Supporting Information: CONTENTS

Reagent Controlled Asymmetric Homologation of Boronic Esters by Enantioenriched Main-Group Chiral Carbenoids

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Supporting Information: EXPERIMENTAL PROCEDURES

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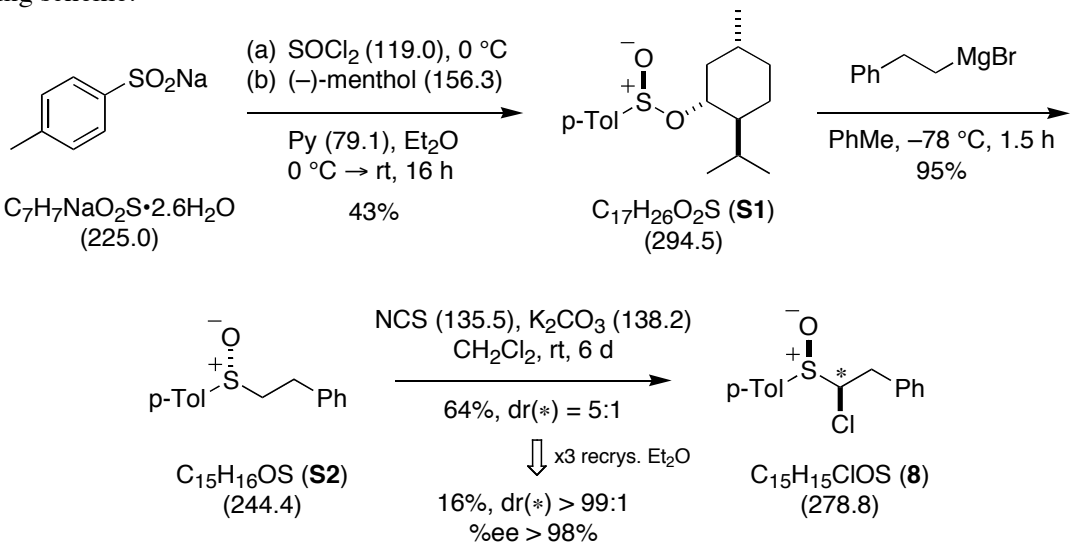
General techniques: All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under an atmosphere of N_2. Tetrahydrofuran (THF) and diethyl ether were freshly distilled from sodium benzophenone ketyl prior to use. Preparative chromatographic separations were performed on silica gel 60 (35-75 μm) and reactions followed by TLC analysis using silica gel 60 plates (2-25 μm) with fluorescent indicator (254 nm) and visualized with UV, phosphomolybdic acid, or p-anisaldehyde. All commercially available reagents were used as received unless otherwise noted.

Melting points were recorded on a melting point stage and are uncorrected. Specific optical rotation data were recorded under the indicated conditions using 1 mL cells with either 0.25 dm or 1.00 dm path length. Infra-red spectra were recorded in Fourier transform mode using a thin film supported between NaCl plates for liquid samples and an ATR probe for solids. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra were recorded in Fourier transform mode at the field strength specified and from the indicated deuterated solvents in standard 5 mm diameter tubes. Chemical shift for ^{1}H and ^{13}C nuclei is quoted in ppm relative to residual solvent signals calibrated as follows: $CDCl_3$ δ_H ($CHCl_3$) = 7.26 ppm, δ_C = 77.2 ppm. Chemical shift in ^{11}B NMR spectra are reported in ppm with external calibration to a BF_3•OEt_2 standard (δ_B = 0.00 ppm). Chemical shift in ^{19}F NMR spectra are reported in ppm with external calibration to a $CFCl_3$ standard (δ_F = 0.00 ppm). Multiplicities in the ^{1}H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Numbers in parentheses following carbon atom chemical shifts refer to the number of attached hydrogen atoms as revealed by the DEPT spectral editing technique. Low (MS) and high resolution (HRMS) mass spectra were obtained using either electron impact (EI), electrospray (ES), or fast atom bombardment (FAB) ionization techniques. Ion mass/charge (m/z) ratios are reported as values in atomic mass units.

– Preparation of enantioenriched chlorosulfoxide 8 –

Chlorosulfoxide **8** was prepared essentially as previously described by Hoffmann and co-workers[1] according to the following scheme:–



(S_S)-Menthyl p-toluenesulfinate (S1): The Andersen menthyl sulfinate (**S1**)[2] was prepared according to the following slight modification of Solladie's procedure.[3] Thus, sodium toluenesulfinate 2.6 hydrate (45.1 g, 200 mmol) was added portionwise to thionyl chloride (51.0 mL, d = 1.63, 83.1 g, 699 mmol) at 0 °C during 30 min. After cessation of the ensuing effervescence, PhMe (50 mL) was added to the resulting sulfinyl chloride and the mixture concentration *in vacuo*. The residue was dissolved in PhMe (50 mL) and again concentrated *in vacuo*. Following repetition of this dissolution/concentration operation, the sulfinyl chloride was dissolved in anhydrous Et_2O (160 mL) and added to a solution of (–)-menthol (39.0 g, 250 mmol) and pyridine (36.0 mL, d = 0.98, 35.2 g, 445 mmol) in Et_2O (90 mL) at 0 °C. A voluminous colorless precipitate appeared immediately. The mixture was stirred at rt for 16 h and then poured into H_2O (50 mL) and the layers separated. The organic phase was washed with 1.5 M aq. HCl (3x50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was recrystallized three times from acetone to yield the title compound (**S1**, 25.4 g, 86.2 mmol, 43%) as colorless needles: mp 107-109 °C (acetone) [lit.[4] mp 106-108 °C (acetone)]; $[\alpha]_D^{23}$ = –204 (c = 2.24, acetone) [lit.[5] $[\alpha]_D$ = –201 (c = 1.5, acetone)]; IR (neat) 2907, 1594, 1492, 1451, 1128, 958 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60 (2H, d, *J* = 8.0 Hz), 7.33 (2H, d, *J* = 8.0 Hz), 4.12 (1H, td, *J* = 10.7, 4.5 Hz), 2.42 (3H, s), 2.28 (1H, dm, *J* = 12.8 Hz), 2.13 (1H, qm, *J* = 7.2 Hz), 1.73-1.64 (2H, m), 1.55-0.79 (5H, m), 0.96 (3H, d, *J* = 6.7 Hz), 0.86 (3H, d, *J* = 7.2 Hz), 0.71 (3H, d, *J* = 7.2 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.3 (0), 142.6 (0), 129.8 (2C, 1), 125.1 (2C, 1), 80.3 (1), 48.0 (1), 43.1 (2), 34.2 (2), 31.9 (1), 25.4 (1), 23.5 (2), 22.5 (3), 21.9 (3), 21.3 (3), 15.9 (3) ppm; MS (EI+) *m/z* 294 (15, $M^{+\bullet}$), 139 (100). Spectroscopic data were in agreement with those previously reported by Watanabe *et al*.[4]

(R_S)-2-Phenylethyl p-tolyl sulfoxide (S2): A vigorously stirred suspension of mechanically activated Mg-turnings (2.04 g, 83.9 mmol) in anhydrous THF (50 mL) under N_2 was treated with neat phenethyl bromide (11.4 mL, d = 1.35, 15.4 g, 83.2 mmol) at a rate sufficient to first initiate, and then subsequently sustain, a gentle

1. Hoffmann, R. W.; Nell, P. G.; Leo, R.; Harms, K. *Chem. Eur. J.* **2000**, *6*, 3359.
2. Andersen, K. K. *Tetrahedron Lett.* **1962**, 93.
3. Solladie, G. *Synthesis* **1981**, 185.
4. Watanabe, Y.; Mase, N.; Tateyama, M.-A.; Toru, T. *Tetrahedron:Asymmetry* **1999**, *10*, 7337.
5. Hajipour, A.; Mallakpour, S.; Afrousheh, A. *Tetrahedron* **1999**, *55*, 2311.

reflux. After the addition was complete, the exotherm ceased and the reaction mixture returned to rt. The THF solvent was then removed *in vacuo* and the residual Grignard reagent taken up in PhMe (50 mL). The resulting solution was cooled to –78 °C and treated with (S_S)-menthyl *p*-toluenesulfinate (**S1**, 20.4 g, 69.2 mmol) in PhMe (100 mL) during 13 min. After stirring at –78 ºC for 1.5 h, the reaction mixture was poured into sat. aq. NH_4Cl (50 mL) and the layers separated. The organic phase was washed with 1.5 M aq. HCl (30 mL) and the combined aqueous phases were extracted with Et_2O (5x30 mL). The combined organic phases were then washed succesively with H_2O (2x30 mL) and brine (2x30 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by filtration through a plug of SiO_2 (∅ = 6.5 cm, depth = 3 cm) eluting with 33% EtOAc in hexanes (200 mL) followed by EtOAc (150 mL). The title compound (**S2**, 16.1 g, 65.9 mmol, 95%) was obtained as a pale yellow oil which solidified upon standing: mp 47-51 °C (acetone); $[\alpha]_D^{21}$ = +99 (c = 2.06, acetone) [lit.[6] $[\alpha]_D$ = +125 (c = 2.24, acetone)]; IR (neat) 3021, 1599, 1492, 1451, 1039, 803, 702 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.53 (2H, d, *J* = 8.2 Hz), 7.37-7.15 (7H, m), 3.14-2.84 (4H, m), 2.42 (3H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.7 (0), 140.5 (0), 139.0 (0), 130.1 (2C, 1), 128.9 (2C, 1), 128.7 (2C, 1), 126.8 (1), 124.2 (2C, 1), 58.5 (2), 28.3 (2), 21.6 (3) ppm; MS (EI+) *m/z* 244 (50, $M^{+\circ}$), 105 (100). NMR spectral data were in agreement with those previously reported by Yoshimura *et al*.[7]

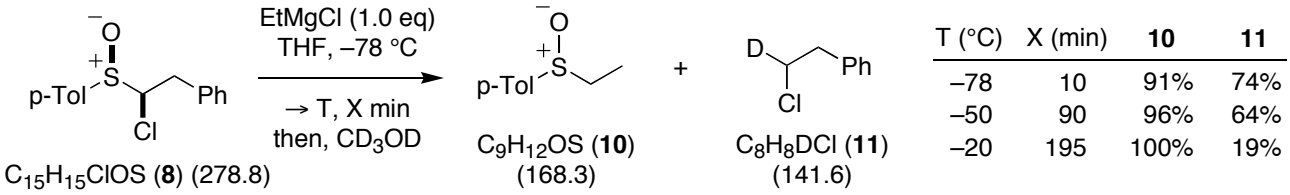
HPLC analysis of **S2** performed with a Daicel Chiralcel® OD-H column, eluting with 1% *i*-PrOH in hexanes at 1.0 mL min^{-1} and monitored by UV at 210 nm, gave peaks: $t_{ret.}$ (**S2**) = 60.4 min, $t_{ret.}$ (*ent*-**S2**) = 69.1 min, which integrated to reveal 96% ee (as compared to a racemic standard).

(R_S,*R*)-1-Chloro-2-phenylethyl p-tolyl sulfoxide (8): According to the method of Satoh and Yamakawa[8] and as applied previously by Hoffmann and co-workers.[1] A solution of (R_S)-2-phenylethyl *p*-tolyl sulfoxide (**S2**, 5.62 g, 23.0 mmol, 96% ee) in CH_2Cl_2 (50 mL) was treated with K_2CO_3 (1.91 g, 13.8 mmol) and *N*-chlorosuccinimide (15.3 g, 115 mmol). The resulting suspension was stirred vigorously at rt for 140 h. After this time, the mixture was poured into Et_2O (100 mL) and washed successively with 5 wt.% aq. NaI (2x200 mL), sat. aq. $Na_2S_2O_3$ (35 mL), and brine (2x50 mL), then dried (Na_2SO_4) and concentrated *in vacuo*. The crude residue was purified by column chromatography to afford sulfoxide **8** (4.11 g, 14.7 mmol, 64%) as a 5.5:1 respective mixture of *syn* and *anti* diastereoisomers (epimeric about C∗; ratio determined by integration of ^1H NMR spectrum). After three recrystallation cycles from Et_2O (conducted at 4 °C), sulfoxide **8** (1.03 g, 3.69 mmol, 16%) was obtained as colorless needles which were diastereoisomerically pure as adjudged by ^1H NMR spectroscopy: mp 81-82 °C (Et_2O) [lit.[1] mp 77-78 °C (acetone)]; $[\alpha]_D^{23}$ = –89.8 (c = 0.62, acetone) [lit.[1] $[\alpha]_D^{20}$ = –91.8 (c = 2.0, acetone)]; IR (neat) 2945, 1604, 1454, 1086, 943, 803, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (2H, d, *J* = 8.2 Hz), 7.39-7.21 (7H, m), 4.67 (1H, dd, *J* = 9.7, 4.4 Hz), 3.64 (1H, dd, *J* = 14.3, 4.4 Hz), 2.72 (1H, dd, *J* = 14.3, 9.7 Hz), 2.44 (3H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.7 (0), 135.6 (0), 135.5 (0), 129.8 (2C, 1), 129.6 (2C, 1), 128.9 (2C, 1), 127.5 (1), 125.8 (2C, 1), 76.7 (1), 37.1 (2), 21.7 (3) ppm; MS (EI+) *m/z* 280 (30, $M(^{37}Cl)^{+\bullet}$) 278 (90, $M(^{35}Cl)^{+\bullet}$), 103 (100). NMR spectral data recorded for **8** were in complete agreement with those previously reported by Hoffmann *et al*.[1]

HPLC analysis of recrystallized **8** performed with a Daicel Chiralcel® OD-H column, eluting with 5% *i*-PrOH in hexanes at 1.0 mL min^{-1} and monitored by UV at 250 nm, gave peaks: $t_{ret.}$ (*ent*-**8**) = 15.3 min, $t_{ret.}$ (**8**) = 23.5 min, which integrated to reveal 98.7% ee (as compared to a racemic standard).

6. Hoffmann, R. W.; Nell, P. G. *Ang. Chem. Int. Ed.* **1999**, *38*, 338.
7. Yoshimura, T.; Yoshizawa, M.; Tsukurimichi, E. *Bull. Chem. Soc. Jpn.* **1987**, *60*, 2491.
8. Satoh, T.; Oohara, T.; Ueda, Y.; Yamakawa, K. *Tetrahedron Lett.* **1988**, *29*, 313.

– Sulfoxide ligand exchange study from 8 (Scheme 2) –



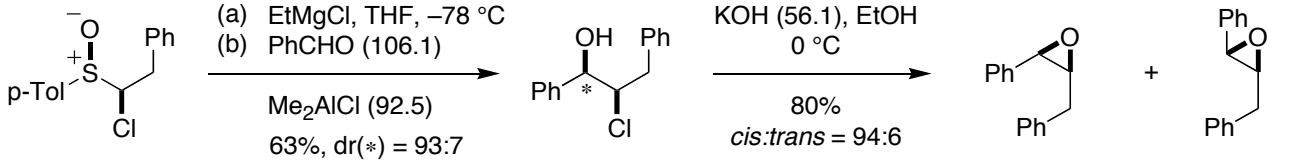
T (°C)	X (min)	**10**	**11**
–78	10	91%	74%
–50	90	96%	64%
–20	195	100%	19%

A stirred solution of sulfoxide **8** (195 mg, 0.70 mmol) in anhydrous THF (2 mL) at –78 °C under N_2 was treated with EtMgCl (0.61 mL, 1.18 M in THF, 0.72 mmol). The mixture was allowed to warm steadily to the indicated temperature (T) during the prescribed time period (X min) at which point d_4-MeOH (0.16 mL, d = 0.89, 142 mg, 3.84 mmol) was added. After warming to rt, the mixture was treated with sat. aq. NH_4Cl (10 mL) and extracted successively with Et_2O (2x10 mL) and EtOAc (2x10 mL). The combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 50% EtOAc in hexanes) to yield, in order of elution, deuterated chloride **11** (%D ≥ 91% by ^{1}H NMR analysis) and ethyl sulfoxide **10** (%D = 0% by ^{1}H NMR analysis), both as colorless oils.

Ethyl p-tolyl sulfoxide (**10**): IR (neat) 2928, 1596, 1492, 1454, 1086, 1045, 1012, 812 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (2H, d, *J* = 8.0 Hz), 7.33 (2H, d, *J* = 8.0 Hz), 2.87 (1H, dq, *J* = 13.4, 7.4 Hz), 2.76 (1H, dq, *J* = 13.4, 7.4 Hz), 2.42 (3H, s), 1.19 (3H, t, *J* = 7.4 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.6 (0), 140.2 (0), 130.0 (2C, 1), 124.4 (2C, 1), 50.5 (2), 21.6 (3), 6.2 (3) ppm; MS (ES+) *m/z* 169 [100, $(M+H)^+$]. ^{1}H and ^{13}C NMR spectral data were in agreement with those previously reported by Evans *et al.*[9]

(2-Chloro-2-deuteroethyl)benzene (**11**): IR (neat) 2950, 1728, 1478, 1412, 1349, 1259, 1097 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.20 (5H, m), 3.70 (1H, t of 1:1:1 triplet, *J* = 7.2, 1.5 Hz), 3.07 (2H, br d, *J* = 7.2 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.2 (0), 129.0 (2C, 1), 128.8 (2C, 1), 127.1 (1), 44.9 (1, 1:1:1 triplet, *J* = 46.3 Hz), 39.3 (2) ppm; MS (EI+) *m/z* 143 (6, $M(^{37}Cl)^{+\bullet}$), 141 (19, $M(^{35}Cl)^{+\bullet}$), 91 (100). Data for **11** were in agreement with those previously reported by Namavari *et al.*[10]

– Repetition of Hoffmann's carbenoid trapping experiment with benzaldehyde (Equation 1) –



(1*R*,2*R*)-2-Chloro-1,3-diphenylpropan-1-ol (S3): The method of Hoffmann and co-workers[1] was followed with slight modification (EtMgCl in place of EtMgBr). Thus, the experiment was conducted in a two compartment reaction vessel fabricated from two single-necked 25 mL RB flasks connected about their equators by way of a short horizontal glass tube (ca. 20 mm length, ∅ (int.) = 4 mm). Each compartment was provided with a magnetic stir bar. The apparatus was maintained under an atmosphere of N_2 and one compartment charged with a solution of isomerically homogenous sulfoxide **8** (59 mg, 0.21 mmol, %ee > 98%) in anhydrous THF (3.5 mL). The other compartment was similarly charged with EtMgCl (2.65 mL, 0.11 M in

9. Evans, D. A.; Faul, M. M.; Colombo, L.; Bisaha, J. J.; Clardy, J.; Cherry, D. *J. Am. Chem. Soc.* **1992**, *114*, 5977.
10. Namavari, M.; Satyamurthy, N.; Barrio, J. R. *J. Fluorine Chem.* **1995**, *72*, 89.

THF, 0.29 mmol) and the entire apparatus was cooled by submergence in a –78 °C cold bath. After allowing a suitable time period for the attainment of thermal equilibrium (ca. 20 min, with stirring), the apparatus was gently tilted to effect the portionwise addition (six portions) of the solution of sulfoxide **8** to the Grignard reagent during 17 min. The connecting tube remained submerged in the cooling bath throughout this operation. The reaction mixture was afforded 30 min to stir at –78 °C during which time the compartment previously occupied by the sulfoxide was charged with a mixture of benzaldehyde (36 μL, d = 1.04, 37 mg, 0.35 mmol) and Me_2AlCl (0.35 mL, 1.0 M in hexanes, 0.35 mmol) in THF (2.5 mL). The apparatus was tilted as before to add the now chilled mixture of benzaldehyde/Me_2AlCl to the carbenoid solution in four portions during 15 min. The reaction mixture was then allowed to warm steadily to –30 ºC over the following 13.5 h before being quenched by the addition of sat. aq. NH_4Cl (1 mL). The layers of the resulting biphasic mixture were separated and the aqueous phase was extracted with *t*-BuOMe (3x10 mL). The combined organic phases were then washed successively with H_2O (5 mL) and brine (5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the title compound (**S3**, 33 mg, 0.134 mmol, 63%, dr(∗) = 93:7 as adjudged by ^{1}H NMR spectral analysis) as a colorless oil: IR (neat) 3423, 3027, 1602, 1495, 1454, 1064, 1028, 746, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, signals attributable to major isomer only) δ 7.47-7.12 (10 H, m), 4.77 (1H, t, *J* = 5.4 Hz), 4.34 (1H, dt, *J* = 9.2, 5.4 Hz), 3.11 (1H, dd, *J* = 14.2, 5.4 Hz), 2.94 (1H, dd, *J* = 14.2, 9.2 Hz), 2.72 (1H, d, *J* = 5.4 Hz, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$, signals attributable to major isomer only) δ 140.3 (0), 137.6 (0), 129.4 (2C, 1), 128.8 (2C, 1), 128.7 (2C, 1), 128.5 (1), 127.1 (1), 126.7 (2C, 1), 76.0 (1), 70.1 (1), 41.1 (2) ppm. ^{1}H and ^{13}C NMR data were in agreement with those previously reported by Hoffmann *et al*.[1]

(2*S*,3*R*)-*cis*-2-Benzyl-3-phenyloxirane (*cis*-12) and (2*S*,3*S*)-*trans*-2-benzyl-3-phenyloxirane (*trans*-12): Following the method of Hoffmann and co-workers,[1] a solution of chlorohydrin **S3** (16 mg, 0.065 mmol, dr(∗) = 93:7) in EtOH (1.5 mL) at 0 °C was treated with an ethanolic solution of KOH (0.32 mL, 0.40 M in EtOH, 0.13 mmol) during 30 s. The resulting mixture was stirred at rt for 19 h and was then treated with NH_4Cl (115 mg, 2.15 mmol) and concentrated *in vacuo*. The residue was partitioned between *t*-BuOMe (10 mL) and sat. aq. NH_4Cl (5 mL) and the layers well shaken and separated. The aqueous phase was extracted with *t*-BuOMe (3x10 mL) and the combined organic phases were washed with brine (2x5 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the title compounds (*cis*-**12** and *trans*-**12**, 11 mg, 0.052 mmol, 80%) as an inseparable mixture of colorless oils (*cis:trans* = 94:6 as adjudged by ^{1}H NMR spectral analysis): IR (neat) 3027, 1602, 1495, 1454, 743, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$, signals attributable to *cis*-**12** only) δ 7.43-7.16 (8H, m), 7.04 (2H, d, *J* = 6.4 Hz), 4.17 (1H, d, *J* = 4.1 Hz), 3.44 (1H, td, *J* = 6.4, 4.1 Hz), 2.77 (1H, dd, *J* = 14.6, 6.4 Hz), 2.56 (1H, dd, *J* = 14.6, 6.4 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$, signals attributable to *cis*-**12** only) δ 137.6 (0), 135.5 (0), 129.0 (2C, 1), 128.7 (2C, 1), 128.3 (2C, 1), 127.9 (1), 126.8 (2C, 1), 126.7 (1), 59.9 (1), 57.8 (1), 33.4 (2) ppm; MS (ES+) *m/z* 211 [42, $(M+H)^+$], 115 (100). ^{1}H and ^{13}C NMR data were in agreement with those previously reported by Hoffmann and Schulze.[11]

HPLC analysis of the mixture of *cis*-**12** and *trans*-**12** obtained in the above experiment using two different chiral stationary phases permitted determination of %ee for both diastereoisomers. Thus, analysis of a racemic sample of **12** exhibiting *cis:trans* ~ 3:1 with a Daicel Chiralcel® AS-RH column, eluting with 40-55% MeCN in H_2O (over 30 min) at 1.0 mL min^{-1} and monitored by UV at 210 nm, gave resolved peaks $t_{ret.}$ (*cis*-**12** + *ent-cis*-**12**) = 19.0 min, $t_{ret.}$ (*trans*-**12**) = 20.4 min, and $t_{ret.}$ (*ent-trans*-**12**) = 26.0 min (Figure S1). Analysis of the same sample with a Daicel Chiralcel® OD-RH column, eluting with 40-55% MeCN in H_2O (over 30 min) at 1.0 mL min^{-1}

11. Schulze, V.; Hoffmann, R. W. *Chem. Eur. J.* **1999**, *5*, 337.

and monitored by UV at 210 nm, gave resolved peaks $t_{ret.}$ (*ent-cis*-**12**) = 26.4 min, $t_{ret.}$ (*ent-trans*-**12**) = 27.6 min, and $t_{ret.}$ (*cis*-**12** + *trans*-**12**) = 28.6 min (Figure S2). Examination of integration values for chromatograms similarly obtained from the enantioenriched sample of *cis*-**12** and *trans*-**12** obtained in the above experiment, revealed %ee (*cis*-**12**) = 98.4% and %ee (*trans*-**12**) > 98% (Figures S3 and S4). Absolute stereochemical configurations for these compounds were previously established by Hoffmann and co-workers.[1]

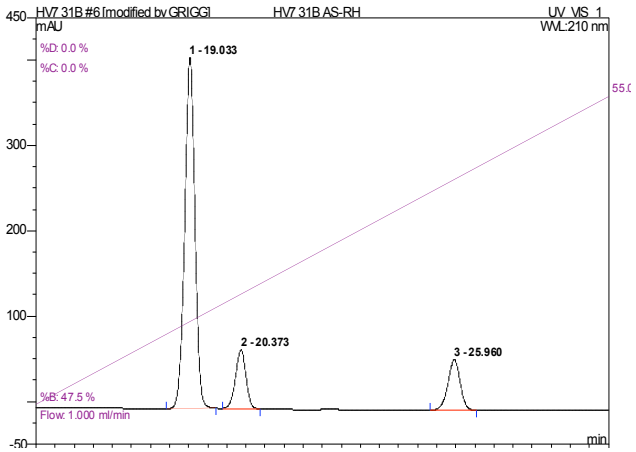


Figure S1. HPLC chromatogram (AS-RH) for *rac*-**12** (*cis:trans* ~ 3:1)

Peak 1 - 19.0 min (74.27%)
Peak 2 - 20.4 min (12.82%)
Peak 3 - 26.0 min (12.90%)

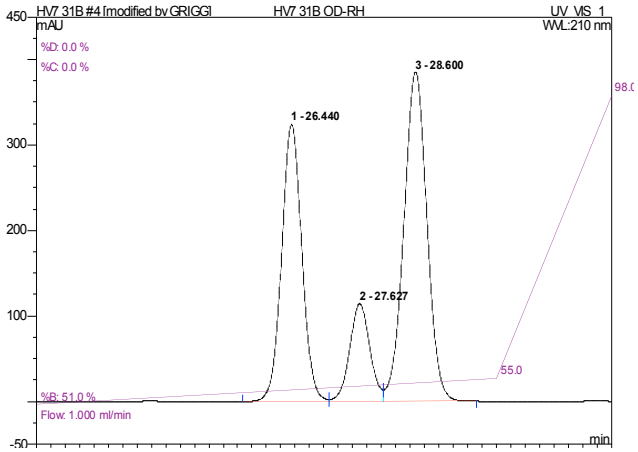


Figure S2. HPLC chromatogram (OD-RH) for *rac*-**12** (*cis:trans* ~ 3:1)

Peak 1 - 26.4 min (36.86%)
Peak 2 - 27.6 min (12.99%)
Peak 3 - 28.6 min (50.15%)

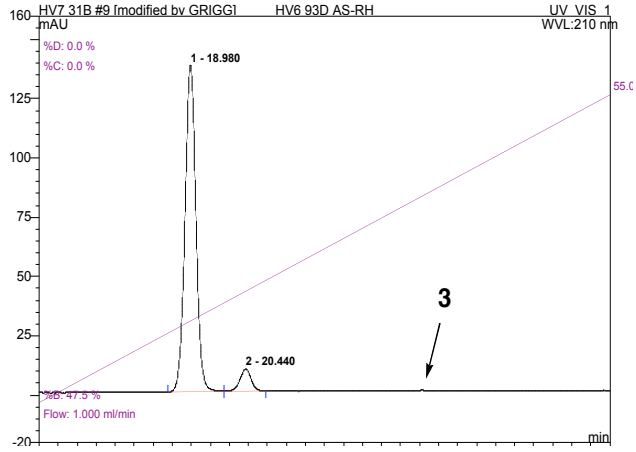


Figure S3. HPLC chromatogram (AS-RH) for enantioenriched **12** (*cis:trans* = 94:6)

Peak 1 - 19.0 min (93.53%)
Peak 2 - 20.4 min (6.47%)
Peak 3 - 26.0 min (< 0.05%)

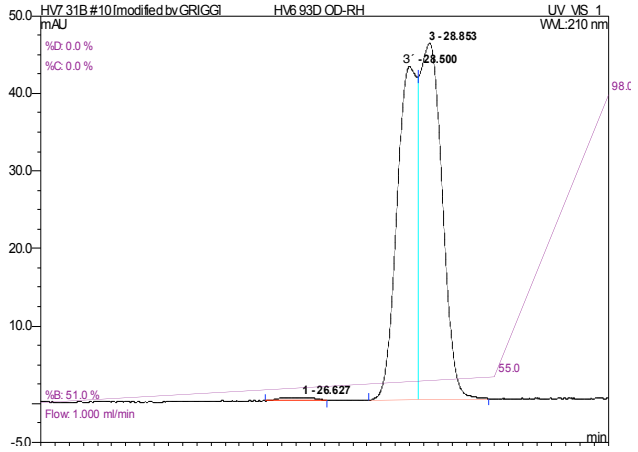
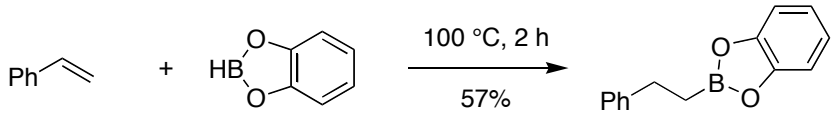


Figure S4. HPLC chromatogram (OD-RH) for enantioenriched **12** (*cis:trans* = 94:6)

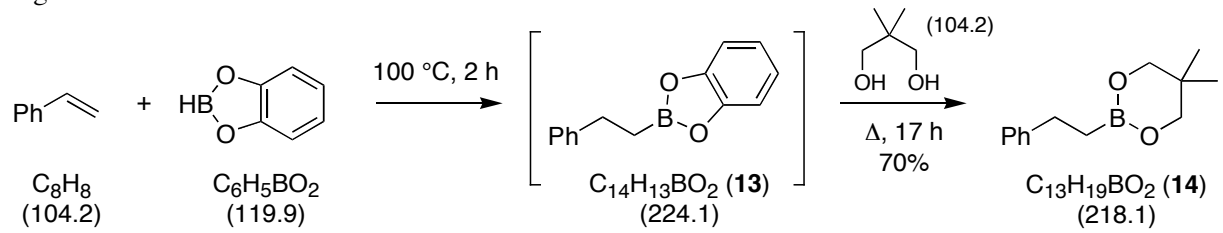
Peak 1 - 26.6 min (0.71%)
Peak 2 - absent (< 0.05%)
Peaks 3,3´ - 28.5-28.9 min (99.29%)

– Preparation of boronic esters 13-19 (Tables 1 and 2) –



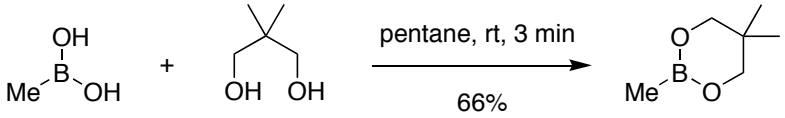
C_8H_8 (104.2) $C_6H_5BO_2$ (119.9) $C_{14}H_{13}BO_2$ (**13**) (224.1)

2-(2-Phenylethyl)benzo-1,3,2-dioxaborole (13): A stirred mixture of styrene (1.15 mL, d = 0.91, 1.05 g, 10.0 mmol) and catecholborane (1.17 mL, d = 1.13, 1.32 g, 11.0 mmol) was heated at 100 °C under N_2 for 2 h. After this time, distillation in a Kugelrohr oven (200 °C, 4.5 mmHg) afforded the title boronic ester **13** (1.28 g, 5.71 mmol, 57%) as a colorless air-sensitive oil which was stored under N_2 and used promptly: IR (neat) 3214, 1602, 1471, 1380, 1235, 1065, 1004, 922, 862, 807, 741, 700 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (7H, m), 7.13-7.05 (2H, m), 2.99 (2H, t, *J* = 8.2 Hz), 1.67 (2H, t, *J* = 8.2 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 148.3 (2C, 0), 128.6 (2C, 1), 128.1 (2C, 1), 126.1 (1), 122.8 (2C, 1), 112.5 (2C, 1), 29.8 (2) ppm [O-<u>C</u> (x2) and B-<u>C</u>H_2 not observed]; MS (EI+) *m/z* 224 (65, $M^{+\bullet}$), 91 (100). ^{11}B NMR spectral data for this compound have been reported by Burgess and van der Donk.[12]



C_8H_8 (104.2) $C_6H_5BO_2$ (119.9) $C_{14}H_{13}BO_2$ (**13**) (224.1) $C_{13}H_{19}BO_2$ (**14**) (218.1)

5,5-Dimethyl-2-(2-phenylethyl)-1,3,2-dioxaborinane (14): A stirred mixture of styrene (1.15 mL, d = 0.91, 1.05 g, 10.0 mmol) and catecholborane (1.17 mL, d = 1.13, 1.32 g, 11.0 mmol) was heated at 100 °C under N_2 for 2 h. After cooling to rt, the resulting boronate (**13**) was added directly to a solution of 2,2-dimethyl-1,3-propanediol (2.60 g, 25.0 mmol) in anhydrous THF (13 mL) and heated to reflux for 17 h. After this time, the mixture was concentrated *in vacuo* and the residue purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the title compound (**14**, 1.53 g, 7.02 mmol, 70%) as a colorless oil: bp 204-206 °C (4.5 mmHg); IR (neat) 2959, 1602, 1475, 1346, 1287, 1250, 1172, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30-7.11 (5H, m), 3.59 (4H, s), 2.71 (2H, t, *J* = 8.2 Hz), 1.08 (2H, t, *J* = 8.2 Hz), 0.93 (6H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.1 (0), 128.3 (2C, 1), 128.1 (2C, 1), 125.5 (1), 72.1 (2C, 2), 31.7 (0), 30.2 (2), 21.9 (2C, 3), 16.7 (2) ppm; MS (FAB+) *m/z* 218 (100, $M^{+\bullet}$); HRMS (ES+) *m/z* 219.1568 (calcd. for $C_{13}H_{20}BO_2$: 219.1556). Boronate **14** was previously reported by Kakiuchi *et al* without characterization data.[13]

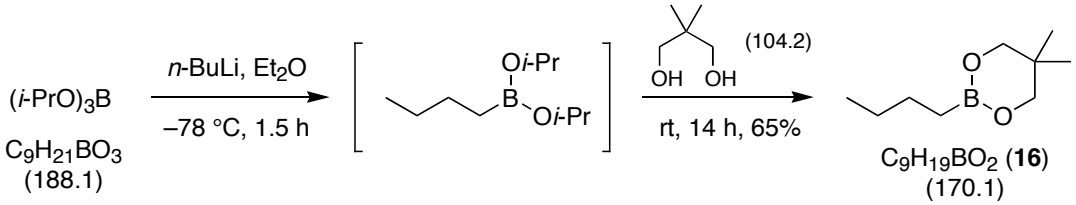


CH_5BO_2 (59.9) $C_5H_{12}O_2$ (104.2) $C_6H_{13}BO_2$ (**15**) (128.0)

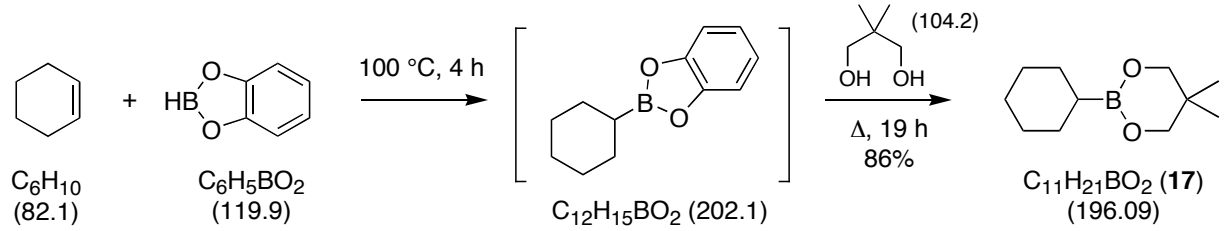
2,5,5-Trimethyl-1,3,2-dioxaborinane (15): Prepared by analogy to Brown's synthesis of 2-*tert*-butyl-1,3,2-dioxaborinane from *tert*-butylboronic acid and 1,3-propanediol.[14] Thus, a mixture of methaneboronic acid (104 mg, 1.74 mmol), 2,2-dimethyl-1,3-propanediol (200 mg, 1.92 mmol), and pentane (1.8 mL) was stirred at rt

12. Burgess, K.; van der Donk, W. A. *Organometallics* **1994**, *13*, 3616.
13. Kakiuchi, F.; Usui, M., Ueno, S.; Chatani, N.; Murai, S. *J. Am. Chem. Soc.* **2004**, *126*, 2706.
14. Srebnik, M.; Cole, T. E.; Ramachandran, P. V.; Brown, H. C. *J. Org. Chem.* **1989**, *54*, 6085.

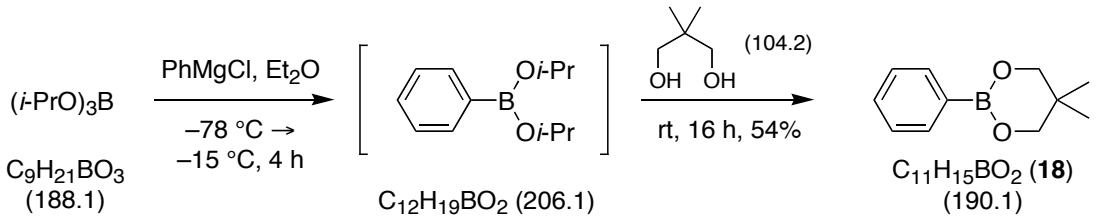
under N_2 for 3 min. After this time, the layers of the resulting biphasic mixture were separated. Careful removal of the pentane solvent by evaporation under one atmosphere of N_2 afforded the title boronate (**15**, 147 mg, 1.15 mmol, 66%) as a colorless oil: IR (neat) 2923, 1714, 1473, 1336, 1248, 1034 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.59 (4H, s), 0.96 (6H, s), 0.20 (3H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.2 (2C, 2), 31.7 (0), 22.0 (2C, 3) ppm [B-$\underline{C}H_3$ not observed]; ^{11}B NMR (160 MHz, $CDCl_3$) δ 30.3 ppm. Boronate **15** was previously reported by Kakiuchi *et al* without characterization data.[13]



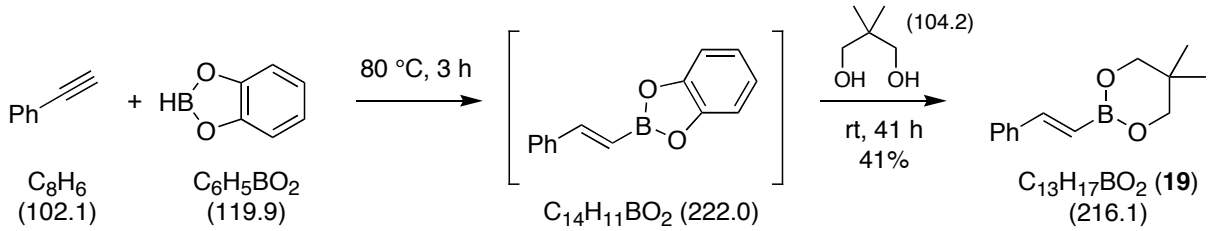
2-Butyl-5,5-dimethyl-1,3,2-dioxaborinane (16): A solution of *n*-butyllithium (6.60 mL, 1.52 M in hexanes, 10.0 mmol) in Et_2O (27 mL) at –78 °C under N_2 was treated with triisopropyl borate (2.30 mL, d = 0.818, 1.88 g, 10.0 mmol) during 1 h. After 20 min at –78 °C, the cold bath was removed and the reaction mixture allowed to warm to rt. Once at rt, the reaction mixture was treated with 2,2-dimethyl-1,3-propanediol (830 mg, 7.97 mmol) and stirred for 14 h. The mixture was then partitioned between Et_2O (100 mL) and sat. aq. NH_4Cl (50 mL) and the layers separated. The organic phase was washed successively with H_2O (2x50 mL) and brine (50 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was distilled at reduced pressure to yield the title boronate (**16**, 876 mg, 5.15 mmol, 65%) as a colorless oil: bp 51-52 ºC (1.5 mmHg); IR (neat) 2956, 2928, 1476, 1412, 1330, 1248, 1179, 1075 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.59 (4H, s), 1.41-1.24 (4H, m), 0.96 (6H, s), 0.88 (3H, t, J = 7.0 Hz), 0.71 (2H, t, J = 7.4 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.1 (2C, 2), 31.8 (0), 26.6 (2), 25.7 (2), 22.0 (2C, 3), 14.8 (2), 14.1 (3) ppm; MS (ES+) *m/z* 209 [100, $(M+K)^+$].



2-Cyclohexyl-5,5-dimethyl-1,3,2-dioxaborinane (17): A stirred mixture of cyclohexene (1.01 mL, d = 0.81, 819 mg, 9.97 mmol) and catecholborane (1.17 mL, d = 1.13, 1.32 g, 11.0 mmol) was heated at 100 °C under N_2 for 4 h. After cooling to rt, the resulting boronate was added directly to a solution of 2,2-dimethyl-1,3-propanediol (2.60 g, 25.0 mmol) in anhydrous THF (13 mL) and heated to reflux for 19 h. After this time, the mixture was concentrated *in vacuo* and the residue purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the title compound (**17**, 1.68 g, 8.57 mmol, 86%) as a colorless air-sensitive oil: IR (neat) 2923, 1476, 1410, 1314, 1253, 1179 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.58 (4H, s), 1.72-1.55 (5H, m), 1.34-1.17 (5H, m), 0.94 (6H, s), 0.91-0.79 (1H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 72.1 (2C, 2), 31.8 (0), 28.4 (2C, 2), 27.6 (2C, 2), 27.1 (2), 25.8 (br), 21.9 (2C, 3) ppm.



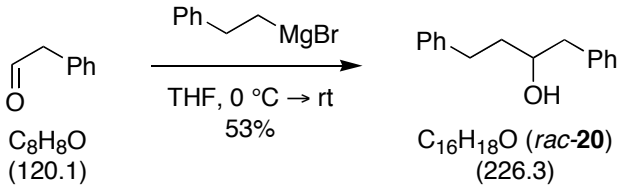
5,5-Dimethyl-2-phenyl-1,3,2-dioxaborinane (18): A solution of phenylmagnesium bromide (14.6 mL, 1.37 M in THF, 20.0 mmol) in Et_2O (52 mL) at –78 °C was slowly treated with triisopropyl borate (4.60 mL, d = 0.82, 3.76 g, 20.0 mmol) during 2 h. The solution was allowed to warm to –15 °C over 4 h and then 2,2-dimethyl-1,3-propanediol (2.19 g, 21.0 mmol) was added in one portion. The resulting mixture was stirred at rt for 16 h and then partitioned between Et_2O (200 mL) and sat. aq. NH_4Cl (100 mL). The layers were separated and the organic phase washed successively with H_2O (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 5% EtOAc in hexanes) to yield the title boronate (**18**, 2.05 g, 10.8 mmol, 54%) as colorless plates: mp 61-63 °C (hexanes) [lit.[15] mp 65-66 °C (hexanes)]; IR (neat) 2956, 1599, 1314, 1133, 696, 642 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (2H, d, *J* = 6.7 Hz), 7.48-7.31 (3H, m), 3.77 (4H, s), 1.02 (6H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.0 (2C, 1), 130.9 (1), 127.8 (2C,1), 72.5 (2C, 2), 32.1 (0), 22.1 (2C, 3) ppm [C-B not observed]; ^{11}B NMR (160 MHz, $CDCl_3$) δ 26.8 ppm. ^1H and ^{11}B NMR spectral data were in agreement with those previously reported by Davis *et al.*[16]



(*E*)-5,5-Dimethyl-2-(2-phenylethenyl)-1,3,2-dioxaborinane (19): A mixture of phenylacetylene (0.55 mL, d = 0.93, 512 mg, 5.01 mmol) and catecholborane (0.59 mL, d = 1.13, 667 mg, 5.56 mmol) were stirred at 80 °C under N_2 for 3 h. After cooling to rt, the resulting orange solid was dissolved in Et_2O (50 mL). Exactly one half of the ethereal solution was treated with 2,2-dimethyl-1,3-propanediol (1.30 g, 12.5 mmol) and stirred at rt under N_2 for 41 h. After this time, the reaction mixture was washed with H_2O (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the title unsaturated boronate (**19**, 220 mg, 1.02 mmol, 41%) as a colorless solid: mp 41-44 °C (pentane, colorless prisms); IR (neat) 2956, 1622, 1478, 1256, 1190, 1078, 998, 749, 693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49 (2H, d, *J* = 7.2 Hz), 7.38-7.23 (4H, m), 6.11 (1H, d, *J* = 18.4 Hz), 3.70 (4H, s), 1.01 (6H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.2 (1), 137.9 (0), 128.6 (2C, 1), 127.1 (2C, 1), 121.0 (1), 72.3 (2C, 2), 31.9 (0), 22.0 (2C, 3) ppm. IR and NMR spectral data were in agreement with those previously reported by Kobayashi *et al.*[17]

15. Bowie, R.; Musgrave, O. *J. Chem. Soc.* **1963**, 3945.
16. Davis, F.; Turchi, I.; Maryanoff, B.; Hutchins, R. *J. Org. Chem.* **1972**, *37*, 1583.
17. Kobayashi, Y.; Nakayama, Y.; Mizojiri, R. *Tetrahedron* **1998**, *54*, 1053.

– Preparation of standards (±)-20-24, HPLC resolution, and configurational assignment for 22 and 23 –



(±)-1,4-Diphenylbutan-2-ol (*rac*-20): A vigorously stirred suspension of mechanically activated Mg-turnings (270 mg, 11.1 mmol) in anhydrous THF (10 mL) under N_2 was treated with neat phenethyl bromide (1.37 mL, d = 1.35, 1.85 g, 10.0 mmol) at a rate sufficient to first initiate, and then subsequently sustain, a gentle reflux. Shortly after the addition was complete, the exotherm ceased and the reaction mixture returned to rt. The solution of the so-formed Grignard reagent was cooled to 0 °C and treated with phenylacetaldehyde (1.17 mL, d = 1.03, 1.21 g, 10.0 mmol) in anhydrous THF (5 mL) during 6 min. The reaction mixture was stirred at 0 °C for 10 min and then allowed to warm to rt. After stirring for 15 h at rt, the mixture was poured into sat. aq. NH_4Cl (10 mL) and the resulting layers well shaken and separated. The aqueous phase was extracted with EtOAc (3x10 mL) and the combined organic phases washed successively with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 6% EtOAc in hexanes) to afford the title carbinol (*rac*-**20**, 1.19 g, 5.26 mmol, 53%) as a viscous oil which crystallized upon standing: mp 43-44 °C (Et_2O-hexanes (1:1), colorless needles) [lit.[18] mp 44 °C]; IR (neat) 3357, 2918, 1602, 1492, 1451, 1084, 1029, 749, 697 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35-7.15 (10H, m), 3.90-3.75 (1H, m), 2.92-2.64 (4H, m), 1.94-1.75 (2H, m), 1.53 (1H, d, *J* = 4.1 Hz, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2 (0), 138.5 (0), 129.6 (2C, 1), 128.8 (2C, 1), 128.63 (2C, 1), 128.57 (2C, 1), 126.7 (1), 126.0 (1), 72.1 (1), 44.3 (2), 38.6 (2), 32.3 (2) ppm; MS (EI+) *m/z* 226 (8, $M^{+\bullet}$), 208 (25), 91 (100). ^1H NMR data were in agreement with those reported previously by Lambert *et al*.[19]

HPLC resolution of *rac*-**20** was achieved with a Daicel Chiralcel® OD-H column, eluting with 5% *i*-PrOH in hexanes at 1.0 mL min^{-1} and monitored by UV at 210 nm, which gave peaks: $t_{ret.}$ (**20**) = 10.9 min, $t_{ret.}$ (*ent*-**20**) = 17.6 min (Figure S5). Assignment of enantiomorphs to the peaks as indicated below was based on the outcome of asymmetric homologation of boronate **14** by carbenoids *ent*-**9** and **26** (Table 1, Entry 7, Figure S15, p. S19 and Table 2, Entry 2, Figure S19, p. S21) and the analogy of these results to those obtained from boronates **16** and **17** for which absolute configuration of product carbinols was established (*vide infra*).

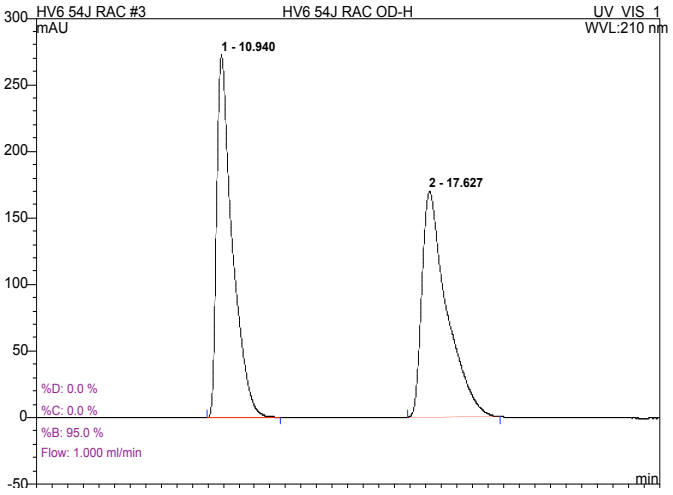
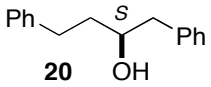
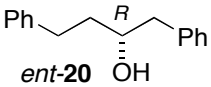


Figure S5. Chromatogram for HPLC resolution of *rac*-**20**.

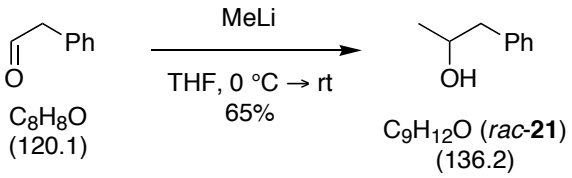
Peak 1 - 10.9 min (50.33%)



Peak 2 - 17.6 min (49.67%)



18. Cornubert, R.; Eggert, H. *Bull. Soc. Chim. Fr.* **1954**, *21*, 522.
19. Lambert, J. B.; Mark, H. W.; Magyar, E. S. *J. Am. Chem. Soc.* **1977**, *99*, 3059.



(±)-1-Phenylpropan-2-ol (*rac*-21): A stirred solution of MeLi (12.5 mL, 1.60 M in Et_2O, 20.0 mmol) in anhydrous THF (16 mL) at 0 °C was treated with phenylacetaldehyde (2.30 mL, d = 1.03, 2.36 g, 19.7 mmol) during 23 min. The resulting mixture was stirred at 0 °C for 30 min and then for a further 3 h at rt. After this time, the mixture was poured into sat. aq. NH_4Cl (50 mL) and the layers separated. The aqueous phase was extracted with Et_2O (3x50 mL) and the combined organic phases were washed successively with H_2O (25 mL) and brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to yield the title carbinol (*rac*-**21**, 1.78 g, 13.1 mmol, 65%) as a pale yellow liquid: bp 71-72 °C (2 mmHg) [lit.[20] bp 65-66 °C (1 mmHg)]; IR (neat) 3358, 2964, 1599, 1451, 1077, 938, 741, 698 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.19 (5H, m), 4.05-3.95 (1H, m), 2.80 (1H, dd, *J* = 13.6, 4.9 Hz), 2.69 (1H, dd, *J* = 13.6, 7.9 Hz), 1.54 (1H, d, *J* = 3.6 Hz, OH), 1.25 (3H, d, *J* = 6.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.7 (0), 129.6 (2C, 1), 128.8 (2C, 1), 126.7 (1), 69.1 (1), 46.0 (2), 23.0 (3) ppm. Spectroscopic data were in agreement with those previously reported by Besse *et al.*[21]

HPLC resolution of *rac*-**21** was achieved with a Daicel Chiralcel® AD column, eluting with 1% *i*-PrOH in hexanes at 0.5 mL min^{-1} and monitored by UV at 210 nm, which gave peaks: $t_{ret.}$ = 33.7 min, $t_{ret.}$ = 36.2 min (Figure S6). Peaks within this chromatogram have not been assigned to particular enantiomorphs because a pure sample of enantioenriched carbinol **21** could not be obtained from asymmetric homologation of **15** by carbenoid **9** (Table 1, Entry 8).

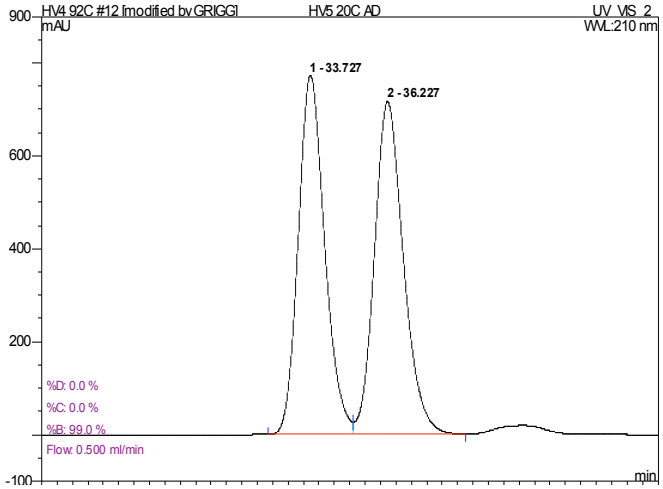
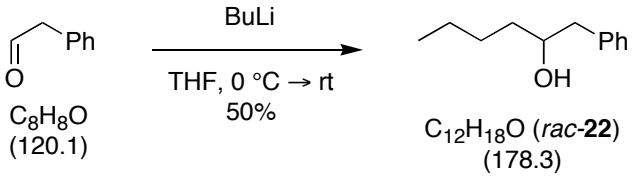


Figure S6. Chromatogram for HPLC resolution of *rac*-**21**.

Peak 1 - 33.7 min (49.57%)

Peak 2 - 36.2 min (50.43%)

20. Snook, M. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1974**, *96*, 860.
21. Besse, P.; Renard, M. F.; Veschambre, H. *Tetrahedron:Asymmetry* **1994**, *5*, 1249.



(±)-1-Phenylhexan-2-ol (*rac*-22): A stirred solution of *n*-BuLi (13.2 mL, 1.51 M in hexanes, 19.9 mmol) in anhydrous THF (15 mL) at 0 °C was treated with phenylacetaldehyde (2.34 mL, d = 1.03, 2.41 g, 20.1 mmol) during 7 min. The resulting mixture was stirred at 0 °C for 1 h and then at rt for 20 h. After this time, the mixture was poured into sat. aq. NH_4Cl (50 mL) and the layers were separated. The aqueous phase was extracted with Et_2O (3x50 mL) and the combined organic phases were washed successively with H_2O (25 mL) and brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to yield the title carbinol (*rac*-**22**, 1.80 g, 10.1 mmol, 51%) as a pale yellow oil: bp 101-102 °C (1.5 mmHg) [lit.[22] bp 100-102 °C (1 mmHg)]; IR (neat) 3373, 2928, 1602, 1454, 1028, 743, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36-7.19 (5H, m), 3.87-3.77 (1H, m), 2.84 (1H, dd, *J* = 13.5, 4.2 Hz), 2.64 (1H, dd, *J* = 13.5, 8.5 Hz), 1.60-1.25 (6H, m), 0.91 (3H, t, *J* = 7.2 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.9 (0), 129.6 (2C, 1), 128.6 (2C, 1), 126.5 (1), 72.8 (1), 44.2 (2), 36.6 (2), 28.1 (2), 22.9 (2), 14.3 (3) ppm. ^1H and ^{13}C NMR spectral data were in agreement with those previously reported by Bonini *et al.*[23]

HPLC resolution of *rac*-**22** was achieved with a Daicel Chiralcel® OD-H column, eluting with 0.5% *i*-PrOH in hexanes at 1.0 mL min^{-1} and monitored by UV at 210 nm, which gave peaks: $t_{ret.}$ (**22**) = 12.3 min, $t_{ret.}$ (*ent*-**22**) = 16.1 min (Figure S7).

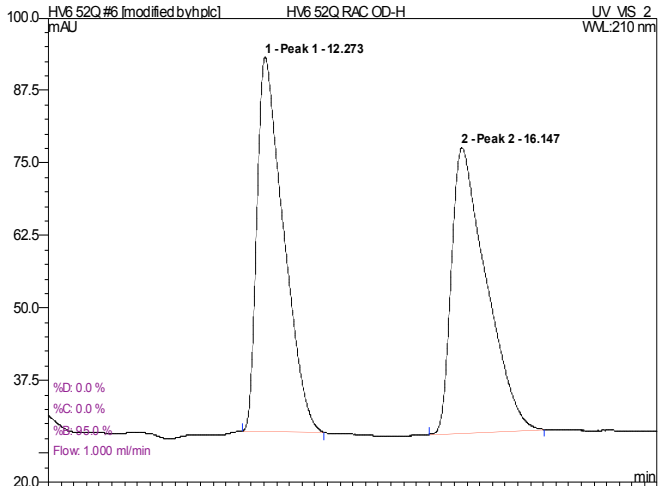
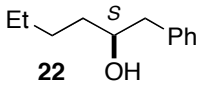
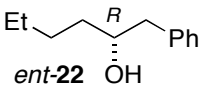


Figure S7. Chromatogram for HPLC resolution of *rac*-**22**.

Peak 1 - 12.3 min (50.02%)



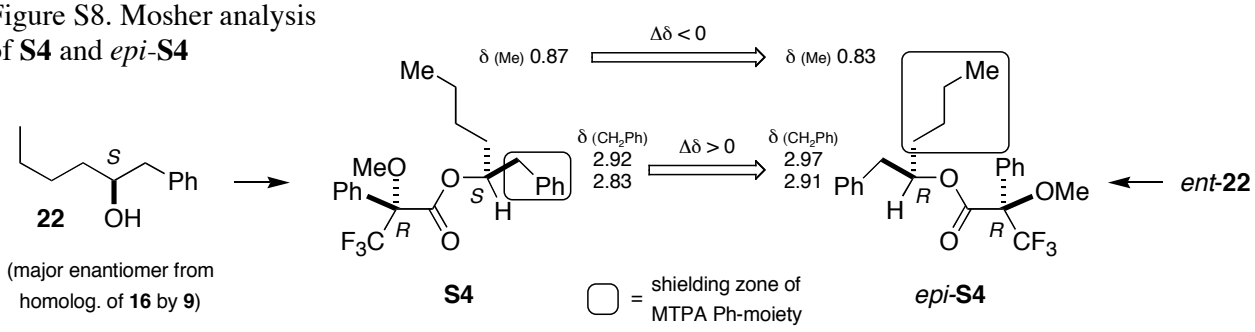
Peak 2 - 16.1 min (49.98%)



To establish absolute configuration for enantiomorphs **22** (*S*) and *ent*-**22** (*R*), diastereomeric mixtures of MTPA-esters (**S4** and *epi*-**S4**) were prepared both from a sample of *rac*-**22** and a sample of enantioenriched **22** (%ee = 70%) obtained from asymmetric homologation of boronate **16** by carbenoid **9** (Table 1, Entry 9). Analysis of ^1H NMR data for the two epimeric components present within the mixtures according to the Mosher configurational correlation model (Figure S8),[24] enabled assignment of (*S*)-configuration to carbinol **22** as illustrated.

22. Uguen, D. *Bull. Soc. Chim. Fr.* **1981**, *2*, 99.
23. Bonini, C.; Federici, C.; Rossi, L.; Righi, G. *J. Org. Chem.* **1995**, *60*, 4803.
24. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

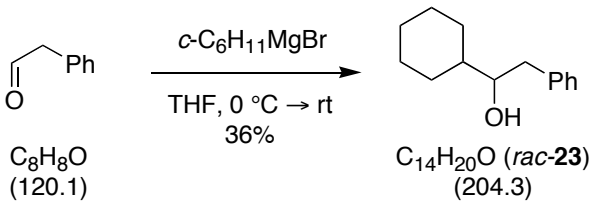
Figure S8. Mosher analysis of **S4** and *epi*-**S4**



Preparation of MTPA ester's S4 and *epi*-S4: Following the method of Li,[25] a mixture of (±)-1-phenylhexan-2-ol (*rac*-**22**, 52 mg, 0.29 mmol), dicyclohexylcarbodiimide (DCC, 171 mg, 0.83 mmol), 4-(dimethylamino)pyridine (DMAP, 5 mg, 0.041 mmol) and (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (96 mg, 0.41 mmol) was reacted in CH_2Cl_2 (3 mL) at rt for 92 h. After this time, the mixture was concentrated *in vacuo* and the residue purified by column chromatography (eluting with 5% Et_2O in hexanes) to afford a 1:1 mixture of **S4** and *epi*-**S4** (82 mg, 0.21 mmol, 71%) as a colorless oil: IR (neat) 2956, 1742, 1454, 1264, 1168, 1023, 993, 696 cm^{-1}; MS (ES+) *m/z* 417 [90, $(M+Na)^+$], 330 (100); HRMS (ES+) *m/z* 417.1651 (calcd. for $C_{22}H_{25}F_3NaO_3$: 417.1653). A diastereomerically enriched sample of **S4**/*epi*-**S4** (dr = 85:15) was similarly prepared from **21** with 70% ee (Table 1, Entry 9). NMR data were unambigously attributed to either **S4** or *epi*-**S4** by comparison of spectra obtained from the isomer mixture with **S4**:*epi*-**S4** = 50:50 to those obtained from the isomer mixture with **S4**:*epi*-**S4** = 85:15.

(*S*)-1-Phenylhex-2-yl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate (**S4**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.16 (8H, m), 7.10 (2H, d, *J* = 6.4 Hz), 5.35 (1H, quintet, *J* = 6.3 Hz), 3.43 (3H, q, $^5J_{HF}$ = 1.0 Hz), 2.92 (1H, dd, *J* = 13.9, 7.5 Hz), 2.83 (1H, dd, *J* = 13.9, 5.8 Hz), 1.70-1.58 (2H, m), 1.41-1.18 (4H, m), 0.87 (3H, t, *J* = 7.1 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4 (0), 137.0 (0), 132.4 (0), 129.6 (1), 129.5 (2C, 1), 128.6 (2C, 1), 128.5 (2C, 1), 127.51 (1), 127.49 (1), 126.7 (1), 123.5 (0, q, $^1J_{C\text{-}F}$ = 287 Hz), 84.7 (0, q, $^2J_{C\text{-}F}$ = 27.4 Hz), 78.1 (1), 55.5 (3, q, $^4J_{C\text{-}F}$ = 1.7 Hz), 40.2 (2), 33.3 (2), 27.6 (2), 22.6 (2), 14.1 (2) ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ –71.88 (3F, s) ppm.

(*R*)-1-Phenylhex-2-yl (*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate (*epi*-**S4**): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42-7.18 (8H, m), 7.12-7.08 (2H, m), 5.37 (1H, quintet, *J* = 6.8 Hz), 3.39 (3H, q, $^5J_{HF}$ = 1.0 Hz), 2.97 (1H, dd, *J* = 13.3, 6.7 Hz), 2.91 (1H, dd, *J* = 13.3, 6.7 Hz), 1.69-1.57 (2H, m), 1.43-1.15 (4H, m), 0.83 (3H, t, *J* = 6.4 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.5 (0), 137.3 (0), 132.5 (0), 129.6 (1), 129.5 (2C, 1), 128.7 (2C, 1), 128.5 (2C, 1), 127.5 (2C, 1), 126.9 (1), 123.5 (0, q, $^1J_{C\text{-}F}$ = 287 Hz), 84.7 (0, q, $^2J_{C\text{-}F}$ = 27.4 Hz), 78.1 (1), 55.5 (3, q, $^4J_{C\text{-}F}$ = 1.7 Hz), 40.3 (2), 33.3 (2), 27.1 (2), 22.6 (2), 14.0 (2) ppm; ^{19}F NMR (470 MHz, $CDCl_3$) δ –71.79 (3F, s) ppm.



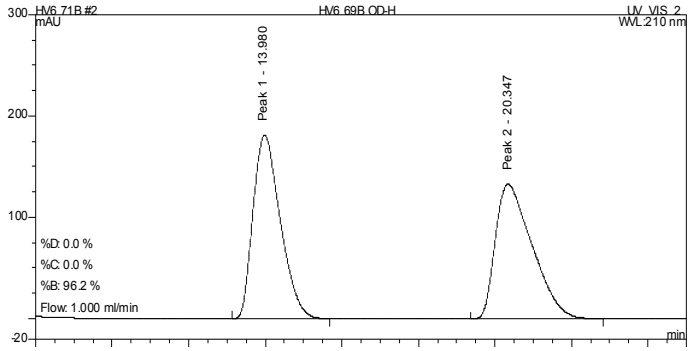
(±)-1-Cyclohexyl-2-phenylethanol (*rac*-23): A vigorously stirred suspension of mechanically activated Mg-turnings (270 mg, 11.1 mmol) in anhydrous THF (14 mL) under N_2 was treated with neat cyclohexyl bromide (1.23 mL, d = 1.32, 1.62 g, 9.93 mmol) at a rate sufficient to first initiate, and then subsequently sustain, a gentle

25. Wei, Z.-L.; Li, Z.-Y.; Lin, G.-Q. *Tetrahedron: Asymmetry* **2001**, *12*, 229.

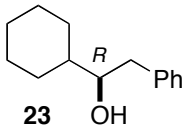
reflux. Shortly after the addition was complete, the exotherm ceased and the reaction mixture returned to rt. The solution of so-formed Grignard reagent was cooled to 0 °C and treated with phenyacetaldehyde (1.17 mL, d = 1.03, 1.21 g, 10.0 mmol) during 2 min. The reaction mixture was stirred at 0 °C for a further 40 min and then at rt for 1 h before pouring into sat. aq. NH_4Cl (50 mL). The layers were separated and the aqueous phase was extracted with Et_2O (3x50 mL). The combined organic phases were then washed successively with H_2O (25 mL) and brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to yield the title carbinol (*rac*-**23**, 731 mg, 3.58 mmol, 36% yield) as colorless solid: mp 55-57 °C (pentane) [lit.[26] mp 57.5 °C (hexanes)]; IR (neat) 3302, 2928, 1602, 1492, 1443, 1034, 749, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35-7.19 (5H, m), 3.58 (1H, ddd, *J* = 9.5, 8.9, 3.6 Hz), 2.89 (1H, dd, *J* = 13.6, 3.3 Hz), 2.60 (1H, dd, *J* = 13.6, 9.5 Hz), 1.97-1.63 (5H, m), 1.50-1.36 (2H, m), 1.35-1.02 (5H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.4 (0), 129.5 (2C, 1), 128.7 (2C, 1), 126.5 (1), 77.0 (1), 43.3 (1), 40.9 (2), 29.5 (2), 28.1 (2), 26.7 (2), 26.5 (2), 26.3 (2) ppm. Data previously reported for carbinol **23** by Ohta *et al* are believed to be in error [mp 173-174 °C (pentane), ^1H NMR spectrum lists 21H with no proton resonating in the 3-5 ppm region].[27]

HPLC resolution of *rac*-**23** was achieved with a Daicel Chiralcel® OD-H column, eluting with 0.38% *i*-PrOH in hexanes at 1.0 mL min^{-1} and monitored by UV at 210 nm, which gave peaks: $t_{ret.}$ (**23**) = 14.0 min, $t_{ret.}$ (*ent*-**23**) = 20.4 min (Figure S9).

Figure S9. Chromatogram for HPLC resolution of *rac*-**23**.

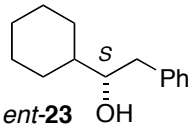


Peak 1 - 14.0 min (50.22%)



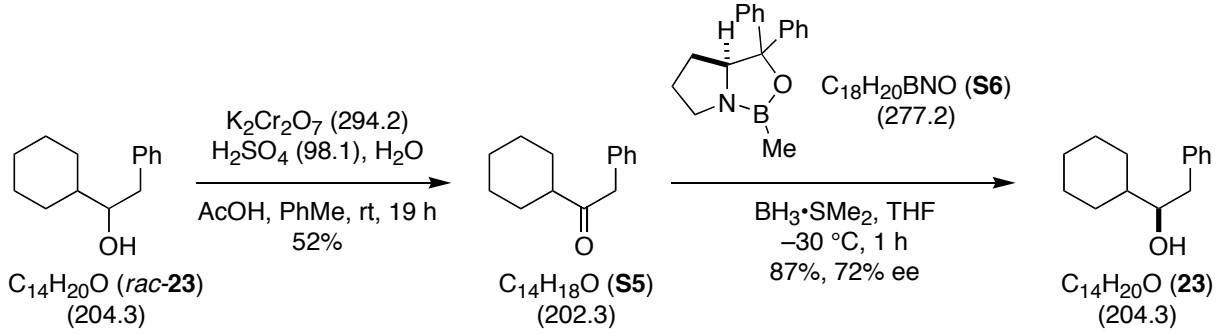
23

Peak 2 - 20.4 min (49.98%)



ent-**23**

To establish absolute configuration for enantiomorphs **23** (*R*) and *ent*-**23** (*S*), an authentic enantioenriched sample of (*R*)-1-cyclohexyl-2-phenylethanol was prepared by reduction of benzyl cyclohexyl ketone (**S5**) with (*S*)-Me-CBS-oxazaborolidine **S6**, as follows:–



26. Perlman, D.; Davidson, D.; Bogert, M. *J. Org. Chem.* **1936**, *1*, 288.
27. Ohta, S.; Yamashita, M.; Arita, K.; Kajiura, T.; Kawasaki, I.; Noda, K.; Izumi, M. *Chem. Pharm. Bull.* **1995**, *43*, 1294.

Benzyl cyclohexyl ketone (S5): Following the method of Jones,[28] a mixture of *rac*-**23** (137 mg, 0.67 mmol), $K_2Cr_2O_7$ (107 mg, 0.36 mmol), H_2SO_4 (110 μL, d = 1.84, 202 mg, 2.06 mmol), H_2O (0.36 mL) and AcOH (35 μL, d = 1.05, 36.7 mg, 0.61 mmol) was stirred vigorously in PhMe (1 mL) at rt for 19 h. After the prescribed work-up, the crude residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to afford the desired ketone (**S5**, 71 mg, 0.35 μmol, 52%) as a pale yellow oil: IR (neat) 2928, 1706, 1495, 1448, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36-7.14 (5H, m), 3.73 (2H, s), 2.46 (1H, tt, *J* = 11.1, 3.3 Hz), 1.88-1.60 (5H, m), 1.43-1.13 (5H, m) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.4 (0), 134.5 (0), 129.6 (2C, 1), 128.7 (2C, 1), 126.9 (1), 50.2 (1), 48.0 (2), 28.6 (2C, 2), 25.9 (2), 25.7 (2C, 2) ppm; MS (ES+) *m/z* 203 [100, $(M+H)^+$]. IR and ^1H NMR data were in agreement with those previously reported by Inaba *et al*.[29]

(*R*)-1-Cyclohexyl-2-phenylethanol (23): Following the method of Corey and co-workers,[30] reduction of ketone **S5** (16 mg, 0.079 mmol) was effected by (*S*)-Me-CBS-oxazaborolidine **S6** (0.17 mL, 1.0 M in PhMe, 0.17 mmol) and borane dimethyl sulfide complex (0.20 mL, 2.0 M in Et_2O, 0.40 mmol) in anhydrous THF (0.4 mL) at –30 °C. Following the prescribed work-up procedure, the residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to yield the title carbinol (**23**, 14 mg, 0.069 mmol, 87% yield) as a colorless solid which gave identical spectral data to those previously obtained for *rac*-**23**.

HPLC analysis of this sample according to the protocol identified for resolution of *rac*-**23** (above) revealed an enantiomeric excess of 72% (Figure S10). Application of the Corey stereocontrol model for reduction of ketone **S5** with catalyst (*S*)-**S6** predicts that the major product from this transformation would be (*R*)-configurated (Figure S11).[30] Peak 1 in the HPLC trace for *rac*-**23** (Figure S9), which corresponds to the major enantiomer (**23**) obtained by asymmetric homologation of boronate **17** by carbenoid **26** (Table 2, Entry 3, Figure S20, p.21), was therefore assigned as being (*R*)-1-cyclohexyl-2-phenylethanol. Peak 2, which was obtained as the major product of asymmetric homologation of boronate **17** by carbenoid *ent*-**9** (Table 1, Entry 10, Figure S17, p. S19), was necessarily therefore assigned as (*S*)-1-cyclohexyl-2-phenylethanol.

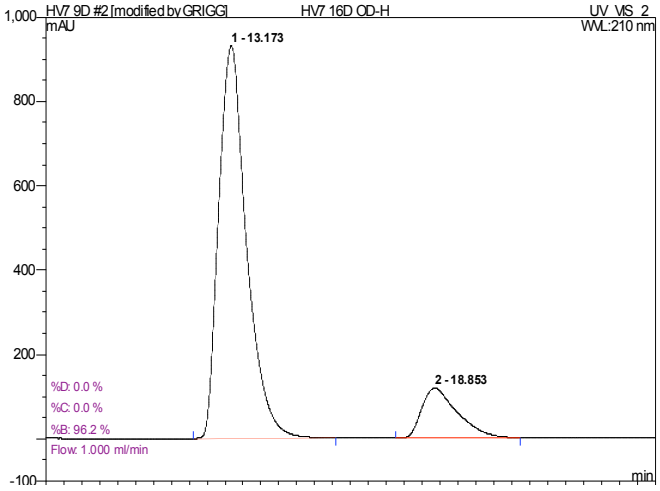


Figure S10. HPLC chromatogram (OD-H) for product of (*S*)-CBS reduction
Peak 1 - 13.2 min (86.04%)
Peak 2 - 18.9 min (13.96%)

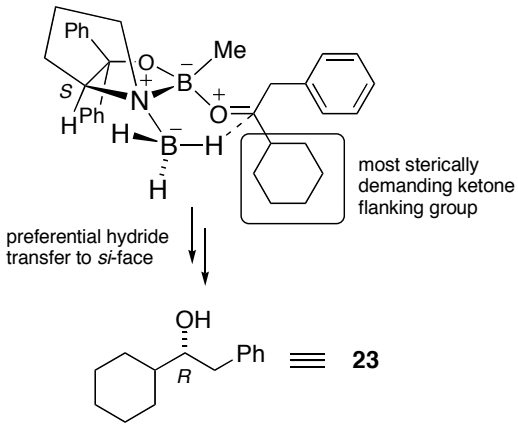
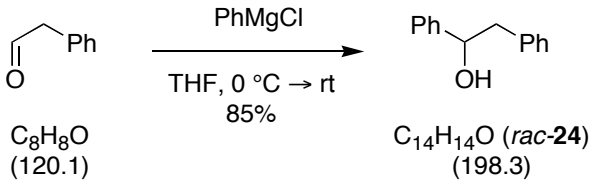


Figure S11. Application of Corey stereocontrol model to ketone **S5** (see ref. 30)

28. Good, R.; Jones, G. *J. Chem. Soc. C* **1970**, 1938.
29. Inaba, S.-I.; Rieke, R. *J. Org. Chem.* **1985**, *50*, 1373.
30. Corey, E.; Helal, C. *Angew. Chem., Int. Ed.* **1998**, *37*, 1986.



(±)-1,2-Diphenylethanol (*rac*-24): A stirred solution of PhMgCl (29.0 mL, 0.70 M in THF, 20.3 mmol) at 0 °C under N_2 was treated with phenylacetaldehyde (2.30 mL, d = 1.03, 2.37 g, 19.7 mmol) during 4 min. The resulting mixture was stirred at 0 °C for a further 30 min and then at rt for 2.5 h before being pouring into sat. aq. NH_4Cl (50 mL). The aqueous phase was extracted with Et_2O (3x50 mL) and the combined organic phases washed successively with H_2O (25 mL) and brine (25 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with 10% EtOAc in hexanes) to yield the title carbinol (*rac*-**24**, 3.32 g, 16.7 mmol, 85%) as a pale yellow liquid that crystallized on standing: mp 64-66 °C (hexanes) [lit.[31] mp 66-67 °C (Skellysolve B)]; IR (neat) 3324, 3027, 2862, 1599, 1451, 1316, 1070, 1039, 776, 696 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38-7.17 (10H, m), 4.90 (1H, ddd, *J* = 8.2, 5.1, 2.6 Hz), 3.05 (1H, dd, *J* = 13.6, 5.1 Hz), 2.98 (1H, dd, *J* = 13.6, 8.2 Hz), 1.96 (1H, br, OH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9 (0), 138.2 (0), 129.7 (2C, 1), 128.7 (2C, 1), 128.6 (2C, 1), 127.8 (1), 126.8 (1), 126.1 (2C, 1), 75.5 (1), 46.3 (2) ppm; MS (ES+) 181 [100, $(M–OH)^+$]. IR, ^1H NMR, and ^{13}C NMR spectral data were in agreement with those previously reported by Knochel and co-workers.[32]

HPLC resolution of *rac*-**24** was achieved with a Daicel Chiralcel® OD-RH column, eluting with 30-45% MeCN in H_2O (over 45 min) at 1.0 mL min^{-1} and monitored by UV at 210 nm, which gave peaks: $t_{ret.}$ (*ent*-**24**) = 24.0 min, $t_{ret.}$ (**24**) = 25.6 min (Figure S12). Assignment of enantiomorphs to the peaks as indicated below was based on the outcome of asymmetric homologation of boronate **18** by carbenoid **9** to yield enantioenriched **24** (Table 1, Entry 11, Figure S18, p. S19) and the analogy of this result to those obtained by asymmetric homologation of boronates **16** and **17** for which absolute configuration of product carbinols was established (*vide supra*).

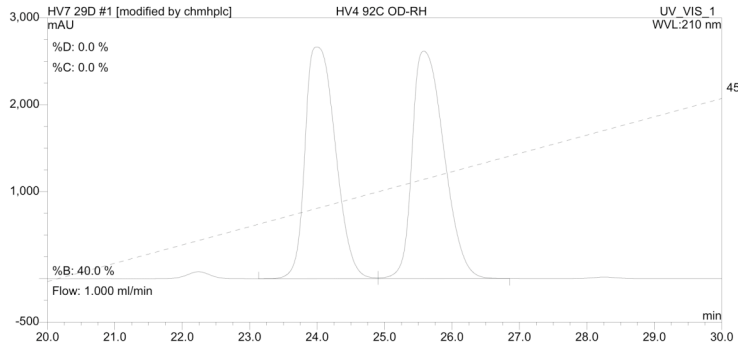
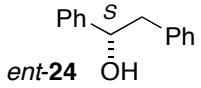
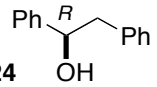


Figure S12. Chromatogram for HPLC resolution of *rac*-**24**.

Peak 1 - 24.0 min (49.18%)



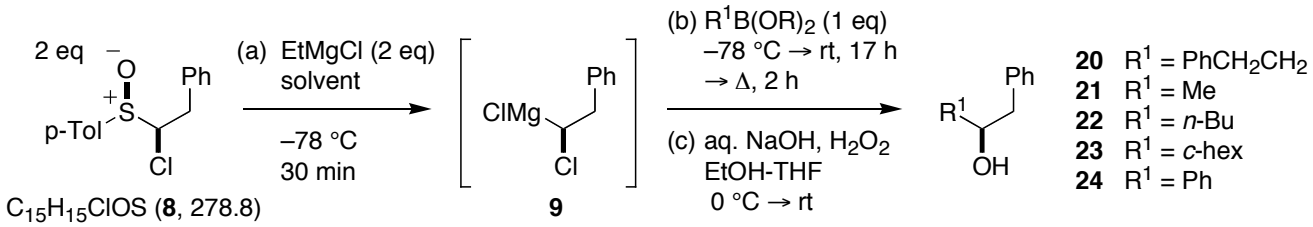
Peak 2 - 25.6 min (50.82%)



31. Meilahn, M. K.; Munk, M. E. *J. Org. Chem.* **1969**, *34*, 1440.
32. Sidduri, A.; Rozema, M. J.; Knochel, P. *J. Org. Chem.* **1993**, *58*, 2694.

– Reagent controlled asymmetric homologation procedures (Tables 1 and 2) –

Asymmetric homologation employing a preformed Mg-carbenoid (Table 1, Entries 2-12):



$C_{15}H_{15}ClOS$ (**8**, 278.8) **9**

The following procedure for homologation of boronate **14** by carbenoid **9** in PhMe solvent to yield enantioenriched carbinol **20** is representative (Table 1, Entry 6, $R^1 = PhCH_2CH_2$).

(*S*)-1,4-Diphenylbutan-2-ol (20): A stirred solution of sulfoxide **8** (291 mg, 1.04 mmol, dr > 99:1, %ee > 98%) in anhydrous PhMe (7 mL) at –78 °C under N_2 was treated carefully with EtMgCl (0.59 mL, 1.76 M in THF, 1.04 mmol) during 18 min. A colorless precipitate was observed to form which hindered stirring. After 30 min, a solution of boronic ester **14** (115 mg, 527 μmol) in PhMe (2 mL) was added during 40 min *via* a syringe pump. The reaction mixture was then allowed to warm slowly to rt over 17 h (*nb*. reaction flask left submerged in cold Dewar bath, but no further dry ice added) and was observed to become homogenous at *ca*. –30 °C. Once at rt, the reaction mixture was heated to a gentle reflux for 2 h and then subsequently cooled to 0 °C. EtOH (1 mL), THF (1 mL), 3.75 M aq. NaOH (0.5 mL, 1.9 mmol) and 30% w/w aq. H_2O_2 (1 mL, 8.8 mmol) were then added successively and the mixture stirred for 3 h before being pouring into sat. aq. NH_4Cl (10 mL). The layers were then separated and the aqueous phase extracted with EtOAc (3x10 mL). The combined organic phases were washed with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with CH_2Cl_2) to afford the desired enantioenriched alcohol (**20**, 57 mg, 252 μmol, 48%) as a colorless oil. Spectral data were identical to those previously obtained for *rac*-**20**.

HPLC analysis using a slightly different chiral stationary phase (Daicel Chiralcel® OD *vs*. OD-H) to that described above for resolution of *rac*-**20** (p. S11), but under otherwise identical conditions, revealed %ee = 82% (Figure S13). For control purposes, resolution of *rac*-**20** on the OD column was demonstrated (Figure S14).

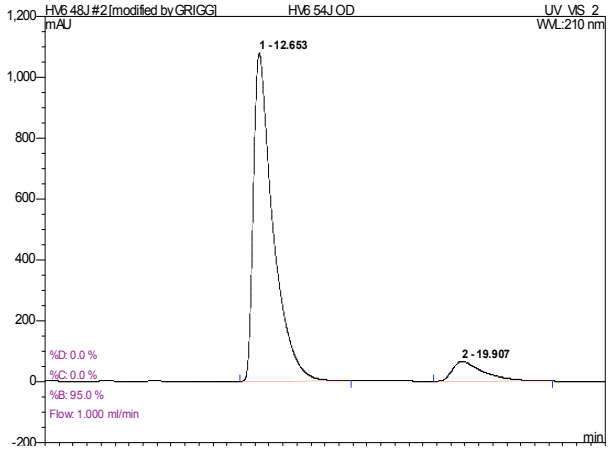


Figure S13. HPLC chromatogram (OD) for enantioenriched **20** (Table 1, Entry 6): **82% ee**
Peak 1 - 12.7 min (91.15%)
Peak 2 - 19.9 min (8.85%)

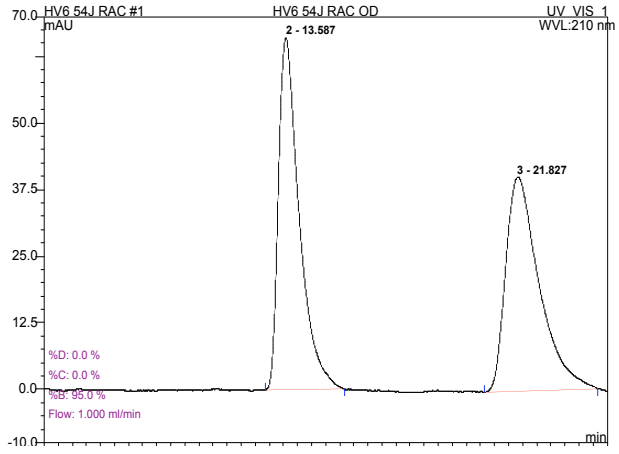


Figure S14. Chromatogram for HPLC resolution of *rac*-**20** on OD column
Peak 1 - 13.6 min (50.62%)
Peak 2 - 21.8 min (49.38%)

Other enantioenriched carbinol products listed in Table 1 were similarly prepared. In each case, spectral data were identical to those obtained from the corresponding racemic sample (pp. S11-S17). HPLC analysis was applied to determine %ee according to the previously established resolution protcols. Selected chromograms (Entries 7, 9-11) are presented below (Figures S15–S18). Carbinol **21** (R^1 = Me, Table 1, Entry 8) was obtained as an inseparable mixture with recovered chlorosulfoxide (**8**) and %ee could not be accurately determined.

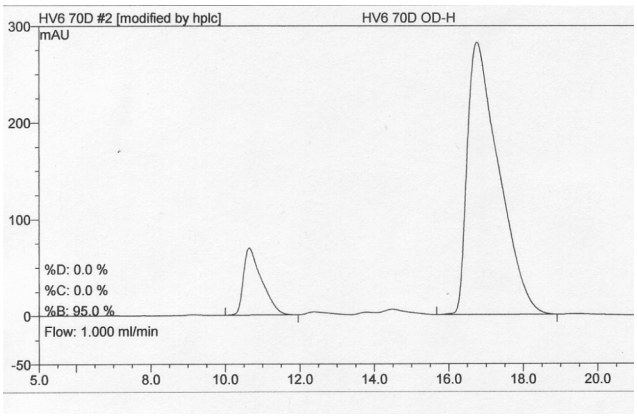


Figure S15. HPLC chromatogram (OD-H) for enantioenriched *ent*-**20** (Table 1, Entry 7): **75% ee**
Peak 1 - 10.6 min (12.51%)
Peak 2 - 16.8 min (87.49%)

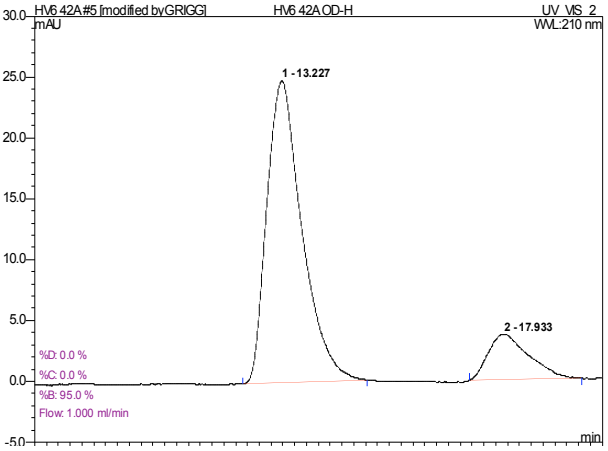


Figure S16. HPLC chromatogram (OD-H) for enantioenriched **22** (Table 1, Entry 9): **70% ee**
Peak 1 - 13.2 min (85.23%)
Peak 2 - 17.9 min (14.77%)

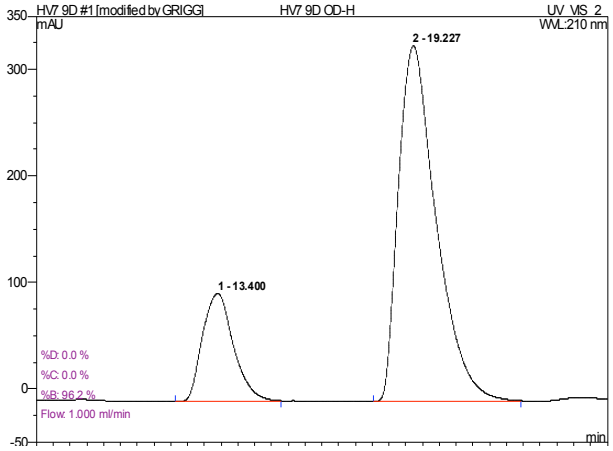


Figure S17. HPLC chromatogram (OD-H) for enantioenriched *ent*-**23** (Table 1, Entry 10): **60% ee**
Peak 1 - 13.4 min (19.89%)
Peak 2 - 19.2 min (80.11%)

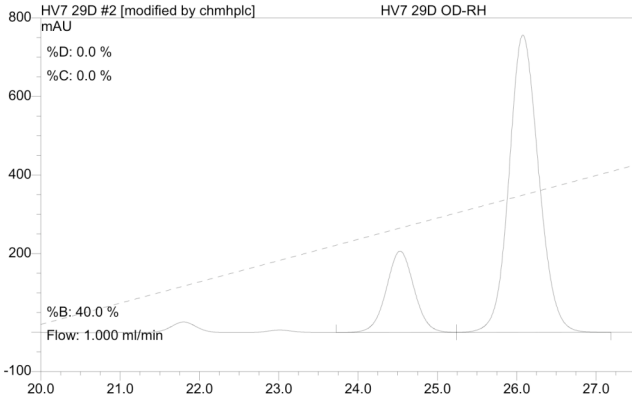
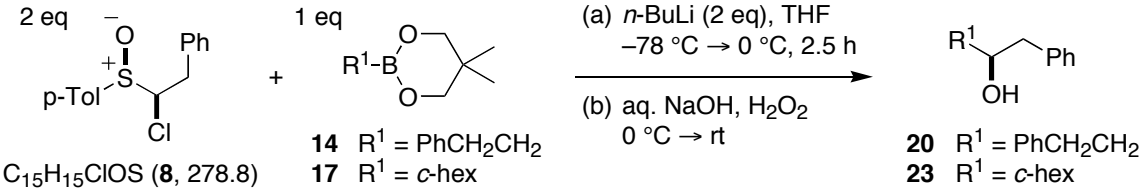


Figure S18. HPLC chromatogram (OD-RH) for enantioenriched **24** (Table 1, Entry 11): **59% ee**
Peak 1 - 24.5 min (20.37%)
Peak 2 - 26.1 min (79.63%)

Asymmetric homologation employing a Li-carbenoid under Barbier conditions (Table 2, Entries 2 and 3):



$C_{15}H_{15}ClOS$ (**8**, 278.8)

14 $R^1 = PhCH_2CH_2$
17 R^1 = *c*-hex

20 $R^1 = PhCH_2CH_2$
23 R^1 = *c*-hex

The following procedure for homologation of boronate **14** by carbenoid **26** to yield enantioenriched carbinol **20** is representative (Table 2, Entry 2, $R^1 = PhCH_2CH_2$).

(*S*)-1,4-Diphenylbutan-2-ol (20): A stirred solution of sulfoxide **8** (136 mg, 488 μmol) and boronic ester **14** (54 mg, 248 μmol) in THF (2 mL) at –78 °C under N_2 was carefully treated with *n*-BuLi (0.32 mL, 1.5 M in hexanes, 480 μmol) (*nb*. *n*-BuLi solution introduced to reaction mixture by running it down the cold flask side-wall during 3 min). The mixture was then allowed to warm to 0 °C with stirring during 2.5 h. After this time, 3.8 M aq. NaOH (0.13 mL, 0.5 mmol) and 8.8 M aq. H_2O_2 (0.20 mL, 1.8 mmol) were added and the resulting biphasic mixture allowed to warm to rt during 2.5 h. The mixture was then poured into 1.5 M aq. HCl (10 mL) and the layers separated. The aqueous phase was extracted with EtOAc (3x10 mL) and the combined organic phases were washed successively with H_2O (10 mL) and brine (10 mL), dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by column chromatography (eluting with CH_2Cl_2) to yield the desired enantio-enriched alcohol (**20**, 39 mg, 173 μmol, 70%) as a colorless oil. Phenethyl chloride (7 mg, 50 μmol, 10%), butyl p-tolyl sulfoxide (51 mg, 260 μmol, 53%), and sulfoxide **8** (32 mg, 115 μmol, 23%, dr (*syn*:*anti*) = 48:52) were also isolated.

Spectral data for **20** were identical to those previously obtained for *rac*-**20** (p. S11). HPLC analysis according to the protocol given above for *rac*-**20**, revealed %ee = 96% (Figure S19, p. S21): $[\alpha]_D^{21} = -5.3$ (c = 0.6, $CHCl_3$).

Phenethyl chloride: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.10 (5H, m), 3.65 (2H, t, *J* = 7.5 Hz), 3.00 (2H, t, *J* = 7.5 Hz) ppm. Data were identical with an authentic sample purchased from a commercial supplier.

Butyl p-tolyl sulfoxide: IR (neat) 2958, 1596, 1492, 1462, 1086, 1037, 812 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (2H, d, *J* = 8.1 Hz), 7.33 (2H, d, *J* = 8.1 Hz), 2.79 (1H, dd, *J* = 6.1, 3.1 Hz), 2.76 (1H, dd, *J* = 6.9, 3.3 Hz), 2.42 (3H, s), 1.79-1.34 (4H, m), 0.92 (3H, t, *J* = 7.3 Hz) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 141.5 (0), 141.0 (0), 130.1 (2C, 1), 124.3 (2C, 1), 57.3 (2), 24.4 (2), 22.1 (2), 21.6 (3), 13.9 (3) ppm; MS (ES+) *m*/*z* 393 [100, $(2M+H)^+$]. Spectroscopic data were in agreement with those reported by Ohta *et al*.[33]

(R_S,*S*)-1-Chloro-2-phenylethyl p-tolyl sulfoxide (*anti*-**8**): IR (neat) 3027, 1596, 1492, 1454, 1146, 1050, 809, 696 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (2H, d, *J* = 8.2 Hz), 7.38-7.22 (7H, m), 4.53 (1H, dd, *J* = 9.7, 2.9 Hz), 3.61 (1H, dd, *J* = 14.3, 2.9 Hz), 3.17 (1H, dd, *J* = 14.3, 9.7 Hz), 2.44 (3H, s) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.1 (0), 137.8 (0), 135.1 (0), 130.01 (2C, 1), 129.97 (2C, 1), 128.8 (2C, 1), 127.6 (1), 126.0 (2C, 1), 77.8 (1), 37.4 (2), 21.7 (3) ppm; MS (ES+) *m*/*z* 279 [100, $(M+H)^+$]. An X-ray crystallographic analysis of *anti*-**8** was reported by Hoffmann and co-workers.[1]

33. Ohta, H.; Okamoto, Y.; Tsuchihashi, G. *Agric. Biol. Chem.* **1985**, *49*, 671.

Enantioenriched carbinol **23** was similarly prepared in 86% yield by asymmetric homologation of boronate **17** by carbenoid **26** (Table 2, Entry 3, R^1 = *c*-hex). HPLC analysis according to the protocol given above for *rac*-**23**, revealed %ee = 87% (Figure S20, p. S21): $[\alpha]_D^{21}$ = +7.0 (c = 1.2, $CHCl_3$).

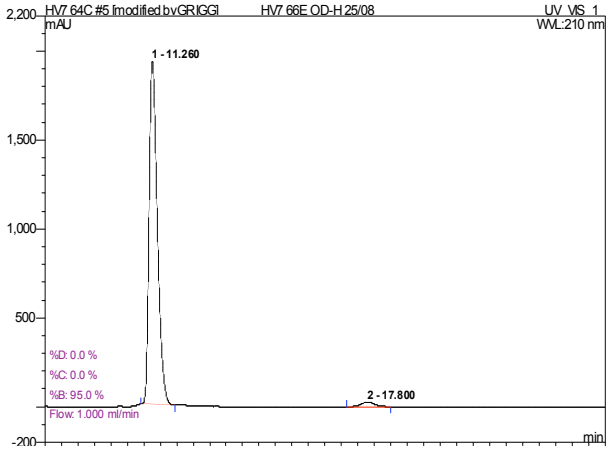


Figure S19. HPLC chromatogram (OD-H) for enantioenriched **20** (Table 2, Entry 2): **96% ee**
Peak 1 - 11.3 min (97.96%)
Peak 2 - 17.8 min (2.04%)

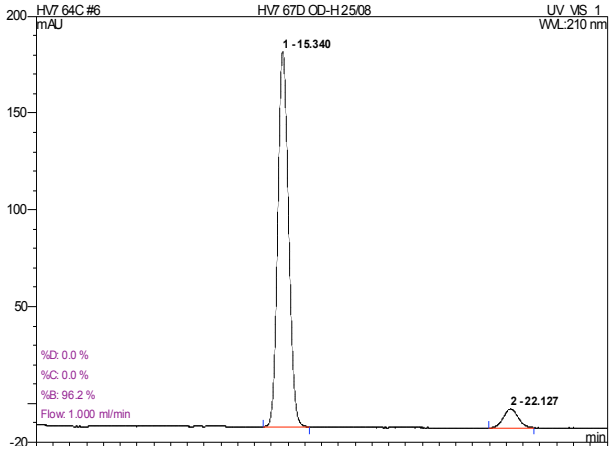


Figure S20. HPLC chromatogram (OD-H) for enantioenriched **23** (Table 2, Entry 3): **87% ee**
Peak 1 - 15.3 min (93.49%)
Peak 2 - 22.1 min (6.51%)