Milbemycin Synthesis: Asymmetric Synthesis of Spiroketals from Methyl α-D-Glucopyranoside

Girish Khandekar, Gareth C. Robinson, Nicholas A. Stacey, Eric J. Thomas*† and Sunil Vather
The Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY, UK

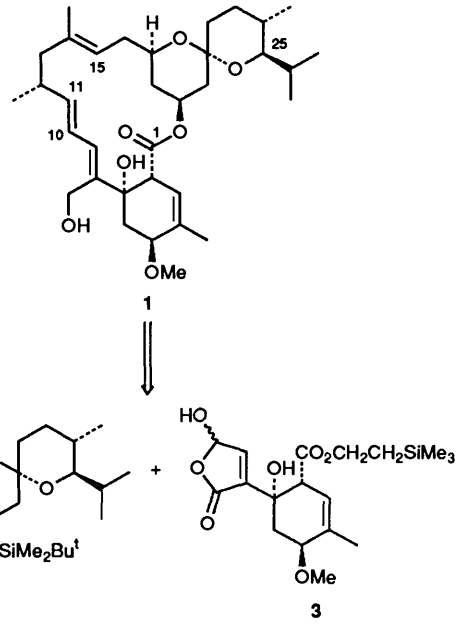
The 6-chloro-4,6-dideoxygalactoside **8** was prepared by selective dichlorination of methyl α-D-glucopyranoside **6** followed by hydrogenolysis, and was converted into the epoxyalkyldithioacetal **10** by treatment with propane-1,3-dithiol, protection, and formation of the epoxide. With nucleophiles, the epoxyalkyldithioacetal underwent opening of the epoxide, whereas with strongly basic reagents abstraction of the dithiane proton at C-2 followed by elimination gave the epoxy hydroxy ketone dithioacetal **34**. This chemistry was used to prepare a series of *anti*-1,3-diols **36**, **38** and **40** and should be useful for natural-product synthesis. Using the vinyllithium reagent derived from iodide **57**, the diol **60** corresponding to the C(11)–C(21) fragment of milbemycin E **1** was prepared, and this was taken through to the spiroketal **64** as a model for a proposed synthesis of the C(11)–C(25) fragment of a milbemycin. The *anti*-diols **36** and **40** were taken through to the spiroketals **74** and **69**, respectively, so providing an asymmetric synthesis of fully functionalised milbemycin spiroketals.

The milbemycins and avermectins are important targets for synthesis because of their potent and useful biological activities.[1-3] A crucial step in a convergent approach to non-aromatic β-milbemycins, *e.g.* milbemycin E **1**, is a Wittig condensation between a phosphonium ylide corresponding to the C(11)–C(25) fragment, *e.g.* **2**, and a hydroxybutenolide, *e.g.* **3**.[3-7] We now report full details of an approach to the asymmetric synthesis of the C(11)–C(25) fragment of milbemycin E, together with an asymmetric synthesis of milbemycin spiroketals.[8]

The C(11)–C(25) fragment **4** of milbemycin E is synthetically equivalent to the open-chain (trihydroxydialkyl)-1,3-dithiane **5**. Since the stereochemistry at C(17) and C(19) corresponds to that at C(5) and C(3) in glucose, methyl α-D-glucopyranoside **6** would appear to be an attractive precursor of species **5**. Indeed, derivatives of glucose have been used as the starting materials in several asymmetric syntheses of milbemycin and avermectin spiroacetals.[9]

A synthesis of spiroketals from methyl D-glucopyranoside **6** has been developed by Redlich.[10] Specifically, the protected 2-(trihydroxyalkyl)dithiane **14** has been prepared from the 4,6-dideoxy-*xylo*-hexopyranoside **13** and was converted into the ketene dithioketal **15** by treatment with butyllithium, which deprotonates the dithiane at C-2 and induces elimination of acetone. Reduction of compound **15** with lithium aluminium hydride then gave the 2-(hydroxyalkyl)-1,3-dithiane **16** which, after exchange of protecting groups, was alkylated, giving the 2,2-bisalkyldithiane **17**, and converted into the spiroketal **18**.[10] This chemistry would appear to be applicable to a synthesis of the spiroketals required for a milbemycin synthesis if the hydroxy substituent at C(6) in methyl D-glucopyranoside could be carried through the synthesis, thus being available for the introduction of the C(11)–C(15) fragment.

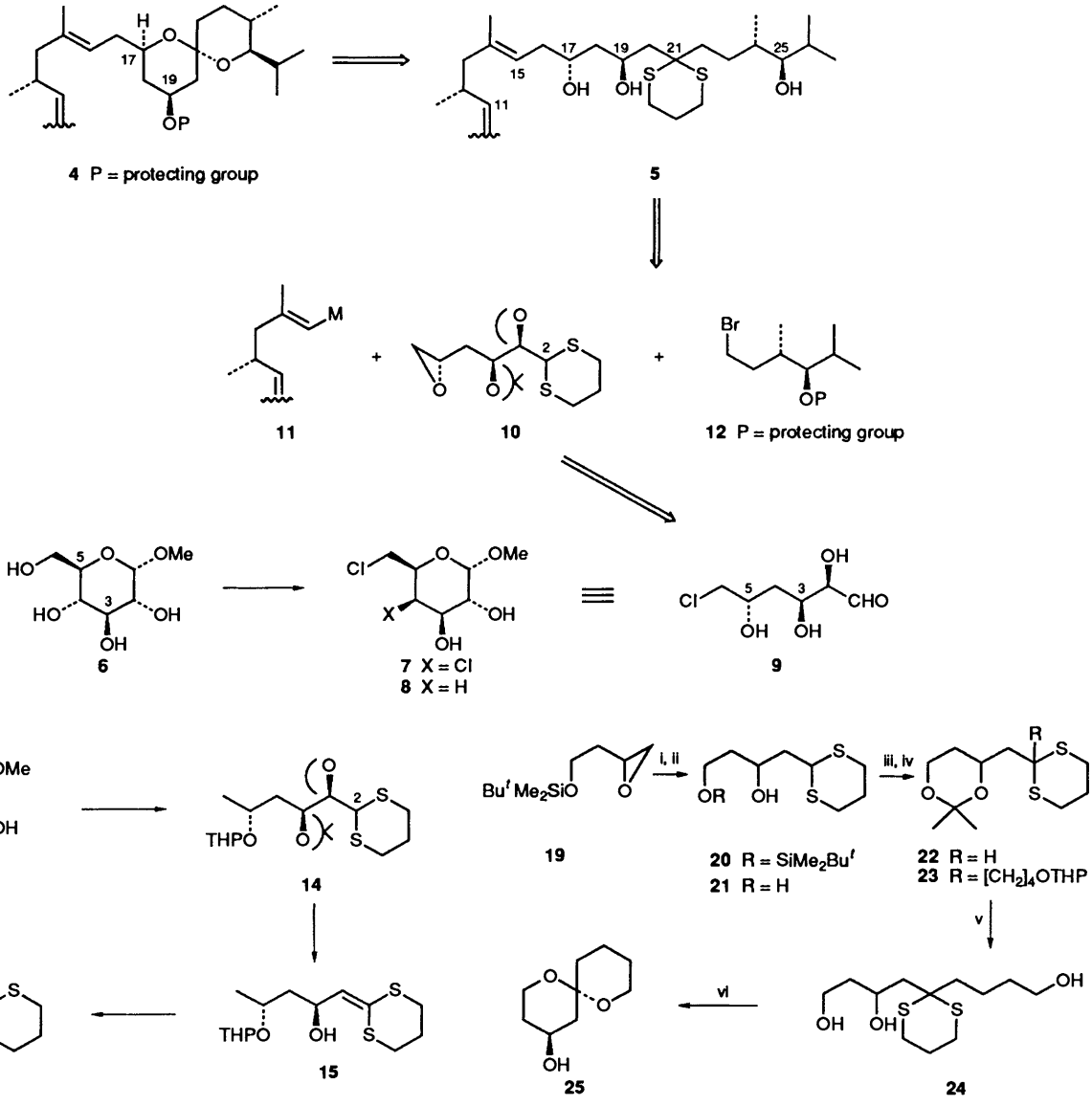
With this approach in mind, the protected 2-(epoxyalkyl)-dithiane **10** was identified as a key intermediate. It was thought that this epoxide would be available from methyl α-D-glucopyranoside **6** since treatment of compound **6** with sulfuryl dichloride is known to give the dichloride **7**,[11] and selective



hydrogenolysis of the dichloride to methyl 6-chloro-4,6-dideoxygalactoside **8** has been reported.[12] This chlorogalactoside is synthetically equivalent to the chlorotrihydroxyaldehyde **9**, and treatment of this with propane-1,3-dithiol, protection, and formation of an epoxide ring should lead to the 2-(epoxyalkyl)-1,3-dithiane **10**. Opening of the epoxide by using a vinyllithium reagent equivalent to partial structure **11** could then be used to introduce the C(11)–C(15) fragment, and alkylation (with bromide **12**) of the thus-formed dithiane available from compound **10** by elimination of acetone, reduction, and protection of the diol, should lead to the introduction of the C(22)–C(25) unit.

The insect pheromone **25**[13] was prepared to gain familiarity with the spiroketal synthesis using dithianes. Alkylation of 1,3-dithiane using the epoxide **19** gave the 2-(hydroxyalkyl)-1,3-dithiane **20**, which was converted into the 2-(acetonido-alkyl)-1,3-dithiane **22** (Scheme 1). Alkylation using 1-bromo-4-(tetrahydropyran-2-yloxy)butane gave compound **23**, and

† *Present address:* The Department of Chemistry, The Victoria University of Manchester, Oxford Road, Manchester, M13 9PL, UK.



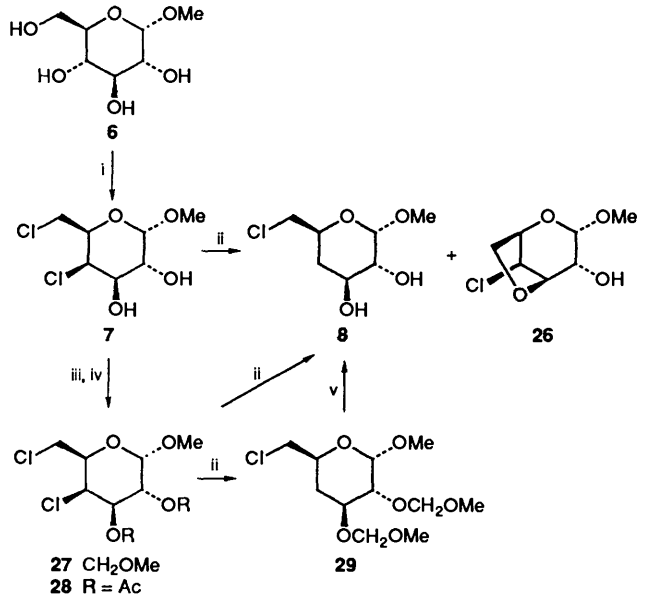
Scheme 1 *Reagents and conditions:* i, 2-lithio-1,3-dithiane, 0 °C, 2 h (**20**, 55%); ii, TBAF, THF (**21**, 82%); iii, $CuSO_4$, H_2SO_4, acetone (**22**, 90%); iv, BuLi, −20 °C, 6 h; then $Br[CH_2]_4OTHP$, −78 °C, 6 h and room temp., overnight (**23**, 48%); v, PTSA, MeOH, 20 °C, 16 h (71%); vi, $HgCl_2$, THF, 20 °C, 3 h (80%).

deprotection followed by treatment with mercury(II) chloride gave the spiroketal **25**.[13]

Synthesis of 2-[(1R,2S,4S)-4,5-*Epoxy*-1,2-*isopropylidenedioxypentyl*]-1,3-*dithiane* **10**.—Following the literature method,[11] methyl α-D-glucopyranoside **6** was converted into the 4,6-dichlorodideoxygalactoside **7** by using sulfuryl dichloride followed by treatment with sodium iodide. Preliminary studies into the reduction of the dichloride **7** and its analogous diiodide[14] using trialkyltin hydrides[15,16] gave mixtures of mono- and bis-reduced products, and so hydrogenolysis procedures were investigated. However, the published procedure[12] which involved the use of relatively large quantities of pyrophoric Raney nickel was considered unsuitable for large-scale work necessary at the beginning of a synthesis, and so an alternative procedure was required.

It was found that the required hydrogenolysis to the monochloro sugar **8** could be achieved using 10% palladium on charcoal as the catalyst in ethanol under basic conditions. However, although yields of up to 65% could be achieved, the reaction was not reproducible and appeared to be very sensitive to sulfur-containing impurities in the starting material. These tended to poison the catalyst and slow down the reaction, so allowing the formation of a side-product which was identified as the bicyclic ether **26** formed by base-catalysed intramolecular displacement of the chlorine at C(6) by the hydroxy group at C(3) (Scheme 2).

To avoid this side-reaction, the dichloro sugar **7** was protected as its bis-methoxymethyl ether **27**. Hydrogenolysis under basic conditions now proceded cleanly to give the protected monochloro sugar **29**, which was deprotected using hydrobromic acid in 1,2-dimethoxyethane (DME) (overall yield ~ 50%). However, as neither the protected dichloro- nor the protected mono-chloro sugars **27** or **29** was crystalline and

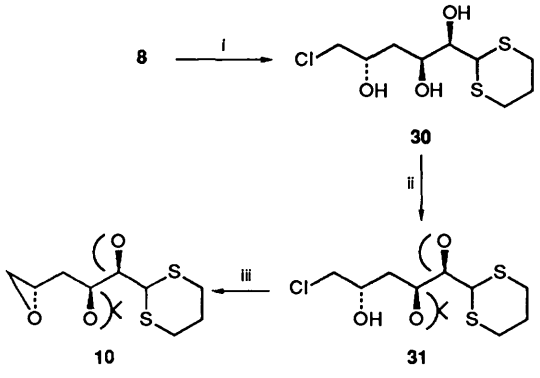


Scheme 2 *Reagents:* i, SO_2Cl_2; then NaI[11]; ii, H_2, Pd/C, KOH, EtOH (64% of **8** from **7**: 72% of **29** from **27**: 93% of **8** from **28**); iii, $EtNPr^i_2$, $ClCH_2OMe$, CH_2Cl_2 (**27**, 92%); iv, Ac_2O, pyridine[17]; v, HBr, DME (80%).

had to be purified by chromatography, it was difficult to prepare large quantities of the monochloro sugar by this route.

A more convenient preparation of the monochloro sugar **8** was devised using the diacetate **28** of the dichloro sugar.[17] This diacetate is highly crystalline and can be prepared from the crude dichloro sugar **7** without any chromatography. Hydrogenolysis of the diacetate in ethanol containing potassium hydroxide is very clean and is accompanied by saponification of the acetoxy substituents *in situ* to give the monochloro sugar **8** directly.

Having prepared the monochloro sugar **8**, we converted it into the dithiane **30** by using propane-1,3-dithiol and conc. hydrochloric acid, and the dithiane was protected as its acetonide **31** using acetone, anhydrous copper sulfate, and an acid catalyst (Scheme 3). Treatment of the chlorohydrin **31** with base gave the epoxide **10**.



Scheme 3 *Reagents:* i, $HS[CH_2]_3SH$, HCl (93%); ii, $CuSO_4$, PTSA, acetone (91%); iii, NaOH, EtOH (74%).

Chemistry of 2-[(1R,2S,4S)-4,5-*Epoxy*-1,2-*isopropylidenedioxypentyl*]-1,3-*dithiane* **10**.—The 2-(epoxyalkyl)-1,3-dithiane **10** had been identified as a key intermediate in our proposed synthesis of milbemycins. By analogy with the work of Redlich,[10] it was expected that strong bases would deprotonate compound **10** at C(2) and lead to ketene dithioketals by loss of acetone. However, it was hoped that nucleophiles would open the epoxide ring rather than deprotonate the dithiane, and so could be used to extend the alkyl chain.

It was found that reaction of the epoxy dithiane **10** with vinylmagnesium bromide in the presence of a copper catalyst proceeded with cleavage of the epoxide ring, but without elimination of acetone, to give the homoallyl alcohol **32** (Scheme 4). Similarly, lithiated methyl phenyl sulfone gave the epoxide-cleaved product **33**. In contrast, butyllithium acted as a base and gave a good yield of the epoxy hydroxy ketene dithioketal **34**, and treatment of the epoxide-opened products **32** and **33** with butyllithium induced elimination of acetone to give the ketene dithioketals **35** and **37**, respectively. Reduction of these with lithium aluminium hydride gave the corresponding dithianes **36** and **38**. With an excess of the sodium salt of 4-methoxybenzyl alcohol, the opening of the epoxide and elimination of acetone could be carried out in a one-pot synthesis to give the *p*-methoxybenzyl ether **39**, reduction of which gave the dihydroxyalkyldithiane **40**.

It would seem that the epoxy dithiane **10** can be used to prepare a range of *anti*-1,3-diols which should prove useful for asymmetric natural-product synthesis.

Synthesis of Milbemycin Spiroketals.—Two approaches were investigated for the introduction of the C(14)–C(15) trisubstituted double bond into milbemycin precursors.

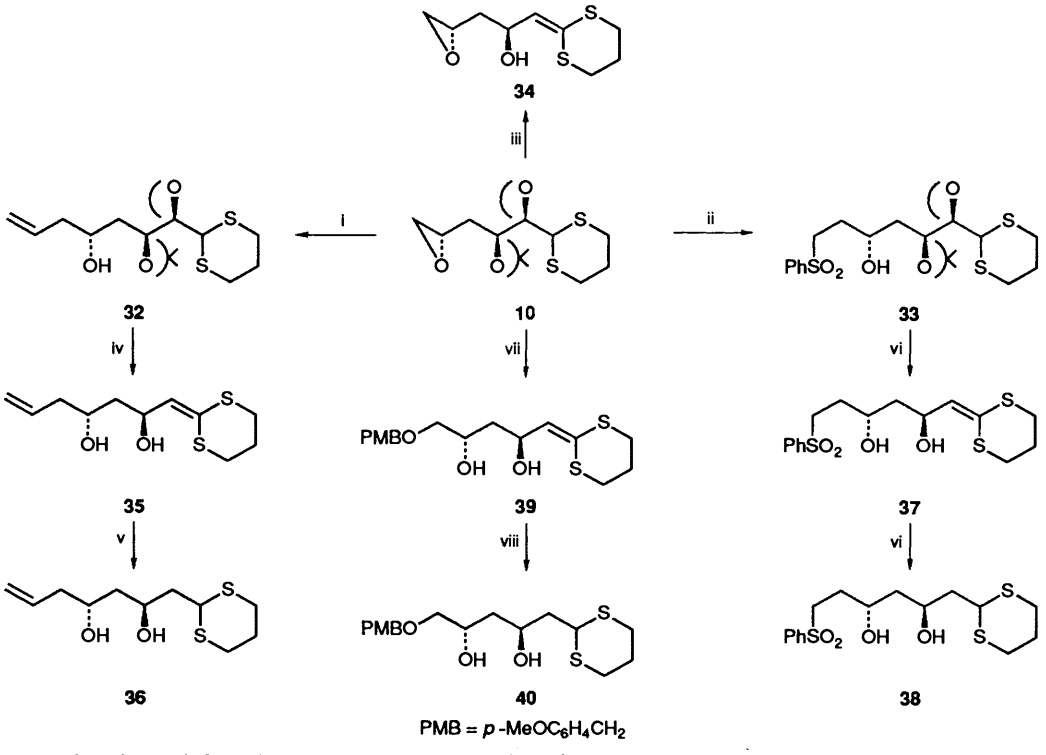
Protection of the dihydroxyalkyldithiane **38** as its acetonide **41**, followed by lithiation of the sulfone and addition to 4-methylpentan-2-one gave a good yield of the diastereoisomeric hydroxy sulfones **42** (Scheme 5). However, reductive elimination of this mixture using sodium amalgam in tetrahydrofuran (THF)–methanol[18] was non-stereoselective, giving a 55:45 mixture of the (*E*)- and (*Z*)-isomers of the alkene **43**, and so this approach was not continued.

Reactions of epoxides **10** and **34** with more complex vinyl organometallic reagents were then examined. The monoprotected diol **44** was prepared as reported in the literature from (*R*)-(+)-citronellal,[19] and was converted into the alkene **46** by oxidative elimination of the selenide **45** (Scheme 6).[20] Addition of bromine to the alkene gave the dibromide **47**, which was treated with potassium *tert*-butoxide[21] to give the alkyne **48** together with small smounts of the isomeric allene **49**. Conversion of the alkyne into the vinyl iodide **50** was carried out using Negishi's procedure in 45% yield.[22]

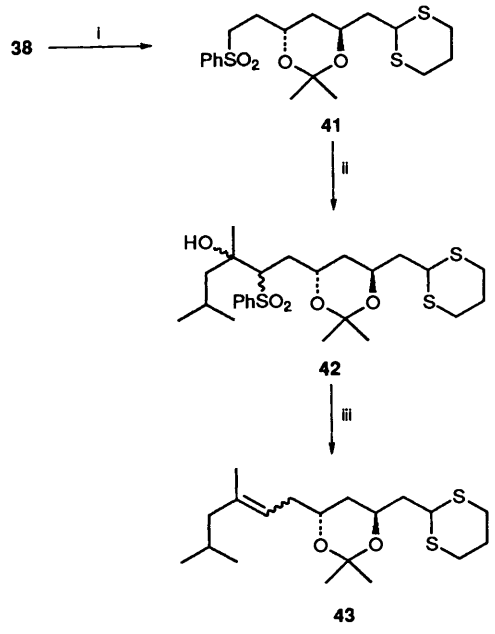
Addition of the organometallic reagent, prepared by addition of butyllithium to the vinyl iodide **50**, to the epoxide **10** was complicated by elimination of acetone. However, addition to the epoxy hydroxy ketene dithioketal **34** which had been deprotonated with one mole equivalent of butyllithium, gave a modest yield of the coupled product **51**. Reduction gave the 2-(dihydroxyalkyl)-1,3-dithiane **52**.

This sequence was repeated using the alkynol **55** prepared from Evans' chiral oxazolidinone **53**.[23] The alkynol[24,25] was protected and taken through to the vinyl iodide **57**, which was coupled with the lithiated epoxy hydroxy ketene dithioketal **34** to give the (dihydroxyalkyl)ketene dithioketal **59** (Scheme 7). However, the yields of product isolated from this reaction were somewhat capricious. If two mole equivalents of the vinyl organometallic reagent were used, a ~32% yield of the coupled product was obtained, but only lower yields, typically 15–18%, were isolated from reactions using one mole equivalent of the reagent. Protection of the hydroxy group of the epoxy hydroxy ketene dithioketal **34** as its [2-(trimethylsilyl)ethoxy]methyl (SEM)-ether **58** did not result in any significant improvement in the yield, and the use of alternative procedures and other metallic species derived from **56** or **57** were not promising in our hands. Although this coupling reaction was somewhat inefficient, in order to evaluate the overall synthetic strategy it was decided to investigate the incorporation of the ketene dithioketal **59** into a spiroketal synthesis.

Reduction of the ketene dithioketal **59** gave the 2-(dihydroxy-



Scheme 4 *Reagents and conditions:* i, CH_2=CHMgBr, THF, CuI (92%); ii, lithiomethyl phenyl sulfone, THF, Et_2O (72%); iii, BuLi, −78 °C, 30 min (87%); iv, BuLi, −78 to 20 °C, 4 h (54%); v, $LiAlH_4$, THF (65%); vi, BuLi, THF, −78 °C; then $LiAlH_4$, room temp. 22 h (78%); vii, sodium *p*-methoxybenzyloxide, DMF, room temp. 3 h (73%); viii, $LiAlH_4$, THF, room temp., 17 h (94%).



Scheme 5 *Reagents and conditions:* i, $CuSO_4$, PTSA, $Me_2C(OMe)_2$, room temp., 16 h (88%); ii, BuLi, −78 °C, 15 min; then 4-methylpentan-2-one (64%); iii, sodium amalgam, THF–MeOH (83%).

alkyl)-1,3-dithiane **60**. This was protected as its acetonide **61** and alkylated using 1-bromo-4-(tetrahydropyran-2-yloxy)-butane and *tert*-butyllithium to give the 2,2-dialkyl-1,3-dithiane **62**. Acid-catalysed deprotection gave the tetraol **63**, which was converted into the spiroketal **64** using mercury(II) chloride in THF.[26]

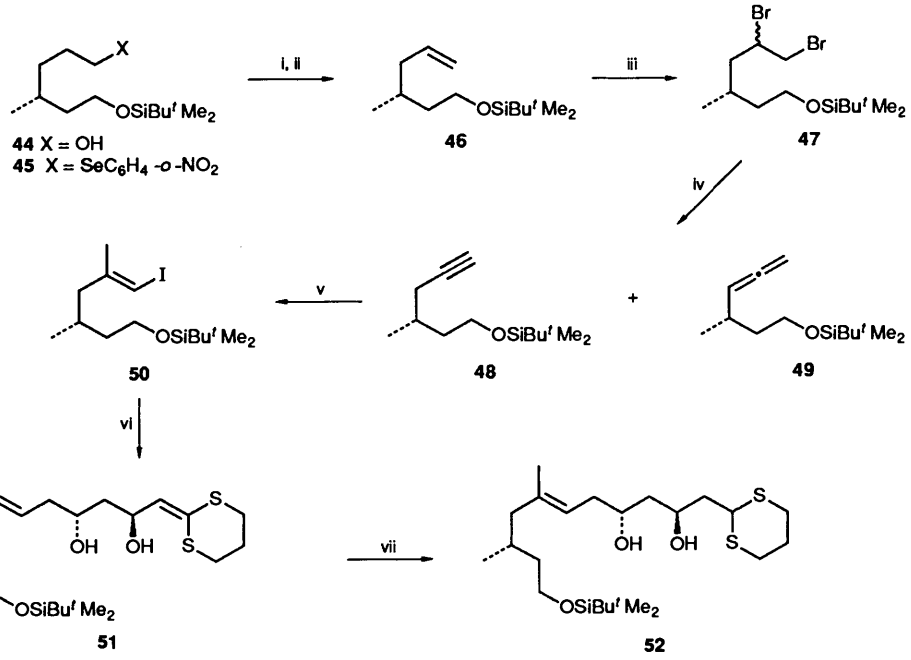
This spiroketal corresponds to the 'upper hemisphere' of a milbemycin lacking only the alkyl substituents at C(24) and C(25). However, its synthesis is limited by the difficulties associated with the coupling of the organometallic reagent prepared from vinyl iodide **57** with the epoxide **34**. Therefore it was decided to investigate procedures for the incorporation of the 2-(dihydroxyalkyl)-1,3-dithianes **36** and **40** into fully substituted spiroketals, leaving the introduction of the C(14)–C(15) double bond until later in the synthesis.

The 2-(dihydroxyalkyl)-1,3-dithiane **40** was protected as its acetonide **65** and alkylated using the silylated bromo alcohol **66**[27] to give the 2,2-dialkyl-1,3-dithiane **67** (Scheme 8). Deprotection under acidic conditions gave the triol **68**, which was cyclised to give the spiroketal **69** using mercury(II) chloride in THF. This spirocyclisation was accompanied by loss of the *p*-methoxybenzyl group from the primary hydroxy substituent.

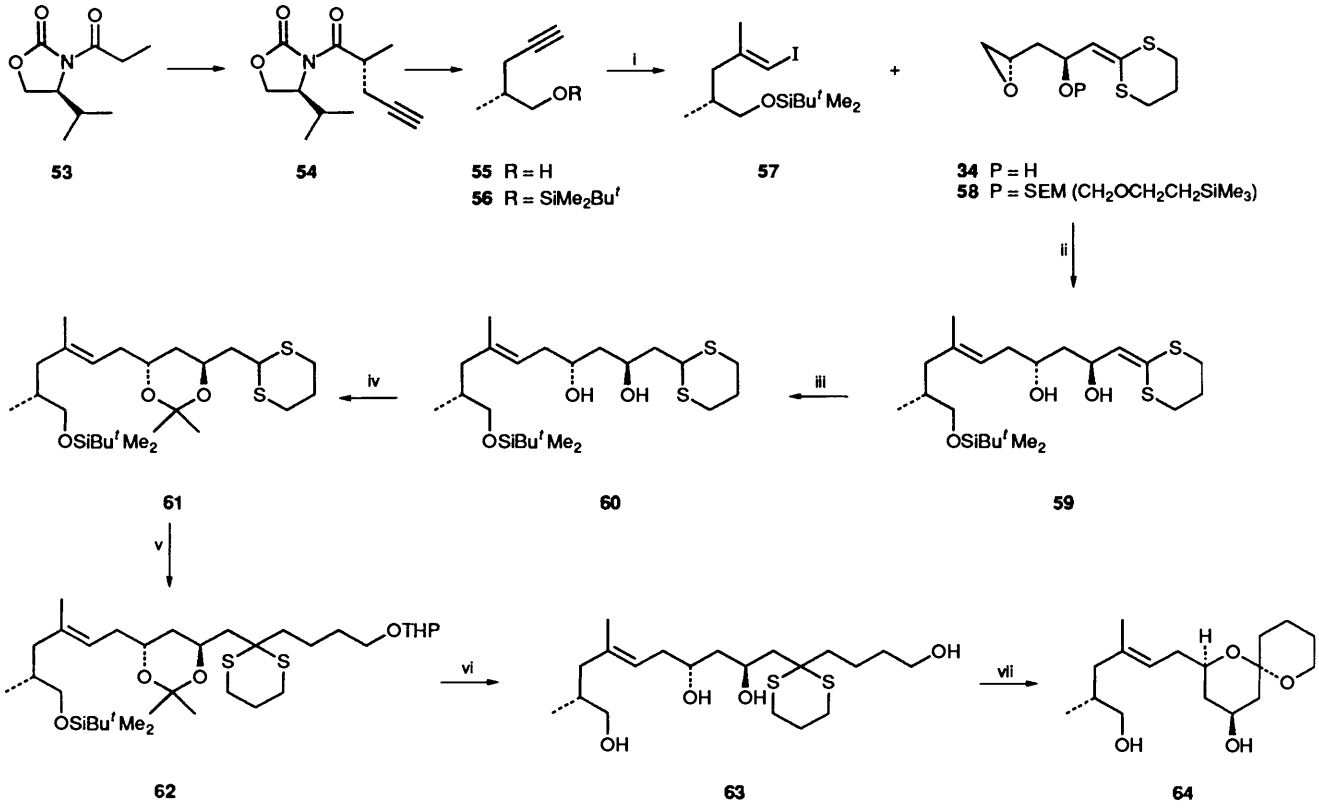
The 2-(dihydroxyalkyl)-1,3-dithiane **36** was similarly taken through to the spiroketal **74**. Protection of the diol gave the acetonide **70**, which was alkylated using the iodide **71**[27] to give the 2,2-dialkyl-1,3-dithiane **72** (Scheme 9). Acid-catalysed deprotection gave the triol **73**, which was cyclised to give the spiroketal **74**.

The structures of these spiroketals were assigned on the basis of their spectroscopic data. The spiroketal **74** was identical with a sample prepared by a different route[27] and incorporated into a synthesis of milbemycin E.[7]

Conclusions.—Spiroketals **69** and **74** possess all the functionality associated with the C(16)–C(25) fragment of milbemycin E **1**.[5] Although the displacement of derivatives of primary alcohols analogous to **69** is notoriously difficult, procedures are available for the conversion of the prop-2-enylspiroketal **74** into the 'upper hemisphere' of milbemycin E.[27,28] An alternative synthesis of spiroketal **74** and the incorporation of this spiroketal into a synthesis of milbemycin E[7] have been reported[27] and full details will be described in following papers. Of general interest in the present work is the conversion of the 6-chloro-4,6-dideoxyglucoside **7** into the 2-(epoxyalkyl)-1,3-dithiane **10** and the epoxy hydroxy ketene dithioketal **34**, and the conversion of these into the *anti*-1,3-diols **36**, **38** and **40**. These homochiral diols should be useful intermediates for asymmetric synthesis.



Scheme 6 *Reagents and conditions:* i, PBu_3, *o*-nitrophenyl selenocyanate (**45**, 94%); ii, aq. H_2O_2, THF, 3 h, room temp. (89%); iii, Br_2, CCl_4 (52%); iv, KOBu^t, 18-crown-6, hexane (**48**, 65%; **49**, 9%); v, Me_3Al, CH_2Cl_2, zirconocene dichloride; then I_2, THF (41%); vi, BuLi; then **34**-Li (27%); vii, $LiAlH_4$.

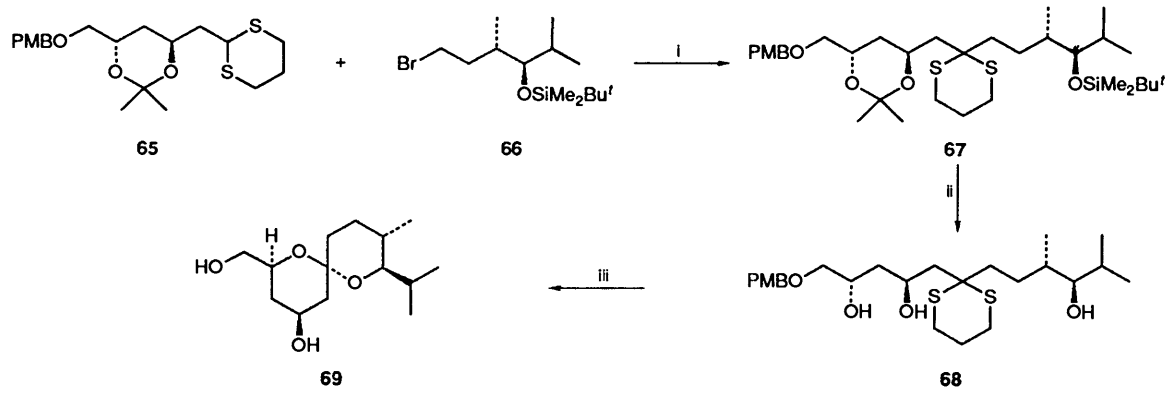


Scheme 7 *Reagents:* i, Me_3Al, zirconocene dichloride; then I_2, THF (69%); ii, BuLi; then **34**-Li (32%); iii, $LiAlH_4$ (73%); iv, $Me_2C(OMe)_2$, PTSA, $CuSO_4$, acetone (62%); v, Bu^{t}Li, Br[CH_2]$_4$OTHP (59%); vi, PTSA, MeOH, THF (86%); vii, $HgCl_2$, THF (73%).

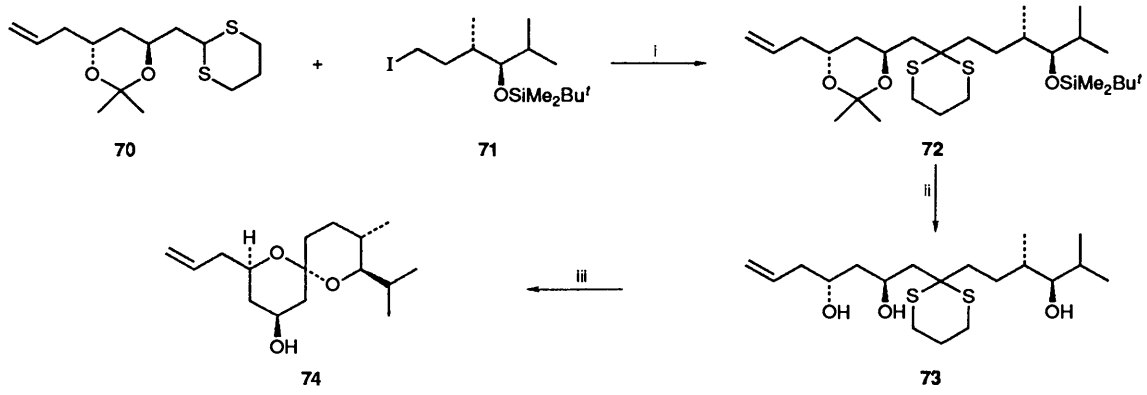
Experimental

For general experimental details see ref. 3. ^{1}H NMR spectra at 400 MHz were measured on a JEOL-JNM-GX400 spectrometer, and those at 270 MHz were measured on a JEOL-JNM-EX270 spectrometer. For mass spectroscopic data of chlorine-containing compounds only the peak corresponding to ^{35}Cl is given. Characteristic groups of peaks were obtained for compounds containing selenium; the peaks corresponding to ^{80}Se are given below. Optical rotations were measured on a Perkin-Elmer 241 polarimeter, and $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Ether refers to diethyl ether. Light petroleum was distilled over the range 40–60 °C.

Methyl 4,6-dichloro-4,6-dideoxy-α-D-galactoside **7** and the corresponding 4,6-diiodo compound were prepared as described in the literature.[11,14] The bis-acetate **28** of the dichloro sugar was prepared from the crude dichloro sugar **7** by using acetic anhydride in pyridine, and was obtained as crystals, m.p. 103–105 °C (from Et_2O) (lit.,[17] 104–106 °C); $[\alpha]_D$ + 207.9 (*c* 1.0,



Scheme 8 *Reagents:* i, Bu^{t}Li, HMPA, THF (33%); ii, aq. acetic acid, THF (66%); iii, $HgCl_2$, THF (70%).



Scheme 9 *Reagents:* i, Bu^{t}Li, HMPA, THF (74%); ii, hydrochloric acid, MeOH (85%); iii, $HgCl_2$, THF (70%).

$CHCl_3$). The (2*R*)-2-methylpent-4-yn-1-ol **55** was prepared by reduction of the oxazolidinone **54** by using lithium aluminium hydride and had $[\alpha]_D$ + 6.32 (*c* 1.1, $CHCl_3$).[24] Mosher's derivativisation confirmed that the enantiomeric excess (e.e.) was greater than 95%. Silyation under the usual conditions with *tert*-butyldimethylsilyl chloride gave the silyl ether **56**.[25]

4-tert-*Butyldimethylsiloxy*-1-(1,3-*dithian*-2-*yl*)*butan*-2-*ol* **20**.—Butyllithium (1.25 cm^3; 1.6 mol dm^{-3} in hexane) was added slowly to a solution of 1,3-dithiane (240 mg, 2 mmol) in THF (2 cm^3) at −40 °C. After 15 h at −30 °C, a solution of 4-*tert*-butyldimethylsiloxy-1,2-epoxybutane **19** (406 mg, 2 mmol) in THF (1 cm^3) was added over a period of 30 min, and the mixture was stirred for 2 h at 0 °C. Water (6 cm^3) was added and the mixture was acidified using hydrochloric acid (0.01 mol dm^{-3}) to pH 4/5 (pH paper) and extracted with ether (50 cm^3). The extract was washed successively with aq. sodium hydrogen carbonate (30 cm^3), aq. potassium hydroxide (30 cm^3; 5%) and brine (30 cm^3). After being dried ($MgSO_4$), the extract was concentrated under reduced pressure, and the residue was chromatographed (ethyl acetate–light petroleum, 1:4) to give the *title compound* **20** (358 mg, 55%) as an oil (Found: M^+, 322.1456. $C_{14}H_{30}O_2S_2Si$ requires *M*, 322.1456); ν_{max}($CHCl_3$)/cm^{-1} 3470, 1260, 1080, 870 and 840; δ_H(300 MHz) 0.04 (6 H, s, $SiMe_2$), 0.84 (9 H, s, $SiCMe_3$), 1.58–2.15 (6 H, m), 2.72–2.95 (4 H, m, SCH_2), 3.51 (1 H, br s, OH), 3.71–3.89 (2 H, m, OCH_2), 4.03–4.15 (1 H, m, C*H*OH) and 4.35 (1 H, dd, *J* 5 and 10, 2-H); *m*/*z* (EI) 322 (M^+, 2%).

4-[(1,3-*Dithian*-2-*yl*)*methyl*]-2,2-*dimethyl*-1,3-*dioxane* **22**.—Tetrabutylammonium fluoride (TBAF) (2 cm^3; 1 mol dm^{-3} in THF) was added to a solution of the silyl ether **20** (322 mg, 1 mmol) in THF at −5 °C. The mixture was stirred at 20 °C for 30 min, diluted with ether (30 cm^3), and washed with brine (30 cm^3) before being dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue (chloroform–methanol, 9:1) gave 4-(1,3-dithian-2-yl)butane-1,3-diol **21** (171 mg, 82%) an an oil; ν_{max}($CHCl_3$)/cm^{-1} 3620, 3400, 1280, 1250, 1060 and 910; δ_H(300 MHz) 1.63–2.20 (6 H, m), 2.75–3.0 (4 H, m, SCH_2), 3.07 and 3.43 (each 1 H, br s, OH), 3.83 (2 H, m, OCH_2), 4.08–4.20 (1 H, m, C*H*OH) and 4.23 (1 H, dd, *J* 5 and 10, 2-H); *m*/*z* (CI, NH_3) 208 (M^+, 10%), 190 (50) and 119 (100).

A mixture of the compound **21** (95 mg, 0.46 mmol), anhydrous copper sulfate (250 mg), conc. sulfuric acid (0.1 cm^3) and acetone (10 cm^3) was stirred at 20 °C for 18 h. The mixture was filtered and solid calcium hydroxide was added to the filtrate until neutral. The mixture was filtered again, and concentrated under reduced pressure. Chromatography of the residue (methanol–light petroleum, 1:9) gave the *title compound* **22** (102 mg, 90%) as a pale yellow oil (Found: M^+, 248.0905. $C_{11}H_{20}O_2S_2$ requires *M*, 248.0905); ν_{max}/cm^{-1} 1270, 1240, 1200, 1160, 1130, 1050, 970, 905, 870 and 820; δ_H(300 MHz) 1.35 and 1.36 (each 3 H, s, Me), 1.58 (2 H, m), 1.69–2.19 (4 H, m), 2.73–2.97 (4 H, m, SCH_2), 3.8 (1 H, ddd, *J* 12, 5 and 2, OCHC*H*), 3.97 (1 H, dt, *J* 12 and 3, OHC*H*), 4.11–4.27 (1 H, m, C*H*OH) and 4.16 (1 H, dd, *J* 5 and 10, 2-H); *m*/*z* (EI), 248 (M^+, 20%) and 190 (55).

2,2-*Dimethyl*-4-({2-[4-(*tetrahydropyran*-2-*yloxy*)*butyl*]-1,3-*dithian*-2-*yl*}*methyl*)-1,3-*dioxane* **23**.—Butyllithium (0.3 cm^3; 2.6 mol dm^{-3} in hexane) was added to a solution of the 2-alkyldithiane **22** (134 mg, 0.54 mmol) in THF (1 cm^3) at −20 °C and the mixture was stirred for 6 h before being cooled to −78 °C. A solution of 1-bromo-4-(tetrahydropyran-2-yloxy)-butane (200 mg, 0.85 mmol) in THF (1 cm^3) was added, and the mixture was stirred at −78 °C for 6 h and at room temperature overnight. Water (5 cm^3) was added, and the mixture was extracted with ether (3 × 20 cm^3). The extracts were dried ($MgSO_4$), and concentrated under reduced pressure, and the residue was chromatographed (ethanol–light

petroleum, 1 : 9) to give the *title compound* **23** (106 mg, 48%) as an oil (Found: M^+, 404.2054. $C_{20}H_{36}O_4S_2$ requires *M*, 404.2055); $\nu_{max}(CHCl_3)/cm^{-1}$ 1270, 1240, 1200, 1160, 1130, 1090, 1075 and 1030; δ_H(300 MHz) 1.35 and 1.48 (each 3 H, s, Me), 1.35–2.20 (18 H, m), 2.72–2.29 (4 H, m, SCH_2), 3.30–3.93 (6 H, overlapping m), 4.00 (1 H, dt, *J* 2.5 and 10, CHO) and 4.57 (1 H, t, *J* 2.5, OCHO); *m/z* (EI) 404 (M^+, 6%).

1,7-*Dioxaspiro*[5.5]*undecan*-4-*ol* **25**.—A solution of the protected triol **23** (90 mg, 0.22 mmol) and toluene-*p*-sulfonic acid (PTSA) (20 mg) in methanol (20 cm^3) was stirred at 20 °C for 16 h and was then concentrated under reduced pressure. The residue was taken up in dichloromethane (30 cm^3) and the solution was washed with water (10 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue gave 4-[2-(4-hydroxybutyl)-1,3-dithian-2-yl]butane-1,3-diol **24** (51 mg, 71%) as an oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 3620, 3420, 1280, 1240, 1170 and 910; δ_H(300 MHz; $CDCl_3$–D_2O) 1.35–2.20 (11 H, m), 2.4 (1 H, dd, *J* 10 and 15), 2.7–3.2 (4 H, m, SCH_2), 3.65 (2 H, t, *J* 5, CH_2OH), 3.73–3.9 (2 H, m, CH_2OH) and 4.14–4.30 (1 H, m, CHOH); *m/z* (CI, NH_3), 280 (M^+, 3%).

Mercury(II) chloride (180 mg) was added to a solution of the triol **24** (80 mg, 0.29 mmol) in THF (3 cm^3) at 20 °C. After 3 h, the mixture was diluted with dichloromethane (30 cm^3) and filtered, and the filtrate was washed successively with water (30 cm^3) and brine (2 × 30 cm^3). After being dried ($MgSO_4$), the organic phase was concentrated under reduced pressure, and the residue was chromatographed (methanol–chloroform, 1 : 9) to give the spiroketal **25**[13] (39 mg, 80%) as an oil.

Hydrogenolysis of Methyl 4,6-*Dichloro*-4,6-*dideoxy*-α-D-*galactoside* **7**.—Methyl 4,6-dichloro-4,6-dideoxy-α-D-galactoside **7**[11] (2.02 g, 10 mmol), 10% palladium on charcoal (600 mg), potassium hydroxide (0.9 g) and ethanol (90 cm^3) were shaken vigorously under hydrogen for 5 h. The mixture was filtered and hydrochloric acid (0.1 mol dm^{-3}) was added to the filtrate to neutrality. The filtrate was then concentrated under reduced pressure, and the residue was taken up in ethyl acetate. The organic solution was washed with water (10 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure to give methyl 6-chloro-4,6-dideoxy-α-D-*xylo*-hexopyranoside **8** (1.51 g, 64%) as crystals, recrystallised from ethyl acetate–light petroleum, m.p. 109 °C (lit.,[12] 110 °C).

In some cases the crude product was a yellow oil, which on chromatography (ethyl acetate) gave two fractions. The less polar was identified as the *bicyclic compound* **26** (~ 20%) as an oil (Found: M^+ − OMe, 163.0161. $C_6H_8ClO_3$ requires *m/z*, 163.0162); ν_{max}/cm^{-1} 3450, 1160, 1080, 965, 930, 900 and 882; δ_H*(300 MHz) 2.70 (1 H, br s, OH), 3.56 (3 H, s, OMe), 3.95 (1 H, dd, *J* 3 and 6), 4.13 (1 H, d, *J* 10, 6-H), 4.25 (1 H, dd, *J* 3 and 10, 6-H), 4.43 (1 H, narrow m), 4.50 (1 H, d, *J* 6), 4.72 (1 H, m) and 4.75 (1 H, d, *J* 3, 3-H); *m/z* (EI) 177 (M^+ − 17, 4%), 163 (M^+ − 31, 3) and 103 (100).

The more polar compound was identified as the required methyl 6-chloro-4,6-dideoxy-α-D-*xylo*-hexopyranoside **8** (~ 45%).

Methyl 4,6-*Dichloro*-4,6-*dideoxy*-2,3-*bis*-O-(*methoxymethyl*)-α-D-*galactoside* **27**.—A solution of methyl 4,6-dichloro-4,6-dideoxy-α-D-galactoside **7** (1.0 g, 4.32 mmol) and diisopropylethylamine (3 cm^3, 17.3 mmol) in dichloromethane (31 cm^3) was heated under reflux for 10 min. Chloromethyl methyl ether (1.65 cm^3, 21.65 mmol) was added dropwise, and the mixture was heated under reflux for 16 h. Water (20 cm^3) was added, and the organic layer was washed with water (2 × 10 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. The residual oil was chromatographed (ethyl acetate–light petroleum, 1 : 4) to give the *title compound* **27** (1.27 g, 92%) as an oil (Found: C, 41.6; H, 6.45. $C_{11}H_{20}Cl_2O_6$ requires C, 41.4; H, 6.30%); $[\alpha]_D$ + 42.4 (*c* 3.65, $CHCl_3$); ν_{max}/cm^{-1} 1210, 1150, 1110, 1030, 980 and 915; δ_H(300 MHz) 3.40, 3.45 and 3.50 (each 3 H, s, OMe), 3.66 (2 H, d, *J* 7, 6-H_2), 3.95 (1 H, dd, *J* 4 and 7, 2-H), 4.10–4.15 (2 H, m), 4.53 (1 H, d, *J* 5, 4-H), 4.70 and 4.76 (each 1 H, d, *J* 8, OHC*H*OMe), 4.83 (2 H, d, *J* 8, 2 × OHC*H*OMe) and 4.88 (1 H, d, *J* 4, 1-H); *m/z* (CI, NH_3) 336 (M^+ + NH_3, 100%).

Hydrogenolysis of Methyl 4,6-*Dichloro*-4,6-*dideoxy*-2,3-*bis*-O-(*methoxymethyl*)-α-D-*galactoside* **27**.—Following the procedure outlined above, the bis-protected galactoside **27** (0.92 g, 2.88 mmol) and potassium hydroxide (0.46 g, 8.2 mmol) in ethanol gave, after chromatography (ethyl acetate–light petroleum, 1 : 2), *methyl* 6-*chloro*-4,6-*dideoxy*-2,3-*bis*-O-(*methoxymethyl*)-α-D-xylo-*hexopyranoside* **29** (0.59 g, 72%) as an oil (Found: C, 46.3; H, 7.40%; M^+ − OMe, 253.0845. $C_{11}H_{21}ClO_6$ requires C, 46.4; H, 7.45%; *M* − OMe, 253.0843); ν_{max}/cm^{-1} 1150, 1115, 1040 and 915; δ_H(300 MHz) 1.48 and 2.12 (each 1 H, m, 4-H), 3.30, 3.34 and 3.38 (each 3 H, s, OMe), 3.48 (3 H, m, 2-H and 6-H_2), 3.86 (2 H, m, 3- and 5-H), 4.63, 4.66, 4.70 and 4.75 (each 1 H, d, *J* 7, OHC*H*OMe) and 4.80 (1 H, d, *J* 3, 1-H); *m/z* (EI) 253 (M^+ − 31, 37%) and 45 (100).

A solution of methyl 6-chloro-4,6-dideoxy-2,3-bis-*O*-(methoxymethyl)-α-D-*xylo*-hexopyranoside **29** (2.31 g, 8.12 mmol) and aq. hydrogen bromide (24%) in 1,2-dimethoxyethane (DME) (45 cm^3) was stirred at 55 °C for 1 h. Aq. sodium hydroxide was added until the solution was neutral, and the mixture was concentrated under reduced pressure. The residue was taken up in ethyl acetate (20 cm^3), and the solution was dried ($MgSO_4$), and concentrated under reduced pressure to leave an oil. Chromatography (ethyl acetate) gave methyl 6-chloro-4,6-dideoxy-α-D-*xylo*-hexopyranoside **8** (1.29 g, 80%).

Hydrogenolysis of Methyl 2,3-*Di*-O-*acetyl*-4,6-*dichloro*-4,6-*dideoxy*-α-D-*galactoside* **28**.—A mixture of the dichlorodiacetate **28** (15 g, 47 mmol), palladium on charcoal (13 g, 10%) and powdered potassium hydroxide (5.2 g, 130 mmol) in ethanol (150 cm^3) was agitated under hydrogen at 140 psi for 6 h. After filtration through silica, the filtrate was concentrated under reduced pressure to give methyl 6-chloro-4,6-dideoxy-α-D-*xylo*-hexopyranoside **8** (8.71 g, 93%) as a solid, m.p. 108 °C (lit.,[12] 110 °C).

(1R,2S,4S)-5-*Chloro*-1-(1′,3′-*dithian*-2′-*yl*)*pentane*-1,2,4-*triol* **30**.—Propane-1,3-dithiol (1.3 cm^3, 13 mmol) was added dropwise to a solution of the chlorodideoxyglucoside **8** (2.0 g, 10 mmol) in conc. hydrochloric acid (3.6 cm^3). After 22 h at room temperature, the mixture was diluted with water (180 cm^3). A solid separated out and was filtered off, and was washed with light petroleum (100 cm^3). The filtrate was neutralised with 880 ammonia and washed with light petroleum to remove residual thiol (5 × 50 cm^3). The filtrate and the precipitate were combined, and concentrated under reduced pressure to leave a solid. This was triturated with acetone (50 cm^3) for 20 min and filtered. The filtrate was concentrated under reduced pressure to give the *title compound* **30** (2.51 g, 93%) as a solid, which was used without further purification. Chromatography (chloroform–methanol, 9 : 1) gave an analytical sample (Found: C, 40.0; H, 6.4; Cl, 13.1; S, 23.2. $C_9H_{17}ClO_3S_2$ requires C, 39.7; H, 6.3; Cl, 12.9; S, 23.5%); $[\alpha]_D$ + 5.4 (*c* 0.5, $CHCl_3$); ν_{max}(Nujol)/cm^{-1} 3480, 3380, 1075 and 1030; δ_H(300 MHz) 1.60 (1 H, br s, OH), 1.70–2.33 (4 H, m, 3-H_2 and 5′-H_2), 2.50 (1 H, d, *J* 10, OH), 2.63–3.00 (4 H, m, 4′- and 6′-H_2), 3.10 (1 H, d, *J* 4, OH), 3.58 (1 H, dd, *J* 6.5 and 11.5, 5-H), 3.70 (1 H, dd, *J* 5 and 11,

* Locants refer to glucose numbering.

5-H), 3.78 (1 H, dd, *J* 2.5 and 8, 1-H), 4.02 (1 H, d, *J* 8, 2'-H) and 4.10–4.25 and 4.30–4.41 (each 1 H, m, 2- and 4-H); *m/z* (CI) 290 ($M + NH_4^+$, 20%) and 119 (100).

(2S,4S,5R)-1-*Chloro*-5-(1',3'-*dithian*-2'-*yl*)-4,5-*isopropylidenedioxy*)*pentan*-2-*ol* **31**.—The 2-(trihydroxyalkyl)dithiane **30** (2.51 g, 9.21 mmol), acetone (125 cm^3; Analar), anhydrous copper sulfate (4.47 g, 27.9 mmol) and PTSA (0.1 g) were stirred for 17 h at room temperature. The mixture was filtered off, and solid calcium hydroxide was added to the filtrate until it was neutral. The mixture was filtered again, and the filtrate was concentrated under reduced pressure to give an oil, which was chromatographed (ethyl acetate–light petroleum, 1 : 1) to give the *title compound* **31** (2.63 g, 91%) as an oil (Found: M^+, 312.0619. $C_{12}H_{21}ClO_3S_2$ requires *M*, 312.0621); $[\alpha]_D$ − 90.8 (*c* 0.5, $CHCl_3$); ν_{max}/cm^{-1} 3450, 1250, 1220, 1070, 915 and 735; δ_H(300 MHz) 1.43 and 1.47 (each 3 H, s, Me), 1.73–2.22 (4 H, m, 3- and 5'-H_2), 2.33 (1 H, br s, OH), 2.78–3.00 (4 H, m, 4'- and 6'-H_2), 3.55 (1 H, dd, *J* 5 and 10, 1-H), 3.68 (1 H, dd, *J* 5 and 11, 1-H), 3.95 (1 H, dd, *J* 5 and 7.5, 5-H), 4.10 (1 H, m, 2-H), 4.15 (1 H, d, *J* 5, 2'-H) and 4.35 (1 H, m, 4-H); *m/z* (EI) 312 (M^+, 8%) and 119 (100).

2-[(1'R,2'S,4'S)-4',5'-*Epoxy*-1',2'-(*isopropylidenedioxy*)-*pentyl*-1,3-*dithiane*{(4R,5S)-4-(1,3-*Dithian*-2-*yl*)-5-[(S)-2,3-*epoxypropyl*]-1,3-*dioxolane*} **10**.—Powdered sodium hydroxide (0.36 g, 9.0 mmol) was added to a solution of the chlorohydrin **31** (2.63 g, 8.4 mmol) in ethanol (45 cm^3) and the mixture was stirred for 30 min at room temperature. Concentration under reduced pressure gave a residue, which was taken up in chloroform (50 cm^3), and the chloroform solution was washed with water (50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue (ethyl acetate–light petroleum, 1 : 2) gave the *title compound* **10** (1.71 g, 74%) as an oil (Found: M^+, 276.0856. $C_{12}H_{20}O_3S_2$ requires *M*, 276.0854); $[\alpha]_D$ − 47.15 (*c* 0.95, $CHCl_3$); ν_{max}/cm^{-1} 1420, 1380, 1370, 1240 and 1160; δ_H(300 MHz) 1.42 and 1.47 (each 3 H, s, Me), 1.78–2.18 (4 H, m, 5-H_2 and 3'-H_2), 2.53 (1 H, dd, *J* 2.5 and 5, 5'-H), 2.78–3.0 (5 H, m, 4- and 6-H_2 and 5'-H), 3.12 (1 H, m, 4'-H), 3.92 (1 H, dd, *J* 5 and 7.5, 1'-H), 4.16 (1 H, d, *J* 7.5, 2-H) and 4.30 (1 H, dt, *J* 5 and 7.5, 2'-H); *m/z* (EI) 276 (M^+, 11%) and 119 (100).

(4R,6S,7R)-7-(1',3'-*Dithian*-2'-*yl*)-6,7-(*isopropylidenedioxy*)-*hept*-1-*en*-4-*ol* **32**.—A solution of vinylmagnesium bromide in THF (3.0 mmol) was added dropwise over a period of 10 min to a solution of the epoxide **10** (0.28 g, 1.0 mmol) and copper(I) iodide (21 mg, 0.1 mmol) in THF at −10 to −15 °C. After 6 h, water (10 cm^3) and ether (10 cm^3) were added, the layers were separated, and the aqueous layer was extracted with more ether (2 × 30 cm^3). The combined extracts were dried ($MgSO_4$), and concentrated under reduced pressure. The residual oil was chromatographed (ethyl acetate–light petroleum, 1 : 3) to give the *title compound* **32** (0.28 g, 92%) as a solid, which was recrystallised from ether–pentane, m.p. 54–56 °C (Found: C, 55.4; H, 8.2. $C_{14}H_{24}O_3S_2$ requires C, 55.2; H, 7.95%); ν_{max}/cm^{-1} 3450, 1380, 1370, 1245, 1060 and 910; δ_H(300 MHz) 1.43 and 1.47 (each 3 H, s, Me), 1.72–2.36 (6 H, m, 3-, 5- and 5'-H_2), 2.18 (1 H, s, OH), 2.77–3.00 (4 H, m, 4'- and 6'-H_2), 3.92–3.96 (2 H, m, 4- and 7-H), 4.15 (1 H, d, *J* 5, 2'-H), 4.37 (1 H, dt, *J* 2.5 and 7.5, 6-H), 5.12–5.20 (2 H, m, 1-H_2) and 5.76–5.93 (1 H, m, 2-H); *m/z* (EI) 304 (M^+, 25%) and 119 (100).

(3S,5S,6R)-6-(1',3'-*Dithian*-2'-*yl*)-5,6-*isopropylidenedioxy*-1-(*phenylsulfonyl*)*hexan*-3-*ol* **33**.—Butyllithium (10.3 mmol; in hexane) was added to a solution of methyl phenyl sulfone (1.67 g, 10.27 mmol) in THF–ether (40 cm^3; 1 : 1) at −78 °C. After 20 min, the suspension was transferred *via* a cannula into a solution of the epoxide **10** (1.42 g, 5.12 mmol) in THF–ether (50 cm^3; 1 : 1) at −78 °C. The mixture was stirred for 45 min at −78 °C, and was allowed to warm to room temperature. Water (40 cm^3) and ether (40 cm^3) were added, and the aqueous layer was extracted with more ether (2 × 20 cm^3). The combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (ethyl acetate–light petroleum, 1 : 1) of the residue gave the *title compound* **33** (1.53 g, 72%) as a solid, which was recrystallised as needles from ether–pentane, m.p. 106–107 °C (Found: $M^+ - C_3H_6O$, 374.0681. $C_{16}H_{22}O_4S_3$ requires *m/z*, 374.0680); $[\alpha]_D$ − 18.1 (*c* 0.49, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 3530, 1310, 1155, 1087 and 730; δ_H(300 MHz) 1.38 and 1.40 (each 3 H, s, Me), 1.67–2.17 (6 H, m, 2-, 4- and 5'-H_2), 2.70 (1 H, br s, OH), 2.78–2.93 (4 H, m, 4'- and 6'-H_2), 3.16–3.26 and 3.30–3.42 (each 1 H, m, 1-H), 3.87–3.97 (2 H, m, 3- and 6-H), 4.12 (1 H, d, *J* 5, 2'-H), 4.27 (1 H, dt, *J* 3, 7, 5-H) and 7.53–7.90 (5 H, m, ArH); *m/z* (EI) 374 (M^+ − 58, 9%) and 225 (100).

(2S,4S)-1-(1',3'-*Dithian*-2'-*ylidene*)-4,5-*epoxypentan*-2-*ol* **34**.—Butyllithium (7.4 mmol; in hexane) was added to a solution of the epoxide **10** (1.02 g, 3.71 mmol) in THF (5 cm^3) at −78 °C. After 30 min, water (10 cm^3) and ether (50 cm^3) were added, and the mixture was warmed to room temperature. The aqueous layer was extracted with ether (2 × 5 cm^3), and the organic phases were combined, dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (ethyl acetate–light petroleum, 1 : 1) of the residue gave the *title compound* **34** (0.71 g, 87%) as an oil (Found: C, 49.6; H, 6.7%; M^+, 218.0434. $C_9H_{14}O_2S_2$ requires C, 49.5; H, 6.5%; *M*, 218.0435); $[\alpha]_D$ − 50.9 (*c* 1.06, $CHCl_3$); ν_{max}/cm^{-1} 3600, 3450, 1580, 1425 and 1040; δ_H(300 MHz) 1.60–1.70 and 1.83–1.91 (each 1 H, m, 5'-H), 2.11–2.20 (2 H, m, 3-H_2), 2.38 (1 H, br s, OH), 2.60 (1 H, dd, *J* 3 and 5, 5-H), 2.81 (1 H, dd, *J* 5 and 7, 5-H), 2.85–3.00 (4 H, m, 4'- and 6'-H_2) 3.08–3.15 (1 H, m, 4-H), 4.83 (1 H, m, 2-H) and 5.93 (1 H, d, *J* 7, 1-H); *m/z* (EI) 218 (M^+, 8%) and 161 (100).

(2S,4R)-1-(1',3'-*Dithian*-2'-*ylidene*)*hept*-6-*ene*-2,4-*diol* **35**.—Butyllithium (0.8 cm^3; 1.4 mol dm^{-3} in hexane) was added to a solution of the acetonide **32** (100 mg, 0.33 mmol) in THF (3 cm^3) at −78 °C, and the mixture was allowed to warm slowly to room temperature. After 4 h, water (5 cm^3) and ether were added, and the ethereal layer was dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (chloroform–methanol, 9 : 1) of the residue gave the *title compound* **35** (43 mg, 54%) as an oil (Found: M^+, 246.0748. $C_{11}H_{18}O_2S_2$ requires *M*, 246.0748); $[\alpha]_D$ − 40.72 (*c* 0.55, $CHCl_3$); ν_{max}/cm^{-1} 3610, 3530, 3080, 1645, 1280, 1130, 1070, 1020, 990 and 915; δ_H(300 MHz) 1.53–1.84 (2 H, m, 3-H_2), 2.06–2.38 (4 H, m, 5- and 5'-H_2), 2.58 (2 H, br s, OH), 2.76–3.05 (4 H, m, 4'- and 6'-H_2), 3.86–4.05 (1 H, m, 4-H), 4.97 (1 H, dt, *J* 8.5 and 5, 2-H), 5.06–5.17 (2 H, m, 7-H_2), 5.76–5.92 (1 H, m, 6-H) and 6.02 (1 H, d, *J* 8.5, 1-H); *m/z* (EI) 246 (M^+, 20%).

(2S,4R)-1-(1',3'-*Dithian*-2'-*yl*)*hept*-6-*ene*-2,4-*diol* **36**.—The heptenylidenedithiane **35** (100 mg, 0.4 mmol) in THF (1.5 cm^3) was added to lithium aluminium hydride (30 mg) and THF (4 cm^3) and the mixture was stirred for 16 h at 20 °C. Water (10 cm^3) was added and the mixture was extracted with ether. The extracts were dried ($MgSO_4$), and concentrated under reduced pressure to leave a residue, which on chromatography (chloroform–methanol, 9 : 1) gave the *title compound* **36** (57 mg, 56%) as an oil (Found: M^+, 248.0907. $C_{11}H_{20}O_2S_2$ requires *M*, 248.0905); ν_{max}/cm^{-1} 3480, 3010, 1640, 1280, 1240, 1070, 1000 and 920; δ_H(300 MHz) 1.55–2.4 (8 H, m), 2.73–3.05 (4 H, m, 4'- and 6'-H_2), 3.0 and 3.5 (each 1 H, br s, OH), 3.9–4.5 (3 H, overlapping m, 2-, 2'- and 4-H), 5.17–5.27 (2 H, m, 7-H_2) and 5.68–5.93 (1 H, m, 6-H); *m/z* (EI) 248 (M^+, 3%).

(2S,4S)-1-(1',3'-*Dithian*-2'-*yl*)-6-*phenylsulfonylhexane*-2,4-*diol* **38**.—Butyllithium (24 mmol; in hexane) was added to a solution of the (phenylsulfonylhexyl)-1,3-dithiane **33** (2.58 g, 6.0 mmol) in THF (45 cm^3) at −78 °C. After 1 h, the mixture was transferred *via* cannula into a suspension of lithium aluminium hydride (0.49 g, 12.89 mmol) in THF (3 cm^3), and the mixture was warmed to room temperature and stirred for 22 h. Aq. sodium hydroxide (3 cm^3; 5 mol dm^{-3}) was added, followed by ether (30 cm^3), and the mixture was filtered. The filtrate was dried ($MgSO_4$), and concentrated under reduced pressure. The residue was triturated with light petroleum (5 cm^3) and ethyl acetate (5 cm^3) to give the *title compound* **38** (1.76 g, 78%) as a solid, which was used without further purification. Recrystallisation from ether–light petroleum gave needles, m.p. 103–104 °C (Found: C, 50.8; H. 6.4. $C_{16}H_{24}O_4S_3$ requires C, 51.0; H, 6.4%); $[\alpha]_D$ + 14.3 (*c* 0.87, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 3360, 1305, 1100 and 1085; δ_H(300 MHz) 1.63 (2 H, t, *J* 5, 1-H_2), 1.78–2.35 (6 H, m), 2.67 (1 H, d, *J* 5, OH), 1.83–2.93 (4 H, m, 4'- and 6'-H_2), 3.16–3.27 and 3.31–3.42 (each 1 H, m, 6-H), 4.00–4.06 and 4.27 (each 1 H, m, C*H*OH), 4.22 (1 H, dd, *J* 6 and 9, 2'-H) and 7.55–7.92 (5 H, m, ArH); *m/z* (CI, NH_3) 394 (M + NH_4^+, 51%) and 377 (MH^+, 77%).

(2S,4S)-1-(1',3'-*Dithian*-2'-*ylidene*)-5-(p-*methoxybenzyloxy*)-*pentane*-2,4-*diol* **39**.—A solution containing the sodium salt of *p*-methoxybenzyl alcohol (2.16 mmol) in DMF (4 cm^3) (prepared as a stock solution by addition of *p*-methoxybenzyl alcohol to a stirred suspension of sodium hydride in DMF) was added at 0 °C to a solution of the epoxide **10** (200 mg, 0.72 mmol) in DMF (1 cm^3). After warming to room temperature, the mixture was stirred for 3 h. Ether (30 cm^3) and saturated aq. ammonium chloride (10 cm^3) were added, and the aqueous phase was extracted with ether (4 × 10 cm^3). The combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (ethyl acetate–light petroleum, gradient elution) of the residue gave the *title compound* **39** (188 mg, 73%) as crystals, which was recrystallised from ether, m.p. 99–100 °C (Found: C, 57.5; H, 6.6. $C_{17}H_{24}O_4S_2$ requires C, 57.3; H, 6.8%); $[\alpha]_D$ + 3.1 (*c* 1.01, $CHCl_3$); ν_{max}/cm^{-1} 3600, 3480, 3020, 1620, 1590, 1520, 1255, 1220, 1090, 1040 and 955; δ_H(270 MHz) 1.66 (2 H, m, 3-H_2), 2.14 (2 H, m, 5'-H_2), 2.76–3.06 (6 H, m, 4'- and 6'-H_2, and 2 × OH), 3.42 (2 H, m, 5-H_2), 3.80 (3 H, s, OMe), 4.08 (1 H, m, 4-H), 4.46 (2 H, s, ArCH_2), 4.9 (1 H, m, 2-H), 5.97 (1 H, d, *J* 9, 1-H) and 6.85 and 7.24 (each 2 H, d, *J* 10, ArH); *m/z* (EI) 235 ($M^+ - C_8H_9O$, 6%) and 121 (100).

(2S,4S)-1-(1',3'-*Dithian*-2'-*yl*)-5-(p-*methoxybenzyloxy*)*pentane*-2,4-*diol* **40**.—A solution of the pentylidene-1,3-dithiane **39** (1.11 g, 3.41 mmol) in THF (40 cm^3) was added to a suspension of lithium aluminium hydride (340 mg, 0.89 mmol) in THF (5 cm^3) at 0 °C. The mixture was allowed to warm to room temperature and was stirred for 17 h. Saturated aq. sodium potassium tartrate (10 cm^3), water (20 cm^3) and ether (60 cm^3) were added, and the layers were separated. The aqueous phase was extracted with ether (4 × 30 cm^3), and the combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure to leave the title compound **40** (1.04 g, 94%) as a solid, which was used without further purification. A sample was chromatographed (ethyl acetate–light petroleum) and was crystallised as needles from ether, m.p. 62–63 °C; ν_{max}/cm^{-1} 3420, 1610, 1585, 1510, 1235, 1080, 1030 and 730; δ_H(270 MHz) 1.60 (2 H, m, 3-H_2), 1.80–2.16 (4 H, m, 1- and 5'-H_2), 2.84 (4 H, m, 4'- and 6'-H_2), 3.00 and 3.21 (each 1 H, br s, OH), 3.43 (2 H, m, 5-H_2), 3.80 (3 H, s, OMe), 4.10 (1 H, m, C*H*OH), 4.24 (2 H, overlapping m, C*H*OH and 2'-H), 4.48 (2 H, s, ArCH_2) and 6.88 and 7.24 (each 2 H, d, *J* 9, ArH); *m/z* (CI, NH_3) 359 (MH^+, 9%) and 121 (100).

(4S,6S)-4-(1',3'-*Dithian*-2'-*ylmethyl*)-2,2-*dimethyl*-6-[2-(*phenylsulfonyl*)*ethyl*]-1,3-*dioxane* **41**.—A mixture of the 2-dihydroxyhexyl-1,3-dithiane **38** (0.45 g, 1.2 mmol), acetone (16 cm^3; Analar), 2,2-dimethoxypropane (0.6 cm^3), anhydrous copper sulfate (1.43 g) and PTSA (16 mg) was stirred at room temperature for 16 h. The mixture was filtered, and solid calcium hydroxide was added to the filtrate until it was neutral. After further filtration, the filtrate was concentrated under reduced pressure, and the residue was chromatographed (ether–light petroleum, 1 : 1) to give the *title compound* **41** (0.44 g, 88%) as a solid, which was recrystallised from ether–light petroleum, m.p. 98–99 °C (Found: C, 54.5; H, 6.9%; M^+, 416.1149. $C_{19}H_{28}O_4S_3$ requires C, 54.8; H, 6.8%; *M*, 416.1150); $[\alpha]_D$ − 15.4 (*c* 1.2, $CHCl_3$); $\nu_{max}(CDCl_3)/cm^{-1}$ 1310, 1225, 1150 and 985; δ_H(300 MHz) 1.25 and 1.28 (each 3 H, s, Me), 1.57 (2 H, t, *J* 9, 4-CH_2), 1.75–2.15 (6 H, m, 5- and 5'-H_2, and 6-CH_2), 2.77–2.88 (4 H, m, 4'- and 6'-H_2), 3.02–3.12 and 3.23–3.35 (each 1 H, m, $PhSO_2CH$), 3.75–3.87 and 3.98–4.10 (each 1 H, m, CHO), 4.12 (1 H, dd, *J* 7 and 9, 2'-H) and 7.53–7.90 (5 H, m, ArH); *m/z* (EI) 416 (M^+, 7%) and 119 (100).

(4R,6S)-4-(3'',5''-*Dimethylhex*-2''-*enyl*)-6-(1',3'-*dithian*-2'-*yl*)-2,2-*dimethyl*-1,3-*dioxane* **43**.—Butyllithium (0.5 mmol) was added to a solution of the 2-(phenylsulfonylhexyl)-1,3-dithiane **41** (0.21 g, 0.5 mmol) in THF (3 cm^3) at −78 °C. After 15 min, a solution of 4-methylpentan-2-one (0.11 g, 1.09 mmol) in THF (1 cm^3) was added, and the mixture was stirred for 45 min. Methanol (1 cm^3) was added, and the mixture was allowed to warm to room temperature before ether (20 cm^3) and water (5 cm^3) were added. The aqueous layer was extracted with ether (3 × 5 cm^3), and the combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue (ether–light petroleum, 1 : 2) gave (7S,9S)-10-(1',3'-*dithian*-2'-*yl*)-7,9-*isopropylidenedioxy*-2,4-*dimethyl*-5-(*phenylsulfonyl*)*decan*-4-*ol* **42** (0.16 g, 64%) as a mixture of diastereoisomers (Found: M^+, 516.0688. $C_{25}H_{40}O_5S_3$ requires *M*, 516.0688); ν_{max}/cm^{-1} 3500, 1290, 1220, 1150, 1130 and 890; *m/z* (EI) 516 (M^+, 1%), 459 (M^+ − 57, 100) and 119 (100).

A solution of the hydroxy-sulfone **42** (99 mg, 0.18 mmol) in THF–methanol (3 cm^3; 2 : 1) was added to a suspension of sodium–mercury amalgam (0.75 g; 5%) in THF (1 cm^3) at 0 °C, and the mixture was stirred for 45 h. The organic solution was decanted off, diluted with ether (10 cm^3), washed with water (5 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (ether–light petroleum, 1 : 20) gave the *title compound* **43** (53 mg, 83%) as an oil (Found: $M^+ - CH_3$, 343.1765. $C_{18}H_{31}O_2S_2$ requires *m/z*, 343.1765); ν_{max}/cm^{-1} 1380, 1220 and 650; δ_H(300 MHz) 0.83–0.88 (6 H, overlapping d, together $HCMe_2$), 1.33 and 1.36 (each 3 H, s, together CMe_2), 1.57 and 1.66 (each 1.5 H, s, 3''-Me), 1.60–2.33 (11 H, m), 2.78–2.90 (4 H, m, 4'- and 6'-H_2), 3.73–3.83 and 4.06–4.14 (each 1 H, m, CHO), 4.16 (1 H, dd, *J* 5 and 10, 2'-H) and 5.08 and 5.16 (each 0.5 H, t, *J* 7, 2''-H); *m/z* (EI) 343 (M^+ − 15, 2%) and 301 (20); (CI, NH_3) 359 (M^+ + 1, 12%).

(3R)-1-(tert-*Butyldimethylsiloxy*)-3-*methyl*-6-(o-*nitrophenylseleno*)*hexane* **45**.—Tributylphosphine (4.6 cm^3, 18.47 mmol) was added dropwise to a mixture of the alcohol **44**[19] (4.0 g, 16.26 mmol) and *o*-nitrophenyl selenocyanate (4.17 g, 18.38 mmol) in THF (45 cm^3). After 4 h, the mixture was concentrated under reduced pressure and the residue was chromatographed (ether–light petroleum, 1 : 3) to give the *title compound* **45** (6.57 g, 94%) as a dark yellow oil (Found: $M^+ - C_4H_9$, 374.0692. $C_{15}H_{24}NO_3SeSi$ requires *m/z*, 374.0691); ν_{max}/cm^{-1} 1575, 1330, 1305, 1250, 1090 and 835; δ_H(300 MHz) 0.06 (6 H, s, $SiCMe_2$), 0.87 (9 H, s, $SiCMe_3$), 0.90 (3 H, d, *J* 7, 3-Me), 1.27–1.87 (7 H, m), 2.88 (2 H, t, *J* 9, 6-H_2), 3.60–3.68 (2 H, m, 1-H_2) and 7.27–8.28

(4 H, m, ArH); *m/z* (EI) 374 ($M^+ - 57$, 78%) and 75 (100); (CI, NH_3) 432 ($M^+ + 1$, 100%).

(4R)-6-(tert-*Butyldimethylsiloxy*)-4-*methylhex*-1-*ene* **46**.—Aq. hydrogen peroxide (22 cm^3; 30%) was added to a solution of the selenide **45** (6.52 g, 15.16 mmol) in THF (30 cm^3) at 0 °C and the mixture was stirred for 15 min at this temperature and for 3 h at room temperature. Light petroleum (100 cm^3) and water (100 cm^3) were added, and the organic extract was washed with brine (100 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (light petroleum) of the residue on base-washed silica gave the *title compound* **46** (3.08 g, 89%) as an oil (Found: C, 68.7; H, 12.6. $C_{13}H_{28}OSi$ requires C, 68.4; H, 12.4%); ν_{max}/cm^{-1} 3080, 1255, 1090, 910, 835 and 725; δ_H(300 MHz) 0.06 (6 H, s, $SiMe_2$), 0.88 (12 H, overlapping s and d, $SiCMe_3$ and 4-Me), 1.25–1.40 (1 H, m), 1.53–1.70 (2 H, m), 1.85–1.95 and 2.05–2.15 (each 1 H, m, 3-H), 3.57–3.70 (2 H, m, 6-H_2), 4.93–5.05 (2 H, m, 1-H_2) and 5.70–5.83 (1 H, m, 2-H); *m/z* (EI) 213 ($M^+ - 15$, 4%), 171 ($M^+ - 57$, 76%) and 141 (100).

(4R)-6-(tert-*Butyldimethylsiloxy*)-4-*methylhex*-1-*yne* **48**.—A solution of bromine in tetrachloromethane (9 cm^3; 1 mol dm^{-3}) was added to a solution of the alkene **46** (1.43 g, 6.23 mmol) in tetrachloromethane (28 cm^3). After 30 min, the mixture was concentrated under reduced pressure. Chromatography (ether–light petroleum, 1:50) gave (4S)-1,2-*dibromo*-6-(tert-*butyldimethylsiloxy*)-4-*methylhexane* **47** (1.27 g, 52%) as an oil (Found: C, 40.0; H, 7.4. $C_{13}H_{28}Br_2OSi$ requires C, 40.2; H, 7.3%); ν_{max}/cm^{-1} 1255, 1100, 840 and 780; δ_H(300 MHz) 0.06 (6 H, s, $SiMe_2$), 0.88 (9 H, s, $SiCMe_3$), 0.9 and 1.00 (each 1.5 H, d, *J* 9, together 4-Me), 1.28–2.17 (5 H, m), 3.58–3.72 (3 H, m), 3.80–3.91 (1 H, m, 1-H) and 4.17–4.29 (1 H, m, 2-H); *m/z* (EI) 331 ($M^+ - 57$, 1%) and 95 (100).

A solution of the dibromide **47** (1.27 g, 3.27 mmol) in hexane (9 cm^3) was added to potassium *tert*-butoxide (1.81 g, 16.16 mmol) and 18-crown-6 (13 mg) and the suspension was heated under reflux for 20 h. Water (10 cm^3) and hexane (30 cm^3) were added, and the aqueous layer was extracted with more hexane (2 × 10 cm^3). The combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (light petroleum) of the residue gave two fractions. The less polar fraction was identified as (4S)-6-(tert-*butyldimethylsiloxy*)-4-*methylhexa*-1,2-*diene* **49** (70 mg, 9%) as an oil (Found: $M^+ - C_4H_9$, 169.1047. $C_9H_{17}OSi$ requires *m/z*, 169.1049); ν_{max}/cm^{-1} 1952, 1460, 1260, 1100, 840 and 778; δ_H(300 MHz) 0.06 (6 H, s, $SiMe_2$), 0.87 (9 H, s, $SiCMe_3$), 1.04 (3 H, d, *J* 7, 4-Me), 1.50–1.61 (3 H, m), 3.65 (2 H, t, *J* 6, 6-H_2), 4.65–4.75 (2 H, m, 1-H_2) and 5.06 (1 H, q, *J* 7, 3-H); *m/z* (CI, NH_3) 227 ($M^+ + 1$, 100%).

The more polar fraction was identified as the *title compound* **48** (0.48 g, 65%) as an oil (Found: C, 68.9; H, 11.70. $C_{13}H_{26}OSi$ requires C, 69.0; H, 11.55%); $[\alpha]_D$ + 42.9 (*c* 0.63, $CHCl_3$); ν_{max}/cm^{-1} 3310, 2120, 1460, 1255, 1085 and 840; δ_H(300 MHz) 0.07 (6 H, s, $SiMe_2$), 0.88 (9 H, s, $SiCMe_3$), 1.03 (3 H, d, *J* 7, 4-Me), 1.38–1.50 and 1.60–1.72 (each 1 H, m, 5-H), 1.76–1.88 (1 H, m, 4-H), 1.96 (1 H, t, *J* 3, 1-H), 2.12 and 2.23 (each 1 H, m, 3-H) and 3.65 (2 H, t, *J* 7, 6-H_2); *m/z* (CI, NH_3) 227 (MH^+, 100%).

(4R,1E)-6-(tert-*Butyldimethylsiloxy*)-1-*iodo*-2,4-*dimethylhex*-1-*ene* **50**.—A solution of trimethylaluminium in degassed dichloromethane (2 cm^3; 1 mol dm^{-3}) was transferred *via* a cannula onto zirconocene dichloride (0.29 g, 1.0 mmol) and the mixture was stirred until a yellow solution was obtained. A solution of the alkyne **48** (0.23 g, 1.0 mmol) in degassed dichloromethane (0.5 cm^3) was added using a cannula, and the mixture was stirred at room temperature for 24 h. After cooling of the mixture to 0 °C, a solution of iodine (0.33 g, 1.20 mmol) in THF (1.5 cm^3) was added, and the mixture was stirred for 15 min at 0 °C. The excess of trimethylaluminium was destroyed by the careful addition of saturated aq. ammonium chloride, and the mixture was filtered. The filtrate was dried ($MgSO_4$), and concentrated under reduced pressure. Light petroleum was added to the residue, and the mixture was shaken for 30 min before being filtered, and the filtrate was concentrated under reduced pressure. Chromatography of the residue (light petroleum) gave two fractions. The less polar fraction was identified as the *title compound* **50** (150 mg, 41%) as an oil (Found: $M^+ - C_4H_9$, 311.0328. $C_{10}H_{20}IOSi$ requires *m/z*, 311.0329); $[\alpha]_D$ + 2.7 (*c* 1.06, $CHCl_3$); ν_{max}/cm^{-1} 1255, 1100, 840 and 780; δ_H(300 MHz) 0.08 (6 H, s, $SiMe_2$), 0.83 (3 H, d, *J* 10, 4-Me), 0.90 (9 H, s, $SiCMe_3$), 1.14–1.35 (2 H, m, 5-H_2), 1.48–1.63 (1 H, m, 4-H), 1.86 (3 H, s, 2-Me), 2.03 (1 H, dd, *J* 7 and 12, 3-H), 2.22 (1 H, dd, *J* 6 and 12, 3-H), 3.60–3.69 (2 H, m, 6-H_2) and 5.83 (1 H, narrow m, 1-H); *m/z* (EI) 311 ($M^+ - 57$, 80%).

The more polar fraction consisted of unchanged alkyne **48** (100 mg recovery).

(2S,4R,9R,6E)-11-(tert-*Butyldimethylsiloxy*)-1-(1′,3′-*dithian*-2′-*ylidene*)-7,9-*dimethylundec*-6-*ene*-2,4-*diol* **51**.—Butyllithium (0.37 mmol) was added to a solution of the epoxy hydroxyketene dithioketal **34** (81 mg, 0.37 mmol) in ether (1 cm^3) at −70 °C. A white suspension formed, and the mixture was stirred at −70 °C for 15 min. Butyllithium (0.39 mmol) was added to a solution of the vinyl iodide **50** (143 mg, 0.39 mmol) in ether (1 cm^3) at −70 °C and, after 15 min, this mixture was added *via* a cannula to the suspension of the lithiated dithioketal **34**. After 30 min, the mixture was allowed to warm to room temperature and was then cooled to 0 °C. After 30 min, water (1 cm^3) and ether (10 cm^3) were added, and the aqueous layer was extracted further with ether (2 × 5 cm^3). The combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography (light petroleum–ethyl acetate, 3:1) of the residue gave the title compound **51** (48 mg, 27%) as a yellow oil; $\nu_{max}(CDCl_3)/cm^{-1}$ 3500, 1580, 1445, 1260 and 1080; δ_H(300 MHz) 0.05 (6 H, s, $SiMe_2$), 0.84 (3 H, d, *J* 7, 9-Me), 0.90 (9 H, s, $SiCMe_3$), 1.23–2.35 (11 H, m), 1.60 (3 H, s, 7-Me), 2.76–3.01 (4 H, m, 4′- and 6′-H_2), 3.58–3.71 (2 H, m, 11-H_2), 3.94 (1 H, m, 4-H), 4.95 (1 H, m, 2-H), 5.15 (1 H, t, *J* 7, 6-H) and 6.01 (1 H, d, *J* 9, 1-H); *m/z* (CI, NH_3) 461 (MH^+, 7%) and 443 ($M^+ - 17$, 100%).

(2S,4R,9R,6E)-11-(tert-*Butyldimethylsiloxy*)-1-(1′,3′-*dithian*-2′-*yl*)-7,9-*dimethylundec*-6-*ene*-2,4-*diol* **52**.—Following the procedure outlined above, the undecenylidenedithiane **51** (51 mg, 0.11 mmol) and lithium aluminium hydride (17 mg, 0.44 mmol) gave the title compound **52** (30 mg, 59%) as an oil after chromatography (ethyl acetate–light petroleum, 1:3); ν_{max}/cm^{-1} 3400, 1250, 1090, 840 and 780; δ_H(300 MHz) 0.06 (6 H, s, $SiMe_2$), 0.81 (3 H, d, *J* 7, 9-Me), 0.90 (9 H, s, $SiCMe_3$), 1.23–2.35 (15 H, m), 1.60 (3 H, s, 7-Me), 2.81–2.95 (4 H, m, 4′- and 6′-H_2), 3.58–3.68 (2 H, m, 11-H_2), 3.90–4.0 (1 H, m, 4-H), 4.25–4.30 (2 H, m, 2- and 2′-H) and 5.13 (1 H, t, *J* 7, 6-H); *m/z* (CI, NH_3) 463 (MH^+, 72%) and 119 (100).

(4R,1E)-5-(tert-*Butyldimethylsiloxy*)-1-*iodo*-2,4-*dimethylpent*-1-*ene* **57**.—Following the procedure outlined above, (4R)-5-(*tert*-butyldimethylsiloxy)-4-methylpent-1-yne[25] **56** (0.31 g, 1.46 mmol) gave the *title compound* **57** (0.35 g, 69%) as an oil (Found: $M^+ - CH_3$, 339.0644. $C_{12}H_{24}IOSi$ requires *m/z*, 339.0643); $[\alpha]_D$ + 4.5 (*c* 0.99, $CHCl_3$); ν_{max}/cm^{-1} 1260, 1095, 840 and 780; δ_H(300 MHz) 0.06 (6 H, s, $SiMe_2$), 0.82 (3 H, d, *J* 7, 4-Me), 0.90 (9 H, s, $SiCMe_3$), 1.70–1.78 (1 H, m, 4-H), 1.82 (3 H, s, 2-Me), 1.95 (1 H, dd, *J* 10 and 15, 3-H), 2.38 (1 H, dd, *J* 7 and 15, 3-H), 3.37 and 3.42 (each 1 H, dd, *J* 4 and 9, 5-H), and 5.83 (1 H, s, 1-H); *m/z* (EI) 339 ($M^+ - 15$, 39%) and 297 (100).

(2S,4R,9R,6E)-10-(tert-*Butyldimethylsiloxy*)-1-(1′,3′-*dithian*-2′-*yl*)-7,9-*dimethyldec*-6-*ene*-2,4-*diol* **60**.—Butyllithium (2.58 mmol) was added to a solution of the vinyl iodide **57** (0.91 g, 2.58 mmol) in ether at −70 °C. After 15 min, this solution was added *via* a cannula to a solution of the epoxy hydroxy ketene dithioketal **34** (0.28 g, 1.29 mol) [which had previously been treated with butyllithium (2.58 mmol) in hexane at −78 °C] in THF at −70 °C, and the mixture was stirred for 4 h at −10 to −20 °C. Work-up as outlined above gave (2*S*,4*R*,9*R*,6*E*)-10-(*tert*-butyldimethylsiloxy)-1-(1′,3′-dithian-2′-ylidene)-7,9-dimethyldec-6-ene-2,4-diol **59** (0.18 g, 32%) as an oil; ν_{max}/cm^{-1} 3400, 1265, 1095, 845 and 785; δ_H(300 MHz) 0.03 (6 H, s, $SiMe_2$), 0.82 (3 H, d, *J* 7, 9-Me), 0.90 (9 H, s, $SiCMe_2$), 1.56–1.83 (5 H, m), 1.62 (3 H, s, 7-Me), 2.16–2.35 (4 H, m), 2.76–3.00 (4 H, m, 4′- and 6′-H_2), 3.35 and 3.48 (each 1 H, dd, *J* 5 and 12, 10-H), 3.92 (1 H, m, 4-H), 4.93 (1 H, m, 2-H), 5.15 (1 H, t, *J* 8, 6-H) and 6.01 (1 H, d, *J* 9, 1-H); *m*/*z* (CI, NH_3) 446 (M^+, 6%) and 429 (100).

Following the procedure outlined above, the decenylidene-1,3-dithiane **59** (330 mg, 0.75 mmol) and lithium aluminium hydride (0.12 g, 3.13 mmol) gave the *title compound* **60** (0.25 g, 73%) as an oil (Found: C, 58.5; H, 10.0. $C_{22}H_{44}O_3S_2Si$ requires C, 58.9; H, 9.9%); ν_{max}/cm^{-1} 3500, 1265, 1090, 845 and 790; δ_H(300 MHz) 0.03 (6 H, s, $SiMe_2$), 0.80 (3 H, d, *J* 7, 9-Me), 0.88 (9 H, s, $SiCMe_3$), 1.65–2.47 (12 H, m), 1.62 (3 H, s, 7-Me), 2.75–2.97 (4 H, m, 4′- and 6′-H_2), 3.08 (1 H, br s, OH), 3.36 (1 H, dd, *J* 7 and 10, 10-H), 3.42 (1 H, dd, *J* 5 and 10, 10-H), 3.90 (1 H, m, 4-H), 4.27 (1 H, dd, *J* 7 and 10, 2′-H), 4.20–4.32 (1 H, m, 2-H) and 5.13 (1 H, t, *J* 8, 6-H); *m*/*z* (CI, NH_3) 449 (MH^+, 100%).

(4R,5″R,6S)-4-[(E)-6-(tert)-*Butyldimethylsiloxy*)-3″,5″-*dimethylhex*-2″-*enyl*]-6-(1′,3′-*dithian*-2′-*ylmethyl*)-2,2-*dimethyl*-1,3-*dioxane* **61**.—The dihydroxydecenyl-1,3-dithiane **60** (0.25 g, 0.55 mmol), acetone (7.5 cm^3; Analar), 2,2-dimethoxypropane (0.4 cm^3), anhydrous copper(II) sulfate (0.65 g) and PTSA (6 mg) were stirred at room temperature for 1.5 h and filtered. Solid calcium hydroxide was added to the filtrate until it was neutral, and the mixture was filtered again and the filtrate was concentrated under reduced pressure. Chromatography of the residue (ether–light petroleum, 1 : 10) gave the *title compound* **61** (0.16 g, 62%) as an oil (Found: $M^+ - C_4H_9$, 431.2110. $C_{21}H_{39}O_3S_2Si$ requires *m*/*z*, 431.2110); ν_{max}/cm^{-1} 1385, 1230, 1090, 840 and 780; δ_H(300 MHz) 0.08 (6 H, s, $SiMe_2$), 0.86 (3 H, d, *J* 7, 5″-Me), 0.95 (9 H, s, $SiCMe_3$), 1.40 and 1.43 (each 3 H, s, Me), 1.65 (3 H, s, 3″-Me), 1.61 (11 H, m), 2.38–3.00 (4 H, m, 4′- and 6′-H_2), 3.39 and 3.47 (each 1 H, dd, *J* 6 and 12, 6″-H), 3.83 (1 H, m, 4-H), 4.12–4.20 (1 H, m, 6-H), 4.73 (1 H, dd, *J* 6 and 10, 2′-H) and 5.15 (1 H, t, *J* 7, 2″-H); *m*/*z* (CI, NH_3) 489 (MH^+, 5%) and 431 ($M^+ - 57$, 100%).

(4R,5″R,6S)-4-[(E)-6″-(tert-*Butyldimethylsiloxy*)-3″,5″-*dimethylhex*-2″-*enyl*]-2,2-*dimethyl*-6-{2′-[4-(*tetrahydropyran*-2-*yloxy*)-*butyl*]-1′,3′-*dithian*-2′-*ylmethyl*}-1,3-*dioxane* **62**.—*tert*-Butyllithium (0.26 mmol) was added to a solution of the decenyldithiane **61** (118 mg, 0.24 mmol) in THF (1 cm^3) at −22 °C. Hexamethylphosphoric triamide (HMPA) (84 mm^3, 0.48 mmol) was added, and the mixture was stirred at −22 °C for 1 h. A solution of 1-bromo-4-(tetrahydropyran-2-yloxy)butane (142 mg, 0.6 mmol) in THF (1 cm^3) was added and the mixture was stirred for 1 h. Water (2 cm^3) and ether (15 cm^3) were added and, after warming to room temperature, the aqueous layer was extracted with more ether (2 × 10 cm^3). The combined organic phases were dried ($MgSO_4$), and concentrated under reduced pressure. Chromatography of the residue (ethyl acetate–light petroleum, 1 : 15) gave the *title compound* **62** (92 mg, 59%) as an oil (Found: M^+, 644.3965. $C_{34}H_{64}O_5S_2Si$ requires *M*, 644.3964); ν_{max}/cm^{-1} 1385, 1230, 1130, 1085, 840 and 780; δ_H(300 MHz) 0.03 (6 H, s, $SiMe_2$), 0.82 and 0.85 (each 1.5 H, d, *J* 7, 5″-Me), 0.88 (9 H, s, $SiCMe_3$), 1.30 and 1.37 (each 3 H, s, Me), 1.50–2.32 (23 H, m), 1.57 (3 H, s, 3″-Me), 2.68–2.88 (4 H, m, 4′- and 6′-H_2), 3.30–3.40 (3 H, m), 3.43–3.55 (1 H, m), 3.7–3.8 (2 H, m), 3.82–3.92 and 4.08–4.18 (each 1 H, m), 4.55–4.58 (1 H, m, OCHO) and 5.12 (1 H, m, 2″-H); *m*/*z* (EI) 644 (M^+, 3%).

(2R,7R,9S,4E)-10-[2′-(4″-*Hydroxybutyl*)-1′,3′-*dithian*-2′-*yl*]-2,4-*dimethyldec*-4-*ene*-1,7,9-*triol* **63**.—The bisalkylated 1,3-dithiane **62** (26 mg, 0.04 mmol) and PTSA (3 mg) were stirred in solution in THF–methanol (1 cm^3; 1:1) for 6 h at room temperature. Solid calcium hydroxide was added until the solution was neutral, the mixture was filtered, and the filtrate was concentrated under reduced pressure. Chromatography of the residue (ethyl acetate–light petroleum, 20 : 1) gave the *title compound* **63** (14 mg, 86%) as a viscous oil (Found: M^+, 406.2211. $C_{20}H_{38}O_4S_2$ requires *M*, 406.2211); ν_{max}/cm^{-1} 3630, 3430, 1280, 1080, 1030 and 840; δ_H(300 MHz) 0.89 (3 H, d, *J* 7, 2-Me), 1.48–2.20 (14 H, m), 1.65 (3 H, s, 4-Me) 2.24 (2 H, t, *J* 6.5), 2.42 (1 H, dd, *J* 9 and 16), 2.72–3.05 (4 H, m, 4′- and 6′-H_2), 3.42 (1 H, dd, *J* 7 and 10, 1-H), 3.47 (1 H, dd, *J* 7 and 12, 1-H), 3.65 (2 H, t, *J* 7, 4″-H_2), 3.92–4.00 (1 H, m, 7-H), 4.22–4.28 (1 H, m, 9-H) and 5.22 (1 H, t, *J* 7, 5-H); *m*/*z* (EI) 406 (M^+, 2%), 388 ($M^+ - 18$, 3) and 171 (100).

(2R,4S,6S)-2-[(5′R,2′E)-6′-*Hydroxy*-3′,5′-*dimethylhex*-2′-*enyl*]-1,7-*dioxaspiro*[5.5]*undecan*-4-*ol* **64**.—A solution of the tetraol **63** (14 mg, 0.035 mmol) and mercury(II) chloride (22 mg, 0.087 mmol) in THF (1 cm^3) was stirred at room temperature for 24 h. Ether (10 cm^3) was added, the mixture was filtered, and the filtrate was concentrated under reduced pressure. Chromatography (ethyl acetate–light petroleum, 10 : 1) gave the *title compound* **64** (7 mg, 73%) as an oil (Found: $M^+ - H_2O$, 280.2041. $C_{17}H_{28}O_3$ requires *m*/*z* 280.2038) further purified by HPLC; ν_{max}/cm^{-1} 3620, 1470, 1390, 1185, 1050, 1030 and 990; δ_H(300 MHz) 0.89 (3 H, d, *J* 7, 5′-Me), 1.14–1.20 and 1.24–1.28 (each 1 H, m), 1.47–1.70 (6 H, m), 1.65 (3 H, s, 3′-Me), 1.83–1.91 (2 H, m), 1.94–2.04 (2 H, m), 2.11 (1 H, dd, *J* 7 and 10, 4′-H), 2.26 (2 H, m, 1′-H_2), 3.44 and 3.51 (each 1 H, dd, *J* 6 and 11, 6′-H), 3.52–3.55 (1 H, m, 2-H), 3.57–3.64 (2 H, m, 8-H_2), 4.10 (1 H, m, 4-H) and 5.28 (1 H, t, *J* 6, 2′-H); *m*/*z* (EI) 280 ($M^+ - 18$, 2%) and 171 (100).

(4S,6S)-4-(1′,3′-*Dithian*-2′-*ylmethyl*)-6-(p-*methoxybenzyloxymethyl*)-2,2-*dimethyl*-1,3-*dioxane* **65**.—The dihydroxypentyl-1,3-dithiane **40** (1.04 g, 2.89 mmol), 2,2-dimethoxypropane (20 cm^3) and PTSA (27 mg, 5 μmol) were stirred in acetone (Analar) for 2 h. Calcium hydroxide was added, the mixture was filtered, and the filtrate was concentrated under reduced pressure to give the *title compound* **65** (1.07 g, 86%) after chromatography (light petroleum–ether, 2 : 1) as an oil (Found: C, 60.1; H, 7.85. $C_{20}H_{30}O_4S_2$ requires C, 60.25; H, 7.6%); ν_{max}/cm^{-1} 1615, 1520, 1385, 1250, 1230, 1040 and 735; δ_H(270 MHz) 1.40 (6 H, s, 2 × Me), 1.48–2.08 (6 H, m, 5-H_2, 4-CH_2, and 5′-H_2), 2.84 (4 H, m, 4′- and 6′-H_2), 3.44 (2 H, m, 6-CH_2), 3.82 (3 H, s, OMe), 4.10 (3 H, m, 4-, 6- and 2′-H), 4.48 and 4.54 (each 1 H, d, *J* 11, ArCH) and 6.86 and 7.24 (each 2 H, d, *J* 11, ArH); *m*/*z* (CI, NH_3) 399 (MH^+, 13%) and 121 (100).

(4S,6S)-4-{2′-[(3″S,4″R)-4″(tert-*Butyldimethylsiloxy*)-3″,5″-*dimethylhexyl*]-1′,3′-*dithian*-2′-*ylmethyl*}-6-(p-*methoxybenzyloxymethyl*)-2,2-*dimethyl*-1,3-*dioxane* **67**.—*tert*-Butyllithium (0.28 mmol; 1.7 mol dm^{-3} in pentane) was added dropwise to a solution of the dithiane **65** (100 mg, 0.25 mmol) in THF (1.5 cm^3) at −78 °C. The mixture was warmed to −40 °C during 30 min, and HMPA (89 mm^3, 0.5 mmol) was added followed by a solution of the bromide **66**[27] (121 mg, 0.37 mmol) in THF (1 cm^3). Saturated aq. ammonium chloride (2 cm^3) was added after 30 min, and the aqueous phase was extracted with ether. The combined extracts were dried (Na_2SO_4), and concentrated

under reduced pressure. Chromatography (light petroleum–ethyl acetate, 3:1) of the residue gave the *title compound* **67** (53 mg, 33%) as an oil (Found: M^+, 641.3767. $C_{34}H_{60}O_5S_2Si$ requires *M*, 641.3729); $[\alpha]_D$ − 19.3 (*c* 3.26, $CHCl_3$); ν_{max}/cm^{-1} 1620, 1590, 1520, 1250, 1230, 1180, 1100, 1040 and 840; δ_H(270 MHz) 0.02 and 0.04 (each 3 H, s, SiMe), 0.84–0.96 (18 H, overlapping peaks, 3 × Me + $SiCMe_3$), 1.34 and 1.40 (each 3 H, s, Me), 1.46–2.20 (12 H, m), 2.76 (4 H, m, 4′- and 6′-H_2), 3.24 (1 H, m, 4″-H), 3.36–3.42 (2 H, m, 6-CH_2), 3.80 (3 H, s, OMe), 4.02 and 4.16 (each 1 H, m, 4- and 6-H), 4.48 and 4.56 (each 1 H, d, *J* 11, ArCH) and 6.88 and 7.26 (each 2 H, d, *J* 8, ArH); *m/z* (CI, NH_3) 642 (MH^+, 3%) and 121 (100).

(2S,4S,6S,8R,9S)-2-*Hydroxymethyl*-8-*isopropyl*-9-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*ol* **69**.—The dialkyldithiane **67** (38 mg, 0.06 mmol), glacial acetic acid (1.5 cm^3), water (0.5 cm^3) and THF (0.5 cm^3) were stirred together for 24 h at 45 °C. The mixture was diluted with ether (10 cm^3) and washed with aq. sodium hydrogen carbonate (2 × 3 cm^3). The aqueous washings were extracted with dichloromethane (3 × 5 cm^3), and the organic phases were combined and dried (Na_2SO_4). After concentration under reduced pressure, chromatography (ether–light petroleum, 8:1) gave (2*S*,4*S*)-1-{2′-[(3″*S*,4″*R*)-4″-hydroxy-3″,5″-dimethylhexyl]-1′,3′-dithian-2′-yl}-5-(*p*-methoxybenzyloxy)pentane-2,4-diol **68** (19 mg, 66%) as an oil; ν_{max}/cm^{-1} 3440, 1615, 1590, 1510, 1240, 1220, 1175, 1090, 1035, 990, 910 and 825; δ_H(300 MHz) 0.84–0.96 (9 H, overlapping doublets, 3 × Me), 1.40–2.48 (15 H, m), 2.72–3.08 (4 H, m, 4′- and 6′-H_2), 3.14 (1 H, m, 4″-H), 3.40 and 3.50 (each 1 H, m, 5-H), 3.82 (3 H, s, OMe), 4.14 and 4.30 (each 1 H, m, 2- and 4-H), 4.50 (2 H, s, ArCH_2) and 6.90 and 7.27 (each 2 H, d, *J* 10, ArH).

Mercury(II) chloride (26 mg, 0.09 mmol) was added to a solution of the triol **68** (19 mg, 0.04 mmol) in THF (1 cm^3) and the mixture was stirred overnight at room temperature. Ether (10 cm^3) was added, and the mixture was washed with water, dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (ether–light petroleum) of the residue gave the *title compound* **69** (7 mg, 70%) as a solid, which was crystallised from ether, m.p. 122–124 °C (Found: MH^+, 259.1909. $C_{14}H_{27}O_4$ requires *m/z*, 259.1935); $[\alpha]_D$ + 93.4 (*c* 0.12, $CHCl_3$); $\nu_{max}(CHCl_3)/cm^{-1}$ 3600, 3440, 1220, 1120, 1080, 1010, 980 and 910; δ_H(400 MHz) 0.79, 0.83 and 0.97 (each 3 H, d, *J* 8, CH*Me*), 1.20–1.31 (2 H, m, 3-H^{ax} and 5-H^{ax}), 1.40–1.70 (6 H, m), 1.83–1.90 (2 H, m, 3-H^{eq} and C*H*Me_2), 1.84–2.05 (2 H, m, 5-H^{eq} and OH), 3.06 (1 H, dd, *J* 10 and 4, 8-H), 3.56 and 3.65 (each 1 H, m, C*H*HOH), 3.74 (1 H, m, 2-H) and 4.19 (1 H, m, 4-H); *m/z* (CI, NH_3) 259 (MH^+, 95%).

(4R,6S)-4-*Allyl*-6-(1′,3′-*dithian*-2′-*ylmethyl*)-2,2-*dimethyl*-1,3-*dioxane* **70**.—Following the procedure outlined above, the diol **36** (0.77 g, 3.1 mmol), acetone (2.5 cm^3), dimethoxypropane (2.5 cm^3) and PTSA gave the title compound **70** (0.79 g, 90%) as an oil, $[\alpha]_D$ − 25.7 (*c* 1, $CHCl_3$); ν_{max}/cm^{-1} 1640, 1280 and 910; δ_H(300 MHz) 1.35 and 1.40 (each 3 H, s, Me), 1.5–2.43 (8 H, m), 2.77–3.0 (4 H, m, 4′- and 6′-H_2), 3.78–3.95 and 4.05–4.16 (each 1 H, m, 4- and 6-H), 4.19 (1 H, dd, *J* 10 and 5, 2′-H), 5.02–5.18 (2 H, m, (CH=C) and 5.72–5.74 (1 H, CH_2=C*H*).

(4R,6S)-4-*Allyl*-6-{2-[(3″S,4″R)-4″-(tert-*butyldimethylsiloxy*)-3″,5″-*dimethylhexyl*]-1′,3′-*dithian*-2′-*ylmethyl*}-2,2-*dimethyl*-1,3-*dioxane* **72**. —*tert*-Butyllithium (0.35 mmol; 1.7 mol dm^{-3} in pentane) and HMPA (0.69 mmol) were added to a solution of the dithiane **70** (100 mg, 0.35 mmol) in THF (1 cm^3) at −22 °C. After 2 h, a solution of the iodide **71**[27] (0.42 mmol) in THF (1 cm^3) was added, and the mixture was stirred at −22 °C for 1 h, and at −20 °C for 12 h. Water (5 cm^3) and ethyl acetate (3 × 10 cm^3) were added, and the combined organic phases were washed successively with hydrochloric acid (0.1 mol dm^{-3}), water, aq. sodium hydrogen carbonate, and water. After being dried (Na_2SO_4), the organic phase was concentrated under reduced pressure, and chromatography (light petroleum–ethyl acetate, 97:3) gave the title compound **72** (136 mg, 74%) as an oil; $[\alpha]_D$ − 17.6 (*c* 2, $CHCl_3$); ν_{max}/cm^{-1} 3070, 1642, 1250, 1220, 1170, 1050, 910, 835 and 770; δ_H(300 MHz) 0.05 and 0.08 (each 3 H, s, SiMe), 0.85–0.96 (18 H, overlapping peaks, 3 × Me + $SiCMe_3$), 1.33 and 1.40 (each 3 H, s, Me), 1.46–2.4 (14 H, m), 2.7–2.91 (4 H, m, 4′- and 6′-H_2), 3.21–3.28, 3.78–3.93 and 4.1–4.23 (each 1 H, m, CHO), 5.03–5.16 (2 H, m, CH_2=) and 5.73–5.9 (1 H, m, CH_2=C*H*); *m/z* (CI, NH_3) 531 (MH^+, 20%) and 473 (100).

(2S,4R)-1-{2′-[(3″S,4″R)-4″-*Hydroxy*-3″,5″-*dimethylhexyl*]-1′,3′-*dithian*-2′-*yl*}*hept*-6-*ene*-2,4-*diol* **73**.—Hydrochloric acid (0.5 cm^3; 1 mol dm^{-3}) was added to a solution of the acetonide **72** (100 mg, 0.189 mmol) in methanol (3 cm^3) and the mixture was stirred for 12 h. Water (5 cm^3) was added, and the mixture was extracted with ethyl acetate. The combined extracts were dried (Na_2SO_4), and concentrated under reduced pressure. Chromatography (ethyl acetate–light petroleum, 2:3) gave the title compound **73** (60 mg, 85%) as an oil; $[\alpha]_D$ + 1.806 (*c* 1.99, $CHCl_3$); ν_{max}/cm^{-1} 3400, 3080, 1735, 1640, 1050, 995 and 910; δ_H(300 MHz) 0.85–1.0 (9 H, overlapping d, 3 × CH*Me*), 1.41–2.2 (14 H, complex m), 2.19 (2 H, t, *J* 7), 2.44 (1 H, dd, *J* 9 and 16), 2.71–3.06 (4 H, m, 4′- and 6′-H_2), 3.14 (1 H, dd, *J* 8 and 5, 4″-H), 3.95–4.05 (1 H, m, 2-H), 4.25–4.38 (1 H, m, 4-H), 5.1–5.21 (2 H, m, 7-H_2) and 5.76–5.91 (1 H, m, 6-H); *m/z* (EI) 376 (M^+, 2%) and 269 (100).

(2R,4S,6S,8R,9S)-2-*Allyl*-8-*isopropyl*-9-*methyl*-1,7-*dioxaspiro*[5.5]*undecan*-4-*ol* **74**.—Following the procedure outlined above the dithiane **73** (100 mg, 0.27 mmol) and mercury(II) chloride (176 mg, 0.65 mmol) in THF (7 cm^3) gave, after chromatography, the spiroketal **74** (50 mg, 70%), $[\alpha]_D$ + 85 (*c* 1.27, $CHCl_3$) [lit.,[27] + 78 (*c* 0.82, $CHCl_3$)], identical by ^1H NMR, IR, and TLC with an authentic sample.[27]

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