3-Heteraglutaraldehydes. Part III.[1] The 1,2-Dithian-4,5-diols and Tetrahydrothiophen-3,4-diols and their Oxidation by Periodate

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Both isomers of the title diols have been prepared by improved methods. The diacetates of the dithiandiols were readily oxidised to stable, crystalline thiolsulphinates, and with difficulty to thiolsulphonates. Bisdisulphides were formed by reaction of a thiol with the thiolsulphinates. Tris(dimethylamino)phosphine abstracted sulphur from the *trans*-thiolsulphinate yielding a contracted ring (sulphoxide), whereas tributylphosphine regenerated disulphide by deoxygenation. The dithiandiols reacted readily with Chloramine-T; the *trans*-compound afforded two isomeric bicyclic sulphenate ester derivatives. Periodate oxidised the tetrahydrothiophendiols to either 3-thiaglutaraldehyde or its 3-oxide, and the dithiandiols to 3,4-dithia-adipaldehyde. The rates of oxidation were compared with those of other cyclic vicinal diols. A number of derivatives were prepared.

3-THIAGLUTARALDEHYDE (5) [2] and the corresponding disulphide 3,4-dithia-adipaldehyde (18) have been known in the form of simple derivatives for many years. We prepared several bisthiosemicarbazones of these compounds in order to examine their anti-tumour properties.[2] The dialdehydes were obtained satisfactorily by literature methods, but it was also of interest to investigate their formation by periodate oxidation of the title diols. This work, now described, continues our study of the oxidation of heterocyclic vicinal diols.

The diols (10) and (15) differ from their cyclic sulphone (1) and ether (2) analogues in that the sulphide [3] and disulphide [4] functions are themselves readily oxidisable by periodate. However, there are several examples [5] of

[1] Part II, J. E. McCormick and R. S. McElhinney, *J.C.S. Perkin I*, 1972, 1335.

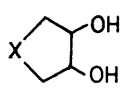
[2] V. C. Barry, M. L. Conalty, J. E. McCormick, R. S. McElhinney, M. R. McInerney, and J. F. O'Sullivan, *J. Medicin. Chem.*, 1970, **13**, 421, and references therein.

[3] C. R. Johnson and J. E. Keiser, *Org. Synth.*, 1966, **46**, 78; C. J. Clayton and N. A. Hughes, *Carbohydrate Res.*, 1967, **4**, 32; R. M. Carlson and P. M. Helquist, *J. Org. Chem.*, 1968, **33**, 2596; J. Kuszmann and P. Sohár, *Carbohydrate Res.*, 1972, **21**, 19.

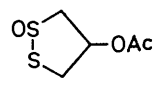
[4] L. Field and R. B. Barbee, *J. Org. Chem.*, 1969, **34**, 36.

[5] L. Hough and M. I. Taha, *J. Chem. Soc.*, 1957, 3994; G. Huber, O. Schier, and J. Druey, *Helv. Chim. Acta*, 1960, **43**, 1787; J. Fernández-Bolaños and M. M. Gallego, *Anales real Soc. espaň. Fís. Quím.*, 1966, **62**, 1005; A. B. Foster, Q. H. Hasan, D. R. Hawkins, and J. M. Webber, *Chem. Comm.*, 1968, 1084. *Cf.* J. Gierer and N.-H. Wallin, *Acta Chem. Scand.*, 1965, **19**, 1502.

preferential diol cleavage in polyhydroxy-sulphides, and sulphide-disulphides have given the corresponding sulphoxide-disulphides in good yield.[6] In general, cyclic



(1) X = SO_2
(2) X = O
(3) X = CH_2



(4)

disulphides are more reactive [7] than linear ones, but it was hoped that at least one of the stereoisomeric diols (15) would yield some disulphide-dialdehyde.

trans-Tetrahydrothiophen-3,4-diol was prepared [8,9] from sodium sulphide and DL-1,4-dichlorobutane-2,3-diol [DL-(14)] by an improved procedure involving a much shorter reaction time. The corresponding *meso*-diol similarly gave *cis*-tetrahydrothiophen-3,4-diol, hitherto obtained [10] in only poor yield and after several stages from *meso*-1,4-dibromobutane-2,3-diol. The dichlorides moreover are derived [11] from the readily available 1,4-dichlorobut-2-ene.

Another lengthy procedure from 1,4-dibromobut-2-ene was earlier used to prepare the 1,2-dithian-4,5-diols.[12] The final step involved oxidation of the 1,4-dimercaptobutane-2,3-diols, which have recently found a number of biochemical applications.[13] We have converted the 1,4-dichlorobutane-2,3-diols (14) into the dithians in relatively good yield by direct reaction with sodium disulphide. Bunte salts were not formed sufficiently readily from the dichlorides to be useful intermediates.[14]

The tetrahydrothiophendiols were characterised as benzoates and mesylates. They were readily oxidised both to [1] the known sulphones and to the sulphoxides.[15] With Chloramine-T they yielded normal sulphimides, although the linear bis-(β-hydroxyethyl) sulphide behaves atypically towards *N*-chlorosulphonamide salts.[16] The yield of sulphimide from the *cis*-diol is almost identical to that from the *trans*-diol. Since the latter can give only a single stereoisomer, the poor yield of *cis*-product probably reflects an inefficient reaction process rather than the formation of considerable amounts of both theoretically possible isomers, *i.e.*, reaction with Chloramine-T is stereoselective. The configuration of the sulphimide from the *cis*-diol has not been determined.

The dithiandiols yielded the known acetates (11) and also mesylates which could be useful alternative sources of 1,2-dithiin.[17] Since the dithians in the present work are crystalline solids and more stable than unsubstituted cyclic disulphides, they afforded a useful opportunity of further contributing to the study of disulphide oxidation.[4,18,19] A difference from the unsubstituted compounds was soon apparent. For these, oxidation can be arrested fairly readily at the dioxide (thiolsulphonate) stage and with more difficulty at the tetroxide. Monoxide (thiolsulphinate) can be isolated in only very low yield.

When the diacetoxydithians (11) were treated with peroxide in acetic acid under conditions which gave 1,2-dithian 1,1-dioxide in good yield,[4] the dioxides (12) were formed to some extent, but these were separable only with difficulty on alumina or silica gel columns from the corresponding monoxides (8). The yield of dioxide could not be increased either by more vigorous reaction conditions or by starting with the monoxide; the products usually consisted of a little monoxide, a little dioxide, and mostly compounds resulting from further oxidation, probably to the disulphonic acid stage. However, when the peroxide oxidation was carried out in the presence of acetic and hydrochloric acids and tungsten trioxide,[4] no crystalline sulphonyl chloride or derivatives thereof could be isolated.

On the other hand, monoxide was readily obtained in good yield after reaction of the dithian (11) with potassium periodate, and only traces of dioxide were formed. Even prolonged reaction under homogeneous conditions with excess of sodium periodate afforded almost exclusively monoxide, in rather better yield than from the potassium salt.[4] A very similar cyclic monoxide acetate (4), that of brugierol, has recently been obtained from natural sources.[20]

Both monoxides and dioxides are highly crystalline stable substances. The *trans*-monoxide can be recovered in good yield after treatment with acetic anhydride for 7 h at 100°, although a longer reaction time causes decomposition as well as some disproportionation to the dioxide. The dioxides are much less sensitive than the monoxides towards iodine vapour, and caution is necessary in interpreting t.l.c. results when using this reagent.

The i.r. spectrum of each monoxide differs characteristically from that of the corresponding dioxide. The monoxide SO stretching vibration (1040—1036 cm^{-1}) is somewhat obscured by the acetate CO bands at 1070—1042 cm^{-1} present, like the other CO absorption at 1246—1200 cm^{-1}, for all four compounds. However the dioxide SO_2 vibrations at *ca.* 1320 and 1130 cm^{-1} are very clear; the dioxides also have peaks at *ca.* 785ms cm^{-1}. All four

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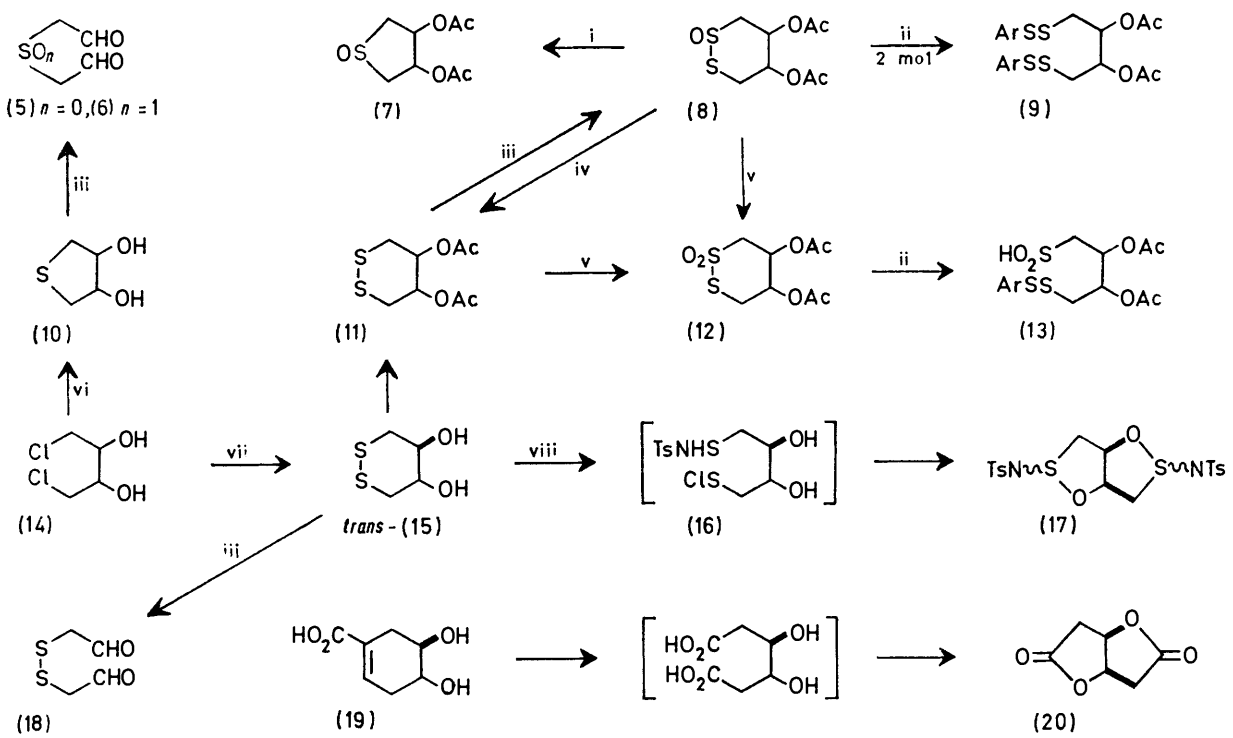
[7] U. Schmidt and P. Grafen, *Angew. Chem. Internat. Edn.*, 1965, **4**, 855.
[8] G. W. Kilmer, M. D. Armstrong, G. B. Brown, and V. du Vigneaud, *J. Biol. Chem.*, 1942, **145**, 495; D. E. Wolf and K. Folkers, *Org. Reactions*, 1951, **6**, 447.
[9] A. I. Kosak and R. L. Holbrook, *Ohio J. Sci.*, 1953, **53**, 370 (*Chem. Abs.*, 1954, **48**, 13,679).
[10] M. Procházka, *Coll. Czech. Chem. Comm.*, 1965, **30**, 1158.
[11] L. N. Owen, *J. Chem. Soc.*, 1949, 243.
[12] (*a*) A. Lüttringhaus, S. Kabuss, H. Prinzbach, and F. Langenbucher, *Annalen*, 1962, **653**, 195; (*b*) W. W. Cleland, *Biochemistry*, 1964, **3**, 480.
[13] W. L. Zahler and W. W. Cleland, *J. Biol. Chem.*, 1968, **243**, 716; M. Carmack and C. J. Kelley, *J. Org. Chem.*, 1968, **33**, 2171.
[14] J. G. Affleck and G. Dougherty, *J. Org. Chem.*, 1950, **15**, 865; H. Distler, *Angew. Chem. Internat. Edn.*, 1967, **6**, 544.
[15] J. E. McCormick and R. S. McElhinney, in preparation; *Chem. Comm.*, 1969, 171.
[16] F. G. Mann, *J. Chem. Soc.*, 1932, 963.
[17] W. Schroth, F. Billig, and G. Reinhold, *Angew. Chem. Internat. Edn.*, 1967, **6**, 698; W. Schroth, F. Billig, and A. Zschunke, *Z. Chem.*, 1969, **9**, 184.
[18] W. E. Savige and J. A. McLaren, in 'Organic Sulfur Compounds,' eds. N. Kharasch and C. Y. Meyers, Pergamon, London, vol. 2, 1966, p. 367.
[19] D. N. Harpp, J. G. Gleason, and D. K. Ash, *J. Org. Chem.*, 1971, **36**, 322; D. N. Harpp and J. G. Gleason, *ibid.*, p. 1314.
[20] A. Kato and M. Numata, *Tetrahedron Letters*, 1972, 203.

compounds absorb at 1382—1376ms cm^{-1}. Peaks at 1160—1153 and 968—950 (*cis*-compounds) and 892—888 cm^{-1} (*trans*-) seem to be characteristic of stereochemistry.

The n.m.r. spectra of all four compounds are more complex than that of the 1,4-dithian [1] which is isomeric with the dioxides. For the pair of derivatives from the *cis*-diacetate (11), the signals from the two sets of acetoxy-protons are considerably further apart than for the two oxides from the *trans*-diacetate. The τ values are characteristic of those reported for axial and equatorial acetoxy-groups in pyranose sugar derivatives.[21] The *cis*-diacetate oxides each have one axial and one equatorial acetoxy-group; in the *trans*-compounds both are equatorial, giving rise to almost coincident resonances. Monoxide is formed from the *trans*-diacetate with a high degree of stereoselectivity, and while the configuration of the *S*-oxide function was not established it is probably the preferred axial. The monoxide product from the *cis*-diacetate contains some of what is presumably the second isomer (t.l.c.), readily eliminated by crystallisation.

Each monoxide (8) reacted readily with *p*-chlorobenzenethiol (2 equiv.) in acetic acid to give the bis-disulphides (9).[22] The *cis*-diacetate dioxide (12) reacted with the thiol (1 equiv.) to give the expected [23] di-sulphide-sulphinic acid (13), requiring sodium methoxide (1 equiv.) for neutralisation, but subsequent reaction with veratryl chloride failed to yield a crystalline di-sulphide-sulphone.

When the *trans*-diacetate (8) was treated with tris-(dimethylamino)phosphine sulphur was abstracted and *trans*-3,4-diacetoxytetrahydrothiophen 1-oxide (7) [15] formed. Although there is much current interest [19,24] in the interaction of trivalent phosphorus with various sulphur functions, thiolsulphinates have apparently not been subjected to such treatment. If the mechanism is similar to that in the case of thiolsulphonates,[19] a transient sulphenate ion would be generated. Unlike the much more stable sulphinate anions, little information is available about sulphenates.[25] The only alkylation studies [26] we could find show that in the anion sulphur exclusively is attacked to yield the sulphoxide; oxygen attack would lead to sulphenate ester, a type of compound nearly always prepared *via* sulphenyl chloride. Apart from gross decomposition products, our reaction mixture consisted, in order of elution, of tris(dimethylamino)phosphine sulphide, a little starting material, and



SCHEME

Reagents: i, $P(NMe_2)_3$; ii, *p*-ClC_6H_4SH; iii, $NaIO_4$; iv, PBu_3; v, H_2O_2–AcOH; vi, Na_2S; vii, Na_2S_2; viii, Chloramine-T.

[21] F. W. Lichtenthaler and P. Emig, *Carbohydrate Res.*, 1968, **7**, 121, and references therein.

[22] L. D. Small, J. H. Bailey, and C. J. Cavallito, *J. Amer. Chem. Soc.*, 1949, **71**, 3565; A. Schöberl and H. Grāfje, *Annalen*, 1958, **617**, 71.

[23] L. Field and R. B. Barbee, *J. Org. Chem.*, 1969, **34**, 1792.

[24] E. J. Corey, *Pure Appl. Chem.*, 1967, **14**, 32; I. Granoth, A. Kalir, and Z. Pelah, *J. Chem. Soc.* (*C*), 1969, 2424; D. H. R. Barton, G. Page, and D. A. Widdowson, *Chem. Comm.*, 1970, 1466; D. H. R. Barton and B. J. Willis, *J.C.S. Perkin I*, 1972, 305.

[25] B. C. Pal, M. Uziel, D. G. Doherty, and W. E. Cohn, *J. Amer. Chem. Soc.*, 1969, **91**, 3634.

[26] K. Fries, *Ber.*, 1912, **45**, 2965; K. Fries and G. Schürmann, *ibid.*, 1919, **52**, 2170, 2182; A. Burawoy and A. Chaudhuri, *J. Chem. Soc.*, 1956, 653.

the sulphoxide (7). Only traces of other components were present, in amounts too small for identification.

Reaction with tributylphosphine took quite a different course. Deoxygenation occurred and the disulphide (11) was isolated in good yield, being eluted before the phosphine oxide. The thiolsulphinate (8) thus resembles thiolsulphonates in that its behaviour towards phosphines depends upon the type of substitution on the phosphorus atom.[19]

The *trans*-diol (15) reacted with Chloramine-T to yield, in the ratio 1 : 3·5, two fairly insoluble compounds which both analysed for $C_{18}H_{20}N_2O_6S_4$. Comparatively little is known of the effect of Chloramine-T on disulphides;[27] the usual product is the sulphimide of an *N*-tosylsulphenamide, RS(NTs)NHTs. These are stable to alcohol, but when the reaction is carried out in alcohol a certain amount of sulphenate ester derivative $RS(NSO_2Ph)OEt$ has been observed.[28] This probably arises *via* initially-formed sulphenyl chloride RSCl.

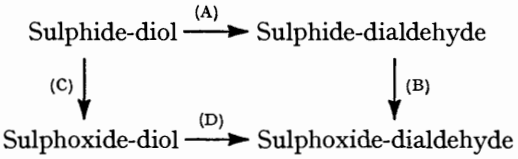
The latter sequence has evidently taken place intramolecularly with the *trans*-diol (15) and the isolated products (which have no i.r. absorption above 1600 cm^{-1} except a weak band at 2900—3000 cm^{-1}) can be formulated as *cis*-fused bicyclic sulphenate ester derivatives (17), isomeric with respect to the configuration at the sulphur atoms. A close stereochemical analogy of this cyclisation is provided by the formation of a *cis*-fused dilactone (20) through ozonolysis of the *trans*-cyclohex-4-ene-1,2-diol (19) arising from chorismic acid.[29] In each case the linear intermediate, which for the disulphide has a structure such as (16), has hydroxy-groups in a *threo*-relationship. When they are *erythro*, bicyclic structures, such as the 1,4:3,6-dianhydrohexitols, are not formed.[30] Of the three possible stereoisomers of *cis*-fused (17), the two isolated probably have at least one *exo*-toluenesulphonamido group, *i.e.*, *cis* to the bridgehead hydrogens.

The *cis*-diol (15) and Chloramine-T under the same conditions gave a very soluble product, difficult to crystallise, and only a little impure toluene-*p*-sulphonamide could be isolated. The reaction with both diols is complex, but it is possible that formation of the compounds (17) requires three equiv. of Chloramine-T [equation (1)].

$$(15) + 3TsNClNa \longrightarrow (17) + TsNH_2 + 3NaCl \quad (1)$$

In fact, the optimum yield was obtained from four equivalents (see Experimental section). The minor (α-) isomer is much less soluble in acetonitrile and while the i.r. spectra are very alike there are major differences in the 650—850 cm^{-1} region.

Reaction of *cis*-tetrahydrothiophen-3,4-diol (10) with sodium periodate (1 mol. equiv.) rapidly gives 3-thiaglutaraldehyde (5) in high yield (route A). If 2 mol. equiv. of reagent and a longer reaction time are used, the product is 3-thiaglutaraldehyde 3-oxide (6) (A, then B);[15] the oxidation of sulphides to the sulphoxide stage by



periodate is clear-cut. The *trans*-diol yields 50—60% of 3-thiaglutaraldehyde after an oxidation time of a few min. Longer reaction times, using 1 mol. equiv. of reagent, cause oxidation (C) of the sulphide function in the diol in preference to that (B) of the dialdehyde-sulphide or (A) of the diol function itself. This follows since bisthiosemicarbazone is isolated in about the same yield after an oxidation time of several h and even then contains no detectable amount of sulphoxide derivative. Reaction (D), which has been shown[15] to be appreciably slower than (A), would occur to only a very limited extent with this amount of periodate. When 2 mol. equiv. of reagent are used, the product after even a few min consists of a mixture of dialdehydes (5) and (6); after 1 h it is virtually pure sulphoxide-dialdehyde (6), probably originating *via* both (B) and (D).

A further comparison of the diols (10) was made by measuring the pH of aqueous solutions in the presence of boric acid. Addition of the *trans*-diol did not lower the pH of a boric acid solution, indicating that a borate complex is not formed.[31,32] The *cis*-diol however does form a complex to some extent (see Table 1). The rate of oxidation by periodate and the ease of borate complex formation are consequences of the geometry or the flexibility of these ring compounds. In the case of *trans*-diols, the sulphide (10) differs from the sulphone (1)[1] and the ether (2),[33] which are oxidised comparatively slowly, and resembles rather, at least in the early stages of oxidation, the cyclopentane (3).[34]

Both disulphide-diols (15) were rapidly oxidised by periodate. *Ca.* 45—55% of dialdehyde (18) was formed from the *cis*-compound within a few min, while the *trans*-diol afforded only slightly less (35—45%). A longer reaction time at room temperature caused total decomposition of the *cis*-diol and did not improve the yield of dialdehyde from the *trans*-diol, while excess of periodate did raise it somewhat. Addition of solutions of each diol

[27] F. Challenger in 'Organic Sulfur Compounds,' ed. N. Kharasch, Pergamon, Oxford, vol. 1, 1961, p. 341; G. Leandri and D. Spinelli, *Ann. Chim. (Italy)*, 1959, **49**, 964.

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[29] J. M. Edwards and L. M. Jackman, *Austral. J. Chem.*, 1965, **18**, 1227.

[30] L. Hough and A. C. Richardson in 'Rodd's Chemistry of Carbon Compounds,' ed. S. Coffey, Elsevier, Amsterdam, vol. IF, 1967, pp. 53, 289; F. J. Hopton and G. H. S. Thomas, *Canad. J. Chem.*, 1969, **47**, 2395; R. P. Linstead, L. N. Owen, and R. F. Webb, *J. Chem. Soc.*, 1953, 1225. But see L. N. Owen and A. G. Peto, *J. Chem. Soc.*, 1955, 2383, on the effect of hetero-atoms on the formation of *trans*-pentalanes.

[31] J. Boëseken, *Adv. Carbohydrate Chem.*, 1949, **4**, 189; J. Dale, *J. Chem. Soc.*, 1961, 914.

[32] M. Procházka and V. Horák, *Coll. Czech. Chem. Comm.*, 1959, **24**, 1509.

[33] H. Klosterman and F. Smith, *J. Amer. Chem. Soc.*, 1952, **74**, 5336.

[34] J. S. Brimacombe, A. B. Foster, M. Stacey, and D. H. Whiffen, *Tetrahedron*, 1958, **4**, 351; G. R. Barker and D. F. Shaw, *J. Chem. Soc.*, 1959, 590.

to boric acid scarcely affected the pH, *i.e.*, neither appeared to form a borate complex. It was noted earlier that both diols readily form cyclic acetals.[12a]

This behaviour towards periodate, borate, and carbonyl compounds may be compared with that of the *cis*- and *trans*-cyclohexane-1,2-diols. These are rapidly oxidised by periodate (the former relatively much faster),[34,35] neither forms a stable borate complex,[31] and both yield cyclic acetals (again the former much more readily).[12a] In contrast, of the five-membered sulphone-diols (1) only the *cis*-compound is rapidly oxidised and forms a borate complex and acetals.[32] Further useful comparisons of isomeric 1,2-diols have been made by Kuhn from i.r. spectra.[36]

The estimated yields of dialdehydes formed by oxidation in the present work are based on the weight of 4-methylthiosemicarbazone obtained. Other derivatives have also been prepared. The most convenient sources of these dialdehydes are the acetals, which may in turn be synthesised by reaction of (*a*) chloroacetal with Na_2S_n [37] or (*b*) vinyl ether with S_nCl_2.[38] We have found method (*a*) preferable for $n = 1$, (*b*) for $n = 2$. Hydrolysis of the sulphide acetal occurs readily; the disulphide is more sensitive to other forms of decomposition, and the conditions for its conversion into carbonyl derivatives are accordingly somewhat critical. The analogous tetramethyldialdehyde evidently reacts without difficulty.[39] An attempt to convert the sulphide-bisphenylhydrazone into the sulphoxide [40] by the peroxide method of Kiang and Mann [41] was abortive.

EXPERIMENTAL

Except where otherwise stated, i.r. peaks recorded are of strong (s) intensity and u.v. spectra refer to solutions in 2-methoxyethanol diluted with methanol. Column chromatography was carried out using alumina (Brockmann grade II—III) or silica gel (30—70 mesh ASTM) (Merck). Other general details are given in ref. 1.

1,4-*Dichlorobutane*-2,3-*diols* (14).—These were made from *trans*-1,4-dichlorobut-2-ene (redistilled Eastman Kodak Practical grade) by the method of Owen.[11] Performic acid yielded the *meso* compound (25—39%), m.p. 127—129° (from benzene; 10 ml g^{-1}) (lit., 127°,[11] 129—132° [42]). Permanganate gave the DL-diol (52—57%), m.p. 60—62° (from chloroform; 1 ml g^{-1}) (lit., 62°,[11] 62—63 and 75° [42]). Some commercial samples of 1,4-dichlorobut-2-ene which evidently contain considerable proportions of *cis*-isomer [43] are best avoided.

Tetrahydrothiophen-3,4-*diols* (10) *and Esters*.—To a boiling solution of DL-1,4-dichlorobutane-2,3-diol (12·72 g, 0·08 mol) in ethanol (100 ml) was added dropwise, over 15 min, sodium sulphide nonahydrate (38·4 g, 0·16 mol) dissolved in water (50 ml). Stirring and refluxing were continued for 5 min more. The mixture was at once cooled and treated below 25° with hydrochloric acid (20%; 27 ml) which lowered the pH to 4; sodium chloride was sometimes filtered off at this stage. The solvent was evaporated and the residue extracted with boiling chloroform (3 × 40 ml). The dark brown solution was evaporated and the residue taken up in ethyl acetate and charcoaled. Concentration to 12 ml and addition of benzene (5 ml) afforded (after 3—4 days) the *trans*-diol (5·91 g, 62%), m.p. 67—71° (lit.,[8] 54—58°).

A mixture of *meso*-1,4-dichlorobutane-2,3-diol (3·18 g), sodium sulphide nonahydrate (9·6 g), and ethanol (30 ml) was swirled and heated under reflux for 15 min. For large scale reactions, the ethanol was preheated to the b.p. After working-up as for the *trans*-isomer, the chloroform extract (1·68 g) was recrystallised from benzene (or ethyl acetate), giving the *cis*-diol (1·32 g, 55%), m.p. 70—72°. A pure sample had m.p. 70·5—72·5° (lit.,[10] 69—71°) (Found: C, 40·2; H, 6·8; S, 26·7. Calc. for $C_4H_8O_2S$: C, 40·0; H, 6·7; S, 26·7%). Yields of 65—70% of material sufficiently pure for further work have often been obtained.

The action of benzoyl chloride and pyridine on the *cis*-diol immediately yielded the dibenzoate (67%), m.p. 79·5—80·5° (from methanol) (lit.,[10] 79—81°; 27%) (Found: C, 65·9; H, 4·9; S, 9·8. Calc. for $C_{18}H_{16}O_4S$: C, 65·9; H, 4·9; S, 9·75%). The *trans*-dibenzoate was made similarly and had m.p. 144—145° (lit.,[10] 143°).

When the *cis*-diol (1·20 g) in dry pyridine (3 ml) was treated dropwise with methanesulphonyl chloride (1·87 ml) at 0—3° and the ice–salt bath removed, the temperature gradually rose to *ca* 35°. After 2 h, ice–water precipitated the *bismethanesulphonate* (2·61 g, 95%), m.p. 111—113° (from methanol) (Found: C, 26·4; H, 4·5; S, 34·5. $C_6H_{12}O_6S_3$ requires C, 26·1; H, 4·35; S, 34·8%); $\nu_{max.}$ 1360, 1335, 1172, 1015, 924, and 866 cm^{-1}. The yield of *trans*-bismethanesulphonate, prepared in the same way, was 94%, m.p. 137·5—140° (lit.,[10] 139—140°; 68%).

Tetrahydro-1-p-*tolyl*-*sulphonyliminothiophen*-3,4-*diols*.—When the diol (1·20 g) was added to a stirred suspension of Chloramine-T (2·96 g, 10·5 mmol) in water (15 ml), a clear solution resulted but soon solid began to separate. Stirring was discontinued and next day the product was filtered off.

The *cis*-diol gave material (2·27 g; m.p. 110—140°) which was crystallised from methanol to yield the *sulphimide* (1·09 g, 38%), m.p. 165°. A pure sample had m.p. 169—170° (decomp.) (Found: C, 45·8; H, 5·3; N, 4·9; S, 22·1. $C_{11}H_{15}NO_4S_2$ requires C, 45·7; H, 5·2; N, 4·8; S, 22·1%); $\nu_{max.}$ 3470 (OH), 1410, 658, and several bands between 1280 and 980 cm^{-1}.

The crude product, m.p. 110—124°, from the *trans*-diol, yielded the *sulphimide* (38%) from acetonitrile. The m.p., 139—141°, was raised to 141·5—143° by a further recrystallisation (Found: C, 45·9; H, 5·25; N, 4·8; S, 22·1%); $\nu_{max.}$ 3300 (OH) and several bands between 1280 and 980 cm^{-1}.

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cis-1,2-*Dithian*-4,5-*diol* (15).—A mixture of sodium sulphide nonahydrate (10·81 g, 0·045 mol) and sulphur (1·44 g) in ethanol (125 ml; 95%) was stirred and refluxed for 10 min. The virtually clear solution was treated dropwise over 5 h with *meso*-1,4-dichlorobutane-2,3-diol (4·77 g, 0·03 mol) in ethanol (75 ml; 95%), stirring and heating throughout. The solvent was evaporated and the residue extracted with boiling chloroform (3 × 25 ml). Further evaporation left a pale yellow solid which was extracted with hot water (20 ml). On cooling, the dithian (1·59 g) separated, m.p. 129—131° (lit.,[12a] 128—129°). Concentration of the mother liquor afforded a further amount (0·38 g, total 43%).

The use of a nitrogen atmosphere, or of a smaller excess (10%) of sodium disulphide, or treatment with hot alkali before extraction,[44] did not significantly affect the yield of dithian. The product however was cleaner when 50% excess of disulphide was employed. A still larger excess (400%) reduced the yield to *ca.* 10%. The yield was also decreased (31—34%) when the dichloride solution was added over 1 h.

Methanesulphonyl chloride and pyridine below 15° gave the *bismethanesulphonate* (91%), m.p. 123·5—124° (decomp.) (from acetone–methanol) (Found: C, 23·4; H, 3·9; S, 40·9. $C_6H_{12}O_6S_4$ requires C, 23·4; H, 3·9; S, 41·6%); $\nu_{max.}$ 1348, 1328, 1168, 980—908 (several peaks), and 845 cm^{-1}.

trans-1,2-*Dithian*-4,5-*diol* (15).—This was obtained from the DL-dichloride by a procedure similar to that used for the *cis*-diol and had m.p. 130—132° (lit.,[12a] 129—130°). The yield (43%) was raised to 51% by a second extraction with chloroform and water of the original residue. Acetone and ethyl acetate were less satisfactory than chloroform. The *bismethanesulphonate* (82%) had m.p. 148—148·5° (decomp.) (from aqueous dimethylformamide) (Found: C, 23·2; H, 3·9; S, 41·8%); $\nu_{max.}$ 1364, 1342, 1175, 1018—944 (several peaks), and 858 cm^{-1}.

cis-4,5-*Diacetoxy*-1,2-*dithian* 1-*Oxide* (8).—A solution of *cis*-4,5-diacetoxy-1,2-dithian (11) (472 mg, 2 mmol) (m.p. 75—76·5°, yield 95% using acetic anhydride–pyridine; lit.,[45] m.p. 74—75°) in acetone (2 ml) was stirred (4 days) in the dark with a suspension of potassium periodate (1·886 g, 8·2 mmol) in water (24 ml). Inorganic salts were filtered off and extraction with chloroform (4 × 10 ml) yielded crystals (488 mg), m.p. 100—109°. These contained (t.l.c.; ether) two major components together with traces of the *cis*-thiolsulphonate (12) and another compound; there was no evidence of starting material. Recrystallisation from ether gave the *thiolsulphinate* (324 mg, 64%), the predominant and faster-moving (t.l.c.) of the major components. A pure sample had m.p. 114—115·5° (Found: C, 38·5; H, 5·0; S, 25·7. $C_8H_{12}O_5S_2$ requires C, 38·1; H, 4·8; S, 25·4%); $\nu_{max.}$ 1735 (C=O), 1236—1204 and 1070—1052 (C–O), 1040 (SO), 1378 m, 1153 m, and 950 m cm^{-1}; τ ($CDCl_3$) 4·15—4·68 (2H, m, 2 × CH), 5·88—6·88 (4H, m, 2 × CH_2), 7·85 (3H, s, CH_3CO_2ax), and 7·97 (3H, s, CH_3CO_2eq).

trans-4,5-*Diacetoxy*-1,2-*dithian* 1-*Oxide* (8).—The *trans*-dithian (11) (2·36 g, 10 mmol) (m.p. 54—55·5°; lit.,[45] m.p. 54—55°) was oxidised as above to yield a crude product (2·51 g), m.p. 139—144°. This consisted [t.l.c.; benzene–methanol (19 : 1)] of a trace of the *trans*-thiolsulphonate (12) and only one other component. The *thiolsulphinate* (1·87 g, 74%) (pure by t.l.c.) had m.p. 147—149·5° (from methanol) (Found: C, 37·9; H, 4·9; S, 25·4%); $\nu_{max.}$ 1732, 1246—1220, 1069—1058, 1036, 1376m, and 888m cm^{-1}; τ ($CDCl_3$) 4·00—5·01 (2H, m, 2 × CH), 6·06—7·13 (4H, m, 2 × CH_2), 7·94 and 7·98 (6H, 2s, 2 × CH_3CO_2eq).

This thiolsulphinate (86%; m.p. 147—149°) was formed after 2 days from solutions of the *trans*-dithian (11) (1·42 g) in acetone (96 ml) and sodium periodate (2·82 g, 2·2 equiv.) in water (120 ml). Acetone was removed from the reaction mixture before work-up as above. After a reaction time of 1 day, starting material could be detected in the crude product. The thiolsulphinate (68%) was also obtained using sodium periodate (1 equiv.) for 7 days.

cis-4,5-*Diacetoxy*-1,2-*dithian* 1,1-*Dioxide* (12).—Hydrogen peroxide (30% w/v; 0·28 ml, 2·5 mmol) in acetic acid (0·5 ml) was added to a solution of *cis*-dithian (11) (236 mg, 1 mmol) in acetic acid (0·75 ml). After 24 h, the mixture was evaporated, finally with methanol (3 portions). The crystalline product (153 mg; m.p. 124—139°) was triturated with water (1 ml) and filtered off. T.l.c. [benzene–methanol (19 : 1)] indicated the presence of the *cis*-thiolsulphinate (8) (slower-moving) and one other substance. The material was combined with more (from, in all, 9 mmol dithian), and a portion (73·5%) was dissolved in benzene (10 ml) and chromatographed on alumina (28 ml), eluting with benzene. Fractions (30 ml) were examined by t.l.c. Fractions 2—3 contained virtually pure cis-*thiolsulphonate* (12) (329 mg, 18·5%), m.p. 148—150° (from methanol) (Found: C, 36·2; H, 4·6; S, 23·5. $C_8H_{12}O_6S_2$ requires C, 35·8; H, 4·5; S, 23·9%); $\nu_{max.}$ 1742, 1240—1200, 1055—1042, 1328 and 1130 (SO_2), 1378m, 1160m, 968, and 785m cm^{-1}; τ ($CDCl_3$) 4·45—4·74 (2H, m, 2 × CH), 6·04—6·62 (4H, m, 2 × CH_2), 7·86 (3H, s, CH_3CO_2ax), and 7·96 (3H, s, CH_3CO_2eq). Fractions 4—6 yielded, after recrystallisation, a further quantity of thiolsulphonate (total 24%), m.p. 147·5—150·5°.

The chromatographic separation just described is not always successful. Increasing the temperature, the time, or the proportion of peroxide in the reaction yielded mixtures of products which did not crystallise.

trans-4,5-*Diacetoxy*-1,2-*dithian* 1,1-*Dioxide* (12).—(*a*) The *trans*-dithian (11) (236 mg) was oxidised like the *cis*-isomer, yielding crystalline material (144 mg) with the same t.l.c. pattern. Oxidation (of 590 mg) for 2 days did not appreciably alter the proportion of the products. The total product (362 mg) from these two reactions, in benzene (4 ml), was chromatographed on alumina (11 ml). Fractions 2—7, eluted by benzene (74 ml), contained virtually pure (t.l.c.) trans-*thiolsulphonate* (12) (156 mg, 17%) as a syrup which slowly crystallised; m.p. 143·5—145·5° (from methanol) (depressed on admixture with the corresponding thiolsulphinate) (Found: C, 35·9; H, 4·7; S, 23·8%); $\nu_{max.}$ 1742, 1240—1218, 1050, 1320, 1130, 1382m, 892m, and 782m cm^{-1}; τ ($CDCl_3$) 4·42—5·08 (2H, m, 2 × CH), 6·23—6·59 (4H, m, 2 × CH_2), and 7·89 and 7·92 (6H, 2s, 2 × CH_3CO_2eq). Again, this method of separation was found to be unreliable.

(*b*) When the *trans*-thiolsulphinate (8) (756 mg, 3 mmol) in acetic acid (6 ml) was warmed for 5 h at 40° with hydrogen peroxide (30% w/v; 0·42 ml, 3·75 mmol), t.l.c. indicated partial conversion into the corresponding thiolsulphonate (12). Chromatography of the crude, crystalline product (445 mg) on silica gel using chloroform as eluant afforded pure (by t.l.c.) thiolsulphonate (161 mg, 20%), m.p. 144—145° (from methanol). Recrystallisation of less pure fractions gave further material (total 34%), m.p. 139—141·5°.

(*c*) The *trans*-thiolsulphinate (8) (504 mg) and acetic anhydride (1 ml) were heated at 100°. The solution was still

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colourless after 11 h but dark brown after 23 h. Evaporation, finally with methanol (3 portions), gave a partially crystalline residue which on trituration with methanol afforded the *trans*-thiolsulphonate (12) (118 mg, 22%), m.p. and mixed m.p. 143—145° (from methanol). With a reaction time of 7 h, the starting material (65%), m.p. 145—148·5°, was recovered.

2,3-*Diacetoxy*-1,4-*bis*-(p-*chlorophenyldithio*)*butanes* (9).—*p*-Chlorobenzenethiol (289 mg, 2 mmol) was mixed with a solution of the *cis*-thiolsulphinate (8) (252 mg) in acetic acid (2 ml) in a stoppered flask. The thiol gradually dissolved and, after 17 h, the solvent was evaporated, finally using methanol. The crystals were dissolved in hot methanol (40 ml) and concentration of the solution gave the meso-*bis-disulphide* (9) (327 mg, 63%), m.p. 112—113·5° (from methanol) (Found: C, 46·3; H, 4·0; Cl, 13·4; S, 24·4. $C_{20}H_{20}Cl_2O_4S_4$ requires C, 45·9; H, 3·8; Cl, 13·6; S, 24·5%); $\nu_{max.}$ 1741, 1482, 1375, 1206, 1095—1019, 920m, and 820 cm^{-1}.

The corresponding product from the *trans*-thiolsulphinate (8) (1·134 g) was recrystallised from methanol (9 ml) to give the DL-*bis-disulphide* (9) (1·44 g, 61%), m.p. 85·5—87° after a second crystallisation (Found: C, 45·7; H, 3·9; Cl, 13·5; S, 24·7%); $\nu_{max.}$ 1724, 1477, 1375, 1232, 1214, 1090—1009, 960, 864m, and 818 cm^{-1}. When the reaction time was 3 days, the yield was no better. Heating at 100° or using ethanol as solvent gave much lower yields.

Reaction of trans-4,5-*Diacetoxy*-1,2-*dithian* 1-*Oxide with Phosphines*.—(*a*) The compound (1·008 g, 4 mmol) dissolved in dry benzene (15 ml) was treated dropwise with freshly-distilled tributylphosphine (0·88 g, 4·4 mmol). After 15 min, the yellow mixture was evaporated and the residual oil dissolved in ether (10 ml) and chromatographed on silica gel (180 g). Fractions 4—10, eluted by ether (280 ml), consisted of pure (by t.l.c.) *trans*-4,5-diacetoxy-1,2-dithian (11) (805 mg, 85%), m.p. and mixed m.p. 52—54° (from light petroleum).

(*b*) Addition of freshly-distilled tris(dimethylamino)-phosphine (1·43 g, 8·8 mmol) as above to a solution of the *trans*-thiolsulphinate (8) (2·02 g, 8 mmol) in dry benzene (30 ml) raised the temperature only slightly. The reaction mixture was evaporated after 10 min and extracted repeatedly with ether (in all, 80 ml, cold, and 90 ml, boiling), leaving a dark brown gum which was discarded. Evaporation and extraction of the solute (2·83 g) with light petroleum (3 × 10 ml) left a residue (1·21 g) which crystallised. This, except for a little gum (28 mg), was dissolved in ether (50 ml) and chromatographed on silica gel (120 g). Fractions (40 ml) were collected and examined by t.l.c. Fractions 2—3, eluted by ether, consisted of tris(dimethylamino)phosphine sulphide (206 mg) (see below). Fractions 6—10, also eluted by ether, afforded starting material (126 mg). Finally, fractions 20—28, eluted by ether–methanol (8 : 2), yielded substantially pure *trans*-3,4-diacetoxytetrahydrothiophen 1-oxide (7) [15] (518 mg, 29%), m.p. and mixed m.p. 79·5—81·5° (from ether–light petroleum).

Distillation of the petroleum-soluble fraction gave material (1·16 g), b.p. 94—118° at 2 mmHg. This was largely tris(dimethylamino)phosphine sulphide, but contained a little sulphoxide (7). In another experiment, the total ether extract was chromatographed on alumina. The first fraction (pure by t.l.c.) was an oil which crystallised in the deep freeze, contained phosphorus, nitrogen, and sulphur (sodium fusion) and had b.p. *ca.* 100° at 2 mmHg, n_D^{17} 1·5120. Tris(dimethylamino)phosphine sulphide has [46] b.p. 63° at 1·2 mmHg, m.p. 29°. Alumina did not satisfactorily separate subsequent fractions *i.e.* sulphoxide (7) and starting material.

Reaction of 1,2-*Dithian*-4,5-*diols with Chloramine-T*.—When a solution of Chloramine-T (563 mg, 2 mmol) in water (4 ml) was treated with the *trans*-diol (15) (76 mg, 0·5 mmol) in water (0·75 ml), a sticky product immediately separated. After 3 h the supernatant liquid was poured off and the residue warmed briefly with methanol (0·5 ml). The resulting solid (270 mg; $\nu_{max.}$ 3240 and 3330 cm^{-1}) was collected and washed well with water (4 ml). An aliquot portion (200 mg) was dissolved in hot acetonitrile (15 ml), concentrated (to 10 ml), and cooled, yielding the α-*isomer* of *cis*-3,7-bis-*p*-tolylsulphonylimino-2,6-dioxa-3,7-dithiabicyclo[3,3,0]octane (17) (19·4 mg, 10·7%). Recrystallisation from acetonitrile (1·35 ml mg^{-1}) gave hair-like crystals, m.p. 255° (decomp.) (Found: C, 44·3; H, 4·1; N, 5·4; S, 26·4. $C_{18}H_{20}N_2O_6S_4$ requires C, 44·25; H, 4·15; N, 5·75; S, 26·25%); $\nu_{max.}$ 1590w, 1398w, 1278, 1145, 1082, 1046, 1016, 950, 850, 814m, 703, and 692 cm^{-1}.

Further concentration (2·5 ml) of the first acetonitrile mother liquor and addition of warm water (3·5 ml) gave the β-*isomer* (67 mg, 37%), needles, m.p. 213·5—216° (decomp.) (from acetonitrile, 0·06 ml mg^{-1}) (Found: C, 44·5; H, 4·25; N, 5·9; S, 26·2%); $\nu_{max.}$ 1590w, 1396w, 1300, 1140, 1083, 1032, 1002, 952, 852, 823, 752, and 670 cm^{-1}.

A final fraction (73 mg) was obtained from the original mother liquor. It had m.p. 107—118° ($\nu_{max.}$ 3230 and 3330 cm^{-1}) and was largely toluene-*p*-sulphonamide.

Use of Chloramine-T (1, 2, 3, and 6 equiv.) as above gave crude product (29, 62, 165, and 234 mg, respectively). The i.r. spectra were similar to that of the product (270 mg) above, and fractional crystallisation yielded comparable proportions of the two isomeric compounds, except that in the ' 6 equiv.' reaction the yield of β-isomer was lower, and of toluene-*p*-sulphonamide higher.

When the *cis*-diol (15) reacted with Chloramine-T (4 equiv.) under the conditions described for the *trans*-diol, again a gummy product separated at once. However this readily dissolved in methanol (0·5 ml). Addition of water gave material (45 mg), m.p. 78—104° ($\nu_{max.}$ 3230 and 3320 cm^{-1}) which probably contained much toluene-*p*-sulphonamide.

Reaction of Thiacycloalkane-1,2-*diols with Boric Acid*.—An aqueous solution (5 ml) containing diol (1 mmol) was treated with 0·4M-boric acid (5 ml) and the pH was taken (Table 1) using a Radiometer (electrodes: glass G202C; calomel K401). The pH values of blank solutions of diol (1 mmol) in water (10 ml) were also noted. The pH of 0·2M-boric acid was found to be 4·85.

TABLE 1

		pH of solution	
Diol		Diol	Diol + boric acid
Disulphide (15)	*cis*	5·6	4·7
	trans	6·1	4·8
Sulphide (10)	*cis*	6·1	4·1
	trans	6·3	4·9
Sulphoxide	*cis*	6·3	3·4
	trans	5·9	4·9
Sulphone (1)	*cis*	5·5	3·5
	trans	5·6	4·8

Periodate Oxidation of Tetrahydrothiophen-3,4-*diols*.—The *cis*-diol (120 mg, 1 mmol) in water (3·3 ml) was treated dropwise at 3° with sodium periodate (214 mg, 1 mmol) in water

[46] H.-J. Vetter and H. Nöth, *Chem. Ber.*, 1963, **96**, 1308.

(5·7 ml). The solution was at once (10—15 min after the beginning of the oxidation) worked up with barium chloride and other reagents as described for 3-thiaglutaraldehyde 3,3-dioxide.[1] Addition of acetic acid (0·2 ml) and 4-methylthiosemicarbazide (210 mg) then caused separation of a colourless solid. Next day the 3-thiaglutaraldehyde bis-(4-methylthiosemicarbazone) (239 mg, 82%) was collected. The m.p. was 185—186° (decomp.) (from dimethylformamide–methanol), undepressed on admixture with a sample [2] prepared from 1,1,5,5-tetramethoxy-3-thiapentane; $\lambda_{max.}$ 274 nm.

A similarly prepared dialdehyde solution yielded (87%) the bis-(2,4-dinitrophenylhydrazone), m.p. and mixed m.p. 216·5—217° (decomp.) (from dimethylformamide–methanol); $\lambda_{max.}$ 349 nm.

The *trans*-diol (0·6 g, 5 mmol) was oxidised similarly and the solution (45 ml) was placed in the refrigerator. A portion (9 ml) was withdrawn 15 min after the beginning of the oxidation, and yielded 3-thiaglutaraldehyde bis-(4-methylthiosemicarbazone) (158 mg, 54%), m.p. and mixed m.p. 182—182·5°. Further portions (9 ml each) were removed after oxidation times of 1, 2, 3, and 4 h, and yielded the same derivative (53, 54, 54, and 54%, respectively). When the oxidation was performed at 16—20°, yields of 43% (m.p. 181—182°; 15 min reaction time) and 42·5% (45 min) were obtained.

Other Derivatives of 3-Thiaglutaraldehyde.—A mixture of 1,1,5,5-tetramethoxy-3-thiapentane (10 mmol) in water (25 ml) and acetic acid (0·75 ml) was refluxed for 5 min and the resulting solution was cooled and treated with phenylhydrazine or hydroxylamine. The *bisphenylhydrazone* (79%), initially a gum, solidified on addition of 75% aqueous methanol. It had m.p. 103—106° (from benzene–light petroleum) (Found: C, 64·6; H, 6·1; N, 18·1; S, 11·0. $C_{16}H_{18}N_4S$ requires C, 64·4; H, 6·0; N, 18·8; S, 10·7%); $\lambda_{max.}$ (95% ethanol) 241, 282, and 305sh nm. The *dioxime* (87%) had m.p. 95—97° (from water) (Found: C, 32·4; H, 5·6; N, 18·9; S, 22·0. $C_4H_8N_2O_2S$ requires C, 32·4; H, 5·4; N, 18·9; S, 21·6%); $\nu_{max.}$ 3170, 1640m, 1435, 1417, 1294, 1218m, 1058m, 986, 920, and 650m cm^{-1}.

When the bisacetal (1 mmol) was stirred for 30 min at 40° with 0·1N-HCl (15 ml), a colourless solution resulted which was cooled and brought to pH 5 by sodium acetate. 4-Benzylthiosemicarbazide (362 mg) in ethanol (15 ml), water (10 ml), and acetic acid (0·8 ml) was added slowly at 40°. The *bis-(4-benzylthiosemicarbazone)* (436 mg) had m.p. 152—154° (from dimethylformamide–25% aqueous methanol) (Found: C, 53·9; H, 5·6; N, 18·8; S, 21·3%. $C_{20}H_{24}N_6S_3$ requires C, 54·0; H, 5·45; N, 18·9; S, 21·65%); $\lambda_{max.}$ 277 nm. When the dialdehyde solution was treated with the thiosemicarbazide (1 equiv.), the only solid product obtained was a little (9%) bisthiosemicarbazone.

Periodate Oxidation of 1,2-Dithian-4,5-diols.—The diols were dissolved in water and oxidised as described for the tetrahydrothiophen-3,4-diols. The effect of oxidation time was studied at two temperature ranges by preparing the bis-(4-methylthiosemicarbazone) as before. The yields recorded in Table 2 are of crude products which melted sharply over 1—2° in the range 153—158°, except as indicated in footnotes. Recrystallisation gave a pure sample, m.p. 162—163°, undepressed on admixture with material prepared as described later from 1,1,6,6-tetraethoxy-3,4-dithiahexane (Found: C, 29·7; H, 4·9; N, 25·2; S, 39·7%).

The more rapid reaction of the *cis*-diol is evident from the colour (light brown) after 2 h at 0—4°, while the corresponding *trans*-diol solution is colourless. Moreover at 16—20°, unless the product from *cis*-diol is worked up as quickly as possible (15—20 min after the beginning of the oxidation), extensive decomposition and separation of iodine take place. Reaction of the *cis*-diol (0—4°) products with 2,4-dinitrophenylhydrazine in methanolic sulphuric acid gave yields of the same order as the bis-(4-methylthiosemicarbazone), but the products were much less pure; difficulty was similarly experienced in preparing the bis-(2,4-dinitrophenylhydrazone) from the bisacetal.

TABLE 2

Yields of bis-(4-methylthiosemicarbazone) after oxidation of 1,2-dithian-4,5-diols at different temperatures

	Yield (%) from *cis*-diol		Yield (%) from *trans*-diol	
Oxidation time (min)	At 0—4°	At 16—20°	At 0—4°	At 16—20°
15—20	22 [a]	47 [c]	22	37
30				36
45		Decomp.		38
60	51 [b]		32	38 [d]
120	51		36	
180	51		43	
240			37	
330	Decomp.			

[a] M.p. 135—152°. [b] 61% (2 equiv. $NaIO_4$). [c] M.p. 152—155°. [d] M.p. 153—154°, shrinks from 80°.

1,1,6,6-*Tetraethoxy-3,4-dithiahexane.*—A solution of ethyl vinyl ether (15·2 ml, 0·16 mol) in dry ether (16 ml) was cooled to 0°. Purified [47] sulphur monochloride (6·4 ml, 0·08 mol) was carefully added dropwise with stirring over 30 min, at 0—4°. The ice–salt bath was removed for 1 h and then replaced by one at 40°. Ethanol (18·5 ml) was run in over 4 min. The orange-yellow mixture was left at room temperature overnight and became brown-black. Calcium carbonate (8 g) was added over 5 min, at 8—10°, followed by water (16 ml) at which the temperature rose slightly. The pH was adjusted to *ca.* 7 by addition of a little more calcium carbonate and the organic layer separated. The aqueous layer was filtered through Celite and extracted with light petroleum (4 × 20 ml). The combined product solutions were washed with saturated aqueous bicarbonate, dried ($MgSO_4$, charcoal), and evaporated, leaving a golden-brown oil (20·89 g). Distillation afforded a main fraction (16·25 g) of b.p. 119—134° at 0·15—0·3 mmHg, n_D^{22} 1·4775, and redistillation of this gave the bisacetal (13·0 g, 55%), b.p. 119—124° at 0·25—0·4 mmHg, n_D^{23} 1·4768 (lit.,[38b] b.p. 150—155° at 8 mmHg).

Derivatives of 3,4-Dithia-adipaldehyde.—The bisacetal (1·19 g, 4 mmol) in acetic acid (4 ml) was treated with a warm solution of reagent [8 mmol; (*a*) 4-methylthiosemicarbazide or (*b*) hydroxylamine hydrochloride–sodium acetate] in water (4 ml) and the mixture was heated for 6—10 min at 100°. It was then bright yellow to dark brown, and was cooled.

(*a*) Crystallisation occurred and the *bis-(4-methylthiosemicarbazone)* (78%, m.p. 161—163°; another time, 92% m.p. 154—155°) was collected. Recrystallisation from dimethylformamide–methanol–water (1 : 5 : 1) with charcoaling gave an almost colourless product of m.p. 163—163·5° (decomp.) (Found: C, 29·7; H, 5·0; N, 26·0; S, 39·6. $C_8H_{16}N_6S_4$ requires C, 29·6; H, 4·9; N, 25·9; S, 39·5%); $\lambda_{max.}$ 276 nm.

[47] Z. S. Ariyan and L. A. Wiles, *J. Chem. Soc.*, 1961, 4510.

(*b*) After 3 h the solution was evaporated and the residue extracted with light petroleum (3 × 10 ml) (discarded) and then with boiling chloroform (3 × 10 ml). After being charcoaled and concentrated (4 ml), the solution deposited the *dioxime* (61%; m.p. 91—94·5°). A pure sample (from chloroform, *ca.* 200 ml g^{-1}) had m.p. 92—96° (Found: C, 26·5; H, 4·4; N, 15·3; S, 35·6. $C_4H_8N_2O_2S_2$ requires C, 26·7; H, 4·4; N, 15·6; S, 35·6%); $\nu_{max.}$ 3170, 1640m, 1465, 1407, 1300, 1217m, 1075, 994, and 942m cm^{-1}.

2,4-Dinitrophenylhydrazine (0·4 g) quickly dissolved in a mixture of bisacetal (298 mg) and acetic acid (20 ml; 80%) at 100°. The bisarylhydrazone soon began to separate and after 10 min the mixture was cooled and treated with water (12 ml), yielding a product (95%), m.p. 193—195° (decomp.), raised to 197·5—199·5° by crystallisation from dimethylformamide–methanol (lit.,[48] 205·5—206°); $\lambda_{max.}$ 355 nm.

The 2,4-dinitrophenylhydrazone was also obtained (88%; m.p. 192°) by heating the bisacetal (1 mmol) with the arylhydrazine (0·4 g) in methanol (20 ml) and sulphuric acid (1·4 ml) for 5 h at 40°. Much less pure products resulted from the same mixture either at room temperature for 24 h or at reflux for 2 min. Attempts to hydrolyse the acetal before treatment with reagent always led to poorer yields, sometimes of inferior products (*e.g.* in 50% methanolic 0·1N-HCl, 5 ml $mmol^{-1}$, at 40 or 100°, or in 50% acetic acid; the odour of aldehyde was readily noticed, but the solutions soon became dark brown).

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[48] N. Kobayasi and M. Fujimaki, *Agric. Biol. Chem.* (*Japan*), 1965, **29**, 698 (*Chem. Abs.*, 1965, **63**, 11,689).