

# Synthesis and reactions of some optically active epoxyketones formally derived from tertiary allylic alcohols

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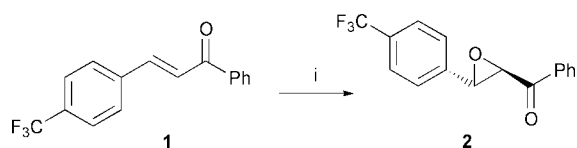
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Received (in Cambridge, UK) 13th October 2000, Accepted 26th February 2001  
First published as an Advance Article on the web 21st March 2001

The epoxyketones **2**, **3** and **7–9** reacted with Grignard reagents in a highly stereocontrolled manner to give the epoxyalcohols **20**, **4–6** and **11–13** in high yields. The epoxyalcohol **12** underwent a Payne rearrangement on base treatment to give the isomer **15** while epoxyalcohols **4**, **5**, **12** and **20** suffered ring-opening (with retention of configuration) using tin(IV) chloride to afford chlorodiols **18**, **17**, **19** and **21** respectively. On the other hand, the alcohols **4**, **5** and **12** reacted with trialkylsilyl chlorides to furnish the chlorodiols **22**, **24** and **23** respectively with inversion of configuration.

Recent advances in the poly( $\alpha$ -amino acid)-catalysed epoxidation of conjugated enones has resulted in ready access to a range of  $\alpha,\beta$ -epoxyketones in single enantiomer form.<sup>1</sup> For example, the enone **1** is converted into the epoxide **2** (a compound required for the present study—see later) using the recently reported reaction conditions that utilise sodium percarbonate as the cheap, easy-to-use oxidant and base (Scheme 1).<sup>2</sup>

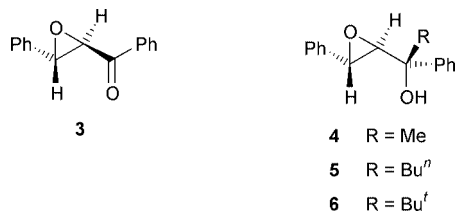


Scheme 1 Reagents and conditions: i)  $\text{Na}_2\text{CO}_3 \cdot 1.5\text{H}_2\text{O}_2$ , poly(L-leucine),  $\text{H}_2\text{O}$ , DME, 18 h, rt, 78%, 97% ee.

As well as expanding the range of readily available, optically active epoxyketones we have been anxious to develop further the chemistry of these compounds through reaction at the carbonyl group and/or the epoxide moiety. In this paper we report in full some of our initial investigations in this area.<sup>3</sup>

## Results and discussion

The epoxyketone **3** suffers attack by a range of Grignard reagents in a highly stereoselective fashion to afford the corresponding tertiary alcohols **4–6**, as essentially single diastereoisomers (dr as determined by  $^1\text{H}$  NMR of the crude product was  $>99:1$  in each case). The yields range from excellent (87%) for the alcohol **4** to a modest 41% for the *tert*-butyl compound **6**.



Similarly, the epoxyketones **7–9** were treated with phenylmagnesium bromide to give single compounds (**11–13** respectively) in each case, with yields ranging from 67 to 97%. Only in

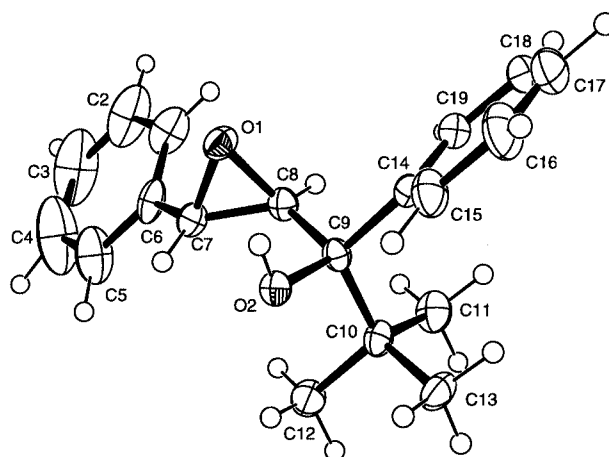
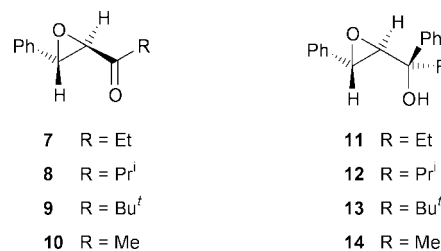
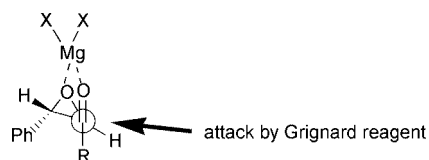


Fig. 1 X-Ray crystal structure of **13**.

the case of the methyl ketone **10** was a mixture of diastereomers obtained on reaction with phenylmagnesium bromide, the major product **14** being contaminated with a small amount of the diastereoisomer **4** (ratio **4** : **14**, 1 : 6).<sup>4</sup>

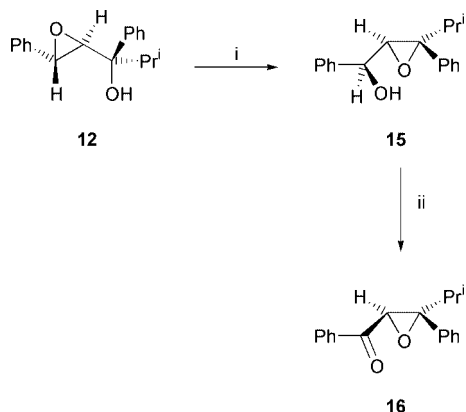


The stereochemistry of the compounds **5**<sup>3</sup> and **13** (Fig. 1) was ascertained by X-ray crystallography. The formation of the tertiary alcohols **4–6** and **11–13** in a stereochemically-controlled manner is explained by chelation of the organomagnesium reagent to the epoxide and carbonyl moieties prior to attack by the nucleophile from the less-hindered *Re*-face (Fig. 2).<sup>4,5</sup> It is interesting to note that the well-known Sharpless asymmetric epoxidation methodology does not work with any degree of success for allylic tertiary alcohols.<sup>6</sup>



**Fig. 2** Chelation controlled attack by Grignard reagents on epoxyketones **3** and **7–9**.

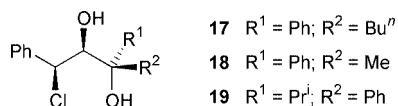
Payne rearrangement<sup>7</sup> of the tertiary alcohol **12** furnished the secondary alcohol **15** as the major product (ratio **12** : **15**, 3 : 97) and subsequent Dess–Martin oxidation of the latter alcohol afforded the epoxyketone **16** (Scheme 2). This illustrates



**Scheme 2** Reagents and conditions: (i) NaOH, Bu<sup>n</sup>OH, 2 h, rt, 97%; (ii) Dess–Martin periodinane, CH<sub>2</sub>Cl<sub>2</sub>, 16 h, rt, 67%.

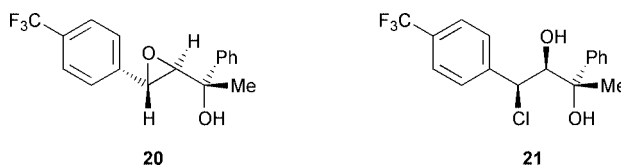
new methodology for the production of epoxides formally derived from  $\beta,\beta$ -disubstituted enones, compounds which do not undergo asymmetric epoxidation directly using poly( $\alpha$ -amino acids) as catalysts.

Attempts to induce a tin(IV) chloride-catalysed semi-pinacol rearrangement<sup>8</sup> on the epoxyalcohol **5** were thwarted by the onset of an epoxide ring-opening reaction, giving the chlorodiols **17**, resulting from opening of the three-membered ring with retention of configuration at the reacting carbon atom. The relative stereochemistry of the substituents in compound **17** was confirmed by X-ray crystallography.<sup>9</sup>

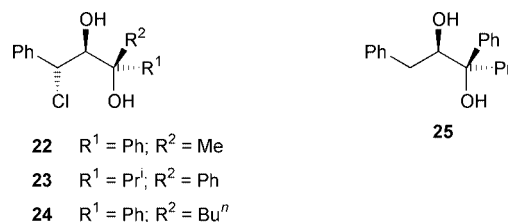


The same protocol performed on the epoxides **4** and **12** gave rise to the corresponding halodiols **18** and **19** respectively. The yields for all three reactions were within the range 80–86%. The mechanism for this reaction is believed to proceed as illustrated in Scheme 3. The Lewis acid coordinates to the oxygen atoms of the epoxide unit and the alcohol moiety. Donation of electrons into the empty d-orbital of the metal can take place from either of the oxygen atoms and normally it would be anticipated that the alcohol group would be the major contributor.<sup>10</sup> However, strong co-ordination to the epoxide oxygen atom leads to favourable neighbouring group participation by the phenyl group and consequent opening of the three-membered ring. Fast, intramolecular migration of chloride ion from the metal (possibly by a caged ion-pair mechanism) would then deliver the nucleophile to the benzylic carbon atom with retention of configuration.<sup>11</sup>

As expected, on the basis of this proposed mechanism, a compound having an electron-poor aromatic ring reacts more slowly: thus the epoxyalcohol **20**, prepared from the ketone **2** in 93% yield using methylmagnesium bromide, reacted sluggishly with tin(IV) chloride (4 h *versus* 1.5 h for complete reaction) yet still gave the chloro-compound **21** in almost quantitative yield.



In a complementary fashion, treatment of the epoxyalcohols **4** and **12** with *tert*-butyldimethylsilyl chloride (5 mol equivalents), in the absence of imidazole, produced the chlorodiols **22** and **23** (60–61% yield) through inversion of configuration at the carbon atom undergoing substitution. Trimethylsilyl chloride (2 mol equivalents) promoted the same reaction, converting the epoxyalcohol **5** into chlorodiol **24** in 57% yield.



Epoxide opening with trialkylsilyl halides has been documented previously with most cases displaying inversion of configuration at the participating carbon centre.<sup>12</sup> Activation of the epoxide unit by the oxaphilic silicon species followed by rear-side attack on the benzylic centre by chloride ion is a generally accepted mechanism leading to the observed products.

In order to clearly establish the stereochemical relationship of the two chlorodiols **19** and **23**, both compounds were hydrodehalogenated, independently, with tri-*n*-butyltin hydride and AIBN in hot toluene to give the diol **25** in each case.

In summary, we have shown that diastereoselective addition of Grignard reagents to non-racemic  $\alpha,\beta$ -epoxyketones generates the corresponding alcohols with excellent diastereoselectivity. A range of transformations of these alcohols has also been presented; further work, aimed at the production of longer carbon chains carrying a variety of substituents at adjacent positions with strictly controlled stereochemistry, is ongoing.

## Experimental

### General procedures

NMR spectra were recorded on Bruker AC200, Bruker AMX400, Bruker Avance 400 or Varian Gemini300 instruments. The following abbreviations are used to describe the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; sept, septet; m, multiplet; br, broad. *J* values are given in Hz. NMR spectral data are referenced to the residual protonated solvent peak (DMSO,  $\delta_{\text{H}}$  2.52) or TMS. Shifts in <sup>13</sup>C NMR spectra have been assigned using DEPT. IR spectra were recorded on a Perkin Elmer Paragon 1000 spectrophotometer. The designations s (sharp) and br (broad) are used to describe the peaks observed in the IR spectrum. Diagnostic signals from the IR spectrum are listed with assignments accompanied by a selection of strong peaks in the fingerprint region to aid further comparisons. Melting points were measured on a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were measured on an Optical Activity AA-1000 polarimeter with a 0.1 dm cell and are quoted in units of 10<sup>-1</sup> deg cm<sup>2</sup> g<sup>-1</sup>. Low resolution EI mass spectra were measured on a Fisons Trio1000 spectrometer; CI and accurate mass spectra were measured on a VG Analytical 7070E double focusing magnetic mass spectrometer. Elemental analysis was performed on a Carlo Erba Elemental Analyser model 1106. Chiral HPLC was performed on a Gilson chromatograph with isocratic pump at a

flow rate of 1 ml min<sup>-1</sup> using a Chiralpak® AD column (4.6 cm × 25 cm) with UV detection at 254 nm.

All reactions were monitored by thin layer chromatography, which was performed on 200–250 µm thickness Merck silica gel plates (60<sub>F254</sub>). Compounds were detected by ultraviolet light or by staining with ceric ammonium molybdate or potassium permanganate solutions followed by heat as a developing agent. Retention factors (*R<sub>f</sub>*) are quoted to the nearest 0.05. Column chromatography was performed on Merck-60 silica gel (230–400 mesh).

Petroleum ether refers to the light petroleum fraction bp 40–60 °C and was distilled prior to use. Tetrahydrofuran and diethyl ether were heated under reflux over (and distilled from) sodium–benzophenone ketyl; CH<sub>2</sub>Cl<sub>2</sub> was heated under reflux over (and distilled from) calcium hydride prior to use; *tert*-butyl alcohol was dried using 3 Å molecular sieves; anhydrous toluene was purchased from Aldrich. All materials were purchased and used directly from commercial suppliers unless otherwise stated.

*trans*-(1*S*,2*R*)-Epoxychalcone<sup>13</sup> (**3**) and (–)-(1*S*,2*R*)-1,2-epoxy-4,4-dimethyl-1-phenylpentan-3-one<sup>13</sup> (**9**) were prepared as described previously.

#### General procedure A for epoxidation of enones: biphasic conditions

The enone (2.90 mmol), urea–H<sub>2</sub>O<sub>2</sub> (324 mg, 3.44 mmol, 1.2 eq), DBU (0.64 cm<sup>3</sup>, 4.3 mmol, 1.5 eq) and polystyrene-supported poly(L-leucine)<sup>14</sup> (2.00 g) or SiO<sub>2</sub>-poly(L-leucine)<sup>15</sup> (5.20 g) were stirred in dry THF (30 cm<sup>3</sup>) until the reaction was judged to be complete by TLC. The catalyst was separated by filtration and washed with EtOAc (150 cm<sup>3</sup>). The filtrate was washed with saturated aqueous sodium sulfite (2 × 50 cm<sup>3</sup>), water (2 × 50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure afforded the crude product.

#### General procedure B for epoxidation of enones: sodium percarbonate conditions

The enone (2.90 mmol), sodium percarbonate (Na<sub>2</sub>CO<sub>3</sub>·1.5H<sub>2</sub>O<sub>2</sub>, 1.35 g, 8.60 mmol, 3.0 eq) and polystyrene-supported poly(L-leucine)<sup>14</sup> (2.00 g) were stirred in a mixture of 1,2-

dimethoxyethane and water [20 cm<sup>3</sup> (1 : 1)] until the reaction was judged to be complete by TLC. The catalyst was separated by filtration and washed with EtOAc (150 cm<sup>3</sup>). The filtrate was washed with saturated aqueous sodium sulfite (2 × 50 cm<sup>3</sup>), water (2 × 50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure afforded the crude product.

#### Recycling of the catalysts

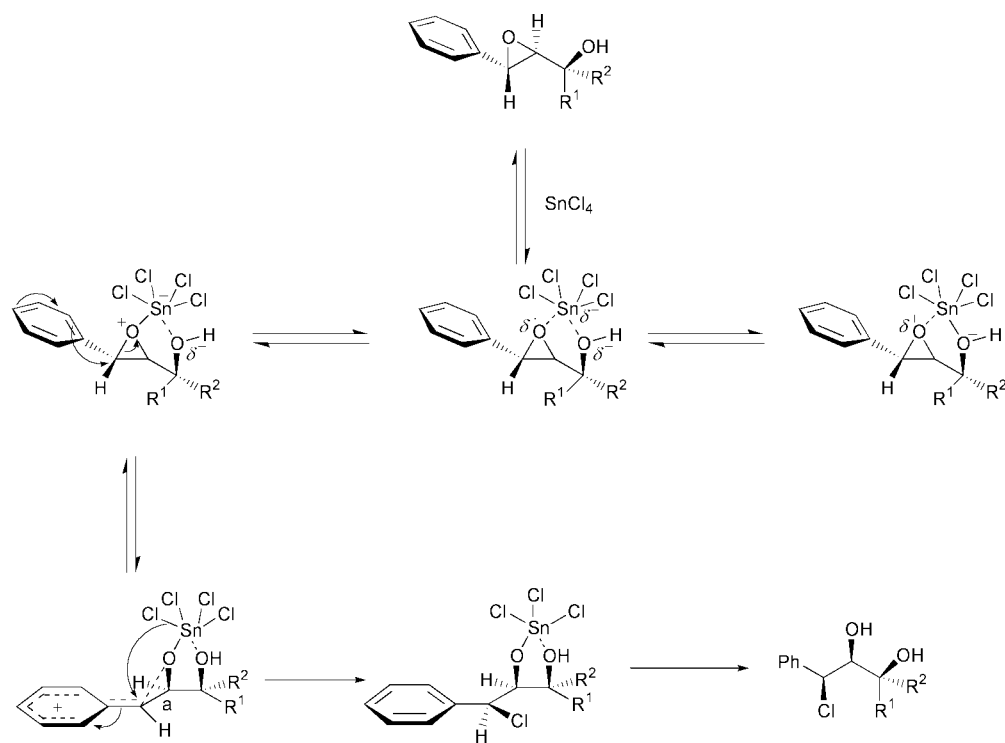
Polystyrene-supported poly(L-leucine) was recycled by washing with water, water–acetone (1 : 1), acetone and EtOAc sequentially before drying on a glass sinter. SiO<sub>2</sub>-poly(L-leucine) is incompatible with aqueous solutions, so the residual urea was removed by washing with EtOH and THF sequentially before drying on a glass sinter.

#### (–)-(1*S*,2*R*)-1,2-Epoxy-3-phenyl-1-(4-trifluoromethylphenyl)propan-3-one (**2**)

Epoxidation of enone **1** (1.00 g, 3.62 mmol) according to general procedure B was complete after 18 hours. Standard workup followed by recrystallisation from *n*-hexane gave the title compound **2** (829 mg, 2.84 mmol, 78%) as white needles, mp 93–96 °C (*n*-hexane); *R<sub>f</sub>* [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.3; [*a*]<sub>D</sub><sup>22</sup> = –205 (*c* 1.0, CHCl<sub>3</sub>); *v*<sub>max</sub>(KBr)/cm<sup>-1</sup> 1684 (C=O), 1659, 1330, 1113, 1069, 854 and 691; *δ*<sub>H</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 4.16 (1 H, d, *J* 1.8, CH), 4.26 (1 H, d, *J* 1.8, CH), 7.49–7.54 (4 H, m, ArH), 7.62–7.69 (3 H, m, ArH), 8.00–8.03 (2 H, m, ArH); *δ*<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 58.4 and 61.0 (CH), 123.9 (q, <sup>1</sup>*J*<sub>C-F</sub> 272, CF<sub>3</sub>), 125.8 (q, <sup>3</sup>*J*<sub>C-F</sub> 4, ArC–C–CF<sub>3</sub>), 126.2, 128.4 and 129.0 (ArCH), 131.3 (q, <sup>2</sup>*J*<sub>C-F</sub> 33, ArC–CF<sub>3</sub>), 134.2 (ArCH), 135.4 and 139.7 (Ar*Cipso*), 192.5 (C=O); HRMS (CI) C<sub>16</sub>H<sub>12</sub>O<sub>2</sub>F<sub>3</sub> [M + H]<sup>+</sup> requires 293.0789, found 293.0792; *m/z* (EI) 105 (5%), 87 (10), 71 (100), 57 (25); ee 97% (Chiralpak® AD; 5% EtOH in *n*-hexane; major enantiomer 23.0 min, minor enantiomer 19.8 min).

#### General procedure for the addition of Grignard reagents to epoxyketones

To a stirred solution of the Grignard reagent (2.8 mmol) in THF (20 cm<sup>3</sup>) at –78 °C was added the epoxyketone (1.4 mmol) as a



Scheme 3

solution in THF (10 cm<sup>3</sup>) under a nitrogen atmosphere. The reaction was stirred at -78 °C for 1.5 h, quenched by addition of saturated aqueous ammonium chloride (10 cm<sup>3</sup>), allowed to warm to room temperature and extracted with EtOAc (3 × 25 cm<sup>3</sup>). The combined organic extracts were washed with water (2 × 50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure gave the crude product which was analysed by NMR to measure the diastereoisomeric ratio of *Re* : *Si* products<sup>16</sup> before purification.

#### (-)-(1*S*,2*R*,3*S*)-1,3-Diphenyl-1,2-epoxybutan-3-ol (4)

Reaction of methylmagnesium bromide (3.0 M in Et<sub>2</sub>O, 1.5 cm<sup>3</sup>, 4.5 mmol) with *trans*-(1*S*,2*R*)-epoxychalcone (**3**) (500 mg, 2.23 mmol) following the general procedure gave the desired tertiary alcohol with a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] followed by recrystallisation from *n*-hexane to give the title compound **4** (468 mg, 1.95 mmol, 87%) as white crystals; mp 100–102 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.3 (Found: C, 79.7; H, 6.8; C<sub>16</sub>H<sub>16</sub>O<sub>2</sub> requires: C, 80.0; H, 6.7%); [α]<sub>D</sub><sup>22</sup> = -45.8 (*c* 0.5, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>-1</sup> 3485 (O–H), 1632, 1497 and 1446; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.70 (3 H, s, C(4)H<sub>3</sub>), 2.85 (1 H, s, C(3)OH), 3.23 (1 H, d, *J* 2.2, CH), 4.03 (1 H, d, *J* 2.2, CH), 7.3 (10 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 27.7 (C(4)H<sub>3</sub>), 55.9 and 68.6 (CH), 71.4 (C(3)*ipso*), 125.21, 125.9, 127.64, 128.4 and 128.6 (ArCH), 136.8 and 143.6 (ArC*ipso*); *m/z* (EI) 121 (34%), 120 (86), 105 (91), 91 (100), 77 (62).

#### (-)-(1*S*,2*R*,3*S*)-1,2-Epoxy-1,3-diphenylheptan-3-ol (5)

To a stirred suspension of magnesium turnings (108 mg, 4.46 mmol) in Et<sub>2</sub>O (10 cm<sup>3</sup>) was added *n*-bromobutane (0.48 cm<sup>3</sup>, 4.5 mmol) under a nitrogen atmosphere at such a rate as to maintain reflux. After complete reaction of the magnesium, THF (10 cm<sup>3</sup>) was added and the contents of the flask were cooled to -78 °C. *trans*-(1*S*,2*R*)-Epoxychalcone (**3**) (500 mg, 2.23 mmol) was added either *via* a solid addition tube or as a solution in THF (5.0 cm<sup>3</sup>). After 4 h, the reaction was quenched and worked up according to the general procedure, except that Et<sub>2</sub>O (3 × 50 cm<sup>3</sup>) was employed instead of EtOAc. The desired tertiary alcohol had a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] and recrystallised from *n*-hexane to afford **5** (378 mg, 1.34 mmol, 60%) as white crystals, mp 82–84 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.4 (Found: C, 80.9; H, 7.8; C<sub>19</sub>H<sub>22</sub>O<sub>2</sub> requires: C, 80.8; H, 7.9%); [α]<sub>D</sub><sup>22</sup> = -50.0 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>-1</sup> 3494 (O–H), 1212, 961 and 881; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.88 (3 H, m, C(7)H<sub>3</sub>), 1.17–1.47 (4 H, m, C(5,6)H<sub>2</sub>), 1.93–2.09 (2 H, m, C(4)H<sub>2</sub>), 2.35 (1 H, s, C(3)OH), 3.35 (1 H, d, *J* 2.2, CH), 3.92 (1 H, d, *J* 2.2, CH), 7.17–7.47 (10 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 14.6 (C(7)H<sub>3</sub>), 23.7 and 25.9 (CH<sub>2</sub>), 41.7 (C(4)H<sub>2</sub>), 55.7 and 68.6 (CH), 73.9 (C(3)*ipso*), 125.7, 126.4, 127.7, 128.8, 129.0 and 129.0 (ArCH), 136.8 and 142.6 (ArC*ipso*); *m/z* (EI) 163 (20%), 120 (83), 105 (100), 91 (81), 77 (59).

#### (-)-(1*S*,2*R*,3*S*)-4,4-Dimethyl-1,3-diphenyl-1,2-epoxypentan-3-ol (6)

Reaction of *tert*-butylmagnesium chloride (2 M in Et<sub>2</sub>O, 1.0 cm<sup>3</sup>, 1.9 mmol) with *trans*-(1*S*,2*R*)-epoxychalcone (**3**) (217 mg, 0.97 mmol) following the general procedure gave a product with a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (9 : 1)] followed by recrystallisation from *n*-hexane to furnish the title compound **6** (113 mg, 0.40 mmol, 41%) as white crystals, mp 99–101 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.5 (Found: C, 80.7; H, 7.9; C<sub>19</sub>H<sub>22</sub>O<sub>2</sub> requires: C, 80.8; H, 7.85%); [α]<sub>D</sub><sup>22</sup> = -95 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>-1</sup> 3526 (O–H), 1495,

1450, 1360, 1170 and 880; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.02 (9 H, s, C(CH<sub>3</sub>)<sub>3</sub>), 2.83 (1 H, s, OH), 3.59 (1 H, d, *J* 2.4, CH), 3.8 (1 H, d, *J* 2.4, CH), 7.17–7.33 (10 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 25.4 (C(CH<sub>3</sub>)<sub>3</sub>), 39.2 (C(CH<sub>3</sub>)<sub>2</sub>), 54.9 and 64.3 (CH), 76.1 (C(3)*ipso*), 125.6, 126.9, 127.2, 128.2 and 128.6 (ArCH), 136.8 and 142.4 (ArC*ipso*); *m/z* (EI) 225 (M<sup>+</sup> - C<sub>4</sub>H<sub>9</sub>, 7%), 207 (18), 105 (100).

#### (-)-(1*S*,2*R*)-1,2-Epoxy-1-phenylpentan-3-one (7)

Epoxidation of 1-phenylpent-1-en-3-one (500 mg, 3.12 mmol) according to general procedure A using SiO<sub>2</sub>-poly(L-leucine) as the catalyst was complete after 18 h. Purification by column chromatography [petroleum ether–Et<sub>2</sub>O (9 : 1)] followed by recrystallisation from MeOH furnished the title compound **7** (138 mg, 0.78 mmol, 25%) as white needles; mp 45–48 °C (MeOH); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.35 (Found: C, 75.3; H, 6.9; C<sub>11</sub>H<sub>12</sub>O<sub>2</sub> requires: C, 75.0; H, 6.9%); [α]<sub>D</sub><sup>22</sup> = -111 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>-1</sup> 2973 (C–H), 1710 (saturated C=O), 1457, 1408, 1173 and 884; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.12 (3 H, t, *J* 7.2, CH<sub>3</sub>), 2.49 (1 H, dq, *J* 18.4, 7.2) and 2.59 (1 H, dq, *J* 18.4, 7.2, CH<sub>2</sub>), 3.52 (1 H, d, *J* 1.9, CH), 3.98 (1 H, d, *J* 1.9, CH), 7.26–7.38 (5 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 7.0 (CH<sub>3</sub>), 31.1 (CH<sub>2</sub>), 58.1 and 63.1 (CH), 125.8, 128.8 and 129.0 (ArCH), 135.4 (ArC*ipso*), 206.5 (C=O); *m/z* (EI) 176 (M<sup>+</sup>, 21%), 131 (12), 120 (41), 91 (100).

#### (-)-(1*S*,2*R*)-1,2-Epoxy-4-methyl-1-phenylpentan-3-one (8)

Epoxidation of 4-methyl-1-phenylpent-1-en-3-one (1.0 g, 5.74 mmol) according to general procedure A using SiO<sub>2</sub>-poly(L-leucine) as the catalyst was complete after 18 h. Purification by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] followed by recrystallisation from *n*-hexane furnished the title compound **8** (621 mg, 3.26 mmol, 57%) as white needles; mp 56–57 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.4 (Found: C, 75.8; H, 7.4; C<sub>12</sub>H<sub>14</sub>O<sub>2</sub> requires: C, 75.8; H, 7.4%); [α]<sub>D</sub><sup>22</sup> = -208 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>-1</sup> 1711 (C=O), 1458, 1417 and 1052; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.16 (3 H, d, *J* 7.0) and 1.17 (3 H, d, *J* 7.0, CH(CH<sub>3</sub>)<sub>2</sub>), 2.83 (1 H, sept, *J* 7.0, C(4)H), 3.61 (1 H, d, *J* 2.0, CH), 3.93 (1 H, d, *J* 2.0, CH), 7.29–7.38 (5 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 17.3 and 18.1 (CH(CH<sub>3</sub>)<sub>2</sub>), 37.0 (C(4)H), 58.4 and 61.9 (CH), 125.7, 128.7 and 129.0 (ArCH), 135.4 (ArC*ipso*), 208.7 (C=O); *m/z* (EI) 190 (M<sup>+</sup>, 4%), 174 (57), 148 (88), 147 (77); ee >99% (Chiralpak<sup>®</sup> AD, 5% EtOH in *n*-hexane; major enantiomer 8.9 min, minor enantiomer 23.4 min).

#### (+)-(1*S*,2*R*,3*R*)-1,2-Epoxy-1,3-diphenylpentan-3-ol (11)

Reaction of phenylmagnesium bromide (1 M in THF, 1.1 cm<sup>3</sup>, 1.1 mmol) with epoxyketone **7** (100 mg, 0.57 mmol) following the general procedure gave a product with a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (12 : 1)] to give the title compound **11** (141 mg, 0.55 mmol, 97%) as a colourless oil; *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.3; [α]<sub>D</sub><sup>22</sup> = +44 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(thin film)/cm<sup>-1</sup> 3454 (O–H), 2972 and 2937 (alkyl C–H), 1495, 1448, 1311, 1060 and 886; δ<sub>H</sub> (200 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.86 (3 H, t, *J* 6.6, CH<sub>3</sub>), 1.93 (2 H, q, *J* 6.6, CH<sub>2</sub>), 2.59 (1 H, br s, OH), 3.41 (1 H, d, *J* 2.2, CH), 4.08 (1 H, d, *J* 2.2, CH), 7.30–7.51 (10 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 7.8 (CH<sub>3</sub>), 32.2 (CH<sub>2</sub>), 56.0 and 68.0 (CH), 74.2 (COH), 125.5, 125.8, 127.4, 128.4, 128.5 and 128.7 (ArCH), 137.0 and 144.4 (ArC*ipso*); *m/z* (EI) 148 (M<sup>+</sup> - C<sub>6</sub>H<sub>5</sub> - C<sub>2</sub>H<sub>5</sub>, 56%), 120 (50), 105 (100), 77 (67).

#### (+)-(1*S*,2*R*,3*R*)-1,2-Epoxy-1,3-diphenyl-4-methylpentan-3-ol (12)

Reaction of phenylmagnesium bromide (1 M in THF, 2.6 cm<sup>3</sup>, 2.6 mmol) with epoxyketone **8** (247 mg, 1.30 mmol) following the general procedure gave a product with a *Re* : *Si* ratio<sup>16</sup> of

>99 : 1. The product was purified by recrystallisation from *n*-hexane to give the title compound **12** (191 mg, 0.94 mmol, 71%) as white needles, mp (*n*-hexane) 106–107 °C;  $R_f$  [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.3 (Found: C, 80.4; H, 7.55; C<sub>18</sub>H<sub>20</sub>O<sub>2</sub> requires: C, 80.6; H, 7.5%);  $[a]_D^{25} = +64$  (*c* 1.0, CHCl<sub>3</sub>);  $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$  3491 (O–H), 1470, 1448, 1287 and 1059;  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.85 (3 H, d, *J* 6.9) and 0.99 (3 H, d, *J* 6.9, CH(CH<sub>3</sub>)<sub>2</sub>), 1.54 (1 H, s, OH), 2.22 (1 H, sept, C(4)H), 3.45 (1 H, d, *J* 2.1, CH), 4.13 (1 H, d, *J* 2.1, CH), 7.25–7.52 (10 H, m, ArH);  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 16.9 and 17.5 (CH(CH<sub>3</sub>)<sub>2</sub>), 36.2 (C(4)H), 56.6 and 67.2 (CH), 76.0 (COH), 125.6, 127.2, 128.3 and 128.6 (ArCH), 136.9 and 144.6 (ArC*ipso*); *m/z* (EI) 225 (M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>, 5%), 147 (45), 120 (36), 105 (100), 91 (87).

#### (+)-(1*S*,2*R*,3*R*)-1,2-Epoxy-4,4-dimethyl-1,3-diphenylpentan-3-ol (**13**)

Reaction of phenylmagnesium bromide (1 M in THF, 2.7 cm<sup>3</sup>, 2.7 mmol) with epoxyketone **9** (279 mg, 1.37 mmol) following the general procedure gave a product with a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The product was purified by recrystallisation from *n*-hexane to furnish the title compound **13** (261 mg, 0.92 mmol, 67%) as white crystals, mp 91–92 °C (*n*-hexane);  $R_f$  [petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.6 (Found: C, 81.2; H, 8.0; C<sub>19</sub>H<sub>22</sub>O<sub>2</sub> requires: C, 80.8; H, 7.9%);  $[a]_D^{25} = +60$  (*c* 1.0, CHCl<sub>3</sub>);  $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$  3470 (O–H), 1498, 1461, 1326 and 979;  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.98 (9 H, s, CH<sub>3</sub>), 2.18 (1 H, s, OH), 3.76 (1 H, d, *J* 2.0, CH), 4.21 (1 H, d, *J* 2.0, CH), 7.35–7.37 (8 H, m, ArH), 7.57–7.59 (2 H, m, ArH);  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 26.6 (C(CH<sub>3</sub>)<sub>3</sub>), 38.2 (C(CH<sub>3</sub>)<sub>3</sub>), 57.9 and 66.4 (CH), 78.3 (COH), 126.3, 127.9, 128.1, 128.2, 129.0 and 129.3 (ArCH), 137.5 and 143.8 (ArC*ipso*); *m/z* (EI) 225 (M<sup>+</sup> – C<sub>4</sub>H<sub>9</sub>, 3%), 207 (4), 105 (100).

#### (–)-(1*S*,2*S*,3*R*)-2,3-Epoxy-4-methyl-1,3-diphenylpentan-1-ol (**15**)

Epoxyalcohol **12** (150 mg, 0.56 mmol) and sodium hydroxide (25.0 mg, 0.61 mmol) were stirred in anhydrous *tert*-butyl alcohol (10 cm<sup>3</sup>) at 30 °C for 2 hours under a nitrogen atmosphere. The reaction mixture was quenched by addition of saturated aqueous ammonium chloride (10 cm<sup>3</sup>) and extracted with EtOAc (3 × 25 cm<sup>3</sup>). The combined organic extracts were washed with water (2 × 50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure gave the crude product which was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] to afford the title compound **15** (146 mg, 0.54 mmol, 97%) as a colourless oil,  $R_f$  [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.35;  $[a]_D^{25} = -171$  (*c* 1.0, CHCl<sub>3</sub>);  $\nu_{\max}(\text{thin film})/\text{cm}^{-1}$  3426 (br, O–H), 2964 (C–H), 1603 (phenyl C=C), 1494, 1445, 1365, 1025, 937, 765 and 701;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.88 (3 H, d, *J* 6.6) and 0.96 (3 H, d, *J* 6.6, CH(CH<sub>3</sub>)<sub>2</sub>), 1.93 (1 H, sept, *J* 6.6, C(4)H), 2.08 (1 H, br s, OH), 3.18 (1 H, d, *J* 8.8, C(2)H), 3.76 (1 H, d, *J* 8.8, C(1)H), 7.27–7.45 (10 H, m, ArH);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 17.4 and 18.8 (CH(CH<sub>3</sub>)<sub>2</sub>), 34.9 (C(4)H), 65.6 (CH), 70.7 (C(3)), 71.8 (CH), 126.1, 127.7, 128.0, 128.1 and 128 (ArCH), 136.9 and 141.8 (ArC*ipso*); HRMS (CI): C<sub>18</sub>H<sub>24</sub>NO<sub>2</sub> [M + NH<sub>4</sub>]<sup>+</sup> requires 286.1807, found 286.1814; *m/z* (EI) 250 (3%), 207 (24), 162 (23), 161 (29), 149 (64), 120 (70), 117 (100), 105 (70), 91 (93), 77 (95).

#### (+)-(2*S*,3*R*)-2,3-Epoxy-4-methyl-1,3-diphenylpentan-1-one (**16**)

Crude epoxyalcohol **15** (50 mg, 0.19 mmol) and Dess–Martin periodinane (89 mg, 0.21 mmol) were stirred in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (10 cm<sup>3</sup>) under a nitrogen atmosphere for 16 hours. The reaction was quenched by addition of a mixture of saturated aqueous sodium bicarbonate and saturated aqueous sodium sulfite [10 cm<sup>3</sup>, (1 : 1)] and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 25 cm<sup>3</sup>). The combined organic extracts were washed with water (2 ×

50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure, followed by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] gave the epoxyketone **16**, which was further purified by recrystallisation from *n*-hexane to afford title compound **16** (34 mg, 0.13 mmol, 67% from epoxyalcohol **12**) as fine white needles, mp 91–92 °C (*n*-hexane);  $R_f$  [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.4 (Found: C, 80.7; H, 6.8; C<sub>18</sub>H<sub>18</sub>O<sub>2</sub> requires: C, 81.2; H, 6.8%);  $[a]_D^{25} = +125$  (*c* 1.0, CHCl<sub>3</sub>);  $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$  2963 (C–H), 1684 (aryl C=O), 1465, 1448 1230, 766;  $\delta_{\text{H}}$  (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.05 (3 H, d, *J* 6.6) and 1.08 (3 H, d, *J* 6.6, CH(CH<sub>3</sub>)<sub>2</sub>), 2.23 (1 H, sept, *J* 6.6, C(4)H), 4.40 (1 H, s, CH), 7.16–7.57 (8 H, m, ArH), 7.83–7.87 (2 H, m, ArH);  $\delta_{\text{C}}$  (75 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 17.8 and 18.6 (CH(CH<sub>3</sub>)<sub>2</sub>), 35.0 (C(4)H), 63.7 (C(2)H), 71.0 (C(3)), 127.7, 127.8, 128.2, 128.6 and 133.4 (ArCH), 134.7 and 136.0 (ArC*ipso*), 193.5 (C=O); *m/z* (EI) 223 (M<sup>+</sup> – C<sub>3</sub>H<sub>7</sub>, 3%), 71 (100).

#### General procedure for epoxide opening with retention of configuration

To a stirred solution of the epoxyalcohol (0.21 mmol) in anhydrous CH<sub>2</sub>Cl<sub>2</sub> (5.0 cm<sup>3</sup>) was added tin(IV) chloride (1 M in CH<sub>2</sub>Cl<sub>2</sub>, 0.25 cm<sup>3</sup>, 0.25 mmol) at –78 °C under a nitrogen atmosphere. Stirring was continued at –78 °C for 1.5 h before quenching by the addition of saturated aqueous ammonium chloride (5.0 cm<sup>3</sup>). The product was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 25 cm<sup>3</sup>) and the combined organic extracts were washed with water (2 × 25 cm<sup>3</sup>) and brine (25 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under reduced pressure gave the crude chlorodiols, which was purified by column chromatography or recrystallisation.

#### (+)-(1*S*,2*S*,3*S*)-1-Chloro-1,3-diphenylheptane-2,3-diol (**17**)

Epoxyalcohol **5** (60 mg, 0.21 mmol) was treated with tin(IV) chloride (1 M in CH<sub>2</sub>Cl<sub>2</sub>, 0.25 cm<sup>3</sup>, 0.25 mmol) following the general procedure. Purification of the crude product by column chromatography [petroleum ether–Et<sub>2</sub>O (4 : 1)] followed by recrystallisation from *n*-hexane furnished the title compound **17** (53 mg, 0.17 mmol, 80%) as white crystals, mp 80–83 °C (*n*-hexane);  $R_f$  [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.2;  $[a]_D^{25} = +26$  (*c* 1.0, CHCl<sub>3</sub>);  $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$  3408 (br, O–H), 2948, 1491, 1447, 1226, 1071, 762 and 699;  $\delta_{\text{H}}$  (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.78 (3 H, t, *J* 7.2, C(7)H<sub>3</sub>), 1.12–1.34 (4 H, m, C(5,6)H<sub>2</sub>), 1.73–1.74 (1 H, m) and 2.18–2.21 (1 H, m, C(4)H<sub>2</sub>), 2.89 (1 H, s, C(3)OH), 3.12 (1 H, d, *J* 9.2, C(2)OH), 4.11 (1 H, dd, *J* 9.2, 2.0, C(2)H), 4.73 (1 H, d, *J* 2.0, C(1)H), 7.24–7.39 (10 H, m, ArH);  $\delta_{\text{C}}$  (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 14.6 (C(7)H<sub>3</sub>), 23.6, 25.7 and 40.6 (CH<sub>2</sub>), 65.2 and 79.4 (CH), 80.9 (C(3)), 125.2, 127.3, 127.6, 128.3, 128.5 and 128.7 (ArCH), 140.7 and 143.3 (ArC*ipso*); HRMS (CI) C<sub>19</sub>H<sub>27</sub>NO<sub>2</sub><sup>35</sup>Cl [M + NH<sub>4</sub>]<sup>+</sup> requires 336.1730, found 336.1734; *m/z* (EI) 163 (43%), 120 (100), 105 (75), 91 (53), 77 (28).

#### (+)-(1*S*,2*S*,3*S*)-1-Chloro-1,3-diphenylbutane-2,3-diol (**18**)

Epoxyalcohol **4** (50 mg, 0.21 mmol) was treated with tin(IV) chloride (1 M in CH<sub>2</sub>Cl<sub>2</sub>, 0.25 cm<sup>3</sup>, 0.25 mmol) following the general procedure. The product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (4 : 1)] followed by recrystallisation from *n*-hexane to yield the title compound **18** (43 mg, 0.16 mmol, 76%) as white crystals, mp 70–71 °C (*n*-hexane);  $R_f$  [petroleum ether–Et<sub>2</sub>O (3 : 2)] 0.4 (Found: C, 69.4; H, 6.2; Cl, 12.6; C<sub>16</sub>H<sub>17</sub>O<sub>2</sub>Cl requires: C, 69.4; H, 6.2; Cl, 12.8%);  $[a]_D^{25} = +46$  (*c* 0.54, CHCl<sub>3</sub>);  $\nu_{\max}(\text{KBr})/\text{cm}^{-1}$  3520 (br, O–H), 3085, 3060, 2978, 2930 (C–H stretch), 1446, 1494 and 1599;  $\delta_{\text{H}}$  (400 MHz; DMSO-*d*<sub>6</sub>) 1.53 (3 H, s, C(4)H<sub>3</sub>), 3.80 (1 H, dd, *J* 8.3, 2.8, C(2)H), 5.14 (1 H, d, *J* 2.8, C(1)H), 5.18 (1 H, s, C(3)OH), 5.26 (1 H, d, *J* 8.3, C(2)OH); HRMS (CI) C<sub>16</sub>H<sub>21</sub>NO<sub>2</sub><sup>35</sup>Cl [M + NH<sub>4</sub>]<sup>+</sup> requires 294.1261, found 294.1259.

**(+)-(1S,2S,3R)-1-Chloro-4-methyl-1,3-diphenylpentane-2,3-diol (19)**

Epoxyalcohol **12** (64 mg, 0.24 mmol) was treated with tin(IV) chloride (1 M in CH<sub>2</sub>Cl<sub>2</sub>, 0.3 cm<sup>3</sup>, 0.3 mmol) following the general procedure. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] to give the title compound **19** (63 mg, 0.21 mmol, 86%) as a colourless oil, *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.45; [*a*]<sub>D</sub><sup>25</sup> = +42 (*c* 1.0, CHCl<sub>3</sub>); δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.55 (3 H, d, *J* 6.9) and 1.07 (3 H, d, *J* 6.9, CH(CH<sub>3</sub>)<sub>2</sub>), 1.38 (1 H, br s, C(3)OH), 2.55 (1 H, sept, *J* 6.9, C(4)H), 2.89 (1 H, d, *J* 4.2, C(2)OH), 4.34 (1 H, dd, *J* 4.2, 6.2, C(2)H), 4.84 (1 H, d, *J* 6.2, C(1)H), 7.19–7.24 (2 H, m, ArH), 7.29–7.37 (6 H, m, ArH), 7.41–7.46 (2 H, m, ArH); δ<sub>C</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 16.5 and 16.6 (CH(CH<sub>3</sub>)<sub>2</sub>), 34.8 (C(4)H), 67.2 and 77.7 (CH), 80.0 (C(3)OH), 126.4, 127.2, 127.9, 128.3, 128.8 and 129.0 (ArCH), 139.4 and 142.2 (ArCipso); HRMS (CI) C<sub>18</sub>H<sub>25</sub>NO<sub>2</sub><sup>35</sup>Cl [M + NH<sub>4</sub>]<sup>+</sup> requires 322.1574, found 322.1576; *m/z* (EI) 149 (60%), 120 (100), 105 (64), 91 (52), 77 (27).

**(–)-(1S,2R,3S)-1,2-Epoxy-3-phenyl-1-(4-trifluoromethylphenyl)butan-3-ol (20)**

Reaction of methylmagnesium bromide (3 M in Et<sub>2</sub>O, 1.1 cm<sup>3</sup>, 3.3 mmol) with epoxyketone **2** (500 mg, 1.7 mmol) following the general procedure gave a *Re* : *Si* ratio<sup>16</sup> of >99 : 1. The crude product was purified by recrystallisation from *n*-hexane to afford the title compound **20** (486 mg, 1.58 mmol, 93%) as white plates, mp 71–73 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.3; [*a*]<sub>D</sub><sup>25</sup> = –51 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>–1</sup> 3534 (br, O–H), 1325 (C–OH), 1169, 1124, 1068, 759, 700 and 645; δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.73 (3 H, s, CH<sub>3</sub>), 2.73 (1 H, br s, COH), 3.21 (1 H, d, *J* 2.2, CH), 4.09 (1 H, d, *J* 2.2, CH), 7.26–7.52 (9 H, m, Ar); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 27.7 (CH<sub>3</sub>), 55.5 and 69.4 (CH), 71.8 (COH), 124.5 (q, <sup>1</sup>*J*<sub>C–F</sub> 272, CF<sub>3</sub>), 125.5 (ArCH), 125.8 (q, <sup>3</sup>*J*<sub>C–F</sub> 4, ArC–C–CF<sub>3</sub>), 126.4, 128.1 and 128.9 (ArCH), 130.7 (q, <sup>2</sup>*J*<sub>C–F</sub> 32, ArC–CF<sub>3</sub>), 141.3 and 143.8 (ArCipso); HRMS (CI) C<sub>17</sub>H<sub>19</sub>NO<sub>2</sub>F<sub>3</sub> [M + NH<sub>4</sub>]<sup>+</sup> requires 326.1368, found 326.1370; *m/z* (EI) 87 (9%), 71 (100), 57 (23).

**(+)-(1S,2S,3S)-1-Chloro-3-phenyl-1-(4-trifluoromethylphenyl)butane-2,3-diol (21)**

Reaction of epoxyalcohol **20** (150 mg, 0.49 mmol) with tin(IV) chloride (1 M in CH<sub>2</sub>Cl<sub>2</sub>, 0.6 cm<sup>3</sup>, 0.6 mmol) according to the general procedure was complete after 4 hours. The crude product was purified by recrystallisation from *n*-hexane to give the title compound **21** (162 mg, 0.47 mmol, 96%) as white needles, mp 97–99 °C (*n*-hexane); *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.2; [*a*]<sub>D</sub><sup>25</sup> = +36 (*c* 1.0, CHCl<sub>3</sub>); ν<sub>max</sub>(KBr)/cm<sup>–1</sup> 3396 (br, O–H), 1330 (C–OH), 1172, 1120, 1070, 763 and 699; δ<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.63 (3 H, s, CH<sub>3</sub>), 2.77 (1 H, s, exchangeable with D<sub>2</sub>O, C(3)OH), 3.11 (1 H, d, *J* 8.8, exchangeable with D<sub>2</sub>O, C(2)OH), 4.10 (1 H, dd, *J* 8.8 and 3.2, C(2)H), 4.83 (1 H, d, *J* 3.2, C(1)H), 7.26–7.46 (9 H, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 29.0 (CH<sub>3</sub>), 63.94 (CH), 77.8 (COH), 79.11 (CH), 124.2 (q, <sup>1</sup>*J*<sub>C–F</sub> 272, CF<sub>3</sub>), 125.0 (ArCH), 125.7 (q, <sup>3</sup>*J*<sub>C–F</sub> 4, ArC–C–CF<sub>3</sub>), 127.8, 128.4 and 129.0 (ArCH), 130.7 (q, <sup>2</sup>*J*<sub>C–F</sub> 33, ArC–CF<sub>3</sub>), 144.1 and 144.6 (ArCipso); HRMS (FAB) C<sub>17</sub>H<sub>15</sub>OF<sub>3</sub><sup>35</sup>Cl [M – H<sub>2</sub>O + H]<sup>+</sup> requires 327.07635, found 327.07527; *m/z* (EI) 188 (27%), 159 (12), 121 (100), 105 (20), 91 (11), 77 (16).

**General procedure for epoxide opening with inversion of configuration**

The epoxyalcohol (0.40 mmol) and TBSCl (300 mg, 2.0 mmol) were stirred in dry DMF (10 cm<sup>3</sup>) under a nitrogen atmosphere for 24 h. The reaction was quenched by addition of water (20 cm<sup>3</sup>) and extracted with EtOAc (3 × 25 cm<sup>3</sup>). The combined organic extracts were washed with water (2 × 50 cm<sup>3</sup>) and brine (50 cm<sup>3</sup>) before drying (MgSO<sub>4</sub>). Removal of the solvent under

reduced pressure gave the crude product, which was purified by column chromatography.

**(1R,2S,3S)-1-Chloro-1,3-diphenylbutane-2,3-diol (22)**

Epoxyalcohol **4** (100 mg, 0.42 mmol) was treated with TBSCl (124 mg, 0.82 mmol) following the general procedure. Purification of the crude product by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] gave the title compound **22** (69 mg, 0.25 mmol, 60%) as a colourless oil; *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.15; δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 1.60 (3 H, s, C(4)H<sub>3</sub>), 1.77 (1 H, s, C(3)OH), 2.71 (1 H, d, *J* 6.6, C(2)OH), 4.44 (1 H, dd, *J* 6.6, 3.3, C(2)H), 4.77 (1 H, d, *J* 3.3, C(1)H), 7.22–7.40 (10 H, m, ArH); δ<sub>C</sub> (75 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 29.7 (C(4)H<sub>3</sub>), 63.6 and 81.7 (CH), 125.1, 127.5, 128.5, 128.6, 128.9 and 129.0 (ArCH), 138.9 and 145.2 (ArCipso); *m/z* (EI) 120 (100%), 105 (20), 91 (35), 77 (14).

**(–)-(1R,2S,3R)-1-Chloro-1,3-diphenyl-4-methylpentane-2,3-diol (23)**

Epoxyalcohol **12** (200 mg, 0.75 mmol) was treated with TBSCl (560 mg, 3.73 mmol) following the general procedure. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] to afford the title compound **23** (140 mg, 0.46 mmol, 61%) as a colourless oil, *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.3; [*a*]<sub>D</sub><sup>25</sup> = –14 (*c* 1.0, CHCl<sub>3</sub>); δ<sub>H</sub> (300 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.70 (3 H, d, *J* 6.6) and 1.03 (3 H, d, *J* 6.6, CH(CH<sub>3</sub>)<sub>2</sub>), 1.86 (1 H, d, *J* 3.3, exchangeable with D<sub>2</sub>O, C(2)OH), 2.47 (1 H, sept, *J* 6.6, C(4)H), 2.82 (1 H, s, exchangeable with D<sub>2</sub>O, C(3)OH), 4.47 (1 H, dd, *J* 7.7, 3.3, C(2)H), 4.60 (1 H, d, *J* 7.7, C(1)H), 7.23–7.38 (8H, m, ArH), 7.50–7.55 (2 H, m, ArH); δ<sub>C</sub> (75 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 16.6 and 16.9 (CH(CH<sub>3</sub>)<sub>2</sub>), 34.7 (C(4)H), 62.4 and 78.2 (CH), 80.7 (COH), 126.2, 126.9, 127.7, 128.3 and 128.6 (ArCH), 138.3 and 142.3 (ArCipso); HRMS (CI) C<sub>18</sub>H<sub>25</sub>NO<sub>2</sub><sup>35</sup>Cl [M + NH<sub>4</sub>]<sup>+</sup> requires 322.15254, found 322.15758; *m/z* (EI) 149 (53%), 120 (54), 105 (100), 91 (67), 77 (53).

**(1R,2S,3S)-1-Chloro-1,3-diphenylheptane-2,3-diol (24)**

Epoxyalcohol **5** (100 mg, 0.35 mmol) was treated with TMSCl (0.05 cm<sup>3</sup>, 0.42 mmol) following the general procedure. Another equivalent of TMSCl was added after 5 hours followed by a further 2.5 equivalents after 27 hours. The crude product was purified by column chromatography [petroleum ether–Et<sub>2</sub>O (6 : 1)] to give the title compound **24** (64 mg, 0.20 mmol, 57%) as a colourless oil, *R*<sub>f</sub> [petroleum ether–Et<sub>2</sub>O (3 : 1)] 0.15; ν<sub>max</sub>(thin film)/cm<sup>–1</sup> 3540 (br, O–H), 1600, 1495, 1453, 1265, 1115 and 967; δ<sub>H</sub> (200 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.75 (3 H, t, *J* 7.1, C(7)H<sub>3</sub>), 1.07–1.27 (4 H, m, C(5,6)H<sub>2</sub>), 1.53 (1 H, s, C(3)OH), 1.69–1.80 (1 H, m) and 2.06–2.16 (1 H, m, C(4)H<sub>2</sub>), 2.93 (1 H, d, *J* 7.1, C(2)OH), 4.44 (1 H, dd, *J* 7.1, 2.8, C(2)H), 4.73 (1 H, d, *J* 2.8, C(1)H), 7.17–7.43 (10 H, m, ArH); δ<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 13.9 (C(7)H<sub>3</sub>), 22.8 and 24.9 (CH<sub>2</sub>), 40.6 (C(4)H<sub>2</sub>), 63.2 (CH), 79.1 (C(3)), 81.1 (CH), 125.6, 127.3, 128.4, 128.6, 128.8 and 129.1 (ArCH), 137.7 and 142.3 (ArCipso); HRMS (FAB) C<sub>19</sub>H<sub>22</sub>O<sup>35</sup>Cl [M – H<sub>2</sub>O + H]<sup>+</sup> requires 301.13592, found 301.13553; *m/z* (EI) 163 (56%), 120 (100), 105 (56), 91 (62), 77 (36).

**(+)-(2S,3R)-4-Methyl-1,3-diphenylpentane-2,3-diol (25)**

A stirred solution of chlorodiols **19** (75 mg, 0.25 mmol) and AIBN (3.0 mg, 0.02 mmol) in anhydrous toluene (10 cm<sup>3</sup>) was degassed by purging with a stream of nitrogen for 15 min. Tri-*n*-butyltin hydride (0.07 cm<sup>3</sup>, 0.28 mmol) was added and the reaction mixture was heated to 90 °C in a nitrogen atmosphere. After 12 hours the reaction was cooled to room temperature and partitioned between CH<sub>3</sub>CN (20 cm<sup>3</sup>) and *n*-hexane (20 cm<sup>3</sup>). The *n*-hexane layer was extracted with further portions of CH<sub>3</sub>CN (3 × 20 cm<sup>3</sup>) and the combined CH<sub>3</sub>CN extracts were

washed with *n*-hexane (4 × 50 cm<sup>3</sup>). Removal of the solvent under reduced pressure gave the crude product which was purified by recrystallisation from *n*-hexane to give title compound **25** (26 mg, 0.1 mmol, 40%). The reaction was also carried out with chlorodiol **24** (87 mg, 0.29 mmol) to give the title compound **25** (19 mg, 0.07 mmol, 24%) as white needles, mp 118–119 °C (*n*-hexane); *R*<sub>f</sub>[petroleum ether–Et<sub>2</sub>O (6 : 1)] 0.1 (Found: C, 80.2; H, 8.3; C<sub>18</sub>H<sub>22</sub>O<sub>2</sub> requires: C, 80.0; H, 8.2%); [*a*]<sub>D</sub><sup>22</sup> = +7 (*c* 0.3, CHCl<sub>3</sub>); *v*<sub>max</sub>(KBr)/cm<sup>-1</sup> 3665 (s, O–H), 3455 (br, O–H), 1495, 1258, 1073, 1006 and 956; *δ*<sub>H</sub> (400 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 0.83 (3 H, d, *J* 6.8) and 0.89 (3 H, d, *J* 6.8, CH(CH<sub>3</sub>)<sub>2</sub>), 1.47 (1 H, d, *J* 3.2, exchangeable with D<sub>2</sub>O, C(2)OH), 2.42 (1 H, s, exchangeable with D<sub>2</sub>O, C(3)OH), 2.44 (1 H, dd, *J*<sub>AX</sub> 10.8, *J*<sub>AB</sub> 14.0, C(1)H<sup>A</sup>H<sup>B</sup>), 2.45 (1 H, sept, *J* 6.8, C(4)H), 3.06 (1 H, dd, *J*<sub>BX</sub> 2.0, *J*<sub>AB</sub> 14.0, C(1)H<sup>A</sup>H<sup>B</sup>), 4.30 (1 H, app dt, *J* 2.0, 10.8, C(2)H), 7.23–7.37 (8 H, m, ArH), 7.51–7.53 (2 H, m, ArH); *δ*<sub>C</sub> (100 MHz; CDCl<sub>3</sub>; Me<sub>4</sub>Si) 17.6 and 17.7 (CH(CH<sub>3</sub>)<sub>2</sub>), 34.0 (C(4)H), 38.0 (C(1)H<sub>2</sub>), 76.6 (C(2)H), 81.1 (C(3)), 127.2, 127.3, 127.6, 128.5, 129.3 and 130.1 (ArCH), 139.9 and 143.0 (ArCipso); *m/z* (EI) 181 (5%), 150 (33), 149 (100), 131 (8), 105 (27), 91 (42), 77 (22).

#### Crystal structure determination (+)-(1*S*,2*R*,3*R*)-1,2-epoxy-4,4-dimethyl-1,3-diphenylpentan-3-ol (**13**) †

Crystal data for **13**: C<sub>19</sub>H<sub>22</sub>O<sub>2</sub>, *M* = 282.4. Mo-Kα radiation (*λ* = 0.71073 Å), trigonal, space group *R*3, *a* = 18.759(2), *c* = 12.2520(16) Å, *U* = 3733.7(8) Å<sup>3</sup>, *Z* = 9, *μ*(Mo-Kα) = 0.072 mm<sup>-1</sup>. Total number of reflections measured = 6683 of which 2168 were unique (*R*<sub>int</sub> = 0.0523). Refinement by full-matrix least squares method on *F*<sup>2</sup> with 278 parameters gave *R*<sub>1</sub> = 0.0336 (*I* > 2.0σ(*I*)), *wR*<sup>2</sup> = 0.0806 (all data). Data were collected on a Stoe IPDS diffractometer. The structure was solved and refined using SHELX97.<sup>17</sup>

† CCDC reference number 151889. See <http://www.rsc.org/suppdata/p1/b0/b008275i/> for crystallographic data in CIF or other electronic format.

#### Acknowledgements

We thank the EPSRC, DTI, GlaxoWellcome and ChiroTech for a studentship (to A. T. G.) under the Asymmetric Synthesis LINK Scheme.

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