroxide remaining (%)	Yield (%) *trans*-Diol	Yield (%) Epoxide	M.p.	2,5-Dihydrothiophen 1,1-dioxide recovered (%)
1A	3 h	Reflux	26	56		159—161°	
2A	6 h	Reflux	0	53		159—160	
3A	24 h	Room	95				*ca.* 100
4F	3 h	Reflux	0	38		157—159	
5F	0·5 h	Reflux	0	*ca.* 12	*ca.* 16		
6F	3 day	40°	0		50	153—161	25
7F	7 day	40°	0		41	122—126	27
8A	7 day	40°	63 †		43	159—161	28
9A	38 day	Room	31		30	152·5—158·5	45
10A	7 day	40°, then	0	31		157—160	22
11A	3 h	reflux	0	49		155—158	28

* For experiments marked A, acetic acid was used; for F, 90% formic acid. † Values of 35 and 54% were obtained in other similar runs, and 87% in a blank experiment without 2,5-dihydrothiophen 1,1-dioxide.

extracted with cold benzene (3 × 12 ml). Evaporation gave a solid (0·72 g) with i.r. spectrum superimposable on that of the dihydrothiophen (25%). The benzene-insoluble material (2·56 g, m.p. 116—138°) was crystallised from water (7 ml) to give the epoxide (1·67 g, 50%), m.p. 153—161° (lit.,[10] 128—130° and 158—160°). The i.r. spectrum had no absorption bands above 3000 cm^{-1}. Hydrolysis of a sample with 10% sulphuric acid (see later) afforded the *trans*-diol (85%, m.p. 158—162°; i.r. spectrum identical with that of an authentic specimen).

Other Experiments with 2,5-*Dihydrothiophen* 1,1-*Dioxide and Peroxide in Acid.*—2,5-Dihydrothiophen 1,1-dioxide (5), hydrogen peroxide, and acid were combined in the ratio 1 mol : 4 mol : 800 ml and reacted under the conditions in Table 1. Remaining peroxide was destroyed by sodium disulphite (95 g $Na_2S_2O_5 \equiv$ 1 mol H_2O_2), and the solution neutralised with sodium acetate (except in experiment 1) before evaporation. Any unchanged dihydrothiophen (5) was extracted with cold benzene and the product was recrystallised and identified by mixed m.p., i.r., and t.l.c. In experiments 4 and 5, extraction of the crude product with hot benzene yielded some ester ($\nu_{max.}$ 1725 cm^{-1}), presumably formate.

Isomerisation of 3,4-*Epoxytetrahydrothiophen* 1,1-*Dioxide* (6) *in Methanol.*—After a sample (0·1 g) was heated under

(*d*) With aqueous perchloric acid in (*c*) replaced by sulphuric acid (4 ml; 10%), the solution was cooled, neutralised ($NaHCO_3$), and evaporated. Boiling methanol extracted the *trans*-diol (241 mg), m.p. and mixed m.p. 159—161° (from ethanol) (confirmed by i.r.).

(*e*) The epoxide (268 mg) was heated under reflux for 3 h with water (1·5 ml) and sulphonyldiacetic acid (150 mg). Neutralisation ($NaHCO_3$), evaporation, and extraction with hot acetone afforded a soluble fraction (330) mg), $\nu_{max.}$ 1710 cm^{-1} (otherwise similar to that of *trans*-diol). Recrystallisation from ethanol gave a mixture (147 mg), m.p. *ca.* 110°; no ester absorption in the i.r., and t.l.c. indicated that this product consisted largely of *trans*-diol (4) and epoxide (6). Treatment with methanesulphonyl chloride–pyridine afforded the bismethanesulphonate of the *trans*-diol, m.p. and mixed m.p. 186—189·5°. On treating the epoxide similarly, the only compound isolated was starting material (66%).

Dimethyl Sulphonyldiacetate.—Sulphonyldiacetic acid (7) was made from thiodiacetic acid (15 g) as described by Backer,[35] except that the solution, after being cooled 1 night in running water, was kept at 40° the next. All the peroxide was now consumed. The solution was evaporated

[34] V. Baliah and T. Rangarajan, *J. Chem. Soc.*, 1954, 3068.
[35] H. J. Backer, *Rec. Trav. chim.*, 1953, **72**, 119.

in vacuo. Addition of ether and filtration gave sulphonyldiacetic acid (9·07 g, 50%), m.p. 185—187° (from acetonitrile) (lit.,[35] 182°). A further amount (3·34 g) was obtained after re-oxidation of the ether-soluble fraction.

When the acid (364 mg, 2 mmol) was heated under reflux for 3 h with methanol (15 ml), most of it (323 mg) was recovered.

The experiment was repeated in the presence of crushed sodium hydrogen sulphate (1 g). After filtration and evaporation, the residue was extracted with boiling benzene (3 × 10 ml). Two crystallisations from benzene–light petroleum gave the dimethyl sulphonyldiacetate (287 mg, 68%), m.p. and mixed m.p. 112—117°. Heating the acid for 8 h under reflux in 3% v/v methanolic sulphuric acid, neutralisation ($NaHCO_3$), extraction with acetone, and recrystallisation, afforded the ester (72%), m.p. 115—117·5°.

cis-*Tetrahydrothiophen*-3,4-*diol* 1,1-*Dioxide*.—(*a*) *cis*-Tetrahydrothiophen-3,4-diol [36] (3·6 g) was oxidised as described for the *trans*-diol yielding the sulphone (3·56 g, 78%), m.p. 129—130° (lit.,[4] 129—131°); it was unnecessary to leave the solution 24 h before heating under reflux.

(*b*) In the method of Procházka and Horák,[5] control of temperature during the early stages of the reaction is difficult. A mixture of the dihydrothiophen (5) (59 g), hydrogen peroxide (65 ml), water (50 ml), t-butyl alcohol (1 ml), and aqueous osmium tetroxide solution (2% w/v; 4 ml) was maintained, without stirring, for 6 h at 5—7° (bath 0°). It was kept overnight in the deep freeze (in the refrigerator, the temperature rose and the final yield was only 30%), then for 8 h at 8—11° (bath 5°), and then 3 days more in the deep freeze, whereafter the peroxide was all consumed. Evaporation *in vacuo*, addition of ethanol (10 ml), chilling, and filtration yielded the *cis*-diol (43·3 g, 57%), m.p. 121—125°, sufficiently pure for further operations. An analytical sample had m.p. and mixed m.p. 129·5—131° (from ethanol). When less (1·5 ml) osmium tetroxide solution was used the solid dissolved more slowly, 7—8 days in the deep freeze (with intermittent warming to 8° as before) being required for total destruction of the peroxide, and the yield of *cis*-diol was 48%.

3,4-*Diacetoxytetrahydrothiophen* 1,1-*Dioxides*.—The diol (304 mg, 2 mmol) was treated with acetic anhydride (0·4 ml) and dry pyridine (0·2 ml) and left overnight. Addition of ice–water and filtration yielded the diacetate. The *trans*-compound (90%) had m.p. 154—157° (from methanol) (lit.,[10] 152—154°); the cis-*isomer* (87%), m.p. 126—127·5° (Found: C, 40·5; H, 5·1; S, 13·7. $C_8H_{12}O_6S$ requires C, 40·7; H, 5·1; S, 13·6%).

trans-*Tetrahydrothiophen*-3,4-*diol Dimethanesulphonate*.—The diol (152 mg) in dry pyridine (0·3 ml) was cooled in ice and treated dropwise with methanesulphonyl chloride (0·19 ml). On removing the bath, a clear solution resulted. After 3 h, ice was added, forming a gum which soon crystallised. Filtration gave the *ester* (169 mg, 55%), m.p. 188—190° (twice from acetone–light petroleum) (Found: C, 23·8; H, 4·0; S, 30·6. $C_6H_{12}O_8S_3$ requires C, 23·4; H, 3·9; S, 31·2%).

3-*Thiaglutaraldehyde* 3,3-*Dioxide*.—*cis*-Tetrahydrothiophen-3,4-diol (3·04 g, 20 mmol) was added over 10 min in portions to a solution of sodium metaperiodate (4·28 g, 20 mmol) in water (100 ml) at 10°. The solution (final volume, 240 ml) was treated at once with barium chloride and worked-up as described [1] for 3-oxaglutaraldehyde.

The solution (228 ml) was treated with 4-methylthiosemicarbazide (3·99 g, 38 mmol) in water (67 ml), followed by acetic acid (2 ml). The resulting crystals (5·33 g, 82%) were collected after 1 day to give the *bis*-(4-*methylthiosemicarbazone*) (14), m.p. 192·5° (decomp.) (from aqueous dimethylformamide) (Found: C, 29·6; H, 5·1; N, 25·7; S, 29·4. $C_8H_{16}N_6O_2S_3$ requires C, 29·6; H, 4·9; N, 25·9; S, 29·6%), $\lambda_{max.}$ (in 2-methoxyethanol diluted with 95% ethanol) 280 nm; *bis*-(2,4-*dinitrophenylhydrazone*), m.p. 225—227·5° (from dimethylformamide–methanol) (Found: C, 37·3; H, 2·7; N, 22·0; S, 6·45. $C_{16}H_{14}N_8O_{10}S$ requires C, 37·6; H, 2·7; N, 22·0; S, 6·3%), $\lambda_{max.}$ (in 2-methoxyethanol diluted with 95% ethanol) 223, 252, and 346 nm.

When the bis-(4-methylthiosemicarbazone) (81 mg, 0·25 mmol) was heated under reflux for 1·5 h [1] with methanolic 2,4-dinitrophenylhydrazine sulphate (1 mmol), filtration of the hot solution gave the bis-(2,4-dinitrophenylhydrazone) (125 mg, 98%), m.p. and mixed m.p. 230—232°. With a reflux time of 15 min, the yield was 76%.

The *dioxime* (31) was obtained by the usual procedures (85%), m.p. 162—162·5° (decomp.) (from water) (Found: C, 26·9; H, 4·5; N, 15·8; S, 17·9. $C_4H_8N_2O_4S$ requires C, 26·7; H, 4·4; N, 15·6; S, 17·8%); the pinkish *bisphenylhydrazone* (13), prepared at 5° and collected after 15 min, had m.p. 160—160·5° (from ethanol) (Found: C, 58·0; H, 5·5; N, 16·8; S, 9·8. $C_{16}H_{18}N_4O_2S$ requires C, 58·2; H, 5·5; N, 17·0; S, 9·7%), $\lambda_{max.}$ 236, 284, and 306 nm, $\nu_{max.}$ 3280 cm^{-1} (NH), τ [$(CD_3)_2CO$] 5·90 (4H, d, *J* 6 Hz, $SO_2{\cdot}CH_2$).

Oxidation of the trans-*Diol* (4).—The diol was treated with periodate and worked up after *t* h with barium chloride as for the *cis*-diol, and converted into the unpurified derivatives $SO_2(CH_2{\cdot}CH{:}NR)_2$ in the yield shown in Table 2. When worked-up immediately (*cf.* the *cis*-diol), negligible amounts of impure derivatives were obtained.

TABLE 2

	Yield (%)			
t/h	R = NH·CS·NHMe	R = NH·$C_6H_3(NO_2)_2$	R = OH	R = NHPh
4	31	30	34	
24	66	67	59	61
48	68	78	68	65

Bis-(β-*acetoxyvinyl*) *Sulphone* (21).—Aqueous 3-thiaglutaraldehyde 3,3-dioxide [from the *cis*-diol (4·5 mmol)] was freeze-dried and the dialdehyde extracted with cold acetone (3 × 23 ml). Evaporation left a gum, which was treated during 30 min with acetic anhydride (0·85 ml, 9 mmol) and pyridine (0·09 ml). Ice–water (3 ml) was added and the insoluble *enol acetate* (44%) was collected, m.p. 124—127° (from methanol) (Found: C, 41·2; H, 4·5; S, 13·3. $C_8H_{10}O_6S$ requires C, 41·0; H, 4·3; S, 13·7%), $\lambda_{max.}$ 234 nm, $\nu_{max.}$ 3090, 1640, and 960 (CH=CH) and 1785 (vinyl ester) cm^{-1}.

2,6-*Dimethoxy*-1,4-*oxathian* 4,4-*Dioxide* (18).—3-Thiaglutaraldehyde 3,3-dioxide [from the *cis*-diol (5 mmol)], was dissolved in methanol (15 ml) containing boron trifluoride–ether (0·2 ml) and warmed (15 min) at 40°. Evaporation next day left a crystalline residue, which on recrystallisation (methanol) gave the *dimethyl ether* (196 mg, 20%), m.p. 149—158°. The analytical sample (a single spot on t.l.c.) had m.p. 159—161° (from benzene) (Found: C, 36·9; H, 6·2; S, 16·1. $C_6H_{12}O_5S$ requires C, 36·7; H,

[36] M. Procházka, *Coll. Czech. Chem. Comm.*, 1965, **30**, 1158.

6·1; S, 16·3%), τ ($CDCl_3$) 5·2 (2H, dd, *J* 8 and 2·5 Hz, 2 × CH), 6·46 (6H, s, 2 × Me), and 6·9 (4H, d, *J* 9·5 Hz, 2 × CH_2).

Attempted acetylation of the dialdehyde with acetic anhydride and boron trifluoride–ether afforded a crude product, which lacked the enol acetate peaks at 1785 and 1640 cm^{-1} but showed absorptions at 3400w and 1750s cm^{-1}. However, after work-up with alcohols the only compounds isolable (in minute yields) from various experiments were the foregoing dimethyl ether (18), the *diethyl ether* (19), m.p. 132·5—133·5° (from benzene–light petroleum) (Found: C, 43·4; H, 7·3; S, 14·4. $C_8H_{16}O_5S$ requires C, 42·9; H, 7·1; S, 14·3%), and 6-*methoxy*-1,4-*oxathian*-2-*yl acetate* 4,4-*dioxide* (20), m.p. 118—121° (from benzene) (Found: C, 37·6; H, 5·4; S, 14·2. $C_7H_{12}O_6S$ requires C, 37·5; H, 5·4; S, 14·3%), $\nu_{max.}$ 1757 cm^{-1} (ester CO).

Oxidation of Bis-(2,2-*dimethoxyethyl*) *Sulphide*.—A solution of the acetal (4·20 g, 20 mmol) in acetic acid (10 ml) and acetic anhydride (10 ml) was stirred and treated dropwise with hydrogen peroxide (5·7 ml) over 15 min at 0—5°. The solution was warmed to room temperature over 3 h and left 3 days more, and finally was warmed for 2 h at 40°. The peroxide was destroyed by adding dimethyl sulphide (1·0 ml) dropwise and standing for 0·5 h. The aqueous acetic acid was evaporated *in vacuo* with repeated addition of portions of methanol, and a syrupy residue (6·36 g) remained.

The preparation of a 2,4-dinitrophenylhydrazone from a sample (121 mg) in methanolic sulphuric acid (0·5 h at room temperature) gave glyoxal bis-(2,4-dinitrophenylhydrazone) (8·5 mg), m.p. and mixed m.p. 312—315° (decomp.) (uncorr.). Evaporation of the methanolic mother liquor gave a residue, from which was prepared, by heating with 2,4-dinitrophenylhydrazine in acetic acid under reflux for 1·25 h the bis-(2,4-dinitrophenylhydrazone) of 3-thiaglutaraldehyde 3,3-dioxide (184 mg, 95%), m.p. and mixed m.p. 229—231° (decomp.). The glyoxal derivative probably arose from Pummerer rearrangement of an intermediate sulphoxide under acidic conditions.

Bis-(β-*hydroxy*-β-*phenylthioethyl*) *Sulphone* (10).—Crude 3-thiaglutaraldehyde 3,3-dioxide [from the *cis*-diol (5 mmol)] was dissolved in cold acetonitrile (2 ml). The resulting solution was treated with benzenethiol (1·03 ml, 10 mmol) and toluene-*p*-sulphonic acid monohydrate (9·4 mg) and set aside overnight at room temperature. Evaporation left an oil which slowly formed the *monothioacetal* (10) (1·08 g, 58%) after trituration with benzene (4 ml), drying, and washing with water (4 ml). Crystallisation, from benzene–light petroleum and then from benzene alone, gave crystals (t.l.c. showed one main spot together with a trace of faster moving material), m.p. 81—86° (Found: C, 52·0; H, 5·0; S, 25·7. $C_{16}H_{18}O_4S_3$ requires C, 51·9; H, 4·9; S, 25·95%), $\nu_{max.}$ 3400 cm^{-1} (OH).

Treatment of the methanolic monothioacetal with aqueous acidic 4-methylthiosemicarbazide and concentration of the resulting opalescent solution gave the bis-(4-methylthiosemicarbazone) (96%), m.p. 195—200° (decomp.).

2-*Acetoxy*-6-*phenylthio*-1,4-*oxathian* 4,4-*Dioxide* (9).—The crude monothioacetal (10) (260 mg, 0·7 mmol) was treated with acetic anhydride–pyridine (0·3 ml, 2 : 1 v/v). Ice–water (4 ml) was added after 30 min and the *acetate* (199 mg, 94%) was isolated after 2 h as crystals (t.l.c. showed one main spot and a very faint slower-moving spot), m.p. 147—149° (from methanol) (Found: C, 47·8; H, 4·7; S, 21·6. $C_{12}H_{14}O_5S_2$ requires C, 47·7; H, 4·6; S, 21·2%), $\nu_{max.}$ 1762 (ester CO) and 1304 and 1138 cm^{-1} (SO_2), τ ($CDCl_3$) 4·0 (1H, dd, *J* 8 and 3 Hz, C*H*·OAc), 4·8 (1H, dd, *J* 10 and 3 Hz, C*H*·SPh), 6·9 (4H, d, *J* 10 Hz, 2 × CH_2), and 7·88 (3H, s, Me).

Bis-(β-*pyrrolidinovinyl*) *Sulphone* (22).—(*a*) The enol acetate (21) (234 mg, 1 mmol) in methanol (2 ml) was treated with pyrrolidine (1·3 ml). After the initial, vigorous reaction had subsided the mixture was heated under reflux (30 min). Evaporation left a deep orange semi-solid to which water (2 ml) was added. The insoluble *enamine* (211 mg, 82%) was collected, and recrystallised from benzene–light petroleum and then from benzene alone, m.p. 160—162° (Found: C, 56·5; H, 8·1; N, 11·0; S, 12·3. $C_{12}H_{20}N_2O_2S$ requires C, 56·3; H, 7·8; N, 10·9; S, 12·5%), $\lambda_{max.}$ 239 and 283 nm, $\nu_{max.}$ 1597 cm^{-1} (CH=CH).

(*b*) A suspension of 1,4-dithian-2,6-diol 1,1-dioxide (15) (92 mg, 0·5 mmol) (see later) in water (2 ml) was treated slowly at 3—5° with pyrrolidine (0·17 ml, *ca.* 2 mmol) in water (2 ml). The enamine (22) (102 mg, 80%), m.p. and mixed m.p. 159—160° (decomp.), separated.

*Bis-*β-(3,4-*dichloroanilino*)*vinyl Sulphone* (23).—Aqueous 3-thiaglutaraldehyde 3,3-dioxide [from the *cis*-diol (304 mg, 2 mmol)] was added to 3,4-dichloroaniline (323 mg, 2 mmol) in methanol (20 ml). Opacity developed after 0·5 h, and after 2 h an oil had separated on the walls of the flask. Methanol was evaporated off and after 0·5 h the yellow gum, which had hardened, was broken up and filtered off. The crude, amorphous product was dissolved by warming briefly (bath at 70°) with methanol (1 ml). Cooling afforded bright yellow crystals. These were dissolved in methanol (60 ml) at 70° (bath) and the solution, after filtration and concentration to 5 ml, yielded the *enamine* (23) (89 mg), m.p. 131·5—132·5° (Found: C, 43·4; H, 2·9; Cl, 31·5; N, 6·15; S, 7·0. $C_{16}H_{12}Cl_4N_2O_2S$ requires C, 43·8; H, 2·7; Cl, 32·4; N, 6·4; S, 7·3%), $\lambda_{max.}$ (in 2-methoxyethanol–methanol) 257 and 285 nm, $\nu_{max.}$ 3390 (NH) and 1640 cm^{-1} (CH=CH).

Brief heating of the enol acetate (21) with 3,4-dichloroaniline in methanol gave only unchanged starting material.

1,4-*Dithian*-2,6-*diol* 4,4-*Dioxide* (15).—Aqueous 3-thiaglutaraldehyde 3,3-dioxide [from the *cis*-diol (20 mmol)] was treated with conc. hydrochloric acid (48 ml) and hydrogen sulphide was passed into the solution during 3·5 h. The mixture was stoppered and set aside overnight at room temperature. It was then treated with charcoal, filtered (Celite), and evaporated to dryness. Water (4 ml) was added and the insoluble white solid (2·62 g) was collected and washed with the minimum amount of water. The crude product was heated under reflux for several min with acetonitrile (180 ml) and filtered hot. The filtrate deposited crystals of the *diol* (1·412 g, 38%), m.p. 160—162° (decomp.). Concentration of the mother liquors to 24 ml caused separation of 3 further fractions of product (in all, 535 mg, 14·5%) m.p. 153—158° (decomp.). The analytical sample (t.l.c. showed one main spot together with 2 slower-moving spots) had m.p. 156—157° (decomp.) (from acetonitrile) (Found: C, 26·6; H, 4·4; S, 34·8. $C_4H_8O_4S_2$ requires C, 26·1; H, 4·3; S, 34·8%), $\nu_{max.}$ 3370 cm^{-1} (OH).

2,6-*Diacetoxy*-1,4-*dithian* 4,4-*Dioxide* (16).—The diol (15) (368 mg, 2 mmol) was treated with acetic anhydride (0·4 ml) and pyridine (0·08 ml), and stirred thoroughly, since solution did not occur. Water (3 ml) was added after 30 min and the *diacetate* (389 mg, 72·5%) was filtered off. Several recrystallisations from methanol gave crystals

(t.l.c. showed one predominant spot and traces of 2 slower-moving spots), m.p. 157—161° (Found: C, 35·6; H, 4·5; S, 24·0. $C_8H_{12}O_6S_2$ requires C, 35·8; H, 4·5; S, 23·9%), $\nu_{max.}$ 1755 and 1740 (ester CO), 1320 and 1129 (SO_2), and 1040 cm^{-1}, τ ($CDCl_3$) 3·66 (2H, t, J 5 Hz, 2 × CH), 6·41 (4H, d, J 5 Hz, 2 × CH_2), and 7·87 (6H, s, 2 × Me).

2,6-*Diacetoxy*-1,4-*dithian* 1,4-*Trioxide* (24).—The diacetate (16) (214 mg, 0·8 mmol) was partially dissolved in acetic acid (2·6 ml) at 40°. The mixture, cooled to room temperature, was treated with hydrogen peroxide (1·1 ml) and set aside for 48 h. Gradually the starting material dissolved completely and crystals (170 mg, 75%) separated. A further amount of crystalline product was obtained by dilution with water (12 ml) and extraction with chloroform (3 × 12 ml). The crude product was shown by t.l.c. to consist of 3 substances; one of these predominated and all were slower moving than the starting material. Recrystallisation from methanol gave crystals, m.p. 161·5—162·5° (decomp.) though the t.l.c. pattern was unchanged. Further recrystallisation, from acetonitrile, gave needles (t.l.c. indicated that they consisted almost entirely of the predominant substance in the crude product) of the *sulphoxide*, m.p. 172·5—173° (decomp.) (Found: C, 33·9; H, 4·3; S, 22·2. $C_8H_{12}O_7S_2$ requires C, 33·8; H, 4·2; S, 22·5%), $\nu_{max.}$ 1760 and 1745 (ester CO), 1348 and 1140 (SO_2), 1080 (SO), and 1052 cm^{-1}.

Reaction of Sulphuryl Chloride with Ethyl Vinyl Ether.—Freshly distilled sulphuryl chloride (8·1 ml, 0·1 mol) was added dropwise over 20 min to a stirred solution of ethyl vinyl ether (28·3 ml, 0·3 mol) in dry ether (150 ml). The temperature rose from 14 to 30° and was brought back to 20°. After 1 h at this temperature, the solution was distilled to give a mixture (12·24 g, 86%), b.p. 30—34° at *ca.* 12 mmHg, $n_D^{19·5}$ 1·4392, chiefly αβ-dichloroethyl ethyl ether (lit.,[37] 40—50° at 15 mmHg, n_D^{20} 1·4436), but probably containing a little β-chlorovinyl ethyl ether, which [37] has slightly lower b.p. and n_D, and reacts similarly with ethanol.

The above product (10·21 g) was heated under reflux for 1 h with ethanol (7 ml) containing a drop of sulphuric acid. The solution was cooled and poured into water and the product was extracted with light petroleum (×4). Washing (sodium carbonate solution, water), drying ($MgSO_4$), and distillation gave chloroacetaldehyde diethyl acetal (8·17 g, 75%), b.p. 43—45° at *ca.* 12 mmHg. After redistillation, a sample had $n_D^{19·5}$ 1·4156 (lit.,[38] 79—81° at 55 mmHg, n_D^{20} 1·4170). Both the dichloride and the diethyl acetal gave chloroacetaldehyde 2,4-dinitrophenylhydrazone nearly quantitatively, m.p. and mixed m.p. 155—157° (decomp.) (lit.,[37] 155°).

Thiodiacetonitrile (33).—A solution of sodium sulphide nonahydrate (264 g, 1·1 mol) in water (300 ml) was cooled to 0° (ice–salt bath) and stirred briskly. Chloroacetonitrile 126·6 ml, 2·0 mol) was added dropwise over 40 min. Stirring was continued and the bath temperature gradually raised (−10 to 0°) over the next 2 h. The internal temperature was in this way maintained at 0—5° throughout the reaction. The almost colourless crystalline product (71·0 g, 63·5%) was filtered off and washed with a little ice-cold water, m.p. 44—46° (lit.,[30] 45·5—46·5°). By extraction of the brown mother liquor with chloroform, the yield can be raised to 67—70%.

Sulphonyldiacetonitrile (32).—(*a*) A solution of sulphide (33) (22·4 g, 0·2 mol) in acetic acid (40 ml) at 20° was treated with hydrogen peroxide (54·4 ml, 0·48 mol) and sulphuric acid (3·4 ml) in acetic acid (60 ml). During the exothermic reaction the temperature was kept below 40° and periodically brought down to 30° until the reaction subsided (*ca.* 1 h on this scale). The solution was then kept at 40° for 3 days. (After a few h, the colour disappeared and after 10 h thick prisms had separated.) Finally, the mixture was chilled and the *sulphone* (23·23 g, 81%) was collected and washed with ice-cold water, m.p. 142—144° undepressed by admixture with a sample prepared under (*b*). In larger scale experiments, the oxidising solution and the sulphide were mixed gradually. A yield of 59% was obtained after reaction for 1 day. At room temperature, the yield was 31% after 2 days and 53% after 6 days and work-up with disulphite.

(*b*) A solution of the dioxime (31) (1·62 g, 9 mmol) in acetonitrile (50 ml) under reflux was treated during 15 min with thionyl chloride (1·44 ml, 19·8 mmol) in acetonitrile (5 ml). Hydrogen chloride was evolved and the solution was heated under reflux for a further 30 min. The solvent was evaporated and the crystalline residue was taken up in methanol (20 ml), treated with charcoal and chloroform (10 ml) to produce long needles of the dinitrile (32) (1·16 g, 89%), m.p. 144—145° (Found: C, 33·7; H, 2·75; N, 19·5; S, 22·5. $C_4H_4N_2O_2S$ requires C, 33·3; H, 2·8; N, 19·4; S, 22·2%).

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[37] D. A. van Dorp, J. F. Arens, and O. Stephenson, *Rec. Trav. chim.*, 1951, **70**, 289; J. F. Arens, *ibid.*, 1955, **74**, 271.
[38] K. Weissermel and M. Lederer, *Chem. Ber.*, 1963, **96**, 77.