

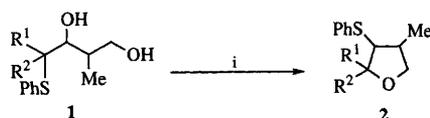
Kinetic resolution in asymmetric *anti* aldol reactions of branched and straight chain racemic 2-phenylsulfanyl aldehydes: asymmetric synthesis of cyclic ethers and lactones by phenylsulfanyl migration

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The kinetic resolution of branched and straight chain 2-phenylsulfanyl aldehydes by the Lewis acid-catalysed asymmetric *anti* aldol reaction followed by reduction to single enantiomers of 1,3-diols and/or acid-catalysed cyclisation with PhS migration provides a route to enantiomerically pure cyclic ethers and lactones with full stereochemical control.

Cyclic ether and lactone subunits are widespread in many natural products and various methods exist for their construction.¹ Enantioselective methodology in particular continues to receive widespread attention.² Our efforts in this area have featured stereoselective aldol reactions and stereospecific phenylsulfanyl rearrangements. This way we have been able to synthesise a wide variety of both racemic and optically active oxygen and nitrogen containing heterocycles.³ Treatment of β -hydroxy sulfides **1** with a catalytic amount of TsOH leads to phenylsulfanyl migration from a tertiary or a secondary centre to the secondary centre initially bearing a hydroxy group and thus, by oxygen or nitrogen participation, to the synthesis of heterocycles **2** (Scheme 1).



Scheme 1 Reagents and conditions: i, TsOH, cat., reflux

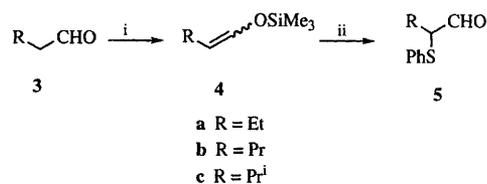
Tertiary to secondary (R^1, R^2 = alkyl, carbocyclic ring) migrations are rapid and high yielding regardless of the stereochemistry of β -hydroxy sulfide **1** (Me and OH, *syn* or *anti*). On the other hand, secondary to secondary (R^1 = alkyl, R^2 = H) migrations require that the stereochemistry of β -hydroxy sulfide **1** be *anti*. This is because a developing *anti* relationship between the phenylsulfanyl group and the methyl group during migration favours cyclisation, but no cyclisation is observed if the phenylsulfanyl group is forced to migrate into a *syn* relationship with the methyl group.⁴ With this background, an extension of our methodology involving secondary to secondary phenylsulfanyl migrations in optically active compounds must by necessity feature an *anti*-selective asymmetric aldol reaction on the 2-phenylsulfanyl aldehydes. We now report the successful extension of secondary to secondary phenylsulfanyl migrations to the synthesis of optically active cyclic ethers and lactones by way of kinetic resolution of racemic 2-phenylsulfanyl aldehydes *via* Lewis acid-catalysed asymmetric *anti* aldol reactions.

Earlier studies in our laboratories involving aldol reactions on racemic 2-phenylsulfanyl aldehyde **5a** with certain metal enolates gave not only excellent aldol (2,3) stereoselectivity but good levels of Felkin (3,4-*anti*) stereoselectivity.⁴ Felkin products always predominated regardless of the stereochemical consequence of the aldol process itself (Me and OH, *syn* or *anti*). Extension of secondary to secondary phenylsulfanyl migrations to produce optically active cyclic ethers and lactones required the use of either optically active aldehydes with achiral enolates (single asymmetric aldol reactions) or the use of

optically active aldehydes with chiral enolates (double asymmetric aldol reactions). Our efforts at the former approach were frustrated by the racemisation of the chiral aldehydes during the reaction.⁵ The basic nature of the lithium enolate used was the main factor. Consequently we had to explore other possibilities.

We had successfully applied the Evans *syn* aldol technology⁶ to the synthesis of optically active spirocyclic heterocycles.^{3a,d} The development by Heathcock⁷ of an *anti*-selective version of the Evans *syn* aldol reaction came at the right time for us as we could see from our earlier results^{3a,c} and from Heathcock's work⁷ that our aldehydes were particularly suitable for this reaction, since they possess an aromatic ring and a sulfur atom, features that seem to play an important role in the developing stereoselectivities.

The aldehydes **5** were prepared in good yields from silyl enol ethers **4** by sulfenylation (Scheme 2). Treatment of commercially



Scheme 2 Reagents and conditions: i, Me_3SiCl , Et_3N , DMF, 80 °C; ii, PhS-Cl, CH_2Cl_2 , -78 °C to room temp.

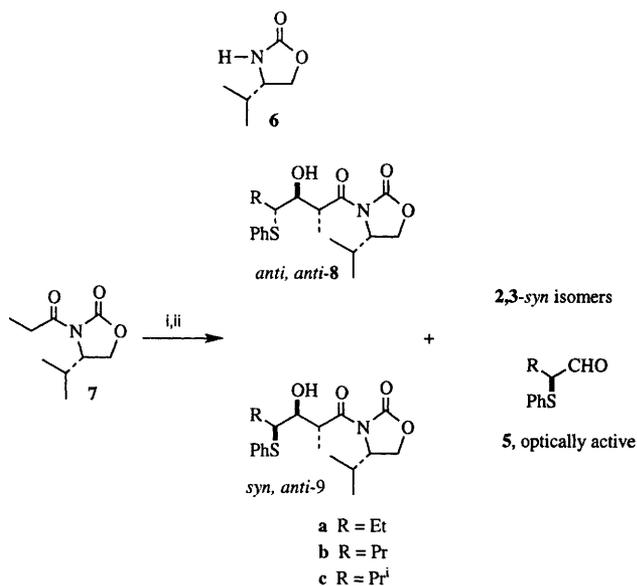
available aldehydes **3** with Me_3SiCl in the presence of triethylamine in DMF at 80 °C gave silyl enol ethers **4** in good yield. Sulfenylation with PhS-Cl, generated *in situ* by the reaction of PhSSPh with sulfuric chloride, was rapid in dichloromethane at room temperature. When aldehydes **5** were condensed with the boron enolate of imide **7** derived from the valine-based auxiliary **6** in the presence of 3.0 equiv. of Et_2AlCl , good *anti* stereoselectivities were observed (Scheme 3). The reactivity imparted to aldehydes **5** by the phenylsulfanyl group was also evident here. Reactions were essentially complete after 1 h at -78 °C. In addition, a preference for the *anti* aldol product arising from Felkin control (PhS and OH *anti* to one another) was also observed. This was nevertheless expected from previous work in these laboratories.⁴ At this juncture, simply based on the ratio of Felkin to non-Felkin products, it was apparent that a kinetic resolution process was in play. The kinetic resolution we initially observed was improved by increasing the amount of aldehyde and Lewis acid which in addition brought about the benefit of both improved aldol (2,3) stereoselectivity and improved Felkin (3,4) stereoselectivity (Table 1, entries 4–6).

To investigate further the process of kinetic resolution in

Table 1 *anti* Aldol reactions of **7** with 2-phenylsulfanyl aldehydes **5**

Entry	R	3 (equiv.)	Et ₂ AlCl (equiv.)	Aldol ratio ^a <i>anti</i> ^b : <i>syn</i>	Felkin ratio 8 : 9	Yield (%) ^c	
						8	9
1	Et	1.5	3.0	89:11	58:31	54	15
2	Pr	1.5	3.0	88:12	66:22	52	19
3	Pr ⁱ	1.5	3.0	81:19	62:19	<i>d</i>	<i>d</i>
4	Et	2.0	4.0	> 97:3	75:25	63	16
5	Pr	2.0	4.0	99.4:0.6	85.4:14.0	75	6
6	Pr ⁱ	2.0	4.0	96:4	89:7	<i>d</i>	<i>d</i>

^a Ratios determined by HPLC. ^b Total **8** + **9**. ^c Yield of purified product. ^d Products inseparable, hence yield not determined.



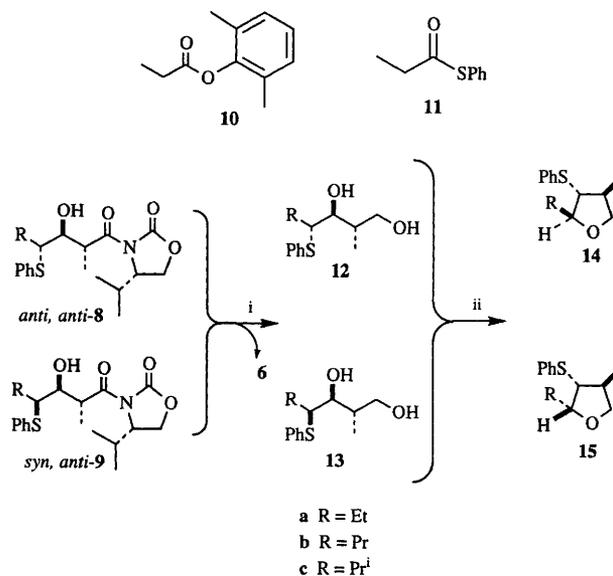
Scheme 3 Reagents and conditions: i, Prⁱ₂NEt, Bu₂BOTf, CH₂Cl₂, 0 °C; ii, 5 × Et₂AlCl; -78 °C

these reactions, we determined the enantiomeric purity of recovered aldehyde (rich in the slower reacting enantiomer) to be 20% ee (for R = Prⁱ, **5c**) after column chromatography by NMR using the chiral shift reagent, Eu(hfc)₃. With the observation that optically active 2-phenylsulfanyl aldehydes racemise during column chromatography,⁸ perhaps a higher ee value for this particular recovered aldehyde enriched in the slower reacting enantiomer would have been realised. Besides this potential danger of racemisation during column chromatography, the slower reacting enantiomer may also have been racemising under the basic reaction conditions. This possibility would explain the fact that in the case of the less sterically hindered open chain aldehydes **5a** and **5b** recovered aldehydes were essentially racemic.

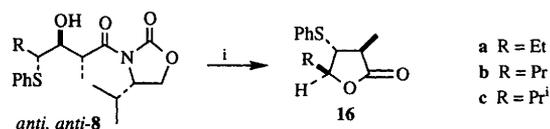
The preference for high Felkin stereoselectivity presumably implies that the faster reacting enantiomer of the aldehydes in this kinetic resolution fits better with the enolate in the Felkin transition state wherein the phenylsulfanyl group occupies the perpendicular position on steric and stereoelectronic grounds. The preference for high Felkin stereoselectivity in this asymmetric aldol reaction of a boron enolate is consistent with earlier results in these laboratories⁹ in spite of the kinetic resolution process. That is to say that the Felkin stereoselectivity also depends on the nature of the enolate geometry and metal counterion. *Z*-Boron enolates give higher Felkin stereoselectivity in reactions with 2-phenylsulfanyl aldehydes than the corresponding *E*-lithium enolates. For instance, the Felkin stereoselectivity in the aldol reaction on aldehyde **5a** for the *E*-lithium enolate derived from 2,6-dimethylphenyl propionate **10** is 2.4:1, while that for the *Z*-boron enolate derived from thioester **11** is 9:1. Higher Felkin stereoselectivity in the aldol

reaction involving boron enolates has been rationalised on the basis of stronger chelation and enolate geometry. Since boron–oxygen bonds are shorter than lithium–oxygen bonds, the aldol transition state is tighter with boron enolates than with lithium enolates. This rationale can also be safely extended to this asymmetric *anti* aldol reaction since the boron enolate used has the normal *Z* configuration. A tighter open chain transition state through which this reaction proceeds would explain the observed high Felkin stereoselectivity. Use of an enantiomerically pure 2-phenylsulfanyl aldehyde, one whose enantiomer fits better with the chiral enolate in the Felkin transition state, in a double stereodifferentiating aldol reaction would be expected to lead to even higher levels of Felkin stereocontrol.

The 2,3-*anti* stereochemistry of the aldol products was confirmed by successful cyclisation to the respective ethers and lactones (Schemes 4 and 5), as secondary to secondary



Scheme 4 Reagents and conditions: i, LiBH₄–H₂O, 0 °C; ii, TsOH, cat., reflux



Scheme 5 Reagents and conditions: i, TsOH, cat., CH₂Cl₂, reflux

phenylsulfanyl migrations take place only from 2,3-*anti* aldols.⁴ The absolute configuration at the 3-hydroxy position is determined from the aldol reaction since the enolate adds to the aldehyde from the top face. The 3,4 relative stereochemistry was confirmed by reduction to the diols and by NMR comparison with the known (R = Et) racemic diols, and also from the coupling constants in the case of lactones. In order to prepare the intermediate optically active diols **12–13** required for

stereospecific cyclisations, lithium borohydride in the presence of an equivalent of water¹⁰ was employed to effect clean reductions leading to high yields and high enantiomeric purities of diols from both Felkin and non-Felkin aldol products with recovery of the chiral auxiliary **6** (Scheme 4). The chemical yields of the products ranged from 69–79%. The enantiomeric purities of the diols as determined by ¹H NMR using Mosher's ester method¹¹ and by comparison with racemic compounds was found to be >98% in all cases. Racemic compounds were synthesised *via* an *anti*-selective aldol reaction between the lithium enolate of 2,6-dimethylphenyl propionate **10** and aldehyde **5**. Stereospecific cyclisation of enantiomerically pure diols *via* an asymmetric episulfonium ion was achieved by treatment of diols **12–13** with a catalytic amount of TsOH under reflux for five minutes. Cyclic ethers **14** and **15** were obtained in essentially enantiomerically pure form (>98% ee) and higher yields (84–91%). The ees of the cyclic ethers were determined by ¹H NMR using the chiral lanthanide shift reagent, Eu(hfc)₃, on both racemic and optically active compounds. As expected, cyclisation proceeded with inversion of configuration at both the migration terminus and origin. Allyl sulfide formation was not observed as it is highly disfavoured in secondary to secondary phenylsulfanyl migrations.¹²

Secondary to secondary phenylsulfanyl migrations also occur in the formation of racemic lactones, provided the stereochemical outcome of the cyclisation is such that the phenylsulfanyl group is *anti* to the methyl group in the product.⁴ Ideally *anti* β-hydroxy acid precursors would be needed for this cyclisation. However, in the present series of compounds, rearrangement to lactones occurred without prior removal of the chiral auxiliary on treatment of the aldol products **8a–c** with 5.0 equiv. of TsOH under reflux in dichloromethane for 1 h. Lactones **16a–c** were obtained as the sole products in moderate to good yields (Scheme 5), with excellent enantiomeric excesses (>98%) as determined by ¹H NMR using Pirkle's chiral solvating alcohol.¹³ The chiral auxiliary was recovered in good yield under these non-destructive conditions. The typical vicinal coupling constants of 10.8–11.5 Hz confirmed the *anti* stereochemical relationship between the phenylsulfanyl group and the methyl group in the product lactones, as well as the 2,3-*anti* stereochemistry of the aldol precursor. As before, no detectable racemisation was observed in these cyclisations.

In conclusion, we have shown that in the absence of ideal non-basic conditions under which potentially enolisable enantiomerically pure 2-phenylsulfanyl aldehydes could be used in asymmetric aldol reactions, kinetic resolutions *via* asymmetric aldol reactions are a viable alternative to provide intermediate enantiomerically pure β-hydroxy sulfides required for secondary to secondary phenylsulfanyl migrations leading to enantiomerically pure cyclic ethers and lactones. Recently, a kinetic resolution of α-tetrahydrofuranal propanals *via* the Evans asymmetric aldol reaction has been observed in studies related to the synthesis of macrodiolide antibiotics pamamycins 607 and 635B subunits.¹⁴

Experimental

Thin layer chromatography (TLC) was carried out on commercially available pre-coated plates (Merck Kieselgel 60F₂₅₄ silica). Column chromatography was carried out on Merck Kieselgel 60 (70–230 mesh) silica, or at slightly greater than atmospheric pressure using Merck Kieselgel 60 (230–400 mesh) unless otherwise stated. High performance liquid chromatography (HPLC) was performed using a Dynamax prepacked silica column with a Gilson model 303 pump and a Cecil Instruments CE 212A UV detector measuring the absorbance between 247–254 nm.

Melting points were measured on a Reichart hot stage microscope and are uncorrected. Infrared spectra were

recorded on a Perkin-Elmer 297 grating spectrophotometer, calibrated against polystyrene. ¹H NMR spectra were recorded on Bruker WM 250 (250 MHz), Bruker AM-400 (400 MHz) and Bruker WP 80 SY (80 MHz) machines while the ¹³C NMR spectra were recorded at 62.5 MHz on a Bruker WM 250 spectrophotometer. Chemical shifts are (δ) are quoted in parts per million relative to tetramethylsilane (δ 0.00) or chloroform (δ 7.25) for ¹H NMR spectra, and relative to chloroform (δ 77.0) for ¹³C NMR spectra. Coupling constants (*J*) are quoted in Hz. Mass spectra were recorded on an AEI Kratos MS 30 machine, or on a VG Trio 2 or VG 7070E machine. The DS503 data system was used for high resolution analysis. Microanalyses were carried out using a Carlo Erba 1106 or Perkin-Elmer 240 automatic analyser. Optical rotation measurements were performed on a Perkin-Elmer 241 Na 589 polarimeter.

All solvents were distilled before use. Tetrahydrofuran (THF) was distilled from lithium aluminium hydride using benzophenone radical as an indicator. Diethyl ether was distilled from lithium aluminium hydride and CH₂Cl₂ from calcium hydride. Benzene was distilled over sodium wire. Dimethylformamide (DMF) was distilled under reduced pressure from calcium hydride and stored over 4 Å molecular sieves. Brine refers to saturated aqueous sodium chloride. Most reagents were either used as received from commercial suppliers or purified by standard methods.

1-Trimethylsilyloxybut-1-ene **4a**

Butanal **3a** (6 cm³, 69 mmol) was added to triethylamine (23.5 cm³, 166 mmol) and trimethylsilyl chloride (Me₃SiCl) (10.6 ml, 83 mmol) in DMF (45 ml) under argon and the mixture stirred at 80 °C for 22 h. The mixture was cooled, light petroleum (bp 30–40 °C) (300 cm³) added, and washed twice quickly with hydrochloric acid (40 cm³ of a 3 mol dm⁻³ solution), saturated sodium hydrogen carbonate (50 cm³) and brine (50 cm³). The organic layer was separated, dried (MgSO₄), and the light petroleum (bp 30–40 °C) carefully removed under reduced pressure to give the silyl enol ether (6.8 g, 68%), as a 2:1 mixture of isomers, bp 42–44 °C/48 mmHg (lit.,¹⁵ bp 56–62 °C/75 mmHg); δ_H(250 MHz; CDCl₃) 6.22 (1 H, m, CHOSiMe₃, *E*), 6.10 (1 H, m, CHOSiMe₃, *Z*), 5.06 (1 H, dt, *J* 7.2 and 14.3, CH=CHOSiMe₃, *E*), 4.50 (1 H, dt, *J* 6.0 and 13.1, CH=CHOSiMe₃, *Z*), 2.14–2.01 (2 H, m, CH₂Me, *Z*), 1.96–1.84 (2 H, m, CH₂Me, *Z*), 0.96 (3 H, t, *J* 3.0, Me, *Z*), 0.92 (3 H, t, *J* 3.2, Me, *E*), 0.17 (9 H, s, SiMe₃, *Z*) and 0.16 (9 H, s, SiMe₃, *E*).

1-Trimethylsilyloxybut-1-ene **4b**

In the same way, pentanal **3b** (5.0 cm³, 47 mmol) and Me₃SiCl (7.2 cm³) gave the silyl enol ether **4b** (4.7 g, 63%) as a colourless liquid and a 1.4:1 mixture of isomers, bp 46–52 °C/36 mmHg; δ_H(250 MHz; CDCl₃) 6.21–6.12 (1 H, m, CH=CHOSiMe₃, *E* and *Z*), 4.98 (1 H, dt, *J* 7.5 and 15.0, CH=CHOSiMe₃, *E*), 4.48 (1 H, dt, *J* 6.0 and 13.2, CH=CHOSiMe₃, *Z*), 2.08–1.99 (2 H, m, CH₂CH=OSiMe₃, *Z*), 2.03 (2 H, dq, *J* 1.5 and 7.2, CH₂CH=CHOSiMe₃, *E*), 1.85 (2 H, dq, *J* 1.2 and 7.1, CH₂CH=CHOSiMe₃, *E*), 1.41–1.26 (2 H, CH₂CH₂CH=CHOSiMe₃, *E* and *Z*), 0.96–0.84 (3 H, m, MeC₂H₄CH=CHOSiMe₃, *E* and *Z*), 0.17 (9 H, s, SiMe₃, *E*) and 0.16 (9 H, s, SiMe₃, *Z*).

3-Methyl-1-trimethylsilyloxybut-1-ene **4c**

In the same way, 3-methylbutanal **3c** (5 cm³, 46.6 mmol) gave the silyl enol ether **4c** (2.82 g, 70%) as a 1.3:1 ratio of isomers, bp 42–44 °C/38 mmHg; δ_H(250 MHz; CDCl₃) 6.20 (1 H, dd, *J* 1.0 and 12.1, CH=CHOSiMe₃, *E*), 6.02 (1 H, dd, *J* 0.92 and 9.0, CH=CHOSiMe₃, *Z*), 4.95 (1 H, dd, *J* 7.8 and 12, CH=CHOSiMe₃, *E*), 4.34 (1 H, dd, *J* 5.9 and 8.9, CH=CHOSiMe₃, *Z*), 2.86–2.71 (1 H, m, CHMe₂, *E*), 2.30–2.11 (1 H, m, CHMe₂, *Z*), 0.96 (3 H, d, *J* 6.7, MeCHMe, *Z*), 0.94 (3 H, d, *J* 5.5, MeCHMe, *E*), 0.17 (9 H, s, SiMe₃, *E*) and 0.16 (9 H, s, SiMe₃, *Z*).

(2*RS*)-2-Phenylsulfanylbutanal 5a

Phenylsulfenyl chloride was prepared *in situ* by the addition of sulfur chloride (SO_2Cl_2) (1.2 cm³, 14.4 mmol) to diphenyl disulfide (3.14 g, 14.4 mmol) and pyridine (15 drops) in dry THF (43 cm³) under argon at room temperature for 1 h, and then added at -78°C to a stirred solution of silyl enol ether **4a** (4.14 g, 29 mmol) in CH_2Cl_2 (15 cm³) at -78°C under argon. The mixture was allowed to warm to room temperature and stirred for a further 1.5 h, the solvent evaporated under reduced pressure and the residue chromatographed (SiO_2 , Et_2O -hexane, 1:10) to give the aldehyde (3.54 g, 68%) as an oil; δ_{H} (250 MHz; CDCl_3) 9.38 (1 H, d, *J* 4.0, CHO), 7.5–7.2 (5 H, m, SPh), 3.44 (1 H, ddd, *J* 7.5, 7.5 and 4.0, *CHSPh*), 1.95–1.61 (2 H, m, CH_2Me) and 1.08 (3 H, t, *J* 7.4, Me).

(2*RS*)-2-Phenylsulfanylpentanal 5b

In the same way, silyl enol ether **4b** (3.7 g, 23.2 mmol) gave the aldehyde **5b** (3.27 g, 72%) as an oil; R_{f} (Et_2O -hexane, 1:10) 0.4; ν_{max} (film)/cm⁻¹ 1734 (C=O) and 1566 (SPh); δ_{H} (250 MHz; CDCl_3) 9.35 (1 H, d, *J* 4.3, CHO), 7.5–7.3 (5 H, m, SPh), 3.52 (1 H, ddd, *J* 4.3, 7.5 and 11.8, *CHSPh*), 1.81–1.39 (4 H, m, C_2H_4) and 0.95 (3 H, t, *J* 7.2, Me); δ_{C} (CDCl_3) 195.3, 132.7, 129.1, 128.1, 56.6, 29.8, 20.1 and 13.7; *m/z* 193 (65%, $\text{M} - 1$), 165 (68, $\text{M} - \text{CHO}$), 110 (44, PhSH), 109 (52, SPh) and 55 (44, C_4H_7) (Found: M^+ , 194.0688. $\text{C}_{11}\text{H}_{14}\text{OS}$ requires M , 194.0681).

(2*RS*)-3-Methyl-2-phenylsulfanylbutanal 5c

In the same way, silyl enol ether **4c** (2.2 g, 14 mmol) gave the aldehyde **5c** (2.20 g, 82%) as an oil; R_{f} (Et_2O -hexane, 1:10) 0.34; ν_{max} (film)/cm⁻¹ 1734 (C=O) and 1566 (SPh); δ_{H} (250 MHz; CDCl_3) 9.34 (1 H, d, *J* 5.4, CHO), 7.4–7.2 (5 H, m, SPh), 3.28 (1 H, dd, *J* 5.4 and 8.5, *CHSPh*), 2.19–2.00 (1 H, m, CHMe_2), 1.18 (3 H, d, *J* 6.7, *MeCHMe*) and 1.08 (3 H, d, *J* 6.8, *MeCHMe*); δ_{C} (CDCl_3) 194.9, 132.6, 132.1, 129.0, 127.7, 64.4, 27.8, 20.6 and 19.9; *m/z* 194 (44%, M^+), 165 (100, $\text{M} - \text{CHO}$), 110 (14, PhSH), 109 (23, SPh) and 55 (16, C_4H_7) (Found: M^+ , 194.0758. $\text{C}_{11}\text{H}_{14}\text{OS}$ requires M , 194.0795).

(4*S*)-3-[(2*R*,3*S*,4*R*)- and (4*S*)-3-[(2*R*,3*S*,4*S*)-3-Hydroxy-2-methyl-4-phenylsulfanyl-1-oxohexyl]-4-(1-methylethyl)-1,3-oxazolidin-2-one, anti,anti-8a and syn,anti-9a

Diisopropylethylamine (0.08 cm³, 0.43 mmol) was added to imide **10** (0.07 g, 0.37 mmol) in CH_2Cl_2 (0.7 cm³) at 0°C under argon followed by dibutylboron triflate (0.45 cm³ of a 1.0 mol dm⁻³ solution in CH_2Cl_2). After 45 min, the enolate was cooled to -78°C and added to a precomplexed and stirred mixture of diethylaluminium chloride (1.5 cm³ of a 1.0 mol dm⁻³ solution in hexane) and aldehyde **5a** (0.134 g, 0.75 mmol) at -78°C . After 1 h at -78°C the reaction was quenched with methanol (2.5 cm³) and 30% hydrogen peroxide (0.50 cm³). The reaction mixture was then allowed to warm to 0°C and held at this temperature for 1 h. Water was added and the layers were separated. The aqueous layer was extracted with diethyl ether and the combined extracts washed with dilute sodium hydrogen carbonate (1.0 mol dm⁻³) and brine, dried (MgSO_4) and evaporated under reduced pressure. The residue, which was a 75:25 mixture, was chromatographed (SiO_2 , CH_2Cl_2 -MeOH, 200:1) to give the aldol **8a** (0.086 g, 63%) as an oil; R_{f} (CH_2Cl_2 -MeOH, 200:1) 0.38; ν_{max} (film)/cm⁻¹ 3512 (OH), 1780 and 1692 (C=O) and 1584 (SPh); δ_{H} (250 MHz; CDCl_3) 7.4–7.2 (5 H, m, SPh), 4.48–4.16 (4 H, m, OCH_2CHN , *MeCHCO*), 4.08 (1 H, dd, *J* 6.3 and 8.7, *CHOH*), 3.76 (1 H, br s, OH), 3.16–3.10 (1 H, m, *CHSPh*), 2.34 (1 H, dq, *J* 3.0, 7.0 and 7.0, CHMe_2), 1.89 (1 H, ddq, *J* 3.3, 7.4 and 14.8, $\text{CH}_A\text{H}_B\text{Me}$), 1.65 (1 H, ddq, *J* 7.4, 9.6 and 14.8, $\text{CH}_A\text{H}_B\text{Me}$), 1.15 (6 H, d and t, *MeCH}_2*, *MeCHCO*), 0.87 (3 H, d, *J* 7.0, *MeCHMe*) and 0.83 (3 H, d, *J* 6.9, *MeCHMe*); δ_{C} (CDCl_3) 176.7, 153.8, 134.5, 131.9, 129.0, 127.1, 76.0, 63.0, 58.7, 55.3, 39.2, 32.6, 28.2, 21.5, 18.0, 14.6, 14.5 and 12.1; *m/z* 365 (58%, M^+), 256 (18, $\text{M} - \text{SPh}$), 130 (100, $\text{C}_6\text{H}_{12}\text{NO}_2$), 109 (44, SPh) and 55 (18, C_4H_7) (Found:

M^+ , 365.1684. $\text{C}_{19}\text{H}_{27}\text{NO}_4\text{S}$ requires M , 365.1453); and the aldol **9a** (0.022, 16%) as an oil; R_{f} (CH_2Cl_2 -MeOH, 200:1) 0.21; δ_{H} (250 MHz; CDCl_3) 7.5–7.2 (5 H, m, SPh), 4.44–4.19 (4 H, m, OCH_2CHN , *CHCO*), 3.95 (1 H, t, *J* 6.0, *CHOH*), 3.13–3.06 (1 H, m, *CHSPh*), 2.32 (1 H, dq, *J* 3.0, 7.0 and 7.0, CHMe_2), 1.93 (1 H, ddq, *J* 3.3, 7.4 and 14.8, $\text{CH}_A\text{H}_B\text{Me}$), 1.58–1.53 (1 H, m, $\text{CH}_A\text{H}_B\text{Me}$), 1.12 (6 H, d and t, *MeCH}_2*, *MeCHCO*), 0.92 (3 H, d, *J* 7.1, *MeCHMe*) and 0.88 (3 H, d, *J* 7.0, *MeCHMe*).

(4*S*)-3-[(2*R*,3*S*,4*R*)- and (4*S*)-3-[(2*R*,3*S*,4*S*)-3-Hydroxy-2-methyl-4-phenylsulfanyl-1-oxoheptyl]-4-(1-methylethyl)-1,3-oxazolidin-2-one, anti,anti-8b and syn,anti-9b

In the same way, imide **7** (0.099 g) and aldehyde **5b** (0.21 g) gave the aldol **8b** (0.152 g, 75%) as needles, mp 85 – 87°C (from EtOAc -hexane); R_{f} (CH_2Cl_2 -MeOH, 200:1) 0.35; ν_{max} (film)/cm⁻¹ 3503 (OH), 1779 and 1698 (C=O) and 1583 (SPh); δ_{H} (250 MHz; CDCl_3) 7.4–7.2 (5 H, m, SPh), 4.42 (1 H, q, *J* 3.9, NCH), 4.38–4.17 (3 H, m, OCH_2 , *CHCO*), 3.78 (1 H, ddd, *J* 3.8, 6.4 and 10.0, *CHOH*), 3.22 (1 H, dt, *J* 3.0 and 9.6, *CHSPh*), 3.00 (1 H, d, *J* 6.2, OH), 2.34 (1 H, dq, *J* 3.8, 7.0 and 7.0, CHMe_2), 1.78–1.26 (4 H, m, RC_2H_4), 1.10 (3 H, d, *J* 6.9, *MeCHCO*), 0.95 (3 H, t, *J* 7.0, *MeCH}_2*), 0.90 (3 H, d, *J* 6.8, *MeCHMe*) and 0.86 (3 H, d, *J* 6.8, *MeCHMe*); δ_{C} (CDCl_3) 176.5, 153.9, 134.5, 131.9, 131.6, 129.0, 127.2, 76.0, 63.0, 58.7, 53.1, 39.1, 30.1, 28.3, 20.6, 18.0, 14.5, 14.4 and 13.9; *m/z*, 379 (64%, M^+), 130 (100, $\text{C}_6\text{H}_{12}\text{NO}_2$), 109 (18, SPh) and 55 (22, C_4H_7) (Found: C, 63.09; H, 7.73; N, 3.55; S, 8.52. $\text{C}_{20}\text{H}_{29}\text{NO}_4\text{S}$ requires C, 63.32; H, 7.65; N, 3.69; S, 8.44%); and the aldol **9b** (0.012 g, 6%) as an oil; R_{f} (CH_2Cl_2 -MeOH, 200:1) 0.20; δ_{H} (250 MHz; CDCl_3) 7.5–7.2 (5 H, m, SPh), 4.51–4.17 (4 H, m, OCH_2CHN , *MeCHCO*), 3.94 (1 H, ddd, *J* 3.4, 5.7 and 9.1, *CHOH*), 3.19 (1 H, ddd, *J* 2.8, 6.1 and 9.7, *CHSPh*), 2.98 (1 H, d, *J* 3.4, OH), 2.33 (1 H, dq, *J* 3.8, 7.0 and 7.0, CHMe_2), 1.87–1.40 (4 H, m, RCH_2CH_2), 1.12 (3 H, d, *J* 6.9, *MeCHCO*) and 0.91–0.89 (t dd, *J* 7.1, 7.0 and 7.0, MeCH_2 , *MeCHMe* and *MeCHMe*); δ_{C} (CDCl_3) 176.5, 153.4, 134.8, 131.7, 129.0, 127.0, 73.1, 63.1, 58.5, 53.1, 40.0, 31.4, 28.5, 20.5, 18.0, 14.6, 14.0 and 13.0.

(4*S*)-3-[(2*R*,3*S*,4*R*)- and (4*S*)-3-[(2*R*,3*S*,4*S*)-3-Hydroxy-2,5-dimethyl-4-phenylsulfanyl-1-oxohexyl]-4-(1-methylethyl)-1,3-oxazolidin-2-one 8c and 9c

In the same way, the imide gave an inseparable mixture of the aldol products **8c** and **9c**; δ_{H} (250 MHz; CDCl_3) 7.5–7.2 [10 H, m, SPh, (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)], 4.64–4.48 [4 H, m, OCH_2CHN , *MeCHCO*, (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)], 4.10 [1 H, dd, *J* 2.9 and 9.4, *CHOH*, (2*R*,3*S*,4*R*)], 3.84 [1 H, t, *J* 6.3, *CHOH*, (2*R*,3*S*,4*S*)], 3.21 [1 H, dd, *J* 3.0 and 6.6, *CHSPh*, (2*R*,3*S*,4*R*)], 3.10 [1 H, dd, *J* 2.6 and 9.4, *CHSPh*, (2*R*,3*S*,4*S*)], 2.53 [2 H, m, CHMe_2 , (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)], 2.46 [1 H, m, Me_2CHSPh , (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)] and 1.30–0.70 [30 H, d + t, Me_5 , (2*R*,3*S*,4*R*) and (2*R*,3*S*,4*S*)].

(2*R*,3*S*,4*R*)-3-Hydroxy-2-methyl-4-phenylsulfanylhexan-1-ol 12a

Lithium borohydride (0.56 cm³ of a 2.0 mol dm⁻³ solution in THF) was added to a stirred solution of the aldol **8a** (0.37 g) in Et_2O (20 cm³) and water (0.02 cm³) under argon at 0°C . After 1–2 h at room temperature, aqueous sodium hydroxide (0.36 cm³ of a 2.5 mol dm⁻³ solution) was added and the mixture stirred until both layers were clear. The mixture was poured into Et_2O (45 cm³) and water (45 cm³). After separation, the aqueous layer was extracted with Et_2O (3 × 45 cm³). The combined extracts were washed with brine (45 cm³), dried (Na_2SO_4) and evaporated under reduced pressure. The residue was chromatographed (SiO_2 , CH_2Cl_2 -MeOH, 100:1) to give recovered chiral auxiliary **6** and the diol (0.192 g, 80%) as an oil; δ_{H} (250 MHz; CDCl_3) 7.42–7.25 (5 H, m, SPh), 3.56 (2 H, distorted ABX system, J_{AX} 4.5 and J_{BX} 6.9, $\text{CH}_X\text{CH}_A\text{H}_B\text{O}$), 3.45 (1 H, dd, *J* 2.5 and 9.2, *CHOH*), 3.20 (1 H,

dt, J 2.8 and 10.5, $CHSPH$), 1.97 (1 H, sym m, CH_xMe), 1.82 (1 H, ddq, J 2.6, 7.4 and 14.8, CH_AH_BMe), 1.52 (1 H, ddq, J 7.4, 10.4 and 14.8, CH_AH_BMe), 1.16 (3 H, t, J 7.4, $MeCH_2$) and 0.74 (3 H, d, J 7.0, $MeCH$); $[\alpha]_D^{20} + 14.6$ (c 3.6 in $CHCl_3$).

(2R,3S,4R)-3-Hydroxy-2-methyl-4-phenylsulfanylheptan-1-ol 12b

In the same way, the aldol **8b** (0.094 g) gave the diol **12b** (0.046 g, 73%) as an oil; $R_f(Et_2O$ –hexane, 5:2) 0.28; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500 (OH) and 1582 (SPH); $\delta_H(250\text{ MHz}; CDCl_3)$ 7.4–7.2 (5 H, m, SPH), 3.56 (2 H, distorted multiplet, $CHOH$, CH_AH_BOH), 3.43 (1 H, dt, J 1.9, 3.9 and 9.4, CH_AH_BOH), 3.29 (1 H, dt, J 2.5, 5.1 and 10.2, $CHSPH$), 3.17 (1 H, t, J 5.2, CH_2OH), 3.07 (1 H, d, J 1.8, $CHOH$), 2.02–1.90 (1 H, m, $CHMe$), 1.81–1.72 (2 H, m, RCH_2CHSPH), 1.55–1.45 (2 H, m, $MeCH_2$), 0.97 (3 H, t, J 6.9, $MeCH_2$) and 0.73 (3 H, d, J 7.0, $MeCH$); $\delta_C(CDCl_3)$ 134.1, 132.0, 129.2, 127.3, 77.3, 68.5, 53.8, 36.7, 28.9, 20.9, 13.9 and 13.2; m/z 254 (40%, M^+), 166 (100, C_4H_9SPH), 109 (38, SPH) and 55 (42, C_4H_7) (Found: M^+ , 254.1326. $C_{14}H_{22}O_2S$ requires M , 236.1475).

(2R,3S,4S)-3-Hydroxy-2-methyl-4-phenylsulfanylhexan-1-ol 13a

In the same way, aldol **9a** (62 mg) gave the diol (30 mg, 74%) as an oil; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.4–7.2 (5 H, m, SPH), 3.63–3.47 (3 H, m, $CHOH$, CH_AH_BOH), 3.81 (1 H, dd, J 2.5 and 4.6, $CHSPH$), 2.63 (2 H, br s, OH), 2.36 (1 H, dddq, J 2.5, 2.5, 6.8 and 6.8, $CHMe$), 2.17–2.01 (1 H, m, $CHMe_2$), 1.21 (3 H, d, J 6.8, $MeCHMe$), 1.04 (3 H, d, J 6.8, $MeCHMe$) and 0.80 (3 H, d, J 7.0 $MeCHCO$).

(2R,3S,4S)-3-Hydroxy-2-methyl-4-phenylsulfanylheptan-1-ol 13b

In the same way, aldol **9b** (0.1 g, 0.26 mmol) gave the diol **13b** (48 mg, 69%) as an oil; $R_f(EtOAc$ –hexane, 1:3); $\nu_{max}(film)/cm^{-1}$ 3422 (OH) and 1583 (SPH); $\delta_H(250\text{ MHz}; CDCl_3)$ 7.5–7.2 (5 H, m, SPH), 3.74 (1 H, dd, J 4.4 and 6.6, $CHOH$), 3.68–3.62 (2 H, m, CH_2O), 3.22 (1 H, ddd, J 3.0, 6.6 and 9.5, $CHSPH$), 2.83 (2 H, br s, OH), 2.20 (1 H, sym m, $CHMe$), 1.79–1.66 (2 H, m, RCH_2CHSPH), 1.58–1.42 (2 H, m, RCH_2R) and 1.13–0.98 (6 H, d and t, $MeCH$ and $MeCH_2$); $\delta_C(CDCl_3)$ 135.2, 133.2, 131.9, 129.0, 127.0, 74.9, 67.0, 53.7, 36.6, 32.0, 20.2, 14.0 and 11.1.

(2R,3S,4R)- and (2R,3S,4S)-3-Hydroxy-2,5-dimethyl-4-phenylsulfanylhexan-1-ol 12c and 13c

In the same way, the mixture of aldols **8c** and **9c** gave the diol **12c** as plates, mp 93–95 °C (from Et_2O –hexane); $R_f(CH_2Cl_2$ – $MeOH$, 20:1) 0.61; $\nu_{max}(CHCl_3)/cm^{-1}$ 3500 (2OH) and 1582 (SPH); $\delta_H(250\text{ MHz}; CDCl_3)$ 7.4–7.2 (5 H, m, SPH), 3.63–3.47 (3 H, m, $CHOH$, CH_AH_BOH), 3.81 (1 H, dd, J 2.5 and 4.6, $CHSPH$), 2.63 (2 H, br s, OH), 2.36 (1 H, dddq, J 2.5, 2.5, 2.5, 6.8 and 6.8, $CHMe$), 2.17–2.01 (1 H, m, $CHMe_2$), 1.21 (3 H, d, J 6.8, $MeCHMe$), 1.04 (3 H, d, J 6.8, $MeCHMe$) and 0.80 (3 H, d, J 7.0, $MeCHCO$); and the diol **13c** as needles, mp 102–104 °C (from Et_2O –hexane); $R_f(CH_2Cl_2$ – $MeOH$, 20:1) 0.53; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.4–7.1 (5 H, m, SPH), 3.96 (1 H, dd, J 2.1 and 9.7, $CHOH$), 3.79 (1 H, dd, J 3.8 and 10.5, CH_AH_BOH), 3.68 (1 H, dd, J 4.9 and 10.4, CH_AH_BOH), 3.08 (1 H, dd, J 3.2 and 9.7, $CHSPH$), 2.43 (1 H, dddq, J 3.3, 3.3, 3.3, 6.8 and 6.8, $CHMe$), 2.32–2.24 (1 H, m, $CHMe_2$), 2.20 (2 H, br s, OH), 1.17 (3 H, d, J 6.7, $MeCHMe$), 0.89 (3 H, d, J 6.8, $MeCHMe$) and 0.69 (3 H, d, J 7.0, $MeCHCO$).

(2S,3R,4S)-2-Ethyl-4-methyl-3-phenylsulfanyltetrahydrofuran 14a

A mixture of the diol **12a** (60 mg) and $TsOH \cdot H_2O$ (37 mg) in benzene under argon was heated under reflux for 7 min. The solvent was removed under vacuum and the residue chromatographed (SiO_2 ; CH_2Cl_2) to give the tetrahydrofuran

(0.047 g, 85%) as an oil; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.5–7.2 (5 H, m, SPH), 3.93 (1 H, dd, J 7.3 and 8.4, CH_AH_BOR), 3.64 (1 H, dt, J 4.0 and 7.9, CHOR), 3.45 (1 H, dd, J 6.8 and 8.5, CH_AH_BOR), 2.74 (1 H, t, J 7.8, $CHSPH$), 2.22 (1 H, septet, J 7.0, $CHMe$), 1.65 (1 H, ddd, J 4.0, 7.0 and 15.0, CH_AH_BMe), 1.48 (1 H, septet, J 7.0, CH_AH_BMe), 1.10 (3 H, d, J 6.8, $MeCH$) and 0.93 (3 H, t, J 7.4, $MeCH_AH_B$); $[\alpha]_D^{20} - 12.3$ (c 0.97 in $CHCl_3$).

(2S,3R,4S)-4-Methyl-3-phenylsulfanyl-2-propyltetrahydrofuran 14b

In the same way, the diol **12b** (0.032 g) and $TsOH \cdot H_2O$ (0.019 g) after 10 min gave the tetrahydrofuran **14b** (0.027 g, 90%) as an oil; $R_f(CH_2Cl_2)$ 0.52; $\nu_{max}(film)/cm^{-1}$ 1584 (SPH); $\delta_H(250\text{ MHz}; CDCl_3)$ 7.5–7.3 (5 H, m, SPH), 4.00 (1 H, t, J 8.4, CH_AH_BOR), 3.76 (1 H, ddd, J 3.5, 7.9 and 11.3, CHOR), 3.53 (1 H, dd, J 6.8 and 8.4, CH_AH_BOR), 2.79 (1 H, t, J 7.8, $CHSPH$), 2.28 (1 H, sym m, $CHMe$), 1.67–1.37 (4 H, m, C_2H_4R), 1.18 (3 H, d, J 6.8, $MeCH$) and 0.96 (3 H, t, J 7.1, $MeCH_2R$); $\delta_C(CDCl_3)$ 130.1, 128.9, 126.3, 83.1, 74.0, 55.4, 37.1, 37.0, 19.4 and 14.0; m/z 236 (42%, M^+), 109 (38, SPH), 55 (100, C_4H_7) and 41 (78, C_3H_5) (Found: M^+ , 236.1349. $C_{14}H_{20}OS$ requires M , 236.1349); $[\alpha]_D^{20} - 1.3$ (c 1.1 in $CHCl_3$).

(2S,3R,4S)-2-Isopropyl-4-methyl-3-phenylsulfanyltetrahydrofuran 14c

In the same way, the diol **12c** (0.049 g) and $TsOH \cdot H_2O$ (0.028 g) gave the tetrahydrofuran **14c** (0.038 g, 84%) as an oil; $R_f(CH_2Cl_2)$ 0.52; $\nu_{max}(film)/cm^{-1}$ 1584 (SPH); $\delta_H(250\text{ MHz}; CDCl_3)$ 7.5–7.2 (5 H, m, SPH), 3.92 (1 H, dd, J 6.7 and 8.5, CH_AH_BOR), 3.50 (1 H, dd, J 5.4 and 7.5, CHOR), 3.44 (1 H, dd, J 6.0 and 8.5, CH_AH_BOR), 2.89 (1 H, t, J 6.5, $CHSPH$), 2.33–2.17 (1 H, m, $CHMe$), 1.92–1.74 (1 H, m, $CHMe_2$), 1.08 (3 H, d, J 6.8, $MeCH$), 0.97 (3 H, d, J 6.9, $MeCHMe$) and 0.92 (3 H, d, J 6.9, $MeCHMe$); m/z 236 (8%, M^+), 110 (60, PhSH) and 43 (100, C_3H_7) (Found: M^+ , 236.1241. $C_{14}H_{20}OS$ requires M , 236.1247); $[\alpha]_D^{20} - 275$ (c 0.2 in $CHCl_3$).

(2R,3R,4S)-2-Ethyl-4-methyl-3-phenylsulfanyltetrahydrofuran 15a

In the same way, the diol **13a** (0.019 g) and $TsOH \cdot H_2O$ (0.012 g) gave the tetrahydrofuran **15a** (0.016 g, 91%) as an oil; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.4–7.2 (5 H, m, SPH), 4.02 (1 H, dd, J 6.4 and 8.5, CH_AH_BOR), 3.69 (1 H, dt, J 4.2 and 7.4, CHOR), 3.51 (1 H, dd, J 6.4 and 8.5, CH_AH_BOR), 3.43 (1 H, t, J 7.4, $CHSPH$), 2.58 (1 H, septet, J 6.8, $CHMe$), 1.77–1.44 (2 H, m, CH_2Me), 1.10 (3 H, d, J 7.0, $MeCH$) and 0.94 (3 H, t, J 7.4, $MeCH_2$); $[\alpha]_D^{20} + 95$ (c 0.6 in $CHCl_3$).

(2R,3R,4S)-4-Methyl-3-phenylsulfanyl-2-propyltetrahydrofuran 15b

In the same way, diol **13b** (0.027 g) and $TsOH \cdot H_2O$ (0.016 g) gave the tetrahydrofuran **15b** (0.021 g, 84%) as an oil; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.5–7.2 (5 H, m, SPH), 4.10 (1 H, dd, J 6.4 and 8.5, CH_AH_BOR), 3.82 (1 H, dt, J 7.5 and 11.3, CHOR), 3.58 (1 H, dd, J 6.4 and 8.5, CH_AH_BOR), 3.49 (1 H, t, J 7.5, $CHSPH$), 2.70–2.57 (1 H, sym m, $CHMe$), 1.69–1.39 (4 H, m, C_2H_4R), 1.17 (3 H, d, J 7.0, $MeCH$) and 0.96 (3 H, t, J 7.1, $MeCH_2$); $[\alpha]_D^{20} + 13.9$ (c 1.1 in $CHCl_3$).

(2R,3R,4S)-2-Isopropyl-4-methyl-3-phenylsulfanyltetrahydrofuran 15c

In the same way, diol **13c** (0.015 g) and $TsOH \cdot H_2O$ (0.009 g) gave the tetrahydrofuran **15c** (0.012 g, 86%) as an oil; $\delta_H(250\text{ MHz}; CDCl_3)$ 7.6–7.1 (5 H, m, SPH), 4.21 (1 H, dd, J 2.6 and 5.7, CH_AH_BOR), 3.95 (1 H, dd, J 6.3, and 8.4, CHOR), 3.64–3.49 (2 H, m, CH_AH_BOR , $CHSPH$), 2.58–2.42 (1 H, m, $CHMe$), 1.86–1.70 (1 H, m, $CHMe_2$), 1.09 (3 H, d, J 7.0, $MeCH$) and 0.90 and 0.85 (each 3 H, d, J 7.0, $CHMe_2$); $[\alpha]_D^{20} + 42$ (c 1.2 in $CHCl_3$).

(2S,3R,4S)-4-Ethyl-2-methyl-3-phenylsulfanyl-4-butanolide 16a

In the same way, the aldol **8a** (20 mg, 0.05 mmol) was refluxed with TsOH·H₂O in CH₂Cl₂ under argon for 1 h. After evaporating the CH₂Cl₂ under reduced pressure, the residue was chromatographed (SiO₂, EtOAc–hexane, 3:17) to give the lactone **16a** (8.9 mg, 69%) as plates; δ_{H} (250 MHz; CDCl₃) 7.5–7.3 (5 H, m, SPh), 4.10 (1 H, ddd, *J* 3.2, 8.3 and 9.5, RCHOR), 2.94 (1 H, dd, *J* 9.5 and 11.5, CHSPh), 2.47 (1 H, dq, *J* 7.1 and 11.5, CHMe), 1.91 (1 H, ddq, *J* 3.2, 7.4 and 14.1, CH_AH_BMe), 1.56 (1 H, septet, *J* 7.4, CH_AH_BMe), 1.31 (3 H, d, *J* 7.1, MeCH) and 1.02 (3 H, t, *J* 7.2, MeCH₂); $[\alpha]_{\text{D}}^{20}$ –46.6 (*c* 0.1 in CHCl₃).

(2S,3R,4S)-2-Methyl-3-phenylsulfanyl-4-propyl-4-butanolide 16b

In the same way, the aldol **8b** (39 mg, 0.1 mmol) gave the lactone **16b** (19 mg, 74%) as cubes, mp 41–43 °C (from Et₂O–hexane); *R*_f(EtOAc–hexane, 3:17) 0.27; ν_{max} (film)/cm^{–1} 1774 (C=O) and 1583 (SPh); δ_{H} (250 MHz; CDCl₃) 7.6–7.3 (5 H, m, SPh), 4.21 (1 H, ddd, *J* 2.7, 11.0 and 12.1, RCHOR), 2.98 (1 H, dd, *J* 9.6 and 11.5, CHSPh), 2.52 (1 H, dq, *J* 7.1 and 11.5, CHMe), 1.97–1.82 (1 H, m, CH_AH_BCH₂Me), 1.68–1.43 (3 H, m, CH_AH_BCH₂Me), 1.38 (3 H, d, *J* 7.0, MeCH) and 0.97 (3 H, t, *J* 7.1, MeCH₂R); δ_{C} (CDCl₃) 176.8, 135.1, 129.4, 129.1, 128.6, 82.8, 55.3, 41.5, 35.1, 19.0, 16.0, 13.8 and 13.1; *m/z* 250 (62%, M⁺), 150 (100, M – C₅H₈O₂), 141 (15, M – SPh) and 109 (59, SPh) (Found: M⁺, 250.1048. C₁₄H₁₈O₂S requires *M*, 250.0844); $[\alpha]_{\text{D}}^{21}$ –23.5 (*c* 1.0 in CHCl₃).

(2S,3R,4S)-4-Isopropyl-2-methyl-3-phenylsulfanyl-4-butanolide 16c

In the same way, the impure aldol **8c** (61 mg, 0.16 mmol) gave the major lactone as needles, mp 66–68 °C (from Et₂O–hexane); *R*_f(Et₂O–hexane, 1:2) 0.40; ν_{max} (film)/cm^{–1} 1769 (C=O) and 1583 (SPh); δ_{H} (250 MHz; CDCl₃) 7.6–7.3 (5 H, m, SPh), 4.13 (1 H, dd, *J* 3.8 and 9.3, RCHOR), 3.13 (1 H, dd, *J* 9.3 and 10.8, CHSPh), 2.59 (1 H, dq, *J* 7.2 and 10.8, CHMe), 2.10 (1 H, dqq, *J* 3.8, 6.9 and 7.0, CHMe₂), 1.36 (3 H, d, *J* 7.1, MeCH), 1.15 (3 H, d, *J* 7.0, MeCHMe) and 0.98 (3 H, d, *J* 6.8, MeCHMe); δ_{C} (CDCl₃) 176.7, 134.8, 130.7, 129.3, 128.9, 86.9, 52.2, 42.1, 29.7, 19.6, 15.8 and 13.4; *m/z* 250.1 (30%, M⁺), 109 (30, SPh), 55.1 (38, C₄H₇) and 41 (100, C₃H₅) (Found: C, 67.02; H, 7.17; S, 12.66. C₁₄H₁₈O₂S requires C, 67.2; H, 7.2; S, 12.8%); $[\alpha]_{\text{D}}^{20}$ –7.8 (*c* 0.6 in CHCl₃).

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