Pinene-derived Iminodiacetic Acid (PIDA): A Powerful Ligand for Stereoselective Synthesis and Iterative Cross-Coupling of Csp^3 Boronate Building Blocks

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Supporting Information

I. General methods

Materials. Commercial reagents were purchased from Sigma-Aldrich, Fisher Scientific, Alfa Aesar, TCI America, or Frontier Scientific, and were used without further purification unless otherwise noted. Pd_2dba_3, RuPhos, PPh_3 and Ag_2O were purchased from Sigma-Aldrich. $P(o\text{-}tol)_3$ was purchased from TCI America. Solvents were purified via passage through packed columns as described by Pangborn and coworkers[1] (THF, Et_2O, CH_3CN, CH_2Cl_2: dry neutral alumina; hexane, benzene, and toluene, dry neutral alumina and Q5 reactant; DMSO, DMF: activated molecular sieves). All water was deionized prior to use. Diisopropylethylamine was freshly distilled under an atmosphere of nitrogen from CaH_2.

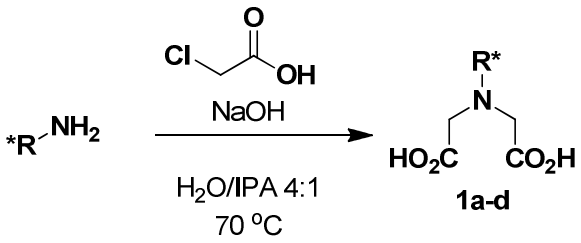
General Experimental Procedures. Unless noted, all reactions were performed in flame-dried round-bottom or modified Schlenk flasks fitted with rubber septa under a positive pressure of argon. Organic solutions were concentrated via rotary evaporation under reduced pressure with a bath temperature of 23 ^oC unless otherwise noted. Reactions were monitored by analytical thin layer chromatography (TLC) performed using the indicated solvent on E. Merck silica gel 60 F254 plates (0.25mm). Compounds were visualized by exposure to a UV lamp (λ = 254 nm), and/or a solution of $KMnO_4$, followed by brief heating using a Varitemp heat gun. Column chromatography was performed using Merck silica gel grade 9385 60Å (230-400 mesh).

[1] Pangborn, A. B.; Giardello, M. A; Grubbs, R. H.; Rosen, R. K.; Timmers, F.J. *Organometallics* **1996**, *15*, 1518-1520.

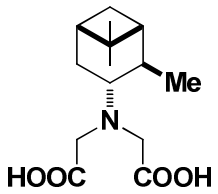
Structural analysis. ^{1}H NMR and ^{13}C NMR spectra were recorded at 20 °C on Varian Unity 500, Varian Unity Inova 500NB or Varian Unity 500 instruments. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane and referenced to residual protium in the NMR solvent ($CHCl_3$, δ = 7.26; acetone, δ = 2.05, center line; 1,1,2,2-tetrachloroethane, 5.95) or to added tetramethylsilane (δ = 0.00). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, m = multiplet, b = broad, app = apparent), coupling constant (*J*) in Hertz (Hz), and integration. Chemical shifts (δ) for ^{13}C NMR are reported in ppm downfield from tetramethylsilane and referenced to carbon resonances in the NMR solvent ($CDCl_3$, δ = 77.0, center line; acetone, δ = 39.5, center line). Carbons bearing boron substituents were not observed (quadrupolar relaxation). ^{11}B NMR were recorded using a Unity Inova 400 instrument and referenced to an external standard of (BF_3•Et_2O). High resolution mass spectra (HRMS) were performed by Furong Sun and Dr. Steve Mullen at the University of Illinois School of Chemical Sciences Mass Spectrometry Laboratory.

II. Experimental procedures

a. Synthesis of 1a – 1d



General procedure for the synthesis of ligands 1a-d:
To a stirred solution of chloroacetic acid (69 mmol, 2.3 equiv) in H_2O (60 ml) at 0 °C was added dropwise 5N NaOH solution (13.8 ml, 69 mmol, 2.3 equiv), keeping the temperature below 15 °C. The amine (30 mmol, 1 equiv) in IPA (30 ml) was then added in one portion. The ice bath was then removed and the reaction heated at 70 °C (oil bath temperature). After stirring for 2.5 h, the reaction turned clear from an initial biphasic mixture. Another 8.1 ml (40.5 mmol, 1.35 equiv) of the 5 N NaOH solution was added, and the reaction stirred for a further 14 h at the same temperature. The third portion of the NaOH solution (8.1 ml, 40.5 mmol, 1. 35 equiv) was then added and stirred for an additional 2 h at 70 °C. The reaction was then heated up to 100 °C. $BaCl_2.H_2O$ (7.69 g, 31.5 mmol, 1.05 equiv) in H_2O (30 ml) was heated until the solid dissolved completely. This heated solution was then added dropwise via pipette into the reaction mixture. After the addition, the reaction was stirred for an additional 15 min, during which the reaction became a thick white suspension. After cooling to room temperature, the white solid was collected by filtration and dried in a vacuum oven set at 100 °C. The mass of the Ba chelate was determined. The Ba chelate was then suspended in H_2O (60 ml) and heated in a 110 °C oil bath until boiling. 5M H_2SO_4 (1.95 equiv relative to the Ba chelate) was added dropwise, followed by rinsing with 5 ml H_2O. The resulting suspension was stirred for another 15 min in the oil bath, then cooled for 5 min and filtered through celite, rinsing with 10 ml H_2O. The filtrate was concentrated to dryness. The solid obtained was then redissolved in Et_2O/CH_2Cl_2 (1:10, 100 ml) and filtered to remove insoluble solids. The CH_2Cl_2 solution was then concentrated *in vacuo* and the solid obtained was used without further purification.



1a

Ligand 1a. The general procedure was followed using (1*R*,2*R*,3*R*,5*S*)-(−)-Isopinocampheylamine (Sigma Aldrich, 4.59 g, 30 mmol), chloroacetic acid (6.52 g, 69 mmol) and NaOH (30 ml, 150 mmol). 11.33 g of the Ba chelate (93%) was obtained. 5.4 ml of 5M H_2SO_4 was used for the hydrolysis, and the ligand **1a** was obtained as an off-white solid (6.63 g, 82 %).

^{1}H-NMR (500 MHz, DMSO-d_6)

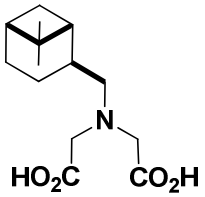
δ 3.45 (s, 4H), 3.23-3.18 (m, 1H), 2.32-2.23 (m, 1H), 2.19-2.12 (m, 1H), 1.91-1.86 (m, 1H), 1.75-1.69 (m, 2H), 1.64-1.60 (m, 1H), 1.15 (s, 3H), 1.03 (d, *J* = 6.5, 3H), 0.92 (s, 3H), 0.79 (d, *J* = 10 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6)

δ 173.5, 62.0, 53.8, 47.3, 40.9, 40.3, 38.7, 33.4, 29.6, 27.9, 23.0, 20.9.

HRMS (ESI+)

Calculated for $C_{14}H_{24}NO_4$:	270.1705
Found:	270.1703



1b

Ligand 1b. The general procedure was followed using (−)-cis-myrtanylamine (Sigma Aldrich, 4.59 g, 30 mmol), chloroacetic acid (6.52 g, 69 mmol) and NaOH (30 ml, 150 mmol). 11.33 g of the Ba chelate (93%) was obtained. 5.4 ml of 5M H_2SO_4 was used for the hydrolysis, and the ligand **1b** was obtained as an off-white solid in about 70-80% purity (1.62 g, 20 %).

^{1}H-NMR (500 MHz, DMSO-d_6)

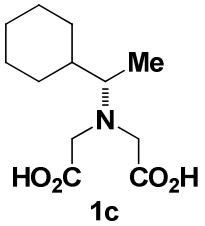
δ 3.36 (s, 4H), 2.56 (d, *J* = 7.5 Hz, 2H), 2.30-2.26 (m, 1H), 2.12-2.09 (m, 1H), 1.93-1.91 (m, 1H), 1.87 – 1.72 (m, 4H), 1.53-1.45 (m, 1H), 1.12 (s, 3H), 0.91 (s, 3H), 0.84 (d, J = 9.5 Hz, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6)

δ 172.4, 59.6, 55.1, 43.5, 40.9, 38.6, 38.2, 32.9, 27.8, 25.8, 22.9, 19.5.

HRMS (ESI+)

Calculated for $C_{14}H_{24}NO_4$:	270.1705
Found:	270.1700



1c

Ligand 1c. The general procedure was followed using (S)-(+)-1-cyclohexylethylamine (Alfa Aesar, 12.72 g, 100 mmol), chloroacetic acid (21.74 g, 230 mmol) and NaOH (100 ml, 500 mmol). 27.84 g of the Ba chelate (74%) was obtained. 14.4 ml of 5M H_2SO_4 was used for the hydrolysis, and the ligand **1c** was obtained as an off-white solid (12.47 g, 51 %).

^{1}H-NMR (500 MHz, DMSO-d_6)

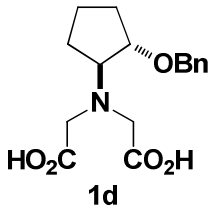
δ 3.37 (d, *J* = 17.5 Hz, 2H), 3.29 (d, *J* = 17.5 Hz, 2H), 2.39 (m, 1H), 1.91 (app d, *J* = 7.5 Hz, 1H), 1.65-1.51 (m, 4H), 1.24-1.03 (m, 5H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.89-0.78 (m, 1H).

^{13}C-NMR (125 MHz, DMSO-d_6)

δ 173.4, 62.6, 53.2, 40.8, 30.0, 29.4, 26.1, 25.8, 25.8, 12.6

HRMS (ESI+)

Calculated for $C_{12}H_{22}NO_4$:	244.1550
Found:	244.1549



1d

Ligand 1d. The general procedure was followed using (1S, 2S)-(+)-2-benzyloxycyclopentylamine (Alfa Aesar, 5 g, 26.1 mmol), chloroacetic acid (5.68 g, 60.1 mmol) and NaOH (26.1 ml, 130.5 mmol). 5.87 g of the Ba chelate (67%) was obtained. 3.40 ml of 5M H_2SO_4 was used for the hydrolysis, and the ligand **1d** was obtained as an off-white solid (3.36 g, 42 %).

^{1}H-NMR (500 MHz, DMSO-d_6)

δ 12.2 (br s, 2H), 7.32-7.24 (m, 5H), 4.42 (d, *J* = 12 Hz, 1H), 4.36 (d, *J* = 11.5 Hz, 1H), 3.76-3.74 (m, 1H), 3.48 (d, *J* = 17.5 Hz, 2H), 3.43 (d, *J* = 18 Hz, 2H), 3.24-3.20 (m, 1H), 1.88-1.82 (m, 1H), 1.82-1.76 (m, 1H), 1.59-1.48 (m, 3H), 1.38-1.30 (m, 1H).

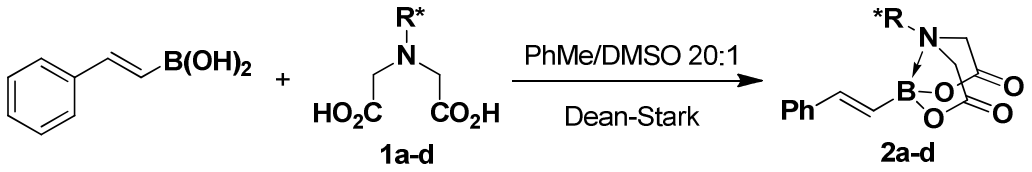
^{13}C-NMR (125 MHz, DMSO-d_6)

δ 173.0, 138.6, 128.1, 127.6, 127.3, 83.0, 70.4, 68.1, 53.6, 29.8, 28.4, 20.9.

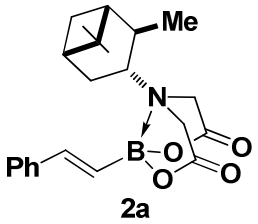
HRMS (ESI+)

Calculated for $C_{16}H_{22}NO_5$:	308.1498
Found:	308.149

b. Synthesis of 2a – 2n



General procedure for the complexation of chiral ligands 1a-d to *trans*-2-phenylvinylboronic acid: To a solution of *trans*-2-phenylvinylboronic acid (1.5 equiv) in toluene (30 ml) and DMSO (1.5 ml) was added the ligand **1** (typically 1-5 mmol, 1 equiv). The flask was fitted with a Dean-Stark trap. The Dean-Stark trap was fitted with an air-cooled condenser vented to ambient atmosphere. The stirred solution was refluxed with azeotropic removal of water for 2 h. The toluene was removed *in vacuo*, and the residue was taken up in 2:1 EtOAc/acetone (60 ml) and washed twice with 1:1 brine/H_2O (30 ml). The aqueous layer was extracted with 2:1 EtOAc/acetone (30 ml) and the combined organic phase washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was then purified by silica gel chromatography, eluting first with Et_2O to remove impurities, then with 1:4 (acetone/Et_2O).



PIDA boronate 2a. The reaction was carried out on a 20 mmol scale with some modifications from the general procedure and purified without the use of silica gel chromatography: To a suspension of *trans*-2-phenylvinylboronic acid (2.96g, 20 mmol) in toluene (200 ml) was added the ligand **1a** (9.68g, 36 mmol). The flask was fitted with a 50 ml Dean-Stark trap and an air-cooled condenser vented to ambient atmosphere. The stirred solution was refluxed with azeotropic removal of water for 2 h. After cooling to room temperature, the crude solid product was collected via vacuum filtration. The filtrate was then concentrated to dryness and Et_2O (50 ml) was added. The resulting white precipitate was collected via vacuum filtration and the combined solids were then washed with additional Et_2O (50 ml). This solid was then taken up in acetone (150 ml) and passed slowly through a pad of silica gel in a 100 ml sintered funnel, eluting with additional acetone (50 ml). The filtrate thus obtained was concentrated and dried *in vacuo*, giving the product (6.74 g, 88%).

TLC (Hexanes:acetone 3:2)

R_f = 0.27, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.47 (d, J = 7 Hz, 1H), 7.35 (t, J = 7 Hz, 1H), 7.29 (t, J = 7.5 Hz, 1H), 7.07 (d, J = 18 Hz, 1H), 6.31 (d, J = 18 Hz, 1H), 4.19 (d, J = 17 Hz, 1H), 3.84 (s, 2H), 3.70 (dt, J = 10, 6.5 Hz, 1H), 3.62 (d, J = 17.5 Hz, 1H), 2.57 – 2.52 (m, 1H), 2.46 – 2.42 (m, 1H), 2.17 (dquint, J = 6.5, 1.5 Hz, 1H), 2.02 (sept, J = 2.5 Hz, 1H), 1.89 (dt, J = 6, 2 Hz, 1H), 1.74 (ddd, J = 15, 6.5, 2.5 Hz, 1H), 1.27 (d, J = 6.5 Hz, 3H), 1.22 (s, 3H), 0.92 (d, J = 11 Hz, 1H), 0.88 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

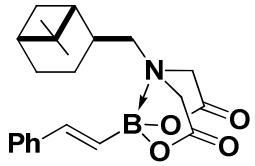
δ 169.5, 166.9, 144.6, 137.6, 128.7, 128.4, 126.7, 68.6, 60.6, 54.4, 49.0, 40.6, 39.1, 38.8, 32.1, 30.3, 27.0, 23.6, 23.4.

^{11}B-NMR (100 MHz, acetone-d_6)

δ 11.9

HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_4$:	382.2190
Found:	382.2187



2b

Boronate ester 2b. The general procedure was followed using *trans*-2-phenylvinylboronic acid (0.22 g, 1.5 mmol), ligand **1b** (0.606g, 2.25 mmol) in 20 ml toluene and 1 ml DMSO. A white solid was obtained (0.387 g, 68%).

TLC (Hexanes:EtOAc:Et_2O 2:2:1)

R_f = 0.20, visualized by short wave UV.

^{1}H-NMR (500 MHz, acetone-d_6)

δ 7.50 (app d, *J* = 7 Hz, 2H), 7.34 (app t, *J* = 7.5 Hz, 2H), 7.28-7.25 (m, 1H), 6.93, (d, *J* = 18 Hz, 1H), 6.33 (d, *J* = 18 Hz, 1H), 4.17-4.08 (m, 4H), 3.45 (dd, *J* = 13.5, 6.5 Hz, 1H), 3.34 (dd, *J* = 13.5, 3 Hz, 1H), 2.74-2.68 (m, 1H), 2.38-2.26 (m, 2H), 2.16-2.11 (m, 1H), 2.01-1.94 (m, 1H), 1.92-1.76 (m, 3H), 1.15 (s, 3H), 1.08 (d, *J* = 10 Hz, 1H), 0.92 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

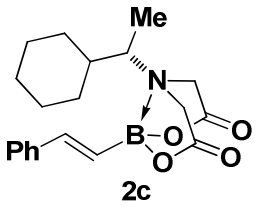
δ 167.8, 167.4, 144.2, 137.6, 128.6, 128.4, 126.7, 66.8, 58.5, 58.4, 47.3, 40.4, 38.1, 37.4, 31.9, 27.3, 25.6, 23.3 (2C).

^{11}B-NMR (100 MHz, acetone-d_6)

δ 11.9

HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_4$:	382.2190
Found:	382.2187



2c

Boronate ester 2c. The general procedure was followed using *trans*-2-phenylvinylboronic acid (0.74 g, 5 mmol), ligand **1c** (1.82 g, 7.5 mmol) in 50 ml toluene and 2.5 ml DMSO. A white solid was obtained (0.311 g, 74%).

TLC (Hexanes:acetone 3:2)

$R_f = 0.38$

^{1}H-NMR (500 MHz, acetone-d_6)

δ 7.52 (d, *J* = 8 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.27 (t, *J* = 7.5 Hz, 1H), 6.96, (d, *J* = 18 Hz, 1H), 6.46 (d, *J* = 18 Hz, 1H), 4.27 (d, *J* = 17 Hz, 1H), 4.19 (d, *J* = 17 Hz, 1H), 4.05 (d, *J* = 14.5 Hz, 1H), 4.02 (d, *J* = 17 Hz, 1H), 3.42-3.38 (m, 1H), 2.05 (m, 1H), 1.86-1.83 (m, 1H), 1.78-1.74 (m, 1H), 1.69-1.62 (m, 2H), 1.50-1.44 (m, 1H), 1.36-1.27 (m, 6H), 1.18-1.-08 (m, 2H).

^{13}C-NMR (125 MHz, $CDCl_3$)

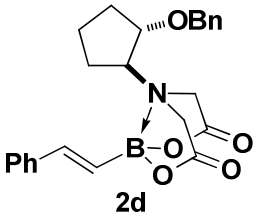
δ 168.5, 167.7, 144.3, 128.6, 128.4, 126.7, 67.6, 56.8, 39.2, 32.1, 27.7, 26.4, 25.7, 25.7, 10.5.

^{11}B-NMR (100 MHz, acetone-d_6)

δ 11.9

HRMS (ESI+)

Calculated for $C_{20}H_{27}BNO_5$:	356.2033
Found:	356.2029



2d

Boronate ester 2d. The general procedure was followed using *trans*-2-phenylvinylboronic acid (0.148 g, 1 mmol), ligand 1d (0.461 g, 1.5 mmol) in 15 ml toluene and 0.5 ml DMSO. An off-white solid was obtained (0.311 g, 74%).

TLC (Hexanes:acetone 3:2)

$R_f = 0.38$

^{1}H-NMR (500 MHz, acetone-d_6)

δ 7.50 (d, *J* = 8 Hz, 2H), 7.38-7.29 (m, 6H), 7.26-7.22 (m, 1H), 7.18-7.13, (m, 1H), 6.96 (d, *J* = 18 Hz, 1H), 6.46 (d, *J* = 18.5 Hz, 1H), 4.62 (d, *J* = 11.5 Hz, 1H), 4.55 (d, *J* = 11 Hz, 1H), 4.41-4.38

(m, 1H), 4.29 (d, *J* = 16.5 Hz, 1H), 4.19 (d, *J* = 17.5 Hz, 1H), 4.14 (d, *J* = 16.5 Hz, 1H), 4.05 (d, *J* = 17 Hz, 1H), 3.70 (q, *J* = 9 Hz, 1H), 2.30-2.25 (m, 1H), 2.20-2.15 (m, 1H), 1.82-1.6 (m, 4H).

^{13}C-NMR (125 MHz, $CDCl_3$)

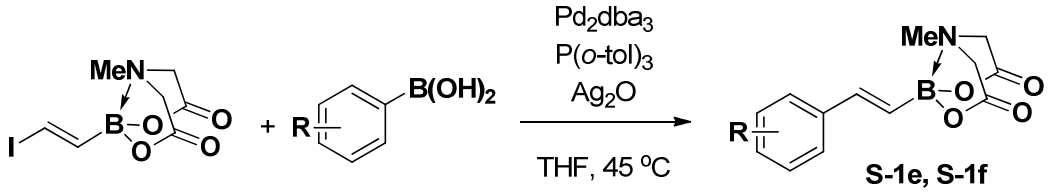
δ 168.8, 167.5, 144.3, 137.5, 136.4, 128.8, 128.6, 128.5, 128.4, 128.3, 126.8, 79.3, 73.4, 72.0, 60.0, 55.4, 29.6, 26.2, 21.1.

^{11}B-NMR (100 MHz, acetone-d_6)

δ 11.8

HRMS (ESI+)

Calculated for $C_{24}H_{27}BNO_5$:	420.1978
Found:	420.1982



General procedure for the synthesis of boronates S-1e and S-1f:

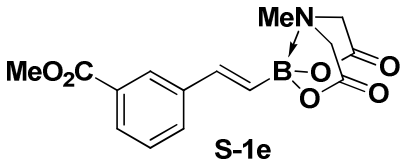
Preparation of boronic acid solution. A 7 ml vial equipped with a stir bar was charged with the boronic acid (2.4 mmol). The vial was taken into the glovebox and THF (6 ml) was added. The mixture was stirred rapidly to give 0.4 M solution of the boronic acid.

Preparation of catalyst stock solution. In a glovebox, to a 7 ml vial equipped with a stir bar was added P(o-tolyl)$_3$ (170 mg, 0.55 mmol) and Pd_2dba_3 (128 mg, 0.14 mmol). THF (14 ml) was added to make a 0.01 M catalyst solution which was stirred at 23 °C for 10 min.

*The freshly prepared catalyst stock solution was immediately for the preparation of **S-1e** and **S-1f**:*

This reaction was carried out in triplicate. A 7 ml vial ("reaction vial") equipped with a stir bar was charged with (*E*)-(2-Iodoethenyl)boronate ester[2] (0.4 mmol), and Ag_2O (1.2 mmol). The vials were taken into the glovebox. To each reaction vial was added 0.5 ml THF. 1.5 ml (0.6 mmol) of the boronic acid solution was added to the reaction vial, followed by 2 ml of the catalyst stock solution (0.02 mmol Pd_2dba_3, 0.08 mmol P(o-tolyl)$_3$). The reaction was then sealed with a cap, removed from the glovebox and placed in a heating block pre-equilibrated at 45 °C. The reaction was stirred for 24 h at 45 °C, then cooled to 23 °C. The reaction mixture was filtered through celite, combining the filtrates from the triplicate reactions. The celite pad was rinsed with THF (2 ×10 ml). The combined filtrate was concentrated *in vacuo*. The crude product was taken up in CH_2Cl_2 and loaded onto a silica gel column. The non-polar impurities were eluted with Et_2O, and the product was eluted with 10-33% Et_2O/acetone.

[2] Lee, S. J.; Anderson, T. M.; Burke, M. D. *Angew. Chem. Int. Ed.* **2010**, *49*, 8860-8863



S-1e

MIDA boronate S-1e. The general procedure was followed using a stock solution of 3-methoxycarbonyl-phenylboronic acid (432 mg, 2.4 mmol) and (*E*)-(2-Iodoethenyl)boronate ester (124 mg, 0.4 mmol) and Ag_2O (278 mg, 1.2 mmol) in each of 3 reaction vials. MIDA boronate **S-1e** (340 mg, 89%) was obtained as a white solid after silica gel chromatography.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.22

^{1}H-NMR (500 MHz, acetone-d_6)

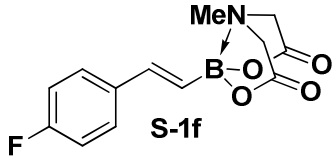
δ 8.14 (t, J = 1.5 Hz, 1H), 7.90 (dt, J = 7.5, 1.5 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 8.0 Hz, 1H), 7.02 (d, J = 18.5 Hz, 1H), 6.47 (d, J = 18.5 Hz, 1H), 4.29 (d, J = 17 Hz, 2H), 4.13 (d, J = 17 Hz, 2H), 3.89 (s, 3H), 3.09 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

δ 168.5, 166.5, 141.1, 139.0, 131.4, 130.9, 129.1, 128.8, 127.3, 61.8, 51.8, 46.8.

HRMS (ESI+)

Calculated for $C_{15}H_{17}BNO_6$:	318.1149
Found:	318.1154



S-1f

MIDA boronate S-1f. The general procedure was followed using a stock solution of 4-fluoro-phenylboronic acid (84 mg, 2.4 mmol) and (*E*)-(2-Iodoethenyl)boronate ester (124 mg, 0.4 mmol) and Ag_2O (278 mg, 1.2 mmol) in each of 3 reaction vials. MIDA boronate **S-1e** (162 mg, 49%) was obtained as a white solid after silica gel chromatography.

TLC (Hexanes:acetone 1:1)

R_f = 0.24, visualized by short wave UV.

^{1}H-NMR (500 MHz, acetone-d_6)

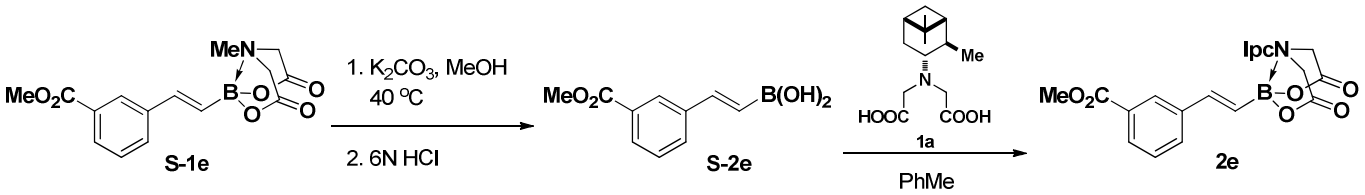
δ 7.58-7.54 (m, 2H), 7.13-7.09 (m, 2H), 6.93 (d, J = 18.5 Hz, 1H), 6.30 (d, J = 18 Hz, 1H), 4.27 (d, J = 17 Hz, 1H), 4.09 (d, J = 16.5 Hz, 1H), 3.06 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

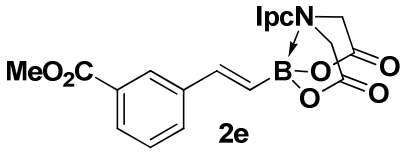
δ 169.1, 163.3 (d, J = 244 Hz), 141.5, 135.7, 129.2 (d, J = 8.8 Hz), 116.0 (d, J = 21.4 Hz), 62.3, 47.4.

HRMS (ESI+)

Calculated for $C_{13}H_{24}BNO_4F$: 278.1000
Found: 278.0998



PIDA boronate 2e. In an unoptimized procedure, to a suspension of **S-1a** (322 mg, 1.02 mmol) in MeOH (10 ml) in a 20 ml vial was added K_2CO_3 (421 mg, 3.05 mmol) under ambient atmosphere. The vial was capped and placed in a heating block pre-heated to 45 °C. The reaction was stirred at 45 °C for 30 min and then allowed to cool to 23 °C. The yellow solution of the boronic ester was poured into 20 ml 6N HCl. The solution was transferred to a separatory funnel and extracted with Et_2O (2 × 25 ml). To the aqueous layer was added brine (10 ml) and the aqueous layer was extracted with 1:1 THF/Et_2O (25 ml). The organic phase was then dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford boronic acid **S-2a**.The boronic acid was then suspended in toluene (30 ml) and **1a** was added. The mixture was refluxed with a Dean-Stark trap for 2 h. The reaction was cooled to 23 °C and concentrated *in vacuo*. CH_2Cl_2 (30 ml) was added and stirred briefly. The excess ligand **1a** was removed by filtration. To the filtrate was added celite, and the suspension was concentrated *in vacuo*. The celite pad was loaded onto a silica gel column and the product purified by flash chromatography (100% Et_2O – 20% acetone/Et_2O) to afford a white solid (298 mg, 67% over 2 steps).



TLC (Hexanes:EtOAc 1:1)

R_f = 0.27, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

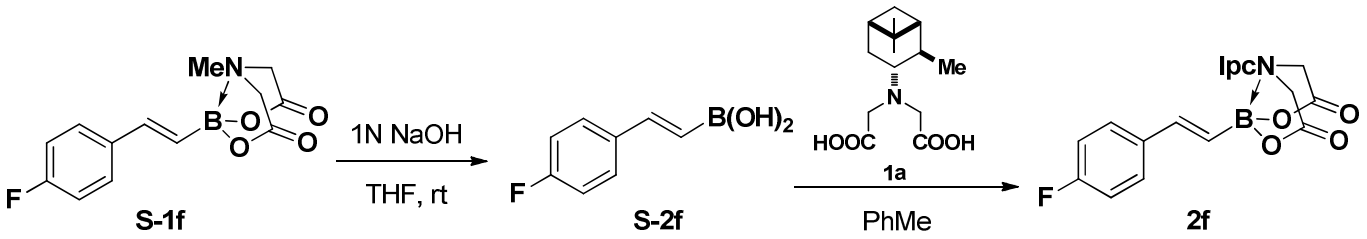
δ 8.14 (s, 1H), 7.95 (d, J = 8 Hz, 1H), 7.63 (d, J = 8 Hz, 1H), 7.43 (t, J = 7.5 Hz, 1H), 7.11 (d, J = 18.5 Hz, 1H), 6.38 (d, J = 18 Hz, 1H), 4.21 (d, J = 17.5 Hz, 1H), 3.93 (s, 3H), 3.88 (d, J = 15.5 Hz, 1H), 3.82 (d, J = 15.5 Hz, 1H), 3.71 (dt, J = 10, 6.5 Hz, 1H), 3.56 (d, J = 17 Hz, 1H), 2.47-2.52 (m, 1H), 2.48-2.43 (m, 1H), 2.18-2.16 (m, 1H), 2.03-2.02 (m, 1H), 1.92-1.90 (m, 1H), 1.74 (ddd, J = 13, 6, 2 Hz, 1H), 1.29 (d, J = 7 Hz, 3H), 1.23 (s, 3H), 0.92 (d, J = 11 Hz, 1H), 0.88 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

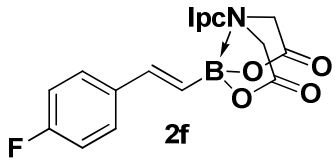
δ 169.5, 166.9 (2H), 143.4, 137.9, 131.2, 130.6, 129.3, 128.7, 127.6, 68.6, 60.6, 54.4, 52.2, 49.0, 40.5, 39.1, 38.8, 32.0, 30.3, 27.0, 23.6, 23.4

HRMS (ESI+)

Calculated for $C_{24}H_{31}BNO_6$: 440.2244
Found: 440.2250



PIDA boronate 2f. To a solution of **S-2b** (139 mg, 0.50 mmol) in THF (5 ml) was added 1N NaOH (1.5 ml, 1.5 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was quenched with the addition of sat. NH_4Cl solution (5 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel, rinsing with Et_2O (5 ml). After phase separation, the aqueous phase extracted with 1:2 THF/Et_2O (2 × 7.5 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid **S-2b**. The solid was suspended up in toluene (20 ml) and **1a** (20 mg, 0.75 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 2 h. After cooling to room temperature, toluene was removed *in vacuo*. CH_2Cl_2 (30 ml) was added and stirred briefly. The excess ligand **1a** was removed by filtration. To the filtrate was added celite, and the suspension was concentrated *in vacuo*. The celite pad was loaded onto a silica gel column and the product purified by flash chromatography (100% Et_2O – 20% acetone/Et_2O) to afford a white solid (136 mg, 68% over 2 steps).



TLC (Hexanes:EtOAc 1:1)

R_f = 0.30, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

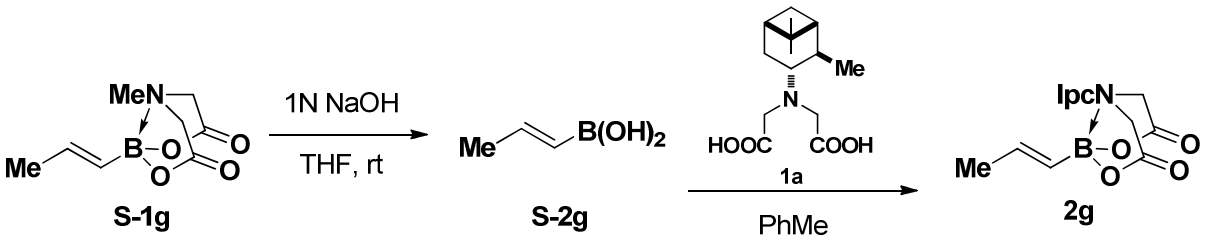
δ 7.44-7.41, (m, 2H), 7.05-7.01 (m, 3H), 6.20 (d, J = 18 Hz, 1H), 4.19 (d, J = 17.5 Hz, 1H), 3.85 (s, 2H), 3.69 (dt, J = 10, 6.5 Hz, 1H), 3.63 (d, J = 17.5 Hz, 1H), 2.52 (tt, J = 12, 2.5 Hz, 1H), 2.44 (ddt, J = 11, 6, 2 Hz, 1H), 2.19-2.16 (m, 1H), 2.03-2.00 (m, 1H), 1.90 (dt, J = 6, 2 Hz, 1H), 1.73 (ddd, J = 15, 6, 2.5 Hz, 1H), 1.28 (d, J = 7 Hz, 3H), 1.22 (s, 3H), 0.92 (d, J = 11 Hz, 1H), 0.88 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

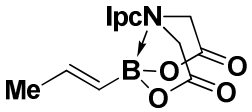
δ 169.5, 166.9, 162.8 (d, J = 247 Hz), 143.3, 133.8, 128.3 (d, J = 7.8 Hz), 115.6 (d, J = 21.4 Hz), 66.6, 60.6, 54.4, 49.0, 40.5, 39.1, 38.8, 32.1, 30.3, 27.0, 23.6, 23.4.

HRMS (ESI+)

Calculated for $C_{22}H_{28}BFNO_4$:	400.2095
Found:	400.2101



PIDA boronate 2g. To a solution of **S-1g**[3] (197 mg, 1 mmol) in THF (10 ml) was added 1N NaOH (3 ml, 3 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was quenched with the addition of sat. NH_4Cl solution (10 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel, rinsing with Et_2O (10 ml). After phase separation, the organic phase was washed with another portion of sat. NH_4Cl solution (10 ml) and the combined aqueous phase extracted with 1:1 THF/Et_2O (15 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid **S-2g** as a white solid. The solid was taken up in toluene (15 ml) and DMSO (0.75 ml) and **1a** (404 mg, 1.5 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 1.5 h. After cooling to room temperature, toluene was removed *in vacuo*. The residue was taken up in 2:1 EtOAc/acetone (15 ml) and washed twice with 1:1 H_2O/brine (10 ml). The aqueous layers were extracted with 2:1 EtOAc/acetone (15 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography, eluting first with Et_2O then with 1:4 acetone/Et_2O to give **2g** as a white solid (166 mg, 52% over 2 steps).



2g

TLC (Hexanes:acetone 3:2)

R_f = 0.41, stained by $KMnO_4$

^{1}H-NMR (500 MHz, acetone-d_6)

δ 6.13 (dq, *J* = 8.5 Hz, 1H), 5.66 (dd, *J* = 17.5, 1.5 Hz, 1H), 4.19 (d, *J* = 18 Hz, 1H), 4.18 (d, *J* = 16 Hz, 1H), 4.09 (d, *J* = 15.5 Hz, 1H), 3.94 (d, *J* = 18 Hz, 1H), 3.87 (dt, *J* = 10, 3 Hz, 1H), 2.57-2.51 (m, 1H), 2.49-2.42 (m, 2H), 2.00 (sept, *J* = 3 Hz, 1H), 1.91 (dt, *J* = 6, 2 Hz, 1H), 1.79 (dd, *J* = 6.5, 1.5 Hz, 3H), 1.61 (ddd, *J* = 15, 6.5, 1.5 Hz, 1H), 1.33 (d, *J* = 7 Hz, 3H), 1.25 (s, 3H), 1.04 (d, *J* = 10.5 Hz, 1H), 0.98 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

δ 170.2, 167.2, 140.8, 67.9, 60.3, 54.5, 49.6, 41.0, 39.0, 38.5, 31.8, 30.3, 26.9, 23.0, 22.9, 20.8.

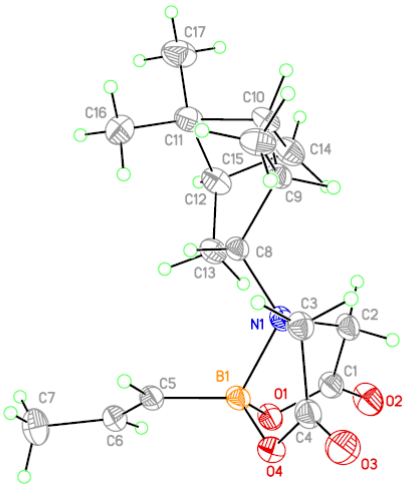
^{11}B-NMR (100 MHz, acetone-d_6)

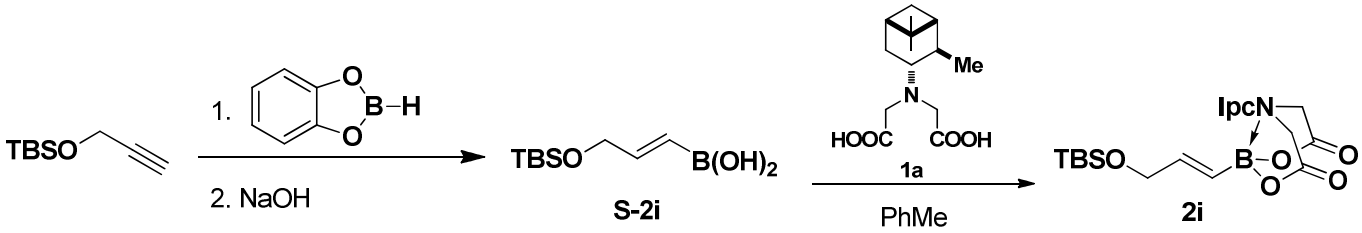
δ 11.5

HRMS (ESI+)

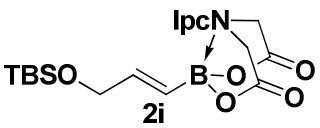
Calculated for $C_{17}H_{27}BNO_4$:	320.2033
Found:	320.2035

[3] Gillis, E. P.; Burke, M. D. Unpublished results.





PIDA boronate 2i. In an unoptimized procedure, TBS-protected propargyl alcohol (5.17 g, 30.4 mmol) was weighed into a dry 20 ml Ichem vial and the vial was sealed with a septum cap. The vial was flushed with N_2 for 20 min, then catecholborane (3.4 ml, 31.9 mmol) was added neat in one portion. The reaction was stirred at 60 °C in a heating block for 15 h. After cooling to room temperature, 4.36 g (approx. 15 mmol) of this crude product was diluted in THF (150 ml) and 1N NaOH (45 ml, 45 mmol) was added. After vigorous stirring for 10 min, the mixture was transferred to a separatory funnel and the phases separated. The organic layer was washed with 1N NaOH (60 ml), then H_2O (60 ml) and 1:1 H_2O/brine (60 ml). The organic phase was then dried over $MgSO_4$, filtered and concentrated to give a yellow oil as the boronic acid **S-2i** (1.48 g, 6.85 mmol). The boronic acid **S-2i** was then dissolved in toluene (60 ml) and DMSO (3 ml). **1a** was then added, and the mixture was heated to reflux with a Dean-Stark trap for 2h. The reaction was then cooled to room temperature. Toluene was then removed *in vacuo*. Et_2O was added to the residue and the precipitate, which is the crude product, was obtained by vacuum filtration. Purification by silica gel chromatography (30-100% EtOAc/hexane) gave a white solid (405 mg, ~30% from boronic acid).



TLC (Hexanes:acetone 3:2)

R_f = 0.51 visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 6.22 (dt, *J* = 17.5, 4Hz, 1H), 5.94 (dt, *J* = 17.5, 2 Hz, 1H), 4.26-4.25 (m, 2H), 4.23 (d, *J* = 18 Hz, 1H), 4.18 (d, *J* = 15.5 Hz, 1H), 4.12 (d, *J* = 15 Hz, 1H), 3.98 (d, *J* = 18 Hz, 1H), 3.86 (dt, *J* = 10.5, 6 Hz, 1H), 2.59-2.53 (m, 1H), 2.49-2.41 (m, 2H), 1.99 (sept, *J* = 3 Hz, 1H), 1.92 (dt, *J* = 6, 2 Hz, 1H), 1.66 (ddd, *J* = 15, 6.5, Hz, 1H), 1.34 (d, *J* = 7 Hz, 3H), 1.25 (s, 3H), 1.07 (d, *J* = 10.5 Hz, 1H), 0.99 (s, 3H), 0.9 (s, 9H), 0.1 (s, 6H).

^{13}C-NMR (125 MHz, $CDCl_3$)

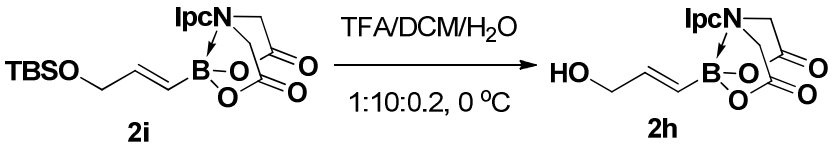
δ 169.7, 167.0, 146.2, 68.4, 64.3, 60.3, 54.2, 49.0, 40.6, 38.9, 38.8, 32.0, 30.8, 30.2, 27.0, 25.9, 23.5 (2C), 15.2, -5.4.

^{11}B-NMR (100 MHz, acetone-d_6)

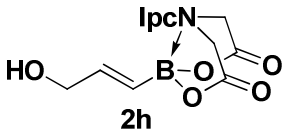
δ 11.8

HRMS (ESI+)

Calculated for $C_{23}H_{41}BNO_5Si$: 450.2847
Found: 450.2845



PIDA boronate 2h. The boronate ester **2i** (1.52 g, 3.38 mmol) was dissolved in CH_2Cl_2 (68 ml) and cooled to 0 °C. H_2O (0.34 ml) followed by TFA (6.80 ml) was then added. The reaction was stirred at 0 °C for 30 min. the reaction was washed briefly with H_2O (30 ml), then twice with sat. aqueous $NaHCO_3$ (30 ml). The combined aqueous layer was washed with CH_2Cl_2 (30 ml). The organic phase was then dried over $MgSO_4$, filtered and concentrated. Following purification by silica gel chromatography (40→80% EtOAc/hexane), a white solid was obtained. (737 mg, 65%).



TLC (Hexanes:acetone 3:2)

R_f = 0.20, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, acetone-d_6)

δ 6.26 (dt, *J* = 18, 4 Hz, 1H), 5.89 (app d, *J* = 17.5 Hz, 1H), 4.12 (d, *J* = 15 Hz, 1H), 4.12 (m, 2H), 3.89 (dt, *J* = 10, 6.5 Hz, 1H), 2.56 (m, 1H), 2.48-2.2 (m, 2H), 1.99 (sept, *J* = 3 Hz, 1H), 1.91 (dt, *J* = 6, 2.5 Hz, 1H), 1.63 (ddd, *J* = 15, 6.5, 5 Hz, 1H), 1.35 (d, *J* = 7 Hz, 3H), 1.25 (s, 3H), 1.06 (d, *J* = 10.5 Hz, 1H), 0.97 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

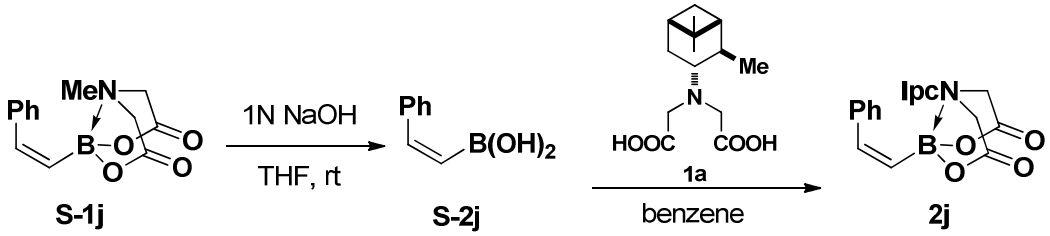
δ 170.8, 167.9, 146.5, 68.5, 64.5, 60.9, 55.2, 50.2, 41.6, 39.6, 39.1, 32.3, 30.9, 27.5, 23.6, 23.6.

^{11}B-NMR (100 MHz, acetone-d_6)

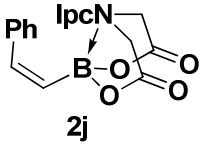
δ 11.8

HRMS (ESI+)

Calculated for $C_{17}H_{27}BNO_5$:	336.1982
Found:	336.1979



PIDA boronate 2j. To a solution of **S-1j**[4] (117 mg, 0.45 mmol) in THF (5 ml) was added 1N NaOH (1.4 ml, 1.4 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was diluted with Et_2O and quenched with the addition of sat. NH_4Cl solution (10 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel. After phase separation, the organic phase was washed with another portion of sat. NH_4Cl solution (10 ml) and the combined aqueous phase extracted with 3:2 THF/Et_2O (10 ml then 5 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid **S-2j** as a white solid. The solid was taken up in benzene (30 ml) and **1a** (182 mg, 0.675 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 2 h. After cooling to room temperature, benzene was removed *in vacuo*. CH_2Cl_2 (30 ml) was added and stirred briefly. The excess ligand **1a** was removed by filtration. To the filtrate was added celite, and the suspension was concentrated *in vacuo*. The celite pad was loaded onto a silica gel column and the product purified by flash chromatography (100% Et_2O – 20% acetone/Et_2O) to afford a white solid (100 mg, 58% over 2 steps) as the pure *cis*-isomer.



TLC (Hexanes:EtOAc 1:1)

R_f = 0.52, visualized by short wave UV.

^{1}H-NMR (500 MHz, acetone-d_6)

δ 7.37 – 7.27 (m, 5H), 5.92 (d, J = 15 Hz, 1H), 4.04 (d, J = 17.5 Hz, 1H), 3.69 (dt, J = 10.5, 6.5 Hz, 1H), 3.29 (d, J = 14.5 Hz, 1H), 3.27 (d, J = 18 Hz, 1H), 2.54 (d, J = 15 Hz, 1H), 2.53-2.48 (m, 1H), 2.43 – 2.39 (m, 1H), 2.00 – 1.98 (m, 1H), 1.97 – 1.94 (m, 1H), 1.85 (dt, J = 6, 2.5 Hz, 1H), 1.50 (ddd, J = 15, 6.5, 2.5 Hz, 1H), 1.25 (s, 3H), 1.02 (s, 3H), 0.99 (d, J = 7 Hz, 3H), 0.82 (d, J = 11 Hz, 1H).

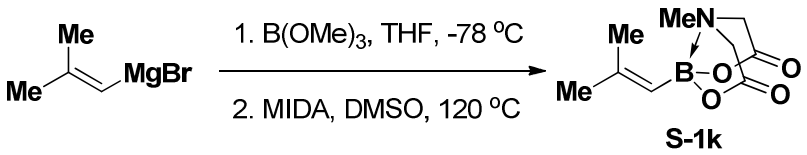
[4] Woerly, E. M.; Struble, J. R.; Palyam, N.; O'Hara, S. P.; Burke M. D. *Tetrahedron* **2011**, *67*, 4333-4343.

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.4, 166.7, 144.8, 139.6, 128.6, 128.0, 127.6, 67.8, 61.5, 55.0, 49.0, 40.7, 38.8, 38.7, 32.1, 30.4, 27.1, 23.3, 23.0.

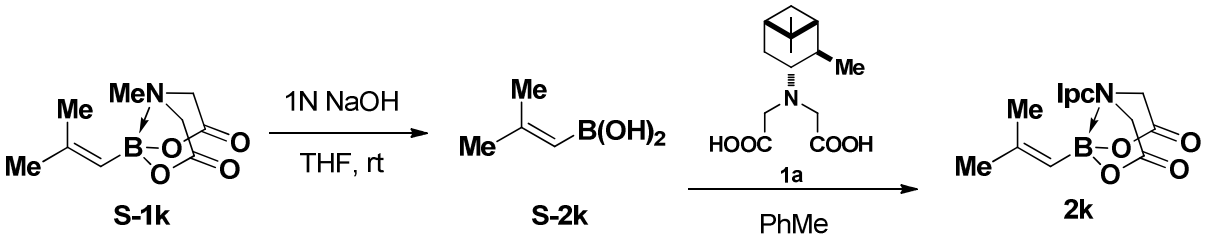
HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_4$:	382.2190
Found:	382.2198

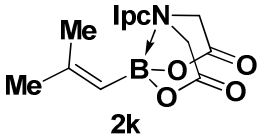


S-1k

MIDA boronate S-1k. To an oven-dried 300-mL 3-neck round-bottomed flask equipped with a magnetic stir bar, two rubber septa (side and center arm) and a thermometer with an adapter (side arm) was added THF (75 mL) and trimethyl borate (6 mL, 53.6 mmol, 1.1 equiv) under an atmosphere of N_2. The solution was cooled to -70 °C (internal temperature) in a dry ice/acetone bath. The Grignard reagent (97.5 mL, 48.75 mmol, 0.50 M in THF) was cannulated directly into the reaction vessel over 30 min. The reaction vessel was removed from the bath after 5 min and allowed to warm to ambient temperature over the course of 3 h resulting in a white slurry. While the slurry of the "ate" complex was warming to ambient temperature, an oven-dried 200-mL 3-neck round-bottomed flask equipped with a magnetic stir bar, a thermometer, a rubber septum and a distillation train (center arm) was charged with MIDA (15.78 g, 107.3 mmol, 2.2 equiv) and DMSO (75 mL). Using a heating mantle and variac, the suspension was brought to an internal temp of 150 °C. The suspension of the "ate" complex was added directly into the DMSO solution of MIDA over the course of 1 h via cannula transfer (Teflon cannula) under a positive pressure of N_2 at a rate such that the internal temperature remained between 120–150 °C. After the addition was completed the reaction vessel was washed with THF (20 mL) and the washes added via cannula transfer to the reaction vessel containing the MIDA solution. The remaining THF and MeOH were allowed to distill off (~15 min). The reaction vessel was allowed to cool to ambient temperature. The reaction mixture was then transferred to a 1 L separatory funnel. To this was added 100 ml of de-ionized water, 100 ml of brine, 150 ml of ethyl acetate, and 100 ml of acetone. After mixing, the organic layer was separated, and the aqueous layer was extracted thrice with 50 mL of 3:2 ethyl acetate: acetone solution. TLC showed no product in the aqueous layer. The combined organic fractions were then washed with 100 mL of brine (3X), and dried by stirring with $MgSO_4$ and Darco. The organic fractions were then concentrated to form a orange-brown oil, which was taken up in 50 ml acetone. Et_2O (400 ml) was slowly added to the acetone solution. 2 phases formed. After vacuum filtration to trap the oil, crystals formed which were recovered by another filtration. The filtrate was concentrated, and the residue taken up in 20 ml of acetone. 100 ml of Et_2O and 100 ml of hexane was added sequentially, and the mixture allowed to crystallize overnight. After filtration, the filtrate was concentrated, the residue taken up in ~ 10 ml acetone, and Et_2O (100 ml) was layered on top and the solution was allowed to stand and crystallize. The crystals were collected by vacuum filtration and the filtrate discarded. An off-white solid was obtained as an inseparable mixture of 2 MIDA boronates (4.43 g, 43%). This mixture was used without further purification for the synthesis of **2k**.



PIDA boronate 2k. In an unoptimized procedure, to a solution of the crude product containing **S-1k** (1.69 g, 8.01 mmol) in THF (80 ml) was added 1N NaOH (24 ml, 24 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was diluted with Et_2O (40 ml) and quenched with the addition of sat. NH_4Cl solution (50 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel. After phase separation, the aqueous phase extracted with 2:1 THF/Et_2O (2 × 30 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid **S-2k**. The solid was taken up in toluene (60 ml) and **1a** (3.23 g, 12.0 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 2 h. After cooling to room temperature, toluene was removed *in vacuo*. CH_2Cl_2 (50 ml) was added and stirred briefly. The excess ligand **1a** was removed by filtration. To the filtrate was added celite, and the suspension was concentrated *in vacuo*. The celite pad was loaded onto a silica gel column and the product purified by flash chromatography (Et_2O – 20% acetone/Et_2O) to afford a white solid (710 mg, 27% over 2 steps) as the pure product.



TLC (Hexanes:EtOAc 1:1)

R_f = 0.30, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

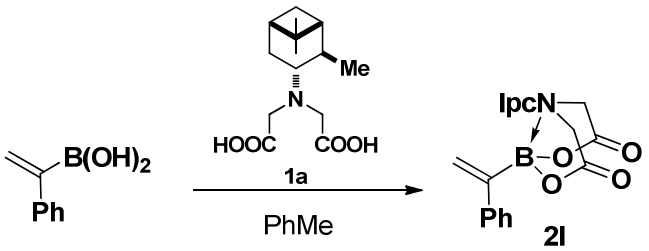
δ 5.12 (s, 1H), 4.10 (d, J = 17 Hz, 1H), 3.76 (d, J = 15.5 Hz, 1H), 3.76 (d, J = 15.5 Hz, 1H), 3.72 (dt, J = 10.5, 6 Hz, 1H), 3.46 (d, J = 17.5 Hz, 1H), 2.47-2.41 (m, 2H), 2.15-2.12 (m, 1H), 1.99-1.98 (m, 1H), 1.91 (dt, J = 6, 2 Hz, 1H), 1.87 (s, 3H), 1.85 (s, 3H), 1.58 (ddd, J = 15, 6, 2 Hz, 1H), 1.30 (d, J = 6.5 Hz, 3H), 1.25 (s, 3H), 0.95 (s, 3H), 0.89 (d, J = 10.5 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

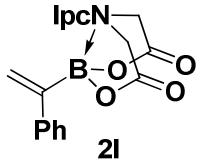
δ 169.6, 166.8, 151.2, 68.5, 61.0, 54.1, 49.1, 40.6, 39.1, 38.9, 32.1, 30.2, 29.7, 27.1, 23.6, 23.3, 21.4

HRMS (ESI+)

Calculated for $C_{18}H_{29}BNO_4$:	334.2190
Found:	334.2191



PIDA boronate 2l. To a solution of 1-phenylvinylboronic acid (296 mg, 2 mmol) was added 1a (808 mg, 3 mmol). The mixture was refluxed with a Dean-Stark trap for 2 h. The reaction was then cooled to 23 °C and concentrated *in vacuo*. The residue was taken up in CH_2Cl_2 and absorbed onto celite. The celite pad was loaded onto a silica gel column and the product purified by flash chromatography (Et_2O – 20% acetone/Et_2O) to give a slightly yellow solid. The solid was triturated with acetone (2 ml) and filtered to obtain a white solid (374 mg, 49%).



TLC (Hexanes:EtOAc 1:1)

R_f = 0.34, visualized by short wave UV

^{1}H-NMR (500 MHz, $CDCl_3$)

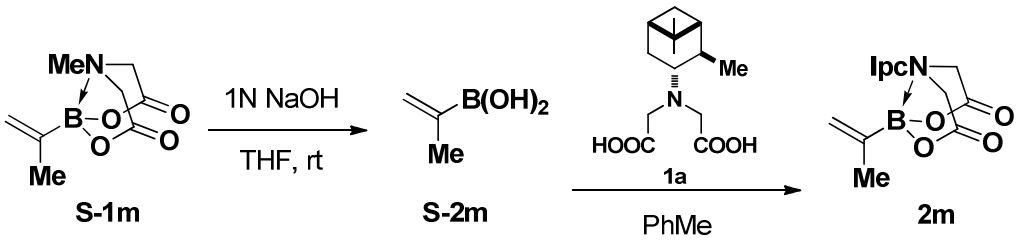
δ 7.37-7.32 (m, 4H), 7.29-7.26 (m, 1H), 5.96 (d, J = 3 Hz, 1H), 5.75 (d, J = 3 Hz, 1H), 4.18 (d, J = 17 Hz, 1H), 3.59 (d, J = 15.5 Hz, 1H), 3.48 (d, J = 17.5 Hz, 1H), 3.48 (m, 1H), 3.25 (d, J = 15.5 Hz, 1H), 2.50-2.45 (m, 1H), 2.39 (ddt, J = 11, 6, 2 Hz, 1H), 1.98-1.94 (m, 1H), 1.81 (dt, J = 6, 2 Hz, 1H), 1.56 (ddd, J = 15.5, 6.5, 2.5 Hz, 1H), 1.21 (s, 3H), 0.94 (d, J = 6.5 Hz, 3H), 0.85 (d, J = 10.5 Hz, 1H), 0.84 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

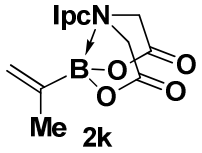
δ 169.1, 166.9, 144.1, 129.3, 128.9, 127.2, 126.8, 67.7, 61.7, 55.3, 48.9, 40.5, 39.0, 38.8, 31.9, 30.0, 27.1, 23.3, 23.1

HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_4$:	382.2190
Found:	382.2192



PIDA boronate 2m. To a solution of **S-1k**[5] (197 mg, 1 mmol) in THF (10 ml) was added 1N NaOH (3 ml, 3 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was quenched with the addition of sat. NH_4Cl solution (10 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel, rinsing with Et_2O (10 ml). After phase separation, the organic phase was washed with another portion of sat. NH_4Cl solution (10 ml) and the combined aqueous phase extracted with 1:1 THF/Et_2O (15 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid **S-2k** as a white solid. (Note: the boronic acid is unstable, should not be dried completely and must be used immediately.) The boronic acid **S-2m** was taken up in toluene (15 ml) and DMSO (0.75 ml) and **1a** (404 mg, 1.5 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 1.5 h. After cooling to room temperature, toluene was removed *in vacuo*. The residue was taken up in 2:1 EtOAc/acetone (15 ml) and washed twice with 1:1 H_2O/brine (10 ml). The aqueous layers were extracted with 2:1 EtOAc/acetone (15 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography, eluting first with Et_2O then with 1:4 acetone/Et_2O to give a white solid as the pure product (153 mg, 48% over 2 steps).



2k

TLC (Hexanes:acetone 3:2)

R_f = 0.44, stained by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 5.57 (br s, 1H), 5.47 (br s, 1H), 4.20, (d, J = 17.5 Hz, 1H), 3.89 (d, J = 16 Hz, 1H), 3.86 (d, J = 16 Hz, 1H), 3.72 (dt, J = 10.5, 6.5 Hz, 1H), 3.62 (d, J = 17.5 Hz, 1H), 2.53 – 2.48 (m, 1H), 2.43 – 2.39 (m, 1H), 2.18 – 2.15 (m, 1H), 1.97 – 1.96 (m, 1H), 1.89 (dt, J = 6, 2 Hz, 1H), 1.86 (s, 3H), 1.56 (ddd, J = 15, 6, 2.5 Hz, 1H), 1.30 (d, J = 7 Hz, 3H), 1.23 (s, 3H), 0.92 (s, 3H), 0.89 (d, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.6, 166.9, 126.0, 68.8, 61.4, 55.2, 49.0, 40.5, 39.1, 38.8, 31.9, 30.3, 27.0, 23.8, 23.4, 22.0.

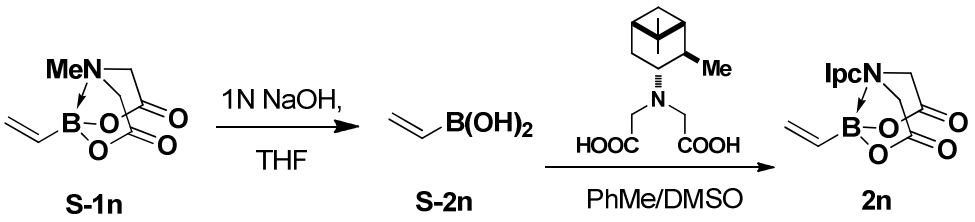
^{11}B-NMR (100 MHz, acetone-d_6)

δ 11.6

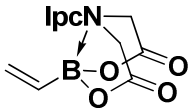
HRMS (ESI+)

Calculated for $C_{17}H_{27}BNO_4$:	320.2033
Found:	320.2034

[5] Woerly, E. M.; Cherney, A. H.; Davis, E. K.; Burke, M. D. *J. Am. Chem. Soc.* **2010**, *132*, 6941-6943. This compound is also available from Sigma-Aldrich (product no. 707252).



To a solution of **S-1h**[6] (183 mg, 1 mmol) in THF (10 ml) was added 1N NaOH (3 ml, 3 mmol) under ambient atmosphere and temperature and stirred vigorously for 15 min. The reaction was quenched with the addition of sat. NH_4Cl solution (10 ml). The mixture was stirred for 3 min, then transferred to a separatory funnel, rinsing with Et_2O (10 ml). After phase separation, the organic phase was washed with another portion of sat. NH_4Cl solution (10 ml) and the combined aqueous phase extracted with 1:1 THF/Et_2O (15 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the boronic acid as a white solid. The solid was taken up in toluene (15 ml) and DMSO (0.75 ml) and **1a** (404 mg, 1.5 mmol) was added. The reaction was heated to reflux with a Dean-Stark trap for 1.5 h. After cooling to room temperature, toluene was removed *in vacuo*. The residue was taken up in 2:1 EtOAc/acetone (15 ml) and washed twice with 1:1 H_2O/brine (10 ml). The aqueous layers were extracted with 2:1 EtOAc/acetone (15 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography, eluting first with Et_2O then with 1:4 acetone/Et_2O to give a white solid as the pure product (153 mg, 55% over 2 steps).



2n

TLC (Hexanes:acetone 3:2)

R_f = 0.39, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 6.04 (dd, J = 19.5, 14 Hz, 1H), 5.11 (dd, J = 13.5, 3.5 Hz, 1H), 5.84 (dd, J = 19, 3.5 Hz, 1H), 4.15 (d, J = 17.5 Hz, 1H), 3.78 (d, J = 15.5 Hz, 1H), 3.73 (d, J = 15.5 Hz, 1H), 3.67 (dt, J = 13, 6.5 Hz, 1H), 3.46 (d, J = 17.5 Hz, 1H), 2.52 – 2.43 (m, 2H), 2.14 (dquint, J = 7, 2 Hz, 1H), 2.02 (sept, J = 3 Hz, 1H), 1.92 (dt, J = 6, 2 Hz, 1H), 1.67 (ddd, J = 15, 6, 2.5 Hz, 1H), 1.30 (d, J = 7 Hz, 3H), 1.26 (s, 3H), 0.95 (s, 3H), 0.90 (d, J = 11 Hz, 1H).

^{13}C-NMR (125 MHz, acetone-d_6)

δ 170.2, 167.8, 130.1, 68.6, 61.0, 55.2, 50.2, 41.6, 39.6, 39.2, 32.3, 31.0, 27.4, 23.6.

^{11}B-NMR (100 MHz, acetone-d_6)

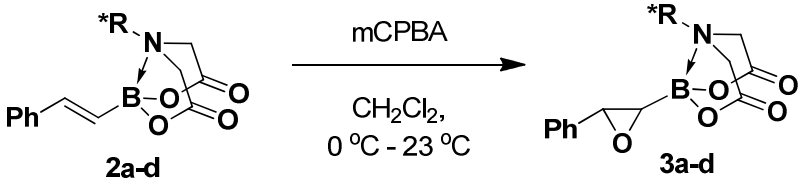
δ 11.3

HRMS (ESI+)

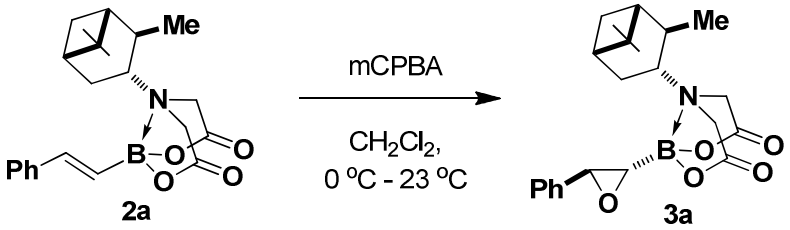
Calculated for $C_{16}H_{25}BNO_4$:	306.1877
Found:	306.1872

[6] Uno, B. E.; Gillis, E. P., Burke, M. D. *Tetrahedron.* **2009**, *65*, 3130-3138. This compound is also available fom Sigma-Aldrich (product no. 704415).

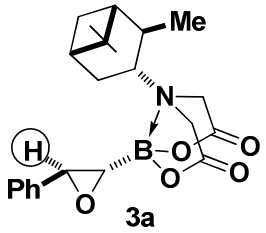
c. Synthesis of 3a – 3n

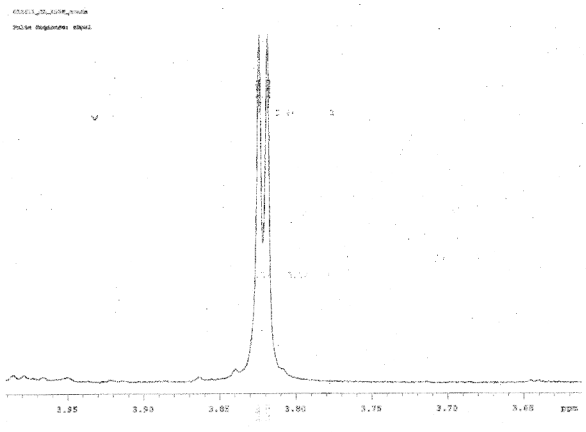


General procedure for the epoxidation of boronate esters 2a-d (Table 1):
To a solution of the boronate ester **2** (0.1 mmol) in CH_2Cl_2 at 0 °C was added mCPBA (max 77%, 43 mg, 0.19 mmol) portionwise over 3 min under ambient atmosphere. The reaction was stirred for 12 h, gradually raising the temperature to rt. The reaction was then concentrated *in vacuo* at 20 °C, and ^{1}H-NMR analysis was carried out. Conversions for all 4 substrates (**2a-d**) are >95%. The peaks from the protons on the epoxide were used to determine the d.r. Note that except for **3a** for which all stereogenic centers have been assigned, the stereochemistry of the epoxide shows only the *relative* i.e. *trans* configuration of the epoxide substituents.



Epoxide **3a**. The general procedure was followed using boronate ester **2a** (38 mg, 0.1 mmol) and mCPBA (43 mg, 0.19 mmol). d.r. >20:1





TLC (Hexanes:acetone 3:2)

R_f = 0.46, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.40-7.35 (m, 4H), 7.33-7.30 (m, 1H), 4.40 (dt, *J* = 10.5, 3.5 Hz, 1H), 4.36 (d, *J* = 18 Hz, 1H), 4.22 (d, *J* = 15 Hz, 1H), 4.14 (d, *J* = 17.5 Hz, 1H), 4.12 (d, *J* = 17.5 Hz, 1H), 3.83 (d, *J* = 2.5 Hz, 1H), 2.92-2.86 (m, 1H), 2.62-2.57 (m, 1H), 2.57 (d, *J* = 2.5 Hz, 1H), 2.53-2.47 (m, 1H), 2.11-2.08 (m, 1H), 2.00 (dt, *J* = 5.5, 2 Hz, 1H), 1.85 (ddd, *J* = 14.5, 4, 2.5 Hz, 1H), 1.45 (d, *J* = 6.5 Hz, 3H), 1.31 (s, 3H), 1.14 (d, *J* = 11 Hz, 1H), 1.10 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

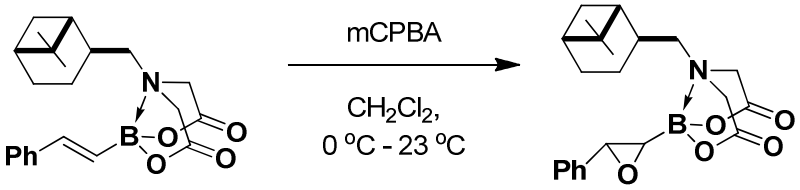
δ 169.1, 166.4, 137.9, 128.5, 128.1, 125.5, 68.1, 61.8, 56.7, 54.7, 49.0, 40.6,. 39.2, 39.0, 32.1, 30.6, 27.1, 23.5, 23.5

^{11}B-NMR (128 MHz, $CDCl_3$)

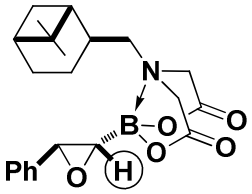
δ 10.5

HRMS (ESI+)

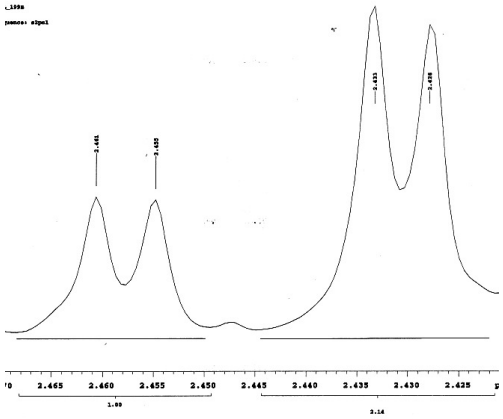
Calculated for $C_{22}H_{29}BNO_5$:	398.2139
Found:	398.2135

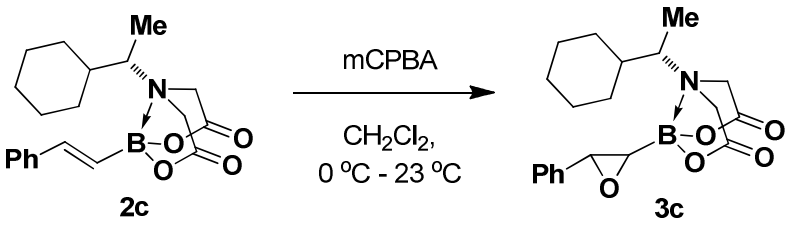


Epoxide **3b**. The general procedure was followed using boronate ester **2b** (38 mg, 0.1 mmol) and mCPBA (43 mg, 0.19 mmol). d.r. = 1.86:1



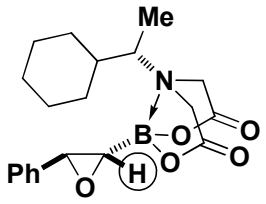
3b



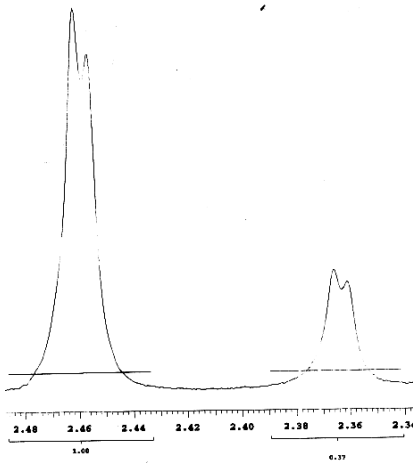


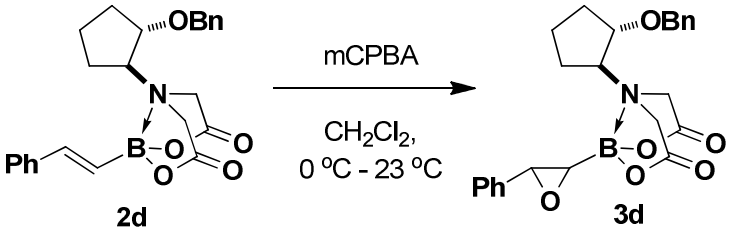
2c **3c**

Epoxide **3c**. The general procedure was followed using boronate ester **2c** (36 mg, 0.1 mmol) and mCPBA (43 mg, 0.19 mmol). d.r. = 2.7:1



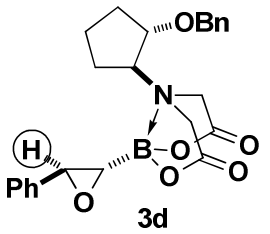
3c



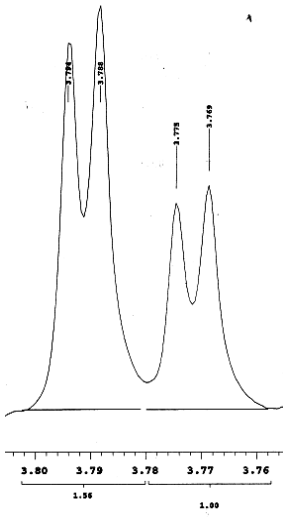


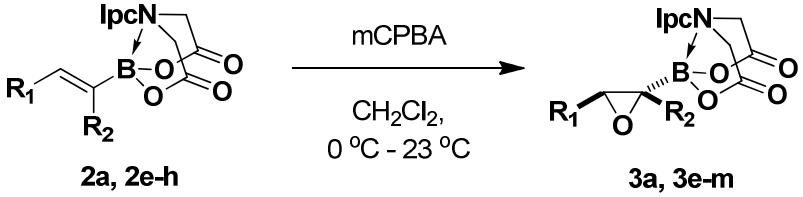
2d **3d**

Epoxide **3d**. The general procedure was followed using boronate ester **2d** (42 mg, 0.1 mmol) and mCPBA (43 mg, 0.19 mmol). d.r. = 1.56:1



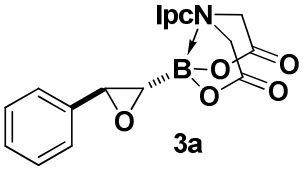
3d





2a, 2e-h 3a, 3e-m

General procedure for the epoxidation of boronate esters 3a, 3e-n (Table 2):
To a solution of the PIDA boronate **2** (0.25 mmol) in CH_2Cl_2 at 0 °C was added mCPBA (max 77%, 106 mg, 0.475 mmol) portionwise over 3 min under ambient atmosphere. The reaction was stirred for 2.5-12 h, gradually raising the temperature to rt in the ice/water bath. The reaction was then concentrated *in vacuo* at 20 °C, and ^{1}H-NMR analysis of the crude reaction mixture was performed to determine the d.r. The crude product was then purified by chromatography on a silica gel or florisil column.



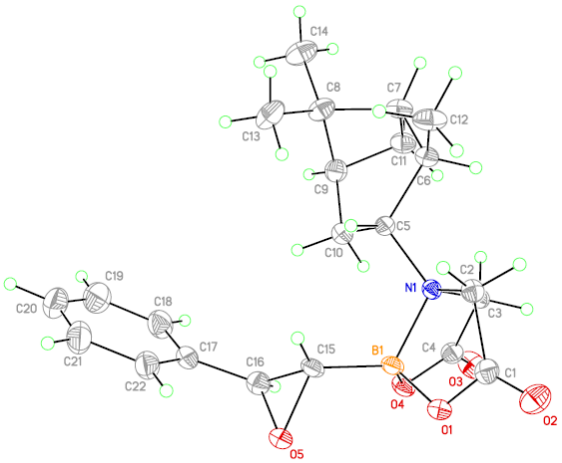
3a

Epoxide 3a. The general procedure was followed using boronate ester **2e** (95 mg, 0.25 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After

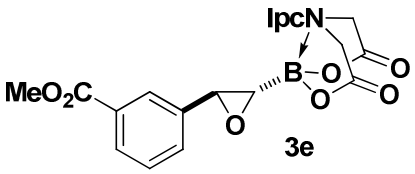
concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (53 mg, 53%). d.r. >20:1. X-ray quality crystals were obtained by making a saturated solution of **3e** in 1 ml of 1,2-dichloroethane and layering it with about 2 ml of hexane. The layers were allowed to slowly mix at room temperature, giving the desired crystals.

The epoxidation of **2a** was also carried out on a 15 mmol scale as follows: A solution of boronate ester **2a** (5.72 g, 15 mmol) in CH_2Cl_2 (300 ml) was cooled to 0 °C. mCPBA (max 77%, 4.47 g, 20 mmol) was added portionwise under ambient atmosphere over 10 min. The reaction was stirred for 8 h, maintaining the bath temperature at 0-10 °C. The reaction was then concentrated to approximately 50 ml of CH_2Cl_2, and Et_2O was added (150 ml). The solution was stirred vigorously for 5 min, and the white solid (crude product) formed was obtained by vacuum filtration. The filtrate was concentrated to approximately 20 ml of CH_2Cl_2 and Et_2O (100 ml) and hexane (50 ml) was added. The white solid formed was collected by vacuum filtration. The filtrate, containing mostly mCPBA, *m*-chlorobenzoic acid and other non-polar impurities, was discarded. The combined white solid was dissolved in a minimum amount of CH_2Cl_2 in a 250 ml Erlenmeyer flask and layered with hexane (CH_2Cl_2:hexane 1:2). The flask was then cooled to -20 °C in a freezer. This recrystallized product was then collected by vacuum filtration and washed with CH_2Cl_2/hexane 1:10. The white solid was then dried *in vacuo* (3.87 g, 65%). Spectral data are identical to that obtained in the reaction in Table 1.

X-ray quality crystals were obtained by making a saturated solution of **3a** in 1 ml of 1,2-dichloroethane and layering it with about 2 ml of hexane. The layers were allowed to slowly mix at room temperature, giving the desired crystals.



3a



3e

Epoxide 3e. The general procedure was followed using boronate ester **2e** (88 mg, 0.2 mmol) and mCPBA (69 mg, 0.4 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2, absorbed onto celite and loaded onto a silica gel column equilibrated with 50% Et_2O/hexane. The non-polar impurities were eluted with 50% Et_2O/hexane. The product was then eluted with 30% EtOAc/hexanes. After

concentration at room temperature, the solid was washed with Et_2O:hexanes 1:1 (5 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (65 mg, 71%). d.r. >20:1.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.33, visualized by UV/vis or $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

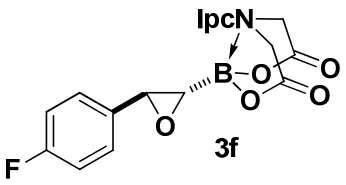
δ 7.98-7.97 (m, 2H), 7.50-7.49 (m, 1H), 7.44-7.41 (m, 1H), 4.39 (dt, J = 10, 6.5 Hz, 1H), 4.25 (d, J = 17.5 Hz, 1H), 4.06 (d, J = 15 Hz, 1H), 4.01 (d, J = 2.5 Hz, 1H), 3.92 (s, 3H), 3.74 (d, J = 15.5 Hz, 1H), 3.49 (d, J = 17 Hz, 1H), 2.76 -2.71 (m, 1H), 2.53-2.45 (m, 1H), 2.49 (d, J = 2.5 Hz, 1H), 2.22-2.20 (m, 1H), 2.08-2.07 (m, 1H), 1.99-1.97 (m, 1H), 1.84 (ddd, J = 15, 5.5, 2.5 Hz, 1H), 1.39 (d, J = 6.5 Hz, 3H), 1.30 (s, 3H), 1.11 (s, 3H), 0.95 (d, J = 11 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.2, 166.8, 166.5, 138.6, 130.5, 130.1, 129.9, 128.6, 126.6, 68.3, 61.7, 56.3, 54.7, 52.2, 49.1, 40.6, 39.2, 38.9, 32.1, 30.6, 27.0, 23.6, 23.5.

HRMS (ESI+)

Calculated for $C_{24}H_{31}BNO_7$:	456.2194
Found:	456.2196



3f

Epoxide 3f. The general procedure was followed using boronate ester **2e** (80 mg, 0.2 mmol) and mCPBA (69 mg, 0.4 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2, absorbed onto celite and loaded onto a silica gel column equilibrated with 50% Et_2O/hexane. The non-polar impurities were eluted with 50% Et_2O/hexane, then with 80% Et_2O/hexanes. The product was then eluted with 30% EtOAc/hexanes. The epoxide was then dried *in vacuo*, giving the product as a white solid (43 mg, 52%). d.r. >17:1.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.39, visualized by UV/vis or $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

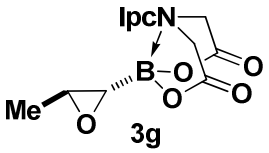
δ 7.27 – 7.25 (m, 2H), 7.05 – 7.01 (m, 2H), 4.38 (dt, J = 10, 6.5 Hz, 1H), 4.24 (d, J = 17.5 Hz, 1H), 4.05 (d, J = 15 Hz, 1H), 3.94 (d, J = 3 Hz, 1H), 3.72 (d, J = 15 Hz, 1H), 3.48 (d, J = 17.5 Hz, 1H), 2.74 – 2.69 (m, 1H), 2.50 (ddt, J = 11, 6, 2 Hz, 1H), 2.45 (d, J = 3 Hz, 1H), 2.22 – 2.17 (m, 1H), 2.09-2.05 (m, 1H), 1.98 (dt, J = 6.5, 2.5 Hz, 1H), 1.84 (ddd, J = 15, 6, 2.5 Hz, 1H), 1.38 (d, J = 6.5 Hz, 3H), 1.30 (s, 3H), 1.09 (s, 3H), 0.94 (d, J = 11 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.2, 166.5, 163.9, 133.9, 127.4 (d, J = 7.8 Hz), 115.7 (d, J = 21.4 Hz), 68.4, 62.0, 56.5, 55.0, 49.3, 40.9, 39.5, 39.2, 32.4, 30.9, 27.3, 23.8, 23.7.

HRMS (ESI+)

Calculated for $C_{22}H_{28}BNO_5F$:	416.2045
Found:	416.2052



3g

Epoxide 3g. The general procedure was followed using boronate ester **2g** (80 mg, 0.25 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (51 mg, 64%). d.r. >20:1.

TLC (Hexanes:acetone 3:2)

R_f = 0.46, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 4.29 (dt, *J* = 10.5, 6.5 Hz, 1H), 4.20 (d, *J* = 17 Hz, 1H), 3.98 (d, *J* = 15 Hz, 1H), 3.65 (d, *J* = 15 Hz, 1H), 3.42 (d, *J* = 17 Hz, 1H), 3.07 (m, 1H), 2.72-2.66 (m, 1H), 2.51-2.45 (m, 1H), 2.17-2.14 (m, 1H), 2.12 (d, *J* = 3 Hz, 1H), 2.05 (sept, *J* = 3 Hz, 1H), 1.94 (dt, *J* = 6, 2.5 Hz, 1H), 1.81 (ddd, *J* = 15, 6. 2.5 Hz, 1H), 1.37 (d, *J* = 5 Hz, 3H), 1.33 (d, *J* = 7 Hz, 3H), 1.27 (s, 3H), 1.04 (s, 3H), 0.92 (d, *J* = 10 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.2, 166.3, 109.7, 67.9, 61.7, 54.6, 53.2, 49.0, 40.6, 39.2, 38.9, 32.1, 30.5, 27.0, 23.6, 23.5.

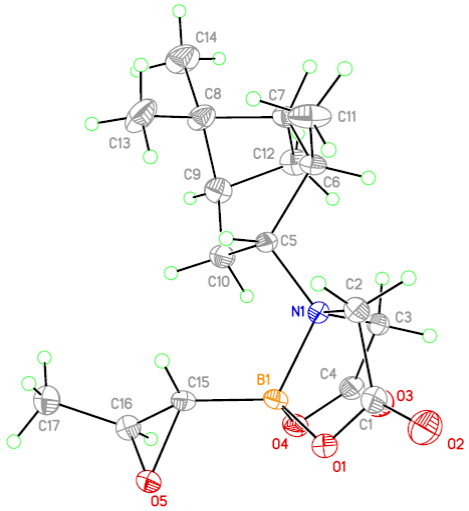
^{11}B-NMR (128 MHz, $CDCl_3$)

δ 10.7

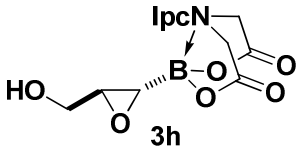
HRMS (ESI+)

Calculated for $C_{17}H_{27}BNO_5$:	336.1982
Found:	336.1977

X-ray quality crystals were obtained by making a saturated solution of **3g** in 1 ml of 1,2-dichloroethane and layering it with about 2 ml of hexane. The layers were allowed to slowly mix at room temperature, giving the desired crystals.



3g



3h

Epoxide 3h. The general procedure was followed using boronate ester **2h** (84 mg, 0.25 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (68 mg, 77%). d.r. >20:1.

TLC (Hexanes:acetone 3:2)

R_f = 0.22, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, acetone-d_6)

δ 4.29 (d, *J* = 18 Hz, 1H), 4.30-4.26 (m, 1H), 4.13 (d, *J* = 15.5 Hz, 1H), 4.06 (d, *J* = 18.5 Hz, 1H), 3.98 (d, *J* = 15.5 Hz, 1H), 3.02 (dt, *J* = 6, 3 Hz, 1H), 2.80-2.74 (m, 1H), 2.57-2.51 (m, 1H), 2.50-2.44 (m, 1H), 1.97 (dt, *J* = 6, 2.5 Hz, 1H), 1.79 (ddd, *J* = 15, 6. 2.5 Hz, 1H), 1.39 (d, *J* = 7.5 Hz, 3H), 1.28 (s, 3H), 1.10 (d, *J* = 10.5 Hz, 1H), 1.05 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

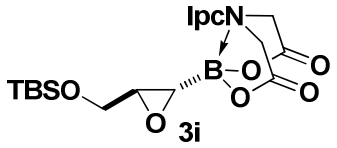
δ 170.7, 167.2, 68.8, 64.1, 61.9, 57.8, 55.4, 50.2, 41.6, 39.7, 39.1, 32.3, 31.2, 27.4, 23.9, 23.7.

^{11}B-NMR (128 MHz, acetone-d_6)

δ 10.8

HRMS (ESI+)

Calculated for $C_{17}H_{27}BNO_6$:	352.1931
Found:	352.1925



Epoxide 3i. The general procedure was followed using boronate ester **2i** (45 mg, 0.1 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (35 mg, 75%). d.r. >20:1.

TLC (Hexanes:acetone 3:2)

R_f = 0.51, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 4.31 (dt, *J* = 10.5, 6 Hz, 1H), 4.21 (d, *J* = 18 Hz, 1H), 4.01 (dd, *J* = 12.5, 2.5 Hz, 1H), 3.99 (d, *J* = 15.5 Hz, 1H), 3.64 (d, *J* = 15 Hz, 1H), 3.63 (dd, *J* = 12.5, 4.5 Hz, 1H), 3.42 (d, *J* = 17 Hz, 1H), 3.17 (quint, *J* = 3 Hz, 1H), 2.70-2.65 (m, 1H), 2.50-2.46 (m, 1H), 2.39 (d, *J* = 3 Hz, 1H), 2.16-2.15 (m, 1H), 2.05 (sept, *J* = 3 Hz, 1H), 1.95 (dt, *J* = 6.5, 2.5 Hz, 1H), 1.81 (ddd, *J* = 15, 6, 3 Hz, 1H), 1.33 (d, *J* = 6.5 Hz, 3H), 1.27 (s, 3H), 1.02 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

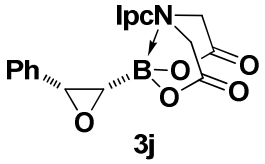
δ 169.2, 166.3, 67.9, 63.2, 61.7, 57.2, 54.6, 49.0, 40.6, 39.2, 38.9, 32.0, 30.5, 27.0, 25.9, 23.5, 23.5, 18.3, -5.3, -5.4.

^{11}B-NMR (128 MHz, $CDCl_3$)

δ 11.3

HRMS (ESI+)

Calculated for $C_{23}H_{41}BNO_6Si$:	466.2796
Found:	466.2798



Epoxide 3j. The general procedure was followed using PIDA boronate **2j** (38 mg, 0.1 mmol) and mCPBA (35 mg, 0.2 mmol) with a reaction time of 11 h. The crude product was purified with a florisil column (80% Et_2O/hexane, then 20% - 40% EtOAc/hexane), giving the product as a white solid (38 mg, 96%). d.r. = 17:1.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.4, stained by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

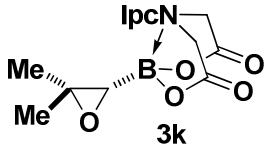
δ 7.36-7.28 (m, 5H), 4.42 (dt, J = 10, 7 Hz, 1H), 4.33 (d, J = 5 Hz, 1H), 4.10 (d, J = 17.5 Hz, 1H), 3.66 (d, J = 15 Hz, 1H), 3.54 (d, J = 15 Hz, 1H), 3.30 (d, J = 17 Hz, 1H), 2.77 – 2.71 (m, 1H), 2.72 (d, J = 5.5 Hz, 1H), 2.47 (ddt, J = 11, 6, 2 Hz, 1H), 2.13 – 2.10 (m, 1H), 2.08 – 2.05 (m, 1H), 1.95 (dt, J = 6, 2 Hz, 1H), 1.80 (ddd, J = 14.5, 6, 2.5 Hz, 1H), 1.34 (d, J = 7 Hz, 3H), 1.29 (s, 3H), 1.10 (s, 3H), 0.89 (d, J = 7 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.1, 165.2, 136.6, 128.2, 127.5, 125.7, 67.8, 61.3, 57.9, 54.5, 49.0, 40.6, 39.1, 39.0, 32.1, 30.5, 27.1, 23.5, 23.4.

HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_5$:	398.2139
Found:	398.2141



3k

Epoxide 3k. The general procedure was followed using boronate ester **2k** (83 mg, 0.25 mmol) and mCPBA (86 mg, 0.5 mmol). The reaction was stopped **after 2.5 h**. The crude product was then taken up in 15 ml of CH_2Cl_2, absorbed onto celite, concentrated *in vacuo* and loaded onto a silica gel column. The product was purified by silica gel chromatography (50% Et_2O/hexanes to 80% Et_2O/hexanes to 30% EtOAc/hexanes). The product was obtained as a white solid (43 mg, 49%). d.r. >20:1.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.42, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

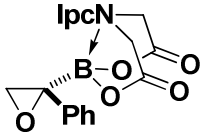
δ 4.28 (dt, J = 10.5, 6 Hz, 1H), 4.18 (d, J = 17.5 Hz, 1H), 3.90 (d, J = 15 Hz, 1H), 3.72 (d, J = 15 Hz, 1H), 3.48 (d, J = 17.5 Hz, 1H), 2.65 – 2.60 (m, 1H), 2.48 – 2.44 (m, 1H), 2.18 (s, 1H), 2.18-2.15 (m, 1H), 2.06 – 2.03 (m, 1H), 1.93 (dt, J = 5.5, 1.5 Hz, 1H), 1.78 (ddd, J = 15, 6.5, 3 Hz, 1H), 1.41 (s, 3H), 1.39 (s, 3H), 1.32 (d, J = 6.5 Hz, 3H), 1.26 (s, 3H), 1.02 (s, 3H), 0.94 (d, J = 11 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.4, 166.2, 67.7, 61.4, 60.1, 54.4, 49.0, 40.7, 39.2, 38.9, 31.9, 30.5, 27.2, 27.0, 23.5 (2C), 20.4

HRMS (ESI+)

Calculated for $C_{18}H_{29}BNO_5$:	350.2139
Found:	350.2138



3l

Epoxide 3l. The general procedure was followed using boronate ester **2l** (95 mg, 0.25 mmol) and mCPBA (86 mg, 0.5 mmol). The crude product was then taken up in 10 ml of CH_2Cl_2, absorbed onto celite, concentrated *in vacuo* and loaded onto a silica gel column. The product was purified by silica gel chromatography (50% Et_2O/hexanes to 30% EtOAc/hexanes to 35% EtOAc/hexanes). The product was obtained as a white solid (74 mg, 75%). d.r. (isolated product) 14:1, d.r. (crude product) = 11:1. Note: d.r. was increased slightly after column purification.

TLC (Hexanes:EtOAc 1:1)

R_f = 0.47, stained by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

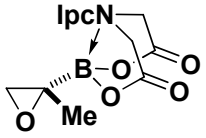
δ 7.54 (d, J = 7 Hz, 2H), 7.31 – 7.27 (m, 2H), 7.22 (dt, J = 7.5, 2 Hz, 1H), 4.24 (d, J = 14.5 Hz, 1H), 4.09 (d, J = 17 Hz, 1H), 4.02 (dt, J = 10.5, 6 Hz, 1H), 3.68 (d, J = 14.5 Hz, 1H), 3.49 (d, J = 17 Hz, 1H), 3.27 (d, J = 7 Hz, 1H), 2.51 (d, J = 6.5 Hz, 1H), 2.29 (ddt, J = 11, 6, 2 Hz, 1H), 2.09 – 2.03 (m, 1H), 1.82 (dt, J = 5.5, 2 Hz, 1H), 1.56 (sept, J = 3.5 Hz, 1H), 1.33 (d, J = 6.5 Hz, 3H), 1.11 (s, 3H), 1.08 (dd, J = 6, 2.5 Hz, 1H), 1.00 – 0.95 (m, 1H), 0.77 (d, J = 11 Hz, 1H), 0.72 (s, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.7, 166.9, 141.4, 128.8, 127.2, 125.2, 67.6, 61.3, 57.7, 55.3, 49.1, 41.0, 39.7, 39.0, 32.0, 29.4, 27.1, 24.0, 23.9.

HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_5$:	398.2139
Found:	398.2141



3m

Epoxide 3h. The general procedure was followed using boronate ester **2h** (80 mg, 0.25 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (49 mg, 49%). d.r. 10:1.

TLC (Hexanes:acetone 3:2)

R_f = 0.40, stained by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 4.54 (dt, J = 10.5, 6.5 Hz, 1H), 4.22 (d, J = 17.5 Hz, 1H), 3.89 (d, J = 15 Hz, 1H), 3.64 (d, J = 15 Hz, 1H), 3.40 (d, J = 17 Hz, 1H), 2.85 (d, J = 5.5 Hz, 1H), 2.71 (m, 1H), 2.58 (d, J = 5 Hz, 1H), 2.49-2.45 (m, 1H), 2.13 (m, 1H), 2.07 (sept, J = 3 Hz, 1H), 1.94 (dt, J = 6, 2 Hz, 1H), 1.74 (ddd, J = 15, 6. 2.5 Hz, 1H), 1.39 (s, 3H), 1.32 (d, J = 7 Hz, 3H), 1.27 (s, 3H), 1.04 (s, 3H), 0.93 (d, J = 11 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

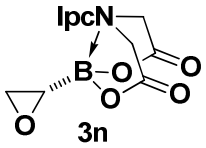
δ 169.3, 166.3, 67.3, 61.4, 55.3, 54.9, 49.0, 40.7, 39.3, 39.0, 32.0, 30.6, 27.0, 23.5, 23.4, 21.2

^{11}B-NMR (96 MHz, $CDCl_3$)

δ 10.8

HRMS (ESI+)

Calculated for $C_{17}H_{27}BNO_5$:	336.1982
Found:	336.1976



3n

Epoxide 3n. The general procedure was followed using boronate ester **2h** (76 mg, 0.25 mmol) and mCPBA (106 mg, 0.475 mmol). The crude product was then taken up in a minimum amount of CH_2Cl_2 and loaded onto a silica gel column equilibrated with 30% Et_2O/hexane. The non-polar impurities were eluted with 30% Et_2O/hexane. The product was then eluted with 2:2:6 (acetone/Et_2O/hexane). After concentration at room temperature, the solid was washed with Et_2O (5-10 ml) to remove residual mCPBA and vacuum filtered. The epoxide was then dried *in vacuo*, giving the product as a white solid (66 mg, 82%). d.r. >20:1.

TLC (Hexanes:acetone 3:2)

R_f = 0.43, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 4.29 (dt, *J* = 10.5, 6.5 Hz, 1H), 4.22 (d, *J* = 17.5 Hz, 1H), 3.98 (d, *J* = 15 Hz, 1H), 3.68 (d, *J* = 15 Hz, 1H), 3.48 (d, *J* = 17 Hz, 1H), 2.87 (dd, *J* = 6, 5 Hz, 1H), 2.78 (dd, *J* = 6, 3.5 Hz, 1H), 2.72-2.66 (m, 1H), 2.51-2.45 (m, 1H), 2.39 (dd, *J* = 5, 3.5 Hz, 1H), 2.18-2.17 (m, 1H), 2.06 (sept, *J* = 3 Hz, 1H), 1.95 (dt, *J* = 6, 2 Hz, 1H), 1.83 (ddd, *J* = 15, 6. 2.5 Hz, 1H), 1.34 (d, *J* = 7 Hz, 3H), 1.27 (s, 3H), 1.03 (s, 3H), 0.92 (d, *J* = 11 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 169.5, 166.6, 68.1, 61.6, 54.7, 49.0, 45.5, 40.6, 39.2, 38.9, 32.0, 30.5, 27.0, 23.5, 23.5.

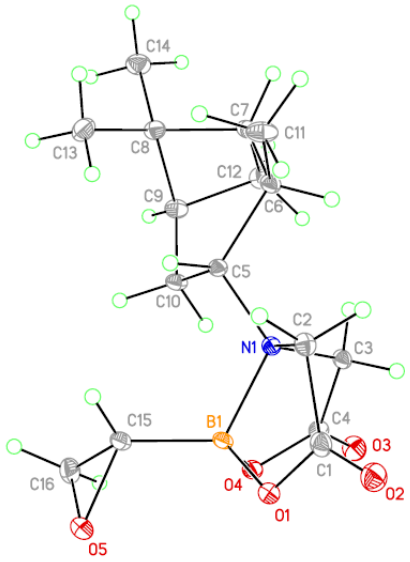
^{11}B-NMR (128 MHz, $CDCl_3$)

δ 11.0

HRMS (ESI+)

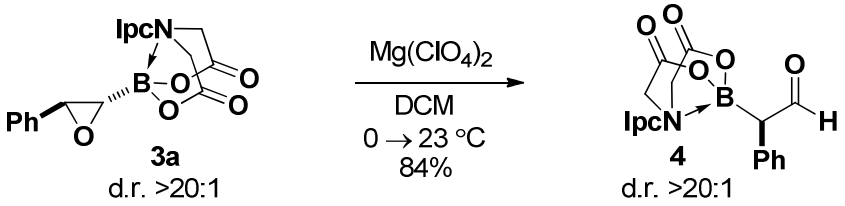
Calculated for $C_{16}H_{25}BNO_5$:	322.1826
Found:	322.1824

X-ray quality crystals were obtained by making a saturated solution of **3h** in 1 ml of 1,2-dichloroethane and layering it with about 2 ml of hexane. The layers were allowed to slowly mix at room temperature, giving the desired crystals.

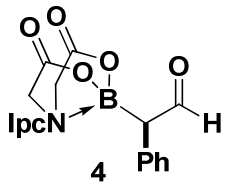


3h

d. Synthesis of 4 – 12 and racemic 12



Aldehyde 4. A dry Schlenk flask was charged with **3a** (795 mg, 2 mmol) and dry CH_2Cl_2 (40 ml) under a nitrogen atmosphere. The flask was flushed with nitrogen and cooled to 0 °C. $Mg(ClO_4)_2$ (2 mmol) was then added in one portion, and the reaction was stirred in the ice/water bath for 2 h. The reaction was then warmed up to room temperature and filtered through celite, washing with additional CH_2Cl_2 (20 ml). The filtrate was then concentrated *in vacuo* at room temperature to afford an off-white solid. No purification of this product was necessary for subsequent reactions. Note: the stereogenic α-carbon of the aldehyde epimerizes on silica gel.



4

^{1}H-NMR (500 MHz, acetone-d_6)

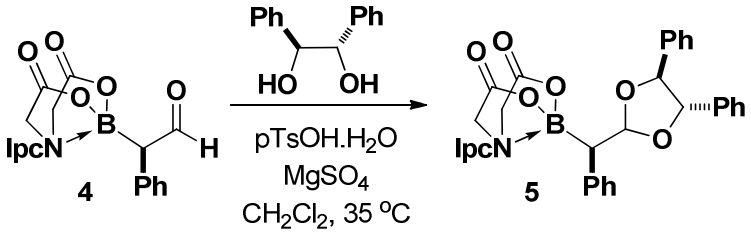
δ 9.88 (d, *J* = 2.5 Hz, 1H), 7.45 (dd, *J* = 7, 1.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 2H), 7.32 (tt, *J* = 7.5, 1.5 Hz, 1H), 4.29 (d, *J* = 18 Hz, 1H), 4.07 (d, *J* = 18 Hz, 1H), 4.04 (d, *J* = 15.5 Hz, 1H), 3.93 (br s, 1H), 3.66 (d, *J* = 10.5, 6 Hz, 1H), 2.98-2.92 (m, 1H), 2.86 (d, *J* = 15.5 Hz, 1H), 2.45 (ddt, *J* = 11, 6, 2 Hz, 1H), 2.38 (ddt, *J* = 13, 6.5, 2 Hz, 1H), 2.11 (sept, *J* = 3 Hz, 1H), 1.88-1.86 (m, 1H), 1.85-1.83 (m, 1H), 1.26 (s, 3H), 1.08 (d, *J* = 11 Hz, 1H), 0.99 (s, 3H), 0.93 (d, *J* = 7 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 199.9, 168.5, 166.1, 134.4, 129.4, 128.7, 127.4, 67.0, 61.6, 55.3, 48.8, 40.6, 38.8, 38.6, 31.6, 30.3, 27.0, 23.1, 23.0.

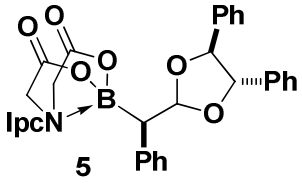
HRMS (ESI+)

Calculated for $C_{22}H_{29}BNO_5$:	398.2139
Found:	398.2140



4

Acetal 6. A 40ml vial equipped with a stir bar was charged with aldehyde **4** (397 mg, 1 mmol), (S,S)-hydrobenzoin (643 mg, 3 mmol) and $MgSO_4$ (1 g). CH_2Cl_2 (20 ml) was added, followed by pTsOH•H_2O (3.8 mg, 0.02 mmol). The vial was flushed briefly with nitrogen and placed in a heat block. The reaction was stirred at 35 °C for 3 h. After cooling to room temperature, the suspension was filtered through celite and the filtrate was concentrated *in vacuo*. The crude product was purified by silica gel chromatography (acetone/Et_2O/hexane 1:4:15 →1:2:7 →1:1:3) to afford 6 (394 mg, 66%) as a white solid.



5

TLC (Hexanes:EtOAc:Et_2O 2:2:1)

R_f = 0.69, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.61, (app d, *J* = 6.5 Hz, 2H), 7.38 (app t, *J* = 7.5 Hz, 2H), 7.32-7.25 (m, 7H), 7.19-7.17 (m, 2H), 7.15-7.13 (m, 2H), 6.04 (d, *J* = 2.5 Hz, 1H), 4.75 (d, *J* = 8 Hz, 1H), 4.31 (d, *J* = 8 Hz, 1H), 4.17

(d, *J* = 17.5 Hz, 1H), 3.79 (dt, *J* = 10, 6 Hz, 1H), 3.44 (d, *J* = 15 Hz, 1H), 3.42 (d, *J* = 17 Hz, 1H), 3.00 (d *J* = 2.5 Hz, 1H), 2.92 (d, *J* = 15 Hz, 1H), 2.77-2.72 (m, 1H), 2.44-2.42 (m, 1H), 2.07 (m, 1H), 1.96 (m, 1H), 1.85-1.81 (m, 2H), 1.26 (s, 3H), 0.96 (s, 3H), 0.91-0.89 (m, 4H).

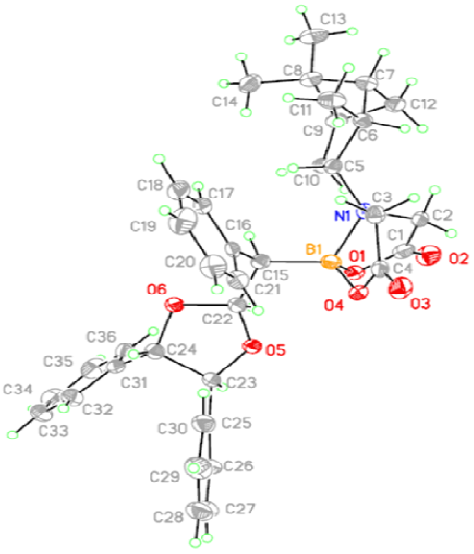
^{13}C-NMR (125 MHz, $CDCl_3$)

δ 168.9, 166.5, 138.7, 137.7, 136.5, 130.8, 128.6, 128.4, 128.3, 128.2, 127.9, 127.2, 126.9, 126.4, 106.1, 87.4, 84.9, 66.4, 61.6, 55.3, 48.8, 40.6, 38.9, 38.8, 31.7, 30.9, 30.3, 27.0, 23.2, 23.1.

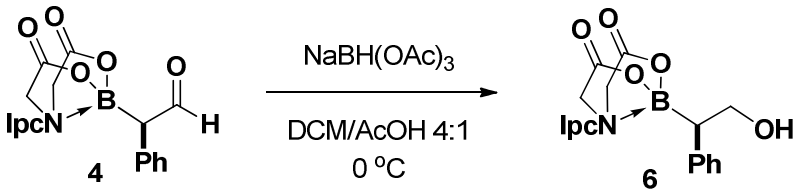
HRMS (ESI+)

Calculated for $C_{36}H_{41}BNO_6$:	594.3027
Found:	594.3028

X-ray quality crystals were obtained by layering a solution of **6** in 1 ml of 1,2-dichloroethane and layering it with about 2 ml of hexane. The layers were allowed to slowly mix at room temperature, giving the desired crystals.

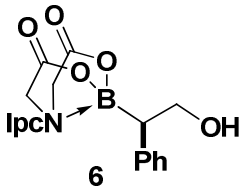


6



Alcohol 5. A dry 100 ml Schlenk flask was charged with aldehyde **4** (2.19 mg, 5.51 mmol) under an atmosphere of nitrogen. CH_2Cl_2 (60 ml) was added and the solution was cooled to -5 °C in an ice/salt bath. AcOH (15 ml) was added slowly. $NaBH(OAc)_3$ (1.75 g, 8.27 mmol) was then added portionwise to the solution over 3 min. The reaction was stirred at 0 °C for 2 h, then a second portion of $NaBH(OAc)_3$ (584 mg, 2.76 mmol) was added over 3 min. A third portion of $NaBH(OAc)_3$ (584 mg, 2.76 mmol) was added over 3 min after another 2 h. The reaction was stirred for another 4 h, then quenched with H_2O (20 ml). The mixture was stirred for 5 min until the organic layer became clear and effervescence ceased. The mixture was then transferred to a separatory funnel. After phase separation, the organic layer was washed H_2O (30 ml), then with phosphate buffer (pH = 7, 0.5 M, 25 ml × 2). The combined aqueous layer was

extracted with DCM (30 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography (30-45% EtOAc/hexane). A white solid was obtained (1.56 g, 71%).



6

TLC (Hexanes:acetone)

R_f = 0.32, visualized by $KMnO_4$

^{1}H-NMR (500 MHz, acetone-d_6)

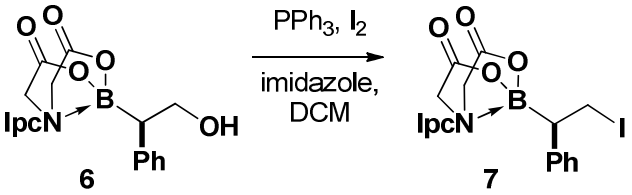
δ 7.39 (app d, *J* = 7.5 Hz, 2H), 7.33 (app t, *J* = 7.5 Hz, 2H), 7.24 (app t, *J* = 7 Hz, 1H), 4.29 (d, *J* = 18 Hz, 1H), 4.07 (d, *J* = 18 Hz, 1H), 4.04 (d, *J* = 15.5 Hz, 1H), 3.66 (d, *J* = 10.5, 6 Hz, 1H), 2.82 (d, *J* = 15 Hz, 1H), 2.82-2.77 (m, 1H), 2.61 (dd, *J* = 6, 4 Hz, 1H), 2.44 (ddt, *J* = 11, 6, 2 Hz, 1H), 2.33 (ddt, *J* = 13, 6.5, 2 Hz, 1H), 2.08 (m, 2H), 1.86 (dt, *J* = 5.5, 2 Hz, 1H), 1.76 (ddd, *J* = 14.5, 6, 2.5 Hz, 1H), 1.27 (s, 3H), 1.05 (d, *J* = 11 Hz, 1H), 1.01 (s, 3H), 0.93 (d, *J* = 7 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 168.9, 166.5, 140.8, 129.4, 128.4, 126.9, 66.6, 65.5, 61.8, 55.2, 48.8, 40.6, 38.8, 38.7, 31.7, 30.2, 27.0, 23.1, 23.0.

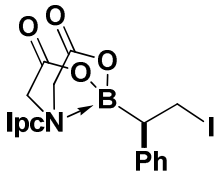
HRMS (ESI+)

Calculated for $C_{22}H_{31}BNO_5$:	400.2295
Found:	400.2297



6 7

Iodide 7. To a dry 25 ml Shclenk flask was added PPh_3 (346 mg, 1.32 mmol), imidazole (112 mg, 1.65 mmol) and a solution of the alcohol 6 (438 mg, 1.10 mmol) in DCM (15 ml) under a positive pressure of N_2. I_2 (335 mg, 1.32 mmol) was then added in one portion. The reaction was stirred for 2 h, then transferred to a separatory funnel and washed with 10 ml H_2O. The aqueous layer was extracted with 10 ml DCM. The combined organic layer was dried over $MgSO_4$, filtered and concentrated. The crude product was purified by silica gel chromatography (40 to 60% EtOAc/hexanes). The off-white solid was then dissolved in DCM (approx. 25 ml) and passed through a pad of activated charcoal. The colorless filtrate was then concentrated *in vacuo* to give a white solid (235 mg, 42%).



7

TLC (Hexanes:EtOAc 1:1)

R_f = 0.42, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

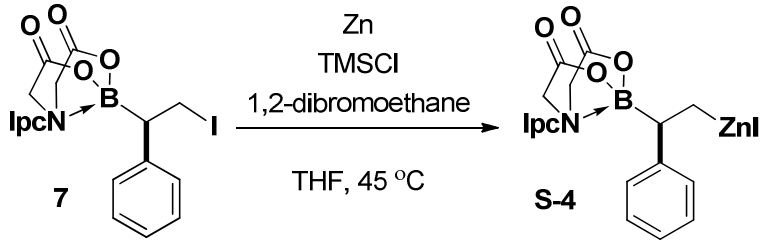
δ 7.38 – 7.26 (m, 5H), 4.15 (d, J = 17 Hz, 1H), 4.01 (dd, J = 10, 3.5 Hz, 1H), 3.69 (dt, J = 10.5, 6 Hz, 1H), 3.55 (dd, J = 12.5, 10 Hz, 1H), 3.40 (d, J = 17.5 Hz, 1H), 3.39 (d, J = 15 Hz, 1H), 2.73 (d, J = 15 Hz, 1H), 2.69 – 2.63 (m, 2H), 2.45 (ddt, J = 11.5, 6, 1 Hz, 1H), 2.08 (sept, J = 3 Hz, 1H), 1.96 – 1.91 (m, 1H), 1.85 (dt, J = 6, 2 Hz, 1H), 1.76 (ddd, J = 15, 6, 2.5 Hz, 1H), 1.26 (s, 3H), 0.97 (s, 3H), 0.88 (d, 1H), 0.85 (d, J = 7 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 168.3, 166.1, 142.1 (2C), 129.3, 127.4 (3C), 66.6, 61.7, 55.5, 48.8, 40.6, 38.8 (2C), 31.7, 30.3, 27.0, 23.1, 22.9.

HRMS (ESI+)

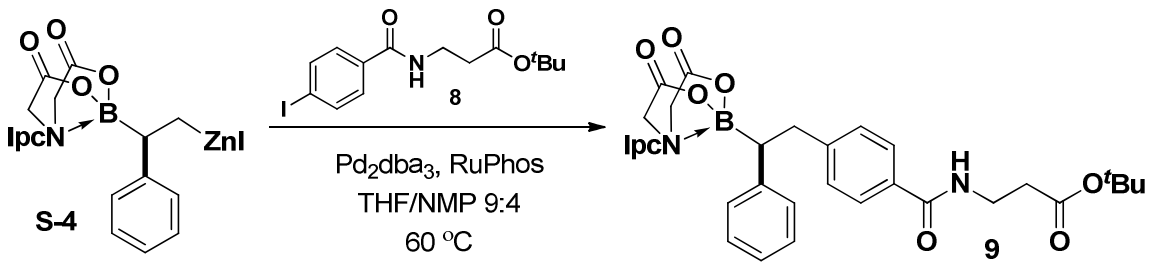
Calculated for $C_{22}H_{30}BNO_4I$:	510.1313
Found:	510.1309



7 **S-4**

Organozinc S-4.

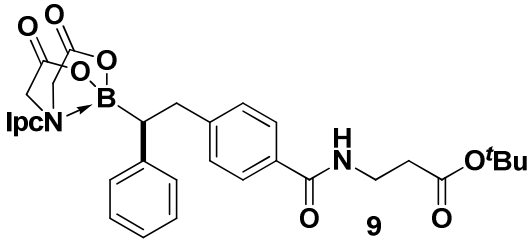
In a glovebox, Zn dust (172 mg, 2.63 mmol) was weighed into a flame-dried 7 ml vial equipped with a stir bar. Another 7 ml vial was charged with a THF solution (1.2 ml) of the iodide **7** (446 mg, 0.876 mmol). Both vials, together with another empty 7 ml vial, were sealed with septum cap and removed from the glovebox. The vial containing Zn dust was placed under argon, and 3 drops of TMSCl followed by 3 drops of 1,2-dibromoethane were added. The THF solution of iodide 7 was then added to the Zn dust in one portion via syringe under argon. The reaction vial was then placed in a heating block and stirred at 45 °C for 1.5 h. The vial was then removed from the block and 3.2 ml of THF was added to form a 0.2 M solution of the organozinc **S-4**.



PIDA boronate 9.

Preparation of catalyst stock solution. A dry 7 ml vial equipped with a star bar was charged with RuPhos[7] (9.5 mg, 0.02 mmol). The vial was brought into the glovebox, and Pd_2dba_3 (4.6 mg, 0.005 mmol) was added. THF (1.5 ml) was added, and the mixture stirred at rt for 3 min.

*The freshly prepared catalyst stock solution was immediately for the preparation of **9**:*
A dry 7 ml vial equipped with a stir bar was charged with iodide **8** (75 mg, 0.2 mmol) and brought into the glovebox. To this was added NMP (1.2 ml) followed by 1.2 ml (0.004 mmol Pd_2dba_3, 0.016 mmol RuPhos) of the catalyst solution. The vial was sealed with a septum cap, stirred briefly and then brought out of the glovebox. The vial was placed in a heating block pre-equilibrated to 60 °C, and the solution of the organozinc reagent **S-4** (1.5 ml, approx. 0.3 mmol) was added over 3 h with the aid of a syringe pump. After the addition was complete, the reaction was stirred for another 2 h at 60 °C, then cooled to rt. The reaction was diluted with Et_2O (10 ml) and washed with sat. NH_4Cl (2 × 5 ml) and H_2O (2 × 5 ml). The combined aqueous layers were extracted with Et_2O (10 ml). The organic phase was then dried over $MgSO_4$, filtered and concentrated. The residue was taken up in DCM (5 ml), absorbed onto celite and loaded onto a silica gel column. The product was obtained as a white solid after column chromatography (92 mg, 73%).



TLC (Hexanes:EtOAc 3:2)

R_f = 0.36, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.49 (d, J = 8.5 Hz, 2H), 7.30-7.13 (m, 4H), 7.14 (app t, J = 7.5 Hz, 1H), 6.96 (d, J = 8 Hz, 2H), 6.72 (t, J = 6 Hz, 1H), 4.16 (d, J = 17.5 Hz, 1H), 3.64 – 3.57 (m, 3H), 3.45 (d, J = 15.5 Hz, 2H), 3.39 (dd, J = 14, 3 Hz, 1H), 3.04 (app t, J = 14 Hz, 1H), 2.66 – 2.61 (m, 1H), 2.51 (t, J = 5.5 Hz, 1H), 2.44 – 2.41 (m, 2H), 2.06 – 2.05 (m, 1H), 1.95 – 1.92 (m, 1H), 1.83 -1.78 (m, 2H), 1.44 (s, 9H), 1.23 (s, 3H), 0.89 (d, J = 7.5 Hz, 1H), 0.87 (s, 3H), 0.81 (d, J = 7 Hz, 3H).

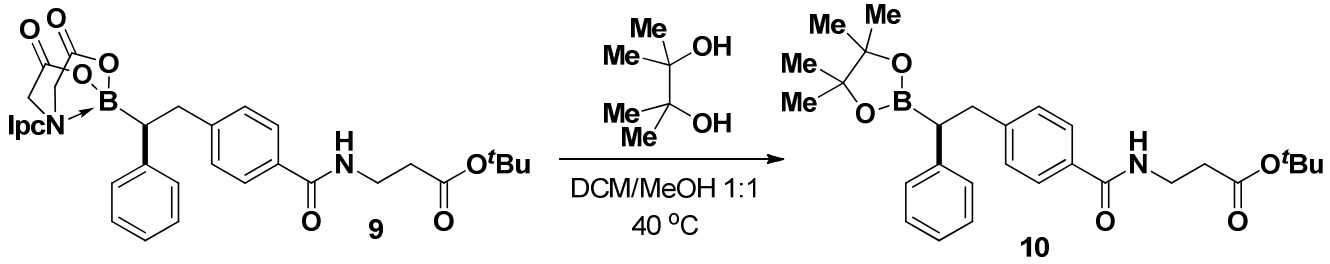
^{13}C-NMR (125 MHz, $CDCl_3$)

δ 172.2, 168.9, 167.3, 166.7, 145.9, 142.1, 131.7, 128.9, 126.5, 126.4, 81.1, 66.4, 62.0, 55.7, 48.8, 40.6, 38.8 (2C), 38.7, 35.3, 35.1, 31.7, 30.3, 28.1, 27.0, 23.0, 22.9.

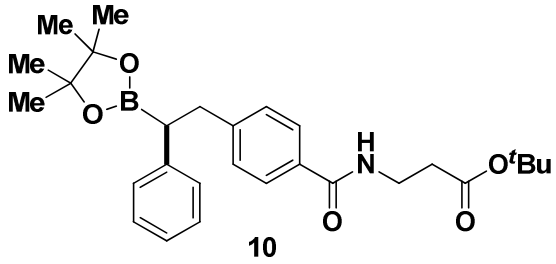
[7] Milne, J. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 13028-13032.

HRMS (ESI+)

Calculated for $C_{36}H_{48}BN_2O_7$:	631.3555
Found:	631.3560



Pinacol ester 10. PIDA boronate **9** (91.3 mg, 0.145 mmol) was dissolved in DCM (1.5 ml) in a 7 ml vial under ambient atmosphere. Pinacol (18 mg, 0.152 mmol) was added, followed by MeOH (1.5 ml). The vial was capped and placed in a heating block and stirred at 40 °C for 3.5 h. The reaction was concentrated *in vacuo*. The residue was azeotroped 5 times with benzene until a white solid was obtained. Benzene (5 ml) was then added and the suspension filtered, rinsing with additional benzene. The filtrate was concentrated *in vacuo* to give a white solid tainted with a light brown color. The crude product was then purified on a florisil column (20 – 30% EtOAc/hexanes), giving **S-5** as a colorless oil that slowly crystallized over time (58.5 mg, 84%). The white solid obtained by filtration (PIDA) was dissolved in MeOH, and concentrated *in vacuo*, azeotroping with benzene to remove residual MeOH. PIDA was recovered in 96% yield (37.6 mg).



TLC (EtOAc:hexanes 3:2)

R_f = 0.59, visualized by short wave UV

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.61 (d, J = 8 Hz, 2H), 7.26 – 7.19 (m, 4H), 7.21 (d, J = 8 Hz, 2H), 7.15 – 7.12 (m, 1H), 6.81 (t, J = 6 Hz, 1H), 3.66 (q, J = 6 Hz, 1H), 3.19 (dd, J = 13.5, 9 Hz, 1H), 2.98 (dd, J = 13.5, 7.5 Hz, 1H), 2.65 (dd, J = 9.5, 7.5 Hz, 1H), 2.54 (t, J = 6.5 Hz, 2H), 1.45 (s, 9H), 1.12 (s, 6H), 1.11 (s, 6H).

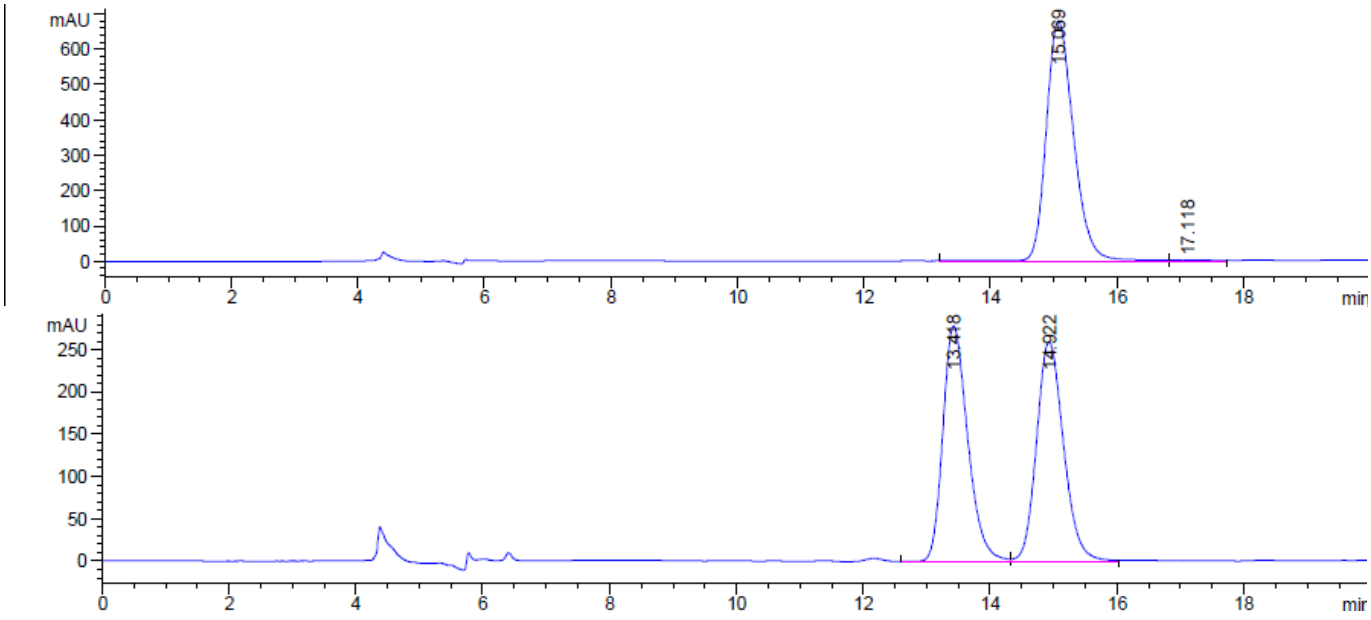
^{13}C-NMR (125 MHz, $CDCl_3$)

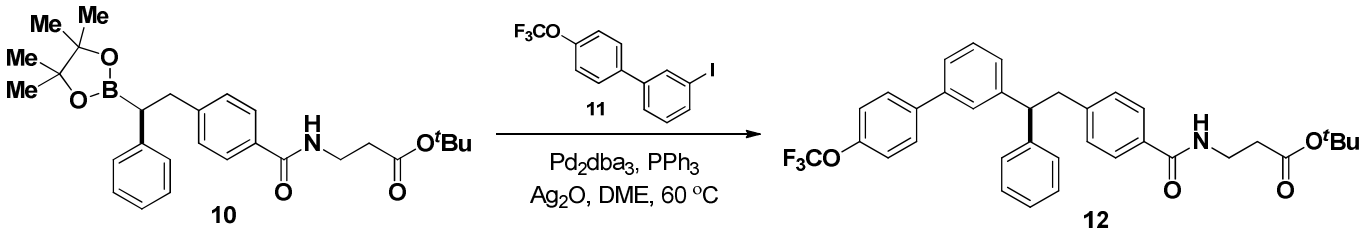
δ 172.2, 167.2, 145.6, 142.0, 131.9, 129.0, 128.3, 126.6 (2C), 125.5, 83.5, 81.1, 38.6, 35.4, 35.1, 28.1, 24.5.

HRMS (ESI+)

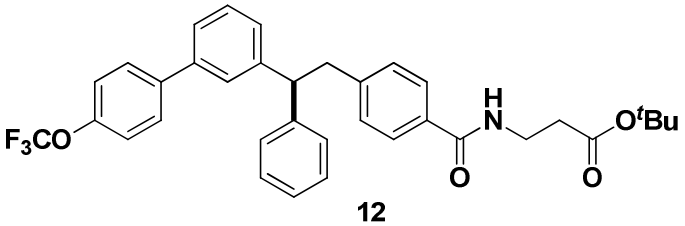
Calculated for $C_{28}H_{39}BNO_5$:	480.2921
Found:	480.2924

The e.r. was determined by chiral HPLC using a ChiraCel OD-H (4.6 × 250 mm) column:
Conditions: 5% IPA/hexane, flow rate = 0.8 ml/min, temperature = 23 °C, detection wavelength = 214 nm
t_r(major) 14.92 min, t_r(minor) 13.42 min; e.r. > 95:5





***t*-butyl ester 12.** A flame-dried 7 ml vial equipped with a stir bar was charged with Ag_2O (5.7 mg, 0.249 mmol) and brought into the glove box. PPh_3 (2.8 mg, 0.0106 mmol) was then added into the vial, followed by a solution of the pinacol boronic ester **10** (9.9 mg, 0.21 mmol) and iodide **11** (6.1 mg, 0.0166 mmol) in DME (0.23 ml). To this mixture was added a solution of Pd_2dba_3 (0.609 mg, 0.00066 mmol) in DME (0.1 ml). The vial was sealed with a cap, brought out of the glove box and stirred at 60 °C for 22.5 h. The reaction was then cooled to room temperature, diluted with THF (1.5 ml) and filtered through celite, eluting with THF. The filtrate was then concentrated *in vacuo*. The crude product was purified by silica gel chromatography (15 – 20% EtOAc/hexanes) to afford a yellow oil as the product (3.9 mg, 40%).



12

TLC (Hexanes:EtOAc 3:2)

R_f = 0.5, visualized by short wave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.58 (d, J = 8 Hz, 2H), 7.48 (dt, J = 6.5, 2 Hz, 2H), 7.34 – 7.37 (m, 1H), 7.26 – 7.18 (m, 3H), 7.08 (d, J = 8.5 Hz, 1H), 6.78 (t, J = 5.5 Hz, 1H), 4.29 (t, J = 7.5 Hz, H), 3.65 (q, J = 6 Hz, 2H), 3.44 (d, J = 8 Hz, 1H), 2.53 (t, J = 6 Hz, 2H), 1.45 (s, 9H).

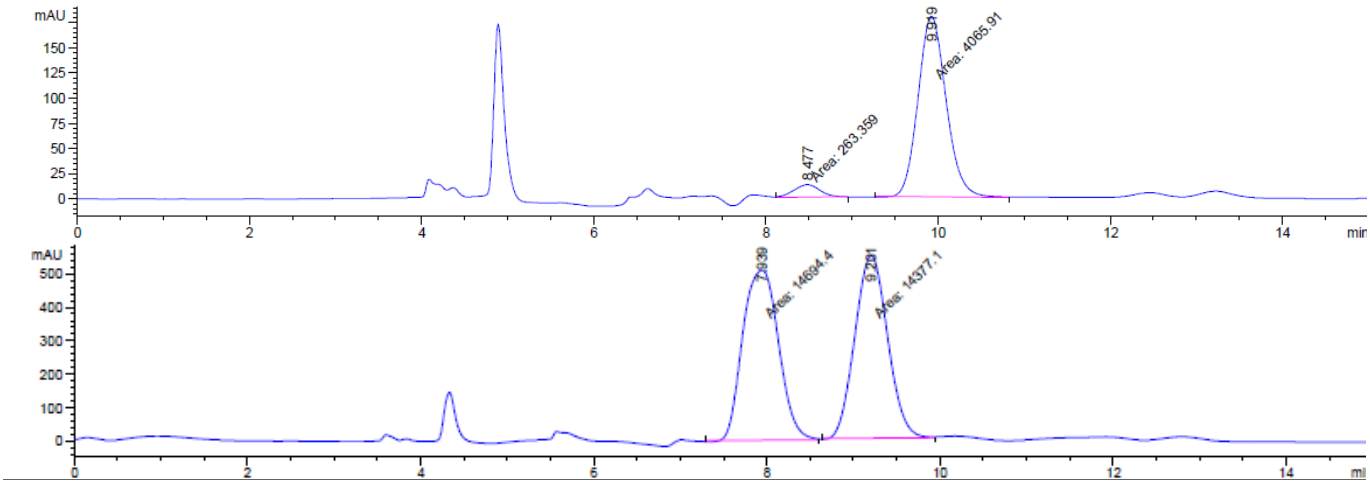
^{13}C-NMR (125 MHz, $CDCl_3$)

δ 172.3, 167.1, 148.6, 144.7, 143.9, 143.7, 139.9, 132.3, 129.3, 129.0, 128.5, 128.5, 128.0, 127.2, 126.9, 126.8, 126.5, 125.2, 121.2, 81.2, 52.9, 42.0, 35.4, 35.1, 28.1.

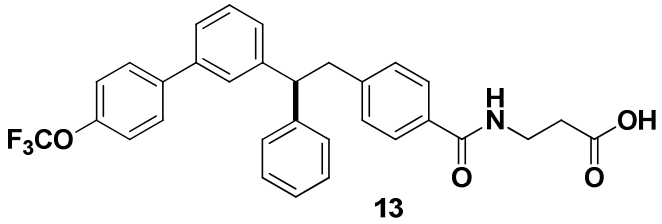
HRMS (ESI+)

Calculated for $C_{35}H_{35}NO_4F_3$:	590.2518
Found:	590.2512

The e.r. was determined by chiral HPLC using a ChiraCel OD-H (4.6 × 250 mm) column:
Conditions: 20% IPA/hexane, flow rate = 0.7 ml/min, temperature = 23 °C, detection wavelength = 214 nm.
t_r(major) 9.92 min, t_r(minor) 8.48 min; e.r. 94: 6



Acid 13. To a solution of the *t*-butyl ester **12** in DCM (0.6 ml) in a 2 ml vial was added TFA (0.1 ml) under ambient atmosphere. The vial was sealed and the reaction was stirred at room temperature for 2 h. The solvent was then removed *in vacuo*, and TFA removed by co-evaporation with DCM. The crude product was then purified by silica gel chromatography (EtOAc – EtOAc + 0.1% AcOH) to afford the product as a white solid (3.0 mg, 85%).



TLC (Hexanes:EtOAc 3:7)

R_f = 0.28, visualized by shortwave UV.

^{1}H-NMR (500 MHz, $CDCl_3$)

δ 7.55 (d, J = 8 Hz, 1H), 7.49 (d, J = 8.5 Hz, 1H), 7.35-7.33 (m, 3H), 7.26 – 7.20 (m, 9 H, 1H), 7.11 (d, J = 8 Hz, 2H), 6.82 (t, J = 6 Hz, 1H), 4.29 (t, J = 8 Hz, 1H), 3.73 (q, J = 6 Hz, 2H), 3.45 (d, J = 7.5 Hz, 2H), 2.74 (t, J = 5.5 Hz, 2H).

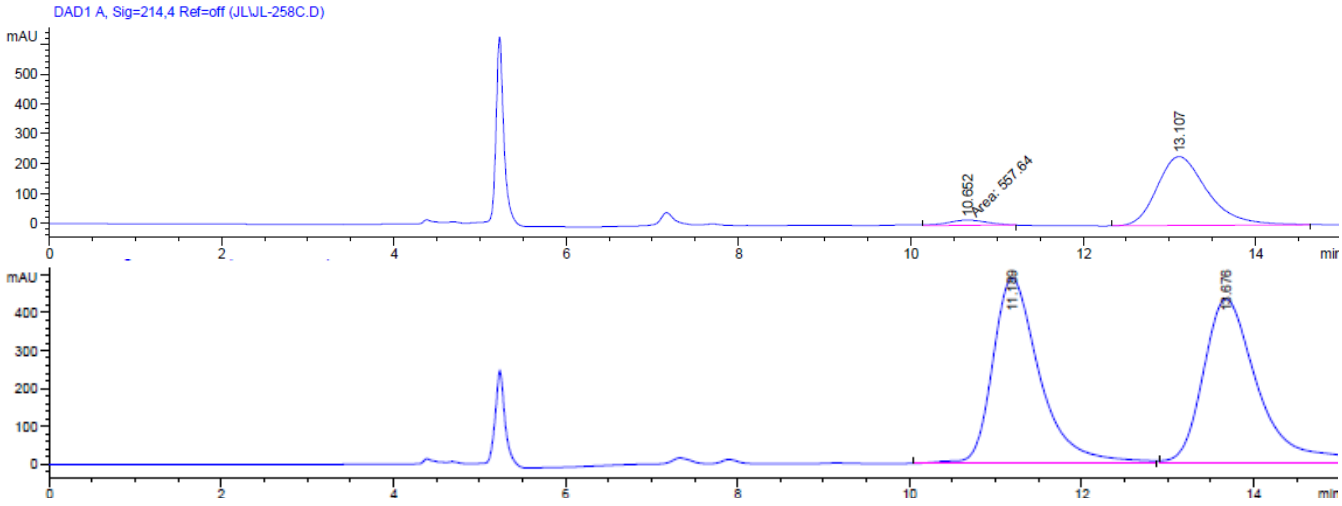
^{13}C-NMR (125 MHz, $CDCl_3$)

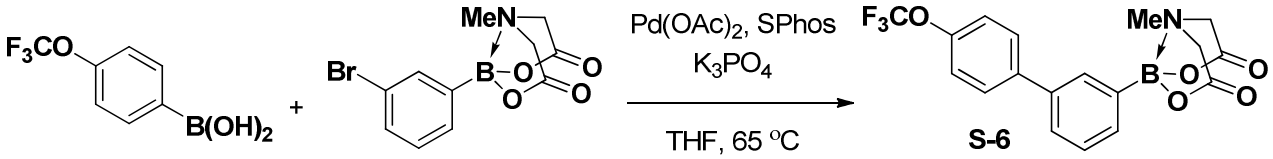
δ 176.4, 167.6, 148.6, 144.7, 144.3, 143.6, 140.0, 139.9, 131.8, 129.3, 129.0, 128.5 (2C), 127.9, 127.2, 126.9, 126.5, 125.2, 121.2, 52.9, 41.9, 35.2, 33.7.

HRMS (ESI+)

Calculated for $C_{31}H_{27}NO_4F_3$:	534.1892
Found:	534.1887

The e.r. was determined by chiral HPLC using a ChiraCel OD-H (4.6 × 250 mm) column:
Conditions: 20% IPA/hexane, flow rate = 0.6 ml/min, temperature = 23 °C, detection wavelength = 214 nm.
t_r(major) 13.11 min, t_r(minor) 10.65 min; e.r. 94:6.





MIDA boronate S-6.

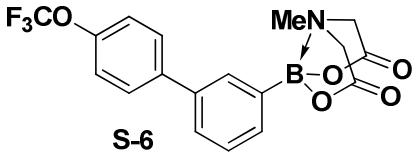
Preparation of catalyst stock solution. A dry 20 ml vial was charged with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol) and SPhos[8] (41 mg, 0.1 mmol) under ambient atmosphere. The vial was taken into the glovebox. THF (12.5 ml) was added and the mixture stirred for 20 min, forming a clear brown solution.

The freshly prepared catalyst stock solution was immediately for the preparation of ***S-6****:*

A 20 ml vial equipped with a stir bar was charged with 3-bromophenyl MIDA boronate[9] (312 mg, 1 mmol) and 4-(trifluoromethoxy)phenylboronic acid (309 mg, 1.5 mmol). This was repeated for another 20 ml vial. Finely ground K_3PO_4 was weighed into each of the 2 reaction vials. THF (5 ml) was added to each of the reaction vials, followed by 5 ml (0.05 mmol $Pd(OAc)_2$, 0.1 mmol SPhos) of the catalyst solution. The reaction vials were sealed with Teflon-lined caps, brought out of the glovebox and stirred at 65 °C in a heating block for 14 h. The reaction was then cooled to rt, then filtered through celite, combining the filtrates from the 2 reactions. The celite pad was washed with additional THF (20 ml). Celite was added to the filtrate and the mixture concentrated *in vacuo*. The celite (containing the absorbed crude product) was loaded onto a silica gel column. The column was eluted with Et_2O to remove non-polar impurities, then

[8] Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461-1473.
[9] Gillis, E. P.; Burke, M. D. *J. Am. Chem. Soc.* **2007**, *129*, 6716-6717. This product is also available from Sigma-Aldrich (product no. 698113).

with 20% acetone/hexanes followed by 30% acetone/hexanes to elute the product. The fractions containing the product were concentrated *in vacuo*, affording the pure product as a white solid (586 mg, 75%).



S-6

TLC (Hexanes:acetone 1:1)

R_f = 0.32, visualized by short wave UV.

^{1}H-NMR (500 MHz, acetone-d_6)

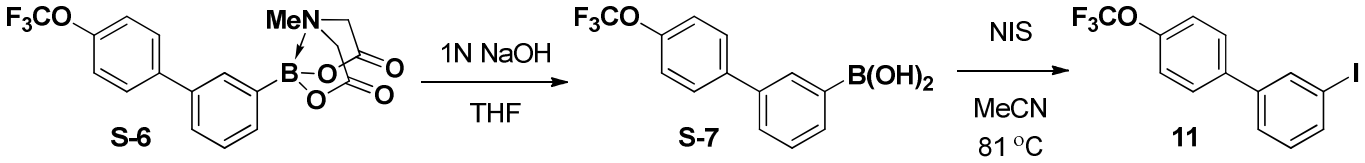
δ 7.84 (app s, 1H), 7.80 (d, J = 9 Hz, 2H), 7.69 (dt, J = 8, 1.5 Hz, 1H), 7.58 (d, J = 7.5 Hz, 1H), 7.49 (t, J = 15 Hz, 1H), 7.42 (d, J = 8.5 Hz, 2H), 4.38 (d, J = 17 Hz, 2H), 4.21 (d, J = 17 Hz, 2H), 2.82 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

δ 169.3, 141.5, 139.8, 132.9, 132.0, 129.6, 129.3, 128.6, 122.2, 62.9, 48.4.

HRMS (ESI+)

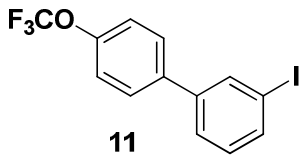
Calculated for $C_{18}H_{16}BNO_5F_3$:	394.1074
Found:	394.1078



S-6 **S-7** **11**

Aryl iodide 11. To a solution of MIDA boronate **S-6** (763 mg, 1.94 mmol) in THF (20 ml) was added 1N NaOH (6 ml) in one portion under ambient atmosphere. The mixture was stirred vigorously for 20 min at rt, then diluted with Et_2O (20 ml) quenched with sat. NH_4Cl (20 ml). The mixture was stirred briefly and transferred to a separatory funnel. After shaking and phase separation, the aqueous layer was washed with THF/Et_2O 1:1 (20 ml). The combined organic phase was dried over $MgSO_4$, filtered and concentrated. The residue was dried *in vacuo* to give an off-white solid (540 mg, 98%). The solid was transferred to a 40 ml and N-iodosuccinimide was added. The vial was sealed with a septum cap and evacuated under high vacuum and back-filled with N_2. This cycle was repeated twice. MeCN was then added, the vial placed in a heating block and the reaction stirred at 81 °C for 36 h. The reaction was cooled to rt and concentrated *in vacuo* to approximately 5 ml of MeCN. After dilution with Et_2O (30 ml), the organic phase was washed with 1M $NaHSO_3$ (30 ml × 2), then with H_2O (30 ml). The combined aqueous phase was extracted with Et_2O (30 ml). The organic layer was dried over $MgSO_4$, filtered and concentrated, giving a brown liquid and a white crystalline solid. This residue was taken up in a minimum amount of Et_2O and loaded onto a silica gel column. The column was flushed with hexanes. The fractions containing product were concentrated *in vacuo*, giving a yellow oil. This yellow oil was further purified by

dissolving it in pentane and passing through a short silica gel pad, eluting with pentane. A colorless oil was obtained (679 mg, 89%).



11

TLC (Hexanes)

R_f = 0.45, visualized by short wave UV

^{1}H-NMR (500 MHz, CD_3CN)

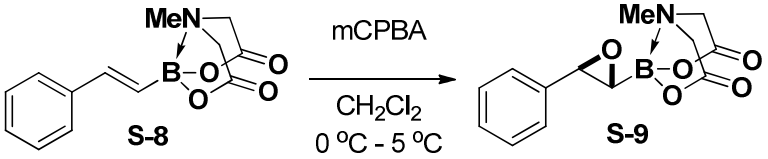
δ 7.91 (t, J = 2 Hz, 1H), 7.70 (ddd, J = 7.5, 1.5, 1 Hz, 1H), 7.55 (dt, J = 8.5, 2 Hz, 2H), 7.51 (ddd, J = 8, 1.5, 1 Hz), 7.29 (dd, J = 9, 1 Hz, 1H), 7.18 (t, J = 8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

δ 149.0, 142.0, 138.3, 136.6, 136.1, 130.5, 128.5, 126.3, 121.5, 121.3, 94.8.

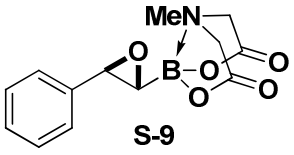
HRMS (EI+)

Calculated for $C_{13}H_8IOF_3$:	363.95723
Found:	363.95628



S-8 **S-9**

MIDA boronate S-9. To a suspension of the MIDA boronate **S-8**[10] (6.37 g, 24.86 g) in DCM (125 ml) at 0 °C was added mCPBA (7.29 g, 42.26 mmol) portionwise over 10 min under ambient atmosphere. The reaction was stirred for 12 h, gradually rising to RT in the ice/water bath. A white suspension was obtained, which was filtered to remove the white solids. The filtrate was concentrated (at 23 °C) to about 5 ml DCM, and the white solids were added back into the rbf. With vigorous stirring, 160 ml of Et_2O was added and the mixture was stirred for 5 min. The white solid (product) was obtained by filtration, rinsing with 40 ml of Et_2O. The filtrate containing impurities and trace amounts of the product, was discarded. The product was then returned to the rbf and stirred with another 100 ml of Et_2O. The white solid was obtained after filtration, rinsing with 50 ml of Et_2O. The solid was then dried *in vacuo*. White solid (6.28 g, 92%).



S-9

TLC (Hexanes:acetone 1:1)

R_f = 0.38, stained by $KMnO_4$

[10] Uno, B. E.; Gillis, E. P.; Burke, M. D. *Tetrahedron* **2009**, *65*, 3130-3138.

^{1}H-NMR (400 MHz, acetone-d_6)

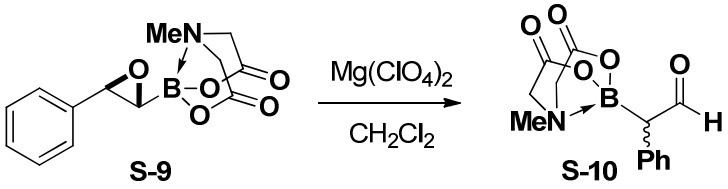
δ 7.37 – 7.27 (m, 5H), 4.36 (d, J = 17.2 Hz, 1H), 4.29 (d, J = 16.8 Hz, 1H), 4.18 (d, J = 17.2 Hz, 1H), 4.04 (d, J = 16.8 Hz, 1H), 3.80 (d, J = 3.2 Hz, 1H), 3.35 (s, 3H), 2.45 (d, J = 2.8 Hz, 1H).

^{13}C-NMR (125 MHz, $CDCl_3$)

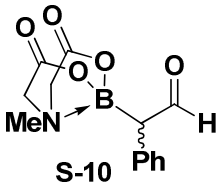
δ 169.3, 168.3, 140.1, 129.2, 128.6, 126.4, 63.0, 62.8, 56.5, 47.0.

HRMS (ESI+)

Calculated for $C_{13}H_{15}NO_5$:	276.1043
Found:	276.1057



MIDA boronate S-10. A flame-dried 300 ml rbf equipped with a stir bar was charged with the MIDA boronate **S-9** (2.59 g, 10 mmol) and DCM (100 ml) under ambient atmosphere. The mixture was stirred to form slightly cloudy solution. $Mg(ClO_4)_2$ (2.23 g, 10 mmol) was then added portionwise over 3 min. The rbf was capped with a cap plug and stirred at rt for 2 h 15 min. The reaction was then filtered through celite, rinsing with 50 ml DCM. The filtrate (slightly cloudy) was concentrated *in vacuo* to give a fluffy white solid. 50 ml Et_2O was added to the solid, and the suspension stirred for 5 min, then vacuum-filtered. The solid was returned to the rbf and stirred with another 40 ml Et_2O for 5 min. The suspension was filtered, and the white solid was dried *in vacuo*. This crude product (2.26 g, 87%) was used without further purification.



TLC (Hexanes:acetone 1:1)

R_f = 0.34, stained by $KMnO_4$.

^{1}H-NMR (500 MHz, acetone-d_6)

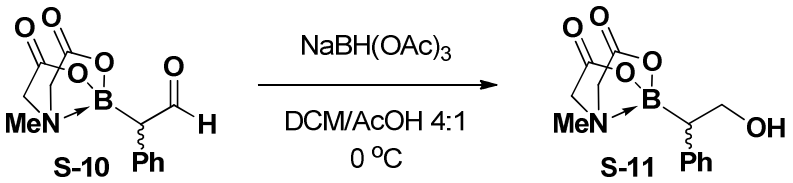
δ 9.82 (d, J = 2.5 Hz, 1H0, 7.37 – 7.25 (m, 4H), 7.26 – 7.23 (m, 1H), 4.28 (d, J = 17 Hz, 1H), 4.26 (d, J = 17 Hz, 1H), 3.74 (d, J = 17 Hz, 1H), 3.72 (br s, 1H), 3.20 (s, 3H).

^{13}C-NMR (125 MHz, acetone-d_6)

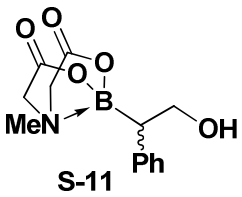
δ 168.2, 137.3, 130.6, 129.3, 127.0, 63.6, 63.3, 47.1.

HRMS (ESI+)

Calculated for $C_{13}H_{15}BNO_5$:	276.1043
Found:	276.1044



MIDA boronate S-11. To a flame-dried 200 ml 3-neck rbf was added MIDA boronate **S-10** (2.26 g, 8.72 mmol) under positive N_2 atm. DCM (100 ml) was added, and the mixture stirred at rt until a homogeneous solution was formed. The solution was cooled to 0 °C in an ice/water bath and AcOH (25 ml) was then added slowly. After stirring for another 5 min, $NaBH(OAc)_3$ (2.77 g, 13.1 mmol, 1.5 eq) was added. The reaction was stirred at 0 °C for 2 h, then another portion of $NaBH(OAc)_3$ (0.92 g, 4.34 mmol, 0.5 eq) was added. After stirring at 0 °C for another 2.5 h, the third portion of $NaBH(OAc)_3$ (0.92 g, 4.34 mmol, 0.5 eq) was added. The reaction was gradually raised to RT, stirring for 11.5 h. 50 ml of H_2O was added slowly to quench the reaction. The mixture was transferred to a 500 ml sep funnel, rinsing with 50 ml DCM. After phase separation, the organic layer was washed with pH 7 phosphate buffer (1 M, 2 × 50 ml). The combined aqueous phase was extracted with 50 ml DCM. The organic phase was dried over $MgSO_4$, filtered and concentrated *in vacuo*. The aqueous layer was thus extracted with EtOAc/acetone 2:1 (150 ml). This organic phase was then washed with brine (50 ml), dried over $MgSO_4$, filtered, combined with the rest of the product and concentrated. AcOH was present, forming a thick oil with the product. 100 ml Et_2O was then added to this oil with vigorous stirring. The white suspension was filtered, washing the white solid with additional Et_2O (50 ml). The solid was dissolved in acetone and transferred into a rbf. The filtrate was concentrated, and additional white solid precipitated with 50 ml Et_2O. The solid was dissolved in acetone, and transferred to the rbf containing the rest of the product dissolved in acetone. An equal volume of hexane was added, and the mixture concentrated *in vacuo* to give a white fluffy solid. Residual water was azeotroped with PhMe, followed by hexane. The white solid was then dried *in vacuo* (1.54 g, 64%, ~ 80-90% purity). This crude product was used without further purification.



TLC (Hexanes:acetone 1:1)

R_f = 0.14, stained by $KMnO_4$.

^{1}H-NMR (500 MHz, acetone-d_6)

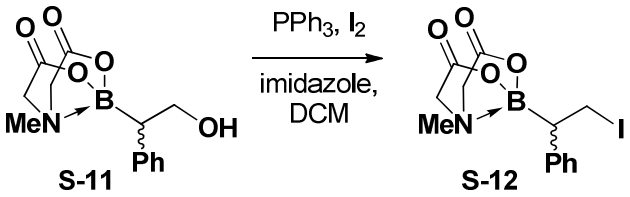
δ 7.28 – 7.27 (m, 2H), 7.23 – 7.20 (m, 2H), 7.11 (tt, J = 7.5, 1Hz, 1H), 4.19 (d, J = 16 Hz, 1H), 4.14 (d, J = 15 Hz, 1H), 4.11 (d, J = 14.5 Hz, 1H), 3.94 (t, J = 9 Hz, 1H), 3.79 (d, J = 8.5 Hz, 1H), 3.66 (d, J = 17 Hz, 1H), 3.15 (s, 3H), 2.56 (t, J = 7.5 Hz, 1H).

^{13}C-NMR (125 MHz, acetone-d_6)

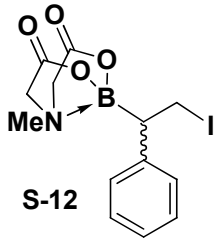
δ 169.0, 168.8, 144.0, 130.0, 128.8, 125.9, 66.1, 63.6, 63.0, 46.7.

HRMS (ESI+)

Calculated for $C_{13}H_{15}NO_5Na$:	300.1019
Found:	300.1018



MIDA boronate S-12. A flame-dried 100 ml Schlenk flask was charged with PPh_3 (1.87 g, 7.12 mmol), imidazole (0.808 g, 11.86 g) and I_2 (1.81 g, 7.12 mmol). DCM (50 ml) was added and the mixture stirred, forming a slightly yellow solution with white solid. After stirring for 5 min, the alcohol **11** (1.315 g, 4.75 mmol) was added as a solid under positive N_2 atmosphere. The reaction was then stirred for 2.5 h. Another 0.1 g of I_2 was added. The reaction was stirred for an additional 1 h. 40 ml H_2O was then added, and the mixture transferred to a separatory funnel. After phase separation, the organic layer was washed with another 30 ml H_2O. The combined aqueous phase was extracted with 50 ml DCM. The organic extracts were then dried over $MgSO_4$, filtered and concentrated to give a white solid. To this solid was added 50 ml Et_2O. The suspension was stirred for 30 min and filtered, washing with additional Et_2O. The white solid was taken up in acetone, absorbed onto celite and loaded onto a silica gel column. The product was purified by chromatography (100% Et_2O to 30% EtOAc/Et_2O to 50% acetone/hexane). The fractions containing the product were concentrated to give a white solid. To remove residual triphenylphosphine oxide, the solid was triturated with acetone (~ 5ml) and Et_2O (20 ml). The suspension was filtered, and the white solid washed again with 50 ml Et_2O. After filtration, the white solid was dried *in vacuo* (736 mg, 40%).



TLC (Hexanes:acetone 3:2)

R_f = 0.28, stained by $KMnO_4$.

^{1}H-NMR (500 MHz, acetone-d_6)

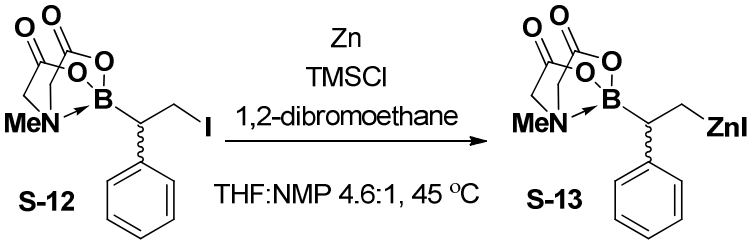
δ 7.32 – 7.21 (m, 5H), 4.27 (d, J = 17 Hz, 1H), 4.10 (d, J = 17 Hz, 1H), 4.08 (d, J = 17 Hz, 1H), 4.00 (dd, J = 10, 3.5 Hz, 1H), 3.53 (dd, J = 13, 10 Hz, 1H), 3.16 (d, J = 16.5 Hz, 1H), 3.02 (s, 3H), 2.66 (dd, J = 13, 2.5 Hz, 1H).

^{13}C-NMR (125 MHz, acetone-d_6)

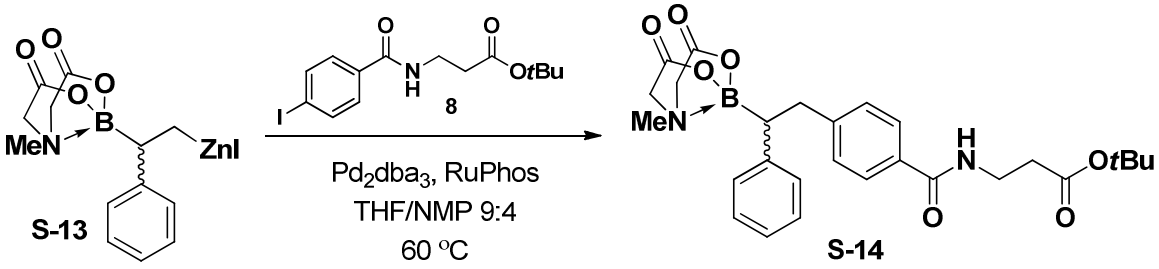
δ 168.4, 167.9, 143.8, 129.7, 129.3, 127.0, 63.3, 63.0, 46.5, 15.5.

HRMS (ESI+)

Calculated for $C_{13}H_{16}NO_4I$: 388.0217
Found: 388.0226



Organozinc S-12. In a glovebox, Zn dust (78.5 mg, 1.2 mmol) was weighed into a flame-dried 7 ml vial equipped with a stir bar. Another 7 ml vial was charged with a THF:NMP 3:1 solution (0.8 ml) of the iodide **S-12** (155 mg, 0.4 mmol). Both vials were sealed with septum caps and removed from the glovebox. The vial containing Zn dust was placed under argon, and 3 drops of TMSCl followed by 3 drops of 1,2-dibromoethane were added. The solution of iodide **S-12** was then added to the Zn dust in one portion via syringe under argon. The reaction vial was then placed in a heating block and stirred at 45 °C for 1.5 h. The vial was then removed from the block and 1.2 ml of THF was added to form a 0.2 M solution of the organozinc **S-13**.



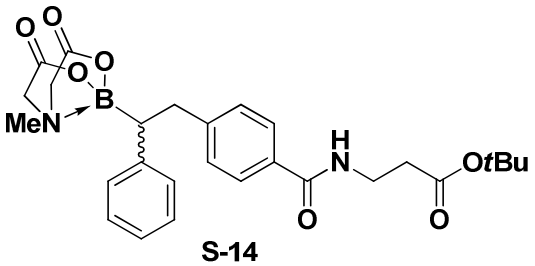
MIDA boronate S-14.

Preparation of catalyst stock solution. A dry 7 ml vial equipped with a star bar was charged with RuPhos[11] (9.5 mg, 0.02 mmol). The vial was brought into the glovebox, and Pd_2dba_3 (4.6 mg, 0.005 mmol) was added. THF (1.5 ml) was added, and the mixture stirred at rt for 3 min.

*The freshly prepared catalyst stock solution was immediately for the preparation of **9**:*
A dry 7 ml vial equipped with a stir bar was charged with iodide **8** (75 mg, 0.2 mmol) and brought into the glovebox. To this was added NMP (0.75 ml) and THF (0.45 ml) followed by 1.2 ml (0.004 mmol Pd_2dba_3, 0.016 mmol RuPhos) of the catalyst solution. The vial was sealed with a septum cap, stirred briefly and then brought out of the glovebox. The vial was placed in a heating block pre-equilibrated to 60 °C, and the solution of the organozinc reagent **S-13** (1.5 ml, approx. 0.3 mmol) was added over 3 h with the aid of a syringe pump. After the addition was complete, the reaction was stirred for another 2 h at 60 °C, then cooled to rt. The reaction was diluted with Et_2O (7 ml) and washed with sat. NH_4Cl (2 × 5 ml) and H_2O (2 × 5 ml). The combined aqueous layers were extracted with THF:Et_2O 1:1 (10 ml). The organic phase was then dried over $MgSO_4$, filtered and concentrated. The residue was taken up in acetone

[11] Milne, J. E.; Buchwald, S. L. *J. Am. Chem. Soc.* **2004**, *126*, 13028-13032.

(5 ml), absorbed onto celite and loaded onto a silica gel column. The product was obtained as a white solid after column chromatography (86 mg, 85%).



S-14

TLC (Hexanes:acetone 1:1)

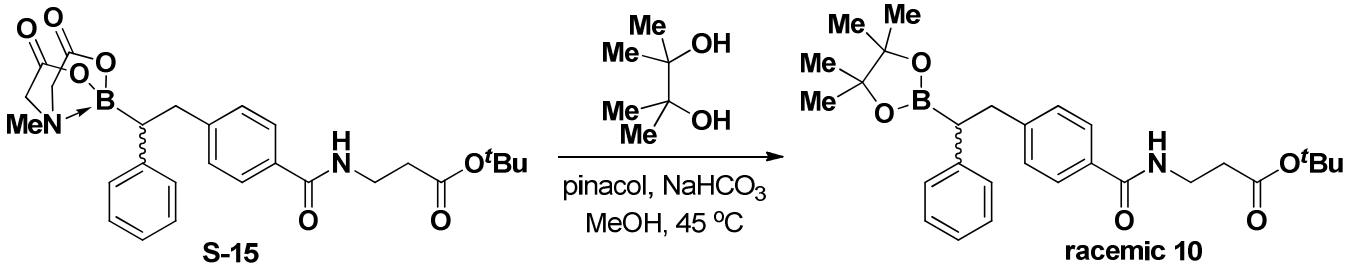
R_f = 0.28, visualized by short wave UV.

^{1}H-NMR (500 MHz, acetone-d_6)

δ 7.60 – 7.57 (m, 1H), 7.58 (d, J = 8 Hz, 1H), 7.17 – 7.11 (m, 4H), 7.05 – 7.01 (m, 1H), 7.02 (d, J = 8 Hz, 1H), 4.26 (d, J = 17.5 Hz, 1H), 4.11 (d, J = 14 Hz, 1H), 4.07 (d, J = 13.5 Hz, 1H), 3.54 (q, J = 7, 2H), 3.31 (dd, J = 14, 3 Hz, 1H), 3.15 (d, J = 17 Hz, 1H), 3.02 (s, 3H), 2.93 (dd, J = 13.5, 12.5 Hz, 1H), 2.59 (dd, J = 12, 3 Hz, 1H), 2.51 (t, J = 7 Hz, 1H), 1.41 (s, 9H).

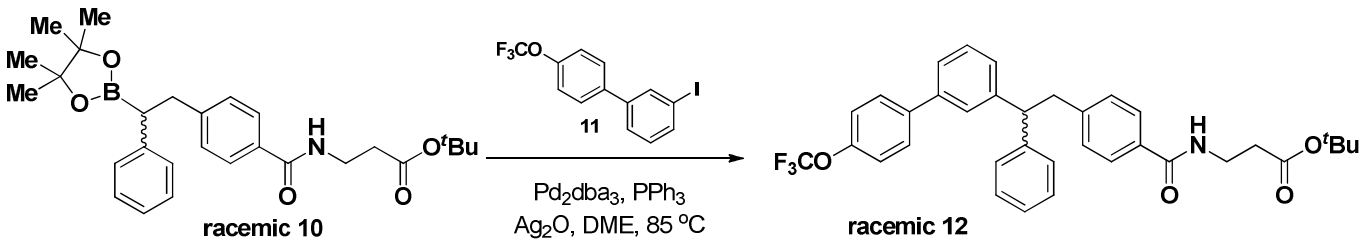
^{13}C-NMR (100 MHz, acetone-d_6)

δ 171.7, 168.9, 168.3, 167.2, 146.7, 143.9, 132.8, 130.2, 129.4, 128.9, 127.4, 126.0, 80.6, 63.5, 63.1, 46.3, 39.3, 36.5, 36.0, 28.2.



S-15 **racemic 10**

Racemic pinacol boronic ester 10. To a 7 ml vial charged with MIDA boronate **S-15** (58 mg, 0.114 mmol), pinacol (20 mg, 0.171 mmol) and $NaHCO_3$ was added MeOH (3 ml) under ambient atmosphere. The vial was capped and placed in a heating block and stirred at 45 °C for 5 h. The reaction was concentrated *in vacuo*. The residue was azeotroped 5 times with benzene until a white solid was obtained. Benzene (5 ml) was then added and the suspension filtered, rinsing with additional benzene. The filtrate was concentrated *in vacuo* to give a colorless oil residue. To this was added hexanes (10 ml), mixed thoroughly. The supernatant hexanes solution was then concentrated *in vacuo* to give the racemic pinacol ester **10**. ^{1}H-NMR data matches that of enantioenriched **10**.

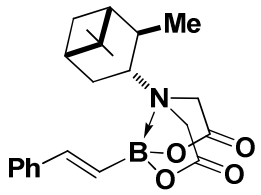
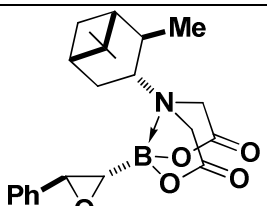
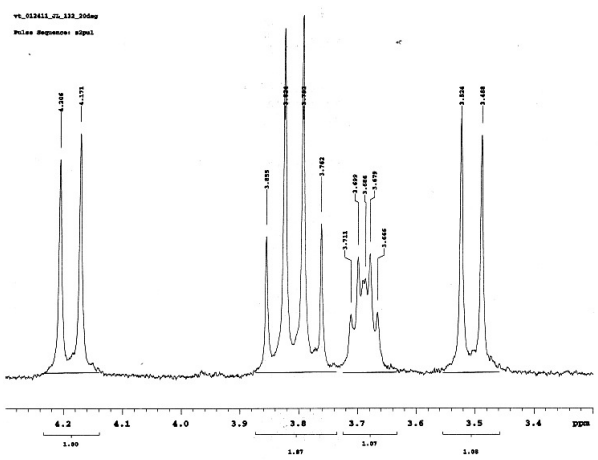
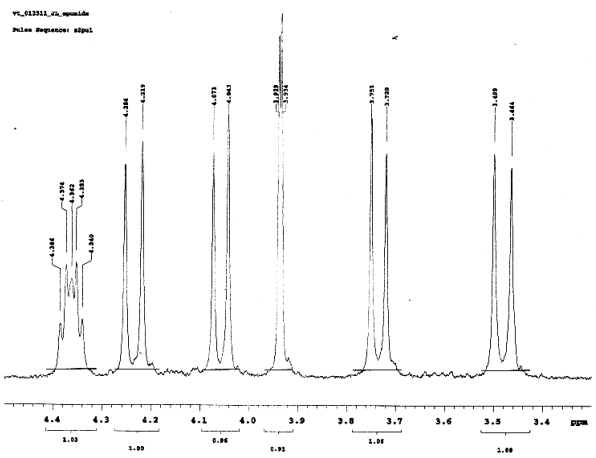
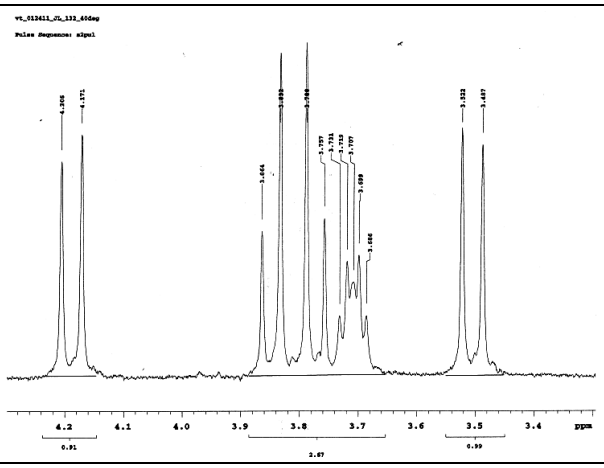
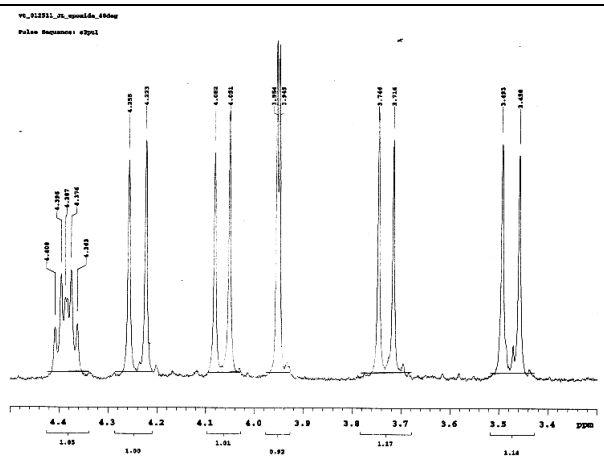


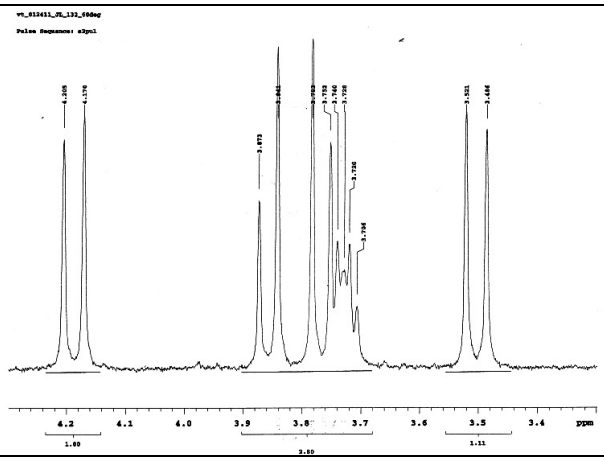
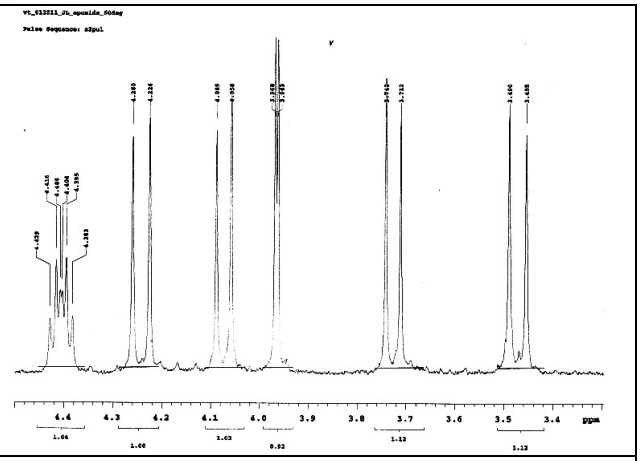
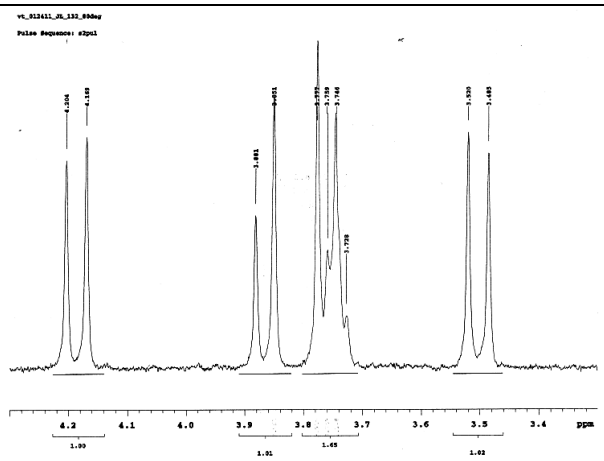
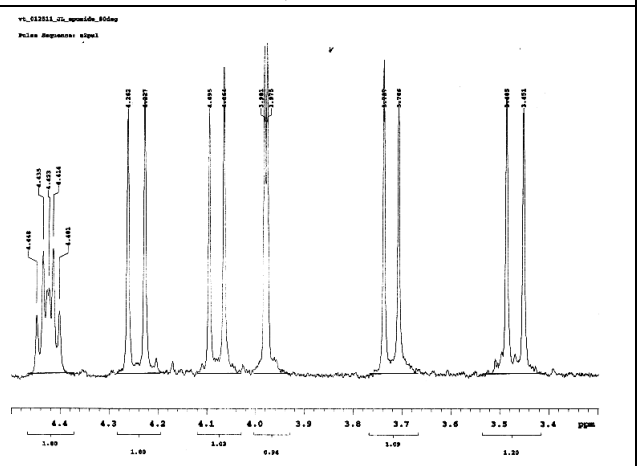
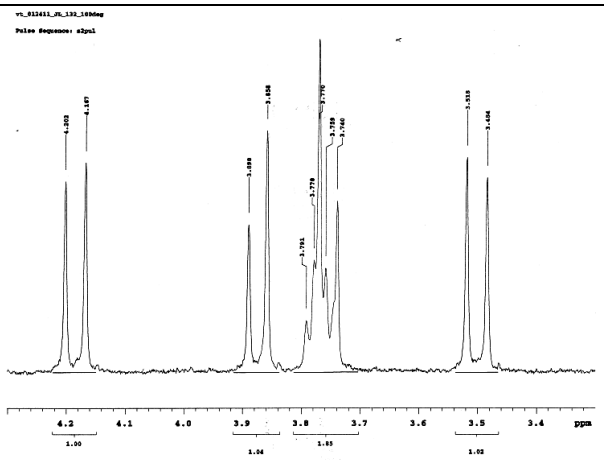
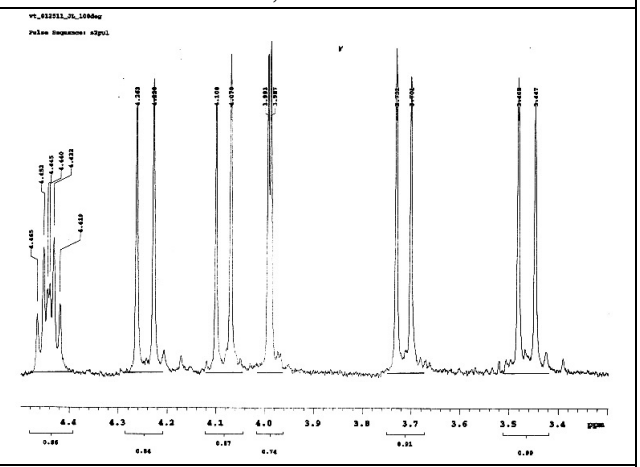
Racemic *t*-butyl ester 12. A flame-dried 7 ml vial equipped with a stir bar was charged with Ag_2O (30.6 mg, 0.132 mmol) and brought into the glove box. PPh_3 (23.1 mg, 0.088 mmol) was then added into the vial, followed by a solution of the racemic pinacol boronic ester **S-7** (52 mg, 0.132 mmol) and iodide 10 (32 mg, 0.088 mmol) in DME (1.6 ml). To this mixture was added a solution of Pd_2dba_3 (4.83 mg, 0.0158 mmol) in DME (1 ml). The vial was sealed with a cap, brought out of the glove box and stirred at 85 °C for 24 h. The reaction was then cooled to room temperature and filtered through celite, eluting with Et_2O. The filtrate was then concentrated *in vacuo*. The crude product was purified by silica gel chromatography (15 – 20% EtOAc/hexanes) to afford a yellow oil as the product (48.5 mg, 93%). ^{1}H-NMR data matches that of enantioenriched **12**.

Racemic acid 12. To a 7 ml vial containing racemic **11** (24 mg, 0.041 mmol) was added TFA:DCM 1:4 (1 ml). The vial was sealed with a septum cap and vented to the atmosphere via a 22-gauge needle. The reaction was stirred at room temperature for 2 h. The solvent was then removed *in vacuo*. Residual TFA was removed by azeotroping with DCM (3 × 5 ml) to give a brown/orange oil. The crude product was purified by silica gel chromatography (EtOAc:hexanes:AcOH 7:3:0.4). The product was obtained as a white solid (16.2 mg, 74%). ^{1}H-NMR data matches that of enantioenriched **12**.

III. Variable-temperature NMR studies

Variable-temperature NMR studies of **2a** and **3a**:
Spectra were collected in 1,1,2,2-tetrachloroethane.

T (°C)	 **2a**	 **3a**
20		
	δ 4.19, J = 17.5 Hz	δ 4.24, J = 17.5 Hz
40		
	δ 4.19, J = 17.5 Hz	δ 4.24, J = 17.5 Hz

60		
	δ 4.19, J = 17.5 Hz	δ 4.24, J = 17 Hz
80		
	δ 4.19, J = 17.5 Hz	δ 4.24, J = 17.5 Hz
100		
	δ 4.19, J = 17.5 Hz	δ 4.25, J = 17.5 Hz