Stereochemically controlled synthesis of substituted 1,2-oxathianes

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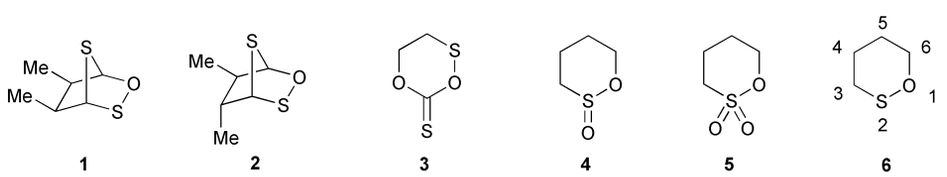
Treatment of a series of 4-sulfanyl-1,3-diols with toluene-*p*-sulfonyl chloride and triethylamine in dichloromethane gives substituted 1,2-oxathianes as single diastereoisomers in high yield by cyclisation with formation of a S–O bond. The cyclisation occurs efficiently and the fate of each stereogenic centre (four in all) of the newly formed oxathiane ring is investigated.

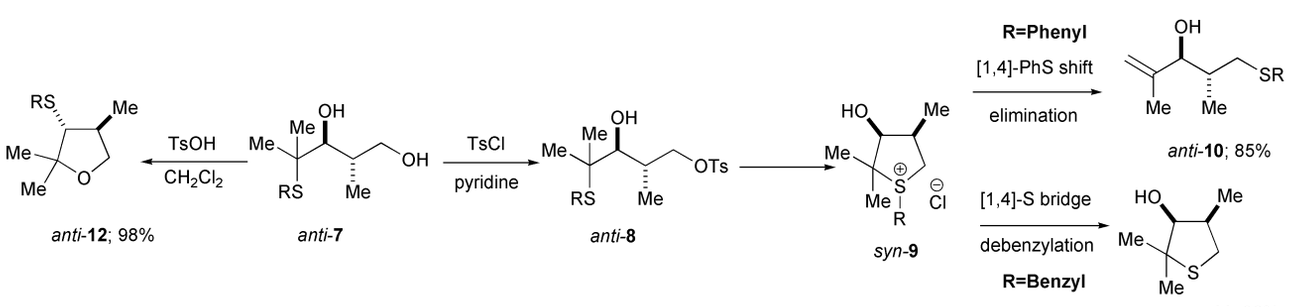
The synthesis of acyclic sulfenic esters is less well documentated than that of the analogous cyclic esters.[1] Amongst these cyclic sulfenates, oxathietanes are the most common.[2] 1,2-Oxathiolane itself is known,[3] but 1,2-oxathianes are rare. There are reports that sulfur-bridged 1,2-oxathianes **1** and **2** are intermediates in the degradation of vinyl sulfides from the onion *Allium cepa*,[4] while oxidised versions, such as **3**, may be reactive species in the inactivation of the flavoenzyme cyclohexanone oxygenase by thiolactones.[5] Stable 1,2-oxathiane 2-oxides *e.g.* **4**, and 2,2-dioxides *e.g.* **5** are well documented,[6] but 1,2-oxathiane **6** itself is unknown (Scheme 1).

In a series of publications,[7,8] we have reported numerous stereospecific [1,2]-RS migrations during the acid-catalysed rearrangements of 1,4-RS-1,3-diols (*e.g.*, *anti*-**7**) to give stereospecifically substituted tetrahydrofurans such as *anti*-**12** in near quantitative yield (Scheme 2). This rearrangement occurs irrespective of the migrating RS substituent (ArS, AlkS or HS),[9] but the relative rates of migration are different. By comparison the nature of R is more relevant to the outcome of the [1,4]-RS participation[10] that occurs when the same diol (*e.g.*, *anti*-**7**) is treated with TsCl in pyridine. When the migrating substituent is SPh, *exo*-elimination of the sulfonium ion *syn*-**9**; R = Ph occurs to give the allylic alcohol *anti*-**10**; R = Ph with an overall [1,4]-SPh shift,[11] whereas, debenzylation of the similar sulfonium ion *syn*-**9**; R = Bn gives the thiolane *syn*-**11** in near perfect yield since benzyl is more susceptible to S_N2 displacement (Scheme 2).[10]

In an attempt to synthesise the same thiolane[10] *syn*-**11**, treatment of the 4-HS-1,3-diol *anti*-**13** with TsCl in pyridine gave *syn*-**11** in only 52%, but, to our surprise the remaining product was the 1,2-oxathiane *syn*-**18** formed in 48% yield (Scheme 3). This 1,2-oxathiane must have come from competitive tosylation of the nucleophilic tertiary SH group (rather than the usually observed chemoselective tosylation of the primary OH group) to give the *S*-tosyl derivative *anti*-**16**. Cyclisation by nucleophilic displacement[12] at sulfur by the primary OH group as the nucleophile and the sulfinate, Ts^-, as the leaving group leads to the 1,2-oxathiane *syn*-**18**. It appears that under these conditions competitive tosylation must occur at about the same rate on the primary OH and the tertiary SH groups (Scheme 3). Full deprotonation of the more acidic SH group (pK_a = 7) in *anti*-**13** (to form the thiolate *anti*-**19**), we argued, would promote tosylation at sulfur since a thiolate is more nucleophilic than a thiol (by at least two orders of magnitude) and much more nucleophilic than the original primary alcohol (Scheme 4). Treatment of the 4-HS-1,3-diol *anti*-**13** with the stronger base Et_3N (pK_{aH} = 9), followed by slow addition of TsCl gave the 1,2-oxathiane *syn*-**18** as the only product in an improved 93% yield.

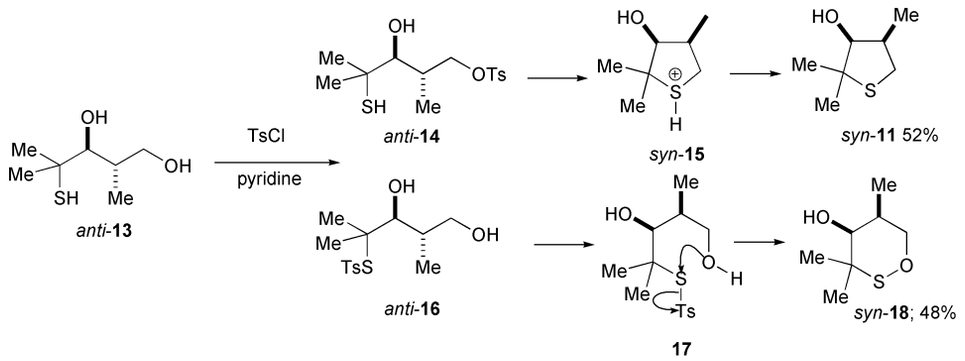


Scheme 1

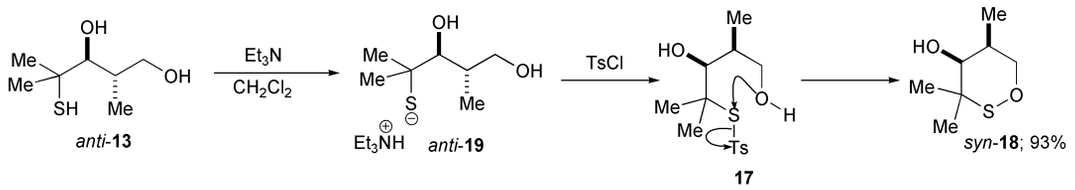


Scheme 2

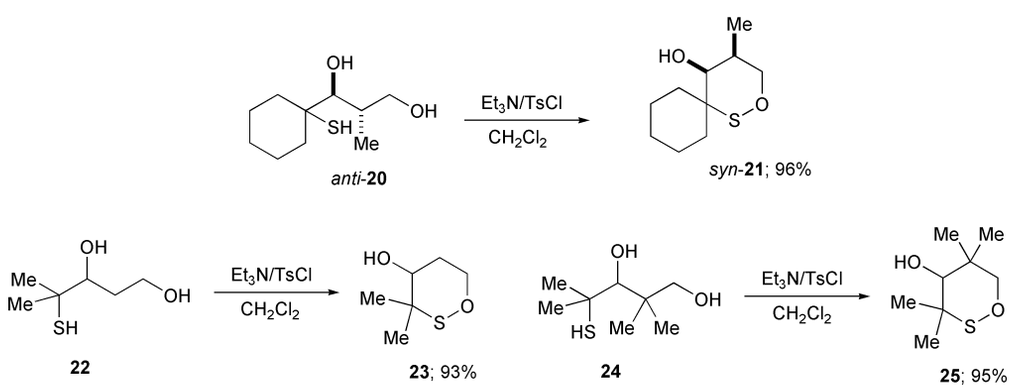
 DOI: 10.1039/b205060a



Scheme 3



Scheme 4

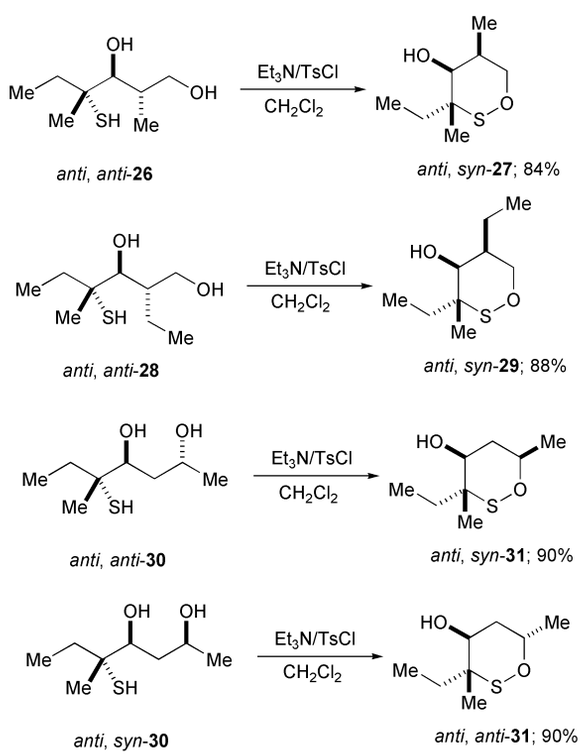


Scheme 5

In an attempt to investigate this ring closure, we cyclised a series of related 4-HS-1,3-diols with variation in stereochemistry and substitution pattern at each carbon atom. The method of preparation of these 4-HS-1,3-diols; *anti*-**13**, *anti*-**20**, **22**, **24**, *anti*,*anti*-**26**, *anti*,*anti*-**28**, *anti*,*anti*-**30** and *anti*,*syn*-**30** has previously been reported.[13] Treatment of diols *anti*-**20**, **22** and **24** with TsCl–Et_3N in CH_2Cl_2 gave the spirocyclic 1,2-oxathiane *syn*-**21** and the substituted 1,2-oxathianes **23** and **25** in near quantitative yield (Scheme 5). The spirocyclic oxathiane *syn*-**21** has one substituent at C-5, as does oxathiane *syn*-**18**. The 1,2-oxathiane **23** has no C-5 substituent, whereas the 1,2-oxathiane **25** has two. This cyclisation with S–O bond formation is independent of the substitution pattern at the C-5 position.

Structural variation at C-3, C-5 and C-6 positions of the oxathiane ring structure was studied with a series of 4-HS-1,3-diols *anti*,*anti*-**26**, *anti*,*anti*-**28**, *anti*,*anti*-**30** and *anti*,*syn*-**30** having a tertiary stereogenic centre at the C-4 position. All cases have either a methyl or ethyl substituent at C-3. Formation of oxathianes *anti*,*syn*-**27** and *anti*,*syn*-**29** illustrates that the cyclisation is efficient with the additional methyl or ethyl substituent at C-5. Furthermore, the diastereoisomeric diols *anti*,*anti*- and *anti*,*syn*-**30** with a methyl group at C-6 each cyclised stereospecifically to a different diastereoisomer of the oxathiane *anti*,*syn*- and *anti*,*anti*-**31**. The stereochemistry remained unchanged – retention of configuration was observed (Scheme 6).

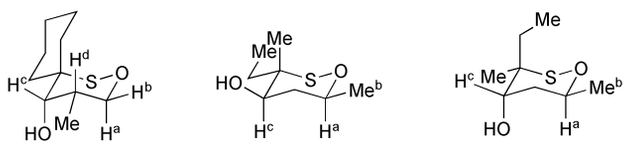
All the compounds we have described have a tertiary thiol group, but this seems to hinder neither the tosylation nor the cyclisation. The diols **30** have a secondary alcohol as a nucleo-



Scheme 6

phile but again cyclisation is not sterically hindered. This cyclisation is again stereospecific with retention of configuration observed at all the carbon atoms. This was confirmed by a 500 MHz NOESY spectrum on both the 1,2-oxathianes *syn*-**21** and *anti*, *syn*-**29**.

These 1,2-oxathianes were identified by NMR and MS (see Table 2). Characteristically, *syn*-**21** has a triplet for $\mathbf{H^a}$ on C-6 next to oxygen (δ 3.4) with large geminal (11.6 Hz) and axial–axial (11.6 Hz) coupling constants, typical of a six-membered ring (Scheme 7). Harpp and Gleason have observed similarly



syn-**21** *anti, syn*-**31** *anti, anti*-**31**

Scheme 7

large geminal coupling in substituted 1,2-oxathiane-2-oxides.[6a] The proton next to the secondary alcohol $\mathbf{H^c}$ is a double doublet with a small equatorial–equatorial (2.1 Hz) coupling and a large (11.2 Hz) coupling to OH. This suggests that the 1,2-oxathiane *syn*-**21** has an axial OH and an equatorial Me group which correlates with *A* values[14] and is in agreement with the 500 MHz NOESY spectrum. The most noticeable features of the ^{13}C NMR spectrum of *syn*-**21** are the CH_2 group next to oxygen (δ 74.5), a CH group (δ 73.3) and a quaternary carbon next to sulfur (δ 51.7). These peaks resemble those of the starting material *anti*-**20** since there is no skeletal reorganisation in this formal oxidation. The molecular ion M^+ is observed in the MS at 100% abundance. The ^{1}H NMR spectra of *anti*,*anti*- and *anti*,*syn*-**31** are more interesting since the methyl group ($\mathbf{Me^b}$) has a choice whether to be in an axial or equatorial conformation. In fact, it is equatorial (by a 500 MHz NOESY) in both diastereoisomers as shown in Scheme 7. This is not that surprising for *anti*, *syn*-**31** since all the larger substituents are equatorial as illustrated by the larger vicinal axial–axial couplings for $\mathbf{H^a}$ and $\mathbf{H^b}$ (Table 2). However, for *anti*, *anti*-**31** the OH and ethyl groups are axial because the OH has a smaller *A* value (0.60) and the Et a similar *A* value (1.79) to that of a methyl group (1.74). Additionally, the equatorial proton $\mathbf{H^c}$ in *anti*, *anti*-**31** appears as a double doublet with small equatorial–equatorial (*J* 3.9 Hz) and equatorial–axial (*J* 2.7 Hz) couplings. We have found similar results with related tetrahydropyrans.[15]

Table 1 1,2-Oxathiolanes from the rearrangement of sulfanyl-1,3-diols with TsCl–Et_3N in CH_2Cl_2

Diol	1,2-Oxathiolane	Yield
anti-**13**	*syn*-**18**	93%
anti-**20**	*syn*-**21**	96%
22	**23**	93%
24	**25**	95%
anti, anti-**26**	*anti, syn*-**27**	84%
anti, anti-**28**	*anti, syn*-**29**	88%
anti, anti-**30**	*anti, syn*-**31**	90%
anti, syn-**30**	*anti, anti*-**31**	90%

In conclusion, we have reported a general method for the synthesis of 4-hydroxy-1,2-oxathianes. The cyclisation is stereospecific with retention at all carbon atoms and occurs irrespective of the developing stereochemistry and the structural nature of the cyclising chain (Table 1). However, the reaction does appear to be sensitive to the strength of the base used, full deprotonation of the thiol is required for high yields to prevent competing thiolane formation. These derivatives were found to be thermally stable at room temperature; no decomposition was observed (by ^{1}H and ^{13}C NMR spectroscopy).

We have further demonstrated the rearrangement of 4-RS-1,3-diols (like *anti*-**7**) with TsCl is dependent on the migrating substituent (R = Ph, Bn and H) and can lead to three structurally diverse compounds; the allylic alcohol *anti*-**10** (when R = Ph),[11] thiolanes *syn*-**11** (when R = Bn)[10] and now the 1,2-oxathiane *syn*-**18** (when R = SH); all of which are formed as single products in near quantitative yield.

Experimental

All solvents were distilled before use. Tetrahydrofuran (THF) and ether were freshly distilled from $LiAlH_4$, whilst dichloromethane (CH_2Cl_2) and toluene were freshly distilled from CaH_2. Triphenylmethane was used as the indicator for THF. *n*-BuLi was titrated against diphenylacetic acid before use. All reactions were carried out under nitrogen using oven-dried glassware. Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography (TLC) was carried out on commercially available pre-coated plates (Merck Kieselgel $60F_{254}$ silica). Proton and carbon NMR spectra were recorded on Bruker WM 200, WM 250, WM400 or WM500 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million downfield from tetramethylsilane. Carbon NMR spectra were recorded with broad proton decoupling and Attached Proton Test (ATP). The symbol * after the carbon shift indicates an even number of attached protons; *i.e.*, CH_2 or quaternary carbons. Mass spectra were recorded on a AEI Kratos MS30 or MS890 machine using a DS503 data system for high resolution analysis.

(4*RS*,5*SR*)-4-Hydroxy-3,3,5-trimethyl-1,2-oxathiane *syn*-18

Toluene-*p*-sulfonyl chloride (0.13 g, 0.61 mmol) was added to a stirred solution of the diol[10] *anti*-**13** (0.1 g, 0.61 mmol) and Et_3N (0.12 g, 0.16 ml, 1.22 mmol) in dichloromethane (5 ml). The solution was stirred for 12 hours. Ether (20 ml) was added and the solution was extracted with HCl (10 ml, 3 M) and evaporated under reduced pressure. The residue was purified by

Table 2 Identification of 1,2-oxathianes, δ H^a, *J*/Hz and % abundance in mass spectrum

	syn-**18**	*syn*-**21**	**23**	**25**	*anti, syn*-**27**	*anti, syn*-**29**	*anti, syn*-**31**	*anti, anti*-**31**
δ H^a	3.4 (dd)	3.4(t)	3.8(m)	3.6(d)	3.4(t)	3.4(t)	4.2(ddq)	4.2(ddq)
$J_{syn}H^a$	0.0	0.0	[a]	—	0.0	0.0	6.3	6.2
$J_{anti}H^a$	11.8	11.6	[a]	—	11.7	11.7	11.5	11.7
$J_{gem}H^a$	11.8	11.6	[a]	11.2	11.7	11.7	—	—
δ H^b	3.8(dd)	3.8(dd)	4.2(m)	3.8(d)	3.8(dd)	3.9(dd)	—	—
$J_{syn}H^b$	4.7	4.8	[a]	—	4.9	4.9	—	—
δ H^c	3.4(dd)	3.3(dd)	3.9(ddd)	3.5(s)	3.4(m)	3.5(m)	3.9(dd)	3.9(dd)
$J_{syn}H^c$	2.0	2.1	3.5	—	2.0	2.0	2.6	2.7
$J_{anti}H^c$	—	—	8.6	—	—	—	7.9	3.9
M^+	100%	100%	100%	90%	55%	65%	15%	20%

[a] Coupling constants were not determined because of coalescence with other signals.

flash chromatography on a silica gel column with light petroleum ether (40–60 °C) (1 : 1) to give the *1,2-oxathiane syn*-**18** (91 mg, 93%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3300 (OH); δ_H(400 MHz, $CDCl_3$) 3.86 (1 H, dd, *J* 11.8 and 4.7, CH_AH_BO), 3.43 (1 H, t, *J* 11.8, CH$_A$$H_B$O), 3.44 (1 H, dd, *J* 11.1 and 2.0, C*H*OH), 2.32 (1 H, d, *J* 11.1, OH), 2.22–2.14 (1 H, m, C*H*Me), 1.59 (3 H, s, Me), 1.09 (3 H, s, Me) and 0.82 (3 H, d, *J* 6.9, C*H*Me); δ_C(100 MHz, $CDCl_3$) 73.7 (CHOH), 73.7* (CH_2O), 51.7* (CS), 31.4 (*C*HMe), 25.2 (Me), 20.7 (Me) and 13.9 (*Me*CH); *m*/*z* 162.1 (100% M), 88.0 (5, M − C_3H_6S) and 74.0 (5, C_3H_6S).

(3*RS*,4*SR*)-5-Hydroxy-4-methyl-1,2-thiaoxaspiro[5.5]undecane *syn*-21

In the same way, the diol[10] *anti*-**20** (16 mg, 0.106 mmol), toluene-*p*-sulfonyl chloride (71 mg, 0.34 mmol) and Et_3N (69.2 mg, 93.2 μl, 0.68 mmol) in CH_2Cl_2 (1 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane syn*-**21** (61.2 mg, 96%) as an oil; R_f [light petroleum ether (40–60 °C) (9 : 1)] 0.5; ν_{max}(film, $CDCl_3$)/cm^{-1} 3300 (OH); δ_H(500 MHz, $CDCl_3$) 3.87 (1 H, dd, *J* 11.6 and 4.8, CH_AH_BO), 3.46 (1 H, t, *J* 11.6, CH$_A$$H_B$O), 3.35 (1 H, dd, *J* 11.2 and 2.1, C*H*OH), 2.37–2.34 (1 H, m, C*H*Me), 2.33 (1 H, d, *J* 11.2, OH), 2.21–2.14 (1 H, m, CH_AH_B), 1.76–1.07 (9 H, m, 4 × CH_2 and CH$_A$$H_B$) and 0.84 (3 H, d, *J* 6.9, MeCH); δ_C(100 MHz, $CDCl_3$) 74.5* (CH_2O), 73.3 (CHOH), 51.7* (CS), 37.6 (*C*HMe), 35.3*, 33.9*, 25.9* and 22.0* (5 × CH_2) and 18.4 (*Me*CH) (Found M^+, 202.1027. $C_{10}H_{18}O_2S$ requires *M*, 202.1027); *m*/*z* 202.1 (100%, M). There was an NOE enhancement (by a 500 MHz NOESY) between the C*H*OH (δ_H 3.35) and C*H*Me (δ_H 2.35) for the oxathiane *anti*, *syn*-**21** signifying a *syn*- relationship.

4-Hydroxy-3,3-dimethyl-1,2-oxathiane 23

In the same way, the diol[10] **22** (16 mg, 0.106 mmol), toluene-*p*-sulfonyl chloride (22 mg, 0.106 mmol) and Et_3N (21.4 mg, 28.8 μl, 0.21 mmol) in CH_2Cl_2 (2 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane* **23** (14.6 mg, 93%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.5; ν_{max}(film, $CDCl_3$)/cm^{-1} 3300 (OH); δ_H(400 MHz, $CDCl_3$) 4.25–4.14 (1 H, m, CH_AH_BO), 3.93 (1 H, ddd, *J* 11.3, 8.6 and 3.5, C*H*OH), 3.87–3.79 (1 H, m, CH$_A$$H_B$O), 2.42 (1 H, br d, *J* 8.6, OH), 2.04–1.70 (2 H, m, CH_2), 1.31 (3 H, s, Me) and 1.24 (3 H, s, Me); δ_C(100 MHz, $CDCl_3$) 75.1* (CH_2O), 73.3 (CHOH), 50.7* (CS), 32.8* (CH_2), 29.3 and 26.8 (2 × Me) (Found M^+, 148.0562. $C_6H_{12}O_2S$ requires *M*, 148.0557); *m*/*z* 148.1 (100%, M).

4-Hydroxy-3,3,5,5-tetramethyl-1,2-oxathiane 25

In the same way, the diol[10] **24** (0.1 g, 0.56 mmol) toluene-*p*-sulfonyl chloride (0.12 g, 0.56 mmol) and Et_3N (0.14 g, 0.15 ml, 1.11 mmol) in CH_2Cl_2 (2 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane* **25** (93 mg, 95%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3350 (OH); δ_H(400 MHz, $CDCl_3$) 3.86 (1 H, AB quartet, *J* 11.2, CH_AH_BO), 3.63 (1 H, AB quartet, *J* 11.2, CH$_A$$H_B$O), 3.55 (1 H, s, C*H*OH), 2.06–1.96 (1 H, br s, OH), 1.49 (3 H, s, Me), 1.07 (3 H, s, Me), 1.05 (3 H, s, Me) and 0.91 (3 H, s, Me); δ_C(100 MHz, $CDCl_3$) 86.5* (CH_2O), 81.5 (CHOH), 49.3* (CS), 37.3* (*C*Me), 25.8, 23.6, 22.0 and 19.4 (4 × Me); *m*/*z* 176.1 (90%, M) and 127.3 (100, M–SOH).

(2*SR*,3*RS*,4*RS*)-2,4-dimethyl-4-sulfanylhexane-1,3-diol *anti,anti*-26

Sodium (0.42 g, stick, 18.6 mmol) was added in portions to a solution of (2*SR*,3*RS*,4*RS*)-2,4-dimethyl-4-(benzylsulfanyl)-hexan-1,3-diol[13] (1 g, 3.73 mmol) in liquid ammonia (150 ml) at −33 °C. The solution was stirred for 8 hours. Saturated NH_4Cl (1 ml) and HCl (5 ml, 3 M) were slowly added and the mixture was extracted with ether (3 × 75 ml). The combined organic layers were dried ($MgSO_4$) and evaporated under reduced pressure. The residue was purified by flash column chromatography on silica gel eluting with ether to give (2*SR*,3*RS*,4*RS*)- *2,4-dimethyl-4-sulfanylhexane-1,3-diol anti,anti*-**26** (0.49 g, 75%) as an oil; R_f [ether] 0.8; ν_{max}(film, $CDCl_3$)/cm^{-1} 3500–3300 (OH); δ_H(400 MHz, $CDCl_3$) 3.85 (1 H, dd, *J* 11.0 and 3.3, CH_ACH$_B$-OH), 3.63 (1 H, dd, *J* 11.0 and 5.9, CH$_A$CH_BOH), 3.44 (1 H, br s, OH), 3.41 (1H, d, *J* 3.9, C*H*OH), 2.85 (1 H, br s, OH), 2.22 (1 H, s, SH), 2.00 (1 H, m, C*H*Me), 1.55–1.74 (4 H, m, 2 × CH_2), 1.37 (3 H, s, Me), 1.08 (3 H, d, *J* 7.2, Me) and 1.01 (3 H, t, *J* 7.3, Me); δ_C(50 MHz, $CDCl_3$) 83.8 (CHOH), 66.1 (CH_2O), 55.4 (CSH), 47.1 (*C*HMe), 29.7 (CH_2), 27.1, 18.4, 11.9 and 9.1 (3 × Me) [Found (M − H_2)$^+$, 170.0872. $C_8H_{18}O_2S$ requires (*M* − H_2), 176.1088]; *m*/*z* 176.1 (15%, M − H_2), 160.1 (40, M − H_2O), 103.1 (35, M − C_3H_6SH) and 75.0 (100, C_3H_6SH).

(3*SR*,4*RS*,5*RS*)-3,5-Dimethyl-3-ethyl-4-hydroxy-1,2-oxathiane *anti, syn*-27

In the same way as for 1,2-oxathiane *syn*-**18**, the diol *anti,anti*-**26** (0.15 g, 0.84 mmol), toluene-*p*-sulfonyl chloride (0.16 g, 0.84 mmol) and Et_3N (0.17 g, 0.24 ml, 1.68 mmol) in CH_2Cl_2 (2 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane anti,syn*-**27** (0.12 g, 84%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3300 (OH); δ_H(400 MHz, $CDCl_3$) 3.84 (1 H, dd, *J* 11.7 and 4.9, CH_AH_BO), 3.44 (1 H, t, *J* 11.7, CH$_A$$H_B$O), 3.42 (1 H, dd, *J* 11.1 and 2.0, C*H*OH), 2.41 (1 H, d, *J* 11.1, OH), 2.03–2.18 (2 H, m, C*H*Me and CH_AH_BMe), 1.81 (1 H, m, CH$_A$$H_B$Me), 1.00 (3 H, t, *J* 7.1, Me), 0.96 (3 H, s, Me) and 0.83 (3 H, d, *J* 7.0, Me); δ_C(100 MHz, $CDCl_3$) 73.5 (CH_2OH), 72.1 (CO), 55.7 (CS), 31.2 (*C*HMe), 28.4 (CH_2), 16.3, 13.9 and 8.0 (3 × Me) (Found M + NH_4^+, 194.3146. $C_8H_{16}O_2S$ + NH_4 requires *M*, 194.3135); *m*/*z* 194.1 (55%, M + NH_4^+), and 176.1 (40, M − H).

(3*SR*,4*RS*,5*RS*)-3,5-Diethyl-4-hydroxy-3-methyl-1,2-oxathiane *anti,syn*-29

In the same way, the diol *anti, anti*-**27** (0.11 g, 0.57 mmol), toluene-*p*-sulfonyl chloride (0.11 g, 0.57 mmol) and Et_3N (0.115 g, 0.16 ml, 1.14 mmol) in CH_2Cl_2 (2 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane anti*, *syn*-**29** (93 mg, 86%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3300 (OH); δ_H(400 MHz, $CDCl_3$) 3.91 (1 H, dd, *J* 11.7 and 4.9, CH_AH_BO), 3.51 (1 H, dd, *J* 11.1 and 2.0, C*H*OH), 3.46 (1 H, t, *J* 11.7, CH$_A$$H_B$O), 2.42 (1 H, d, *J* 11.1, OH), 1.19–1.91 (5 H, m, C*H*CH_2Me and 2 × CH_2Me), 1.02 (3 H, t, *J* 7.1, Me), 0.95 (3H, s, Me) and 0.83 (3H, t, *J* 7.1, Me); δ_C(100 MHz, $CDCl_3$) 72.9 (CH_2OH), 69.8 (CO), 55.5* (CS), 31.9 (*C*HCH_2Me), 28.5 and 20.5 (2 × CH_2), 16.3, 14.1 and 7.9 (3 × Me) (Found M^+, 190.1024. $C_9H_{18}O_2S$ requires *M*, 190.1028); *m*/*z* 190 (65%, M + NH_4^+) and 141 (40, M − SOH).

(2*SR*,4*SR*,5*RS*)-5-Methyl-5-(benzylsulfanyl)heptane-2,4-diol by the method of Prasad[16]

Diethylmethoxyborane (0.7 ml, 1 M in THF, 0.7 mmol) was added slowly to a solution of (4*SR*,5*RS*) 4-hydroxy-5-methyl-5-(benzylsulfanyl)heptan-2-one[13] (0.18 g, 0.7 mmol) in THF–methanol (10 ml, 4 : 1) at −78 °C. The solution was stirred for 30 min, $NaBH_4$ (52 mg, 1.4 mmol) was added and the solution stirred for 1 hour. Acetic acid (2 ml) was added and the solution allowed to warm to room temperature. The solution was extracted with ether (3 × 50 ml) and washed with $NaHCO_3$ (50 ml). The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was puri-

fied by column chromatography eluting with light petroleum ether (40–60 °C) (1 : 1) to give (2*SR*,4*SR*,5*RS*)-*5-methyl-5-(benzylsulfanyl)heptane-2,4-diol* (0.17 g, 91%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.15; ν_{max}(film, $CDCl_3$)/cm^{-1} 3500–3350 (OH, broad); δ_H(400 MHz, $CDCl_3$) 7.19–7.35 (5 H, m, Ph), 3.48–3.98 (5 H, m, 2 × C*H*OH, OH and CH_2Ph), 1.51–1.71 (4 H, m, 2 × CH_2), 1.24 (3 H, s, Me), 1.18 (3 H, d, *J* 7.1, MeCHOH), 0.86 (3 H, t, *J* 7.3, Me); δ_C(50 MHz, $CDCl_3$) 137.6, 128.9, 128.6 and 127.1 (Ph), 77.0 (*C*HOH), 68.9 (*C*HOH), 53.1 (CS), 38.4, 33.1 and 27.86 (3 × CH_2), 23.9, 21.7 and 8.7 (3 × Me) (Found M^+, 268.4892. $C_{15}H_{24}O_2S$ requires *M*, 268.4158; *m*/*z* 268 (5%, M^+) and 91 (100, CH_2Ph).

(2*SR*,4*SR*,5*RS*)-5-Methyl-5-(sulfanyl)heptane-2,4-diol *anti*,*syn*-30

The above diol (1 g, 3.73 mmol) and sodium (0.42 g, stick, 18.65 mmol) in liquid NH_3 (150 ml) gave, after column chromatography on silica gel eluting with ether (2*SR*,4*SR*,5*RS*)-*5-methyl-5-(sulfanyl)heptane-2,4-diol anti*,*syn*-**30** (0.49 g, 75%) as an oil; R_f [ether] 0.8; ν_{max}(film, $CDCl_3$)/cm^{-1} 3500–3300 (OH); δ_H(400 MHz, $CDCl_3$) 4.12 (1 H, m, C*H*OHMe), 3.74 (1 H, dd, *J* 6.4 and 1.8, C*H*OHCH_2), 3.22 (2 H, br s, OH), 1.46–1.76 (4 H, m, 2 × CH_2), 1.42 (1 H, s, SH), 1.26 (3 H, s, Me), 1.19 (3 H, d, *J* 6.9, MeCHOH) and 0.99 (3 H, t, *J* 7.4, Me); δ_C(50 MHz, $CDCl_3$) 78.7, 68.9, (2 × CHOH), 53.8 (CSH), 38.8 (*C*H_2-CHOH), 31.80 (CH_2), 24.0, 22.9 and 8.8 (3 × Me) [Found $(M - H_2)^+$, 170.0872. $C_8H_{18}O_2S$ requires ($M - H_2$), 176.1088]; *m*/*z* 176.1 (15%, $M - H_2$), 160.1 (40, $M - H_2O$), 103.1 (35, $M - C_3H_6SH$) and 75.0 (100, C_3H_6SH).

(2*RS*,4*SR*,5*RS*)-5-Methyl-5-(benzylsulfanyl)heptane-2,4-diol by the method of Evans[17]

Tetramethylammonium triacetoxyborohydride (0.88g, 3.36 mmol) was added to a solution of MeCN–acetic acid (4 ml, 1 : 1) and stirred for 1 hour. The solution was cooled to −20 °C. (4*SR*,5*RS*)-4-Hydroxy-5-methyl-5-(benzylsulfanyl)heptan-2-one (0.11 g, 0.42 mmol) in MeCN (1 ml) was slowly added. The solution was kept at −20 °C for 4 days. The solution was extracted with ether (3 × 50 ml) and the combined organic extracts washed with $NaHCO_3$ (3 × 20 ml). The combined organic extracts were dried over $MgSO_4$ and evaporated under reduced pressure to give a crude separable mixture of (92 : 8) diastereoisomers. The residue was purified by column chromatography eluting with light petroleum ether (40–60 °C) (1 : 1) to give (2*RS*,4*SR*,5*RS*)*-5-methyl-5-(benzylsulfanyl)heptane-2,4-diol* as an oil (89 mg, 80%); R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.25; ν_{max}(film, $CDCl_3$)/cm^{-1} 3500–3350 (OH, broad); δ_H(400 MHz, $CDCl_3$) 7.19–7.34 (5 H, m, Ph), 3.95 (1 H, m, C*H*OH), 3.50–3.68 (3 H, m, C*H*OH and CH_2Ph), 3.43 (1 H, br s, OH), 1.51–1.71 (4 H, m, 2 × CH_2), 1.21 (3 H, s, Me), 1.12 (3 H, d, *J* 7.4, Me) and 0.86 (3 H, t, *J* 7.4, Me); δ_C(50 MHz, $CDCl_3$) 138.0, 128.9, 128.6 and 127.1 (Ph), 77.2 (CHOH), 68.9 (CHOH), 55.9 (CS), 38.5, 32.7 and 29.3 (3 × CH_2), 23.9, 22.7 and 8.76 (3 × Me) (Found M^+, 268.4892. $C_{15}H_{24}O_2S$ requires *M*, 268.4158); *m*/*z* 268 (5%, M^+) and 91 (100, CH_2Ph).

(2*RS*,4*SR*,5*RS*)-5-Methyl-5-sulfanylheptane-2,4-diol *anti*,*anti*-30

The above diol (1 g, 3.73 mmol) and sodium (0.42 g, stick, 18.65 mmol) in liquid NH_3 (150 ml) gave, after column chromatography on silica gel eluting with ether the (2*RS*,4*SR*,5*RS*)*-5-methyl-5-sulfanylheptane-2,4-diol anti,anti*-**30** (0.49 g, 75%) as an oil; R_f [ether] 0.8; ν_{max}(film, $CDCl_3$)/cm^{-1} 3500–3300 (OH); δ_H(400 MHz, $CDCl_3$) 4.05 (1H, m, C*H*OHMe), 3.65 (1H, dd, *J* 6.8 and 1.5, C*H*OHCH_2), 3.20 (2H, br s, OH), 1.42–1.75 (4 H, m, 2 × CH_2), 1.40 (1 H, s, SH), 1.25 (3 H, s, Me), 1.21 (3 H, d, *J* 6.8, MeCHOH) and 1.05 (3 H, t, *J* 7.4, Me); δ_C(50 MHz, $CDCl_3$) 79.7, 68.9 (2 × CHOH), 54.1 (CSH), 38.9 (*C*H_2-CHOH), 31.8 (CH_2), 25.3, 24.1 and 8.9 (3 × Me) [Found $(M - H_2)^+$, 170.0872. $C_8H_{18}O_2S$ requires ($M - H_2$), 176.1088)]; *m*/*z* 176.1 (15%, $M - H_2$), 160.1 (40, $M - H_2O$), 103.1 (35, $M - C_3H_6SH$) and 75.0 (100, C_3H_6SH).

(3*RS*,4*RS*,6*SR*)-3,6-Dimethyl-3-ethyl-4-hydroxy-1,2-oxathiane *anti,syn*-31

In the same way, the diol *anti,anti*-**30** (44 mg, 0.25 mmol), toluene-*p*-sulfonyl chloride (47 mg, 0.25 mmol) and Et_3N (0.1 g, 0.14 ml, 0.50 mmol) in CH_2Cl_2 (1 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane anti, syn*- **31** (39 mg, 90%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3444 (OH); δ_H(400 MHz, $CDCl_3$) 4.17 (1 H, ddq, *J* 11.5, 6.3 and 6.2, OC*H*Me), 3.89 (1 H, dd, *J* 7.9 and 2.6, C*H*OH), 1.60–2.15 (5 H, m, CH_2CHO*H* and CH_2Me), 1.16 (3 H, d, *J* 6.2, CHOMe), 1.09 (3 H, t, *J* 7.2, CH_2Me), 0.93 (3 H, s, Me); δ_C(100 MHz, $CDCl_3$) 75.1 (CHO), 69.0 (CHOH), 53.8* (CS), 36.8 and 28.5 (2 × CH_2), 22.2, 15.6 and 8.0 (3 × Me) (Found M + NH_4^+, 194.3133. $C_8H_{16}O_2S$ + NH_4 requires *M*, 194.3135); *m*/*z* 194 (15, M + NH_4^+) and 176 (40, M − SOH).

(3*RS*,4*RS*,6*RS*)-3,6-Dimethyl-3-ethyl-4-hydroxy-1,2-oxathiane *anti,anti*-31

In the same way as for 1,2-oxathiane *syn*-**18**, the diol *anti, syn*-**30** (0.11 g, 0.61 mmol), toluene-*p*-sulfonyl chloride (0.13 g, 0.61 mmol) and Et_3N (0.12 g, 0.16 ml, 1.21 mmol) in CH_2Cl_2 (1 ml) gave, after flash column chromatography on silica gel eluting with light petroleum ether (40–60 °C) (1 : 1) the *1,2-oxathiane anti,anti*-**31** (96 mg, 90%) as an oil; R_f [light petroleum ether (40–60 °C) (1 : 1)] 0.6; ν_{max}(film, $CDCl_3$)/cm^{-1} 3444 (OH); δ_H(400 MHz, $CDCl_3$) 4.18 (1 H, ddq, *J* 11.7, 6.2 and 6.1, OC*H*Me), 3.86 (1 H, dd, *J* 3.9 and 2.7, C*H*OH), 1.51–2.11 (5 H, m, CH_2CHO*H* and CH_2Me), 1.19 (3 H, d, *J* 6.1, CHOMe), 1.05 (3 H, t, *J* 7.1, CH_2Me) and 0.93 (3 H, s, Me); δ_C(100 MHz, $CDCl_3$) 75.1 (CHO), 69.0 (CHOH), 53.8 (CS), 36.8 and 28.5 (2 × CH_2), 22.2, 15.6 and 8.0 (3 × Me) (Found M + NH_4^+, 194.3140. $C_8H_{16}O_2S$ + NH_4 requires *M*, 194.3135); *m*/*z* 194 (20, M + NH_4^+) and 176 (40, M − SOH).

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