Lithiated Carbamates: Chiral Carbenoids for Iterative Homologation of Boranes and Boronic Esters

Jake L. Stymiest, Guillaume Dutheuil, Adeem Mahmood, Varinder K. Aggarwal*

School of Chemistry, University of Bristol, Cantock’s Close, Bristol BS8 1TS (UK)

v.aggarwal@bristol.ac.uk

Table of Contents

1) General Information S2

2) Experimental Procedures & Data S3

3) Chiral HPLC/GC Traces 3 (a-d, f-j) S20

4) ¹H NMR for Mosher Ester of 3e S29

5) Chiral HPLC data for Amines 5-7 S31

6) ¹H NMR & Chiral HPLC for Et₂BPh Experiment to give 3a & 3d S34

7) ¹H NMR of β-CH₃ Doublet in 9 (ent-9) & 10 (ent-10) S37

8) Chiral HPLC Data for Compounds 8 (ent-8) [after oxidation to 3a (ent-3a)] & 9 (ent-9) & 10 (ent-10) S39

9) References S43
1. General Information

All air and water sensitive reactions were carried out in oven dried glassware under a nitrogen atmosphere. Solvents were dried by standard methods.\textsuperscript{1} NMR spectra were recorded on JEOL 270 MHz or JEOL 400 MHz spectrometers using tetramethylsilane as the internal standard (0.00 ppm). CDCl\textsubscript{3} was used as an internal standard for \textsuperscript{13}C NMR spectra (77.0 ppm). CI mass spectra were obtained using a VG Platform mass spectrometer. All IR data was obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Analytical TLC was done on aluminium backed plates (1.5 x 5 cm) pre-coated (0.25 mm) with silica gel (Merck, Silica Gel 60 F\textsubscript{254}). Compounds were visualized by exposure to UV light or by dipping the plates in solutions of 0.3% ninhydrin /97% EtOH /3% AcOH (w/v/v) or 5% (NH\textsubscript{4})\textsubscript{2}Mo\textsubscript{7}O\textsubscript{24} • 4 H\textsubscript{2}O in 95% EtOH (w/v) followed by heating. Flash chromatography was done on silica gel (Merck Kieselgel 60). Melting points were determined with a Kofler hot stage apparatus and were not corrected. Optical rotations were obtained on a Perkin-Elmer 241MC polarimeter. Chiral HPLC separations were done on Agilent 1100 series normal or reversed phase high performance liquid chromatography units using HP Chemstation for LC or LC/MS. Daicel Chiralcel OJ or OD columns (0.46x 25 cm) were used for normal phase separations whereas a ChromTech Chiral-AGP (\alpha-Acid-Glycoprotein) column (4.0 x 25mm) was used for reversed phase separations when required. When analysis on HPLC was not possible separations were carried out using chiral GC on an Agilent Technologies 6890N Network GC system equipped with Chiral GC Top Enhanced software and a Supelco Alpha DEX\textsuperscript{TM} 120 fused silica capillary column (30m x 0.25mm x 0.25\textmu m).

Triethylborane, trichloroborane and phenylboronic acid, purchased from the Aldrich Chemical Company and ethyl boronic acid from Lancaster were used without further purification. \textit{sBuLi} was purchased as a 1.3 M solution in cyclohexane from either Fluka or Acros Chemical Companies. \textit{N,N,N,N-Tetramethylethylenediamine} (TMEDA) was purchased from Aldrich and distilled over CaH\textsubscript{2} prior to use. \textit{(-)-Sparteine} was purchased from Alpha Aesar and distilled under reduced pressure over CaH\textsubscript{2} prior to use. Phenyl pinacol boronic ester was synthesized according to literature procedures.\textsuperscript{2} The
boranes, "Hexyl-B-9BBN\textsuperscript{3} and Ph-B-9BBN,\textsuperscript{4} were also synthesized according to literature procedures.

**Experimental Procedures and Data**

**Preparation of Boranes and Boronic Esters**

\[
\text{B(OH)}_2 \xrightarrow{\text{pinacol, MgSO}_4, \text{Et}_2\text{O}} \text{B-O} \]

**9-Isopropyl-9-bora-bicyclo[3.3.1]nonane (Pr-B-9BBN).** A 100 mL Schlenk flask was charged MeO-B-9BBN (1 M in hexane, 20.0 mL, 20.0 mmol). The solvent was removed under reduced pressure using Schlenk technique. The resulting oil was dissolved in dry Et\textsubscript{2}O (30 mL) and cooled to –78 °C. To this solution was added iso-propyl magnesium chloride (2 M solution in THF, 10.0 mL, 20.0 mmol) dropwise over 40 min. After addition, the cooling bath was removed and the reaction was warmed to rt and stirred for an additional 1h. The volatiles were removed under reduced pressure (inert atmosphere) and the white residue was extracted with hexane (2× 50 mL) using Schlenk technique. The combined organic extractions were concentrated in vacuo (inert atmosphere) to yield the product (2.99g, 93%) as a colourless oil which was used without further purification.

\begin{align*}
1^H \text{NMR (300 MHz, CDCl}_3) \delta 1.10 (d, J = 5.7 \text{ Hz, 6H }), 1.15-1.23 (m, 2H), 1.48 (hept, J = 5.7 \text{ Hz, 1H}), 1.62-1.89 (m, 12H); \quad 13^C \text{NMR (75 MHz, CDCl}_3) \delta 33.3, 31.6, 23.3, 19.2, 16.4; \quad 11^B \text{NMR (96 MHz, CDCl}_3) \delta 84.0.
\end{align*}

**Ethyl Pinacol Boronic Ester [Et-B-(pinacol)].** The same procedure that was used for the synthesis of Ph-B-(pinacol) was used.\textsuperscript{2} A mixture of boronic acid (1.48 g, 20.0 mmol), anhydrous pinacol (2.38 g, 20.0 mmol) and MgSO\textsubscript{4} (2.43 g, 20.0 mmol) in Et\textsubscript{2}O (25 mL) was stirred at rt for 20h. The reaction mixture was filtered and the filtrate gently
concentrated *in vacuo* (≥ 20 mmHg) at rt. This afforded the product as a colourless oil (3.00 g, 96%). $^1$H NMR (CDCl$_3$, 270 MHz) δ 1.92 (s, 12H), 0.88 (t, $J = 7.0$ Hz, 3H), 0.68 (q, $J = 7.0$ Hz, 2H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) δ 82.6, 24.6, 7.4, 3.8 (br); $^{11}$B NMR (CDCl$_3$, 96 MHz) δ 32.0.

**Preparation of Carbamates 1 (a-e).**

![Diagram of 2a]

*N,N*-Diisopropyl-carbamic acid 3-phenyl-propyl ester (2a). This was the general procedure used to synthesize carbamates (2a, b', c-e) from the respective alcohols. To a solution of *N,N*-diisopropylcarbamoyl chloride (9.49 g, 58.0 mmol) and NEt$_3$ (8.15 mL, 58.0 mmol) in CH$_2$Cl$_2$ (100 mL) was added 3-phenyl-propan-1-ol (7.70 mL, 57.0 mmol). This mixture was then heated to reflux and stirred for 24h. The reaction was cooled to rt and H$_2$O (100 mL) was added. The aqueous layer was extracted with CH$_2$Cl$_2$ (3 x 75 mL) and the combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo* to give the crude product as an orange oil. The crude oil was purified by flash chromatography (10% EtOAc/Petrol) to yield 2a as a colourless oil (13.19 g, 88%). All spectral data were in accordance with literature values.$^5$ $^1$H NMR (CDCl$_3$, 270 MHz), δ 7.15-7.30 (m, 5H), 4.11 (t, $J = 6.5$ Hz, 2H), 3.90 (br. m, 2H), 2.71 (t, $J = 7.5$ Hz, 2H), 1.98 (m, 2H), 1.21 (d, $J = 6.9$ Hz, 12H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) δ 155.9, 141.6, 128.5, 128.4, 126.0, 64.1, 45.7 (br), 32.7, 31.0, 21.1 (br).

![Diagram of 2b']

*N,N*-Diisopropyl-carbamic acid pent-4-enyl ester (2b'). (88%) From condensation of 4-penten-1-ol and *N,N*-diisopropylcarbamoyl chloride (SiO$_2$, 10% EtOAc/Petrol) yielded
the product as a colourless oil. IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$ 3078, 2970, 2934, 1687; $^1$H NMR (CDCl$_3$, 270 MHz) $\delta$ 5.75 (ddt, $J = 16.9$, 10.2, 6.6 Hz, 1H), 4.97 (dd, $J = 16.9$, 1.5 Hz, 1H), 4.91 (dd, $J = 10.2$, 1.5 Hz, 1H), 4.02 (t, $J = 6.5$ Hz, 2H), 3.92 (br. m, 2H), 2.09 (m, 2H), 1.70 (m, 2H), 1.33 (d, $J = 6.9$ Hz, 12H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) $\delta$ 155.8, 137.8, 115.1, 64.0, 46.0 (br), 30.4, 28.4, 21.0 (br); HRMS(ESI) calcd. for C$_{12}$H$_{23}$NO$_2$Na (M+Na) 236.1621. Found 236.1611.

$N,N$-Diisopropyl-carbamic acid 5-methyl-hex-4-enyl ester (2b). To a solution of Grubbs 2$^{\text{nd}}$ Generation catalyst (1 mol%, 98 mg, 0.12 mmol) in CH$_2$Cl$_2$ (2 mL) was added simultaneously carbamate 2b' (2.45 g, 11.5 mmol) and 2-methyl-2-butene (25 mL). After stirring at rt for 12h, DMSO$^6$ (0.45 mL, 5.75 mmol) was added and the reaction was stirred for an additional 12h at rt. The mixture was then concentrated in vacuo and the residue was subjected to flash chromatography (SiO$_2$, 5% EtOAc/hexane) to afford 2b as a pale yellow oil (2.30 g, 83%). IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$ 2968, 2932, 1689; $^1$H NMR (CDCl$_3$, 270 MHz) $\delta$ 5.07 (t, $J = 7.0$ Hz, 1H), 4.02 (t, $J = 6.6$ Hz, 2H), 3.85 (br. m, 2H), 2.02 (m, 2H), 1.63 (s, 3H), 1.62 (m, 2H), 1.54 (s, 3H), 1.15 (d, $J = 6.9$ Hz, 12H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) $\delta$ 155.9, 132.2, 123.6, 64.3, 44.5 (br), 29.3, 25.7, 24.7, 21.0 (br), 17.6; HRMS(ESI) calcd. for C$_{14}$H$_{27}$NO$_2$Na (M+Na) 264.1934. Found 264.1925.

5-(tert-Butyl-dimethyl-silanyloxy)-3,3-dimethyl-pentan-1-ol (2c'). To a suspension of NaH (1.68 g, 42.0 mmol) in THF (40 mL) at 0 °C was added 3,3-dimethyl-pent-1,5-diol$^7$ (5.02 g, 38 mmol) in THF (15 mL) dropwise. This mixture was then stirred for 1h at 0 °C and TBDMS-Cl (5.80 g, 38 mmol) was added. This mixture was warmed to rt and stirred for 16h. The reaction was carefully quenched with H$_2$O and the organic layer was diluted with Et$_2$O (100 mL). The layers were separated and the organic layer was washed with
NaHCO₃ (sat.), dried (MgSO₄) and concentrated in vacuo to give crude 2c'. The product was purified by flash chromatography (SiO₂, 100% hexane to 20% EtOAc/hexane) to yield 2c' (7.03 g, 75%). All spectral data corresponded to literature values.¹ H NMR (CDCl₃, 270 MHz) δ 3.66 (t, J = 6.9 Hz, 4H), 1.54 (t, J = 6.9 Hz, 2H), 1.50 (m, 4H), 0.90 (s, 6H), 0.85 (s, 9H), 0.03 (s, 6H); ¹³C NMR (CDCl₃, 67.5 MHz) δ 60.3, 59.6, 44.4, 43.9, 31.6, 28.1, 26.0, 18.4, -5.3.

**N,N-Diisopropyl-carbamic acid 5-(tert-butyl-dimethyl-silanyloxy)-3,3-dimethyl-pentyl ester (2c).** (81%) From condensation of alcohol 2c’ and N,N-diisopropyl carbamoyl chloride gave 2c as a colourless oil (SiO₂, 20% EtOAc/Petrol). This compound is known in the literature but no data is given.⁹ IR νₘₐₓ (neat) / cm⁻¹ 2958, 2930, 2858, 1693; ¹H NMR (CDCl₃, 270 MHz) δ 4.06 (m, 2H), 3.83 (br. m, 2H), 3.62 (t, J = 7.2 Hz, 2H), 1.55 (m, 2H), 1.44 (t, J = 7.2 Hz, 2H), 1.13 (d, J = 6.8 Hz, 12H), 0.88 (s, 6H), 0.81 (s, 9H), -0.02 (s, 6H); ¹³C NMR (CDCl₃, 67.5 MHz) δ 155.7, 61.9, 59.9, 45.7 (br), 44.5, 40.8, 31.6, 27.7, 26.0, 21.0 (br), 18.2, -5.3; HRMS(ESI) calcd. for C₂₀H₄₃NO₃SiNa (M+Na) 396.2904. Found 396.2902.

**N,N-Diisopropyl-carbamic acid isobutyl ester (2d).** (72%) From condensation of isobutyl alcohol and N,N-diisopropylcarbamoyl chloride gave 2d as a colourless oil (SiO₂, 10% EtOAc/Petrol). IR νₘₐₓ (neat) / cm⁻¹ 2966, 2936, 2875, 1688; ¹H NMR (CDCl₃, 270 MHz) δ 3.90 (br. m, 2H), 3.80 (d, J = 6.3 Hz, 2H), 1.90 (m, 1H), 1.50 (d, J = 6.9 Hz, 12H), 0.89 (d, J = 6.6 Hz, 6H); ¹³C NMR (CDCl₃, 67.5 MHz) δ 156.0, 71.0, 45.7 (br), 44.5, 40.8, 31.6, 27.7, 26.0, 21.0 (br), 19.4; HRMS(ESI) calcd. for C₁₁H₂₃NO₂Na (M+Na) 224.1621. Found 224.1611.
**N,N-Diisopropyl-carbamic acid ethyl ester (2e).** (92%) From condensation of ethanol and N,N-diisopropylcarbamoyl chloride gave 2e as a colourless oil (SiO₂, 2% Et₂O/Petrol). IR ν<sub>max</sub> (neat) / cm<sup>-1</sup> 2970, 2935, 1687, 1434, 1308, 1289, 1063; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 270 MHz) δ 4.08 (q, <i>J</i> = 7.2 Hz, 2H), 3.85 (br. m, 2H), 1.23 (t, <i>J</i> = 7.2 Hz, 3H), 1.15 (d, <i>J</i> = 6.7 Hz, 12H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 67.5 MHz) δ 155.6, 60.1, 45.4 (br), 20.8 (br), 14.4; HRMS(ESI) calcd. for C<sub>9</sub>H<sub>19</sub>NO<sub>2</sub>Na (M+Na) 196.1308. Found 196.1299.

**Preparation of Chiral Alcohols from Carbamates 2 (a-e).**

**Representative Procedure for Asymmetric Lithiation/Borylation of Carbamates with Trialkylboranes (including R<sup>2</sup>-B-9BBN, R<sup>2</sup> = iPr or nHex)**

(S)-1-Phenylpentan-3-ol (3a). To a solution of 2a (270 mg, 1.0 mmol) and (-)-sparteine (304 mg, 1.3 mmol) in dry Et₂O (5 mL) at –78 °C was added sBuLi (1.3 M in cyclohexane, 1.0 mL, 1.3 mmol) dropwise. This mixture was then stirred at –78 °C for 5h. A solution of BEt₃ (1 M in Et₂O, 1.3 mL, 1.3 mmol) was added dropwise. The reaction was stirred for a further 40 min at –78 °C and then warmed to rt. The reaction mixture was then cooled to 0 °C and a solution of NaOH (2 M)/H₂O₂ (30%) (2:1 v/v, 4.0 mL) was added dropwise. This mixture was stirred for 1h at rt and quenched with 2 M NaOH (10 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic layers were dried (MgSO₄) and concentrated in
The crude product was purified by flash chromatography (SiO$_2$, 10% EtOAc/Petrol) to yield the product as a white solid (149 mg, 91%). All analytical and spectral data corresponded to that reported in the literature.$^{10}$ Mp 34-36 °C (Lit. 36-38 °C)$^{10a}$; $^1$H NMR (CDCl$_3$, 270 MHz) δ 7.15-7.33 (m, 5H), 3.56 (tt, $J = 7.6, 4.7$ Hz, 1H), 2.81 (ddd, $J = 13.8, 9.6, 6.0$ Hz, 1H), 2.67 (ddd, $J = 13.8, 9.6, 6.8$ Hz, 1H), 1.78 (m, 2H), 1.50 (m, 3H), 0.93 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) 142.3, 128.5, 128.4, 125.9, 72.7, 38.7, 32.2, 30.4, 10.0; $[\alpha]^{22}_D = +25.0$ (c 0.95, CH$_2$Cl$_2$) (e.r. = 98:2), [Lit.$^{10a}$] $[\alpha]^{21}_D = +23.8$ (c 3.01, CHCl$_3$)]. $t_{R} = 9.66$ min (R-minor), 14.81 min (S-major), Daicel Chiracel-OD column, 5% iPrOH in hexane 1 mL/min. [Lit. $t_{R} = 11.4$ min (R-minor), 16.7 min (S-major) Chiracel-OD column, 5% iPrOH in hexane 1 mL/min].$^{11}$ The racemic material (rac-3a) was prepared as above substituting N,N,N,N-tetramethylethlenediamine (TMEDA) for (-)-sparteine. The racemic syntheses for all alcohols and amines were completed in this manner.

(S)-1-Phenyl-nonan-3-ol (3b). (90%) (SiO$_2$, 10% EtOAc/Petrol) all spectral data matched that for the racemate as reported in the literature.$^{12}$ $^1$H NMR (CDCl$_3$, 270 MHz) δ 7.14-7.32 (m, 5H), 3.55-3.65 (m, 1H), 2.57-2.79 (m, 2H), 1.58-1.80 (m, 2H), 1.56 (br. s, 1H), 1.18-1.50 (m, 10H), 0.88 (t, $J = 6.6$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) δ 142.3, 128.6, 128.3, 125.9, 71.5, 39.2, 37.7, 32.2, 31.9, 29.5, 25.7, 22.7, 14.2; $[\alpha]^{21}_D = +4.2$ (c 1.9, MeOH) (e.r. = 97.5:2.5). $t_{R} = 8.9$ min (R-minor), 13.5 min (S-major) Daicel Chiracel-OD column 5% iPrOH in hexane 1 mL/min.

(R)-4-Methyl-1-phenyl-pentan-3-ol (3c). (81%) SiO$_2$ (10% EtOAc/Petrol) all spectral data reported corresponded literature values.$^{13}$ $^1$H NMR (CDCl$_3$, 270 MHz) δ 7.16-7.32
(m, 5H), 3.40 (m, 1H), 2.80 (ddd, J = 13.9, 9.8, 6.4 Hz, 1H), 2.60 (ddd, J = 13.9, 9.8, 6.4 Hz, 1H), 1.65-1.85 (m, 3H), 1.41 (br. s, 1H), 0.92 (d, J = 8.0 Hz, 6H); 13C NMR (CDCl3, 100 MHz) δ 142.3, 128.4, 128.3, 125.7, 75.5, 36.0, 33.7, 32.4, 18.7, 17.1; [α]21D = +35.5 (c 0.9, MeOH) (e.r. = 98:2). [Lit.13 [α]21D + 36.0 (c 3.10, EtOH) for 97:3 e.r.].

(S)-7-Methyl-6-octen-3-ol (3e). (90%) SiO2 (10% EtOAc/Petrol) all spectral data reported matched that for the racemate of 3e.14 1H NMR (CDCl3, 270 MHz) δ 5.10 (t, J = 7.2 Hz, 1H), 3.49 (tt, J = 7.4, 4.8 Hz, 1H), 2.05 (m, 2H), 1.67 (m, 1H), 1.65 (s, 3H), 1.58 (s, 3H), 1.42 (m, 3H), 1.25 (m, 1H), 0.90 (t, J = 7.4 Hz, 3H); 13C NMR (CDCl3, 67.5 MHz) δ 132.1, 124.3, 123.4, 73.2, 36.9, 30.3, 25.8, 24.5, 17.7, 10.0; [α]21D = +4.7 (c 0.8, MeOH) (e.r. = 97:3). Preparation of the (+)-MTPA esters of rac-3e and (S)-3e by the standard method15 and analysis by 1H NMR (CDCl3, 400 MHz) indicated an e.r. of 97:3 based on integration of C-1 triplets (vide infra).

(S)-7-(tert-Butyl-dimethyl-silyloxy)-5,5-dimethyl-heptan-3-ol (3g). (67%) (SiO2, 10% EtOAc/Petrol): IR νmax (neat) / cm⁻¹ 3332, 2957, 1464, 1254; 1H NMR (CDCl3, 270 MHz) δ 3.64-3.68 (m, 3H), 1.82 (ddd, J = 14.6, 7.8, 6.4 Hz, 1H), 1.52 (dd, J = 14.6, 8.8, 1H), 1.19-1.42 (m, 5H), 0.93 (s, 3H), 0.90 (s, 3H), 0.88 (m, 12H), 0.01 (s, 6H); 13C NMR (CDCl3, 67.5 MHz) δ 70.2, 60.6, 48.3, 43.3, 32.5, 32.2, 28.9, 26.0, 18.4, 10.0, -5.3; HRMS(ESI) calcd. for C15H34O2SiNa 297.2214. Found 297.2220; [α]22D = +16.0 (c 2.25, CH2Cl2) (e.r. = 95:5); Chiral GC on Supelco Alpha DEX™ 120 fused silica capillary
Representative Procedure for Asymmetric Lithiation/Borylation of Carbamates with Ph-B-9BBN.

(R)-1,3-Diphenylpropanol (3d). To a solution of 2a (270 mg, 1.0 mmol) and (-)-sparteine (304 mg, 1.3 mmol) in dry Et<sub>2</sub>O (5 mL) at –78 °C was added sBuLi (1.3 M in cyclohexane, 1.0 mL, 1.3 mmol) dropwise. This mixture was stirred at –78 °C for 5h and a solution of Ph-B-9BBN (1 M in Et<sub>2</sub>O, 1.3 mL, 1.3 mmol) was added dropwise. The reaction was stirred for 35 min at –78 °C and a solution of MgBr<sub>2</sub> (239 mg, 1.3 mmol) in Et<sub>2</sub>O (5 mL) was added. This mixture was stirred for 20 min at –78 °C and then warmed to rt. The reaction mixture was then cooled to 0 °C and a solution of NaOH (2 M)/H<sub>2</sub>O<sub>2</sub> (30%) (2:1 v/v, 4.0 mL) was added dropwise. This mixture was stirred for 2h at rt and quenched with 2 M NaOH (10 mL). The layers were separated and the aqueous layer was extracted with Et<sub>2</sub>O (3 x 15 mL). The combined organic layers were dried (MgSO<sub>4</sub>) and concentrated in vacuo. The crude product was purified by flash chromatography (SiO<sub>2</sub>, 10% EtOAc/Petrol) to yield the product as a white solid (199 mg, 94%). All spectral data matched those reported in literature. Mp 45-47 °C (Lit. 48-49 °C). ¹H NMR (CDCl<sub>3</sub>, 270 MHz) δ 7.05-7.39 (m, 10H), 4.61 (apparent t, J = 8.0 Hz, 1H), 2.64 (m, 2H), 2.06 (m, 2H), 1.83 (br. s, 1H); ¹³C NMR (CDCl<sub>3</sub>, 67.5 MHz) 144.7, 141.9, 128.6, 128.5, 128.4, 127.7, 126.0, 125.9, 76.7, 40.6, 32.2; [α]<sup>21</sup>D = + 16.0 (c 0.70, CH<sub>2</sub>Cl<sub>2</sub>) (e.r. = 97:3), [Lit [α]<sup>22</sup>D = + 16.7 (c 0.70, CH<sub>2</sub>Cl<sub>2</sub>)]. t<sub>R</sub> = 20.2 min (S-minor), 24.2 min (R-major) Daicel Chiracel-OD column, 5% iPrOH in hexane 1 mL/min. [Lit. t<sub>R</sub> = 38.2 min (R-minor), 43.5 min (S-major) Chiracel-OD column, (1:19) iPrOH/hexane 1 mL/min].
(R)-5-Methyl-1-Phenyl-4-hexen-1-ol (3f). (65%) (SiO₂, 10% EtOAc/Petrol) all spectral data reported matched that of literature.¹⁷ ¹H NMR (CDCl₃, 270 MHz) δ 7.20-7.42 (m, 5H), 5.13 (dd, J = 8.4, 5.5 Hz, 1H), 4.65 (dd, J = 7.5, 5.7 Hz, 1H), 2.39 (m, 1H), 2.06 (m, 2H), 1.78 (m, 2H), 1.69 (s, 3H), 1.57 (s, 3H); ¹³C NMR (CDCl₃, 67.5 MHz) δ 144.9, 132.3, 128.5, 127.5, 126.0, 123.9, 74.3, 39.1, 25.8, 24.6, 17.8; [α]²²D = + 10.0 (c 4.40, CH₂Cl₂) (e.r. = 95:5). [Lit.¹⁸ [α]²¹D = + 13.4 (c 1.24, CHCl₃)]. tᵣ = 14.4 min (R-minor), 16.7 min (S-minor) Daicel Chiralcel-OD column, 5% iPrOH in hexane 1 mL/min.

5-(tert-Butyl-dimethyl-silanyloxy)-3,3-dimethyl-1-phenyl-pentan-1-ol (3h). (65%) (SiO₂, 10% EtOAc/Petrol). IR νmax (neat) / cm⁻¹ 3432, 2954, 2928, 2857, 1254; ¹H NMR (CDCl₃, 270 MHz) δ 7.19-7.35 (m, 5H), 4.83 (ddd, J = 9.6, 4.0, 2.5 Hz, 1H), 3.78 (m, 2H), 3.60 (d, J = 4.0 Hz, 1H), 2.03 (ddd, J = 14.6, 8.8, 6.0 Hz, 1H), 1.94 (dd, J = 14.6, 9.6 Hz, 1H), 1.52 (ddd, J = 14.6, 2.5 Hz, 1H), 1.42 (dt, J = 14.6, 4.9 Hz, 1H), 1.08 (s, 3H), 1.00 (s, 3H), 0.93 (s, 9H), 0.11 (s, 6H); ¹³C NMR (CDCl₃, 67.5 MHz) 147.3, 128.4, 126.9, 125.6, 76.6, 60.8, 51.4, 43.1, 32.6, 29.2, 28.8, 26.1, 18.5, -5.2; HRMS(ESI) calcd. for C₁₉H₃₄O₂SiNa (M+Na) 345.2220. Found 345.2215; [α]²¹D = + 21.0 (c 6.90, CH₂Cl₂) (e.r. = 97:3); tᵣ = 9.9 min (S-minor), 14.0 min (R-major) Daicel Chiralcel-OD column, 1% iPrOH in hexane 1 mL/min.

(R)-2-Methyl-1-phenyl-propan-1-ol (3i). (70%) SiO₂ (10% EtOAc/Petrol) all spectral data reported matched that of literature.¹⁹ ¹H NMR (CDCl₃, 270 MHz) δ 7.21-7.38 (m,
5H), 4.26 (dd, J = 6.9, 3.2 Hz, 1H), 2.02 (m, 1H), 1.80 (d, 3.2 Hz, 1H), 0.98 (d, J = 6.9 Hz, 3H), 0.78 (d, J = 6.9 Hz, 3H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) δ 143.7, 128.2, 127.4, 126.7, 80.1, 35.4, 19.1, 18.3; [α]$^{23}$D = + 46.0 (c 3.90, Et$_2$O) (e.r. = 98:2) [Lit.$^{19b}$ [α]$^{21}$D = + 52.1 (c 1.06, Et$_2$O) for 95:5 e.r.]; $t_R = 13.6$ min (S-minor), 14.7 min (R-major) Daicel Chiracel-OD column, 5% iPrOH in hexane 1 mL/min.

**Representative Procedure for Asymmetric Lithiation/Borylation of Carbamates with Boronic Esters.**

![Chemical Structure](image)

(S)-1-Phenylpentan-3-ol (3a). To a solution of 2a (270 mg, 1.0 mmol) and (-)-sparteine (304 mg, 1.3 mmol) in dry Et$_2$O (5 mL) at −78 °C was added $s$BuLi (1.3 M in cyclohexane, 1.0 mL, 1.3 mmol) dropwise. This mixture was stirred at −78 °C for 5h. A solution of Et-B-(pinacol) (1 M in Et$_2$O, 1.3 mL, 1.3 mmol) was added dropwise and the reaction was stirred for a further 35 min at −78 °C. A solution of MgBr$_2$ (239 mg, 1.3 mmol) in Et$_2$O (5 mL) was added and this mixture was stirred at −78 °C for 20 min, warmed to rt and then heated to reflux and stirred for ≥12h. The reaction mixture was then cooled to 0 °C and a solution of NaOH (2 M)/H$_2$O$_2$ (30%) (2:1 v/v, 4.0 mL) was added dropwise. This mixture was stirred for 1h at rt and quenched with 2 M NaOH (10 mL). The layers were separated and the aqueous layer was extracted with Et$_2$O (3 x 15 mL). The combined organic layers were dried (MgSO$_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography (SiO$_2$, 10% EtOAc/Petrol) to yield the product as a white solid (148 mg, 90%). All spectral data matched that of the above synthesis with BEt$_3$. Compounds *ent-3a, 3e, 3f, 3h-3j* were all synthesized using the above method from reaction of respective lithiated carbamates with Et-B-(pinacol) or Ph-B-(pinacol). All spectral data matched that of the above compounds synthesized from reaction of representative lithiated carbamates with Et$_3$B or Ph-B-9BBN boranes (*vide supra*).
(R)-1-Phenyl-ethanol (3j). (70%) SiO\textsubscript{2} (10\% EtOAc/Petrol) all spectral data reported matched that of the commercially available enantiomer ent-3j.\textsuperscript{20} \textsuperscript{1}H NMR (CDCl\textsubscript{3}, 270 MHz) δ 7.23-7.29 (m, 5H), 4.88 (q, J = 6.5 Hz, 1H), 1.97 (br. s, 1H), 1.49 (d, J = 6.5 Hz, 3H); \textsuperscript{13}C NMR (CDCl\textsubscript{3}, 67.5 MHz) δ 146.0, 128.5, 127.4, 125.6, 70.3, 25.3; \([\alpha]\)\textsuperscript{23}_D = + 40.0 (c 2.30, MeOH) (e.r. = 97:3). [For (S) enantiomer Lit. \([\alpha]\)\textsuperscript{21}_D = - 45.0 (c 5.00, MeOH)].\textsuperscript{20} \textit{t}_R = 15.0 min (R-major), 19.7 min (S-minor), Daicel Chiracel-OD column, 2.5\% \textit{iPrOH} in hexane 1 mL/min. This was confirmed under the same conditions using ent-3j.\textsuperscript{20} 

Representative example for synthesis of amines from boronic esters.

(S)-Benzyl-(1-ethyl-3-phenyl-propyl)-amine (5).\textsuperscript{21} To a solution of carbamate 2a (270 mg, 1.0 mmol) and (-)-sparteine (0.31 mL, 1.3 mmol) in dry Et\textsubscript{2}O (5 mL) at \(-78 \degree\)C was added sBuLi (1.3 M in cyclohexane, 1.0 mL, 1.3 mmol) dropwise. This mixture was stirred at \(-78 \degree\)C for 5h. A solution of Et\textit{B}-(pinacol) (1 M in Et\textsubscript{2}O, 1.3 mL, 1.3 mmol) was then slowly added and the mixture was stirred at \(-78 \degree\)C for 30 min. A solution of MgBr\textsubscript{2} (239 mg, 1.3 mmol) in Et\textsubscript{2}O (5 mL) was added and the reaction was stirred for an additional 20 min at \(-78 \degree\)C. The reaction was then warmed to rt, heated to reflux and stirred for \(\geq 12\)h. The reaction mixture was cooled to rt and H\textsubscript{2}O (15 mL) was added. The layers were separated and the aqueous layer was extracted with Et\textsubscript{2}O (10 x 2 mL). The combined organic extracts were dried (MgSO\textsubscript{4}) and gently concentrated \textit{in vacuo} to yield the crude boronic ester 8. Crude 8 was dissolved in dry CH\textsubscript{2}Cl\textsubscript{2} (3 mL) and cooled to 0 \degree\)C. A solution of BCl\textsubscript{3} (1 M in CH\textsubscript{2}Cl\textsubscript{2}, 5.0 mL, 5.0 mmol) was then added dropwise. Upon completion, the reaction was warmed to rt and stirred for 4h. The solution was then
concentrated *in vacuo* (inert atmosphere) to complete dryness. The residue was redissolved in CH$_2$Cl$_2$ (6 mL) and cooled to 0 °C. Neat benzyl azide (0.34 mL, 3.0 mmol) was then slowly added. This mixture was allowed to reach rt slowly (o/n) and then quenched with 2 M NaOH. The organic layer was separated and the aqueous layer was extracted further with CH$_2$Cl$_2$ (3 x 15 mL). The combined organic extracts were dried (MgSO$_4$) and concentrated *in vacuo* to afford the crude product 5. The crude compound was purified by flash chromatography (SiO$_2$, 10% to 20% EtOAc/Petrol) to yield 5 as a pale yellow oil (190 mg, 63%). IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$ 3290, 3062, 3027, 1634; $^1$H NMR (CDCl$_3$, 270 MHz) $\delta$ 7.13-7.36 (m, 10H), 3.79 (d, $J = 12.7$ Hz, 1H), 3.74 (d, $J = 12.7$ Hz, 1H), 2.67 (apparent dd, $J = 9.3$, 6.9 Hz, 2H), 2.57 (apparent pent, $J = 6.0$ Hz, 1H), 1.75 (dddd, $J = 16.1$, 9.3, 6.9, 6.0 Hz, 2H), 1.65 (br. s, 1H), 1.52 (apparent qd, $J = 7.4$, 6.0 Hz, 2H), 0.92 (t, $J = 7.4$ Hz, 3H); $^{13}$C NMR (CDCl$_3$, 67.5 MHz) $\delta$ 142.8, 141.0, 128.5, 128.4, 128.3, 126.9, 125.8, 57.7, 51.1, 34.5, 32.1, 26.3, 9.9; HRMS(ESI) calcd. for C$_{18}$H$_{24}$N (M+1) 254.1903. Found 254.1897; $[\alpha]_{D}^{21}$ = -7.5 (c 1.60, MeOH) (for e.r = 96:2)

**Preparation of Acetamide 5' from amine 5.**

![Acetamide 5'](image)

*(S)-N-(1-Ethyl-3-phenyl-propyl)-acetamide (5').* To a solution of amine 5 (50 mg, 0.2 mmol) in EtOH (2 mL) was added 10% Pd/C (5 mg). This mixture was stirred under an H$_2$ atmosphere for 18h. The reaction was then filtered and concentrated to yield the deprotected amine (33 mg, 0.2 mmol) in quantitative yield. The crude amine (33 mg, 0.2 mmol) was dissolved in pyridine (1.5 mL) and Ac$_2$O (20 $\mu$L, 0.4 mmol) was added. This mixture was stirred at rt for 12h and HCl (1 M, 10 mL) was added. The aqueous layer was extracted with EtOAc (3 x 10 mL) and the combined organic extracts were dried (MgSO$_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography (SiO$_2$, 20% to 50% EtOAc/Petrol) to yield acetamide 5' (32 mg, 94%) for analysis by chiral HPLC. IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$ 3278, 3085, 3027, 2964, 2931; $^1$H NMR (CDCl$_3$, 270 MHz) $\delta$ 7.16-7.32 (m, 5H), 5.23 (br. d, $J = 8.8$ Hz, 1H), 3.93
(apparent d pent., \( J = 8.8, 5.1 \) Hz, 1H), 2.65 (apparent t, \( J = 7.8 \) Hz, 2H), 1.95 (s, 3H), 1.75-1.94 (m, 1H), 1.48-1.70 (m, 2H), 1.32-1.45 (m, 1H), 0.89 (t, \( J = 7.8 \) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 67.5 MHz) \( \delta \) 169.8, 142.0, 128.5, 128.4, 125.9, 50.7, 36.6, 32.5, 28.1, 23.6, 10.2; HRMS(ESI) calcd. for C\(_{13}\)H\(_{19}\)NONa (M+Na) 228.1359. Found 228.1351; \([\alpha]^{22}_D = -28.0 \) (c 0.70, CH\(_2\)Cl\(_2\)) (e.r. = 98:2) \( t_R = 8.5 \) min (R-minor), 12.6 min (S-major), Daicel Chiracel-OJ column, 10% iPrOH in hexane 1 mL/min.

(R)-Benzyl-(1,3-diphenyl-propyl)-amine (6). (67%) Pale yellow oil using same procedure as for 5 with substitution of Et-B-pinacol with Ph-B-pinacol. IR \( \nu_{\text{max}} \) (neat) / cm\(^{-1}\) 3250, 3083, 3060, 3025, 2920, 1452; \(^1\)H NMR (CDCl\(_3\), 270 MHz) \( \delta \) 7.09-7.55 (m, 15H), 3.66 (apparent t, \( J = 5.8 \) Hz, 1H), 3.65 (d, \( J = 13.1 \) Hz, 1H), 3.55 (d, \( J = 13.1 \) Hz, 1H), 2.58 (m, 2H), 2.05 (m, 2H), 1.71 (br. s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 67.5 MHz) \( \delta \) 144.1, 142.2, 140.8, 128.5, 128.4, 128.3, 127.8, 127.2, 125.9, 62.2, 51.6, 39.9, 32.7; HRMS(ESI) calcd. for C\(_{22}\)H\(_{24}\)N (M+1) 302.1896. Found 302.1903; \([\alpha]^{22}_D = +23.4 \) (c 2.40, CHCl\(_3\)) (e.r. = 98:2) \( t_R = 13.2 \) min (S-minor), 16.4 min (R-major) Chromtech Chiral-AGP column, 1.5% iPrOH in 10 mM NaOAc buffer (pH 4.5), 0.9 mL/min.

(R)-Benzyl-(2-methyl-1-phenyl-propyl)-amine (7). (50%) Pale yellow oil using the same procedure as for 5 starting from 2d with substitution of Et-B-pinacol with Ph-B-pinacol. IR \( \nu_{\text{max}} \) (neat) / cm\(^{-1}\) 3270, 3062, 3027, 2959, 1453; \(^1\)H NMR (CDCl\(_3\), 270 MHz) \( \delta \) 7.19-7.39 (m, 10H), 3.65 (d, \( J = 13.3 \) Hz, 1H), 3.47 (d, \( J = 13.3 \) Hz, 1H), 3.35 (d, \( J = 7.0 \) Hz, 1H), 1.88 (apparent d sept, \( J = 7.0, 6.8 \) Hz, 1H), 1.71 (br. s, 1H), 0.97 (d, \( J = 6.8 \) Hz, 3H), 0.75 (d, \( J = 6.8 \) Hz, 3H); \(^{13}\)C NMR (CDCl\(_3\), 67.5 MHz) \( \delta \) 143.0, 141.1, 128.4,
128.2, 128.1, 126.5, 68.8, 51.8, 34.6, 19.8, 19.6; HRMS(ESI) calcd. for C$_{17}$H$_{22}$N (M+1) 240.1738. Found 240.1746; $[\alpha]^{22}_D = +63.1$ (c 1.40, CHCl$_3$) (e.r. = 97:3) t$_R = 2.9$ min (S-minor), 3.5 min (R-major) Chromtech Chiral-AGP column, 2% iPrOH in 10 mM NaOAc buffer (pH 4.5), 0.9 mL/min.

**Iterative Homologation of Boronic Esters**

(S)-3-(1-Phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8). To a solution of 2a (2.24 g, 8.5 mmol) and (-)-sparteine (1.99 g, 8.5 mmol) in dry Et$_2$O (40 mL) at –78 °C under Argon was added sBuLi (1.3 M in cyclohexane, 6.50 mL, 8.5 mmol) dropwise. This mixture was then stirred at –78 °C for 5h. A solution of Et-B-(pinacol) (0.78 g, 5.0 mmol) in Et$_2$O (10 mL) was added dropwise. The reaction was stirred for a further 30 min at –78 °C before a solution of MgBr$_2$ [freshly made from stirring Mg turnings (0.31 g, 12.8 mmol) and 1,2-dibromoethane (1.60 g, 8.5 mmol) in Et$_2$O (17 mL) at rt for 4h] was added. The reaction was stirred for a further 30 min at –78 °C, warmed to rt, heated to reflux and then stirred for $\geq$ 12h. The reaction mixture was then cooled to rt and quenched with water (40 mL). The layers were separated and the aqueous layer was extracted with Et$_2$O (3 x 40 mL). The combined organic layers were dried (MgSO$_4$) and concentrated in vacuo. The crude product was purified by flash chromatography (SiO$_2$, 1% Et$_2$O/Petrol) to yield 8 as a pale yellow oil (1.06 g, 78%). IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$: 3027, 2977, 2929, 2860, 1610; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 7.16-7.30 (m, 5H), 2.59-2.65 (m, 2H), 1.78-1.86 (m, 1H), 1.67-1.76 (m, 1H), 1.48-1.59 (m, 2H), 1.28 (s, 12H), 0.97-1.04 (m, 1H), 0.93 (t, $J = 8.1$ Hz, 3H); $^{11}$C NMR (CDCl$_3$, 100 MHz) 143.0, 128.3, 128.1, 125.5, 82.8, 35.6, 33.2, 24.8, 24.1, 13.6; $^{11}$B NMR (CDCl$_3$, 96 MHz) $\delta$ 33.6; MS (EI) 274 (M$^+$), 146 (M$^+$-HB(pin)), 91 (Ph-CH$_2$); HRMS(Cl$^+$) calcd. for C$_{17}$H$_{28}$BO$_2$ 275.2182. Found 275.2174; $[\alpha]^{22}_D = +8.3$ (c 2.16, CHCl$_3$) (e.r. = 98:2).
(R)-3-(1-Phenylpentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (ent-8). The (R) enantiomer, ent-8 was synthesized as above on a 3.0 mmol scale using O’Brien’s (+)-sparteine surrogate, (+)-11 (0.87 g, 4.5 mmol), in place of (-)-sparteine, to yield ent-8 as a colourless oil (0.61 g, 75%). \([\alpha]^{23}_D = -8.2\left(c\ 2.56,\ CHCl_3\right)\) (e.r. = 97:3).

5-Phenyl-3-(S)-ethylpentan-2-(R)-ol (9). To a solution of 2e (0.43 g, 2.5 mmol) and (-)-sparteine (0.59 g, 2.5 mmol) in dry Et₂O (13 mL) at −78 °C under Argon was added sBuLi (1.3 M in cyclohexane, 1.9 mL, 2.5 mmol) dropwise. This mixture was stirred at −78 °C for 5h. A solution of boronic ester 8 (0.27 g, 1.0 mmol) in Et₂O (2.0 mL) was added dropwise. The reaction was stirred for a further 30 min at −78 °C before a solution of MgBr₂ [freshly made from stirring Mg turnings (91 mg, 3.75 mmol) and 1,2-dibromoethane (470 mg, 2.5 mmol) in Et₂O (5.0 mL) at rt for 4h] was added. The reaction mixture was stirred for a further 30 min at −78 °C, warmed to rt, then heated to reflux and stirred for ≥ 12h. The reaction was cooled to 0 °C and a solution of NaOH (2 M)/H₂O₂ (30%) (2:1 v/v, 6.0 mL) was added dropwise. This mixture was stirred for 30 min at 0 °C and then diluted with water (10 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 15 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo. The crude product was purified by flash chromatography (SiO₂, 20% Et₂O/Petrol) to yield an inseparable mixture of the expected alcohol 9 and the first homologated product 3a (from oxidation of unreacted starting boronic ester 8) as a colourless oil [181 mg, 9/3a = 85:15 mol%, \(0.82\ mmol\ 9\ (82\%),\ 0.14\ mmol\ 3a\ (14\%)\)]. IR \(\nu_\text{max}\) (neat) / cm⁻¹: 3362, 3027, 2963, 1604; \(^1\)H NMR (CDCl₃, 400 MHz) major only: 7.16-7.30 (m, 5H), 3.78-3.84 (m, 1H), 2.62 (ddd, \(J = 13.6, 10.4, 5.7\ Hz, 1H\)), 2.51 (ddd, \(J = 13.6, 10.4, 5.7\ Hz, 1H\)).
= 13.6, 10.4, 6.2 Hz, 1H), 1.55-1.66 (m, 1H), 1.49-1.53 (m, 1H), 1.41-1.47 (m, 1H), 1.22-
1.33 (m, 2H), 1.18 (d, J = 6.4 Hz, 3H), 0.87 (t, J = 7.3 Hz, 3H); ^13^C NMR (CDCl$_3$, 100
MHz) 143.0, 128.6, 128.5, 125.8, 69.4, 46.2, 33.9, 31.2, 22.3, 20.3, 11.8; MS (EI) 192
(M$^+$), 174 (M$^+$-H$_2$O), 145, 104, 91 (Ph-CH$_2^+$), 77 (Ph$^+$), 51; HRMS(EI$^+$) calcd. for
C$_{12}$H$_{18}$O 192.1514. Found 192.1512; [\(\alpha\)]$_{22}^D$ = + 1.9 (c 1.05, MeOH) (e.r. > 98:2,^26 d.r. =
96:4^27).

5-Phenyl-3-(R)-ethylpentan-2-(S)-ol (ent-9). Isomer ent-9 was synthesized under the
same conditions as 9 from 0.44 mmol of first homologated boronic ester ent-8, using
O’Brien’s (+)-sparteine surrogate (+)-11, in place of (-)-sparteine, to yield an inseparable
mixture of alcohol ent-9 and alcohol ent-3a (from oxidation of unreacted starting boronic
ester ent-8) as a colourless oil [68 mg, ent-9/ent-3a = 74:26 mol%,^25 0.27 mmol ent-9
(63%), 0.09 mmol ent-3a (21%)]. [\(\alpha\)]$_{24}^D$ = − 4.4 (c 1.35, MeOH) (e.r. > 98:2,^25 d.r. =
90:10^27).

5-Phenyl-3-(S)-ethylpentan-2-(S)-ol (10). Isomer 10 was synthesized using the same
procedure as above for 9 from 0.64 mmol of boronic ester 8, using O’Brien’s (+)-
sparteine surrogate (+)-11 in place of (-)-sparteine to yield an inseparable mixture of
alcohol 10 and alcohol 3a (from oxidation of unreacted starting boronic ester 8) as a
colourless oil [87 mg, 10/3a = 86:14 mol%,^25 0.40 mmol 10 (63%), 0.06 mmol 3a
(10%)]. IR $\nu_{\text{max}}$ (neat) / cm$^{-1}$ 3354, 3027, 2963, 1604; $^1$H NMR (CDCl$_3$, 400 MHz) major
only $\delta$ 7.16-7.30 (m, 5H), 3.86-3.92 (m, 1H), 2.59-2.69 (m, 2H), 1.73-1.82 (m, 1H), 1.51-
1.59 (m, 1H), 1.43-1.51 (m, 2H), 1.33-1.39 (m, 1H), 1.18 (d, J = 6.4 Hz, 3H), 0.93 (t, J =
7.3 Hz, 3H); $^{13}$C NMR (CDCl$_3$, 100 MHz) 142.8, 128.4, 128.3, 125.7, 69.1, 46.0, 33.8, 31.0, 22.1, 19.7, 11.6; HRMS(ESI) calcd. for C$_{12}$H$_{18}$O 192.1514. Found 192.1517; $[\alpha]^{22}_D = +1.7$ (c 1.77, MeOH) (e.r. > 98:2, $^{25}$ d.r. = 94:6).$^{27}$

5-Phenyl-3-($R$)-ethylpentan-2-($R$)-ol (ent-10). Isomer ent-10 was synthesized in the same manner as 10 from 0.45 mmol of first homologated boronic ester ent-8 to yield an inseparable mixture of alcohol ent-10 and alcohol ent-3a (from oxidation of unreacted starting boronic ester ent-8) as a colourless oil [67 mg, ent-10/ent-3a = 80:20 mol%, $^{25}$ 0.29 mmol ent-10 (64%), 0.07 mmol ent-3a, (16%)]. $[\alpha]^{24}_D = -1.6$ (c 0.64, MeOH) (e.r. > 98:2, $^{25}$ d.r. = 94:6).$^{27}$
Chiral Data for Alcohols 3 (a-d, f-j).

*rac*-3a Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (210 nm).

![Graph for rac-3a](image)

3a Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 98:2).

![Graph for 3a](image)

*ent*-3a Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).

![Graph for ent-3a](image)
**rac-3b** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min ($\lambda = 210$ nm).

3b Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).
**rac-3c** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (210 nm).

![Graph of rac-3c](image)

**3c** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 98:2).

![Graph of 3c](image)
**rac-3d** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (λ = 254 nm).

![Graph 1](image1)

**3d** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).

![Graph 2](image2)
**rac-3f** Daicel OD-Chiracel column, 2.5:97.5 iPrOH/Hexane, 1 mL/min, (210 nm).

![Graph 1](image1)

**3f** Daicel OD-Chiracel column, 2.5:97.5 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).

![Graph 2](image2)
**rac-3g** Chiral GC Supelco Alpha-Dex™ column 80 °C for 100 min then 10 °C/min up to 180 °C hold for 5.0 min.

**3g** Chiral GC Supelco Alpha-Dex™ column 80 °C for 100 min then 10 °C/min up to 180 °C hold for 5.0 min (e.r. = 95:5).
**rac-3h** Daicel OD-Chiracel column, 1:99 iPrOH/Hexane, 1 mL/min (λ = 210 nm).

![Graph of rac-3h](image)

**3h** Daicel OD-Chiracel column, 1:99 iPrOH/Hexane, 1 mL/min (e.r. = 98:2).

![Graph of 3h](image)
**rac-3i** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (210 nm).

![Graph 1](image1)

**rac-3i** Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 98:2).

![Graph 2](image2)
**rac-3j** Daicel OD-Chiracel column, 2.5:97.5 iPrOH/Hexane, 1 mL/min (210 nm).

![Chromatogram of rac-3j](image)

**3j** Daicel OD-Chiracel column, 2.5:97.5 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).

![Chromatogram of 3j](image)
$^1$H NMR spectra for Mosher esters of (±)-3e and 3e (CDCl$_3$, 400 MHz) $\gamma$ CH$_3$ triplets.

Mosher ester of (±)-3e
Mosher ester of 3e
Chiral HPLC Data for Amines 5 (as Acetamide), 6 & 7.

*N*-Acetamide 5’ [From (±)-5] Daicel Chiracel-OJ column, 10:90 *i*PrOH/Hexane, 1 mL/min (250 nm).

*N*-Acetamide 5’ [from 5] Daicel Chiracel-OJ column, 10:90 *i*PrOH/Hexane, 1 mL/min (e.r. = 98:6) (250 nm).
(±)-6 Chromtech Chiral-AGP column, 1.5:98.5 iPrOH /10 mM NaOAc buffer (pH 4.5), 0.9 mL/min (220 nm).

6 Chromtech Chiral-AGP column, 1.5:98.5 iPrOH /10 mM NaOAc buffer (pH 4.5), 0.9 mL/min (e.r. = 98:2).
(±)-7 Chromtech Chiral-AGP column, 2:98 iPrOH/10 mM NaOAc buffer (pH 4.5), 0.9 mL/min (220 nm).

7 Chromtech Chiral-AGP column, 2:98 iPrOH/10 mM NaOAc buffer (pH 4.5), 0.9 mL/min (e.r. = 97:3).
Chiral HPLC and $^1$H NMR (CDCl$_3$, 400 MHz) of mixture of 3a and 3d (see below): Daicel OD-Chiracel column, 5% iPrOH/Hexane, 1mL/min (210 nm).

\[ \text{Ph} - \overset{\text{Li}}{\text{OCb}} \xrightarrow{sBuLi}
\text{(-)-sparteine}
\text{Ph} - \overset{\text{Et}}{\text{OCb}} \xrightarrow{1.\text{PhEt}_2\text{B}} \xrightarrow{2.\text{H}_2\text{O}_2}
\text{Ph} - \overset{\text{OH}}{\text{Et}} \xrightarrow{+}
\text{Ph} - \overset{\text{OH}}{\text{Ph}} \\
3a \quad (32\%, 96:4 \text{ e.r.}) \quad + \quad 3d \quad (42\%, 78:22 \text{ e.r.}) \\

\begin{align*}
\text{Area: 860.512, Ret: 15.513, Area: 11645.9, Ret: 20.221} \\
\text{Area: 43548.8, Ret: 24.109} \\
\text{Area: 19197.7, Ret: 16.977}
\end{align*}
Chiral HPLC data from synthesis of 3a and 3d (0.75:1 mixture) from treatment of 16 with "BuLi [to give lithiated carbamate (1a) without sparteine present] followed by trapping with Et₂BPh.

\[
\begin{align*}
\text{Ph} & \quad \text{O} \quad \text{Cb} \quad \text{SnBu} & \\
2a & \quad \text{sBuLi} & \quad \text{(-)-sparteine} & \\
& \quad \text{Ph} & \quad \text{O} \quad \text{Cb} & \\
16 & \quad 1.\text{"BuLi} & \quad 2.\text{PhEt}_2\text{B} & \\
& \quad 3.\text{H}_2\text{O}_2 & \\
& \quad \text{OH} & \quad \text{Et} & \\
3a & \quad (32\%, 97:3 \text{ e.r.}) & \\
3d & \quad (48\%, 97:3 \text{ e.r.}) & \\
\end{align*}
\]
$^1$H NMR of CH$_3$ doublets $\beta$ to OH (CDCl$_3$, 400MHz).
3a (from oxidation of 8) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 98:2).

ent-3a (from oxidation of ent-8) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. = 97:3).
(±)-9 & (±)-10 (including inseparable first homologated alcohols 3a and ent-3a) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (210 nm).

\[ t_R = 7.1 \text{ min (R)-ent-3a, 7.3 min (2S,3S)-10, 7.4 min (S)-3a, 7.9 min (2S,3R)-ent-9, 8.5 min (2R,3R)-ent-10, 9.4 min (2R,3S)-9.} \]
9 (including inseparable first homologated alcohols 3a and ent-3a) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. > 98:2) (210 nm).

9 (including inseparable first homologated alcohols 3a and ent-3a) Daicel OJ-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. > 98:2) (210 nm).
10 (including inseparable first homologated alcohols 3a and \textit{ent-3a}) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. > 98:2) (210 nm).

\textit{ent-10} (including inseparable first homologated alcohols 3a and \textit{ent-3a}) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. > 98:2) (210 nm).
ent-9 (including inseparable first homologated alcohols 3a and ent-3a) Daicel OD-Chiracel column, 5:95 iPrOH/Hexane, 1 mL/min (e.r. > 98:2) (210 nm).

References

The (S)-enantiomer, ent-3j, was purchased from Fluka > 97:3, S:R by GC analysis.

A sample of boronic ester product 8 (50 mg, 0.18 mmol) was taken up in Et₂O (1mL) and cooled to 0 °C. A solution of NaOH (2 M)/H₂O₂ (30%) (2:1 v/v, 1.0 mL) was then added dropwise. After stirring for 30 min at 0 °C, water (2 mL) was added and the layers were separated. The aqueous layer was then extracted with Et₂O (3 x 2 mL). The combined organic layers were dried (MgSO₄) and concentrated in vacuo, furnishing the crude expected alcohol 3a (e.r. = 98:2); tᵣ = 9.7 min (R-minor), 14.8 min (S-major) Daicel Chiracel-OD column, 5% iPrOH in hexane 1 mL/min. [Lit. tᵣ = 11.4 min (R-minor), 16.7 min (S-major) Chiracel-OD column, 5% iPrOH in hexane 1 mL/min]

Ratio determined by HPLC: tᵣ = 7.6 min (2R,3R)-ent-10 and (2S,3R)-ent-9, 8.1 min (2R,3S)-9, 9.7 min (R)-ent-3a, 11.2 min (2S,3S)-10, 14.8 min (S)-3a (Daicel Chiracel-OD column, 5% iPrOH in hexane 1 mL/min).

Determined by using two different HPLC conditions: OD₂⁵ and OJ: tᵣ = 7.1 min (R)-ent-3a, 7.3 min (2S,3S)-10, 7.4 min (S)-3a, 7.9 min (2S,3R)-ent-9, 8.5 min (2R,3R)-ent-10, 9.4 min (2R,3S)-9. Daicel Chiracel-OJ column, 5% iPrOH in hexane 1 mL/min).

Determined by integration of ¹H-NMR (CDCl₃, 400 MHz) of the signals corresponding to the CH₃ β to the alcohol functionality in 9 (ent-9) and 10 (ent-10).