Asymmetric synthesis of tetrahydrofurans by competitive [1,2]-phenylsulfanyl (PhS) migrations under thermodynamic control

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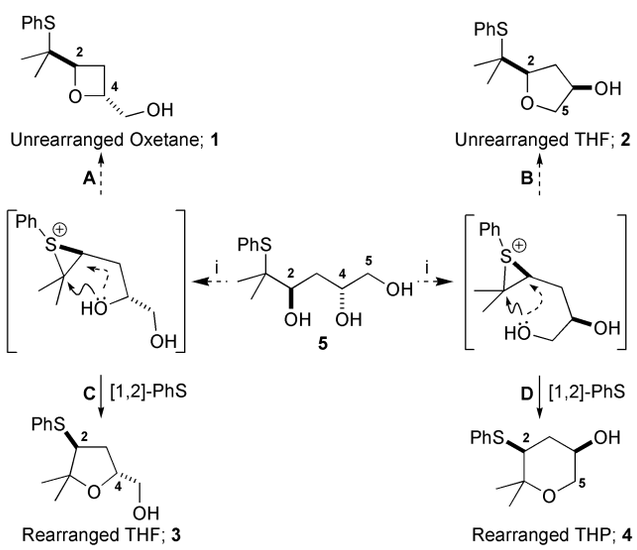
Triols were prepared in enantiomerically enriched form by a short route that included a Sharpless asymmetric dihydroxylation; treatment of these triols with toluene-*p*-sulfonic acid gave THFs as thermodynamic products.

In a short series of papers[1] we reported the outcome of sulfanyl[2] mediated competitive cyclisations between two hydroxy groups of 2,4,5-triols (bearing a phenylsulfanyl group at C-1). For these types of compounds four modes of cyclisation are conceptually possible: routes **A** to **D** (Scheme 1).



Scheme 1 *Reagents*: i, TsOH, CH_2Cl_2.

Route **A** could be ignored because oxetanes (*e.g.* **1**) are too high in energy to be isolated from these cyclisation reactions.[3] We wished to ascertain which of the modes of cyclisation, **B** (to give the 'unrearranged'[4] THF **2**), **C** (to give the 'rearranged'[4] THF **3**) or **D** (to give the rearranged THP **4**) would be operative under acid catalysis. In a closely related study Gruttadauria has reported the outcome of selenium-mediated competitive cyclisations, with the observation that THFs were formed under kinetic conditions but these THFs slowly equilibrated (**E**) to THPs (Scheme 2).[5] More recently Borhan has examined the same problem in the context of epoxide opening and showed that THFs are produced under kinetic conditions. By incorporation of a phenylsulfanyl group the regiochemistry of the epoxide opening could be reversed (*cf.* **F** and **G**, Scheme 2) to give isomeric THFs.[6]

Three sets of diastereomeric 2,4,5-triols were prepared so that their cyclisations could be studied. Each of the three sets had a different migration origin in order that we could demonstrate the generality of the cyclisation outcome. In the first series (triols **5** and **8**) the sulfanyl group was bound to a *gem*-dimethyl substituted carbon atom (Fig. 1). The second pair

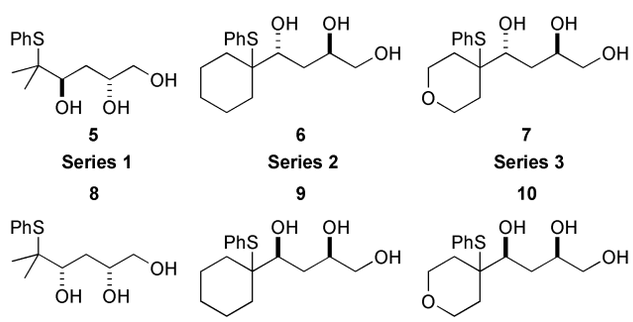


Fig. 1 2,4,5-Triols for cyclisation reactions.

of triols (**6** and **9**) had a cyclohexane ring present and the final set (triols **7** and **10**) had a THP ring present in order that we could prepare some unusual dioxaspirocycles that are not trivial to prepare by other routes.[7] The triols could be synthesised asymmetrically: Sharpless asymmetric dihydroxylation (AD)[8] of a homoallylic ketone being the key step in our route to these compounds.

In each case the synthesis started from an α-phenylsulfanyl aldehyde (**11**, **12** or **13**), compounds which were easily synthesised on a large scale by sulfenylation of the appropriate silyl enol ethers with phenylsulfenyl chloride (Scheme 3).[9] Addition of allylmagnesium bromide to each of the aldehydes to give the homoallylic alcohols (**14**–**16**) was followed by oxidation with Corey's PCC reagent[10] to give good yields of the homoallylic ketones (**17**–**19**). We were pleased to observe that no trace of double bond isomerisation to give the conjugated enones was observed.

The AD reaction gave optimum enantiomeric excess (73–84%) for the diols (**20**–**22**) when Sharpless' PYR ligand was used.[11a] Reaction using the commercially available AD mixes (which contain the PHAL ligand[11b]) resulted in much lower enantioselectivities (typically 30%). The final stage of the stereocontrolled triol synthesis was a 1,3-diastereoselective reduction

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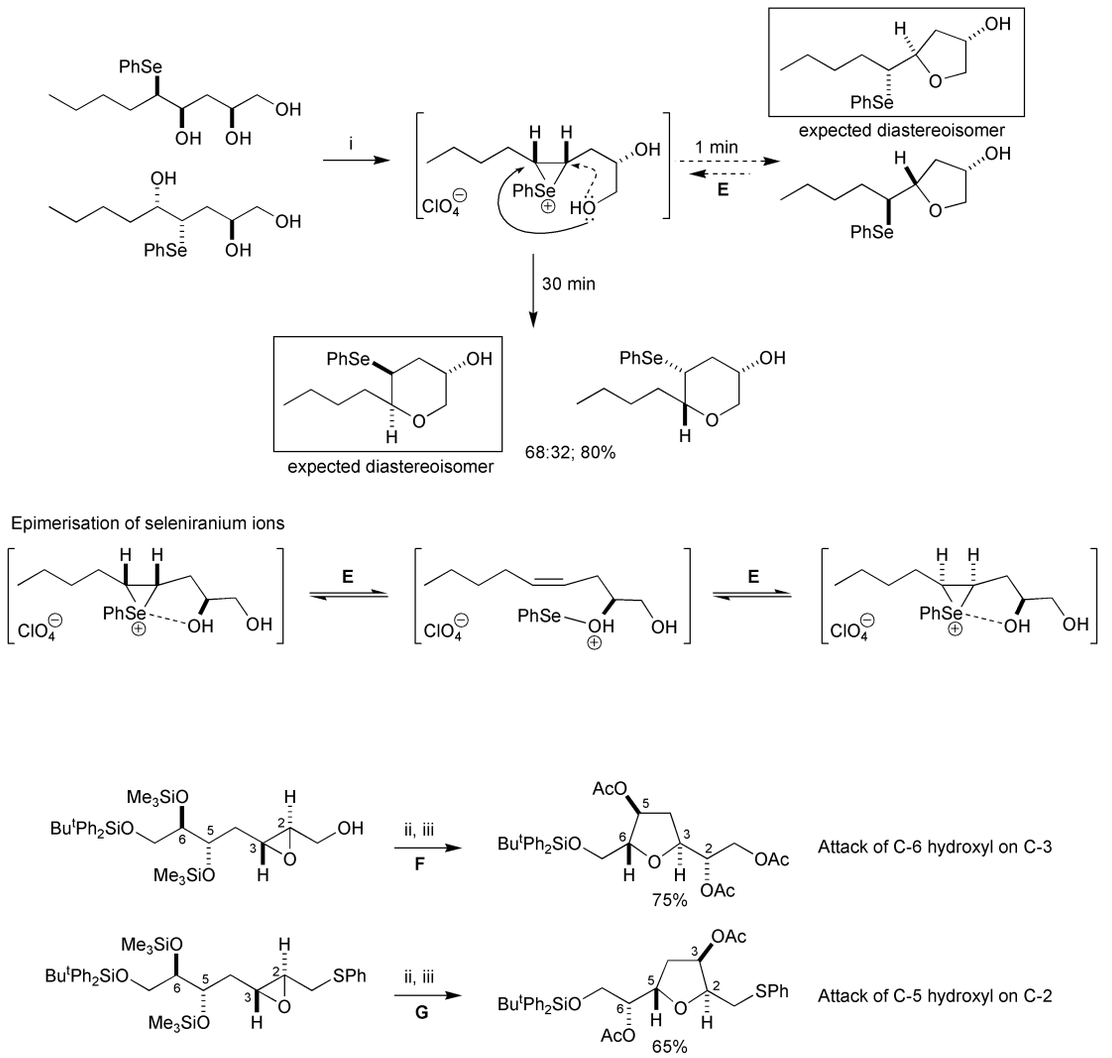
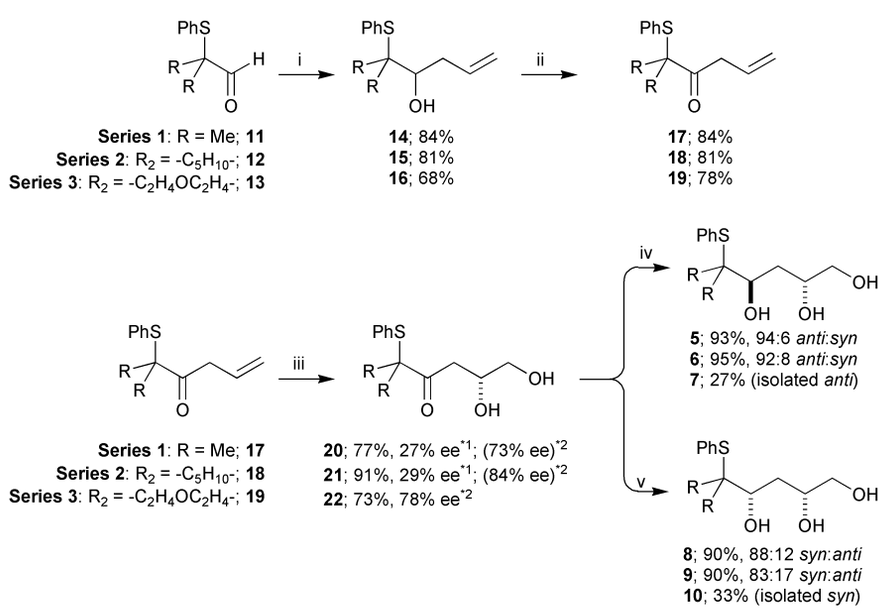


Scheme 2 *Reagents*: i, $HClO_4$, CH_2Cl_2, rt; ii, $BF_3{\cdot}OEt_2$, Et_2O, 0 °C to rt; iii, Ac_2O, pyridine, 60 °C.



Scheme 3 *Reagents*: i, $CH_2{=}CHCH_2MgBr$, Et_2O, rt; ii, PCC, CH_2Cl_2, rt; iii, $K_2OsO_2(OH)_4$, chiral ligand, K_2CO_3, $K_3Fe(CN)_6$, Bu^tOH–H_2O, 0 °C; iv, Me_4N^+ $BH(OAc)_3^-$, AcOH–MeCN, −20 °C, 7 days; v, Et_2BOMe, THF–MeOH, −78 °C then $NaBH_4$. *Chiral ligand used was either: (1) $(DHQD)_2PHAL$ or (2) $(DHQD)_2PYR$.

to give either the 2,4-*anti*[12] (**5**–**7**) or the 2,4-*syn*[13] diastereoisomers (**8**–**10**) of each triol. Racemic standards of the triols could also be prepared in large quantities by racemic dihydroxylation[14] of the homoallylic alcohols (**14**–**16**) and straightforward separation of the 2,4-related diastereoisomers by column chromatography. Little diastereoselection was observed in the

Table 1 Product distribution for the acid catalysed rearrangement of triol **6**

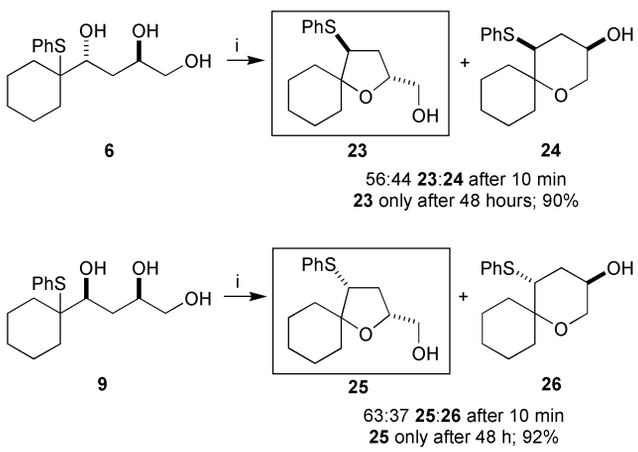
Reaction time/hours	Product ratio, THF **23**:THP **24**
0.167	56:44
1.25	66:34
24	96:4
48	>98:2

Table 2 Product distribution for the acid catalysed rearrangement of triol **9**

Reaction time/hours	Product ratio, THF **25**:THP **26**
0.167	63:37
1.33	71:29
24	89:11
48	>98:2

racemic dihydroxylation reaction but in this way large quantities of the triols were made available to study the cyclisations.

To begin with, the triols **6** and **9** (from the second set) were subjected to our standard conditions for cyclisation: a ten-minute reflux with five mol% toluene-*p*-sulfonic acid in dichloromethane. To our initial disappointment triol **6** gave a 56:44 mixture of THF **23** and THP **24** (Scheme 4, Table 1). Previously we have shown that these cyclisation reactions are under thermodynamic control,[15,16] so resubmitting this mixture to the reaction conditions, or taking a fresh sample of the triol **6**, and heating to reflux in dichloromethane for 48 hours led to the complete conversion into the spirocyclic THF **23** (Scheme 4). Similarly, the *syn*-triol **9** gave an initial product distribution of 63:37 THF **25**:THP **26**, but after a prolonged reflux (48 hours) gave only THF **25** (Scheme 4, Table 2).



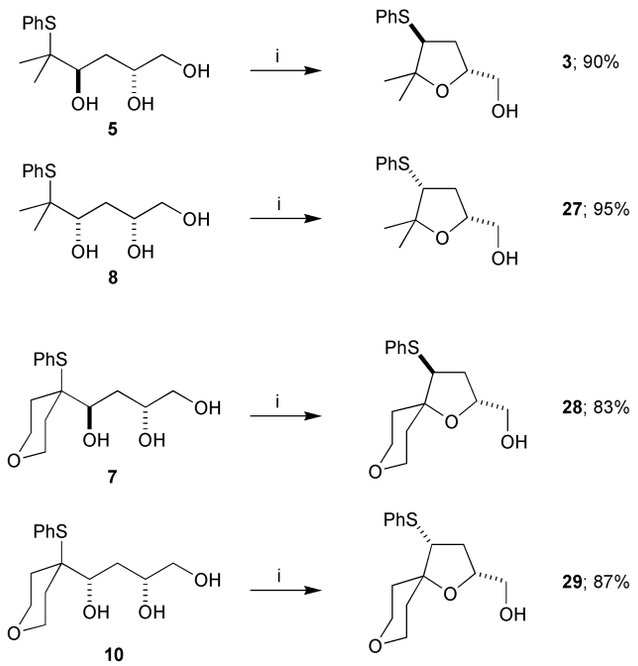
Scheme 4 *Reagents*: i, TsOH, CH_2Cl_2, 40 °C.

Rearrangement of the two other structurally related sets of triols (**5** and **8**) and (**7** and **10**) again led to THF–THP mixtures after short reaction times. Longer reaction times (48 hours) gave the rearranged THFs **3** and **27** (for the second series) and **28** and **29** (for the third series) (Scheme 5).

The THFs and THPs are clearly distinguished by their ^{1}H NMR spectra. The methine proton on the carbon atom bound to the PhS group appears as a double doublet for the THPs (with typical $^3J_{ax\text{-}ax}$ and $^3J_{ax\text{-}eq}$ coupling constants), whereas for the THFs this methine signal appears as a triplet (or at least a double doublet with very similar coupling constants). We were also able to prove unambiguously that the stereochemistry in the triol precursor is faithfully translated into the cyclised product (*i.e.* with stereochemical inversion taking place at C-2). This proof was obtained by single crystal X-ray diffraction on the 3,5-dinitrobenzoate ester **30** (Fig. 2, Table 3) of the *syn*-THP **4** (derived from *anti*-triol **5**).

Table 3 Summary of crystal data, data collection, structure solution and refinement data for compound **30**

Empirical formula	$C_{20}H_{20}N_2O_7S$
Formula weight (M)	432.44 g mol^{-1}
Crystal system	Orthorhombic
Unit cell dimensions	a = 8.527(2) Å, α = 90°
	b = 21.517(3) Å, β = 90°
	c = 22.053(3) Å, γ = 90°
Volume	4046.2(12) Å^3
Temperature	210(2) K
Space group	*Pbca*
Z	8
Absorption coefficient (μ)	1.830 mm^{-1}
Reflections collected	3905
Independent reflections	2511 (R_{int} = 0.0249)
Final R indices [I>2σ(I)]	$R1$ = 0.0434, w$R2$ = 0.0897
R indices (all data)	$R1$ = 0.0724, w$R2$ = 0.1006



Scheme 5 *Reagents*: i, TsOH, CH_2Cl_2, 40 °C, 48 h.

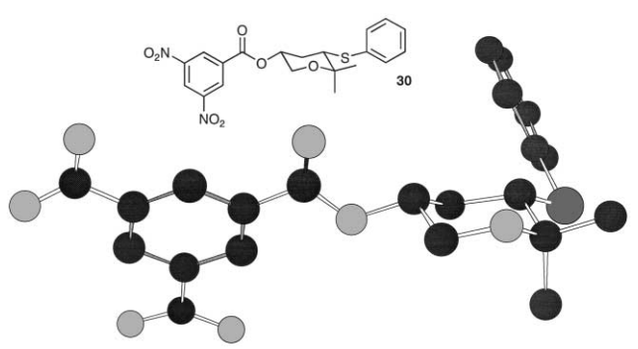


Fig. 2 X-Ray crystal structure of the 3,5-dinitrobenzoate derivative **30** of the *syn*-THP **4** formed by rearrangement of *anti*-triol **5**.

It was possible to follow the course of the [1,2]-PhS rearrangement in $CDCl_3$ over a period of 24 hours by NMR. Fig. 3 shows the 3.0–5.0 ppm region for a selection of ^{1}H NMR spectra recorded during this period. The initial spectrum (top of Fig. 3) is that of the triol **5**. After two hours at 40 °C the spectrum clearly shows a mixture of four compounds: the triol **5**, and each of the three cyclisation products **2**, **3** and **4** (*i.e.* resulting from cyclisations **B**, **C** and **D**, Scheme 1). At much longer reaction times (*e.g.* 9 hours) almost none of the unrearranged THF **2** remains, but THF **3** and THP **4** are still present in a ratio of 1:1. The final spectrum, recorded after 36 hours,

Table 4 Molecular modelling data obtained using MOPAC software with PM3 parameters

Compound number	Compound type	Energy range/kcal mol^{-1}
1	Oxetane	−82.9 to −77.2
2	Unrearranged THF	−98.1 to −95.0
4	Rearranged THP	−101.0 to −98.2
3	Rearranged THF	−103.9 to −97.8

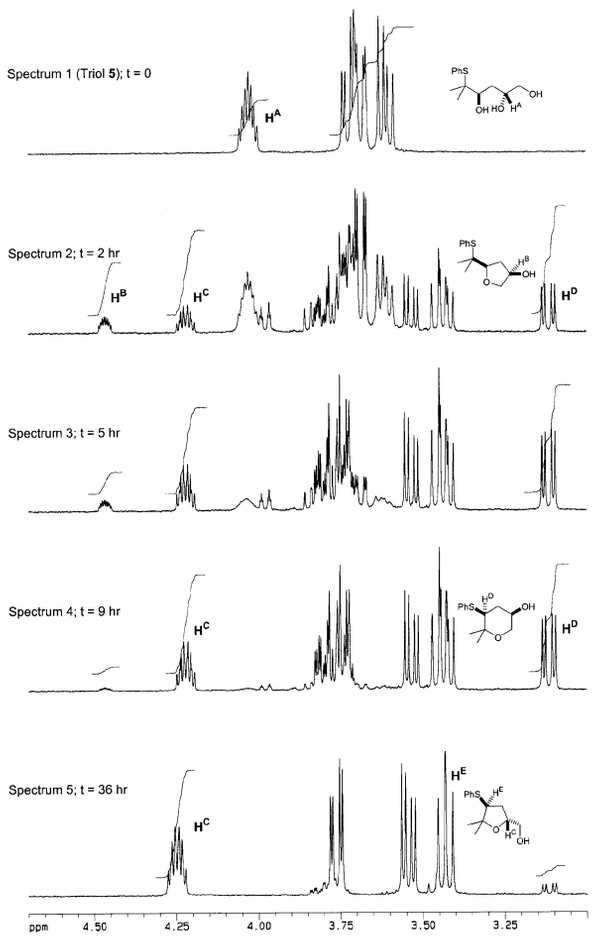


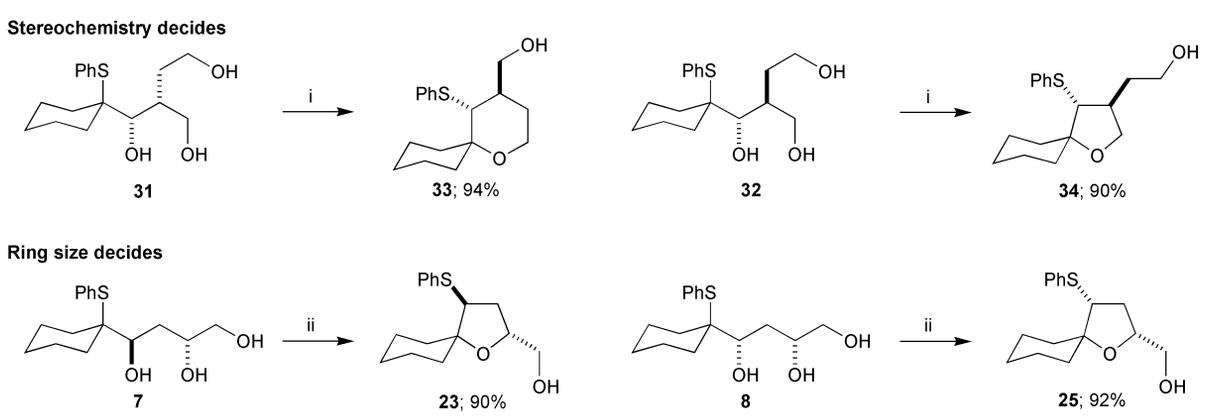
Fig. 3 ^{1}H NMR spectra recorded in $CDCl_3$ at 40 °C at specified intervals to show the rearrangement of triol **5** under equilibrating conditions. Spectrum 1 shows triol **5** immediately after addition of TsOH (OH couplings removed); spectrum 2 shows four compounds present: triol **5** (δ_H ~ 4.0), unrearranged THF **2** (δ_H ~ 4.5), THF **3** (δ_H ~ 4.2) and THP **4** (δ_H ~ 3.1); spectrum 4 reveals only two major components present: THF **3** and THP **4**; and finally spectrum 5 shows equilibration nearing completion: THF **3** is now the major component [note the presence of the characteristic THF signal δ_H ~ 3.45 (1 H, t)].

shows that most of the THP **4** has now disappeared, a clear demonstration that the rearranged THF **3** is the thermodynamic cyclisation product.

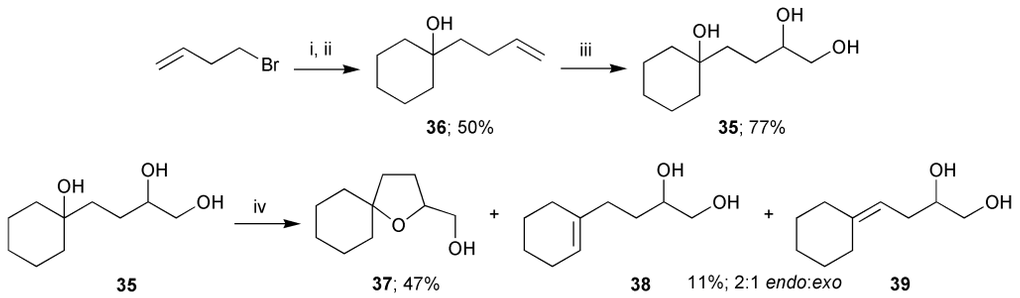
We used semi-empirical molecular orbital calculations to model the products of these cyclisations given their fairly low molecular complexity. We calculated a number of minimum energy conformations for each of the products using PM3 parameters. The data are summarised in Table 4. The modelling data is in good agreement with the actual experimental outcome and these results gave us the confidence to use computer modelling to make predictions about the cyclisations of other closely related compounds.

In contrast to other systems we have studied,[17] ring-size has become more important than the relative stereochemistry (Scheme 6): triols **31** and **32** rearrange to give 3,4-*anti* THP **33** and 3,4-*anti* THF **34**, respectively. That a 2,4-*syn* THF (*e.g.* **25**) is preferred to the alternative 2,4-*anti* THP (*e.g.* **26**, Scheme 4, where one of the two substituents would enter an axial environment) is perhaps not surprising. However, the 2,4-*anti* THF (*e.g.* **23**) is preferred to the 2,4-*syn* THP (*e.g.* **24**, Scheme 4), where both groups could now be equatorial. We presume that the factor governing the cyclisation outcome for the 2,4,5-triols (the degree of substitution being equal for both ring sizes) is the *gem*-disubstituted migration origin. In the THPs one of the C–C bonds is forced to be axial; presumably the 1,3-diaxial interactions are too severe and the flatter THF rings are preferred.

In order to demonstrate further the important role of the sulfanyl group in determining the outcome of these cyclisations, we prepared the triol **35** in racemic form, to compare the acid catalysed cyclisation of this triol with the results obtained for the sulfanyl compounds. Triol **35** was prepared by addition of but-3-enyl-1-magnesium bromide to cyclohexanone, followed by racemic dihydroxylation of the alkene **36** (Scheme 7). A prolonged reflux (3 days) of triol **35** with toluene-*p*-sulfonic acid in dichloromethane was required for the starting material to be consumed. Analysis of the crude reaction mixture revealed the presence of three products: the THF **37** and the two elimination products **38** and **39**, which we were unable to separate by chromatography. No THP could be detected. Acid catalysed diol cyclisations are well known to be complicated by competing mechanisms and often result in poor yields;[18] this cyclisation was no exception. A combination of stepwise and concerted substitution pathways is likely to occur, and when



Scheme 6 *Reagents*: i, TsOH, C_6H_6, 80 °C; ii, TsOH, CH_2Cl_2, 40 °C.



Scheme 7 *Reagents*: i, Mg, Et_2O; ii, cyclohexanone; iii, $K_2OsO_2(OH)_4$, quinuclidine, $K_3Fe(CN)_6$, K_2CO_3, Bu^{t}OH–H_2O; iv, TsOH, CH_2Cl_2, 40 °C, 3 days.

the stepwise mechanism operates a competing E1 pathway is generally found. This reaction demonstrates the importance of sulfur in our cyclisation reactions; the phenylsulfanyl group plays a vital role in controlling the mechanism of the reaction. Stereochemical inversion is always observed even where the electrophilic carbon atom may display a near planar geometry. For this reason no departure from stereospecific cyclisation has ever been observed for cyclisations with [1,2]-PhS migration.

In summary we have demonstrated a viable route for the asymmetric synthesis of 2,4,5-triols and provided firm evidence that [1,2]-PhS rearrangements are under thermodynamic control. For a simple class of triols **5**–**10** the most stable products are the THFs **3**,**23**,**25** and **27**–**29** (Schemes 4 and 5). We believe that the difference in product stability between the 5- and 6-membered rings can be attributed to the *gem*-disubstituted migration origin. In other cases we have investigated whether the relative stability of products may be dependent on ring-size, stereochemistry or a thermodynamic Thorpe–Ingold effect.[19,20] We are now looking at applying these cyclisation reactions to the synthesis of C_2-symmetrical *bis*-THFs (*e.g.* **40**) and *bis*-THPs (*e.g.* **41**), which may be interesting compounds in their own right (Fig. 4).

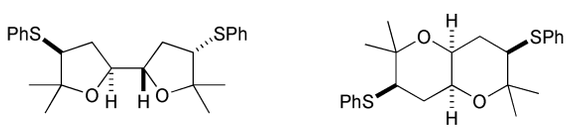


Fig. 4 C_2-symmetrical *bis*-THF and THPs.

Experimental

All solvents were distilled before use. Tetrahydrofuran and diethyl ether were freshly distilled from lithium aluminium hydride whilst dichloromethane and acetonitrile were freshly distilled from calcium hydride. Triphenylmethane was used as an indicator for tetrahydrofuran. Pyridine was dried by distillation from calcium hydride and was stored over 4 Å molecular sieves. All non-aqueous reactions were carried out under argon using oven-dried glassware.

Flash column chromatography was carried out using Merck Kieselgel 60 (230–400 mesh). Thin layer chromatography was performed on commercially available pre-coated plates (Merck silica Kieselgel $60F_{254}$). Preparative HPLC was performed using a Zorbax SIL prepacked silica column (21.2 mm id × 25 cm) with a Gilson model 303 pump and a Cecil Instruments CE 212A UV detection system measuring the absorbance at 254 nm. Analytical HPLC was performed using either a Zorbax RX-C8 prepacked reverse phase silica column or a Daicel Chiralpak AD column with a Spectra-Physics SP8800 pump, a Spectra-Physics SP8450 UV detection system and a ChromJet single channel integrator.

Proton and carbon NMR spectra were recorded on Bruker DPX 250, AM 400, DRX 400 or DRX 500 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million (ppm) downfield of tetramethylsilane. Coupling constants J are quoted in Hz and are not rationalised. The symbol* after the proton NMR chemical shift indicates that the signal disappears after a D_2O "shake". Carbon NMR spectra were recorded with broad band proton decoupling and Attached Proton Test. The symbols $^+$ and $^-$ after the carbon NMR chemical shift indicate odd and even numbers of attached protons respectively.

Melting points were measured on a Stuart Scientific SMP1 melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer 1600 FTIR spectrophotometer. Electron Impact (EI) mass spectra were recorded on a Kratos double focusing magnetic sector instrument using a DS503 data system for high-resolution analysis. Fast atom bombardment (FAB) mass spectra were obtained from a Kratos MS 890 instrument. Electrospray (+ES) mass spectra were recorded using a Brucker Bio-Apex FT-ICR instrument and LCMS using a Hewlett Packard HPLC system, eluting with an acetonitrile-water gradient, in conjunction with positive and negative ion electrospray mass spectrometry.

Optical rotations were recorded on a Perkin–Elmer 241 polarimeter (using the sodium D line; 589 nm) and $[a]_D$ are given in units of 10^{-1} deg dm^2 g^{-1}.

(3*RS*,5*SR*)-2,2-Dimethyl-3-phenylsulfanyltetrahydrofuran-5-ylmethanol 3

Toluene-*p*-sulfonic acid (1.7 mg, 9.0 μmol, 5 mol%) was added to a stirred solution of the *anti*-triol **5** (50 mg, 195 μmol) in dichloromethane (2.5 cm^3). The reaction temperature was raised to 50 °C to initiate reflux and heating continued for 48 hours. The mixture was cooled to room temperature and then filtered through a short plug of silica, eluting with dichloromethane, and the solvent was evaporated under reduced pressure to give a crude product. Purification by column chromatography [light petroleum (bp 40–60 °C)–diethyl ether, 1:1] gave the *^{3,5}anti-tetrahydrofuran* **3** (42 mg, 90%) after 48 hours as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 1:1] 0.12; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3593 (O–H), 3052, 2978, 2929, 2879, 1583, 1480, 1420, 1382, 1369, 1142, 1091, 1034 and 896; δ_H(250 MHz; $CDCl_3$) 7.44–7.19 (5 H, m, PhS), 4.17 (1 H, dtd, J 8.3, 4.8 and 3.3 Hz, CH–O), 3.68 (1 H, ddd, J 11.5, 5.3 and 3.0 Hz, CH_AH$_B$OH), 3.46 (1 H, ddd, J 11.8, 7.3 and 4.8 Hz, CH$_A$-H_BOH), 3.36 (1 H, dd, J 9.5 and 8.5 Hz, CHSPh), 2.34 (1 H, ddd, J 13.0, 8.3 and 4.8 Hz, CH_AH$_B$), 2.13 (1 H, ddd, J 13.0, 9.3 and 8.5 Hz, CH$_A$$H_B$), 2.03* (1 H, dd, J 7.0 and 5.8 Hz, OH), 1.29 (3 H, s, Me$_A$) and 1.27 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$) 135.6$^-$ (*i*-PhS), 131.2$^+$, 129.0$^+$, 126.9$^+$ (*p*-PhS), 83.6$^-$ (C–O), 75.6$^+$ (CHOH), 65.2$^-$ (CH_2OH), 55.1$^+$ (CHSPh), 35.7$^-$ (CH_2), 27.5$^+$ (Me) and 22.2$^+$ (Me); *m*/*z* (EI) 238 (41%, M$^+$), 207 (22, M$^+$ − CH_2OH), 180 (94, M$^+$ − Me_2CO), 169 (26), 149 (100, $C_3H_4SPh^+$), 131 (82) and 119 (61); (Found: M$^+$, 236.1027. $C_{13}H_{18}O_2S$ requires M, 238.1027).

(2*R*,4*R*)-5-Methyl-5-phenylsulfanylhexane-1,2,4-triol 5

Glacial acetic acid (20 cm^3) was added to a stirred suspension of tetramethylammonium triacetoxyborohydride[12] (8.0 g, 30.4

mmol, 10 eq.) in acetonitrile (20 cm^3) and the resulting mixture stirred for 30 minutes at room temperature to give a colourless solution. This solution was cooled to −30 °C and a solution of β-hydroxyketone **20** (1.00 g, 3.93 mmol) in acetonitrile (5 cm^3) was added. The solution was then transferred to a freezer (–25 °C) for 1 week. The reaction was quenched by addition of aqueous sodium potassium tartrate solution (1.0 mol dm^{-3}, 10 cm^3) and the mixture allowed to warm slowly to room temperature. The reaction mixture was then diluted with dichloromethane (10 cm^3) and washed with saturated aqueous sodium bicarbonate solution. The aqueous layer was extracted with dichloromethane (4 × 10 cm^3), the combined organic layers dried over anhydrous magnesium sulfate and the solvent removed under vacuum to give a crude product. Purification by column chromatography (silica, ethyl acetate) gave *syn*-triol **8** (56 mg, 6%) as an oil, R_f(ethyl acetate) 0.23 (see below) and *anti-triol* **5** (880 mg, 87%) as a white amorphous solid; R_f(ethyl acetate) 0.13; retention time/min (isocratic HPLC 62:38 MeCN:H_2O; 0.1% CF_3CO_2H, 0.1% Et_3N; flow rate 1 cm^3 min^{-1}) 5.58; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3615 (O–H), 3472 (O–H), 3059, 2934 and 2856; δ_H(400 MHz; $CDCl_3$) 7.54–7.46 (2 H, m, PhS), 7.42–7.29 (3 H, m, PhS), 4.02–3.93 (1 H, m, C*H*OH), 3.66 (1 H, ddd, *J* 10.9, 6.7 and 3.6 Hz, CH_AH_BOH), 3.61 (1 H, dt, *J* 10.4 and 2.2 Hz, PhSCC*H*OH), 3.54 (1 H, ddd, *J* 11.3, 6.8 and 5.1 Hz, CH$_A$$H_B$OH), 3.23* (1 H, s, OH), 2.59* (1 H, d, *J* 5.5 Hz, OH), 2.14* (1 H, t, *J* 5.8 Hz, CH_2OH), 1.66 (1 H, ddt, *J* 13.9, 7.8 and 2.0 Hz, CH_AH_B), 1.56 (1 H, ddd, *J* 14.1, 10.4 and 4.2 Hz, CH$_A$$H_B$), 1.25 (3 H, s, Me$_A$) and 1.21 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$) 137.4$^+$ (*m*-PhS), 130.1$^-$ (*i*-PhS), 129.4$^+$ (*p*-PhS), 128.9$^+$ (*o*-PhS), 71.7$^+$ (CHOH), 70.2$^+$ (CHOH), 66.8$^-$ (CH_2OH), 55.2$^-$ (CSPh), 33.4$^-$ (CH_2), 25.7$^+$ (Me) and 22.0$^+$ (Me); *m*/*z* (+FAB) 279 (20%, MNa^+), 257 (17, MH^+), 239 (94), 154 (97), 151 (100, Me_2CSPh^+), 136 (82), 129 (100) and 110 (37, $PhSH^+$); (Found: MNa^+, 279.1014. $C_{13}H_{20}O_3SNa$ requires 279.1025).

(1*R*,3*R*)-[1-(Phenylsulfanyl)cyclohexyl]butane-1,3,4-triol 6

By the method described for compound **5**, glacial acetic acid (7.5 cm^3), tetramethylammonium triacetoxyborohydride (3.58 g, 13.6 mmol, 8 eq.) in acetonitrile (7.5 cm^3) and β-hydroxyketone **21** (500 mg, 1.70 mmol) in acetonitrile (2 cm^3) gave a crude product after one week. Purification by column chromatography (silica, ethyl acetate) gave *syn*-triol **9** (see below) (40 mg, 8%) as an oil; R_f(ethyl acetate) 0.22 and *anti-triol* **6** (437 mg, 87%) as an amorphous white solid; R_f(ethyl acetate) 0.32; retention time/min (isocratic HPLC 62:38 H_2O:MeCN; 0.1% CF_3CO_2H, 0.1% Et_3N; flow rate 1 cm^3 min^{-1}) 14.01; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3615 (O–H), 3472 (O–H), 3069, 2936 and 2856; δ_H(400 MHz; $CDCl_3$) 7.54–7.50 (2 H, m, PhS), 7.43–7.30 (3 H, m, PhS), 4.01–3.93 (1 H, m, C*H*OH), 3.64 (1 H, ddd, *J* 11.0, 6.8 and 3.6 Hz, CH_AH_BOH), 3.61 (1 H, dt, *J* 10.6 and 2.3 Hz, PhSCCHOH), 3.53 (1 H, ddd, *J* 11.8, 6.9 and 5.2 Hz, CH$_A$$H_B$OH), 3.24* (1 H, s, OH), 2.59* (1 H, d, *J* 5.5 Hz, OH); 2.14* (1 H, t, *J* 6.0 Hz, OH), 2.06–1.14 (12 H, m); δ_C(100.6 MHz; $CDCl_3$) 137.2$^+$, 129.9$^-$ (*i*-PhS), 129.2$^+$, 129.0$^+$, 71.4$^+$ (CHOH), 70.3$^+$ (CHOH), 66.8$^-$ (CH_2OH), 61.4$^-$ (CSPh), 33.4$^-$, 30.5$^-$, 29.6$^-$, 26.2$^-$, 21.8$^-$ and 21.8$^-$; *m*/*z* (EI) 296 (5%, M^+), 278 (12), 191 (100, $C_6H_{10}SPh^+$), 181 (33), 169 (37), 149 (19), 131 (76), 119 (56) and 110 (52, $PhSH^+$); (Found: M^+, 296.1443. $C_{16}H_{24}O_3S$ requires *M*, 296.1446).

(1*R*,3*R*)-1-[4-(Phenylsulfanyl)tetrahydropyran-4-yl]butane-1,3,4-triol 7

By the method described for compound **5**, glacial acetic acid (5 cm^3), tetramethylammonium triacetoxyborohydride (2.35 g, 8.96 mmol, 8 eq.) in acetonitrile (5 cm^3) and β-hydroxyketone **22** (330 mg, 1.12 mmol) in acetonitrile (1.6 cm^3) gave a crude product after one week. Purification by column chromatography (silica, ethyl acetate–methanol 49:1) gave the *anti-triol* **7** as an oil (90 mg, 27%); R_f(ethyl acetate–methanol, 49:1) 0.28; $[\alpha]_D$ +8.8 (*c*. 0.49 in $CHCl_3$; 78% ee); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3610 (O–H), 3472 (O–H), 2961 (C–H), 2869 (C–H), 1582 (PhS) and 1102 (C–O); δ_H(400 MHz; $CDCl_3$) 7.52–7.45 (2 H, m, PhS), 7.38–7.30 (3 H, m, PhS), 4.05 (1 H, dd, *J* 11.5 and 2.0 Hz, OCH_{eq}H$_{ax}$), 4.00–3.97 (2 H, m, OCH$_{eq}$$H_{ax}$), 3.83–3.77 (2 H, m, C*H*OHCH$_2$C*H*OH), 3.66 (1 H, dd, *J* 7.5 and 3.5 Hz, CH_AH_BOH) 3.69 (1 H, br dd, *J* 10.5 and 2.0 Hz, OCH_{eq}H$_{ax}$), 3.54 (1 H, dd, *J* 11.0 and 7.5 Hz, CH$_A$$H_B$OH), 3.30 (1 H, br s, OH), 2.83 (1 H, br s, OH), 2.47 (1 H, br s, OH), 1.95 (1 H, ddd, *J* 14.5, 11.5 and 5.0 Hz, CCH$_{eq}$$H_{ax}$), 1.83–1.78 (2 H, m, C$H_2$CHOH), 1.62 (1 H, ddd, *J* 14.5, 10.5 and 4.0 Hz, CCH$_{eq}$$H_{ax}$), 1.48 (1 H, br dd, *J* 14.5 and 2.0 Hz, CCH_{eq}H$_{ax}$) and 1.31 (1 H, br dd, *J* 14.5 and 2.0 Hz, CCH_{eq}H$_{ax}$); δ_C(100.6 MHz; $CDCl_3$) 137.9$^+$ (PhS), 130.2$^-$ (*i*-PhS), 129.7$^+$ (*p*-PhS), 129.4$^+$ (PhS), 72.5$^+$ (CHOH), 70.2$^+$ (CHOH), 67.4$^-$ (CH_2OH), 64.1$^-$(*C*H_2O*C*H$_2$), 64.0$^-$ (CH$_2$O*C*H$_2$), 57.2$^-$ (CSPh), 34.0$^-$ (*C*H$_2$CHOH), 30.4$^-$ (*C*H$_2$C*C*H$_2$); *m*/*z* (EI) 298 (36%, M^+), 193 (M^+–$C_4H_9O_3$), 153 (96, M^+–PhS–2 × H_2O), 135 (56, M^+–PhS–3 × H_2O); (Found: M^+, 298.1238. $C_{15}H_{22}O_4S$ requires *M*, 298.1239).

(2*R*,4*S*)-5-Methyl-5-phenylsulfanylhexane-1,2,4-triol 8

A 1.0 mol dm^{-3} solution of diethylmethoxyborane[13] in tetrahydrofuran (2.0 cm^3, 0.3 mmol) was added to a solution of β-hydroxyketone **20** (500 mg, 1.97 mmol) in tetrahydrofuran–methanol (4:1) (50 cm^3) at −78 °C, under an atmosphere of argon. The mixture was stirred for 5 minutes and then sodium borohydride (94.6 mg, 2.50 mmol) was added and the solution allowed to stir for 8 hours. Glacial acetic acid (3 cm^3) was added and stirring continued for a further 5 minutes. The solution was then neutralised with saturated aqueous sodium bicarbonate solution (30 cm^3) and extracted with diethyl ether (3 × 15 cm^3). The organic extracts were dried over anhydrous magnesium sulfate and the solvent was removed under reduced pressure to give a crude product. This product was redissolved in methanol (5 cm^3) and stirred for 5 minutes before removing the methanol under reduced pressure. This cycle was repeated until TLC showed no spots with R_f(diethyl ether) > 0.5. The crude product was purified by column chromatography (silica, ethyl acetate) to give *anti-triol* **5** (54 mg, 11%) as a white solid, R_f(ethyl acetate) 0.13 (see above) and *syn-triol* **8** (399 mg, 79%) as an oil; R_f(ethyl acetate) 0.24; retention time/min (isocratic HPLC 62:38 MeCN:H_2O; 0.1% CF_3CO_2H, 0.1% Et_3N; flow rate 1 cm^3 min^{-1}) 6.75; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3486 (O–H), 3057, 2982, 2931, 2874 and 1422; δ_H(400 MHz; $CDCl_3$) 7.55–7.46 (2 H, m, PhS), 7.44–7.28 (3 H, m, PhS), 3.94* (1 H, s, OH), 3.93–3.83 (1 H, m, C*H*OH), 3.65* (1 H, s, OH), 3.65–3.53 (2 H, m, CH_AH_BOH and PhSCC*H*OH), 3.48 (1 H, dt, *J* 11.3 and 5.7 Hz, CH$_A$$H_B$OH), 2.25* (1 H, t, *J* 6.2 Hz, CH_2OH), 1.67–1.53 (2 H, m, CH_AH_B and CH$_A$$H_B$), 1.26 (3 H, s, Me$_A$) and 1.19 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$) 137.4$^+$ (*m*-PhS), 129.9$^-$ (*i*-PhS), 129.4$^+$ (*p*-PhS), 128.9$^+$ (*o*-PhS), 75.4$^+$ (CHOH), 72.2$^+$ (CHOH), 66.7$^-$ (CH_2OH), 55.1$^-$ (CSPh), 32.8$^-$ (CH_2), 25.6$^+$ (Me) and 21.8$^+$ (Me); *m*/*z* (+FAB) 279 (100%, MNa^+), 257 (3, MH^+), 239 (27), 151 (38, Me_2CSPh^+), 129 (33), 110 (15, $PhSH^+$) and 77 (25); (Found: MNa^+, 279.1015. $C_{13}H_{20}O_3SNa$ requires 279.1025).

(1*S*,3*R*)-[1-(Phenylsulfanyl)cyclohexyl]butane-1,3,4-triol 9

By the method described for compound **8**, diethylmethoxyborane (1.1 cm^3 of a 1.0 mol dm^{-3} solution in tetrahydrofuran, 1.1 mmol), β-hydroxyketone **21** (300 mg, 1.02 mmol) in tetrahydrofuran–methanol (4:1) (20 cm^3) and sodium borohydride (76.5 mg, 2.03 mmol) gave a crude product. Purification by column chromatography (silica, ethyl acetate) gave *anti-triol* **6** (45 mg, 15%) as an oil; R_f(ethyl acetate) 0.30 and *syn-triol* **9** (226 mg, 75%) as an oil; R_f(ethyl acetate) 0.22; retention time/min (isocratic HPLC 62:38 H_2O:MeCN; 0.1% CF_3CO_2H, 0.1%

Et_3N; flow rate 1 cm^3 min^{-1}) 17.77; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3686 (O–H), 3599 (O–H), 3056, 2986, 2937, 2860, 1605, 1474 and 1394; δ_H(400 MHz; $CDCl_3$) 7.53–7.47 (2 H, m, PhS), 7.42–7.31 (3 H, m, PhS), 3.94* (1 H, s, OH), 3.90–3.83 (1 H, m, C*H*OH), 3.75* (1 H, s, OH), 3.62 (1 H, ddd, *J* 10.9, 6.3 and 3.8 Hz, CH_AH_BOH), 3.58–3.52 (1 H, m, PhSCC*H*OH), 3.49 (1 H, dt, *J* 11.3 and 5.8 Hz, CH_AH_BOH), 2.14* (1 H, t, *J* 6.2 Hz, CH_2OH), 2.02 (1 H, qt, *J* 12.8 and 3.9 Hz), 1.89–1.52 (8 H, m) and 1.45–1.14 (3 H, m); δ_C(100.6 MHz; $CDCl_3$) 137.3$^+$, 129.7$^-$ (*i*-PhS), 129.3$^+$, 129.0$^+$, 75.1$^+$ (CHOH), 72.4$^+$ (CHOH), 66.8$^-$ (CH_2OH), 61.3$^-$ (CSPh), 32.8$^-$, 30.2$^-$, 29.2$^-$, 26.2$^-$, 21.8$^-$ and 21.7$^-$; *m*/*z* (+FAB) 296 (16%, M^+), 279 (64, $M^+ - OH$), 169 (73), 154 (100) and 109 (34); (Found: M^+, 296.1446. $C_{16}H_{24}O_3S$ requires *M*, 296.1446).

(1*S*,3*R*)-1-[4-(Phenylsulfanyl)tetrahydropyran-4-yl]butane-1,3,4-triol 10

By the method described for compound **8**, diethylmethoxyborane (2.3 cm^3 of a 1.0 mol dm^{-3} solution in tetrahydrofuran, 2.3 mmol), β-hydroxyketone **22** (599 mg, 2.10 mmol) in tetrahydrofuran–methanol (4:1) (40 cm^3) and sodium borohydride (159 mg, 4.20 mmol) gave a crude product after 8 hours. Purification by column chromatography (silica, ethyl acetate, 4% methanol) gave the *syn-triol* **10** as an oil (0.21g, 33%); R_f(ethyl acetate–methanol, 24:1) 0.40; $[a]_D$ −10.7 (*c*. 0.6 in $CHCl_3$; 78% ee); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3610 (O–H), 2962 (C–H), 2870 (C–H) and 1103 (C–O); δ_H(400 MHz; $CDCl_3$) 7.49–7.43 (2 H, m, PhS), 7.36–7.27 (3 H, m, PhS), 4.03 (1 H, dd, *J* 11.5 and 2.0 Hz, $OCH_{ax}H_{eq}$), 3.96 (1 H, dd, *J* 11.5 and 2.0 Hz, $OCH_{ax}H_{eq}$), 3.91–3.84 (1 H, m, CH_2CHOH), 3.80–3.72 (2 H, m, $OCH_{ax}H_{eq}$), 3.83–3.74 (2 H, m, CH_AH_BOH and CC*H*OH), 3.49 (1 H, dd, *J* 11.0 and 6.0 Hz, CH_AH_BOH), 1.96 (1 H, ddd, *J* 14.0, 12.0 and 5.5 Hz, CH_AH_BCHOH), 1.83 (1 H, br d, *J* 14.0 Hz, CH_AH_BCHOH), 1.83 (1 H, ddd, *J* 14.0, 12.0 and 5.0 Hz, CCH_AH_B), 1.63 (1 H, dt, *J* 14.0 and 10.0 Hz, $CCH_{ax}H_{eq}$), 1.40 (1 H, dd, *J* 12.0 and 1.5 Hz, $CCH_{ax}H_{eq}$) and 1.23 (1 H, dd, *J* 14.5 and 1.5 Hz, $CCH_{ax}H_{eq}$); δ_C(100.6 MHz; $CDCl_3$) 136.5$^+$ (PhS), 128.5$^-$ (*i*-PhS), 128.4$^+$ (*p*-PhS), 128.1$^+$ (PhS), 74.5$^+$ (CH_2CHOH), 71.5$^+$ (CCHOH), 65.7$^-$ (CH_2OH), 62.8$^-$ (CH_2OCH_2), 62.5$^-$ (CH_2OCH_2), 56.2$^-$ (CSPh), 28.8$^-$ (CH_2CCH_2) and 28.5$^-$ (CH_2CCH_2); *m*/*z* (+ES) 321 (100%, MNa^+); (Found: MNa^+, 321.1144. $C_{15}H_{22}O_4SNa$ requires *M*, 321.1137).

(2*RS*,4*SR*)-5-Methyl-5-phenylsulfanylhexane-1,2,4-triol 5 and (2*RS*,4*RS*)-5-Methyl-5-phenylsulfanylhexane-1,2,4-triol 8

Potassium ferricyanide (26.4 g, 80.0 mmol, 3 eq.), potassium carbonate (11.1 g, 80.0 mmol, 3 eq.), osmium(III) chloride hydrate (59.4 mg, 20 μmol, 0.7 mol%) and quinuclidine (105 mg, 944 μmol, 3.5 mol%) were placed in a round bottom flask and stirred gently. Water (140 cm^3) and 2-methylpropan-2-ol (140 cm^3) were added, the flask was sealed and the solution stirred vigorously. Once the solids had completely dissolved the alkene **14** (6.00 g, 27.0 mmol) was added in one portion. Stirring was continued until TLC or LCMS indicated complete consumption of starting material. Sodium sulfite was then added in one portion (121 g, 960 mmol) and stirring continued for a further 30 minutes. The solution was transferred to a separating funnel, diluted with ethyl acetate (200 cm^3) and the aqueous layer separated. The aqueous layer was then extracted with ethyl acetate (3 × 150 cm^3). The combined organic extracts were washed with water (200 cm^3) and brine (200 cm^3), dried over anhydrous magnesium sulfate and finally, the solvent was evaporated under reduced pressure to give a crude product. Analytical HPLC (isocratic 38:62 MeCN:H_2O; 0.1% CF_3CO_2H, 0.1% Et_3N; flow rate 1 cm^3 min^{-1}) indicated an *anti*:*syn* mixture of 43:57 (retention times: 5.66 min, 6.64 min, respectively). Purification by column chromatography (silica, ethyl acetate) gave *syn-triol* **7** (3.53 g, 51%) as an oil; R_f(ethyl acetate) 0.24, spectroscopically identical to the enantiomerically enriched sample and *anti-triol* **5** (2.98 g, 43%) as a white amorphous solid. Crystallisation from chloroform gave *anti-triol* **5** as needles, mp 108–109 °C (from chloroform); R_f(ethyl acetate) 0.13, spectroscopically identical to the enantiomerically enriched sample.

(2*RS*,4*SR*)-[1-(Phenylsulfanyl)cyclohexyl]butane-1,2,4-triol 6 and (2*RS*,4*RS*)-[1-(Phenylsulfanyl)cyclohexyl]butane-1,2,4-triol 9

By the method described for triols **5** and **8**, potassium ferricyanide (1.86 g, 5.66 mmol, 3 eq.), potassium carbonate (0.782 g, 5.66 mmol, 3 eq.), osmium(III) chloride hydrate (4.2 mg, 14 μmol, 0.7 mol%), quinuclidine (7.4 mg, 67 μmol, 3.5 mol%) and alkene **15** (500 mg, 1.91 mmol) in 2-methylpropan-2-ol (10 cm^3) and water (10 cm^3) gave a crude product. Analytical HPLC (isocratic 38:62 MeCN:H_2O; 0.1% CF_3CO_2H, 0.1% Et_3N; flow rate 1 cm^3 min^{-1}) indicated an *syn*:*anti* mixture of 58:42 (retention times: 4.20 min, 4.74 min, respectively). Purification by column chromatography (silica, ethyl acetate) gave *anti-triol* **6** (215 mg, 38%) as a white amorphous solid; R_f(ethyl acetate) 0.32, spectroscopically identical to the enantiomerically enriched sample and *syn-triol* **9** (288 mg, 51%) as an oil; R_f(ethyl acetate) 0.22, spectroscopically identical to the enantiomerically enriched sample.

(3*RS*)-2-Methyl-2-phenylsulfanylhex-5-en-3-ol 14

A solution of allylmagnesium bromide in diethyl ether (1.0 mol dm^{-3}, 56 cm^3, 56 mmol) was added to a stirred solution of aldehyde **11** (9.92 g, 55 mmol) in diethyl ether (100 cm^3) at 0 °C under an atmosphere of argon. After the addition was complete the reaction was allowed to warm to room temperature and stirring continued for 2 hours. Saturated aqueous ammonium chloride solution (80 cm^3) was added and the product was extracted with diethyl ether (3 × 50 cm^3). The combined organic extracts were washed with water (70 cm^3) and saturated brine (70 cm^3) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure to give a crude product which was purified by column chromatography [silica, light petroleum (40–60 °C)–diethyl ether, 9:1] to give the *alcohol* **14** (12.1 g, 99%) as a pale yellow oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.17; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3478 (O–H), 3078, 2934, 2856, 1640 (C=C) and 1583 (PhS); δ_H(250 MHz; $CDCl_3$) 7.55–7.51 (2 H, m, PhS), 7.39–7.30 (3 H, m, PhS), 5.90–5.81 (1 H, m, C*H*=CH_2), 5.16–5.06 (2 H, m, CH=CH_2), 3.38 (1 H, td, *J* 10.0 and 2.4 Hz, C*H*OH), 2.83* (1 H, dd, *J* 2.2 and 1.3 Hz, OH), 2.35–2.23 (1 H, m, $CH_AH_BCH{=}CH_2$), 2.21–2.14 (1 H, m, $CH_AH_BCH{=}CH_2$), 1.28 (3 H, s, Me_A) and 1.23 (3 H, s, Me_B); δ_C(100.6 MHz; $CDCl_3$) 137.5$^+$, 136.1$^+$, 130.4$^-$ (*i*-PhS), 129.2$^+$, 128.8$^+$, 117.0$^-$ (CH=CH_2), 74.6$^+$ (COH), 55.0$^-$ (CSPh), 35.5$^-$ ($CH_2CH{=}CH_2$), 25.6$^+$ (Me_A) and 22.5$^+$ (Me_B); *m*/*z* (EI) 222 (10%, M^+), 181 (9, $Me_2C(SPh)CHOH^+$), 151 (100, Me_2CSPh^+), 110 (91, $PhSH^+$), 95 (26) and 71 (29); (Found: M^+, 222.1078. $C_{13}H_{18}OS$ requires *M*, 222.1078).

(1*RS*)-1-[1-(Phenylsulfanyl)cyclohexyl]but-3-en-1-ol 15

By the method described for compound **14**, a solution of allylmagnesium bromide in diethyl ether (1.0 mol dm^{-3}, 40 cm^3, 40 mmol) and aldehyde **12** (8.80 g, 40 mmol) in diethyl ether (150 cm^3) gave a crude product which was purified by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 9:1] to give the *alcohol* **15** (10.06 g, 96%) as a pale yellow oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.17; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3495 (O–H), 3074, 2971, 2931, 2870, 1641 (C=C) and 1582 (PhS); δ_H(500 MHz; $CDCl_3$) 7.55–7.50 (2 H, m, PhS), 7.39–7.29 (3 H, m, PhS), 5.89 (1 H, ddt, *J* 17.1, 10.1 and 6.9 Hz, C*H*=CH_2), 5.11 (1 H, dd, *J* 17.3 and 1.5 Hz, CH=C$H_{trans}H_{cis}$), 5.08 (1 H, d, *J* 10.6 Hz, CH=C$H_{trans}H_{cis}$), 3.35 (1 H,

d, *J* 10.0 Hz, C*H*OH), 2.89* (1 H, s, OH), 2.47 (1 H, dd, *J* 14.1 and 5.4 Hz, CH_AH_B), 2.25–2.17 (1 H, m, CH$_A$*H*$_B$) 1.97 (1 H, qt, *J* 12.9 and 3.8 Hz), 1.85 (1 H, qt, *J* 12.2 and 3.4 Hz), 1.79–1.48 (6 H, m, 6 × CH_2), 1.44–1.36 (1 H, m) and 1.23 (1 H, qt, *J* 12.5 and 3.8 Hz); δ_C(100.6 MHz; $CDCl_3$) 137.3$^+$, 136.5$^+$, 130.2$^-$ (*i*-PhS), 129.0$^+$, 128.9$^+$, 116.8$^-$ (CH=*C*H$_2$), 74.3$^+$ (COH), 60.9$^-$ (CSPh), 35.5$^-$, 30.5$^-$, 29.9$^-$, 26.2$^-$ and 21.8$^-$; *m*/*z* (EI) 262 (3%, M^+), 203 (3), 191 (66, $C_6H_{10}SPh^+$), 135 (27), 110 (73, $PhSH^+$) and 83 (100) and 91 (98); (Found: M^+, 262.1387. $C_{16}H_{22}OS$ requires *M*, 262.1391).

(1*RS*)-1-[4-(Phenylsulfanyl)tetrahydropyran-4-yl]but-3-en-1-ol 16

By the method described for compound **14**, allylmagnesium bromide in diethyl ether (1.0 mol dm^{-3}, 35 cm^3, 0.035 mol, 1.2 eq.) and aldehyde **13** (6.39g, 0.029 mol) in dry tetrahydrofuran (120 cm^3) gave a crude product which was recrystallised from chloroform to give the *alcohol* **16** as prisms (5.15g, 68%), mp 84–86 °C (chloroform); R_f[light petroleum (bp 40–60 °C)–diethyl ether, 1:1] 0.21; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3579 (O–H), 3070 (C–H), 3040 (C–H), 2962 (C–H), 2867 (C–H), 1640 (C=C) and 1104 (C–O); δ_H(400 MHz; $CDCl_3$) 7.50–7.48 (2 H, m, PhS), 7.36–7.25 (3 H, m, PhS), 5.87 (1 H, dddd, *J* 16.0, 10.0, 7.0 and 7.0 Hz, *H*C=CH$_2$), 5.16–5.10 (2 H, m, HC=C*H*$_2$), 4.04–3.98 (2 H, m, CH_AH_BO), 3.83–3.80 (2 H, m, CH$_A$*H*$_B$O), 3.39 (1 H, dt, *J* 10.0 and 3.0 Hz, C*H*OH), 2.74 (1 H, d, *J* 3.0 Hz, OH), 2.55 (1 H, br dd, *J* 14.0 and 6.0 Hz, CHCH_AH_B), 2.26–2.17 (1 H, m, CHCH$_A$*H*$_B$), 2.02 (1 H, ddd, *J* 14.5, 11.5 and 5.0 Hz, CC$H_{ax}H_{eq}$), 1.86 (1 H, ddd, *J* 14.5, 11.5 and 5.0 Hz, CC$H_{ax}H_{eq}$), 1.48 (1 H, dd, 14.5 and 2.0 Hz, CCH$_{ax}$*H*$_{eq}$) and 1.34 (1 H, dd, *J* 14.5 and 2.0 Hz, CCH$_{ax}$*H*$_{eq}$); δ_C(100.6 MHz; $CDCl_3$), 137.9$^+$ (PhS), 136.4$^+$ (*C*H=CH$_2$), 130.1$^-$ (*i*-PhS), 129.7$^+$ (*p*-PhS), 129.4$^+$ (PhS), 117.7$^-$ (CH=*C*H$_2$), 75.0$^+$ (CHOH), 64.2$^-$ (*C*H$_2$OCH$_2$), 64.0$^-$ (CH$_2$O*C*H$_2$), 57.8$^-$ (CSPh), 35.9$^-$ (*C*H$_2$CHOH), 30.6$^-$ (*C*H$_2$CCH$_2$) and 30.3$^-$ (CH$_2$C*C*H$_2$); *m*/*z* (EI) 264 (46%, M^+), 193 (100, $M^+ - C_4H_6O$), 137 (47, $M^+ - PhS - H_2O$), 109 (45, PhS^+) and 83 (39, $C_5H_7O^+$); (Found: M^+, 264.1194. $C_{15}H_{20}O_2S$ requires *M*, 264.1184); (Found: C, 68.19; H, 7.58. $C_{15}H_{20}O_2S$ requires C, 68.15; H, 7.63%).

2-Methyl-2-phenylsulfanylhex-5-en-3-one 17

Alcohol **14** (8.00 g, 36.0 mmol) was added in one portion, under argon at 0 °C to a stirred solution of pyridinium chlorochromate (PCC)[10] (10.1 g, 46.8 mmol) in dichloromethane (150 cm^3). The solution was allowed to warm to room temperature and stirred until the reaction was judged complete by TLC. Dry diethyl ether (50 cm^3) was added and the supernatant liquor decanted from a black gum. The insoluble residues were washed 5 times with ether (50 cm^3) and the combined ethereal extracts were filtered through a plug of florisil, which was washed with more diethyl ether. The solvent was removed under reduced pressure to give a crude product as a pale yellow–green oil. Purification by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 9:1] gave the *ketone* **17** (6.66 g, 84%) as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.35; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3080, 2972, 2931, 1701 (C=O), 1642 (C=C) and 1584 (PhS); δ_H(250 MHz; $CDCl_3$) 7.38–7.25 (5 H, m, PhS), 6.05–5.92 (1 H, m, C*H*=CH$_2$), 5.23–5.14 (2 H, m, CH=C*H*$_2$), 3.59 (2 H, dt, *J* 6.8 and 1.5 Hz, CH$_2$CO) and 1.40 (6 H, s, 2 × Me); δ_C(100.6 MHz; $CDCl_3$) 205.7$^-$ (C=O), 136.2$^+$, 131.8$^+$, 131.0$^-$ (*i*-PhS), 129.3$^+$, 129.0$^+$, 118.2$^-$ (CH=*C*H$_2$), 56.4$^-$ (CSPh), 41.0$^-$ (*C*H$_2$C=O) and 24.3$^+$ (2 × Me); *m*/*z* (EI) 220 (8%, M^+), 151 (100, Me_2CSPh^+), 110 (14, $PhSH^+$), 109 (14, PhS^+), 84 (35) and 73 (17); (Found: M^+, 220.0923. $C_{13}H_{16}OS$ requires *M*, 220.0922).

1-[1-(Phenylsulfanyl)cyclohexyl]but-3-en-1-one 18

By the method described for compound **17**, alcohol **15** (10.0 g, 38 mmol) and pyridinium chlorochromate (10.8 g, 50 mmol) in dichloromethane (100 cm^3) gave a crude product as a pale green oil. Purification by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 9:1] gave the *ketone* **18** (8.04 g, 81%) as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.39; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3052, 2838, 2858, 1697 (C=O) and 1641 (C=C); δ_H(250 MHz; $CDCl_3$) 7.34–7.24 (5 H, m, PhS), 6.03 (1 H, ddt, *J* 17.1, 10.3 and 6.9 Hz, C*H*=CH$_2$), 5.21 (1 H, dd, *J* 10.1 and 1.4 Hz, CH=CH$_{trans}H_{cis}$), 5.19 (1 H, dd, *J* 17.1 and 1.6 Hz, CH=CH$_{trans}H_{cis}$), 3.57 (2 H, dt, *J* 6.8 and 1.0 Hz, CH$_2$C=O), 1.99–1.91 (2 H, m, CH$_2$), 1.82–1.64 (4 H, m, 2 × CH$_2$), 1.49–1.38 (2 H, m, CH$_2$) and 1.38–1.26 (2 H, m, CH$_2$); δ_C(100.6 MHz; $CDCl_3$) 204.4$^-$ (C=O), 136.5$^+$, 132.0$^+$, 130.0$^-$ (*i*-PhS), 129.3$^+$, 128.8$^+$, 118.1$^-$ (CH=*C*H$_2$), 61.2$^-$ (CSPh), 41.0$^-$, 32.5$^-$, 25.5$^-$ and 23.1$^-$; *m*/*z* (EI) 260 (4%, M^+), 191 (100, $C_6H_{10}SPh^+$), 123 (16), 110 (9, $PhSH^+$) and 81 (44); (Found: M^+, 260.1242. $C_{16}H_{20}OS$ requires *M*, 260.1235).

1-[4-(Phenylsulfanyl)tetrahydropyran-4-yl]but-3-en-1-one 19

By the method described for compound **17**, the alcohol **16** (2.21 g, 8.4 mmol) and pyridinium chlorochromate (2.71 g, 12.5 mmol) in dichloromethane (25 cm^3) gave a crude product. Purification by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 9:1] gave the *ketone* **19** as an oil (1.709 g, 78%); R_f[light petroleum (bp 40–60 °C)–diethyl ether, 3:1] 0.23; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3073 (C–H), 3041 (C–H), 2931 (C–H), 2867 (C–H), 1699 (C=O), 1641 (C=C), 1576 (PhS) and 1104 (C=O); δ_H(400 MHz; $CDCl_3$) 7.34–7.25 (5 H, m, PhS), 6.00 (1 H, ddt, *J* 17.0, 10.0 and 7.0 Hz, C*H*CH$_2$), 5.21 (1 H, dd, *J* 10.0 and 1.5 Hz, C=CH$_A$*H*$_B$), 5.19 (1 H, dd, *J* 17.0 and 1.5 Hz, C=C*H*$_A$H$_B$), 3.94 (2 H, ddd, *J* 12.0, 7.5 and 3.5 Hz, OC$H_{ax}H_{eq}$), 3.58–3.52 (4 H, m, OCH$_{ax}$*H*$_{eq}$ and CHC*H*$_2$), 2.01 (2 H, ddd, *J* 14.0, 7.5 and 3.5 Hz, CC$H_{ax}H_{eq}$) and 1.84 (2 H, ddd, *J* 14.0, 7.0 and 3.5 Hz, CCH$_{ax}$*H*$_{eq}$); δ_C(100.6 MHz; $CDCl_3$) 203.9$^-$ (C=O), 136.9$^+$ (PhS), 136.9$^-$ (*i*-PhS), 131.8$^+$ (*C*H=CH$_2$), 130.0$^+$ (*p*-PhS), 129.4$^+$ (PhS), 119.0$^-$ (HC=*C*H$_2$), 64.7$^-$ (CH$_2$OCH$_2$), 58.8$^-$ (CSPh), 41.4$^-$ (CH$_2$C=O), and 32.3$^-$ (*C*H$_2$C*C*H$_2$); *m*/*z* (EI) 262.1 (18%, M^+), 193 (100, $C_5H_8OSPh^+$) and 109 (12, PhS^+); (Found: M^+, 262.1019. $C_{15}H_{18}O_2S$ requires *M*, 262.1027).

(5*R*)-5,6-Dihydroxy-2-methyl-2-phenylsulfanylhexan-3-one 20

Alkene **17** (3.10 g, 14.1 mmol) was added to a vigorously stirred solution of AD-mix-β (19.7 g) in a mixture of 2-methylpropan-2-ol (70 cm^3) and water (70 cm^3). The reaction was stirred at room temperature† until judged complete by TLC or LCMS. Sodium sulfite (7.50 g, 59.3 mmol, 12 eq.) was then added and stirring continued for 30 minutes. The mixture was transferred to a separating funnel and ethyl acetate (50 cm^3) was added. The solution was extracted a further three times with ethyl acetate (25 cm^3). The combined organic extracts were washed with water (25 cm^3), saturated brine (25 cm^3) and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give a crude product which was purified by column chromatography (silica, ethyl acetate) to give the *diol* **20** (3.57 g, 77%) as an oil; R_f(ethyl acetate) 0.42; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3591 (br, O–H), 3057, 2972, 2931, 2876, 1691 (C=O), 1541, 1474, 1439, 1385, 1367, 1102, 1051, 1026 and 909; retention time/min (Chiralpak AD column; hexane–ethanol, 9:1) 15.5 (63.6%) and 17.3 (36.4); δ_H(250 MHz; $CDCl_3$) 7.39–7.27 (5 H, m, PhS), 4.23–4.12 (1 H, m, C*H*OH), 3.71 (1 H, ddd, *J* 11.1, 6.0 and 3.7 Hz, CH_AH_BOH), 3.56 (1 H, dt, *J* 11.3 and 5.6 Hz, CH$_A$*H*$_B$OH), 3.39* (1 H, d, *J* 3.1 Hz, CHO*H*), 3.04 (1 H, dd, *J* 17.7 and 3.8 Hz, CH_AH_BC=O), 2.95 (1 H, dd, *J* 17.7 and 8.3 Hz, CH$_A$*H*$_B$C=O), 2.07* (1 H, br t, *J* 6.1 Hz, CH$_2$O*H*), 1.44 (3 H, s, Me$_A$) and 1.41 (3 H, s, Me$_B$); δ_C(100.6 MHz;

† When the temperature was reduced to 0 °C only a small improvement in enantiomeric excess was noticed.

Table 5 Effect of varying ligand[8,11] and temperature on the enantiomeric excess of the AD reaction of alkene **17**

Ligand	Temperature	Peaks	Enantiomeric excess
CLB[8]	25 °C	15.4 (55.1%) and 17.2 (44.9)	10.2%
PHAL (AD-mix-β)[11b]	25 °C	15.8 (63.6%) and 17.7 (36.4)	27.2%
PHAL	25 °C	15.5 (67.2%) and 17.3 (32.8)	34.4%
PHN[11c]	25 °C	15.5 (61.3%) and 17.3 (38.7)	22.6%
PYR[11a]	25 °C	15.7 (80.3%) and 17.6 (19.7)	60.6%
PYR	10 °C	16.4 (83.9%) and 18.6 (16.1)	67.8%
PYR	0 °C	16.9 (86.3%) and 19.0 (13.7)	72.6%

Table 6 Comparison of enantiomeric excess in the AD reaction of alkene **18** using the PYR ligand and the standard PHAL ligand

Ligand	Temperature	Peaks	Enantiomeric Excess
PHAL (AD-mix-β)	25 °C	13.8 (64.4%) and 15.0 (35.6)	29.0%
PYR	0 °C	14.4 (91.8%) and 15.8 (8.2)	83.6%

$CDCl_3$) 208.9$^-$ (C=O), 136.3$^+$ (*m*-PhS), 130.7$^-$ (*i*-PhS), 129.5$^+$ (*p*-PhS), 128.9$^+$ (*o*-PhS), 68.8$^+$ (CHOH), 66.0$^-$ (CH_2OH), 56.2$^-$ (CSPh), 38.8$^-$ (CH_2), 24.3$^+$ (Me) and 24.2$^+$ (Me); *m*/*z* (EI) 254 (5%, M^+), 151 (82, Me_2CSPh^+) and 109 (100, PhS^+); (Found: M^+, 254.0971. $C_{13}H_{18}O_3S$ requires *M*, 254.0977).

(3*R*)-3,4-Dihydroxy-1-[1-(phenylsulfanyl)cyclohexyl]butan-1-one 21

By the method described for compound **20**, alkene **18** (3.00 g, 11.5 mmol) and AD-mix-β (16.5 g) in 2-methylpropan-2-ol (75 cm^3) and water (75 cm^3) gave a crude product which was purified by column chromatography (silica, ethyl acetate) to give the *diol* **21** (3.07 g, 91%) as a pale yellow oil; R_f(ethyl acetate) 0.42; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3584 (br, O–H), 3056, 3048, 3987, 2938, 2859, 1685 (C=O), 1621, 1586, 1541, 1474, 1382, 1102, 1069, 1055, 1025 and 909; δ_H(250 MHz; $CDCl_3$) 7.38–7.26 (5 H, m, PhS), 4.20 (1 H, ddq, *J* 9.0, 6.2 and 3.1 Hz, C*H*OH), 3.71 (1 H, ddd, *J* 11.1, 6.0 and 3.6 Hz, CH_AH_BOH), 3.54 (1 H, dt, *J* 11.4 and 5.7 Hz, CH_AH_BOH), 3.53* (1 H, d, *J* 2.8 Hz, CHO*H*), 3.03 (1 H, dd, *J* 17.7 and 2.9 Hz, CH_AH_BC=O), 2.89 (1 H, dd, *J* 17.7 and 9.1 Hz, CH_AH_BC=O), 2.13* (1 H, br t, *J* 5.3 Hz, CH_2OH) and 2.04–1.23 (10 H, m); δ_C(100.6 MHz; $CDCl_3$) 207.8$^-$ (C=O), 136.5$^+$, 129.7$^-$ (*i*-PhS), 129.6$^+$, 128.9$^+$, 68.8$^+$ (CHOH), 66.0$^-$ (CH_2OH), 60.9$^-$ (CSPh), 38.7$^-$ (CH_2C=O), 32.6$^-$, 32.4$^-$, 25.4$^-$, 23.2$^-$ and 23.0$^-$; *m*/*z* (EI) 294 (4%, M^+), 191 (100, $C_6H_{10}SPh^+$), 149 (5), 123 (15) and 81 (46); (Found: M^+, 294.1287. $C_{16}H_{22}O_3S$ requires *M*, 294.1290).

(3*S*)-3,4-Dihydroxy-1-[4-(phenylsulfanyl)tetrahydropyran-4-yl]butan-1-one *ent*-22

By the method described for compound **20**, alkene **19** (50 mg, 0.19 mmol) and AD-mix-α (283 mg) in 2-methylpropan-2-ol (1.5 cm^3) and water (1.5 cm^3) gave a crude product after 24 hours which was purified by column chromatography (silica, ethyl acetate) to give the *diol ent*-**22** (35 mg, 63%) as a yellow oil; R_f(ethyl acetate) 0.38; retention time/min (Chiralpak AD column; hexane:ethanol, 9:1, flow rate 1 $cm^3\ min^{-1}$) 33.4 (37%) and 36.3 (63); $[a]_D$ −0.5 (*c*. 0.88 in $CHCl_3$; 26% ee), spectroscopically identical to **22**.

(5*R*)-5,6-Dihydroxy-2-methyl-2-phenylsulfanylhexan-3-one 20

The alkene **17** (42.0 mg, 200 μmol) was added to a stirred solution of osmium tetroxide (2% w/v solution in water, 25 μl, 2 μmol, 1 mol%), ligand (10 μmol, 5 mol%; see Table 5), potassium carbonate (83 mg, 600 μmol) and potassium ferricyanide (198 mg, 600 μmol) dissolved in a mixture of water (2 cm^3) and 2-methylpropan-2-ol (2 cm^3). The reaction mixture was excluded from light and stirred for 36 hours at the appropriate temperature (0–25°C). Sodium sulfite (250 mg, 1.98 mmol) was added and stirring continued for 30 minutes. The organic layer was separated and the aqueous layer was washed with ethyl acetate (4 × 50 cm^3). The combined organic extracts were washed with water (50 cm^3), then brine (50 cm^3), and finally dried over sodium sulfate. The solvent was removed under reduced pressure to give the crude diol **20** which was analysed by Chiral HPLC (Chiralpak AD column; eluting with hexane–ethanol, 9:1; flow rate 1 $cm^3\ min^{-1}$).

(3*R*)-3,4-Dihydroxy-1-[1-(phenylsulfanyl)cyclohexyl]butan-1-one 21

By the previous method described for compound **20**, alkene **18** (52.0 mg, 0.20 mmol), osmium tetroxide (2% w/v solution in water, 25 μl, 2 μmol, 1 mol%), ligand (10 μmol, 5 mol%), potassium ferricyanide (198 mg, 0.6 mmol) and potassium carbonate (83.0 mg, 0.6 mmol) in a mixture of 2-methylpropan-2-ol (2 cm^3) and water (2 cm^3) gave the crude diol **21** which was analysed by Chiral HPLC (Chiralpak AD column; hexane–ethanol, 9:1) (Table 6).

(3*R*)-3,4-Dihydroxy-1-[4-(phenylsulfanyl)tetrahydropyran-4-yl]butan-1-one 22

By the previous method described for compound **20**, alkene **19** (500 mg, 1.9 mmol), osmium tetroxide (2% w/v solution in water, 240 μl, 19 μmol, 1 mol%), $(DHQD)_2PYR$ (84 mg, 95 μmol, 5 mol%), potassium carbonate (790 mg, 5.7 mmol) and potassium ferricyanide (1.88 g, 5.7 mmol) in a mixture of water (20 cm^3) and 2-methylpropan-2-ol (20 cm^3) at 0 °C gave a crude product. Purification by column chromatography (silica, ethyl acetate) gave the *diol* **22** as a viscous oil (410 mg, 73%); R_f(ethyl acetate) 0.38; retention time/min (Chiralpak AD column; hexane–ethanol, 9:1, flow rate 1 $cm^3\ min^{-1}$) 34.3 (89%) and 37.4 (11); $[a]_D$ +13.0 (*c*. 1.23 in $CHCl_3$; 78% ee); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3593 (O–H), 2967 (O–H), 2868 (C–H), 2868 (C–H), 2868 (C–H), 1691 (C=O) and 1104 (C–O); δ_H(400 MHz; $CDCl_3$) 7.36–7.24 (5 H, m, PhS), 4.18–4.26 (1 H, m, C*H*OH), 4.20–3.91 (2 H, m, CH_AH_BO), 3.71 (2 H, dd, *J* 11.5 and 3.5 Hz, CH_2OH), 3.58–3.53 (2 H, m, CH_AH_BO), 2.94 (1 H, dd, *J* 17.5 and 7.0 Hz, O=CCH_AH_B), 2.93 (1 H, dd, *J* 17.5 and 5.0 Hz, O=CCH_AH_B), 2.00–1.97 (2 H, m, $CCH_{ax}H_{eq}$) 1.83 (1 H, ddd, *J* 13.0, 5.0 and 3.5 Hz, $CCH_{ax}H_{eq}$) and 1.79 (1 H, ddd, *J* 12.5, 5.0 and 3.0 Hz, $CCH_{ax}H_{eq}$); δ_C(100.6 MHz; $CDCl_3$) 204.6$^-$ (C=O), 134.6$^+$ (PhS), 127.9$^+$ (*p*-PhS), 127.2$^+$ (PhS), 127.1$^-$ (*i*-PhS), 66.8$^+$ (CH_2CHOH), 64.1$^-$ (CH_2OH), 62.3$^+$ (CH_2OCH_2), 62.1$^+$ (CH_2OCH_2), 56.3$^-$ (CSPh), 37.1$^+$ (CH_2C=O), 20.9$^-$ (CH_2CCH_2) and 29.7$^-$ (CH_2CCH_2); *m*/*z* (EI) 296 (38%, M^+), 193 (100, $M^+–C_4H_7O_3$) and 109 (22, PhS^+); (Found: M^+, 296.1093. $C_{15}H_{20}O_4S$ requires *M*, 296.1082).

(2*RS*,4*SR*)-(4-Phenylsulfanyl-1-oxaspiro[4.5]dec-2-yl)methanol 23

By the method described for compound **3**, toluene-*p*-sulfonic acid (4.8 mg, 25 μmol) and a solution of *anti*-triol **6** (70 mg,

0.240 mmol) in dichloromethane (2 cm^3) gave the ^{2,4}*anti-tetrahydrofuran* **23** (59 mg, 90%) after 48 hours as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 1:1] 0.18; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3591 (O–H), 3056, 2986, 2938, 2861, 1584, 1480, 1448, 1439, 1146, 1090, 1039, 1026, 964 and 909; δ_H(250 MHz; $CDCl_3$) 7.44–7.36 (3 H, m, PhS), 7.33–7.16 (2 H, m, PhS), 4.20 (1 H, dddd, *J* 7.9, 6.0, 4.7 and 3.2 Hz, CH–O), 3.71 (1 H, ddd, *J* 11.5, 5.6 and 3.2 Hz, C$H_A$$H_B$OH), 3.45 (1 H, ddd, 11.7, 7.2 and 4.7 Hz, CH$_A$$H_B$OH), 3.36 (1 H, t, *J* 7.9 Hz, CHSPh), 2.32 (1 H, ddd, *J* 13.0, 8.0 and 6.0 Hz, C$H_A$$H_B$), 2.10 (1 H, dt, *J* 13.0 and 7.9 Hz, CH$_A$$H_B$), 1.90* (1 H, dd, *J* 7.2 and 5.7 Hz, OH) and 1.76–1.14 (10 H, m); δ_C(100.6 MHz; $CDCl_3$) 135.9$^-$ (*i*-PhS), 131.0$^+$, 129.0$^+$, 126.7$^+$, 84.5$^-$ (C–O), 75.6$^+$ (CH–O), 65.2$^-$ (CH_2OH), 55.2$^+$ (CHSPh), 37.0$^-$, 35.5$^-$, 30.9$^-$, 25.6$^-$, 23.3$^-$ and 22.2$^-$; *m*/*z* (EI) 278 (18%, M^+), 180 (56, $M^+ - C_6H_{10}O$), 149 (100, $C_3H_4SPh^+$) and 110 (15, $PhSH^+$); (Found: M^+, 278.1343. $C_{16}H_{22}O_2S$ requires *M*, 278.1340).

(2*RS*,4*RS*)-(4-Phenylsulfanyl-1-oxaspiro[4.5]dec-2-yl)methanol 25

By the method described for compound **3**, toluene-*p*-sulfonic acid (5.0 mg, 26 μmol) and a solution of *syn*-triol **9** (62.2 mg, 0.210 mmol) in dichloromethane (2 cm^3) gave the ^{2,4}*syn-tetrahydrofuran* **25** (53 mg, 92%) after 48 hours as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 1:1] 0.17; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3589 (O–H), 1584, 1480, 1448, 1146, 1091, 1025, 958 and 908; δ_H(250 MHz; $CDCl_3$) 7.45–7.37 (2 H, m, PhS), 7.34–7.17 (3 H, m, PhS), 4.08 (1 H, dddd, *J* 8.6, 6.8, 5.4 and 3.2 Hz, CH–O), 3.72 (1 H, ddd, *J* 11.5, 6.2 and 3.3 Hz, C$H_A$$H_B$OH), 3.54 (1 H, ddd, *J* 11.7, 6.5 and 5.4 Hz, CH$_A$$H_B$OH), 3.46 (1 H, dd, *J* 8.7 and 7.1 Hz, CHSPh), 2.38 (1 H, dt, *J* 12.9 and 6.9 Hz, C$H_A$$H_B$), 2.01 (1 H, t, *J* 6.6 Hz, OH), 1.96 (1 H, dt, *J* 12.9 and 8.7 Hz, CH$_A$$H_B$) and 1.77–1.11 (10 H, m); δ_C(100.6 MHz; $CDCl_3$) 135.6$^-$ (*i*-PhS), 131.4$^+$, 129.0$^+$, 126.9$^+$, 83.9$^-$ (C–O), 76.5$^+$ (CH–O), 65.2$^-$ (CH_2OH), 55.8$^+$ (CHSPh), 36.1$^-$, 35.4$^-$, 33.6$^-$, 25.6$^-$, 23.1$^-$ and 22.4$^-$; *m*/*z* (EI) 278 (25%, M^+), 180 (82, $M^+ - C_6H_{10}O$), 149 (100, $C_3H_4SPh^+$), 131 (22) and 110 (24, $PhSH^+$); (Found: M^+, 278.1347. $C_{16}H_{22}O_2S$ requires *M*, 278.1340).

(3*RS*,5*RS*)-2,2-Dimethyl-3-phenylsulfanyltetrahydrofuran-5-ylmethanol 27

By the method described for compound **3**, toluene-*p*-sulfonic acid (1.7 mg, 9.0 μmol) and a solution of *syn*-triol **8** (50 mg, 195 μmol) in dichloromethane (2.5 cm^3) gave the ^{3,5}*syn-tetrahydrofuran* **27** (44 mg, 95%) after 48 hours as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 1:1] 0.09; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3593 (O–H), 3054, 2978, 2881, 1584, 1480, 1422, 1142, 1091 and 1034; δ_H(400 MHz; $CDCl_3$) 7.46–7.23 (5 H, m, PhS), 4.12–4.04 (1 H, m, CH–O), 3.70 (1 H, ddd, *J* 11.5, 6.0 and 3.3 Hz, C$H_A$$H_B$OH), 3.52 (1 H, ddd, *J* 11.5, 6.5 and 5.3 Hz, CH$_A$$H_B$OH), 3.49 (1 H, dd, *J* 10.3 and 6.8 Hz, CHSPh), 2.36 (1 H, dt, *J* 13.0 and 6.5 Hz, C$H_A$$H_B$), 1.97 (1 H, dt, *J* 13.0 and 10.1 Hz, CH$_A$$H_B$), 1.31 (3 H, s, Me$_A$) and 1.29 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$) 135.6$^-$ (*i*-PhS), 131.6$^+$, 129.1$^+$, 126.7$^+$ (*p*-PhS), 83.5$^-$ (C–O), 75.8$^+$ (CHOH), 64.9$^-$ (CH_2OH), 56.0$^+$ (CHSPh), 35.6$^-$ (CH_2), 27.8$^+$ (Me) and 25.1$^+$ (Me); *m*/*z* (EI) 238 (43%, M^+), 136 (100), 135 (34) and 110 (24, PhS^+); (Found: M^+, 238.1022. $C_{13}H_{18}O_2S$ requires *M*, 238.1027).

(2*R*,4*S*)-2-Hydroxymethyl-4-phenylsulfanyl-1,8-dioxaspiro-[4.5]decane 28

Amberlyst® (0.35 g) was added to a solution of the triol **7** (53 mg, 0.18 mmol) in dry dichloromethane (20 cm^3). The solution was heated to reflux for 48 hours and the residue was filtered and purified by column chromatography (silica, diethyl ether) to give the ^{2,4}*anti-tetrahydrofuran* **28** as an oil (42 mg, 83%); R_f(diethyl ether) 0.36; $[a]_D$ +4.2 (*c*. 0.7 in $CHCl_3$; 78% ee); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3348 (O–H), 2785 (C–H), 2654 (C–H), 1584 (PhS) and 1106 (C–O); δ_H(400 MHz; $CDCl_3$) 7.41 (2 H, dd, *J* 8.0 and 1.5 Hz, PhS), 7.31–7.22 (3 H, m, PhS), 4.20 (1 H, dtd, *J* 11.0, 5.5 and 3.5 Hz, OCH), 3.82 (1 H, ddd, *J* 11.0, 5.0 and 2.5 Hz, OCH$_2$), 3.80–3.68 (4 H, m, OCH$_2$), 3.51–3.44 (1 H, m, OCH$_2$), 3.37 (1 H, t, *J* 8.0 Hz, CHSPh), 2.34 (1 H, ddd, *J* 13.0, 8.0 and 7.0 Hz, CH$_2$), 2.10 (1 H, dt, *J* 13.0 and 8.5 Hz, CH$_2$), 1.96 (1 H, ddd, *J* 13.5, 11.0 and 4.5 Hz, CH$_{eq}$$H_{ax}$), 1.90 (1 H, ddd, *J* 13.5, 11.0 and 5.5 Hz, CH$_{eq}$$H_{ax}$), 1.59 (1 H, dq, *J* 13.5 and 2.5 Hz, CH_{eq}H$_{ax}$) and 1.38 (1 H, dq, *J* 13.5 and 2.5 Hz, CH_{eq}H$_{ax}$); δ_C(100.6 MHz; $CDCl_3$) 134.2$^-$ (*i*-PhS), 130.4$^+$ (PhS), 128.1$^+$ (PhS), 126.0$^+$ (*p*-PhS), 80.9$^-$ (OC$_q$), 74.9$^+$ (O*C*HCH$_2$), 64.1$^-$ (OCH$_2$), 63.8$^-$ (OCH$_2$), 63.2$^-$ (OCH$_2$), 54.2$^+$ (CHSPh), 35.9$^-$ (CH$_2$), 33.9$^-$ (CH$_2$) and 30.3$^-$ (CH$_2$); *m*/*z* (EI) 280 (31%, M^+), 251 (3), 201 (5), 151 (9), 119 (36), 100 (5) and 69 (100); (Found: M^+, 280.1120. $C_{15}H_{20}O_3S$ requires *M*, 280.1133).

(2*R*,4*R*)-2-Hydroxymethyl-4-phenylsulfanyl-1,8-dioxaspiro-[4.5]decane 29

By the method described for compound **28**, Amberlyst® (0.35 g) and a solution of the triol **10** (67 mg, 0.22 mmol) in dry dichloromethane (20 cm^3) gave a crude product after heating to reflux for 24 hours. The filtered residue was purified by column chromatography (silica, diethyl ether) to give the ^{2,4}*syn-tetrahydrofuran* **29** as an oil (52 mg, 87%); R_f(diethyl ether) 0.33; $[a]_D$ +1.5 (*c*. 1.18 in $CHCl_3$; 78% ee); $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3267 (O–H), 2818 (C–H), 1582 (PhS) and 1103 (C–O); δ_H(400 MHz; $CDCl_3$) 7.45–7.39 (2 H, m, PhS), 7.33–7.20 (3 H, m, PhS), 4.10 (1 H, dtd, *J* 12.0, 6.5 and 3.5 Hz, OCH), 3.82 (1 H, ddd, *J* 11.0, 5.0 and 2.5 Hz, OCH$_2$), 3.78–3.67 (4 H, m, OCH$_2$), 3.55 (1 H, dt, *J* 11.5 and 5.5 Hz, OCH$_2$), 3.46 (1 H, t, *J* 7.5 Hz, CHSPh), 2.40 (1 H, dt, *J* 13.5 and 7.0 Hz, CH$_2$), 2.05–1.90 (2 H, m, CH$_2$), 1.81 (1 H, ddd, *J* 13.5, 10.5 and 6.5 Hz, CH$_{eq}$$H_{ax}$), 1.60 (1 H, dq, *J* 13.5 and 2.5 Hz, CH_{eq}H$_{ax}$) and 1.48 (1 H, dq, *J* 13.5 and 2.5 Hz, CH_{eq}H$_{ax}$); δ_C(100.6 MHz; $CDCl_3$) 135.4$^-$ (*i*-PhS), 132.1$^+$ (PhS), 129.5$^+$ (PhS), 127.6$^+$ (*p*-PhS), 81.8$^-$ (OC$_q$), 77.2$^+$ (O*C*HCH$_2$), 65.5$^-$ (OCH$_2$), 65.1$^-$ (OCH$_2$), 64.8$^-$ (OCH$_2$), 56.1$^+$ (CHSPh), 36.6$^-$ (CH$_2$), 35.4$^-$ (CH$_2$) and 34.5$^-$ (CH$_2$); *m*/*z* (EI) 280 (21%, M^+), 251 (2), 222 (4), 169 (48), 119 (37), 100 (5) and 69 (100); (Found: M^+, 280.1143. $C_{15}H_{20}O_3S$ requires *M*, 280.1133).

(3*RS*,5*SR*)-2,2-Dimethyl-3-phenylsulfanyltetrahydropyran-5-yl 3,5-dinitrobenzoate 30 and (3*RS*,5*SR*)-2,2-Dimethyl-3-phenylsulfanyltetrahydrofuran-5-ylmethyl 3,5-dinitrobenzoate

A 1:1 mixture of alcohols **3** and **4** (98 mg, 412 μmol) was dissolved in pyridine (2.5 cm^3) and 3,5-dinitrobenzoyl chloride (97 mg, 421 μmol) was added. The resulting pale yellow solution was stirred under argon for 1 hour and diluted with diethyl ether (4 cm^3), at which point a cloudy white precipitate was formed. Dilute hydrochloric acid (15 cm^3, 2.0 mol dm^{-3}) was added and the aqueous layer extracted twice with diethyl ether (10 cm^3). The combined organic fractions were dried over anhydrous magnesium sulfate and the solvent evaporated under reduced pressure to give a crude product as a pale yellow solid. The residue was purified by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 4:1] to give the *tetrahydropyran* **30** (51 mg, 29%) as bright yellow needles which were recrystallised from hexane–chloroform (9:1), mp 128–130 °C (from hexane–chloroform); R_f[light petroleum (bp 40–60 °C)–diethyl ether, 4:1] 0.25; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3101, 2880, 1735 (C=O), 1628, 1549 (NO_2), 1478, 1462, 1346 (NO_2), 1290, 1256, 1169, 1138, 1088 and 990; δ_H(400 MHz; $CDCl_3$) 9.23 (1 H, t, *J* 2.2 Hz, *p*-Ar), 9.13 (2 H, d, *J* 2.1 Hz, *o*-Ar), 7.48–7.43 (2 H, m, PhS), 7.36–7.26 (3 H, m, PhS), 5.10 (1 H, tt, *J* 10.2 and 5.1 Hz, CH–O), 3.95 (1 H, ddd, *J* 11.2, 5.3 and 2.0 Hz, CH_{eq}H$_{ax}$O), 3.67 (1 H, dd, *J* 11.1 and 10.1 Hz, CH$_{eq}$$H_{ax}$O), 3.18 (1 H, dd, *J* 12.3 and 4.2 Hz, CHSPh), 2.48 (1 H, dtd, *J* 12.8, 4.7 and 2.0 Hz, CH_{eq}H$_{ax}$), 2.07 (1 H, dt, *J* 12.5 and 11.0 Hz, CH$_{eq}$$H_{ax}$), 1.48 (3 H, s, Me$_A$) and 1.40 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$)

161.6$^-$ (C=O), 148.7$^-$ (C–NO_2), 134.6$^-$, 133.6$^-$, 132.3$^+$, 129.5$^+$, 129.3$^+$, 127.6$^+$, 122.6$^+$, 75.4$^-$ (C–O), 70.6$^+$ (CH–O), 62.1$^-$ (CH_2O), 53.1$^+$ (CSPh), 33.4$^-$ (CH_2), 28.4$^+$ (CH_3) and 18.4$^+$ (CH_3); *m/z* (EI) 432 (100%, M$^+$), 220 (19), 195 (37), 162 (20) and 136 (56); (Found: M$^+$, 432.0971. $C_{20}H_{20}N_2O_7S$ requires *M*, 432.0991) CCDC 192684. See http://www.rsc.org/suppdata/p1/b2/b208556a/ for crystallographic files in .cif or other electronic format. Also, the *tetrahydrofuran* (42 mg, 24%) as pale yellow needles which were recrystallised from hexane–chloroform (9:1), mp 141–142 °C (from hexane–chloroform); R_f[light petroleum (bp 40–60 °C)–diethyl ether, 4:1] 0.15; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3112, 2859, 1734 (C=O), 1628, 1549 (NO_2), 1481, 1347 (NO_2), 1290 and 991; δ_H(400 MHz; $CDCl_3$) 9.24 (1 H, t, *J* 2.1 Hz, *p*-Ar), 9.16 (2 H, d, *J* 2.2 Hz, *o*-Ar), 7.45–7.41 (2 H, m, PhS), 7.32–7.21 (3 H, m, PhS), 4.52–4.36 (3 H, m, CH–O, CH_AH$_B$O and CH$_A$$H_B$O), 3.43 (1 H, t, *J* 9.0 Hz, CHSPh), 2.40–2.25 (2 H, m, CH_AH$_B$ and CH$_A$$H_B$), 1.32 (3 H, s, Me$_A$) and 1.31 (3 H, s, Me$_B$); δ_C(100.6 MHz; $CDCl_3$) 162.5$^-$ (C=O), 148.7$^-$ (C–NO_2), 135.1$^-$, 133.7$^-$, 131.6$^+$, 129.5$^+$, 129.2$^+$, 127.3$^+$, 122.5$^+$, 84.1$^-$ (C–O), 72.8$^+$ (CH–O), 68.9$^-$ (CH_2O), 55.3$^+$ (CSPh), 36.3$^-$ (CH_2), 27.8$^+$ (CH_3) and 22.4$^+$ (CH_3); *m/z* (+ES) 455 (8%, MNa$^+$), 413 (36), 373 (35), 316 (16) and 261 (100); (Found: MNa$^+$, 455.0893. $C_{20}H_{20}N_2O_7SNa$ requires 455.0883).

(3*RS*)-1-(Cyclohexan-1-ol)butane-3,4-diol 35

By the method described for compound **5**, potassium ferricyanide (6.40 g, 19.4 mmol), potassium carbonate (2.68 g, 19.4 mmol), osmium(III) chloride hydrate (5.6 mg, 65.4 μmol, 0.7 mol%), quinuclidine (104 mg, 0.930 mmol, 3.5 mol%) and alkene **36** (1.0 g, 6.48 mmol) in 2-methylpropan-2-ol (35 cm^3) and water (35 cm^3) gave a crude product. Purification by column chromatography (silica, ethyl acetate) gave *triol* **35** (940 mg, 77%) as an oil; R_f(ethyl acetate) 0.10; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3595 (O–H), 3396 (br, O–H), 2935, 2859, 1449, 1390 and 1348; δ_H(200 MHz; $CDCl_3$) 3.79–3.57 (2 H, m, C*H*OH and CH_A-H$_B$OH), 3.47 (1 H, dd, *J* 8.4 and 5.6 Hz, CH$_A$$H_B$OH), 2.86* (3 H, br s, 3 × OH), 1.69–1.21 (14 H, m); δ_C(100.6 MHz; $CDCl_3$) 72.7$^+$ (CH–OH), 71.3$^-$ (C–OH), 66.7$^-$ (C–OH), 37.9$^-$, 37.8$^-$, 37.1$^-$, 26.5$^-$, 25.8$^-$, 22.3$^-$ and 22.2$^-$; *m/z* (+FIB) 189 (20%, MH$^+$), 171 (54), 154 (100), 137 (70), 136 (86) and 107 (28); (Found: MH$^+$, 189.1497. $C_{10}H_{20}O_3$ requires *M*, 189.1491).

1-(Cyclohexan-1-ol)but-3-ene 36

4-Bromobut-1-ene (5.0 g, 3.76 cm^3, 37.0 mmol) was slowly added to a stirred suspension of magnesium turnings (0.99 g, 40.7 mmol, 1.1 eq.) and one small crystal of iodine in diethyl ether (50 cm^3) at 0 °C under argon. The solution was allowed to warm to room temperature once the addition was complete and stirred for 2 hours. The reaction was again cooled to 0 °C and cyclohexanone (3.99 g, 4.22 cm^3, 40.7 mmol) in diethyl ether (5 cm^3) slowly added. Once the addition was complete the mixture was warmed to ambient temperature and stirring continued for 1 hour. Saturated aqueous ammonium chloride solution was then slowly added and the mixture transferred to a separating funnel. The aqueous layer was extracted three times with diethyl ether (30 cm^3) and the combined organic extracts washed with water (30 cm^3), saturated brine (30 cm^3) and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to give a crude product. Purification by column chromatography [silica, light petroleum (bp 40–60°C)–diethyl ether, 4:1] gave the *alkene* **36** (2.88 g, 50%) as an oil; R_f[light petroleum (bp 40–60°C)–diethyl ether, 4:1] 0.16; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3596 (O–H), 2926, 2857, 1639 (C=C), 1449, 1382, 1346 and 1148; δ_H(400 MHz; $CDCl_3$) 5.86 (1 H, ddt, *J* 16.8, 10.1 and 6.6 Hz, C*H*=CH$_2$), 5.04 (1 H, dq, *J* 17.1 and 1.7 Hz, CH_{trans}H$_{cis}$=CH), 4.99–4.91 (1 H, m, CH$_{trans}$$H_{cis}$=CH), 2.25–2.09 (2 H, m, CH_2CH=CH$_2$) and 1.94–1.17 (13 H, m); δ_C(100.6 MHz; $CDCl_3$) 139.3$^+$ (C*H*=CH$_2$), 114.3$^-$ (CH=CH_2), 71.4$^-$ (C–OH), 41.4$^-$, 37.5$^-$, 27.5$^-$, 25.8$^-$ and 22.2$^-$; *m/z* (EI) 136 (2%, M$^+$ − H_2O), 99 (52, M$^+$ − CH_2CH_2CH=CH_2), 84 (42), 55 (78, CH_2CH_2CH=CH_2^+) and 49 (100).

(2*RS*)-(1-Oxaspiro[4.5]dec-2-yl)methanol 37, (2*RS*)-4-Cyclohexylidenebutane-1,2-diol 38 and (2*RS*)-4-(Cyclohex-1-ene)-butane-1,2-diol 39

By the method described for compound **23**, triol **35** (143 mg, 761 μmol) and toluene-*p*-sulfonic acid (20 mg, 106 μmol) in dichloromethane (5 ml) gave a crude product after three days whose ^{1}H NMR spectrum indicated the presence of three components. Purification by column chromatography [silica, light petroleum (bp 40–60 °C)–diethyl ether, 9:1] gave the *tetrahydrofuran* **37** (67 mg, 47%) as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.25; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3583 (O–H), 3056, 2934, 2858, 1449, 1401, 1361, 1331, 1311, 1093, 1068, 1039, 1023 and 908; δ_H(250 MHz; $CDCl_3$) 4.15–4.03 (1 H, m, CH–O), 3.67 (1 H, ddd, *J* 11.3, 6.0 and 3.5 Hz, CH_AH$_B$OH), 3.45 (1 H, dt, 11.5 and 6.0 Hz, CH$_A$$H_B$OH), 2.05* (1 H, t, *J* 6.3 Hz, OH) and 2.02–1.26 (14 H, m); δ_C(100.6 MHz; $CDCl_3$) 83.4$^-$ (C–O), 78.1$^+$ (CH–O), 65.3$^-$ (CH_2OH), 38.4$^-$, 37.3$^-$, 36.0$^-$, 27.1$^-$, 25.7$^-$, 24.1$^-$ and 23.7$^-$; *m/z* (EI) 170 (25%, M$^+$), 139 (100, M$^+$–CH_2OH), 127 (81), 121 (69), 114 (14), 95 (32), 83 (31), 81 (32) and 67 (30); (Found: M$^+$, 170.1310. $C_{10}H_{18}O_2$ requires *M*, 170.1307) and the *alkenes endo*-**38** and *exo*-**39** (16 mg, 11%; 2:1, *endo*:*exo*) as an oil; R_f[light petroleum (bp 40–60 °C)–diethyl ether, 9:1] 0.06; $\nu_{max}(CH_2Cl_2)$/cm^{-1} 3585 (br, O–H), 2931, 2857 and 1642 (C=C); δ_H(200 MHz; $CDCl_3$) 5.44 (1 H, br s, *endo* CH=C), 5.09 (1 H, br t, *J* 7.6 Hz, *exo* CH=C), 3.78–3.58 (4 H, m), 3.54–3.38 (2 H, m) and 2.43–1.39 (24 H, m); δ_C(100.6 MHz; $CDCl_3$) 143.8$^-$ (*exo* CH=*C*), 137.3$^-$ (*endo* CH=*C*), 121.6$^+$ (*endo* *C*H=C), 115.7$^+$ (*exo* *C*H=C), 72.2$^+$ (*endo* and *exo* CH–OH), 66.8$^-$ (*endo* CH_2OH), 66.3$^-$ (*exo* CH_2OH), 37.3$^-$ (*exo* CH_2), 34.1$^-$ (*endo* CH_2), 31.2$^-$ (*exo* CH_2), 31.0$^-$ (*endo* CH_2), 28.8$^-$ (*exo* CH_2), 28.7$^-$ (*exo* CH_2), 28.2$^-$ (*endo* CH_2), 27.9$^-$ (*exo* CH_2), 26.8$^-$ (*exo* CH_2), 25.2$^-$ (*endo* CH_2), 22.9$^-$ (*endo* CH_2) and 22.5$^-$ (*endo* CH_2); (Found: MNa$^+$, 193.1192. $C_{10}H_{18}O_2$Na requires *M*, 193.1199).

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