Stereoretentive Suzuki-Miyaura Coupling of Haloallenes Enables Fully Stereocontrolled Access to (-)-Peridinin

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Supporting Information

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Complete version of truncated reference:
1. (a) Lewis, P.; Stefanovic, N.; Pete, J.; Calkin, A.C.; Giunti, S.; Thallas-Bonke, V.; Jandeleit-Dahm, K.A.; Allen, T.J.; Kola, I.; Cooper, M.E.; de Haan, J.B. *Circulation* **2007**, *115*, 2178-2187.

I. General methods

Materials. Commercial reagents were purchased from Sigma-Aldrich, Fisher Scientific, Alfa Aesar, TCI America, Strem Chemicals Inc., or Frontier Scientific and were used without further purification unless otherwise noted. (-)-Actinol was a generous gift from DSM Nutritional Products in Basel, Switzerland. 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. Triethylamine, diisopropylamine, pyridine, and 2,6-lutidine were freshly distilled under an atmosphere of nitrogen from CaH_2. The following compounds were prepared according to known literature procedures: iodoallene **BB$_4$**,[2] haloallenes **2**,[3] alkyne **4**,[4] dibromolactone **8**,[5] and vinyl germane **11**.[6] Isoprenyl MIDA boronate **9** is commercially available from Sigma-Aldrich (product number 707252).

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 or nitrogen. Organic solutions were concentrated via rotary evaporation under reduced pressure with a bath temperature of 35 – 40 ^{o}C. Reactions were monitored by analytical thin layer chromatography (TLC) performed using the indicated solvent on E. Merck silica gel 60

[1] Pangborn, A.B.; Giardello, M.A; Grubbs, R.H.; Rosen, R.K.; Timmers, F.J. *Organometallics* **1996**, *15*, 1518.
[2] Vaz, B.; Pereira, R.; Perez, M.; Alvarez, R.; de Lera, A.R. *J. Org. Chem*. **2008**, *73*, 6534.
[3] Elsevier, C.J.; Vermeer, P.; Gedanken, A.; Runge, W. *J. Org. Chem.* **1985**, *50*, 364.
[4] Furuichi, N.; Hara, H.; Osaki, T.; Nakano, M.; Mori, H.; Katsumura, S. *J. Org. Chem.* **2004**, *69*, 7949.
[5] Sorg, A.; Blank, F.; Bruckner, R. *Synlett* **2005**, *8*, 1286.
[6] David-Quillot, F.; Marsacq, D.; Balland, A.; Thibonnet, J.; Abarbri, M.; Duchene, A. *Synthesis* **2003**, *3*, 448.

F254 plates (0.25mm). Compounds were visualized by exposure to a UV lamp (λ = 254 nm) and/or a solution of basic $KMnO_4$ followed by brief heating using a Varitemp heat gun. MIDA boronates are compatible with standard silica gel chromatography, including standard loading techniques. Column chromatography was performed using standard methods[7] or on a Teledyne-Isco CombiFlash Rf purification system using Merck silica gel grade 9385 60Å (230-400 mesh). For loading, compounds were adsorbed onto non acid-washed Celite *in vacuo* from an acetone solution. Specifically, for a 1 g mixture of crude material the sample is dissolved in reagent grade acetone (25 to 50 mL) and to the flask is added Celite 454 Filter Aid (5 to 15 g). The mixture is then concentrated *in vacuo* to afford a powder, which is then loaded on top of a silica gel column. The procedure is typically repeated with a small amount of acetone (5 mL) and Celite (2 g) to ensure quantitative transfer.

Structural analysis. ^{1}H NMR spectra were recorded at 23 °C on one of the following instruments: Varian Unity 400, Varian Unity 500, Varian Unity Inova 500NB. 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; CD_2HCN, δ = 1.94, center line; acetone-d_6, δ = 2.05, center line) 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, sext = sextet, sept = septet, m = multiplet, b = broad, app = apparent), coupling constant (*J*) in Hertz (Hz), and integration. ^{13}C NMR spectra were recorded at 23 °C on a Varian Unity 400 or Varian Unity 500. Chemical shifts (δ) are reported in ppm downfield from tetramethylsilane and referenced to carbon resonances in the NMR solvent ($CDCl_3$, δ = 77.0, center line; $\mathbf{C}D_3CN$, δ = 1.30, center line; acetone-d_6, δ = 29.80, center line) or to added tetramethylsilane (δ = 0.00). Carbons bearing boron substituents were not observed (quadrupolar relaxation). ^{11}B NMR were recorded at 23 °C on a General Electric GN300WB or a Varian 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, Dr. Steve Mullen, and Beth Eves at the University of Illinois School of Chemical Sciences Mass Spectrometry Laboratory. Infrared spectra were collected from a thin film on NaCl plates on a Perkin-Elmer Spectrum BX FT-IR spectrometer, a Mattson Galaxy Series FT-IR 5000 spectrometer or a Mattson Infinity Gold FT-IR spectrometer. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}). Specific rotations were measured on a Jasco DIP-370 Digital Polarimeter. Gas chromatography analysis was conducted on an Agilent Technologies 7890A instrument. GC yields are based on a dodecane internal standard using an Agilent Technologies HP-5 column (part number 19091J-413). The stereoretention values were determined by GC analysis with an Agilent Technologies chiral β-cyclodextrin stationary phase (part number 112-2532). X-ray crystallographic analyses were carried out by Dr. Scott Wilson and Dr. Danielle Gray at the University of Illinois George L. Clark X-Ray facility.

[7] Still, W.C.; Kahn, M.; Mitra, A.; *J. Org. Chem.* **1978**, *43*, 2923.

II. Experimental procedures

Haloallenes 2a-e.
The general reaction scheme for the synthesis of haloallenes **2a-e** is shown below and reaction references are provided (Figure 1):[8, 9, 10, 11]

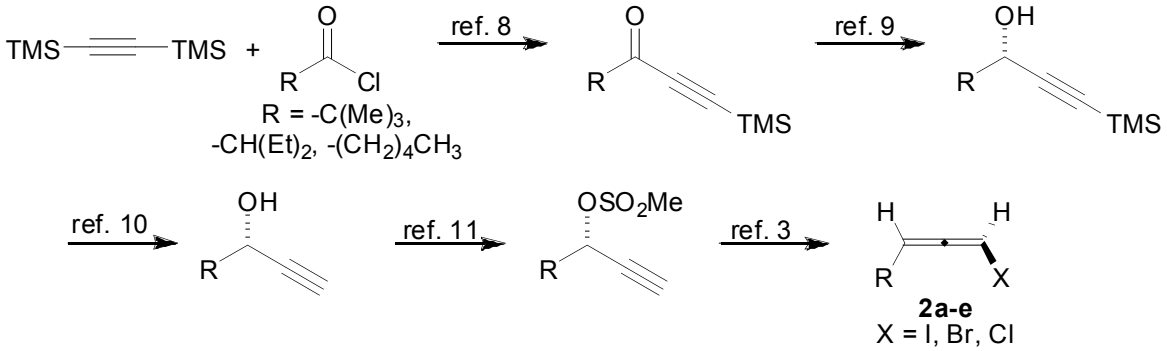
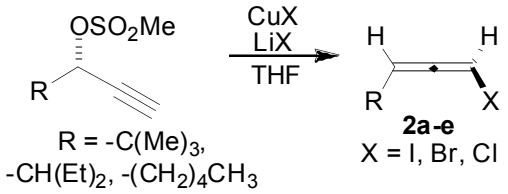


Figure 1. Synthesis of haloallenes **2a-e**



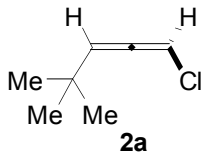
General procedure for the synthesis of haloallenes 2a-e.[3]

Preparation of $LiCuX_2$:
The purity of copper (I) iodide was found to be critical to the enantiopurity of the products **2c-e**. High purity (>99.999%) copper (I) iodide was purchased from Strem or prepared by recrystallization.[12]

In a glovebox, to a Schlenk flask equipped with a stir bar and charged with copper (I) halide (4 eq) was added THF (6 M with respect to the copper halide). Lithium halide (2 eq) and THF (0.6 M with respect to the lithium halide) were added to a separate vial. The Schlenk flask and vial were sealed, removed from the glovebox, and placed under an argon atmosphere. The copper (I) halide suspension was cooled to -78° C. The lithium halide solution was cannula transferred into the Schlenk flask. The mixture was stirred at -78 °C for 30 minutes and then stirred at 23 °C for 30 minutes. The resulting cuprate solution was cooled to 0 °C. A solution of enantioenriched mesylate (1 eq) in THF (0.3 M with respect to the mesylate) was added dropwise *via* cannula to the cuprate solution. The reaction proceeded with stirring at reflux for 1 hr 45 minutes. After

[8] Representative procedure: Bach, J.; Berenguer, R.; Garcia, J.; Loscertales, T.; Vilarrasa, J. *J. Org. Chem.* **1996**, *61*, 9021.
[9] Representative procedure: Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738.
[10] Representative procedure: Fouad, F.S.; Wright, J.M.; Plourde, G.; Purohit, A.D.; Wyatt, J.K.; El-Shafey, A.; Hynd, G.; Crasto, C.F.; Lin, Y.; Jones, G.B. *J. Org. Chem.* **2005**, *70*, 9789.
[11] Westmijze, H.; Vermeer, P. *Synthesis* **1979**, 390.
[12] Fang, L. Y.; Kauffman, G.B. *Inorganic Syntheses* **1983**, *22*, 101.

cooling the resulting mixture to 23 °C, the solution was transferred to a separatory funnel containing 1:1 NH_4Cl (sat. aq.):NH_4OH (14.8 M) and shaken. The layers were separated. The aqueous layer was extracted with Et_2O. The combined organic layers were washed with brine, dried over magnesium sulfate, filtered, and concentrated *in vacuo* to afford the crude haloallene. This oil was purified via flash chromatography on silica gel (100% petroleum ether) to afford haloallenes **2a-e** as oils.



2a

(*R*)-**1-chloro-4,4-dimethyl-1,2-pentadiene,** (*R*)-**2a.**[3] The general procedure was followed using CuCl (1.37 g, 13.9 mmol) in THF (2 mL), LiCl (0.30 g, 6.9 mmol) in THF (11 mL) and (*S*)-4,4-dimethylpent-1-yn-3-yl methanesulfonate (0.66 g, 3.5 mmol, 99:1 e.r.) in THF (11 mL). The work up used NH_4Cl:NH_4OH (150 mL), Et_2O (2 x 125 mL), and brine (15 mL). Flash chromatography (100% petroleum ether) gave chloroallene (*R*)-**2a** as a clear, pale yellow oil (0.075 g, 17%).

TLC (petroleum ether)

R_f = 0.72, visualized by short wave UV

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

δ 6.05 (d, *J* = 5.5 Hz, 1H), 5.61 (d, *J* = 5.5 Hz, 1H), 1.09 (s, 9H).

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

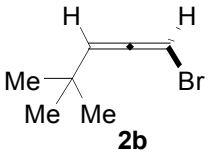
δ 199.5, 113.3, 89.3, 33.0, 29.5

HRMS (EI+)

Calculated for $C_7H_{11}Cl$:	130.0549
Found:	130.0543

$[\alpha]_D^{24}$ -139.8 (*c* 0.9, $CHCl_3$)

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 2.0 min, t_r (minor) 2.2 min; temperature: 80 °C; 6.5 mL/min.: 93.9:6.1 e.r.



2b

(*R*)-**1-bromo-4,4-dimethyl-1,2-pentadiene,** (*R*)-**2b.**[3] The general procedure was followed using CuBr (1.92 g, 13.3 mmol) in THF (2 mL), LiBr (0.58 g, 6.7 mmol) in THF (11 mL) and (*S*)-4,4-dimethylpent-1-yn-3-yl methanesulfonate (0.64 g, 3.3 mmol, 99:1 e.r.) in THF (11 mL). The

work up used NH_4Cl:NH_4OH (150 mL), Et_2O (2 x 125 mL), and brine (15 mL). Flash chromatography (100% petroleum ether) gave bromoallene (*R*)-**2b** as a clear, yellow oil (0.080 g, 14%).

TLC (petroleum ether)
R_f = 0.69, visualized by short wave UV

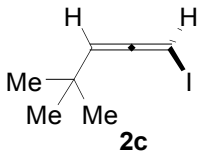
^{1}H-NMR (500 MHz, $CDCl_3$)
δ 5.98 (d, *J* = 5.5 Hz, 1H), 5.36 (d, *J* = 5.5 Hz, 1H), 1.09 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$)
δ 199.6, 112.1, 73.1, 32.5, 29.6

HRMS (EI+)
Calculated for $C_7H_{11}Br$: 174.0044
Found: 174.0039

$[\alpha]_D^{24}$ -183.0 (*c* 1.0, $CHCl_3$)

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 3.2 min, t_r (minor) 3.6 min; temperature: 80 °C; 6.5 mL/min.: 94.2:5.8 e.r.



2c

(*R*)-**1-iodo-4,4-dimethyl-1,2-pentadiene,** (*R*)-**2c.**[3] The general procedure was followed using CuI (8.03 g, 42.2 mmol) in THF (7 mL), LiI (2.86 g, 21.4 mmol) in THF (35 mL) and (*S*)-4,4-dimethylpent-1-yn-3-yl methanesulfonate (2.0 g, 10.5 mmol, 99:1 e.r.) in THF (35 mL). The work up used NH_4Cl:NH_4OH (400 mL), Et_2O (2 x 100 mL), and brine (100 mL). Flash chromatography (100% petroleum ether) gave iodoallene (*R*)-**2c** as a clear, yellow oil (1.98 g, 85%).

TLC (petroleum ether)
R_f = 0.74, visualized by short wave UV

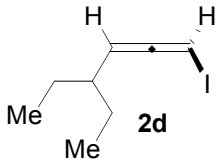
^{1}H-NMR (500 MHz, $CDCl_3$)
δ 5.71 (d, *J* = 6 Hz, 1H), 5.06 (d, *J* = 6 Hz, 1H), 1.08 (s, 9H).

^{13}C-NMR (125 MHz, $CDCl_3$)
δ 203.3, 107.7, 36.5, 31.8, 29.7

HRMS (EI+)
Calculated for $C_7H_{11}I$: 221.9906
Found: 221.9919

$[\alpha]_D^{23}$ -264.2 (*c* 1.8, $CHCl_3$)

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 2.7 min, t_r (minor) 3.0 min; temperature: 100 °C; 6.5 mL/min.: 89.5:10.5 e.r.



2d

(*R*)-**1-iodo-4-ethyl-1,2-hexadiene,** (*R*)-**2d.** The general procedure was followed using CuI (7.48 g, 39.3 mmol) in THF (6.5 mL), LiI (2.58 g, 19.3 mmol) in THF (33 mL) and (*S*)-4-ethylhex-1-yn-3-yl methanesulfonate (1.98 g, 9.7 mmol, approximately 99:1 e.r.) in THF (33 mL). The work up used NH_4Cl:NH_4OH (400 mL), Et_2O (1 x 100 mL), and brine (100 mL). Flash chromatography (100% petroleum ether) gave iodoallene (*R*)-**2d** as a clear, yellow oil (2.1 g, 91%).

TLC (petroleum ether)
R_f = 0.71, visualized by short wave UV

^{1}H-NMR (500 MHz, $CDCl_3$)
δ 5.67 (dd, *J* = 6, 1.5 Hz, 1H), 4.95 (dd, *J* = 8, 6 Hz, 1H), 2.03 – 1.96 (m, 1H), 1.57 – 1.43 (m, 2H), 1.41 – 1.29 (m, 2H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H).

^{13}C-NMR (125 MHz, $CDCl_3$)
δ 205.0, 100.1, 42.0, 35.7, 27.4, 27.1, 11.7, 11.5

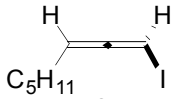
HRMS (EI+)

Calculated for $C_8H_{13}I$:	236.0062
Found:	236.0048

$[\alpha]_D^{25}$ -309.2 (*c* 0.9, $CHCl_3$)
Absolute stereochemical assignment was made according to the Lowe-Brewster rules[13] and by analogy to known haloallenes **2a-c**.[3]

The ee was determined by chiral GC using a Cyclodex B column:
t_r (major) 4.2 min, t_r (minor) 4.6 min; temperature: 110 °C; 6.5 mL/min.: 91.0:9.0 e.r.

[13] Maehr, H. *Tetrahedron: Asymmetry* **1992**, *3*, 735.



2e

(*R*)-**1-iodo-1,2-octadiene,** (*R*)-**2e.**[3] The general procedure was followed using CuI (5.59 g, 29.4 mmol) in THF (5 mL), LiI (1.97 g, 14.7 mmol) in THF (25 mL) and (*S*)-oct-1-yn-3-yl methanesulfonate (1.50 g, 7.3 mmol, approximately 97:13 e.r.) in THF (12.5 mL). The work up used NH_4Cl:NH_4OH (300 mL), Et_2O (2 x 125 mL), and brine (30 mL). Flash chromatography (100% petroleum ether) gave iodoallene (*R*)-**2e** as a clear, yellow oil (1.24 g, 74%).

TLC (petroleum ether)

R_f = 0.63, visualized by short wave UV

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

δ 5.68 (ddd, *J* = 5.5, 2.5, 2.5 Hz, 1H), 5.11 (dt, *J* = 7, 6 Hz, 1H), 2.19 – 2.06 (m, 2H), 1.54 – 1.35 (m, 2H), 1.34 – 1.27 (m, 4H), 0.91 – 0.90 (m, 3H).

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

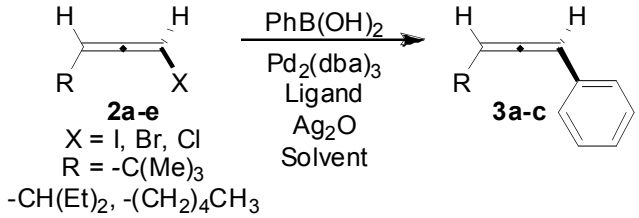
δ 205.4, 96.5, 35.5, 31.2, 28.1, 27.5, 22.4, 14.0

HRMS (EI+)

Calculated for $C_8H_{13}I$:	236.0062
Found:	236.0045

$[\alpha]_D^{23}$ -166.9 (*c* 1.6, $CHCl_3$)

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 5.6 min, t_r (minor) 6.2 min; temperature: 110 °C; 6.5 mL/min: 69.8:30.2 e.r.



General procedure for cross-coupling reactions in Table 1, Entries 1-11 and 13-14:

Preparation of catalyst stock solution. In a glovebox, to a 7 mL vial equipped with a stir bar and charged with phosphine ligand was added a premixed solution of $Pd_2(dba)_3$ in THF. The solution was stirred at 23 °C for 20 min.

The freshly prepared catalyst stock solution was used in the following reaction:
In a glovebox, to a 7 mL vial equipped with a stir bar and charged with base (0.14 mmol) was added the reaction solvent (1.2 mL). A stock solution of $PhB(OH)_2$ (125.4 mg, 1.0 mmol) in THF (3.0 mL) was prepared. An aliquot (0.20 mL, corresponding to 8.4 mg of boronic acid, 0.069 mmol) of this solution was added to the reaction vial. A stock solution of haloallene:dodecane (2:1 molar ratio) in THF (0.23 M with respect to the haloallene) was prepared. An aliquot (0.20 mL, corresponding to 0.045 mmol haloallene) was added to the reaction vial. An aliquot of the prepared catalyst stock solution (0.20 mL, corresponding to 4 mol% $Pd_2(dba)_3$ and 16 mol% ligand) was added to the reaction vial. The vial was sealed with a septum cap and removed from the glovebox. Degassed DI H_2O (0.15 mL) was added. The solution was stirred at 23 ^oC for 1.5 hr in a subdued light environment. Activated carbon, Darco G-60 (~50 mg) was added to the reaction solution.[14] The solution was stirred at 23 ^oC under air for 20 min. The solution was dried over $MgSO_4$ and filtered through a plug of Celite. The resulting solution was analyzed by GC.

Entry 1: Synthesis of (*S*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^oC for 10 min. A portion (1.4 mL) of this solution was added to a vial containing recrystallized PPh_3 (13.8 mg, 0.053 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (32.5 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of chloroallene (*R*)-**2a** (17.6 mg, 0.13 mmol) and dodecane (11.3 mg, 0.066 mmol) in THF (0.60 mL) was prepared. An aliquot (0.20 mL) of this chloroallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2a** was determined by chiral GC using a Cyclodex B column: 93.9:6.1 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 15.8:84.2 e.r.
Stereoretention = -78%, (*S*)-**3a** was the major product, corresponding to net stereoinversion
GC yield based on the dodecane internal standard = 83%

Entry 2: Synthesis of (*S*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^oC for 10 min. A portion (1.4 mL) of this solution was added to a vial containing recrystallized PPh_3 (13.8 mg, 0.053 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (33.1 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of bromoallene (*R*)-**2b** (23.3 mg, 0.13 mmol) and dodecane (11.2 mg, 0.066 mmol) in THF (0.60 mL) was prepared. An aliquot (0.20 mL) of this bromoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

[14] The addition of Darco proved important in preserving the enantiopurity of the product. Working up the reaction without Darco led to a decrease in stereoretention over time. For further discussion on the use of Darco see: Molander, G.A.; Sommers, E.M.; Baker, S.R. *J. Org. Chem*. **2006**, *71*, 1563.

Based on the average of two runs:
The e.r. of (*R*)-**2b** was determined by chiral GC using a Cyclodex B column: 94.2:5.8 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 15.5:84.5 e.r.
Stereoretention = -78%, (*S*)-**3a** was the major product, corresponding to net stereoinversion
GC yield based on the dodecane internal standard = 61%

Entry 3: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^oC for 10 min. A portion (1.4 mL) of this solution was added to a vial containing recrystallized PPh_3 (13.8 mg, 0.053 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (34.1 mg, 0.15 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (90.7 mg, 0.41 mmol) and dodecane (35.3 mg, 0.21 mmol) in THF (1.8 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 78.4:21.6 e.r.
Stereoretention = 72%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 49%

Entry 4: Synthesis of (*R*)-**3b.**
Following the general procedure, a solution of $Pd_2(dba)_3$ (15.5 mg, 0.017 mmol) in THF (2.0 mL) was prepared and stirred at 23 ^oC for 10 min. This entire solution was added to a vial containing recrystallized PPh_3 (18.2 mg, 0.069 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (30.1 mg, 0.13 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2d** (36.5 mg, 0.15 mmol) and dodecane (13.4 mg, 0.079 mmol) in THF (0.6 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2d** was determined by chiral GC using a Cyclodex B column: 91.0:9.0 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 73.8:26.2 e.r.
Stereoretention = 58%, (*R*)-**3b** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 16%

Entry 5: Synthesis of (*R*)-**3c.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^oC for 10 min. A portion (1.4 mL) of this solution was added to a vial containing recrystallized PPh_3 (13.8 mg, 0.053 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (31.6 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution

of iodoallene (*R*)-**2e** (31.8 mg, 0.13 mmol) and dodecane (11.0 mg, 0.065 mmol) in THF (0.6 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2e** was determined by chiral GC using a Cyclodex B column: 69.8:30.2 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 55:45 e.r.
Stereoretention = 25%, (*R*)-**3c** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 10%

Entry 6: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (69.4 mg, 0.076 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^{o}C for 10 min. A portion (0.8 mL) of this solution was added to a vial containing trifurylphosphine (7.1 mg, 0.031 mmol). This catalyst stock solution was stirred at 23 ^{o}C for 20 min. Ag_2O (30.9 mg, 0.13 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (113.5 mg, 0.51 mmol) and dodecane (38.2 mg, 0.22 mmol) in THF (2.2 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 81.6:18.4 e.r.
Stereoretention = 80%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 59%

Entry 7: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^{o}C for 10 min. A portion (0.8 mL) of this solution was added to a vial containing PCy_3 (9.1 mg, 0.032 mmol). This catalyst stock solution was stirred at 23 ^{o}C for 20 min. Ag_2O (33.9 mg, 0.15 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (90.7 mg, 0.41 mmol) and dodecane (35.3 mg, 0.21 mmol) in THF (1.8 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 69.8:30.2 e.r.
Stereoretention = 50%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 10%

Entry 8: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (69.4 mg, 0.076 mmol) in THF (8.0 mL) was prepared and stirred at 23 °C for 10 min. A portion (0.8 mL) of this solution was added to a vial containing P^tBu_2Me (6.1 mg, 0.038 mmol). This catalyst stock solution was stirred at 23 °C for 20 min. Ag_2O (33.0 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (113.5 mg, 0.51 mmol) and dodecane (38.2 mg, 0.22 mmol) in THF (2.2 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 78.0:22.0 e.r.
Stereoretention = 71%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 15%

Entry 9: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 °C for 10 min. A portion (0.8 mL) of this solution was added to a vial containing P(*o*-tol)$_3$ (8.4 mg, 0.028 mmol). This catalyst stock solution was stirred at 23 °C for 20 min. Ag_2O (31.9 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (90.7 mg, 0.41 mmol) and dodecane (35.3 mg, 0.21 mmol) in THF (1.8 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 85.9:14.1 e.r.
Stereoretention = 91%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 58%

Entry 10: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 °C for 10 min. A portion (0.8 mL) of this solution was added to a vial containing P^tBu_3 (6.7 mg, 0.033 mmol). This catalyst stock solution was stirred at 23 °C for 20 min. Ag_2O (31.7 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (90.7 mg, 0.41 mmol) and dodecane (35.3 mg, 0.21 mmol) in THF (1.8 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 86.7:13.3 e.r.
Stereoretention = 93%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 38%

Entry 11: Synthesis of (*R*)-**3a.**
Following the general procedure, a stock solution of $Pd_2(dba)_3$ (68.0 mg, 0.074 mmol) in THF (8.0 mL) was prepared and stirred at 23 ^oC for 10 min. A portion (0.8 mL) of this solution was added to a vial containing XPhos[15] (14.8 mg, 0.031 mmol). This catalyst stock solution was stirred at 23 ^oC for 20 min. Ag_2O (32.2 mg, 0.14 mmol) was suspended in THF (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2c** (90.7 mg, 0.41 mmol) and dodecane (35.3 mg, 0.21 mmol) in THF (1.8 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 86.0:14.0 e.r.
Stereoretention = 91%, (*R*)-**3a** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 42%

Entry 12: Synthesis of (*R*)-**3a.**
Preparation of catalyst solution. In a glovebox, to a 20 mL vial equipped with a stir bar and charged with XPhos (133.1 mg, 0.28 mmol) and $Pd_2(dba)_3$ (63.4 mg, 0.069 mmol) was added THF (7.5 mL). The solution was stirred at 23 °C for 20 min.

The freshly prepared catalyst solution was used in the following reaction:
In a glovebox, to a 100 mL round bottom flask equipped with a stir bar and charged with $PhB(OH)_2$ (306.5 mg, 2.5 mmol) and Ag_2O (1.16 g, 5.0 mmol) was added iodoallene (*R*)-**2c** (334.4 mg, 1.5 mmol) as a solution in hexanes (55 mL). The prepared catalyst solution was added in one portion. The flask was sealed with a septum and removed from the glovebox. Degassed DI H_2O (6.0 mL) was added. The solution was stirred in a subdued light environment at 23 ^oC for 1.5 hr. Activated carbon, Darco G-60 (800 mg) was added to the reaction solution. The solution was stirred at 23 ^oC under air for 20 min. The aqueous layer was removed and the organic layer was dried over $MgSO_4$ and filtered through a plug of Celite. The resulting clear, yellow solution was concentrated *in vacuo*, and the resulting residue was purified via flash chromatography on silica gel (100% petroleum ether) to afford the cross coupled product (*R*)-**3a** as a pale yellow oil (157.6 mg, 61%).

The e.r. of (*R*)-**2c** was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 89.5:10.5 e.r.
Stereoretention = >99%, (*R*)-**3a** was the major product, corresponding to net stereoretention

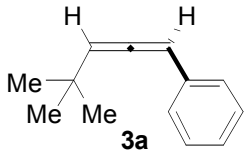
[15] Martin, R.; Buchwald, S.L. *Acc. Chem. Res.* **2008**, *41*, 1461.

Entry 13: Synthesis of (*R*)-**3b.**
Following the general procedure, a solution of $Pd_2(dba)_3$ (15.5 mg, 0.017 mmol) in THF (2.0 mL) was prepared and stirred at 23 °C for 10 min. This entire solution was added to a vial containing XPhos (17.0 mg, 0.036 mmol). This catalyst stock solution was stirred at 23 °C for 20 min. Ag_2O (30.1 mg, 0.13 mmol) was suspended in hexanes (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2d** (33.7 mg, 0.14 mmol) and dodecane (14.2 mg, 0.083 mmol) in hexanes (0.6 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2d** was determined by chiral GC using a Cyclodex B column: 91.0:9.0 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 91.0:9.0 e.r.
Stereoretention = >99%, (*R*)-**3b** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 64%

Entry 14: Synthesis of (*R*)-**3c.**
Following the general procedure, a solution of $Pd_2(dba)_3$ (15.5 mg, 0.017 mmol) in THF (2.0 mL) was prepared and stirred at 23 °C for 10 min. This entire solution was added to a vial containing XPhos (17.0 mg, 0.036 mmol). This catalyst stock solution was stirred at 23 °C for 20 min. Ag_2O (33.6 mg, 0.14 mmol) was suspended in hexanes (1.2 mL). An aliquot (0.20 mL) of the boronic acid stock solution was added. A stock solution of iodoallene (*R*)-**2e** (31.6 mg, 0.13 mmol) and dodecane (13.4 mg, 0.079 mmol) in hexanes (0.6 mL) was prepared. An aliquot (0.20 mL) of this iodoallene stock solution was added to the reaction vial. An aliquot (0.20 mL) of the prepared catalyst stock solution was added and the general procedure was followed for the remainder of the experiment.

Based on the average of two runs:
The e.r. of (*R*)-**2e** was determined by chiral GC using a Cyclodex B column: 69.8:30.2 e.r.
The e.r. of the product was determined by chiral GC using a Cyclodex B column: 66.8:33.2 e.r.
Stereoretention = 85%, (*R*)-**3c** was the major product, corresponding to net stereoretention
GC yield based on the dodecane internal standard = 30%



3a

(*R*)-**(4,4-dimethylpenta-1,2-dien-1-yl)benzene,** (*R*)-**3a.**[16]

TLC (petroleum ether)
R_f = 0.55, visualized by short wave UV

[16] Elsevier, C.J.; Vermeer, P. *J. Org. Chem.* **1985**, *50*, 3042.

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

δ 7.35 – 7.28 (m, 4H), 7.19 (tt, *J* = 6.5, 2 Hz, 1H), 6.27 (d, *J* = 6.5 Hz, 1H), 5.64 (d, *J* = 6.5 Hz, 1H), 1.13 (s, 9H).

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

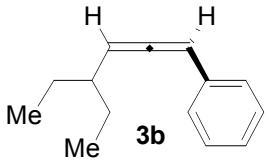
δ 203.1, 136.1, 129.4, 127.5, 127.1, 107.3, 96.8, 33.2, 30.4

HRMS (EI+)

Calculated for $C_{13}H_{16}$:	172.1252
Found:	172.1236

$[\alpha]_D^{25}$ -301.8 (*c* 1.1, $CHCl_3$)

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 13.3 min, t_r (minor) 14.2 min; temperature: 100 °C; 6.5 mL/min: 89.5:10.5 e.r.



3b

(*R*)-**(4-ethylhexa-1,2-dien-1-yl)benzene,** (*R*)-**3b.**

TLC (petroleum ether)

R_f = 0.49, visualized by short wave UV

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

δ 7.32 – 7.27 (m, 4H), 7.20 – 7.15 (m, 1H), 6.14 (dd, *J* = 6.5, 2 Hz, 1H), 5.40 (dd, *J* = 7, 7.5 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.57 – 1.46 (m, 2H), 1.46 – 1.34 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.5, 3H).

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

δ 204.9, 135.2, 128.5, 126.5, 98.9, 94.5, 94.5, 43.1, 27.7, 27.4, 11.9, 11.7

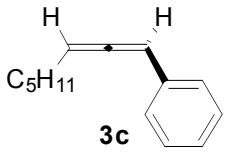
HRMS (EI+)

Calculated for $C_{14}H_{18}$:	186.1409
Found:	186.1420

$[\alpha]_D^{25}$ -169.1 (*c* 0.6, $CHCl_3$)

Absolute stereochemical assignment was made according to the Lowe-Brewster rules and by analogy to known haloallene **3a**.[16]

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 19.5 min, t_r (minor) 20.3 min; temperature: 110 °C; 6.5 mL/min: 73.8:26.2 e.r.



3c

(*R*)-**octa-1,2-dien-1-ylbenzene,** (*R*)-**3c.**

TLC (petroleum ether)

R_f = 0.57, visualized by short wave UV

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

δ 7.27 (d, *J* = 1 Hz, 4H), 7.16 – 7.13 (m, 1H), 6.11 – 6.08 (m, 1H), 5.54 (dd, *J* = 7, 6.5 Hz, 1H), 2.12 – 2.08 (m, 2H), 1.50 – 1.44 (m, 2H), 1.36 – 1.27 (m, 4H), 0.88 – 0.85 (m, 3H).

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

δ 205.1, 135.2, 128.5, 126.6, 126.6 95.1, 94.5, 31.4, 28.8, 28.7, 22.5, 14.1

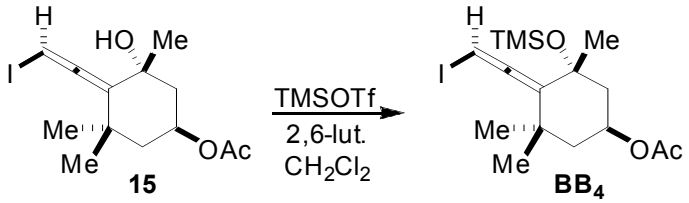
HRMS (EI+)

Calculated for $C_{14}H_{18}$:	186.1409
Found:	186.1416

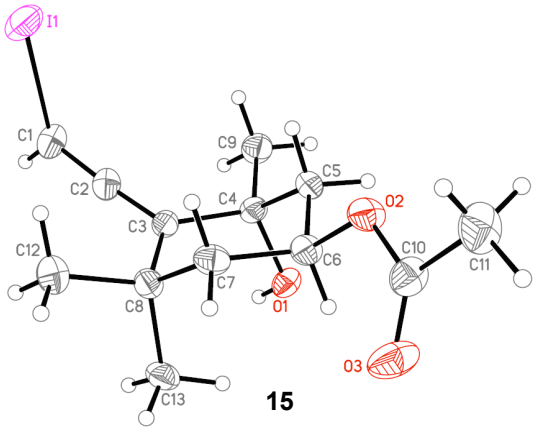
$[\alpha]_D^{25}$ -66.7 (*c* 1.4, $CHCl_3$)

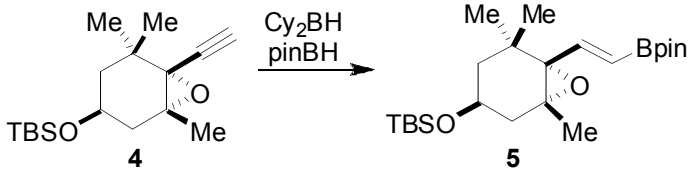
Absolute stereochemical assignment was made according to the Lowe-Brewster rules and by analogy to known haloallene **3a**.[16]

The e.r. was determined by chiral GC using a Cyclodex B column:
t_r (major) 26.2 min, t_r (minor) 26.9 min; temperature: 110 °C; 6.5 mL/min: 63.0:37.0 e.r.



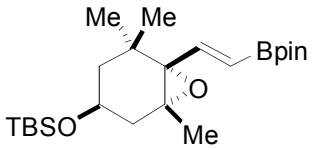
Iodoallene BB_4. Iodoallene **BB_4** was prepared as previously described.[2] X-ray quality crystals of the unprotected iodoallene starting material **15** were grown by layering hexane onto a dissolved solution of the allene in Et_2O. The sample was placed in a -20 °C freezer. Crystals formed overnight. To the best of our knowledge, this is the first reported example of a crystal structure of an iodoallene.[17]





Pinacol ester 5. In a glovebox, to a 20 mL vial equipped with a stir bar and charged with alkyne **4** (2.57 g, 8.7 mmol) was added solid dicyclohexylborane[18] (203.4 mg, 1.1 mmol).[19] The vial was sealed with a septum cap and removed from the glovebox. To the vial was added neat pinacol borane (1.4 mL, 9.6 mmol). The solution was stirred at 23 °C for 13 hr. The resulting thick white paste was dissolved in Et_2O, dry loaded onto Celite, and purified via flash chromatography on silica gel (Hexanes:EtOAc 95:5) to afford pinacol ester **5** as a white solid (3.0 g, 81%).

[17] A search of the Cambridge Crystallographic Database was conducted on 3/17/2010.
[18] Abiko, A. *Org. Synth.* **2002**, *79*, 103.
[19] Shirakawa, K.; Arase, A.; Hoshi, M. *Synthesis* **2004**, *11*, 1814.



5

TLC (Hexanes:EtOAc 9:1)

R_f = 0.50, stained by $KMnO_4$

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

δ 6.68 (d, *J* = 18 Hz, 1H), 5.54 (d, *J* = 18 Hz, 1H), 3.72 (m, 1H), 2.09 (ddd, *J* = 14.5, 5, 1 Hz, 1H), 1.50 (dd, *J* = 14.5, 8 Hz, 1H), 1.36 (ddd, *J* = 13, 3.5, 1Hz, 1H), 1.14 (s, 12H), 1.10 (m, 1H), 1.03 (s, 3H), 1.02 (s, 3H), 0.81 (s, 3H), 0.75 (s, 9H), -0.090 (s, 3H), -0.094 (s, 3H).

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

δ 147.9, 82.9, 70.9, 66.0, 64.5, 46.9, 41.1, 34.5, 29.3, 25.7, 24.7, 24.6, 19.9, 17.9, -4.9, -4.9

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

δ 31.1

HRMS (ESI+)

Calculated for $C_{23}H_{44}BO_4Si$: 423.3102

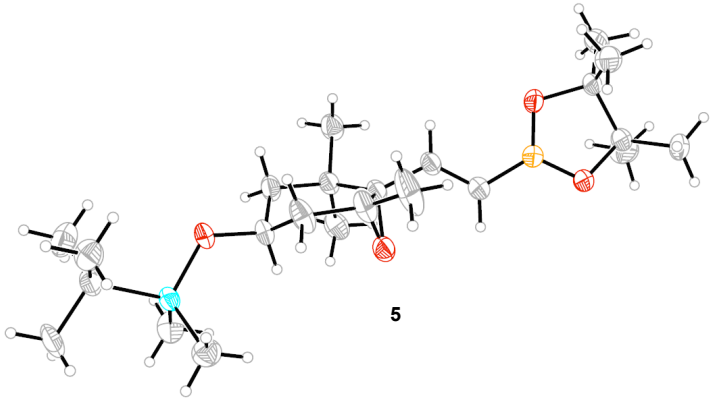
Found: 423.3120

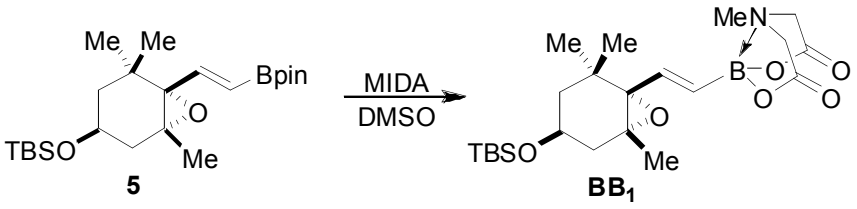
IR (thin film, cm^{-1})

2976, 2953, 2926, 2854, 1635, 1462, 1379, 1344, 1321, 1250, 1198, 1144, 1072, 966, 922, 881, 835, 775, 667, 650, 567.

$[\alpha]_D^{27}$ -75.6 (*c* 1.1, $CHCl_3$)

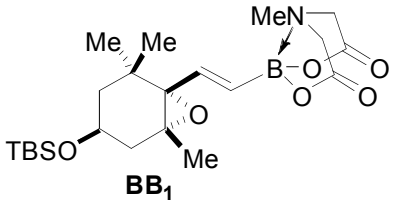
X-ray quality crystals were grown by layering pentane onto a dissolved solution of **5** in acetone. After the layers slowly mixed, the solvent was allowed to slowly evaporate to yield crystals.





5 **BB$_1$**

MIDA boronate BB$_1$. To a 250 mL round bottom flask equipped with a stir bar and charged with pinacol ester **5** (2.54 g, 6.0 mmol) was added *N*-methyliminodiacetic acid, MIDA, (5.48 g, 37.2 mmol) and DMSO (60 mL). The flask was sealed and the reaction stirred at 65 ^{o}C for 10.5 hr. The resulting solution was poured into 500 mL H_2O. The mixture was diluted with 250 mL EtOAc and shaken. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 150 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an acetone solution and purified via flash chromatography on silica gel (Et_2O:Acetone 100:0 → 40:60) to afford MIDA boronate **BB$_1$** as a white solid (1.18 g, 44%) and unreacted starting material (1.18 g recovered). The unreacted starting material was subjected to two additional cycles of the above procedure to afford MIDA boronate **BB$_1$** as a white solid (1.98 g total, 73%).



BB$_1$

TLC (Et_2O:MeCN 4:1)

R_f = 0.44, stained by $KMnO_4$

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

δ 6.39 (d, *J* = 18 Hz, 1H), 5.71 (d, *J* = 18 Hz, 1H), 4.23 (dd, *J* = 17, 2 Hz, 2H), 4.06 (dd, *J* = 17, 4 Hz, 2H), 3.88 (m, 1H), 3.01 (s, 3H), 2.21 (ddd, *J* = 14, 5, 1 Hz, 1H), 1.66 (dd, *J* = 14.5, 8.5 Hz, 1H), 1.50 (ddd, *J* = 14, 5, 1 Hz, 1H), 1.30 – 1.19 (m, 1H), 1.15 (s, 3H), 1.14 (s, 3H), 0.93 (s, 3H), 0.88 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H).

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

δ 169.0, 140.7, 71.4, 66.5, 65.6, 62.3, 47.9, 47.5, 42.1, 35.4, 29.8, 26.2, 25.4, 20.4, 18.5, -4.6, -4.6

^{11}B-NMR (96 MHz, d_6-acetone)

δ 11.5

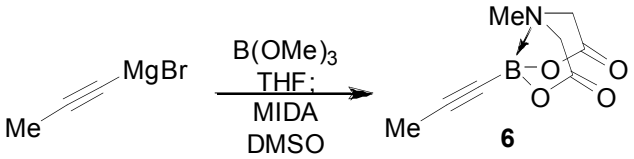
HRMS (ESI+)

Calculated for $C_{22}H_{39}BNO_6Si$:	452.2640
Found:	452.2657

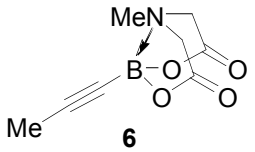
IR (thin film, cm^{-1})

2953, 2929, 2856, 1780, 1753, 1637, 1460, 1389, 1340, 1294, 1255, 1090, 1034, 1007, 953, 881, 858, 837, 773, 681, 588, 513.

$[\alpha]_D^{25}$ -55.7 (*c* 1.0, $CHCl_3$)



Propynyl MIDA boronate 6. To a 300 mL 3-neck round bottom flask equipped with a stir bar was added $B(OMe)_3$ (5.9 mL, 53 mmol) and THF (50 mL). The solution was cooled to -78 °C. Propynylmagnesium bromide (0.5 M in THF, 100 mL, 50 mmol) was added dropwise *via* cannula over 45 min. The resulting solution was stirred at -78 °C for 1.5 hr, followed by stirring at 23 °C for 2 hr. In a separate 500 mL 3-neck round bottom flask equipped with a stir bar, internal thermometer, 500 mL addition funnel, and distillation apparatus was added MIDA (15.0 g, 102 mmol) and DMSO (50 mL). The solution was heated with an oil bath to an internal temperature of 110 - 115 °C.[20] The borate suspension was transferred to the addition funnel and was continuously agitated with a stream of nitrogen. The borate suspension was added dropwise to the hot MIDA solution over 2 hr 50 min, keeping the internal temperature between 105 and 115 °C. After full addition of the borate suspension, the reaction solution was cooled to 60 °C and placed under vacuum (300 mTorr) to distill the reaction to dryness. The resulting foam was cooled to 23 °C and dissolved in 200 mL EtOAc, 50 mL acetone, and 75 mL H_2O and poured into 200 mL EtOAc:Acetone (1:1) and 75 mL brine. The mixture was shaken and the aqueous layer was removed and extracted with EtOAc (1 x 100 mL). The combined organic phases were washed with brine (2 x 20 mL). The brine wash was back extracted with EtOAc:Acetone (2:1, 1 x 75 mL) The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting yellow solid was dissolved in 100 mL THF and 1000 mL Et_2O was added to precipitate the product. The resulting solid was collected by vacuum filtration to yield propynyl MIDA boronate **6** as a white solid (7.48 g, 77%).



TLC (Et_2O:Acetone 2:1)

R_f = 0.28, stained by $KMnO_4$

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

δ 4.22 (d, *J* = 17 Hz, 2H), 4.05 (d, *J* = 17 Hz, 2H), 3.18 (s, 3H), 1.83 (s, 3H).

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

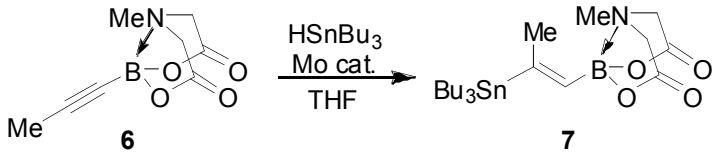
[20] Dick, G.R.; Knapp, D.M.; Gillis, E.P.; Burke, M.D. **2010**, *submitted.*

δ 168.6, 62.1, 48.2, 41.1, 4.0

^{11}B-NMR (96 MHz, d_6-acetone)
δ 6.8

HRMS (ESI+)
Calculated for $C_8H_{11}BNO_4$: 196.0781
Found: 196.0784

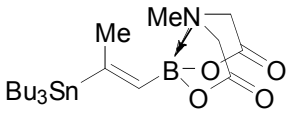
IR (thin film, cm^{-1})
3009, 2957, 2203, 1790, 1462, 1342, 1290, 1260, 1192, 1169, 1092, 994, 882, 858, 706.



6 **7**

Mo cat. = $[Mo(allyl)Br(CO)_2(CH_3CN)_2]$

MIDA boronate 7. In a glovebox, to a 500 mL round bottom flask equipped with a stir bar and charged with propynyl MIDA boronate **6** (5.65 g, 29.0 mmol) was added $[Mo(allyl)Br(CO)_2(CH_3CN)_2]$[21] (705.4 mg, 1.98 mmol). The round bottom was sealed with a septum, removed from the glovebox, and placed under a nitrogen atmosphere. THF (140 mL) was added and the solution was cooled to 0 °C. To the resulting solution was added Bu_3SnH (7.6 mL, 28.2 mmol) dropwise over 45 min to give a dark brown solution. The reaction solution was recharged with a solution of $[Mo(allyl)Br(CO)_2(CH_3CN)_2]$ (700. mg, 1.97 mmol) in THF (6 mL) in one portion, followed by Bu_3SnH (7.6 mL, 28.2 mmol) dropwise over 10 min. The cold bath was removed and the reaction solution was stirred at 23 °C for 2.5 hr. The resulting dark brown solution was concentrated *in vacuo*. The resulting foam was dissolved in hexanes and loaded onto a silica gel column. Purification via flash chromatography (Et_2O:MeCN 100:0 → 80:20) afforded MIDA boronate **7** as a pale yellow foam (11.8 g, 84%).



7

TLC (Et_2O:MeCN 4:1)
R_f = 0.70, stained by $KMnO_4$

[21] Miguel, D.; Perez-Martinez, J.A.; Riera, V. *Organometallics* **1994**, *13*, 1336.

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

δ 5.74 (q, *J* = 1.5 Hz, 1H), 4.17 (d, *J* = 17 Hz, 2H), 3.98 (d, *J* = 17 Hz, 2H), 3.03 (s, 3H), 2.11 (d, *J* = 1.5 Hz, 3H), 1.64 – 1.45 (m, 6H), 1.34 (app sext, *J* = 7.5 Hz, 6H), 1.02 – 0.86 (m, 15H).

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

δ 168.9, 161.1, 62.1, 46.9, 29.6, 27.7, 24.0, 13.7, 9.4

^{11}B-NMR (96 MHz, d_6-acetone)

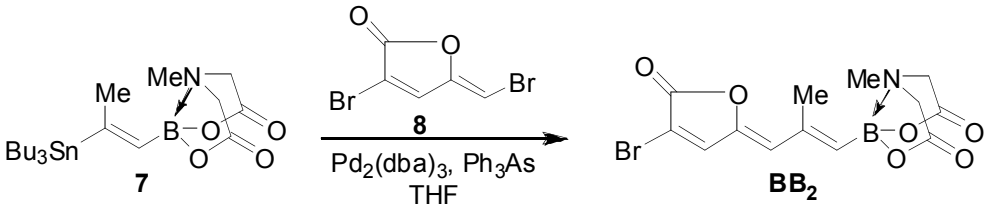
δ 10.4

HRMS (ESI+)

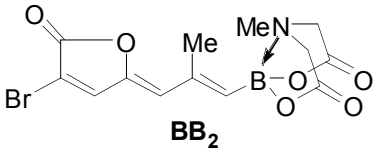
Calculated for $C_{20}H_{39}BNO_4Sn$:	488.2002
Found:	488.2008

IR (thin film, cm^{-1})

3002, 2957, 2926, 2872, 2853, 1767, 1587, 1461, 1376, 1337, 1293, 1125, 1022, 922, 873, 822, 760, 733, 689, 660, 593.



MIDA boronate BB_2. In a glovebox, to a 1000 mL round bottom equipped with a stir bar, MIDA boronate **7** (23.1 g, 47.6 mmol), and dibromolactone **8**[22] (13.2 g, 51.9 mmol) was added $Pd_2(dba)_3$ (1.31 g, 1.4 mmol) and $AsPh_3$ (878.0 mg, 2.9 mmol). The round bottom was sealed with a septum, removed from the glovebox, and placed under a nitrogen atmosphere. THF (250 mL) was added and the flask was sealed under a nitrogen atmosphere. The reaction solution was stirred at 60 °C for 3 hr and was then cooled to 23 °C. The resulting dark yellow solution was concentrated *in vacuo*. The resulting solid was dry loaded onto Celite from an acetone solution and purified via flash chromatography on silica gel (Et_2O:Acetone 100:0 → 50:50) to afford MIDA boronate **BB_2** as a pale yellow solid (13.6 g, 77%).



TLC (Et_2O:Acetone 4:1)

R_f = 0.24, stained by $KMnO_4$

[22] Sorg, A.; Blank, F.; Bruckner, R. *Synlett* **2005**, *8*, 1286.

^{1}H-NMR (500 MHz, d_6-acetone)
δ 7.96 (d, J = 0.5 Hz, 1H), 6.03 (dd, J = 1, 0.5 Hz, 1H), 5.92 (app quint, J = 1 Hz, 1H), 4.26 (d, J = 17 Hz, 2H), 4.10 (d, J = 17 Hz, 2H), 3.10 (s, 3H), 2.23 (d, J = 1 Hz, 3H).

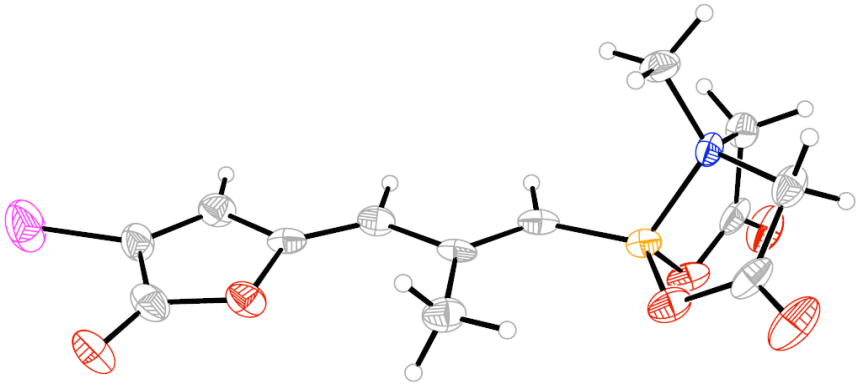
^{13}C-NMR (125 MHz, d_6-acetone)
δ 168.8, 166.0, 146.6, 145.8, 145.1, 122.1, 110.6, 62.5, 47.2, 18.6

^{11}B-NMR (96 MHz, d_6-acetone)
δ 11.2

HRMS (ESI+)
Calculated for $C_{13}H_{14}BBrNO_6$: 370.0098
Found: 370.0089

IR (thin film, cm^{-1})
3011, 2957, 2919, 2229, 1765, 1630, 1590, 1454, 1338, 1292, 1188, 1125, 891, 866, 821, 751, 710, 563.

X-ray quality crystals were grown by layering Et_2O onto a dissolved solution of **BB_2** in acetone. The layers slowly mixed, forming crystals.

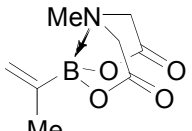


BB_2

9

Isoprenyl MIDA boronate 9. To a 500 mL 3-neck round bottom flask equipped with a stir bar was added $B(OMe)_3$ (12.0 mL, 105 mmol) and THF (100 mL). The solution was cooled to -78 °C. Isoprenylmagnesium bromide (0.5 M in THF, 200 mL, 100 mmol) was added dropwise *via* cannula over 2 hr. The resulting solution was stirred at -78 °C for 1.5 hr, followed by stirring at 23 °C for 2 hr. To a separate 1000 mL 3-neck round bottom flask equipped with a stir bar, internal thermometer, 500 mL addition funnel, and distillation apparatus was added MIDA (29.9

g, 203 mmol) and DMSO (100 mL). The solution was heated with an oil bath to an internal temperature of 110 - 115 °C.[20] The borate suspension was transferred to the addition funnel and was continuously agitated with a stream of nitrogen. The borate suspension was added dropwise to the hot MIDA solution over 2 hr, keeping the internal temperature between 100 and 115 °C. After full addition of the borate suspension, the reaction solution was cooled to 60 °C and placed under vacuum (250 mTorr) to distill the reaction to dryness. The resulting foam was cooled to 23 °C and dissolved in 400 mL EtOAc and 150 mL H_2O and poured into 400 mL EtOAc:Acetone (1:1) and 150 mL brine. The mixture was shaken and the aqueous layer was removed and extracted with EtOAc (2 x 200 mL). The combined organic phases were washed with brine (2 x 20 mL). The brine wash was back extracted with EtOAc:Acetone (2:1, 1 x 75 mL) The combined organic phases were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting white solid was suspended in 150 mL THF and 1500 mL of Et_2O was added to precipitate the product. The resulting solid was collected by vacuum filtration to yield isoprenyl MIDA boronate **9** as a white solid (15.91 g, 81%).



9

TLC (Et_2O:MeCN 4:1)
R_f = 0.43, stained by $KMnO_4$

^{1}H-NMR (500 MHz, d_6-acetone)
δ 5.45 (bs, 1H), 5.32 (d, *J* = 2.5 Hz, 1H), 4.21 (d, *J* = 17 Hz, 2H), 4.03 (d, *J* = 17 Hz, 2H), 3.00 (s, 3H), 1.78 (s, 3H).

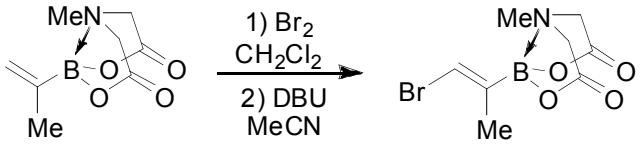
^{13}C-NMR (100 MHz, d_6-acetone)
δ 169.1, 124.4, 62.5, 47.0, 22.0

^{11}B-NMR (128 MHz, d_6-acetone)
δ 11.2

HRMS (ESI+)

Calculated for $C_8H_{13}BNO_4$:	198.0938
Found:	198.0934

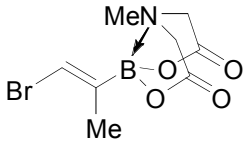
IR (thin film, cm^{-1})
3059, 2999, 2956, 2918, 1757, 1456, 1340, 1294, 1250, 1190, 1149, 1063, 1024, 993, 966, 926, 860, 741, 710, 638, 592, 567.



9 **10**

MIDA Boronate 10. To a 500 mL round bottom flask equipped with a stir bar and charged with isoprenyl MIDA boronate **9** (11.88 g, 60.3 mmol) was added CH_2Cl_2 (525 mL). The resulting clear, colorless solution was cooled to 0 ^oC in an ice bath. Neat bromine (4.7 mL, 91.4 mmol) was added dropwise over 15 minutes to give a cloudy orange solution. The solution was warmed to 23 ^oC over 1 hr and then heated to reflux for 2 hr. The resulting orange solution was cooled to 23 ^oC and concentrated *in vacuo* to give a yellow solid. This solid was azeotroped with CH_2Cl_2 (2 x 100 mL) to remove residual bromine.

The resulting white solid was suspended in MeCN (525 mL). 1,8-Diazabicyclo[5.4.0]undec-7-ene (DBU, 28 mL, 187.4 mmol) was added in one portion. The resulting mixture stirred at 23 ^oC for 1 hr to give a clear, brown solution. The solution was poured into a separatory funnel containing EtOAc:Acetone (4:1, 1000 mL) and 1 M aq. HCl (600 mL). After shaking, the layers were separated. The organic layer was washed with saturated aqueous sodium bisulfite:brine (3:2, 1 x 210 mL) and then brine (1 x 100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting oil was dissolved in 60 mL EtOAc and 20 mL acetone. Et_2O was added in 20 mL portions to precipitate the product. The resulting solid was collected by vacuum filtration to afford MIDA boronate **10** as a white solid (11.03 g, 67%).



10

TLC (Et_2O:MeCN 4:1)

R_f = 0.60, stained by $KMnO_4$

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

δ 6.55 (q, *J* = 1.5 Hz, 1H), 4.31 (d, *J* = 17 Hz, 2H), 4.15 (d, *J* = 17 Hz, 2H), 3.04 (s, 3H), 1.79 (d, *J* = 1.5 Hz, 3H).

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

δ 168.7, 115.3, 62.8, 47.3, 18.6

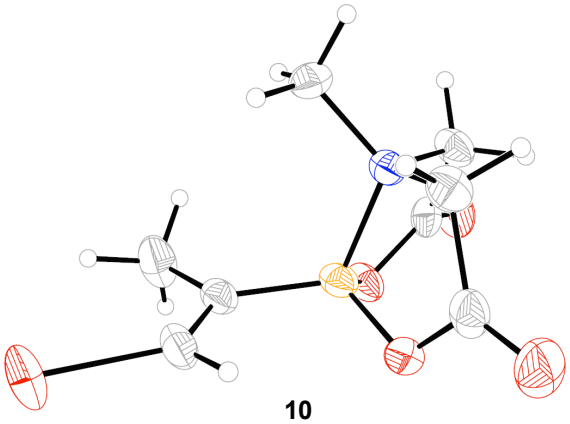
^{11}B-NMR (128 MHz, d_6-acetone)

δ 10.9

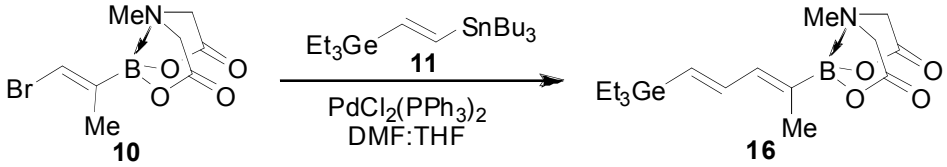
HRMS (ESI+)
Calculated for $C_8H_{12}BBrNO_4$: 276.0043
Found: 276.0040

IR (thin film, cm^{-1})
3082, 3012, 2954, 2924, 2858, 1768, 1593, 1454, 1336, 1282, 1182, 1041, 891, 864, 798, 721, 694, 586.

X-ray quality crystals were grown by layering pentane onto a dissolved solution of **10** in acetone. The layers slowly mixed, forming crystals.

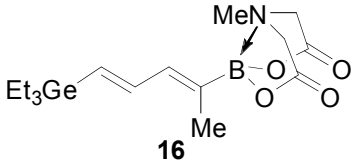


10



MIDA Boronate 16.[23] In a glovebox, to a 500 mL round bottom flask equipped with a stir bar and charged with MIDA boronate **10** (5.35 g, 19.4 mmol) was added *trans*-bis(triphenylphosphine)palladium dichloride (680.0 mg, 0.97 mmol). The round bottom was sealed with a septum, removed from the glovebox and placed under nitrogen. THF (40 mL) and DMF (150 mL) were added to give a clear, yellow solution. (*E*)-triethyl(2-(tributylstannyl)vinyl)germane **11** (11.1 g, 23.3 mmol) was added in one portion. The round bottom was sealed under nitrogen and the solution was stirred at 60 °C for 20.5 hr. The dark brown reaction solution was cooled to 23 °C and was poured into a separatory funnel containing 400 mL H_2O:brine (1:1) and 250 mL EtOAc. After shaking, the layers were separated. The aqueous layer was extracted with EtOAc (2 x 150 mL). The combined organic layers were washed with H_2O:brine (1:1, 2 x 100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an acetone solution and purified by flash chromatography on silica gel (Et_2O:MeCN 100:0 → 70:30) to afford MIDA boronate **16** as a pale yellow solid (5.5 g, 74%).

[23] Halogen-masked ICC and bis-metallated Ge/Sn building blocks have recently been reported from our laboratories: Lee, S.J.; Burke, M.D. **2010**, *manuscript in preparation*.



16

TLC (Et_2O:MeCN 4:1)

R_f = 0.57, stained by $KMnO_4$

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

δ 6.95 (dd, *J* = 18, 10.5 Hz, 1H), 6.38 (d, *J* = 10.5 Hz, 1H), 6.05 (d, *J* = 18 Hz, 1H), 4.21 (d, *J* = 17 Hz, 2H), 4.05 (d, *J* = 17 Hz, 2H), 2.99 (s, 3H), 1.82 (d, *J* = 1 Hz, 3H), 1.05 (t, *J* = 8 Hz, 9H), 0.83 (q, *J* = 8 Hz, 6H).

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

δ 169.2, 141.0, 139.5, 133.3, 62.7, 47.1, 15.1, 9.2, 4.8

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

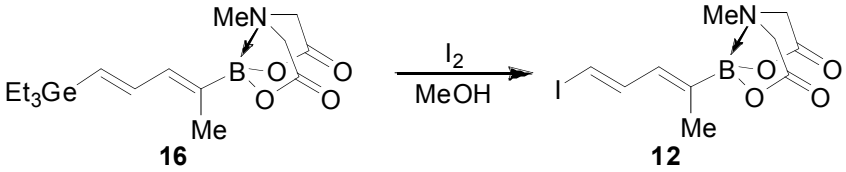
δ 11.7

HRMS (ESI+)

Calculated for $C_{16}H_{29}BGeNO_4$:	384.1408
Found:	384.1430

IR (thin film, cm^{-1})

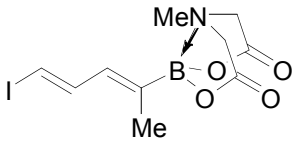
3006, 2953, 2929, 2908, 2872, 1763, 1564, 1460, 1338, 1294, 1254, 1174, 1026, 991, 889, 850, 731, 708, 575.



16 **12**

MIDA Boronate 12. In a subdued light environment, to a 300 mL round bottom flask equipped with a stir bar and charged with MIDA boronate **16** (6.29 g, 16.5 mmol) was added MeOH (450 mL) to give a clear, pale yellow solution. The solution was cooled to -78 ^oC. A solution of iodine (12.57 g, 49.5 mmol) in MeOH (150 mL) was added to the cooled reaction solution dropwise via cannula over 45 min. After stirring at -78 ^oC for 3 hr, 200 mL saturated aqueous sodium bisulfite and 150 mL EtOAc were added in one portion to give a clear, yellow solution. The cold bath was removed and replaced with a 23 ^oC water bath. The reaction solution was warmed to 23 ^oC over 30 min. The solution was poured into a separatory funnel containing 500 mL H_2O and 500 mL EtOAc. After shaking, the layers were separated and the aqueous layer was extracted with EtOAc (2 x 250 mL). The combined organic layers were washed with saturated aqueous sodium bisulfite (1 x 150 mL) and brine (1 x 150 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dry loaded

onto Celite from an acetone solution and purified by flash chromatography on silica gel (Et_2O:MeCN 100:0 → 80:20) to afford MIDA boronate **12** as a pale yellow solid (4.43 g, 77%).



12

TLC (Et_2O:MeCN 4:1)

R_f = 0.48, visualized by short wave UV

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

δ 7.48 (dd, *J* = 14.5, 11 Hz, 1H), 6.59 (d, *J* = 14.5 Hz, 1H), 6.34 (d, *J* = 11 Hz, 1H), 4.22 (d, *J* = 17 Hz, 2H), 4.05 (d, *J* = 17 Hz, 2H), 2.98 (s, 3H), 1.77 (s, 3H).

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

δ 169.1, 142.7, 136.3, 82.1, 62.6, 47.1, 15.3

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

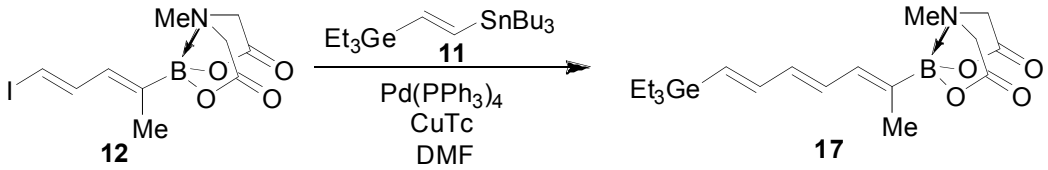
δ 11.5

HRMS (ESI+)

Calculated for $C_{10}H_{14}BINO_4$:	350.0061
Found:	350.0067

IR (thin film, cm^{-1})

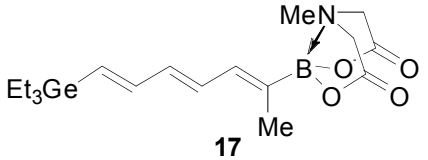
3049, 3008, 2956, 2870, 1766, 1612, 1454, 1336, 1292, 1248, 1227, 1194, 1167, 1119, 1032, 962, 889, 850, 710.



MIDA Boronate 17. In a glovebox, to a 300 mL round bottom flask equipped with a stir bar and charged with MIDA boronate **12** (4.43 g, 12.6 mmol) was added copper(I) thiophene-2-carboxylate[24] (CuTc, 3.60 g, 18.9 mmol) and tetrakis(triphenylphosphine)palladium (735.6 mg, 0.64 mmol). The round bottom was sealed with a septum, removed from the glovebox and placed under nitrogen. DMF (120 mL) was added to give a dark green solution. This solution was cooled to 0 °C. (*E*)-triethyl(2-(tributylstannyl)vinyl)germane **11** (7.20 g, 15.1 mmol) was added in one portion to give a dark brown solution. The 0 °C bath was removed. The round bottom was sealed under nitrogen and the solution was stirred at 23 °C in a subdued light

[24] Allred, G.D.; Liebeskind, L.S. *J. Am. Chem. Soc.* **1996**, *118*, 2748.

environment for 4 hr. The dark brown reaction solution was poured into a separatory funnel containing 400 mL H_2O:brine (1:1) and 400 mL EtOAc. After shaking, the layers were separated. The aqueous layer was extracted with EtOAc (2 x 200 mL). The combined organic layers were washed with H_2O (2 x 200 mL) and brine (1 x 150 mL). The aqueous washes were back extracted with EtOAc (1 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an acetone solution and purified by flash chromatography on silica gel (Et_2O:MeCN 100:0 → 80:20) to afford MIDA boronate **17** as a pale yellow solid (2.94 g, 58%).



17

TLC (Et_2O:MeCN 4:1)

R_f = 0.52, stained by $KMnO_4$ and visualized by short wave UV

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

δ 6.72 – 6.63 (m, 2H), 6.42 (d, *J* = 10.5 Hz, 1H), 6.29 (dd, *J* = 14.5, 10.5 Hz, 1H), 6.07 (d, *J* = 18.5 Hz, 1H), 4.21 (d, *J* = 17 Hz, 2H), 4.04 (d, *J* = 17 Hz, 2H), 2.97 (s, 3H), 1.82 (d, *J* = 1.5 Hz, 3 H), 1.04 (t, *J* = 8 Hz, 9H), 0.82 (q, *J* = 8 Hz, 6H).

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

δ 169.1, 145.7, 137.0, 136.6, 133.0, 129.5, 62.6, 47.1, 15.2, 9.1, 4.8

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

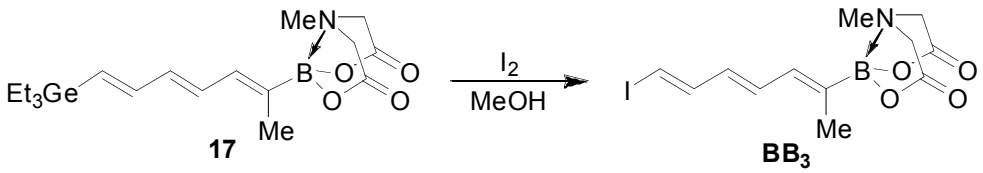
δ 11.8

HRMS (ESI+)

Calculated for $C_{18}H_{31}BGeNO_4$:	410.1558
Found:	410.1567

IR (thin film, cm^{-1})

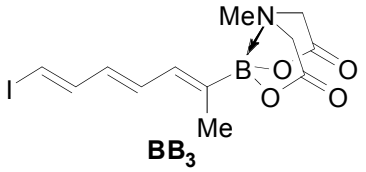
3016, 2954, 2906, 2872, 1765, 1599, 1458, 1427, 1338, 1296, 1248, 1174, 1026, 999, 968, 891, 847, 769, 708, 650, 577.



17 **BB$_3$**

MIDA Boronate BB$_3$. In a subdued light environment, to a 500 mL round bottom flask equipped with a stir bar and charged with MIDA boronate **17** (2.94 g, 7.2 mmol) was added MeOH (180 mL) to give a cloudy, pale yellow solution. The solution was cooled to -78 ^oC. A solution of iodine (5.57 g, 21.9 mmol) in MeOH (60 mL) was added to the cooled reaction

solution dropwise via cannula over 15 min. After stirring at -78 °C for 3 hr, 100 mL saturated aqueous sodium bisulfite and 100 mL EtOAc were added in one portion to give a clear, yellow solution. The cold bath was removed and replaced with a 23 °C water bath. The reaction solution was warmed to 23 °C over 30 min. The solution was poured into a separatory funnel containing 400 mL H_2O and 500 mL EtOAc. After shaking, the layers were separated and the aqueous layer was extracted with EtOAc (2 x 100 mL). The combined organic layers were washed with saturated aqueous sodium bisulfite (1 x 100 mL) and brine (1 x 100 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dissolved in a small amount of acetone and the product was precipitated with Et_2O. The resulting pale yellow solid was triturated with Et_2O (4 x 100 mL) to afford MIDA boronate **BB_3** as a pale yellow solid (2.01 g, 75%).



BB_3

TLC (Et_2O:MeCN 4:1)

R_f = 0.50, stained by $KMnO_4$ and visualized by short wave UV

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

δ 7.23 (ddd, *J* = 14.5, 11, 0.5 Hz, 1H), 6.75 (dd, *J* = 15, 11 Hz, 1H), 6.55 (d, *J* = 14.5 Hz, 1H), 6.38 (dd, *J* = 11.5, 1.5 Hz, 1H), 6.28 (dd, *J* = 15, 11 Hz, 1H), 4.22 (d, *J* = 17 Hz, 2H), 4.05 (d, *J* = 17 Hz, 2H), 2.98 (s, 3H), 1.80 (d, *J* = 1.5 Hz, 3H).

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

δ 169.1, 146.8, 136.3, 133.5, 130.4, 79.7, 62.7, 47.1, 15.4

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

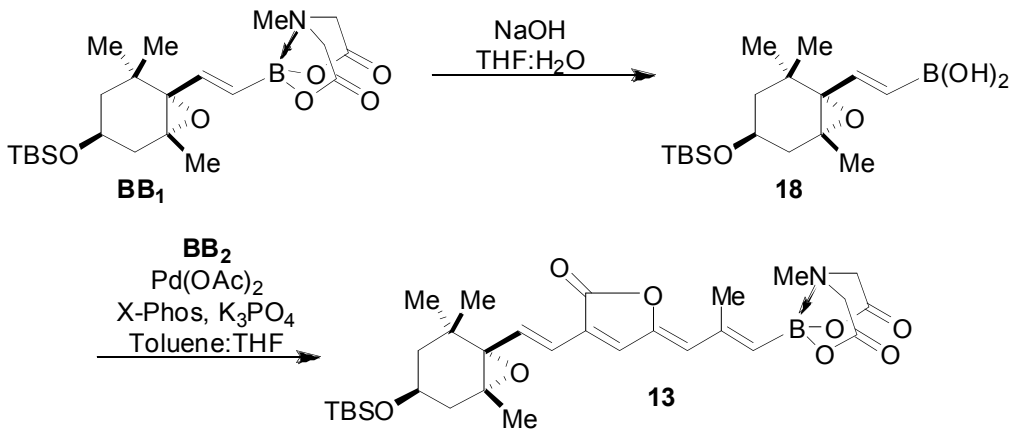
δ 11.7

HRMS (ESI+)

Calculated for $C_{12}H_{16}BINO_4$:	376.0217
Found:	376.0213

IR (thin film, cm^{-1})

3045, 3006, 2956, 2929, 2870, 1768, 1699, 1547, 1454, 1338, 1292, 1250, 1213, 1169, 1140, 1119, 1036, 989, 889, 862, 843, 710.



MIDA boronate 13. To a 20 mL vial equipped with a stir bar and charged with MIDA boronate **BB$_1$** (500.7 mg, 1.1 mmol) was added THF (11 mL) and 1M aq. NaOH (3.3 mL). The mixture was vigorously stirred at 23 °C for 15 minutes. The reaction mixture was then poured into aqueous sodium phosphate buffer (0.5 M, pH 7.0, 10 mL) and diluted with Et_2O (10 mL). The mixture was shaken and the layers were separated. The aqueous phase was extracted with THF:Et_2O (1:1, 2 x 10 mL). (On some occasions phosphate salts precipitated during the extraction process and were redissolved by the addition of water.) The combined organics were dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. Residual solvent was co-evaporated with toluene. The boronic acid **18** was isolated as a white solid (358.5 mg, 95%).

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

δ 6.82 (m, 3H), 5.65 (d, *J* = 18 Hz, 1H), 3.87 (m, 1H), 2.21 (ddd, *J* = 14.5, 5, 1 Hz, 1H), 1.66 (dd, *J* = 14.5, 8 Hz, 1H), 1.50 (ddd, *J* = 13, 4, 1.5 Hz, 1H), 1.30 – 1.18 (m, 1H), 1.16 (s, 3H), 1.12 (s, 3H), 0.91 (s, 3H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H).

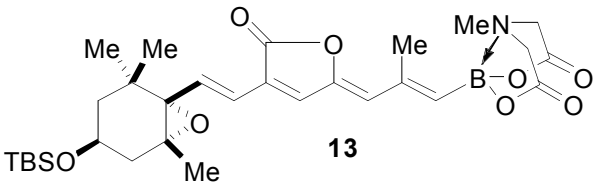
^{13}C-NMR (125 MHz, d_6-acetone)

δ 145.9, 71.5, 66.4, 65.6, 47.8, 42.0, 35.3, 29.7, 26.2, 25.4, 20.2, 18.5, -4.6, -4.6

The boronic acid **18** *was used immediately in the following reaction:*

Preparation of catalyst solution. In a glovebox, to a 7 mL vial charged with XPhos (46.3 mg, 0.10 mmol) and $Pd(OAc)_2$ (11.8 mg, 0.053 mmol) was added THF (2.5 mL). The solution was stirred at 23 °C for 20 min to afford a clear, brown solution.

The freshly prepared catalyst solution was used in the following reaction:
In a glovebox, to a 40 mL vial charged with MIDA boronate **BB$_2$** (285.3 mg, 0.77 mmol) was added finely ground anhydrous K_3PO_4 (481.3 mg, 2.3 mmol). The prepared boronic acid (358.5 mg, 1.1 mmol) was added as a solution in THF:Toluene (1:2, 12.5 mL). The prepared catalyst solution was added in one portion. The vial was sealed with a septum cap and removed from the glovebox. The solution was stirred in a subdued light environment at 45 ^{o}C for 24.5 hr. The reaction mixture was filtered through a pad of Celite, concentrated *in vacuo*, dry loaded onto Celite from an acetone solution, and purified via flash chromatography on florisil (Et_2O:MeCN 100:0 → 80:20) to afford MIDA boronate **13** as a pale yellow solid (358.0 mg, 79%).



13

TLC (Et_2O:MeCN 4:1)

R_f = 0.69, visualized by short wave and long wave UV

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

δ 7.52 (s, 1H), 7.19 (d, *J* = 15.5 Hz, 1H), 6.40 (d, *J* = 15.5 Hz, 1H), 5.93 (s, 1H), 5.82 (s, 1H), 4.26 (d, *J* = 17 Hz, 2H), 4.10 (d, *J* = 17 Hz, 2H), 3.89 (m, 1H), 3.09 (s, 3H), 2.28 – 2.21 (m, 4H), 1.71 (dd, *J* = 14.5, 8.5 Hz, 1H), 1.53 (ddd, *J* = 13, 3.5, 1.5 Hz, 1H), 1.35 – 1.23 (m, 1H), 1.20 (s, 3H), 1.16 (s, 3H), 0.95 (s, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

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

δ 169.2, 168.8, 147.2, 146.4, 138.7, 134.9, 126.5, 122.3, 121.0, 70.7, 67.7, 65.5, 62.5, 47.6, 47.2, 42.0, 35.7, 29.6, 26.2, 25.4, 20.1, 18.7, 18.6, -4.6, -4.6

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

δ 11.1

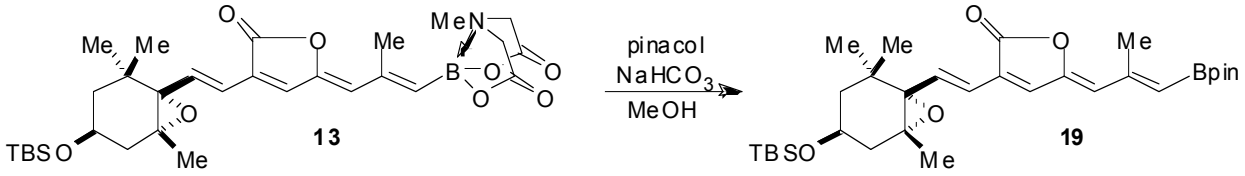
HRMS (ESI+)

Calculated for $C_{30}H_{45}BNO_8Si$:	586.3008
Found:	586.2983

IR (thin film, cm^{-1})

3003, 2956, 2929, 2856, 1765, 1630, 1591, 1387, 1338, 1292, 1255, 1188, 1155, 1124, 1089, 1028, 989, 893, 862, 837, 773, 735, 582.

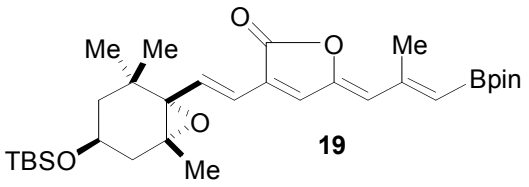
$[\alpha]_D^{28}$ -93.5 (*c* 0.85, $CHCl_3$)



13 **19**

Pinacol ester 19. To a 20 mL vial equipped with a stir bar and charged with MIDA boronate **13** (338.2 mg, 0.58 mmol) was added pinacol (110.3 mg, 0.93 mmol) and solid $NaHCO_3$ (252.6 mg, 3.0 mmol). MeOH (5.8 mL) was added and the suspension was stirred in a subdued light environment at 45 °C for 3 hr. The mixture was filtered through a pad of Celite, eluting with EtOAc (125 mL). The collected solution was concentrated *in vacuo*. The resulting residue was azeotroped with toluene (2 x 5 mL) and was then dissolved in toluene (5.8 mL). To remove residual pinacol, finely ground $CaCl_2$ (337.8 mg, 3.0 mmol) and solid $NaHCO_3$ (252.3 mg, 3.0 mmol) were added. The suspension was stirred at 23 °C for 1.5 hr and was then filtered through

a pad of Celite, eluting with EtOAc (125 mL). The collected solution was concentrated *in vacuo* to afford pinacol ester **19** as a deep red solid (318.3 mg, 99%).



19

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

δ 7.54 (s, 1H), 7.22 (d, *J* = 15.5 Hz, 1H), 6.42 (d, *J* = 15.5 Hz, 1H), 5.95 (s, 1H), 5.65 (s, 1H), 3.90 (m, 1H), 2.36 (s, 3H), 2.25 (ddd, *J* = 14.5, 5, 1 Hz, 1H), 1.72 (dd, *J* = 14.5, 8.5 Hz, 1H), 1.53 (ddd, *J* = 13, 3.5, 1 Hz, 1H), 1.34 – 1.23 (m, 13 H), 1.20 (s, 3H), 1.17 (s, 3H), 0.95 (s, 3H), 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

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

δ 168.9, 153.0, 148.8, 138.3, 135.5, 127.3, 122.2, 119.2, 83.7, 70.7, 67.7, 65.4, 47.6, 41.9, 35.6, 29.6, 26.2, 25.4, 25.1, 20.2, 20.1, 18.5, -4.5, -4.6

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

δ 30.9

HRMS (ESI+)

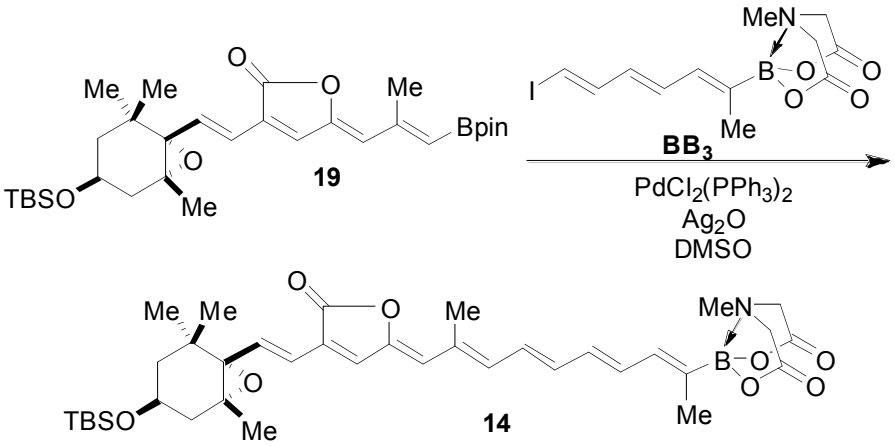
Calculated for $C_{31}H_{50}BO_6Si$: 557.3470

Found: 557.3483

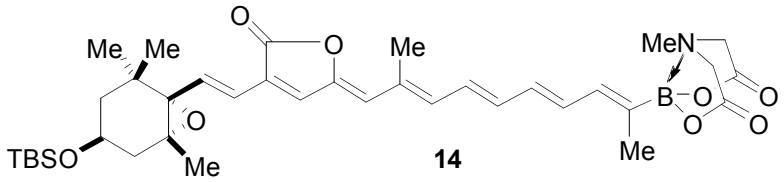
IR (thin film, cm^{-1})

2956, 2929, 2858, 1765, 1593, 1371, 1257, 1144, 1080, 1032, 976, 953, 852, 837, 775, 580.

$[\alpha]_D^{25}$ -24.4 (*c* 1.1, $CHCl_3$)



MIDA boronate 14. In a glovebox, to a 7 mL vial equipped with a stir bar and charged with pinacol ester **19** (105.7 mg, 0.19 mmol), MIDA boronate **BB$_3$** (100.3 mg, 0.27 mmol), and Ag_2O (141.2 mg, 0.61 mmol) was added *trans*-bis(triphenylphosphine)palladium dichloride (9.0 mg, 0.013 mmol) and DMSO (2.0 mL). The vial was sealed with a cap and removed from the glovebox. The solution was stirred in a subdued light environment at 45 ^{o}C for 12 hr. The reaction mixture was poured into a separatory funnel containing EtOAc (30 mL). The organic layer was washed with H_2O:brine (5:1, 3 x 15 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an acetone solution, and purified via reverse phase flash chromatography on C18 silica gel (H_2O:MeCN 95:5 → 0:100) to afford MIDA boronate **14** as an orange solid (57.6 mg, 45%).



TLC (Et_2O:MeCN 4:1)

R_f = 0.51, visualized by visible light (yellow/orange)

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

δ 7.50 (s, 1H), 7.16 (d, *J* = 16 Hz, 1H), 6.81 (dd, *J* = 14.5, 11.5 Hz, 1H), 6.79 (dd, *J* = 14, 12 Hz, 1H), 6.63 (dd, *J* = 14, 11.5 Hz, 1H), 6.58 (d, *J* = 12, 1.5 Hz, 1H), 6.52 (d, *J* = 11 Hz, 1H), 6.50 (dd, *J* = 12, 11 Hz, 1H), 6.39 (d, *J* = 16 Hz, 1H), 6.00 (s, 1H), 4.23 (d, *J* = 17 Hz, 2H), 4.06 (d, *J* = 17 Hz, 2H), 3.90 (m, 1H), 2.98 (s, 3H), 2.25 (ddd, *J* = 9.5, 5, 1.5 Hz, 1H), 2.21 (s, 3H), 1.85 (d, *J* = 1.5 Hz, 3H), 1.71 (dd, *J* = 14.5, 8 Hz, 1H), 1.52 (ddd, *J* = 13, 3.5, 1.5 Hz, 1H), 1.31 (dd, *J* = 13, 10 Hz, 1H), 1.20 (s, 3H), 1.17 (s, 3H), 0.95 (s, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H).

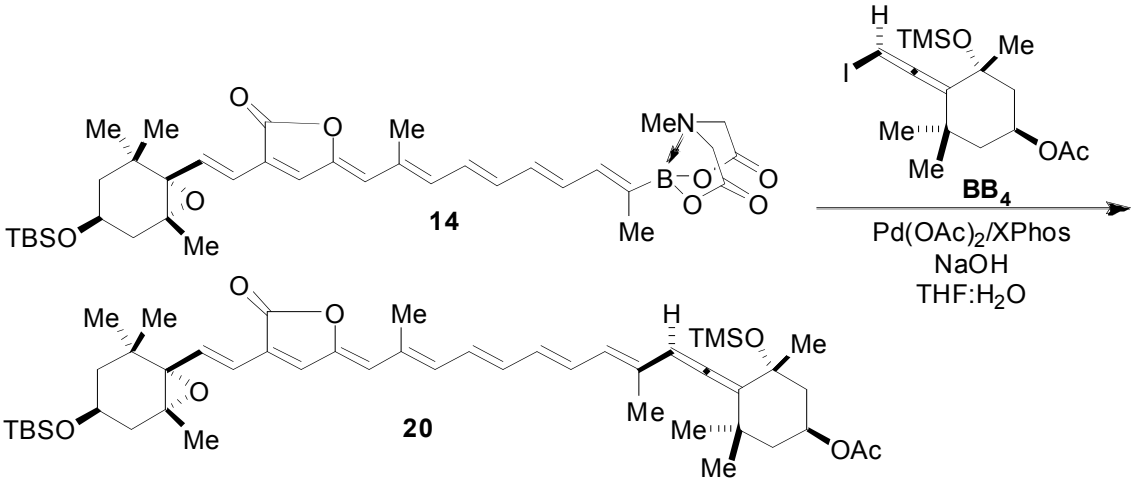
^{13}C-NMR (125 MHz, d_6-acetone)
δ 169.1, 169.1, 148.0, 138.8, 138.2, 137.9, 137.2, 134.9, 134.5, 134.4, 131.9, 130.3, 125.4, 122.6, 119.6, 70.8, 67.8, 65.5, 62.7, 47.7, 47.1, 42.0, 35.7, 29.7, 26.2, 25.4, 20.2, 18.6, 15.5, 15.4, -4.6, -4.6

^{11}B-NMR (128 MHz, d_6-acetone)
δ 12.0

HRMS (ESI+)
Calculated for $C_{37}H_{53}BNO_8Si$: 678.3634
Found: 678.3633

IR (thin film, cm^{-1})
3016, 2956, 2929, 2856, 1757, 1612, 1529, 1462, 1381, 1342, 1298, 1250, 1184, 1084, 1036, 989, 837, 775, 586.

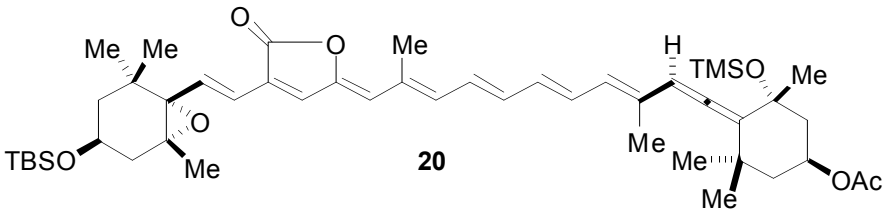
$[\alpha]_D^{29}$ -23.2 (*c* 1.21, $CHCl_3$)



Protected peridinin 20.
Preparation of catalyst stock solution. In a glovebox, to a 7 mL vial equipped with a stir bar and charged with XPhos (30.4 mg, 0.064 mmol) and $Pd(OAc)_2$ (7.3 mg, 0.033 mmol) was added THF (degassed, inhibited with 250 ppm BHT, 2.0 mL). The solution was stirred at 23 °C for 10 min to afford a clear, brown solution.

The freshly prepared catalyst stock solution was used in the following reaction:
In a glovebox, to a 7 mL vial equipped with a stir bar and charged with MIDA boronate **14** (45.2 mg, 0.067 mmol) was added finely ground NaOH (18.7 mg, 0.47 mmol). Iodoallene **BB$_4$** (37.2 mg, 0.088 mmol) was added as a solution in THF (degassed, inhibited with 250 ppm BHT, 2.0 mL). A portion of the prepared catalyst solution (0.20 mL, which contains 0.0033 mmol $Pd(OAc)_2$ and 0.0064 mmol XPhos) was added in one portion. The vial was sealed with a septum cap and removed from the glovebox. Degassed DI H_2O (0.45 mL) was added. The solution was stirred in a subdued light environment at 23 ^oC for 1.5 hr. The reaction mixture was

poured into aqueous sodium phosphate buffer (0.25 M, pH 7.0, 10 mL) and diluted with Et_2O (20 mL). The mixture was shaken and the layers were separated. The aqueous phase was extracted with Et_2O (1 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an Et_2O solution, and purified via reverse phase flash chromatography on C18 silica gel (H_2O:Acetone 7:3 → 0:100) to afford protected peridinin **20** as a red solid (32.6 mg, 60%).



TLC (Hexane:EtOAc 4:1)

R_f = 0.56, visualized by visible light (orange)

A crude NMR for the reaction can be found in the NMR spectra section of the SI.

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

δ 7.15 (d, *J* = 15.5 Hz, 1H), 7.01 (s, 1H), 6.61 (dd, *J* = 14.5, 11.5 Hz, 1H), 6.60 (dd, *J* = 14, 11 Hz, 1H), 6.51 (dd, *J* = 14, 11 Hz, 1H), 6.43 (d, *J* = 11.5 Hz, 1H), 6.37 (dd, *J* = 14, 11 Hz, 1H), 6.34 (d, *J* = 15.5 Hz, 1H), 6.09 (d, *J* = 11.5 Hz, 1H), 5.99 (s, 1H), 5.72 (s, 1H), 5.34 (tt, *J* = 11.5, 4.5 Hz, 1H), 3.90 – 3.80 (m, 1H), 2.26 (ddd, *J* = 14.5, 5, 1 Hz, 1H), 2.23 (s, 3H), 2.03 (s, 3H), 1.96 (ddd, *J* = 12.5, 4, 2 Hz, 1H), 1.79 (s, 3H), 1.65 (dd, *J* = 14.5, 8 Hz, 1H), 1.50 (ddd, *J* = 13, 3.5, 1.5 Hz, 1H), 1.40 (m, 1H), 1.36 (s, 3H), 1.33 (s, 3H), 1.32 – 1.20 (m, 3H), 1.19 (s, 3H), 1.17 (s, 3H), 1.04 (s, 3H), 0.95 (s, 3H), 0.88 (s, 9H), 0.11 (s, 9H), 0.051 (s, 3H), 0.047 (s, 3H).

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

δ 202.5, 170.4, 168.7, 146.7, 138.0, 137.2, 136.2, 134.3, 133.9, 133.8, 132.7, 131.6, 128.8, 127.7, 124.8, 121.6, 119.1, 117.0, 102.7, 74.8, 70.6, 68.3, 67.5, 64.6, 47.7, 47.0, 45.7, 41.3, 35.8, 35.1, 32.3, 30.3, 29.4, 28.8, 25.9, 25.0, 21.4, 20.0, 18.1, 15.4, 14.1, 2.2, -4.7, -4.8

HRMS (ESI+)

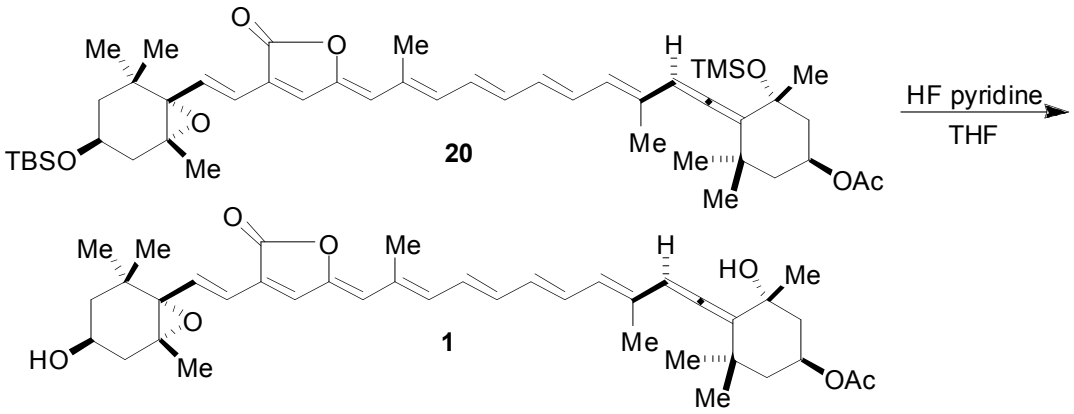
Calculated for $C_{48}H_{73}O_7Si_2$: 817.4895

Found: 817.4895

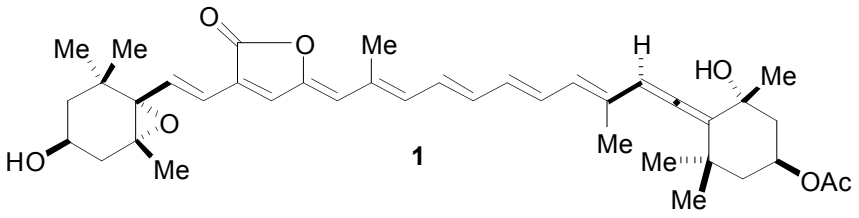
IR (thin film, cm^{-1})

2960, 2929, 2858, 1961, 1755, 1630, 1523, 1454, 1377, 1250, 1161, 1120, 1078, 1036, 987, 839.

$[\alpha]_D^{28}$ -40.3 (*c* 1.6, $CHCl_3$)



Peridinin 1. To a 7 mL polyethylene vial containing a stir bar was added protected peridinin **20** (31.3 mg, 0.038 mmol) as a solution in THF (2.0 mL). HF•pyridine (70% HF in pyridine, 0.10 mL, 5.5 mmol) was added in one portion. The solution was stirred in a subdued light environment at 23 °C for 1 hr. An additional portion of HF•pyridine (70% HF in pyridine, 0.10 mL, 5.5 mmol) was added. The solution was stirred at 23 °C for an additional 2 hr. The reaction was quenched by slow, dropwise addition of saturated aqueous $NaHCO_3$ until effervescence ceased (caution: slow addition is important to avoid uncontrolled effervescence). The reaction solution was then poured into saturated aqueous $NaHCO_3$ (10 mL) and diluted with Et_2O (20 mL). The mixture was shaken and the layers were separated. The aqueous phase was extracted with Et_2O (1 x 10 mL). The combined organics were dried over $MgSO_4$, filtered, and then concentrated *in vacuo*. The resulting residue was dry loaded onto Celite from an Et_2O solution, and purified via flash chromatography on florisil (Hexane:EtOAc 100:0 → 0:100) to afford peridinin **1** as a red solid (15.7 mg, 65%).



TLC (Hexane:Acetone 7:3)

R_f = 0.20, visualized by visible light (orange)

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

δ 7.15 (d, *J* = 16 Hz, 1H), 7.02 (s, 1H), 6.61 (dd, *J* = 14, 11.5 Hz, 1H), 6.60 (dd, *J* = 14, 11.5 Hz, 1H), 6.51 (dd, *J* = 14, 10.5 Hz, 1H), 6.43 (d, *J* = 11.5 Hz, 1H), 6.37 (dd, *J* = 14.5, 10.5 Hz, 1H), 6.35 (d, *J* = 15.5 Hz, 1H), 6.09 (d, *J* = 11.5 Hz, 1H), 6.05 (s, 1H), 5.73 (s, 1H), 5.37 (tt, *J* = 11.5, 4.5 Hz, 1H), 3.90 (m, 1H), 2.38 (ddd, *J* = 14.5, 5, 1.5 Hz, 1H), 2.27 (ddd, *J* = 14, 4, 2 Hz, 1H), 2.22 (s, 3H), 2.03 (s, 3H), 1.98 (ddd, *J* = 12.5, 4, 2 Hz, 1H), 1.80 (s, 3H), 1.69 – 1.60 (m, 2H), 1.50 (dd, *J* = 14, 11 Hz, 1H), 1.40 (m, 1H), 1.38 (s, 3H), 1.35 (m, 1H), 1.35 (s, 3H), 1.26 (m, 1H), 1.199 (s, 3H), 1.195 (s, 3H), 1.06 (s, 3H), 0.97 (s, 3H).

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

δ 202.6, 170.4, 168.7, 146.7, 138.0, 137.2, 136.3, 134.0, 133.9, 133.6, 133.0, 131.5, 128.9, 128.1, 124.7, 121.8, 119.2, 117.6, 103.3, 72.6, 70.4, 67.9, 67.5, 64.2, 47.1, 45.4, 45.2, 40.9, 35.8, 35.3, 32.0, 31.2, 29.5, 29.1, 24.9, 21.4, 19.8, 15.4, 14.0

HRMS (ESI+)
Calculated for $C_{39}H_{51}O_7$: 631.3635
Found: 631.3629

IR (thin film, cm^{-1})
3496, 3016, 2962, 2926, 2856, 1928, 1743, 1635, 1523, 1456, 1365, 1250, 1163, 1124, 1030, 984, 908, 756.

$[\alpha]_D^{28}$ -22.9 ± 5.7 (*c* 1.1, MeOH)

^{1}H NMR data for peridinin: δ_H/ppm

Natural peridinin (literature reference[25]; 400 MHz, $CDCl_3$)	Synthetic peridinin (500 MHz, $CDCl_3$)
7.17	7.15
7.02	7.02
6.61	6.61
6.61	6.60
6.51	6.51
6.45	6.43
6.38	6.37
6.38	6.35
6.11	6.09
6.05	6.05
5.74	5.73
5.38	5.37
3.91	3.90
2.40	2.38
2.28	2.27
2.229	2.22
2.041	2.03
2.00	1.98
1.801	1.80
1.64	1.69-1.60
1.63	1.69-1.60
1.51	1.50
1.40	1.40
1.385	1.38
1.352	1.35
1.35	1.35
1.27	1.26
1.207	1.199
1.203	1.195
1.069	1.06
0.976	0.97

[25] Haugan, J.A.; Englert, G.; Aakermann, T.; Glinz, E.; Liaaen-Jensen, S. *Acta Chemica Scandinavica* **1994**, *48*, 769.

^{13}C NMR data for peridinin: δ_C/ppm

Natural peridinin (literature reference[25]; 100 MHz, $CDCl_3$)	Synthetic peridinin (125 MHz, $CDCl_3$)
202.6	202.6
170.4	170.4
168.8	168.7
146.8	146.7
138.0	138.0
137.2	137.2
136.3	136.3
134.0	134.0
133.9	133.9
133.7	133.6
133.0	133.0
131.5	131.5
128.9	128.9
128.2	128.1
124.8	124.7
121.8	121.8
119.2	119.2
117.6	117.6
103.3	103.3
72.7	72.6
70.5	70.4
68.0	67.9
67.5	67.5
64.2	64.2
47.1	47.1
45.4	45.4
45.2	45.2
41.0	40.9
35.8	35.8
35.3	35.3
32.1	32.0
31.3	31.2
29.5	29.5
29.2	29.1
24.9	24.9
21.4	21.4
19.9	19.8
15.4	15.4
14.0	14.0