Simple, Efficient, and Modular Syntheses of Polyene Natural Products via Iterative Cross-Coupling

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SUPPORTING INFORMATION

I. General Methods

Materials. $Pd(PPh_3)_4$ was a generous gift from Sigma-Aldrich. Commercial reagents were purchased from Sigma-Aldrich, Strem, Fisher Scientific, Alfa Aesar, or Lancaster Synthesis and were used without further purification unless otherwise noted. 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). Triethylamine and 2,6-lutidine were freshly distilled under an atmosphere of nitrogen from CaH_2. The following compounds were prepared according to literature precedent: (*E*)-(2-bromoethenyl)dibromoborane (**3**)[2], (*E*)-1-chloro-2-iodoethylene (**17**)[3], (1*E*,3*E*)-2-methyl-4-(2,6,6-trimethylcyclohex-1-enyl)buta-1,3-dienylboronic acid (**20**)[4], (*E*)-3-bromobut-2-enal (**22**)[5], (*E*)-2-(tributylstannyl)vinylzinc chloride (**15**)[6], (*E*)-methyl 10-iododec-9-enoate (**35**)[7], diol (**37**)[8], dichlomethylpinacolboronic ester (**42**) [9].

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

[2] Hyuga, S.; Chiba, Y.; Yamashina, N.; Hara, S.; Suzuki, A. *Chem. Lett.* **1987**, 1757-1760.

[3] (a) Negishi, E. I.; Okukado, N.; Lovich, S. F.; Luo, F. T. *J. Org. Chem.* **1984**, *49*, 2629-2632. (b) Organ, M. G.; Ghasemi, H. *J. Org. Chem.* **2004**, *69*, 695-700.

[4] Uenishi, J.; Matsui, K.; Wada, A.; *Tetrahedron Lett.* **2003**, *44*, 3093-3096.

[5] Romo, D.; Rzasa, R.M.; Shea, H.A.; Park, K.; Langenhan, J.M.; Sun, L.; Akhiezer, A.; Liu, J.O. *J. Am. Chem. Soc.* **1998**, *120*, 12237-12254

[6] Pihko, P.M.; Koskinen, A.M.P. *Synlett* **1999**, *12*, 1966-1968.

[7] Zhang, W.; Sun, M.; Salomon, R.G. *J. Org. Chem.* **2006**, *71*, 5607.

[8] Paterson, I.; Florence, G.J.; Gerlach, K.; Scott, J.P.; Sereining, N. *J. Am. Chem. Soc.* **2001**, *123*, 9525-9544.

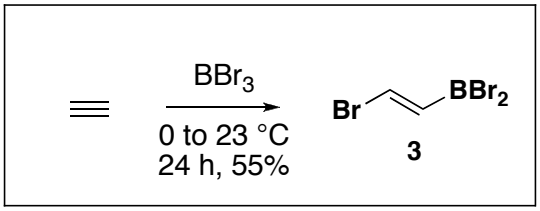
[9] (a) Wuts, P.G.M.; Thompson, P.A. *J. Organomet. Chem.* **1982**, *234*, 137-141. (b) Raheem, I.T.; Goodman, S.N.; Jacobsen, E.N. *J. Am. Chem. Soc.* **2004**, *126*, 706-707.

General Experimental Procedures. All palladium-mediated cross-coupling reactions were set up in a glove box and performed under an atmosphere of argon or nitrogen in oven- or flame-dried I-Chem or Wheaton vials sealed with PTFE-lined plastic caps unless otherwise indicated. All other reactions were performed in oven- or flame-dried round-bottom or modified Schlenk flasks fitted with rubber septa under a positive pressure of argon or nitrogen unless otherwise indicated. Organic solutions were concentrated *via* rotary evaporation under reduced pressure. Reactions were monitored by analytical thin layer chromatography (TLC) performed using the indicated solvent on E. Merck silica gel 60 F254 plates (0.25 mm). Compounds were visualized by exposure to a UV lamp (λ = 254 and 365 nm), a solution of $KMnO_4$, a solution of ceric ammonium molybdate (CAM), or an acidic solution of *p*-anisaldehyde followed by brief heating using a Varitemp heat gun. Flash column chromatography was performed as described by Still and coworkers[10] using EM Merck silica gel 60 (230-400 mesh) and/or Aldrich Florisil® (an activated magnesium silicate: 100-200 mesh).

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 ($CDCl_3$, δ = 7.26; CD_3CN, δ = 1.93; $(CD_3)_2CO$, δ = 2.04; DMSO-d_6, δ = 2.49, center line). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, sext = sextet, dd = doublet of doublets, dt = doublet of triplets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, m = multiplet, br = broad), coupling constant (*J*) in Hertz (Hz), and integration. Based on ^{1}H NMR analysis, unless otherwise indicated the isomeric purity of all olefin-containing compounds was judged to be >95:5 *E*:*Z* (^{1}H and ^{13}C NMR spectra of all compounds are provided in SI.B). MIDA boronates were judged to be stable to long-term storage based on the observation of no change ^{1}H NMR spectra after the indicated time. (^{1}H NMR spectra of **BB$_1$** and **14** collected both before and after storage on the benchtop under air for 1 year and 5 months are included in SI.B). ^{13}C NMR spectra were recorded at 23 °C on one of the following instruments: Varian Unity 400, Varian Unity 500 or Varian Unity Inova 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; $\mathbf{C}D_3CN$, δ = 1.30; $(\mathbf{C}D_3)_2CO$, δ = 29.8; DMSO-d_6, δ = 39.5, center line). **Carbons bearing boron substituents were not reported (quadrupolar relaxation)**. ^{11}B NMR were recorded using a General Electric GN300WB 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. Infrared spectra were collected from a thin film on NaCl plates or as a KBr pellet on a Mattson Galaxy Series FTIR 5000 spectrometer with internal referencing. Absorption maxima (ν_{max}) are reported in wavenumbers (cm^{-1}). X-ray crystallographic analyses of **BB$_1$** and **14** were carried out by Dr. Scott Wilson at the University of Illinois George L. Clark X-Ray facility.

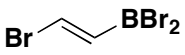
[10] Still, W.C.; Kahn, M.; Mitra, A.; *J. Org. Chem.* **1978**, *43*, 2923-2925.

II. Synthesis of BB_1–BB_3 and selective cross-coupling reactions



(*E*)-(2-bromoethenyl)dibromoborane (3)[2]

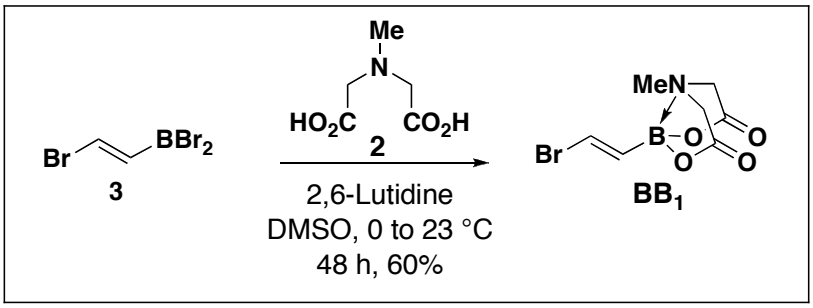
In a subdued light environment, an oven-dried 100 mL one-neck round bottom flask equipped with a magnetic stir bar and a rubber septum was flushed with acetylene gas three-times using a five-inch balloon attached to a needle. The flask was attached to three balloons filled with acetylene gas and cooled to 0 °C. To the flask at 0 °C was added boron tribromide (75.0 g, 299.4 mmol) dropwise *via* syringe over 15 min with stirring. The reaction mixture was allowed to warm to 23 °C and then stirred at 23 °C for 24 hr. (*Each balloon was refilled with acetylene gas after the acetylene gas in the balloon was consumed; if a needle became clogged during the reaction mixture it was replaced with a new one*). The resulting dark-blue crude mixture was distilled *three-times* under high vacuum connected with two dry ice/acetone traps to provide **3** (45.20 g, 163.4 mmol) as a colorless oil in 55 % yield. (bp = 50-55 °C/13 mmHg). (*The fractional vacuum distillation was carried out at 23 °C for 30 minutes before heating to remove a small amount of residual boron tribromide and then the crude mixture was slowly heated to around 65 °C using an oil-bath until distillation was completed. The oil-bath temperature was carefully maintained below 70 °C to inhibit a polymerization reaction*). The triply distilled title compound **3** was used immediately in the next reaction.



3

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

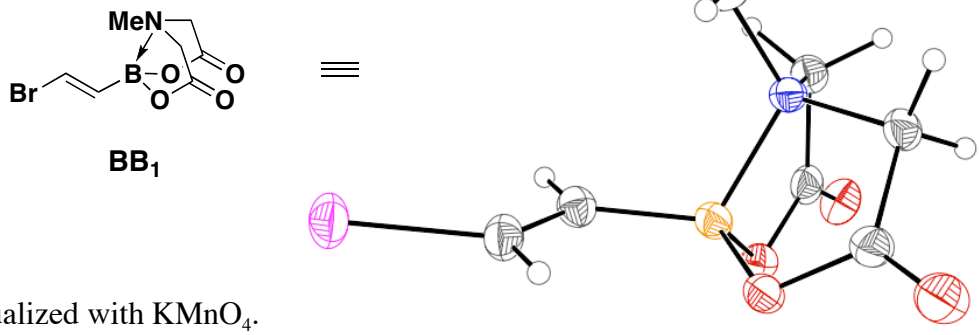
δ 7.97 (d, *J* = 15.0 Hz, 1H), 7.08 (d, *J* = 15.0 Hz, 1H)



(*E*)-(2-bromoethenyl)boronate ester (BB_1)

This reaction was conducted in a subdued light environment in an oven-dried 500 mL three-neck round bottom flask equipped with a magnetic stir bar. To a stirred mixture of *N*-methyliminodiacetic acid (MIDA, **2**) (16.93 g, 113.9 mmol, 1.50 eq.) and 2,6-lutidine (17.69 mL, 151.86 mmol, 2.0 eq.) in DMSO (250 mL) at 0 °C under nitrogen was added freshly distilled **3** (21.00 g, 75.93 mmol) dropwise *via* syringe over 15 min. The reaction mixture was allowed to warm to 23 °C and then stirred at 23 °C for 48 h. The resulting yellow mixture was treated with water (300 mL) and extracted with THF:diethyl ether 1:1 (3 ×

500 mL). The combined organic phases were washed with brine (3 × 350 mL), dried over anhydrous magnesium sulfate, and concentrated in vacuo to provide a light yellow solid. The crude product was purified by flash chromatography on silica gel (EtOAc:petroleum ether 1:1 → EtOAc → EtOAc:MeCN 9:1) to give the title compound **BB$_1$** as a colorless crystalline solid (11.98 g, 45.75 mmol, 60%). Crystals suitable for X-ray crystallography analysis were grown by slow evaporation from ethyl acetate at 23 °C. ***This material was stored under air at 23 °C for one year and six months without decomposition.***



BB$_1$

TLC (EtOAc)

R_f = 0.46, visualized with $KMnO_4$.

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

δ 6.69 (d, *J* = 15.0 Hz, 1H), 6.33 (d, *J* = 14.5 Hz, 1H), 3.97 (d, *J* = 17.0 Hz, 2H), 3.82 (d, *J* = 17.0 Hz, 2H), 2.80 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN)

δ 169.0, 118.8, 62.6, 47.9.

^{11}B NMR (100 MHz, CD_3CN)

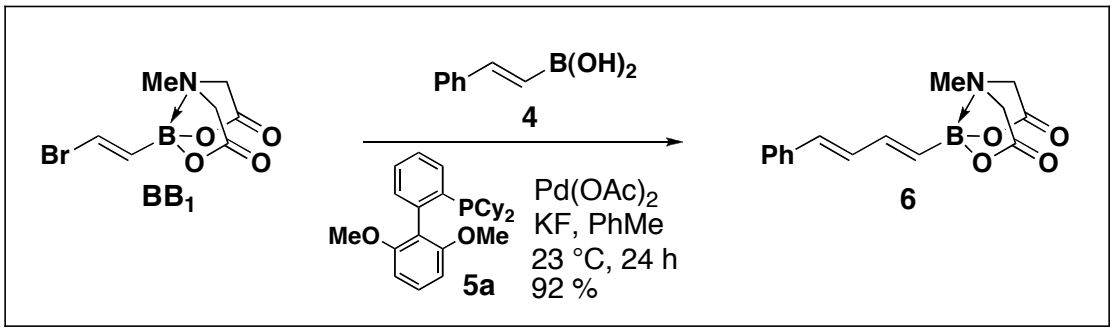
δ 10.5.

HRMS (ESI)

Calculated for $C_7H_{10}NO_4BrB$ $(M+H)^+$:	261.9886
Found:	261.9874

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

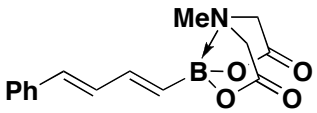
3006, 2962, 1755, 1589, 1451, 1338, 1286, 1196, 1152, 1118, 1080, 1025, 1009, 961, 893, 872, 773, 678.



(*E*,*E*)-1,3-butadienyl-(4-phenyl)boronate ester (6)

A solution of the catalyst was prepared as follows: A 20 mL Wheaton vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (5.60 mg, 0.025 mmol, 1.0 eq.) and 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a)** (20.5 mg, 0.050 mmol, 2.0 eq.). Toluene (3.00 mL) was added and the vial was sealed with a PTFE-lined plastic cap. The resulting mixture was stirred at 23 °C for 45 min. resulting in a yellow Pd/**5a** catalyst solution (0.00833 N Pd in toluene).

This catalyst solution was then utilized in the following procedure: A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with $\mathbf{BB_1}$ (0.262 g, 1.00 mmol, 1.0 eq.), *trans*-2-phenylvinylboronic acid (**4**) (0.229 g, 1.50 mmol, 1.5 eq.), KF (0.116 g, 2.00 mmol, 2.0 eq.; based on $\mathbf{BB_1}$), toluene (7.0 mL), and the catalyst solution (1.20 mL, 0.01 mmol, 1.0 mol% Pd). The vial was then sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred for 24 hr at 23 °C. The resulting heterogeneous yellow mixture was diluted with acetonitrile (10.0 mL), filtered through short pad Celite using acetonitrile (100 mL), and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (EtOAc:Petroleum ether 1:1 → EtOAc → EtOAc:MeCN 2:1) to give the title compound **6** as a colorless crystalline solid (0.263 g, 0.922 mmol, 92%). Dienyl boronate **6** was stable to storage for at least two weeks on the benchtop under air both as a solid and as a solution in DMSO-d_6.



6

TLC (EtOAc)

R_f = 0.85, visualized by UV lamp (λ = 254 nm) or with $KMnO_4$.

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

δ 7.48 (d, *J* = 7.5 Hz, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 1H), 6.93 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.65 (d, *J* = 15.5 Hz, 1H), 6.63 (dd, *J* = 17.0, 10.5 Hz, 1H), 5.78 (d, *J* = 17.5 Hz, 1H), 4.24 (d, *J* = 17.5 Hz, 2H), 4.03 (d, *J* = 17.0 Hz, 2H), 2.78 (s, 3H).

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

δ 169.3, 142.0, 136.9, 132.9, 130.9, 128.7, 127.8, 126.5, 61.4, 46.8.

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

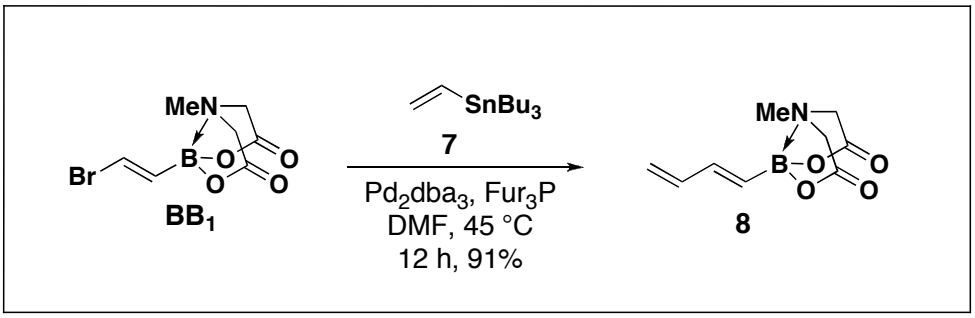
δ 11.4.

HRMS (ESI)

Calculated for $C_{15}H_{17}NO_4B$ $(M+H)^+$:	286.1251
Found:	286.1249

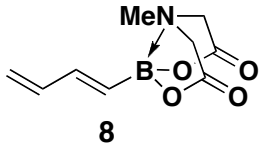
IR (thin film, cm^{-1})

2967, 1741, 1698, 1682, 1651, 1556, 1446, 1338, 1309, 1258, 1113, 1082, 1013, 950, 885, 865, 750, 694, 654.



(*E*,*E*)-1,3-butadienyl-boronate ester (8)

A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with **BB_1** (0.262 g, 1.00 mmol, 1.0 eq.), Pd_2dba_3 (0.037 g, 0.040 mmol, 4.0 mol% Pd), Fur_3P (0.021 g, 0.090 mmol, 9.0 mol%), DMF (8.0 mL) and tributyl(vinyl)tin (**7**) (0.346 mL, 1.15 mmol, 1.15 eq.). The vial was then sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred for 12 h at 45 °C. The resulting reddish mixture was diluted with brine (50 mL) and then extracted with ethyl acetate (3 × 100 mL). The combined organic fractions were dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (EtOAc:Petroleum ether 1:1 → EtOAc → EtOAc:MeCN 15:1) to give the title compound **8** as a colorless crystalline solid (0.190 g, 0.909 mmol, 91%).



TLC (EtOAc)

R_f = 0.46, visualized with $KMnO_4$.

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

δ 6.56 (dd, *J* = 17.5, 10.5 Hz, 1H), 6.43 (dtd, *J* = 17.0, 10.0, 0.5 Hz, 1H), 5.66 (dd, *J* = 17.5, 0.5 Hz, 1H), 5.28 (ddt, *J* = 17.0, 2.0, 0.5 Hz, 1H), 5.14 (ddt, *J* = 10.0, 2.0, 0.5 Hz, 1H), 3.96 (d, *J* = 17.0 Hz, 2H), 3.79 (d, *J* = 17.0 Hz, 2H), 2.76 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN)

δ 169.5, 144.3, 140.1, 119.0, 62.3, 47.6.

^{11}B NMR (100 MHz, CD_3CN)

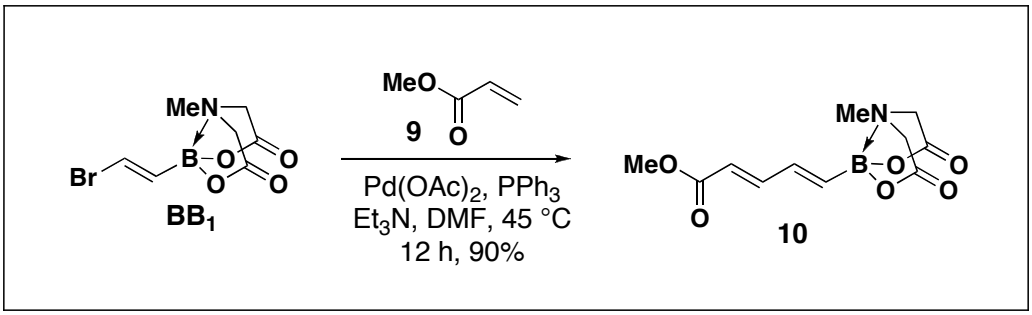
δ 10.9.

HRMS (ESI)

Calculated for $C_9H_{12}BNO_4Na$ $(M+Na)^+$:	232.0757
Found	232.0757

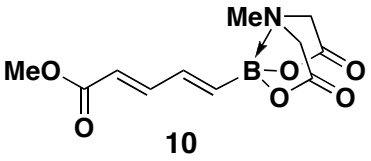
IR (thin film, cm^{-1})

3006, 2960, 1770, 1710, 1636, 1592, 1460, 1424, 1338, 1286, 1194, 1154, 1125, 1088, 1024, 958, 893, 874, 837, 719, 648.



(*E*,*E*)-1,3-butadienyl-(4-methylester)boronate ester (10)

A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with **BB_1** (0.262 g, 1.00 mmol, 1.0 eq.), PPh_3 (0.0159 g, 0.060 mmol, 6.0 mol%), $Pd(OAc)_2$ (0.0067 g, 0.030 mmol, 3.0 mol% Pd), Et_3N (0.279 mL, 2.00 mmol, 2.0 eq.; based on **BB_1**), methyl acrylate (**9**) (0.136 mL, 1.50 mmol, 1.5 eq.), and DMF (7.0 mL). The vial was sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred at 45 °C for 12 h. The resulting mixture was diluted with brine (50 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (EtOAc:Petroleum ether 1:1 → EtOAc → EtOAc:MeCN 15:1) to give the title compound **10** as a light yellow solid (0.240 g, 0.898 mmol, 90%).



TLC (EtOAc)

R_f = 0.33, visualized by UV lamp (λ = 254 nm).

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

δ 7.20 (dd, *J* = 15.5, 10.5 Hz, 1H), 6.68 (dd, *J* = 17.0, 10.5 Hz, 1H), 6.02 (d, *J* = 17.5 Hz, 1H), 5.89 (d, *J* = 15.5 Hz, 1H), 4.11 (d, *J* = 17.0 Hz, 2H), 3.79 (d, *J* = 17.0 Hz, 2H), 3.67 (s, 3H), 2.82 (s, 3H).

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

δ 168.8, 167.3, 145.4, 140.9, 122.4, 61.7, 51.6, 47.2.

^{11}B NMR (100 MHz, $CDCl_3$)

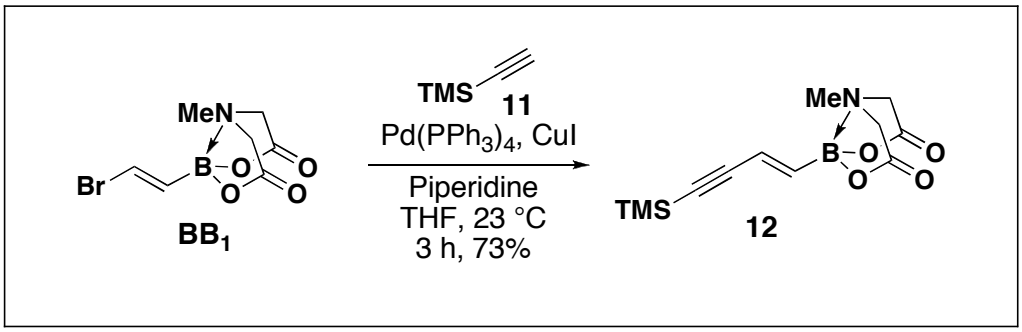
δ 9.9.

HRMS (ESI)

Calculated for $C_{11}H_{14}BNO_6Na$ $(M+Na)^+$:	290.0812
Found:	290.0812

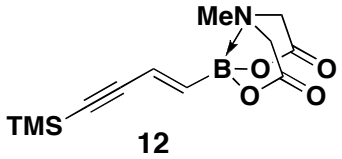
IR (thin film, cm^{-1})

3005, 1751, 1734, 1718, 1701, 1696, 1685, 1654, 1595, 1560, 1437, 1334, 1281, 1233, 1129, 991, 863, 716, 662.



(*E*)-2-trimethylsilylethyleneboronate ester (12)

A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with **BB_1** (0.262 g, 1.00 mmol, 1.0 eq.), $Pd(PPh)_4$ (0.058 g, 0.050 mmol, 5.0 mol%), CuI (0.019 g, 0.100 mmol, 10.0 mol%), piperidine (0.227 mL, 2.30 mmol, 3.0 eq.), THF (5.0 mL), and trimethylsilylacetylene (**11**) (0.166 mL, 1.15 mmol, 1.5 eq.). The vial was then sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred at 23 °C for 3 h. The resulting mixture was diluted with EtOAc (5.0 mL) and filtered through a short pad of silica gel using EtOAc (100 mL). The filtrate was concentrated in vacuo, and the resulting crude product was purified by flash chromatography on silica gel (EtOAc:Petroleum ether 1:1 → EtOAc) to give the title compound **12** as a colorless crystalline solid (0.203 g, 0.728 mmol, 73%).



TLC (EtOAc)

R_f = 0.60, visualized by UV lamp (λ = 254 nm) or with $KMnO_4$.

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

δ 6.12 (d, *J* = 18.0 Hz, 1H), 6.04 (d, *J* = 18.5 Hz, 1H), 4.08 (d, *J* = 17.0 Hz, 2H), 3.70 (d, *J* = 17.0 Hz, 2H), 2.82 (s, 3H), 0.15 (s, 9H).

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

δ 168.7, 123.7, 104.6, 96.4, 61.6, 47.2, –0.2.

^{11}B NMR (100 MHz, $CDCl_3$)

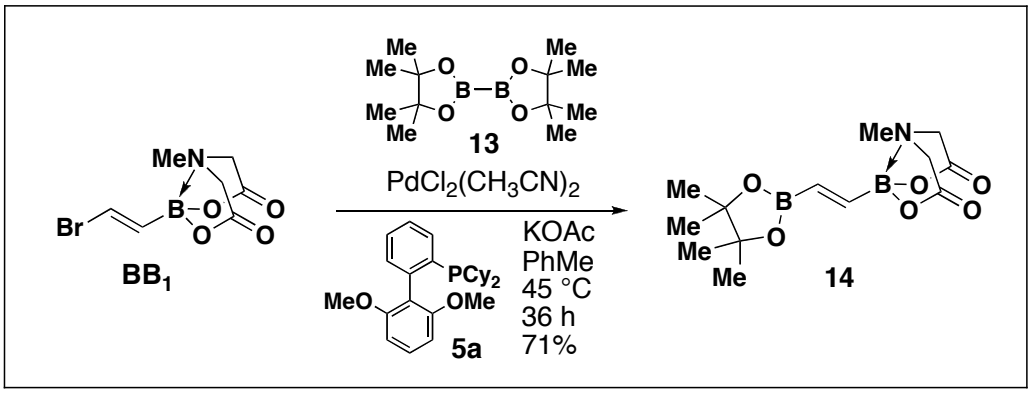
δ 11.5.

HRMS (ESI)

Calculated for $C_{12}H_{19}B\,NO_4Si\,(M+H)^+$:	280.1176
Found:	280.1178

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

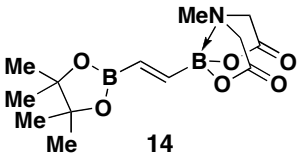
3016, 2959, 2898, 2152, 1760, 1600, 1451, 1423, 1342, 1293, 1251, 1170, 1116, 1066, 1025, 1003, 953, 842, 760, 734, 679.



(*E*)-(2-pinacolethenyl)boronate ester (14)

A solution of the catalyst was prepared as follows: A 20 mL Wheaton vial equipped with a magnetic stir bar was charged with $PdCl_2(CH_3CN)_2$ (7.9 mg, 0.030 mmol, 1.0 eq.) and 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a**) (38.0 mg, 0.090 mmol, 3.0 eq.). Toluene (3.00 mL) was added and the vial was sealed with a PTFE-lined plastic cap. The resulting mixture was stirred at 23 °C for 30 min yielding a clear yellow Pd/**5a** catalyst solution.

This catalyst solution was then utilized in the following procedure: A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with $\mathbf{BB_1}$ (0.262 g, 1.00 mmol, 1.0 eq.), bis(pinacolato)diboron (**13**) (0.324 g, 1.25 mmol, 1.25 eq.), potassium acetate (0.297 g, 3.00 mmol, 3.0 eq.), toluene (5.0 mL), and catalyst solution (3.0 mL, 3.0 mol% Pd). The vial was sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred for 36 h at 45 °C. The resulting heterogeneous mixture was diluted with ethyl acetate (5.0 mL) and filtered through short pad of Celite. Concentration of the filtrate in vacuo provided a light yellow solid. This crude product was purified by flash chromatography on silica gel (EtOAc:Petroleum ether 1:1 → EtOAc → EtOAc:MeCN 15:1) to give the title compound **14** as a colorless crystalline solid (0.219 g, 0.710 mmol, 71%). Crystals suitable for X-ray crystallography analysis were grown by slow evaporation from EtOAc at 23 °C. ***This material was stored under air at 23 °C for one year and six months without decomposition.***



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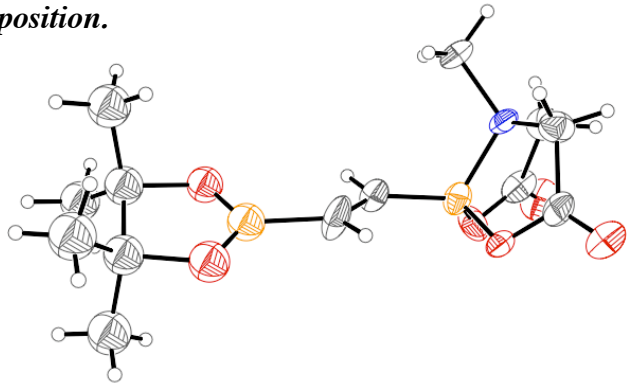


TLC (EtOAc)

R_f = 0.23, visualized with $KMnO_4$.

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

δ 6.67 (d, *J* = 20.5 Hz, 1H), 6.11 (d, *J* = 21.0 Hz, 1H), 3.96 (d, *J* = 17.0 Hz, 2H), 3.80 (d, *J* = 17.0 Hz, 2H), 2.76 (s, 3H), 1.22 (s, 12H).

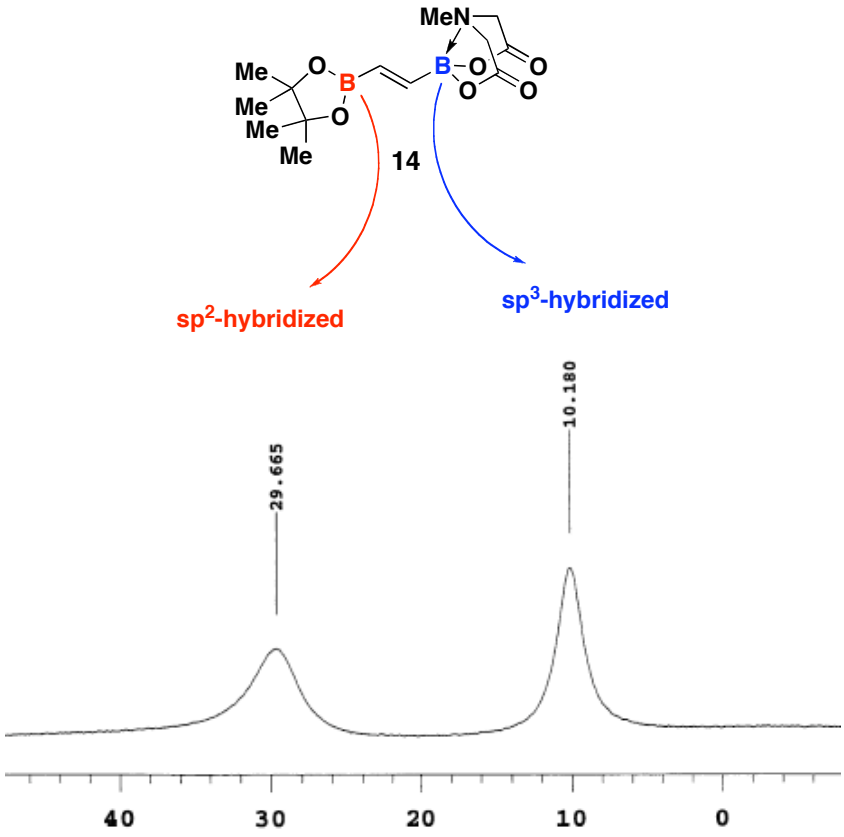
^{13}C NMR (125 MHz, CD_3CN)

δ 169.4, 84.1, 62.5, 47.7, 25.1.

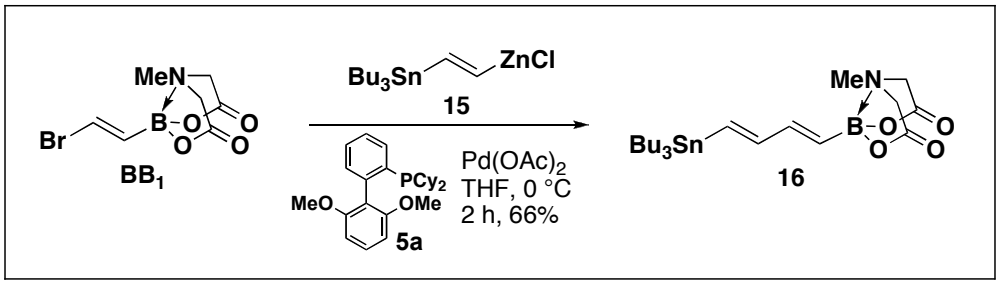
HRMS (ESI)

Calculated for $C_{13}H_{22}NO_6B_2$ $(M+H)^+$:	310.1633
Found:	310.1638

^{11}B NMR (100 MHz, CD_3CN)
δ 29.7 (sp^2), 10.2 (sp^3).



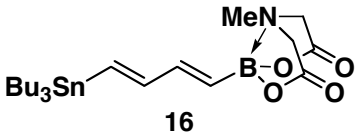
IR (thin film, cm^{-1})
2979, 1762, 1701, 1654, 1560, 1458, 1374, 1332, 1297, 1144, 1110, 1088, 1024, 967, 878, 847, 809, 673.



(*E*,*E*)-1,3-butadienyl-4-(tributylstannyl)boronate ester (16)

A solution of the catalyst was prepared as follows: To a 4 mL vial equipped with a magnetic stir bar and containing 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a**) (15.2 mg, 0.037 mmol, 2.0 eq.) was added a solution of $Pd(OAc)_2$ in THF (0.095 M, 0.19 mL, 0.018 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and maintained at 23 °C with stirring for 15 min. yielding a clear yellow Pd/**5a** catalyst solution.

This catalyst solution was then utilized in the following procedure: (*E*)-2-(tributylstannyl)vinylzinc chloride (**15**) was prepared according to literature precedent[6]: To a solution of *trans*-1,2-bis(tri-*n*-butylstannyl)ethylene (231 mg, 0.382 mmol, 2.0 eq.) in THF (0.4 mL) at –78 °C was added *n*-butyllithium (1.55 M in hexanes, 0.27 mL, 0.42 mmol, 2.2 eq.). After 30 min at –78 °C, a freshly prepared solution of $ZnCl_2$ (57 mg, 0.42 mmol, 2.2 eq.) in THF (0.84 mL) was added causing rapid decoloration. The solution was then warmed to –20 ˚C. During the formation of Negishi reagent **15**, to a slurry of $\mathbf{BB_1}$ (50 mg, 0.191 mmol, 1.0 eq.) in THF (0.2 mL) at 23 °C was added the catalyst stock solution described above (0.10 mL, 0.0095 mmol Pd, 5 mol% Pd) and the resulting slurry was stirred for 30 min before cooling to 0 °C. Negishi reagent **15** was then cannulated into the $\mathbf{BB_1}$ solution over 5 min. After 2 h at 0 °C the reaction was diluted with EtOAc (10 mL) and then concentrated in vacuo. The resulting red oil was dissolved in EtOAc and filtered through a short pad of silica gel with a copious amount of EtOAc, and the filtrate was concentrated in vacuo. The resulting crude product was purified by flash chromatography on silica gel (EtOAc:hexanes 1:1 → EtOAc) to yield **16** as a pale yellow foam (62.2 mg, 0.125 mmol, 66%).



TLC (EtOAc)

R_f = 0.45, visualized with $KMnO_4$.

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

δ 6.65 (dd, *J* = 9.5, 18.5 Hz, 1H), 6.52 (dd, *J* = 10.0, 17.5 Hz, 1H), 6.31 (d, *J* = 18.5 Hz, 1H), 5.63 (d, *J* = 17.0 Hz, 1H), 4.21 (d, *J* = 17.0 Hz, 2H), 4.03 (d, *J* = 17.0 Hz, 2H), 3.00 (s, 3H), 1.54 (m, 6H), 1.32 (m, 6H), 0.95 (t, *J* = 8.0 Hz, 6H), 0.88 (t, *J* = 7.5 Hz, 9H).

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

δ 169.0, 150.2, 146.2, 135.2, 62.3, 47.3, 29.9, 27.9, 13.9, 9.9.

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

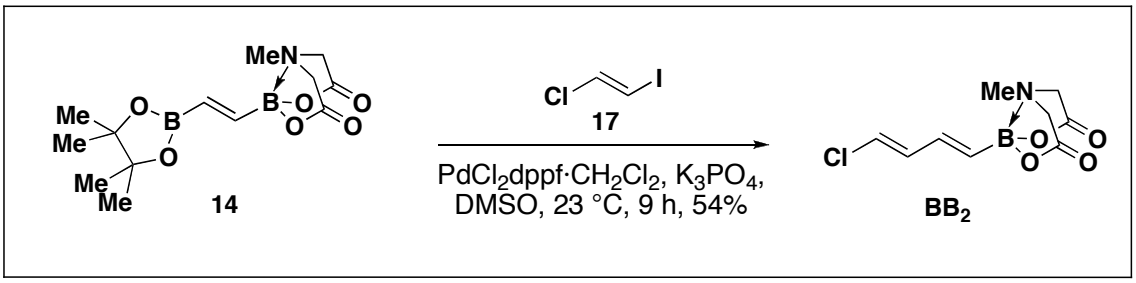
δ 11.3.

HRMS (CI+)

Calculated for $C_{21}H_{39}O_4NBSn$ $(M+H)^+$:	500.1994
Found:	500.1992

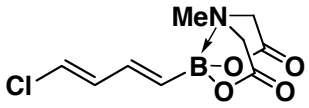
IR (thin film, cm^{-1})

2955, 2925, 2871, 2848, 1762, 1616, 1557, 1463, 1338, 1289, 1167, 1116, 1022, 957, 873, 844.



(*E*,*E*)-1,3-butadienyl-(4-chloro)boronate (BB_2)

To a 20 mL I-Chem vial equipped with a stir bar was added **14** (320 mg, 1.05 mmol, 1.0 eq.), finely ground anhydrous K_3PO_4 (669 mg, 3.15 mmol, 3.0 eq.), $PdCl_2dppf{\cdot}CH_2Cl_2$ (26 mg, 0.32 mmol, 3 mol%), and (*E*)-1-chloro-2-iodoethylene (**17**)[3] (396 mg, 2.10 mmol, 2.0 eq.). The vial was sealed with a PTFE-lined cap and DMSO (8.4 mL) was added via syringe. The resulting mixture was stirred at 23 °C for 9 h. The reaction was quenched with the addition of 0.5 M pH 7 phosphate buffer (8 mL) and the resulting mixture was extracted with THF:Et_2O 1:1 (4 x 15 mL). The combined organic extracts were washed with brine (25 mL), dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was diluted with acetone (15 mL) and concentrated onto Florisil®. The resulting powder was dry-loaded on top of a silica gel column and flash chromatography was performed (hexanes:EtOAc 1:1 → EtOAc → EtOAc:MeCN 9:1) to yield **BB_2** as a colorless crystalline solid (139 mg, 0.571 mmol, 54%).



TLC (EtOAc)

R_f = 0.35, visualized with $KMnO_4$.

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

δ 6.58 (dd, *J* = 10.5, 13.0 Hz, 1H), 6.53 (dd, *J* = 10.5, 16.5 Hz, 1H), 6.43 (d, *J* = 13.0 Hz, 1H), 5.68 (d, *J* = 17.0 Hz, 1H), 3.94 (d, *J* = 17.0 Hz, 2H), 3.78 (d, *J* = 17.0 Hz, 2H), 2.75 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN)

δ 169.3, 139.3, 136.6, 123.1, 62.4, 47.7.

^{11}B NMR (100 MHz, CD_3CN)

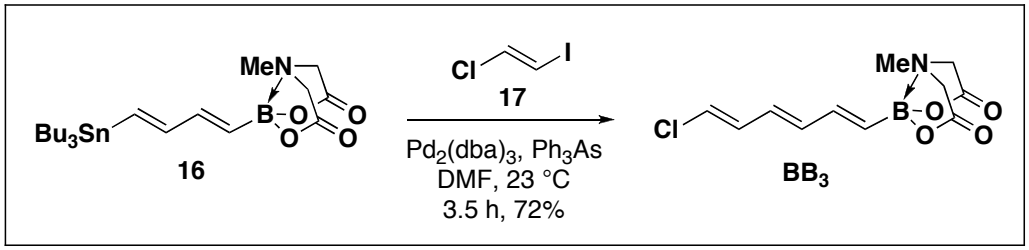
δ 11.1.

HRMS (EI+)

Calculated for $C_9H_{11}O_4NClB$ $(M)^+$:	243.0469
Found:	243.0467

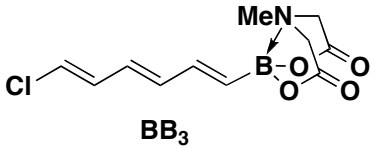
IR (thin film, cm^{-1})

3019, 1767, 1289, 1215, 1026, 1003, 760, 669.



(*E*,*E*,*E*)-(6-chloro)-1,3,5-hexatrienylboronate ester (BB_3)

A 30 mL Wheaton vial equipped with a magnetic stir bar was charged with $Pd_2(dba)_3$ (0.021 g, 0.023 mmol, 1.5 mol%), Ph_3As (0.014 g, 0.046 mmol, 3.0 mol%), **16** (0.760 g, 1.53 mmol, 1.0 eq.) as a solution in DMF (5.0 mL), and finally (*E*)-1-chloro-2-iodoethylene (0.575 g, 3.05 mmol, 2.0 eq.). The vial was sealed with a PTFE-lined plastic cap, and the reaction mixture was stirred at 23 °C for 3.5 h. To the resulting deep reddish mixture was then added saturated aqueous $Na_2S_2O_3$ (50 mL) and the resulting mixture was extracted with EtOAc (3 × 85 mL). The combined organic extracts were washed with brine (3 × 50 mL), dried over anhydrous magnesium sulfate, and concentrated in vacuo to provide an orange solid. This crude product was purified by flash chromatography on Florisil® (petroleum ether:EtOAc 1:1 → EtOAc → EtOAc:MeCN 9:1) to give the title compound **BB_3** as a light yellow solid (0.297 g, 1.10 mmol, 72%).



TLC (EtOAc)

R_f = 0.46, visualized by UV lamp (λ = 254 nm) or with $KMnO_4$.

^{1}H NMR (400 MHz, CD_3CN)

δ 6.61-6.53 (m, 2H), 6.39-6.25 (m, 3H), 5.72 (d, *J* = 17.6 Hz, 1H), 3.95 (d, *J* = 16.8 Hz, 2H), 3.79 (d, *J* = 16.8 Hz, 2H), 2.75 (s, 3H).

^{13}C NMR (100 MHz, CD_3CN)

δ 169.4, 143.1, 136.4, 134.6, 130.2, 122.3, 62.3, 47.6.

^{11}B NMR (100 MHz, CD_3CN)

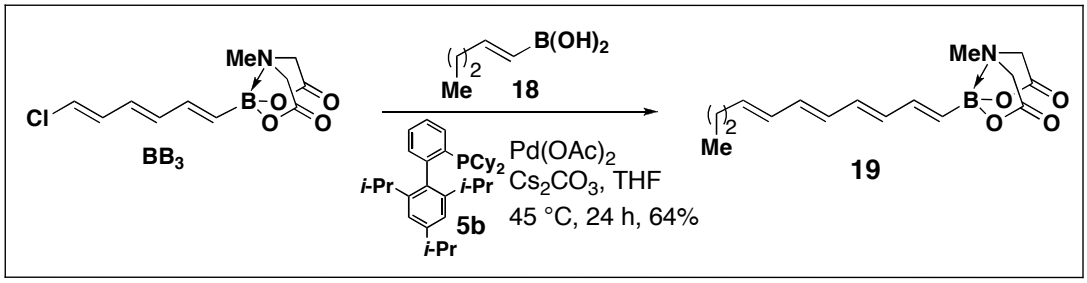
δ 10.7.

HRMS (ESI)

Calculated for $C_{11}H_{14}BNO_4Cl$ $(M+H)^+$:	270.0704
Found:	270.0717

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

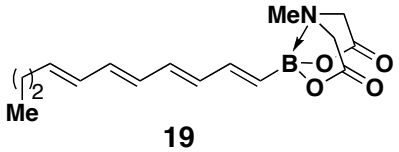
3010, 1764, 1620, 1562, 1458, 1337, 1288, 1235, 1191, 1154, 1116, 1083, 1006, 955, 891, 862, 829, 721.



(*E*,*E*,*E*,*E*)-1,3,5,7-undecatetraenylboronate ester (19)

A solution of the palladium catalyst was prepared as follows: To a 4 mL vial equipped with a stir bar and containing 2-dicyclohexylphosphino-2',4',6'-tri-*iso*-propyl-1,1'-biphenyl (**5b**) (3.0 mg, 0.0063 mmol, 2.0 eq.) in THF (0.577 mL) was added a solution of $Pd(OAc)_2$ in THF (0.00547 M, 0.577 mL, 0.0032 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and stirred at 23 °C for 15 min.

This catalyst solution was then utilized in the following procedure: To a 7 mL vial equipped with a magnetic stir bar and containing $\mathbf{BB_3}$ (11.0 mg, 0.0408 mmol, 1.0 eq.) was added (*E*)-1-penten-1-ylboronic acid (**18**) (7.0 mg, 0.0612 mmol, 1.5 eq.), Cs_2CO_3 (39.9 mg, 0.122 mmol, 3.0 eq.), THF (0.835 mL) and the catalyst solution (0.298 mL, 2 mol% Pd). The resulting mixture was then sealed with a PTFE-lined plastic cap and stirred at 45 °C for 24 h. ($\mathbf{BB_3}$ and product **19** were best separated on TLC plates by eluting twice with EtOAc). The resulting heterogeneous mixture was diluted with ethyl acetate (~1.0 mL) and filtered through a thin pad of Florisil® with copious amounts of EtOAc. The crude product was purified by flash chromatography on Florisil® (petroleum ether:EtOAc 1:1 → EtOAc → EtOAc:MeCN 15:1) to give the title compound **19** as a yellow solid (7.9 mg, 0.0261 mmol, 64%).



19

TLC (EtOAc)

R_f = 0.48, visualized by UV lamp (λ = 254 and 365 nm) or with $KMnO_4$.

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

δ 6.60 (dd, *J* = 9.5, 17.0 Hz, 1H), 6.36-6.25 (m, 3H), 6.20 (dd, *J* = 10.0, 14.5 Hz, 1H), 6.12 (dd, *J* = 10.5, 15.0 Hz, 1H), 5.76 (td, *J* = 7.0, 15.5 Hz, 1H), 5.67 (d, *J* = 17.5 Hz, 1H), 4.22 (d, *J* = 16.5 Hz, 2H), 4.02 (d, *J* = 17.0 Hz, 2H), 2.99 (s, 3H), 2.07 (app q, *J* = 7.5 Hz, 2H), 1.40-1.36 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H).

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

δ 169.0, 143.4, 136.3, 135.1, 135.0, 134.8, 131.7, 131.5, 62.3, 47.3, 35.5, 23.1, 13.9.

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

δ 11.2.

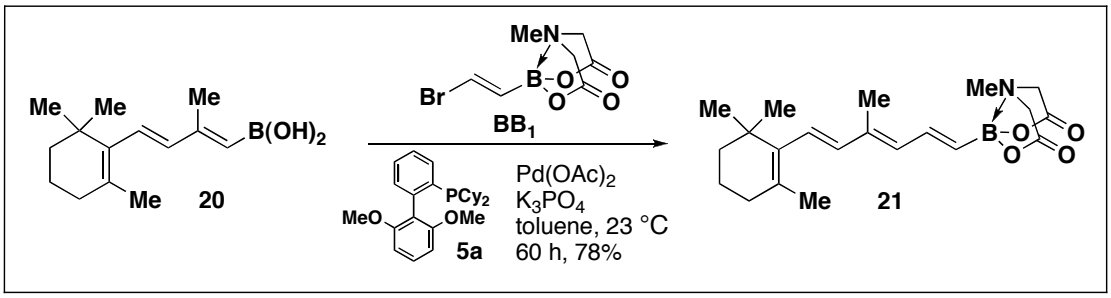
HRMS (ESI)

Calculated for $C_{16}H_{23}BNO_4$ $(M+H)^+$:	304.1720
Found:	304.1711

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

3008, 2961, 2929, 2858, 1766, 1744, 1459, 1342, 1294, 1254, 1155, 1124, 1010, 988, 955, 868.

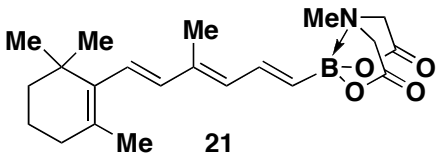
III. Total synthesis of all-*trans*-retinal (23)



Boronate ester 21

A solution of the catalyst was prepared as follows: To a 4 mL vial equipped with a stir bar and containing 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a**) (23.1 mg, 0.056 mmol, 2.0 eq.) was added a solution of $Pd(OAc)_2$ in toluene (0.038 M, 0.740 mL, 0.028 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and maintained at 65 °C with stirring for 15 min.

This catalyst solution was then utilized in the following procedure: To a 40 mL I-Chem vial equipped with a magnetic stir bar and containing a solution of **20**[4] in toluene (estimated 0.17 M, 11.5 mL, 1.96 mmol, 1.5 eq.) was added anhydrous K_3PO_4 as a finely ground powder (0.833 g, 3.92 mmol, 3.0 eq.), $\mathbf{BB_1}$ (0.342 g, 1.30 mmol, 1.0 eq.), and the catalyst solution (0.688 mL, 0.026 mmol Pd, 2 mol% Pd). The resulting mixture was sealed with a PTFE-lined cap and stirred at 23 °C for 60 h. The mixture was then filtered through a pad of silica gel with copious amounts of acetonitrile. To the resulting solution was added Florisil® and the solvent was removed in vacuo. The resulting powder was dry-loaded on top of a silica gel column and flash chromatography was performed (hexanes:EtOAc 1:1 → EtOAc → EtOAC:MeCN 9:1) to yield the title compound **21** as a yellow powder (0.377 g, 1.02 mmol, 78%).



TLC (EtOAc)

R_f = 0.45, visualized with $KMnO_4$.

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

δ 6.98 (dd, *J* = 11.0, 17.0 Hz, 1H), 6.23 (d, *J* = 16.0 Hz, 1H), 6.13 (d, *J* = 11.5 Hz, 1H), 6.10 (d, *J* = 16.0 Hz, 1H), 5.71 (d, *J* = 17.0 Hz, 1H), 4.21 (d, *J* = 17.0 Hz, 2H), 4.03 (d, *J* = 17.0 Hz, 2H), 3.00 (s, 3H), 2.01 (app t, *J* = 6.0 Hz, 2H), 1.94 (d, *J* = 1.0 Hz, 3H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.63-1.58 (m, 2H), 1.48-1.45 (m, 2H), 1.01 (s, 6H).

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

δ 169.1, 140.9, 139.3, 138.7, 136.7, 133.1, 129.6, 127.9, 62.2, 47.4, 40.2, 34.8, 33.5, 29.2, 21.9, 19.9, 12.7.

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

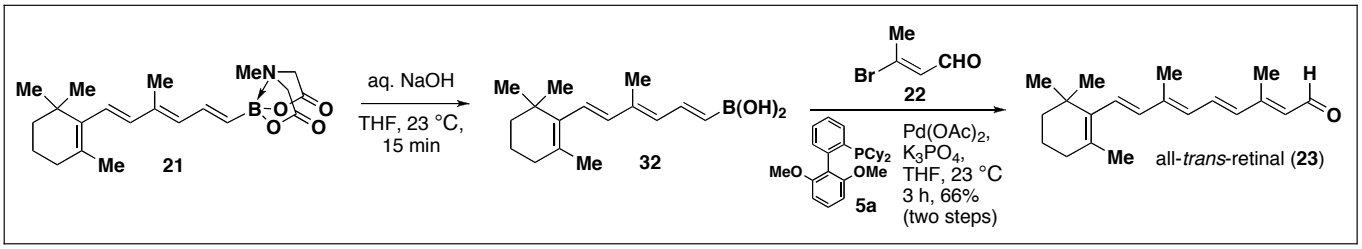
δ 11.7.

HRMS (FAB)

Calculated for $C_{21}H_{31}NBO_4$ $(M+H)^+$:	372.2346
Found:	372.2350

IR (KBr Pellet, cm^{-1})

3021, 2959, 2925, 2865, 1773, 1457, 1338, 1301, 1025, 986, 867.



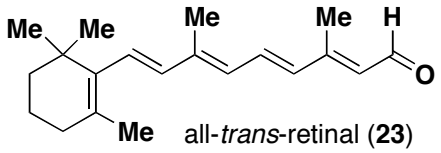
All-*trans*-retinal (23)

*MIDA boronate **21** was converted to boronic acid **32** via the following procedure*: In a 7 mL Wheaton vial, to a stirred solution of **21** (35.9 mg, 0.101 mmol, 1.0 eq.) in THF (1.44 mL) at 23 °C was added 1 M aq. NaOH (0.30 mL, 0.30 mmol, 3.0 eq.) and the resulting mixture was stirred for 15 min. The reaction was then quenched with the addition of 0.5 M pH 7 phosphate buffer (1.5 mL) and diluted with Et_2O (1.5 mL). The layers were separated and the aqueous layer was extracted with THF:Et_2O 1:1 (3 x 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo until a small amount of THF (~1 mL) remained, yielding a solution of **32**; TLC: (EtOAc) $R_f = 0.70$, visualized by $KMnO_4$.

A solution of the palladium catalyst was prepared as follows: To a 1.5 mL vial equipped with a magnetic stir bar and containing 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a**) (3.6 mg, 0.0088 mmol, 2.0 eq.) was added a solution of $Pd(OAc)_2$ in toluene (0.038 M , 0.115 mL, 0.0044 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and maintained at 65 °C with stirring for 15 min.

This catalyst solution was then utilized in the following procedure: To a 4 mL vial equipped with a magnetic stir bar and containing enal **22**[5] (10 mg, 0.067 mmol, 1.0 eq.) was added boronic acid **32** as a solution in THF (estimated 0.101 M, 1 mL, 0.101 mmol, 1.5 eq.), anhydrous K_3PO_4 as a finely ground powder (42.6 mg, 0.201 mmol, 3.0 eq.), and the catalyst stock solution described above (0.035 mL, 0.0013 mmol Pd, 2 mol% Pd). The resulting mixture was sealed with a PTFE-lined cap and stirred at 23 °C for 5 h. The reaction was then quenched with the addition of saturated aqueous $NaHCO_3$ (2 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The crude material was purified by flash chromatography (hexanes:EtOAc 32:1) to yield all-*trans*-retinal (**23**) as a bright yellow solid (12.6 mg, 0.044 mmol, 66%). ^1H NMR[11], ^{13}C NMR[12], HRMS, and IR[13] analysis of synthetic **23** were fully consistent with the data reported for the isolated natural product.

[11] Patel, D. J. *Nature* **1969**, *221*, 825.
[12] Englert, G. *Helv. Chim. Acta* **1975**, *58*, 2367.
[13] Rockley, N.L.; Halley, B.A.; Rockley, M.G.; Nelson, E.C. *Analytical Biochemistry* **1983**, *133*, 314-321.



all-*trans*-retinal (**23**)

TLC (hexanes:EtOAc 7:3)

R_f = 0.65, visualized with $KMnO_4$.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 10.10 (d, *J* = 8.4 Hz, 1H), 7.14 (dd, *J* = 11.2, 14.8 Hz, 1H), 6.37 (d, *J* = 14.8 Hz, 1H), 6.33 (d, *J* = 16.8 Hz, 1H), 6.18 (d, *J* = 11.2 Hz, 1H), 6.16 (d, *J* = 16.4 Hz, 1H), 5.97 (d, *J* = 8.4 Hz, 1H), 2.32 (d, *J* = 1.2 Hz, 3H), 2.06-2.00 (m, 2H)**,** 2.03 (d, *J* = 0.8 Hz, 3H), 1.72 (d, *J* = 0.8 Hz, 3H), 1.65-1.58 (m, 2H), 1.48-1.45 (m, 2H), 1.03 (s, 6H).

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

δ 191.1, 154.8, 141.3, 137.6, 137.0, 134.5, 132.5, 130.5, 129.7, 129.4, 129.0, 39.6, 34.3, 33.1, 29.0, 21.8, 19.2, 13.1, 13.0.

HRMS (FAB)

Calculated for $C_{20}H_{29}O$ $(M+H)^+$:	285.2218
Found:	285.2219

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

2961, 2929, 1865, 2253, 1655, 1573, 1456, 1386, 1334, 1216, 1164, 1135, 968, 908, 734.

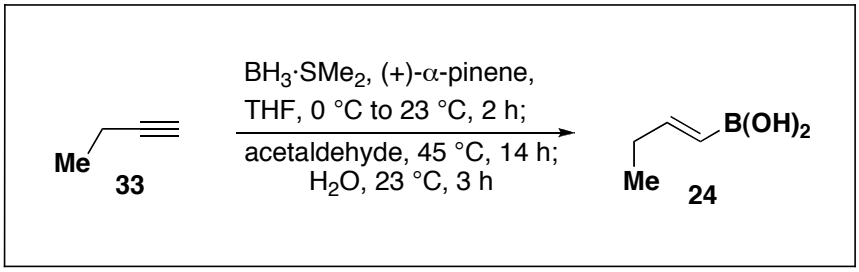
Partial ^{1}H NMR data for natural[11] and synthetic all-*trans*-retinal: δ_H/ppm (integration)

Natural **23** (220 MHz, $CDCl_3$)	Synthetic **23** (400 MHz, $CDCl_3$)
10.12 (1H)	10.10 (1H)
7.15 (1H)	7.14 (1H)
6.37 (1H)	6.37 (1H)
6.36 (1H)	6.33 (1H)
6.20 (1H)	6.18 (1H)
6.18 (1H)	6.16 (1H)
5.98 (1H)	5.97 (1H)
2.33 (3H)	2.32 (3H)
2.03 (3H)	2.03 (3H)
1.72 (3H)	1.72 (3H)
1.04 (6H)	1.03 (6H)

^{13}C NMR data for natural[12] and synthetic all-*trans*-retinal: δ_C/ppm

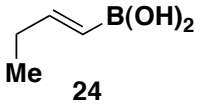
Natural **23** (22.63 MHz, $CDCl_3$)	Synthetic **23** (100 MHz, $CDCl_3$)
190.7	191.1
154.5	154.8
141.1	141.3
137.6	137.6
137.1	137.0
134.5	134.5
132.4	132.5
130.3	130.5
129.6	129.7
129.4	129.4
128.9	129.0
39.6	39.6
34.1	34.3
33.2	33.1
29.0	29.0
21.7	21.8
19.3	19.2
13.0	13.1
13.0	13.0

IV. Total synthesis of β-parinaric acid (27)



(*E*)-1-Butenylboronic acid (24)

In an unoptimized procedure, a 150 mL bomb flask equipped with a magnetic stir bar was charged with BH_3•SMe_2 (1.8 mL, 19.4 mmol, 1.0 eq.) and THF (11 mL). The solution was cooled to 0 °C and (+)-α-pinene (6.3 mL, 39.7 mmol, 2.0 eq.) was added dropwise. The solution was stirred at 0 °C for 10 min then allowed to warm to 23 °C and stirred at 23 °C for 2 h, during which time a white precipitate formed. The solution was then recooled to 0 °C and an excess of 1-butyne (**33**) was condensed into the reaction via a balloon resulting in a clear, colorless solution. The flask was then sealed with a Teflon screw cap and was stirred at 0 °C for 30 min, warmed to 23 °C, and stirred at 23 °C for 1.5 h. The solution was recooled to 0 °C and acetaldehyde (10.4 mL, 185 mmol, 9.5 eq.) was added. The bomb flask was resealed with the Teflon screw cap and the reaction was stirred at 40 °C for 14 h. The reaction was allowed to cool to 23 °C and water (5 mL) was added. After stirring for 3 h at 23 °C, the solution was diluted with EtOAc (50 mL), dried over $MgSO_4$, and concentrated in vacuo. The resulting residue was taken up in hexanes (50 mL) and the resulting mixture was extracted with 10% aqueous NaOH (2 x 10 mL). The combined aqueous extractions were washed with hexanes (2 x 20 mL) and then acidified to pH 2-3 with concentrated hydrochloric acid. The acidified aqueous layer was then extracted with EtOAc (3 x 30 mL), and the combined organic extracts were washed with saturated aq. $NaHCO_3$ (50 mL), dried over $MgSO_4$, and concentrated in vacuo to yield the title compound **24** as a colorless solid (0.928 g, 9.3 mmol, 48%).



TLC (EtOAc)

R_f = 0.68, visualized with $KMnO_4$.

^{1}H NMR (500 MHz, DMSO-d_6 : D_2O 95:5)

δ 6.49 (td, *J* = 6.5, 17.5 Hz, 1H), 5.32 (d, *J* = 18.0 Hz, 1H), 2.08 (m, 2H), 0.96 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6 : D_2O 95:5)

δ 151.5, 27.7, 12.5.

^{11}B NMR (100 MHz, DMSO-d_6 : D_2O 95:5)

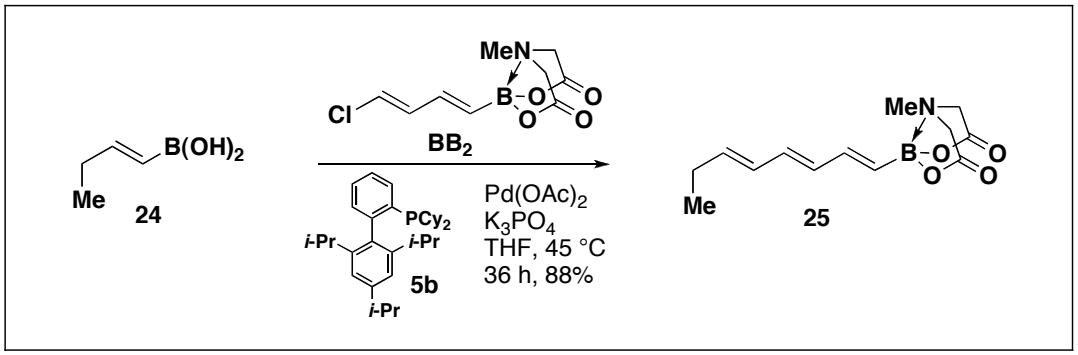
δ 28.8.

HRMS (EI+)

Calculated for $C_4H_9O_2B$ $(M)^+$:	100.0696
Found:	100.0696

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

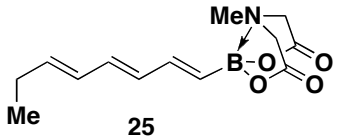
3235, 2970, 1633, 1633, 1356, 1233, 1154, 994.



(*E*,*E*,*E*)-1,3,5-Octatrienylboronate ester (25)

A solution of the palladium catalyst was prepared as follows: To a 4 mL vial equipped with a magnetic stir bar and containing 2-dicyclohexylphosphino-2',4',6'-tri-*iso*-propyl-1,1'-biphenyl (**5b**) (17.3 mg, 0.036 mmol, 2.0 eq.) was added a solution of $Pd(OAc)_2$ in THF (0.0109 M, 1.664 mL, 0.018 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and stirred at 23 °C for 30 min.

This catalyst solution was then utilized in the following procedure: To a 20 mL I-Chem vial equipped with a stir bar and containing (*E*)-1-butenylboronic acid (**24**) (113 mg, 1.13 mmol, 2.0 eq.) was added $\mathbf{BB_2}$ (138 mg, 0.521 mmol, 1.0 eq.), anhydrous K_3PO_4 as a finely ground powder (301 mg, 1.42 mmol, 2.5 eq.), THF (7.9 mL), and the catalyst solution (0.780 mL, 0.0085 mmol Pd, 1.5 mol% Pd). The resulting mixture was sealed with a PTFE-lined cap and stirred at 45 °C for 23 h. ($\mathbf{BB_2}$ and product **25** were best separated on TLC plates by eluting three times with hexanes:EtOAc 2:3). The mixture was then filtered through a pad of silica gel with copious amounts of acetonitrile. To the resulting solution was added Florisil® gel and then the solvent was removed in vacuo. The resulting powder was dry-loaded on top of a silica gel column and flash chromatography was performed (Et_2O → Et_2O:MeCN 4:1) to yield the title compound **25** as a yellow powder (120 mg, 0.456 mmol, 88%).



TLC (EtOAc)

R_f = 0.35, visualized by UV lamp (λ = 254 nm).

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

δ 6.56 (dd, *J* = 10.0, 17.5 Hz, 1H), 6.26 (dd, *J* = 10.5, 15.0 Hz, 1H), 6.19 (dd, *J* = 10.0, 15.0 Hz, 1H), 6.10 (tdd, *J* = 1.5, 10.0, 15.0 Hz, 1H), 5.80 (td, *J* = 6.5, 15.0 Hz, 1H), 5.63 (d, *J* = 17.0 Hz, 1H), 4.19 (d, *J* = 17.0 Hz, 2H), 4.02 (d, *J* = 17.0 Hz, 2H), 2.98 (s, 3H), 2.11 (m, 2H), 0.98 (t, *J* = 7.5 Hz, 3H).

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

δ 168.0, 143.5, 138.3, 134.8, 133.6, 130.4, 62.3, 47.3, 26.4, 13.8.

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

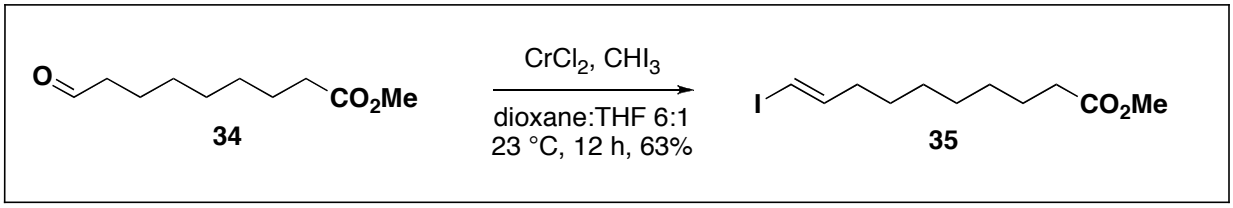
δ 11.6.

HRMS (EI+)

Calculated for $C_{13}H_{18}O_4NB$ $(M)^+$:	263.1329
Found:	263.1331

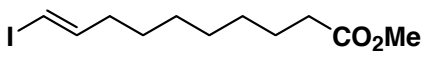
IR (thin film, cm^{-1})

3017, 1768, 1216, 1026, 1010, 756, 668.



Vinyl iodide 35

In an unoptimized procedure, to a suspension of $CrCl_2$ (454 mg, 3.75 mmol, 7.0 eq.) in THF (1.5 mL) at 23 °C was added dropwise a solution of (*E*)-methyl 10-iododec-9-enoate (**34**)[7] (100 mg, 0.537 mmol, 1.0 eq.) and iodoform (422 mg, 1.07 mmol, 2.0 eq.) in dioxane (9.2 mL). After stirring for 12 h, the reaction mixture was diluted with Et_2O (10 mL) and poured into water (10 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 15 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$, and concentrated in vacuo. Purification of the crude product by flash chromatography (hexanes → hexanes:EtOAc 9:1) provided the title compound **35** as a yellow oil (105 mg, 0.337 mmol, 63%). ^1H NMR indicated an *E*:*Z* ratio of 10:1.



35

TLC (hexanes:EtOAc 4:1)

R_f = 0.45, visualized with $KMnO_4$.

^1H NMR (400 MHz, $CDCl_3$)

δ 6.49 (td, *J* = 7.2, 14.4 Hz, 1H), 5.96 (td, *J* = 1.6, 14.0 Hz, 1H), 3.66 (s, 3H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.03 (dq, *J* = 1.2, 6.8 Hz, 2H), 1.64-1.56 (m, 2H), 1.42-1.33 (m, 2H), 1.33-1.24 (m, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)

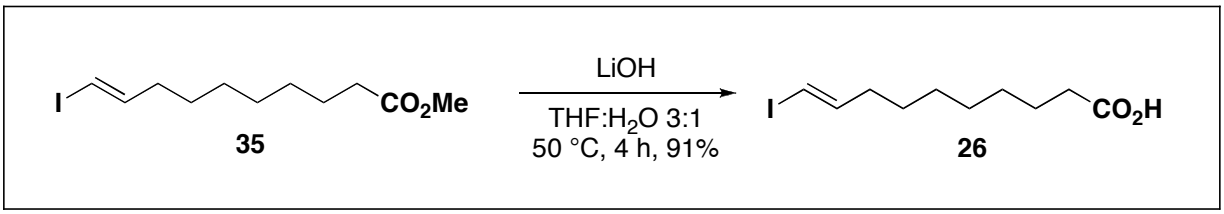
δ 174.2, 146.6, 74.4, 51.5, 36.0, 34.0, 29.0, 28.9, 28.7, 28.2, 24.8.

HRMS (CI+)

Calculated for $C_{11}H_{20}O_2I$ $(M+H)^+$:	311.0508
Found:	311.0508

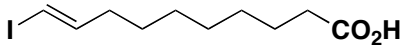
IR (thin film, cm^{-1})

2927, 2855, 1738, 1435, 1197, 1172, 946.



Carboxylic acid 26

To a stirred solution **35** (51.0 mg, 0.164 mmol, 1.0 eq.) in THF:H_2O 3:1 (3.3 mL) was added LiOH (69.0 mg, 1.64 mmol, 10.0 eq.). The reaction was stirred at 50 °C for 4 h before diluting with Et_2O (5 mL) and pouring into 1 M aqueous HCl (5 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4, and concentrated in vacuo. Purification of the crude product by flash chromatography (hexanes:EtOAc 5:1 → EtOAc) provided **26** as a pale yellow solid (44.0 mg, 0.149 mmol, 91%). ^{1}H NMR indicated an *E*:*Z* ratio of 10:1



26

TLC (hexanes:EtOAc 4:1)

R_f = 0.14, visualized with $KMnO_4$.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 11.32 (br s, 1H), 6.50 (td, *J* = 7.2, 14.4 Hz, 1H), 5.97 (td, *J* = 1.6, 14.4 Hz, 1H), 2.35 (t, *J* = 7.6 Hz, 2H), 2.04 (m, 2H), 1.66-1.59 (m, 2H), 1.41-1.25 (m, 8H).

^{13}C NMR (100 MHz, $CDCl_3$)

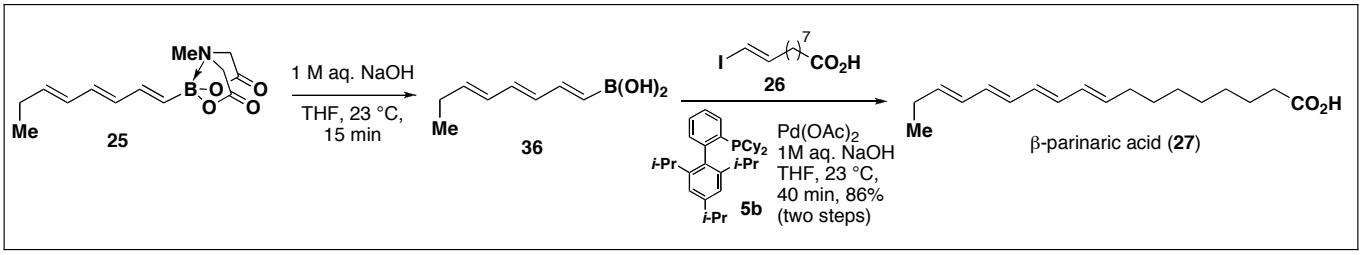
δ 180.0, 146.6, 74.4, 36.0, 34.0, 29.0, 28.9, 28.7, 28.2, 24.6.

HRMS (CI+)

Calculated for $C_{10}H_{18}O_2I$ $(M+H)^+$:	297.0352
Found:	297.0351

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

3300-2500 (br), 2928, 2851, 1694, 1464, 1407, 1282, 1185, 936.

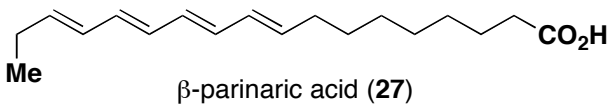


β-parinaric acid (27)

*MIDA boronate **25** was converted to boronic acid **36** via the following procedure*: To a stirred solution of **25** (24.7 mg, 0.094 mmol, 1.0 eq.) in THF (1.34 mL) at 23 °C was added 1 M aq. NaOH (0.28 mL, 0.28 mmol, 3.0 eq.) and the resulting mixture was stirred at 23 °C for 15 min. The reaction was then quenched with the addition of 0.5 M pH 7 phosphate buffer (1.5 mL) and diluted with Et_2O (1.5 mL). The layers were separated and the aqueous layer was extracted with THF:Et_2O 1:1 (3 x 3 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo until a small amount of THF (~3.7 mL) remained, yielding a solution of **36**; TLC (EtOAc): R_f = 0.63, visualized with $KMnO_4$.

A solution of the palladium catalyst was prepared as follows: To a 4 mL vial equipped with a magnetic stir bar and containing 2-dicyclohexylphosphino-2',4',6'-tri-*iso*-propyl-1,1'-biphenyl ligand (**5b**) (2.1 mg, 0.0044 mmol, 2.0 eq.) was added a solution of $Pd(OAc)_2$ in THF (0.004 M, 0.545 mL, 0.0022 mmol, 1.0 eq.). The vial was sealed with a PTFE-lined cap and stirred at 23 °C for 30 min.

This catalyst solution was then utilized in the following procedure: To a 20-mL I-Chem vial equipped with a magnetic stir bar and containing **26** (18.5 mg, 0.062 mmol, 1.0 eq.; *E*:*Z* 7:1 by ^{1}H NMR) was added boronic acid **36** (3.7 mL, estimated 0.094 mmol, 1.5 eq.) and the catalyst solution described above (0.31 mL, 0.0013 mmol Pd, 2 mol% Pd). The resulting mixture was sealed with a teflon-lined septum cap and 1 M aqueous NaOH (0.19 mL, 0.190 mmol, 3.0 eq.) was added. The reaction was stirred at 23 °C for 40 min and was then quenched with the addition of saturated aqueous NH_4Cl (3 mL). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 5 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo. The resulting crude product was purified by flash chromatography (hexanes:Et_2O 4:1 → Et_2O) to yield β-parinaric acid **27** as a fluorescent solid (14.8 mg, 0.054 mmol, 86%). ^{1}H NMR indicated a 7:1 mixture of β-parinaric acid:9-(*Z*) parinaric acid (arising from 7:1 *E*:*Z* mixture of starting material **26**). ^{1}H NMR and ^{13}C NMR analysis of synthetic **27** were fully consistent with the data previously reported for β-parinaric acid.[14,15]



β-parinaric acid (**27**)

TLC (hexanes:Et_2O 1:1)

R_f = 0.26, visualized by UV lamp (λ = 254 and 365 nm).

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

δ 10.96 (br s, 1H), 6.22-6.00 (m, 6H), 5.73 (td, *J* = 7.0 Hz, 15.0 Hz, 1H), 5.68 (td, *J* = 7.0, 15.0 Hz, 1H), 2.34 (t, *J* = 7.5 Hz, 2H), 2.11-2.06 (m, 4H), 1.64-1.61 (m, 2H), 1.43-1.25 (m, 8H), 1.01 (t, *J* = 7.5 Hz, 3H).

[14] Kuklev, D.V.; Smith, W.L. *Chemistry and Physics of Lipids* **2004**, *131*, 215-222.
[15] Smith, R.M. *Journal of Chemical Research* **1981**, *41*, 477-490.

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

δ 179.4, 136.6, 135.0, 132.5, 132.4, 130.9, 130.8, 130.6, 129.6, 33.9, 32.8, 29.2, 29.1, 29.0, 28.9, 25.9, 24.6, 13.5.

HRMS (ESI+)

Calculated for $C_{18}H_{28}O_2Na$ $(M + Na)^+$: 299.1987
Found: 299.1990

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

3428, 3020, 2930, 1641, 1215, 761, 669.

^{1}H NMR data for β-parinaric acid: δ_H/ppm (integration)

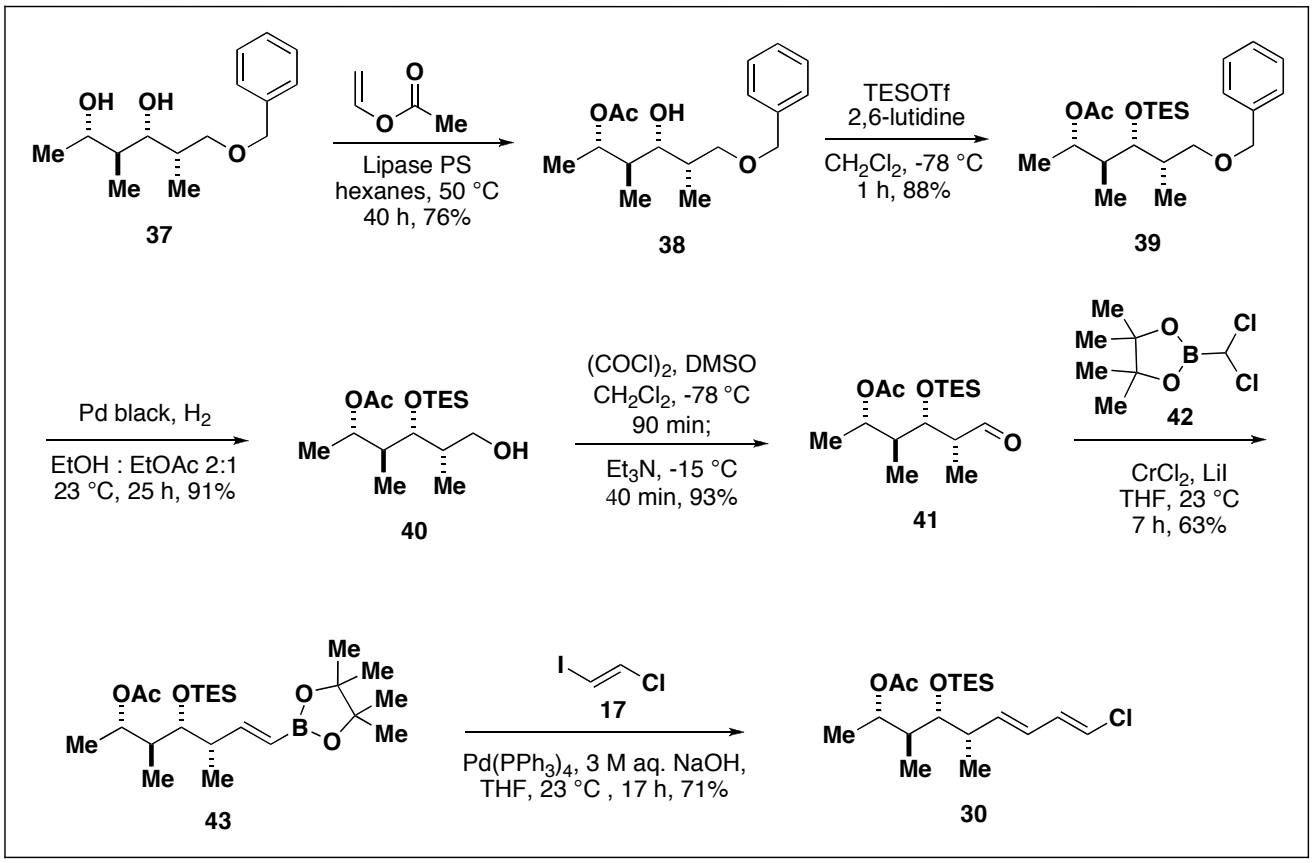
Previously reported **27**[14] (300 MHz, $CDCl_3$)	Synthetic **27** (500 MHz, $CDCl_3$)
6.08 (6H)	6.22-6.00 (6H)
5.75 (2H)	5.73 (1H), 5.68 (1H)
2.32 (2H)	2.34 (2H)
2.11 (2H), 2.10 (2H)	2.11-2.06 (4H)
1.60 (2H)	1.64-1.61 (2H)
1.29 (8H)	1.43-1.25 (8H)
1.08 (3H)	1.01 (3H)

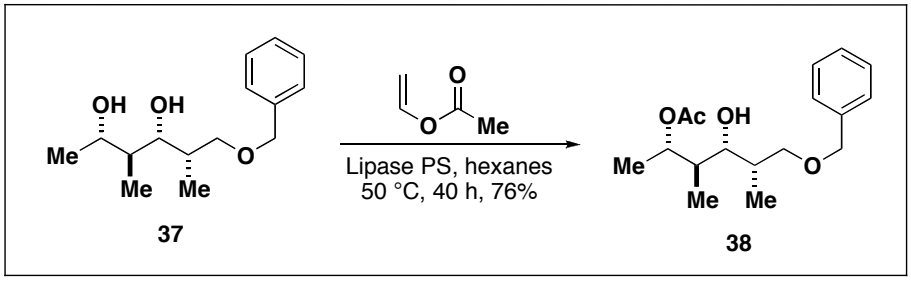
^{13}C NMR data for β-parinaric acid: δ_C/ppm

Previously reported **27**[14] (125 MHz, $CDCl_3$)	Synthetic **27** (125 MHz, $CDCl_3$)
179.0	179.4
137.0	136.6
135.4	135.0
132.9	132.5
132.8	132.4
131.3	130.9
131.3	130.8
131.1	130.6
130.0	129.6
34.2	33.9
33.2	32.8
29.6	29.2
29.5	29.1
29.4	29.0
29.4	28.9
26.3	25.9
25.1	24.6
13.9	13.5

V. Synthesis of ½ of the amphotericin B macrolide (31)

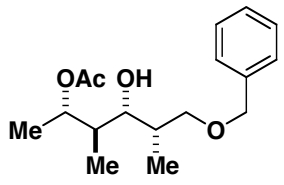
Figure S1. Synthesis of **30**.





Acetate 38

A 200 mL recovery flask was charged with diol **37**[8] (1.18 g, 4.69 mmol, 1.0 eq.), Lipase PS (295 mg, 0.25 mass eq), and hexanes (115 mL) and the resulting slurry was stirred at 50 °C for 15 min. Vinyl acetate (4.33 mL, 47.0 mmol, 10.0 eq) was then added and the reaction mixture was stirred at 50 °C for 40 h. The resulting mixture was cooled to 23 °C and filtered, and the residual enzyme was washed copiously with Et_2O. The filtrate was then concentrated in vacuo and the resulting viscous, light yellow oil was purified by flash column chromatography (hexanes:EtOAc 15:1 → 1:1) to yield **38** as a pale yellow oil (1.05 g, 3.57 mmol, 76%).



38

TLC (hexanes:EtOAc 1:1)

R_f = 0.60, visualized with *p*-anisaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.37-7.29 (m, 5H), 5.32 (dq, *J* = 4.0, 6.4 Hz,1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.49 (d, *J* = 12.0 Hz, 1H), 3.61-3.53 (m, 3H), 2.66 (d, *J* = 3.2 Hz, 1H), 2.03 (s, 3H), 1.97-1.91 (m, 1H), 1.91-1.84 (m, 1H), 1.16 (d, *J* = 6.4 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 6.8 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$)

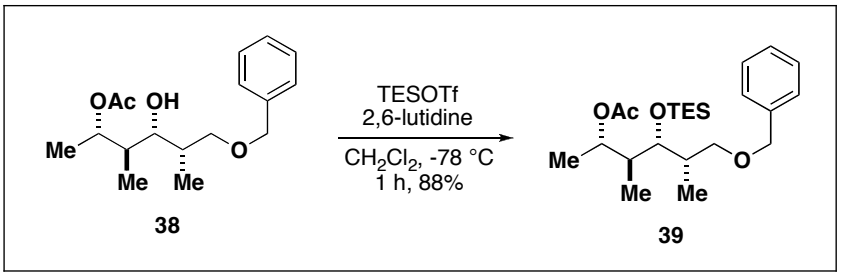
170.4, 138.0, 128.4, 127.7, 127.6, 75.5, 74.9, 73.4, 71.4, 39.6, 34.7, 21.5, 13.8, 10.0, 9.1.

HRMS (CI+)

Calculated for $C_{17}H_{27}O_4$ $(M+H)^+$:	295.1909
Found:	295.1905

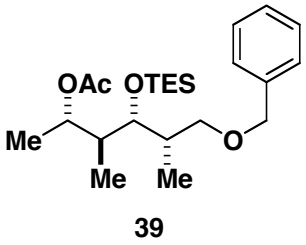
IR (thin film, cm^{-1})

3497, 2970, 2925, 2873, 1731, 1714, 1453, 1371, 1244, 1101, 1053, 1020, 737, 698.



Triethylsilyl ether 39

To a stirred solution of **38** (5.98 g, 20.31 mmol, 1.0 eq.) in CH_2Cl_2 (230 mL) at 0 °C was added 2,6-lutidine (7.84 mL, 67.35 mmol, 3.3 eq.) and the resulting solution was cooled to –78 °C. Triethylsilyl trifluoromethanesulfonate (7.11 mL, 31.43 mmol, 1.5 eq.) was then added dropwise and the resulting solution was stirred at –78 °C for 1 h. The reaction was then quenched with the addition of saturated aqueous $NaHCO_3$ (115 mL) and allowed to warm to 23 °C. The layers were separated and the aqueous layer was extracted with Et_2O (3 x 200 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo to give a yellow oil. Purification by flash chromatography (hexanes:EtOAc 7:1 → 1:1) provided **39** as a yellow oil (7.34g, 17.96 mmol, 88%).



39

TLC (hexanes:EtOAc 3:1)

R_f = 0.67, visualized with *p*-anisaldehyde.

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

δ 7.35-7.26 (m, 5H), 5.00 (app qn, *J* = 6.5 Hz, 1H), 4.49 (d, *J* = 11.5 Hz, 1H), 4.43 (d, *J* = 11.5 Hz, 1H), 3.85 (dd, *J* = 2.5, 7.0 Hz, 1H), 3.35 (app t, *J* = 8.5 Hz, 1H), 3.22 (dd, *J* = 6.0, 9.0 Hz, 1H), 1.96-1.86 (m, 2H), 1.91 (s, 3H), 1.14 (d, *J* = 6.5 Hz, 3H), 0.95 (t, *J* = 8.5 Hz, 9H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H), 0.60 (m, 6H).

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

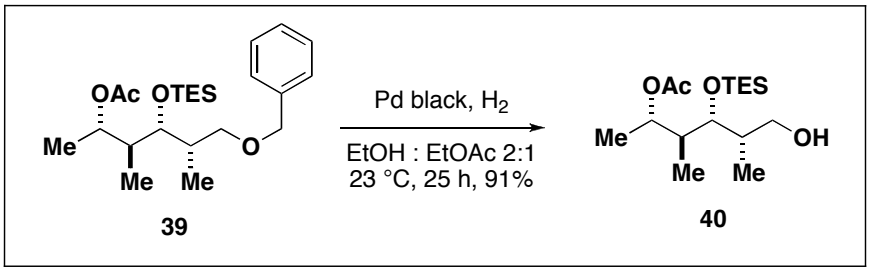
δ 170.4, 138.6, 128.3, 127.7, 127.4, 73.7, 72.9, 72.2, 71.7, 42.6, 35.5, 21.3, 16.1, 11.2, 11.0, 7.0, 5.4.

HRMS (ESI+)

Calculated for $C_{23}H_{41}O_4Si$ $(M+H)^+$:	409.2774
Found:	409.2765

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

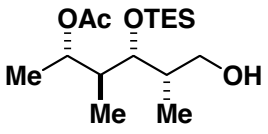
2953, 2875, 1734, 1453, 1369, 1243, 1093, 1046, 1005, 736, 696, 654.



Primary alcohol 40

Caution: palladium black is pyrophoric and should be maintained under inert atmosphere at all times. For this reaction, EtOH and EtOAc were freshly distilled over activated 4Å molecular sieves.

To a 25 mL three-neck round-bottomed flask equipped with a magnetic stir bar was added palladium black (17.3 mg, 0.163 mmol, 0.6 eq.). To this flask was then added via cannula a solution of benzyl ether **39** (111.0 mg, 0.271 mmol, 1.0 eq.) in EtOH:EtOAc 2:1 (4.65mL). The reaction flask was purged with H_2 (balloon) and stirred at 23 °C for 25 h under a positive pressure of H_2 (balloon). The resulting mixture was then filtered under N_2 pressure through a short column of Celite, flushing with copious amounts of EtOH (Pd residue kept under solvent at all times). Purification by flash chromatography (hexanes:EtOAc 12:1 → 4:1) yielded primary alcohol **40** as a pale yellow oil (79.1 mg, 0.248 mmol, 91%).



40

TLC (hexanes:EtOAc 1:1)

R_f = 0.56, visualized with *p*-anisaldehyde.

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

δ 5.01 (app qn, *J* = 6.0 Hz, 1H), 3.85 (dd, *J* = 2.0, 6.0 Hz, 1H), 3.47 (m, 2H), 2.01 (s, 3H), 1.93 (m, 1H), 1.79 (m, 1H), 1.16 (d, *J* = 6.5 Hz, 3H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.89 (d, *J* = 7.5 Hz, 3H), 0.84 (d, *J* = 7.0 Hz, 3H), 0.62 (q, *J* = 8.0 Hz, 6H).

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

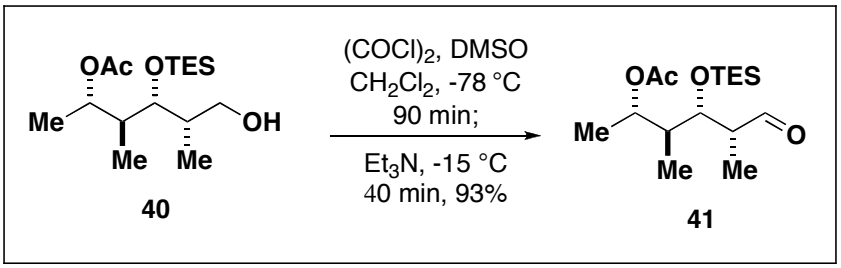
δ 170.7, 72.4, 71.7, 66.2, 42.8, 38.0, 21.4, 16.5, 11.2, 11.2, 7.0, 5.3.

HRMS (ESI+)

Calculated for $C_{16}H_{35}O_4Si$ $(M+H)^+$:	319.2305
Found:	319.2310

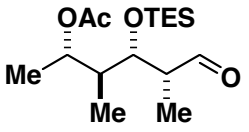
IR (thin film, cm^{-1})

3457, 2954, 2873, 1731, 1714, 1371, 1245, 1044.



Aldehyde 41

To a stirred solution of oxalyl chloride (3.44 mL, 40.1 mmol, 5.0 eq.) in CH_2Cl_2 (20 mL) at –78 °C was added dropwise DMSO (5.70 mL, 80.2 mmol, 10.0 eq.) and the resulting solution was stirred at –78 ˚C for 30 min. To the reaction was then added via cannula a solution of alcohol **40** (2.56 g, 8.02 mmol, 1.0 eq.) in CH_2Cl_2 (55.7 mL) and the resulting solution was stirred at –78 °C for 1.5 h. Triethylamine (28 mL, 201 mmol, 25.0 eq.) was then added and the resulting mixture was allowed to warm to –15 °C over 40 min. The reaction was then quenched with the addition of saturated aqueous NH_4Cl (50 mL). The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over $MgSO_4$, and concentrated in vacuo to yield aldehyde **41** as a yellow oil (2.36 g, 7.46 mmol, 93%).



41

TLC (hexanes:EtOAc 1:1)

R_f = 0.76, stained by *p*-anisaldehyde.

^{1}H NMR (400 MHz, $CDCl_3$)

δ 9.67 (d, *J* = 0.8 Hz, 1H), 4.99 (app qn, *J* = 6.4 Hz, 1H), 4.21 (dd, *J* = 2.8, 6.0 Hz, 1H), 2.44 (ddq, *J* = 0.8, 3.2, 7.2 Hz, 1H), 2.03 (s, 3H), 1.95 (m, 1H), 1.18 (d, *J* = 6.4 Hz, 3H), 1.14 (d, *J* = 7.2 Hz, 3H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.90 (d, *J* = 6.8 Hz, 3H), 0.58 (q, *J* = 7.6 Hz, 6H).

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

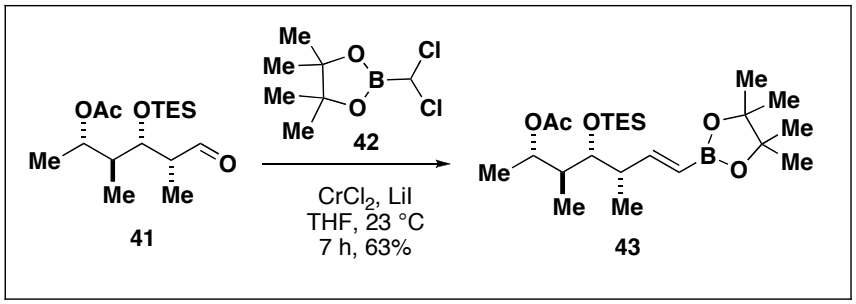
δ 204.7, 170.3, 71.2, 71.2, 49.4, 42.7, 21.3, 16.3, 11.2, 8.3, 6.9, 5.2.

HRMS (ESI+)

Calculated for $C_{16}H_{32}O_4SiNa$ $(M+Na)^+$:	339.1968
Found:	339.1972

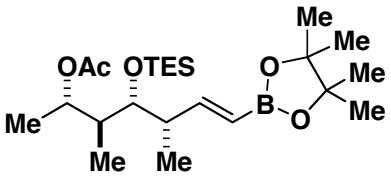
IR (thin film, cm^{-1})

2953, 2877, 1731, 1708, 1458, 1372, 1241, 1049, 1010, 946, 740.



Pinacolboronic ester 43

To a stirred slurry of $CrCl_2$ (0.204 g, 1.66 mmol, 18.0 eq.) in THF (2 mL) at 23 °C was added a solution of aldehyde **41** (29.2 mg, 0.0923 mmol, 1.0 eq.) and dichlomethylpinacolboronic ester **42**[9] (0.117 g, 0.554 mmol, 6.0 eq.) in THF (0.18 mL). A solution of LiI (0.149 g, 1.11 mmol, 12.0 eq.) in THF (0.3 mL) was then added and the resulting slurry was stirred at 23 °C for 7 h. The reaction was then poured into ice water (2 mL) and extracted with Et_2O (2 x 5 mL). The combined organic extracts were dried over $MgSO_4$, filtered through Celite, and concentrated in vacuo. The crude material was purified by flash chromatography on Florisil® (hexanes:EtOAc 35:1 → 3:1) to provide the title compound **43** as a pale yellow oil (25.7 mg, 0. 58 mmol, 63%).



43

TLC (hexanes:EtOAc 1:1)

R_f = 0.87, visualized with *p*-anisaldehyde.

^{1}H-NMR (400 MHz, $CDCl_3$)

δ 6.58 (dd, *J* = 6.8, 18.0 Hz, 1H), 5.43 (dd, *J* = 1.2, 18.0 Hz, 1H), 5.04 (app qn, *J* = 6.4 Hz, 1H), 3.57 (dd, *J* = 4.8, 6.6 Hz, 1H), 2.45-2.36 (m, 1H), 2.01 (s, 3H), 1.91 (m, 1H), 1.26 (s, 12H), 1.12 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 7.2 Hz, 3H), 0.95 (t, *J* = 7.6 Hz, 9H), 0.87 (d, *J* = 7.2 Hz, 3H), 0.60 (q, *J* = 8.0 Hz, 6H).

^{13}C-NMR (100 MHz, $CDCl_3$)

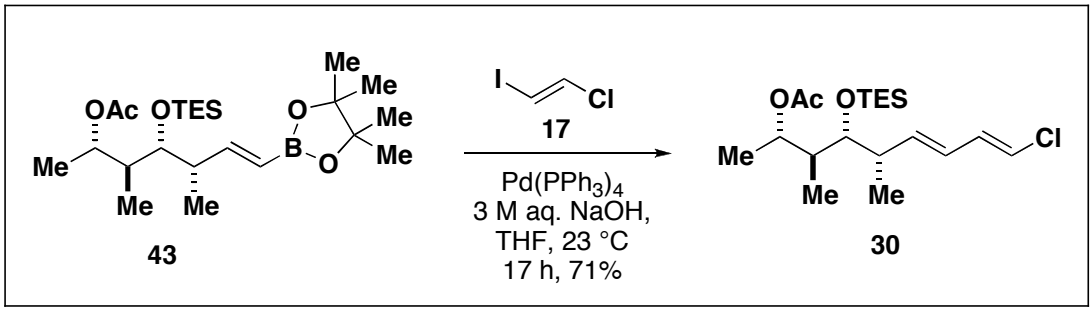
δ 177.2, 158.2, 83.0, 71.5, 42.3, 42.0, 24.8, 24.7, 21.5, 15.7, 13.4, 11.2, 7.1, 5.4.

HRMS (CI+)

Calculated for $C_{23}H_{46}BO_5Si$ $(M+H)^+$:	441.3208
Found:	441.3210

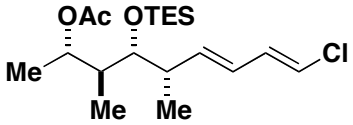
IR (thin film, cm^{-1})

2974, 2873, 1736, 1636, 1458, 1359, 1322, 1241, 1145, 1004, 970, 848, 731.



Dienylchloride 30

A 15 mL round-bottomed flask equipped with a stir bar was charged with pinacol boronic ester **43** (126.9 mg, 0.288 mmol, 1.5 eq.). To this flask was then added a solution of (*E*)-1-chloro-2-iodoethylene (**17**)[3] (36.2 mg, 0.192 mmol, 1.0 eq.) and $Pd(PPh_3)_4$ (16.6 mg, 0.0144 mmol, 5 mol%) as a solution in THF (4.5 mL) followed by 3 M aqueous NaOH (0.192 mL, 0.576 mmol, 2.0 eq.). The resulting mixture was stirred at 23 °C for 17 h and then the reaction was quenched with saturated aqueous NH_4Cl (5 mL). The resulting mixture was diluted with diethyl ether (5 mL) and the layers were separated. The aqueous layer was extracted with diethyl ether (3 x 5 mL) and the combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. Purification of the resulting residue by flash chromatography (hexanes:EtOAc 35:1 → 5:1 with 1% Et_3N (*v*/*v*) added to all eluents) provided dienylchloride **30** as a yellow oil (51.0 mg, 0.136 mmol, 71%).



30

TLC (hexanes:EtOAc 10:1)

R_f = 0.34, visualized with $KMnO_4$.

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

δ 6.41 (dd, *J* = 11.5, 13.0 Hz, 1H), 6.11 (d, *J* = 13.0 Hz, 1H), 5.96 (dd, *J* = 11.0, 15.5 Hz, 1H), 5.65 (dd, *J* = 8.0, 15.5 Hz, 1H), 5.05 (app qn, *J* = 6.5 Hz, 1H), 3.50 (app t, *J* = 5.5 Hz, 1H), 2.37 (m, 1H), 2.01 (s, 3H), 1.88 (m, 1H), 1.13 (d, *J* = 6.0 Hz, 3H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 8.0 Hz, 9H), 0.89 (d, *J* = 7.0 Hz, 3H), 0.60 (q, *J* = 7.5 Hz, 6H).

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

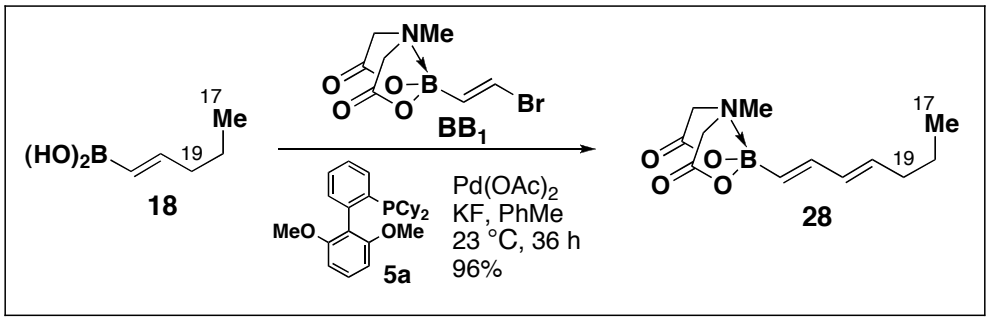
δ 170.2, 139.2, 133.7, 125.6, 119.0, 71.6, 71.4, 42.2, 40.3, 21.4, 16.4, 15.5, 11.2, 7.0, 5.4.

HRMS (CI+)

Calculated for $C_{19}H_{36}ClO_3Si$ $(M+H)^+$:	375.2122
Found:	375.2122

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

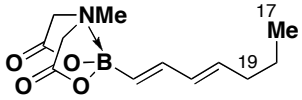
2960, 2873, 1735, 1241, 1015, 800, 655.



(*E*,*E*)-1,3-heptadienylboronate ester (28)

A solution of the catalyst was prepared as follows: An oven-dried Wheaton vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (5.60 mg, 0.025 mmol, 1.0 eq.) and 2-dicyclohexylphosphino-2',6'-dimethoxy-1,1'-biphenyl (**5a**) (20.5 mg, 0.050 mmol, 2.0 eq.). Toluene (3.00 mL) was added and the vial was sealed with a PTFE-lined plastic cap. The resulting mixture was stirred at 23 °C for 45 min. resulting in a yellow Pd/**5a** catalyst solution (0.00833 N Pd in toluene).

This catalyst solution was then utilized in the following procedure: An oven-dried Wheaton vial equipped with a magnetic stir bar was charged with **BB$_1$** (0.262 g, 1.00 mmol, 1.0 eq.), (*E*)-1-pentenylboronic acid **18** (0.171 g, 1.50 mmol, 1.5 eq.), KF (0.116 g, 2.00 mmol, 2.0 eq.), toluene (7.0 mL) and the catalyst solution (1.20 mL, 0.01 mmol, 1.0 mol% Pd). The vial was then sealed with PTFE-lined plastic cap, and the reaction mixture was stirred at 23 °C for 36 h. The resulting heterogeneous light yellow mixture was diluted with acetonitrile (10.0 mL) and filtered through a short pad of Celite. The filtrate was concentrated in vacuo. The crude product was then purified by flash chromatography on silica gel (petroleum ether:EtOAc 1:1 → EtOAc → EtOAc:MeCN 9:1) to give the title compound **28** as a colorless crystalline solid (0.241 g, 0.959 mmol, 96%).



28

TLC (EtOAc)

R_f = 0.46, visualized by UV lamp (λ = 254 nm) or with $KMnO_4$.

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

δ 6.53 (dd, *J* = 17.5, 10.0 Hz, 1H), 6.06 (dd, *J* = 15.0, 10.5 Hz, 1H), 5.74 (dt, *J* = 15.0, 7.0 Hz, 1H), 5.40 (d, *J* = 17.5 Hz, 1H), 4.06 (d, *J* = 17.0 Hz, 2H), 3.70 (d, *J* = 17.0 Hz, 2H), 2.79 (s, 3H), 2.02 (app q, *J* = 7.0 Hz, 2H), 1.37 (app sext, *J* = 7.5 Hz, 2H), 0.86 (t, *J* = 7.5 Hz, 3H).

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

δ 168.9, 144.4, 137.3, 132.2, 61.4, 47.0, 34.6, 22.2, 13.7.

^{11}B NMR (100 MHz, CD_3CN)

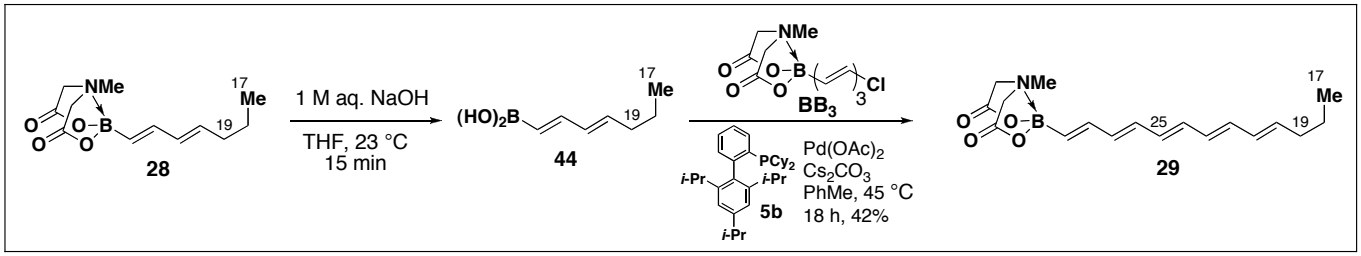
δ 10.8.

HRMS (ESI+)

Calculated for $C_{12}H_{19}BNO_4$ $(M+H)^+$:	252.1407
Found:	252.1404

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

2958, 1762, 1647, 1604, 1458, 1337, 1297, 1196, 1153, 1120, 1084, 1005, 954, 868, 720.

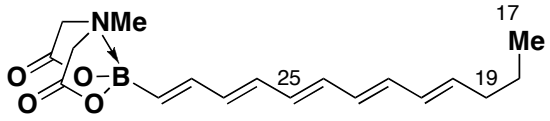


(*E*,*E*,*E*,*E*,*E*)-1,3,5,7,9-decapentenyl-(10-propyl) boronate ester (29)

*MIDA boronate **28** was converted to (E,E)-1,3-heptadienyl boronic acid **44** via the following procedure:* To a stirred mixture of **28** (25.6 mg, 0.102 mmol, 1.0 eq.) in THF (1.0 mL) at 23 °C was added 1N NaOH (aq.) (0.306 mL, 0.306 mmol, 3.0 eq.) *via* syringe. The reaction mixture was stirred at 23 °C for 15 min. The resulting mixture was treated with 1.0 N phosphate buffer solution (pH 7, 0.5 mL) and diluted with Et_2O (1.0 mL). The organic layer was separated and aqueous layer was extracted with THF:Et_2O 1:1 (3 × 1.50 mL). The combined organic layers were dried over anhydrous magnesium sulfate. After filtration, the resulting colorless solution was concentrated to ~ 0.50 mL volume of THF in vacuo. THF (5.0 mL) was added and concentrated again to ~ 0.25 mL volume of THF in vacuo. The isolated yield of boronic acid **44** was assumed to be 90% based on **28**, and a 0.1836 N solution of boronic acid **44** in THF (0.0918 mmol/0.50 mL of THF) was prepared using a 1.0 mL (*v*/*v*) volumetric vial. This solution was immediately used in the next reaction without further purification. TLC (EtOAc) R_f = 0.88, visualized by UV lamp (λ = 254 nm) *or* with $KMnO_4$.

A solution of the catalyst was prepared as follows: A 20 mL Wheaton vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (5.60 mg, 0.025 mmol, 1.0 eq.) and 2-dicyclohexylphosphino-2'.4',6'-tri-*iso*-propyl-1,1'-biphenyl (**5b**) (24.5 mg, 0.050 mmol, 2.0 eq.). Toluene (3.0 mL) was added and the vial was sealed with a PTFE-lined plastic cap. The resulting mixture was stirred at 23 °C for 1 h to yield a reddish Pd/**5b** catalyst solution (0.00833 N Pd in toluene).

This catalyst solution was then utilized in the following procedure: A 10 mL Wheaton vial equipped with a magnetic stir bar was charged with $\mathbf{BB_3}$ (16.5 mg, 0.0612 mmol, 1.0 eq.), Cs_2CO_3 (40.0 mg, 0.1224 mmol, 2.0 eq.), the 0.1836 N boronic acid **44** in THF solution (0.0918 mmol, 0.50 mL), and the catalyst solution (0.110 mL, 1.5 mol% Pd). Toluene (1.64 mL) was then added and the vial was sealed with a PTFE-lined plastic cap and stirred for 18 h at 45 °C. The resulting deep orange mixture was diluted with EtOAc (5.0 mL) and filtered through a short pad of Florisil®. The filtrate was concentrated in vacuo to provide an orange solid. The crude product was purified by flash chromatography on Florisil® (petroleum ether:EtOAc 1:1 → EtOAc → EtOAc:MeCN 9:1) to give the title compound **29** as a light yellow solid (8.40 mg, 0.0255 mmol, 42%).



29

TLC (EtOAc)

R_f = 0.48, visualized by UV lamp (λ = 365 nm) *or* with $KMnO_4$

^{1}H NMR (400 MHz, CD_3CN)

δ 6.60 (dd, *J* = 17.2, 9.6 Hz, 1H), 6.39-6.17 (m, 6H), 6.12 (ddt, *J* = 15.2, 10.4, 1.6 Hz, 1H), 5.77 (dt, *J* = 15.2, 7.2 Hz, 1H), 5.63 (d, *J* = 17.2 Hz, 1H), 3.93 (d, *J* = 16.8 Hz, 2H), 3.77 (d, *J* = 16.8 Hz, 2H), 2.74 (s, 3H), 2.07 (app q, *J* = 7.2 Hz, 2H), 1.40 (app sext, *J* = 7.2 Hz, 2H), 0.88 (t, *J* = 7.2 Hz, 3H).

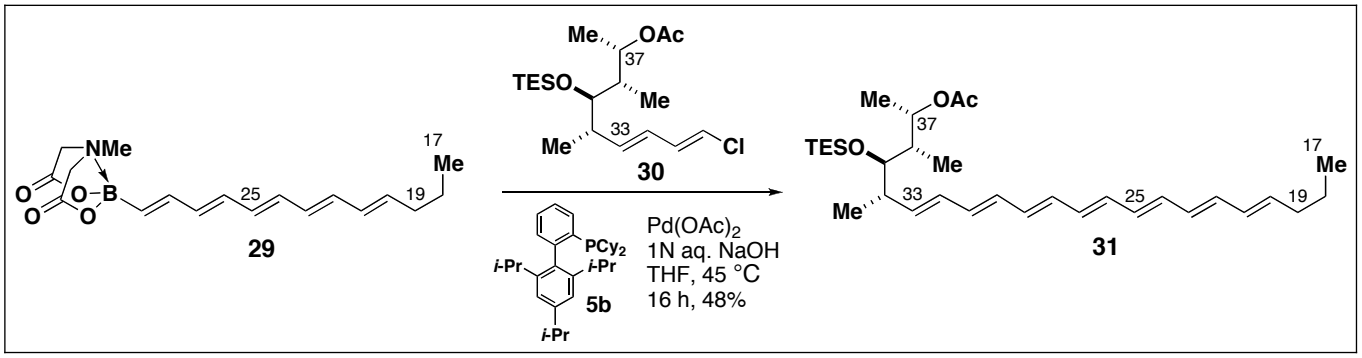
^{13}C NMR (100 MHz, CD_3CN)
δ 169.4, 143.9, 137.0, 135.3, 135.2, 135.0, 133.0, 131.6, 62.3, 47.6, 35.6, 23.1, 13.9.

^{11}B NMR (100 MHz, CD_3CN)
δ 10.4.

HRMS (ESI)

Calcd for $C_{18}H_{25}BNO_4$ $(M+H)^+$:	330.1877
Found:	330.1886

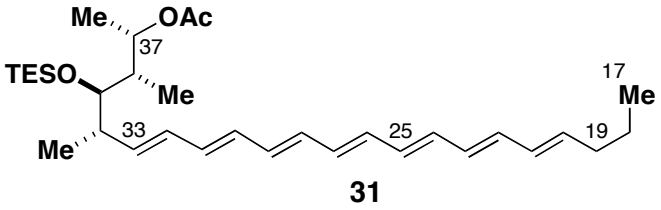
IR (thin film, cm^{-1})
2926, 2359, 1763, 1678, 1463, 1294, 1008, 668.



1/2 of the amphotericin B macrolide (31)

A solution of the catalyst was prepared as follows: An oven-dried Wheaton vial equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (5.60 mg, 0.025 mmol, 1.0 eq.) and 2-dicyclohexylphosphino-2'.4',6'-tri-*iso*-propyl-1,1'-biphenyl (**5b**) (24.5 mg, 0.050 mmol, 2.0 eq.). Toluene (3.0 mL) was added and the vial was sealed with a PTFE-lined plastic cap. The resulting mixture was stirred at 23 °C for 1 h to yield a reddish Pd/**5b** catalyst solution (0.00833 N Pd in toluene).

This catalyst solution was then utilized in the following procedure: An oven-dried Wheaton vial equipped with a magnetic stir bar was charged with **30** (7.0 mg, 0.0187 mmol, 1.0 eq.), **29** (14.0 mg, 0.0421 mmol, 2.25 eq.), the catalyst solution (0.034 mL, 1.5 mol% Pd), and THF (1.50 mL), and the vial was sealed with a PTFE-lined plastic cap. Degassed 1N NaOH (aq.) (0.211 mL, 0.211 mmol, 5.00 eq. based on **29**) was added into the vial *via* syringe. The yellow reaction mixture was stirred for 15 min at 23 °C and then stirred at 45 °C for 16 hr. The resulting heterogeneous deep reddish mixture was diluted with ethyl acetate (5.0 mL) and dried over anhydrous magnesium sulfate. The orange solution was filtered through short pad Florisil® and the filtrate was concentrated in vacuo to provide an orange solid. The crude product was purified by flash chromatography on Florisil® (petroleum ether:EtOAc 60:1) to give the title compound **31** as a yellow solid (4.60 mg, 0.0090 mmol, 48%).



31

TLC (EtOAc: Petroleum ether 1:35)

R_f = 0.40, visualized by UV lamp (λ = 365 nm) *or* with CAM

^{1}H NMR (400 MHz, $CDCl_3$)

δ 6.24-6.18 (m, 10H), 6.11-6.02 (m, 2H), 5.71 (dt, *J* = 14.8, 7.2 Hz, 1H), 5.62 (dd, *J* = 14.8, 8.4 Hz, 1H), 5.03 (qn, *J* = 6.4 Hz, 1H), 3.49 (t, *J* = 5.6 Hz, 1H), 2.38 (app sext, *J* = 6.8 Hz, 1H), 2.06 (app q, *J* = 7.2 Hz, 2H), 1.99 (s, 3H), 1.88 (app sext, *J* = 6.4 Hz, 1H), 1.39 (sext, *J* = 7.2 Hz, 2H), 1.11 (d, *J* = 6.4 Hz, 3H), 0.98 (d, *J* = 6.4 Hz, 3H), 0.94 (t, *J* = 8.0 Hz, 9H), 0.88 (t, *J* = 7.6 Hz, 3H), 0.87 (d, *J* = 7.6 Hz, 3H), 0.59 (q, *J* = 8.0 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$)

δ 170.3, 138.8, 135.8, 133.5, 133.3, 133.2, 133.1, 132.9, 132.7, 132.5, 131.5, 130.9, 130.8, 130.1, 71.6, 42.3, 40.5, 35.0, 29.7, 22.5, 21.4, 16.4, 15.7, 13.7, 11.2, 7.0, 5.4.

HRMS (ESI)

Calculated for $C_{32}H_{53}O_3Si$ $(M+H)^+$: 513.3764

Found: 513.3771

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

3011, 2957, 2928, 2875, 1736, 1456, 1372, 1243, 1069, 1006, 950, 840, 739.