Enantiocontrolled Synthesis of (+)-Boronolide

Toshio Honda,* Satomi Horiuchi, Hirotake Mizutani, and Kazuo Kanai

Institute of Medicinal Chemistry, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142, Japan

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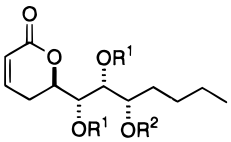
(+)-Boronolide **1**, a δ-lactonic polyacetoxy natural product isolated from the bark and branches of *Tetradenia fruticosa* and from the leaves of *Tetradenia barberae*, has been stereoselectively synthesized, the key steps being the chemoselective Sharpless asymmetric dihydroxylation of (*E*)-1-(*tert*-butyldimethylsiloxy)-7-dodecen-5-yne (**6**), Lindlar reduction of the triple bond of diacetate **9**, and further diastereoselective dihydroxylation of the resulting *cis*-olefin **5**.

δ-Lactonic compounds possessing polyhydroxy or polyacetoxy side chains have attracted increasing attention due to their biological activity. Examples of such compounds include boronolide **1** and its deacetylated **2** and dideacetylated derivatives **3**. (+)-Boronolide **1**, a polyacetoxy natural product, has been isolated from the bark and branches of *Tetradenia fruticosa*[1] and from the leaves of *Tetradenia barberae*,[2] which have been used as a local folk medicine in Madagascar and southern Africa.[3] Deacetylated and dideacetylated derivatives have been obtained from *Tetradenia riparia*, a central-Africa species widely used as a tribial medicine. The extracts of the root of these plants were employed typically by the Zulu as an emetic, while an infusion of the leaf has been reported to be effective against malaria. The absolute configuration of **1** has been determined by X-ray analysis[4] and by chemical degradation.[2]

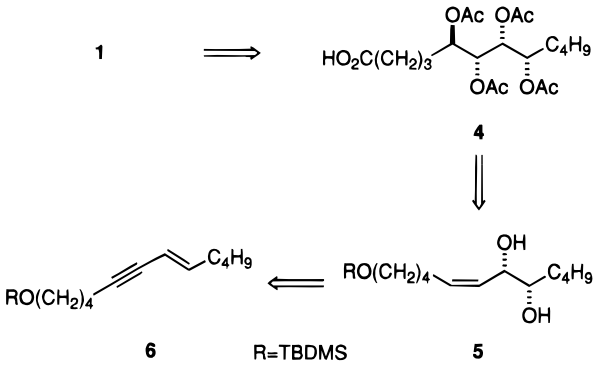
Two total syntheses of boronolide have been reported to date. The first synthesis of **1** has been achieved by Jefford *et al.*[5] in six steps in 4.4% overall yield from the acrolein dimer; however, this synthesis afforded boronolide in racemic form. Recently, a nonracemic synthesis was reported by Nagano *et al.*[6] in seven steps in 5.2% overall yield starting from the D-glucose derivative, which itself required a three-step synthesis.



1 : $R^1 = R^2 = Ac$
2 : $R^1 = R^2 = H$
3 : $R^1 = H$, $R^2 = Ac$

As part of our continuing work on the synthesis of physiologically active natural lactonic compounds, we became interested in developing a general synthetic route capable of providing not only boronolide **1** but also its congeners with desired stereo- and enantioselectivities, since the stereoisomers of **1** would also be of interest from the view point of biological testing. We would like to report herein an asymmetric synthesis of **1** by employing the Sharpless catalytic asymmetric dihydroxylation reaction (AD reaction).[7] The key feature of our synthesis of **1** is based on the enantio- and chemoselective AD reaction of 1,3-enyne **6**,[8] followed by Lindlar reduction of the triple bond and further diastereoselective dihydroxylation of the resulting *cis*-olefin **5** (Scheme 1).

Scheme 1



1,3-Enyne **6**, prepared by palladium-catalyzed cross-coupling reaction of (*E*)-1-iodo-1-hexene[9] with acetylene derivative **7**, was subjected to the AD reaction with AD-mix-α under standard conditions[7,8] to give acetylene diol **8** with 94% ee[10] in 96% yield. To achieve high diastereoselectivity for the second dihydroxylation reaction, we prepared three substrates as follows. Lindlar reduction of the triple bond of **8** gave *cis*-olefin **5** in low yield; however, diacetate **9**, prepared by acetylation of diol **8** with acetic anhydride in pyridine, was easily reduced to the corresponding *cis*-olefin **10** in quantitative yield.

⊗ Abstract published in *Advance ACS Abstracts,* July 1, 1996.

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(10) The ee was determined by HPLC analysis of the bis-benzoyl ester of **6** using a Chiralcel OD column (Daicel Chemical Industries, LTD.).

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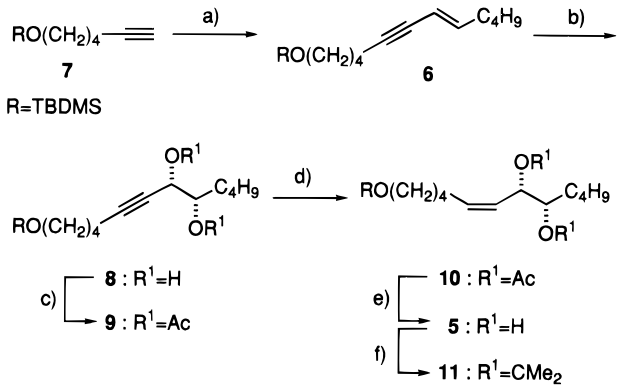
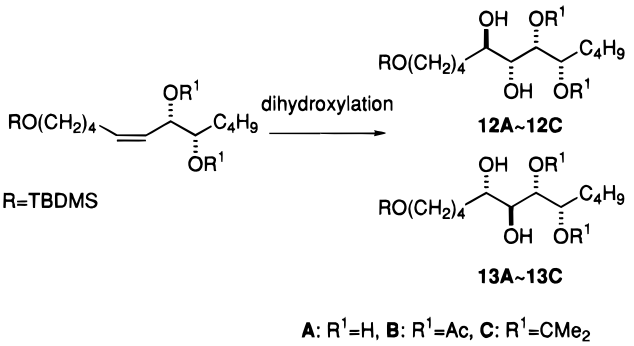
Scheme 2[a]



[a] Reagents and conditions: (a) (*E*)-1-iodo-1-hexene, $(Ph_3P)_2PdCl_2$, CuI, Et_2NH, rt (95%); (b) AD-mix-α, $CH_3SO_2NH_2$, *t*-BuOH−H_2O, 0 °C (96%, 94% ee); (c) Ac_2O, Py, rt (99%); (d) Lindlar catalyst, H_2, AcOEt, rt (quant); (e) K_2CO_3, MeOH, 0 °C to rt (99%); (f) PPTS, CH_2Cl_2, 2,2-dimethoxypropane, 0 °C to rt (86%).

Table 1. Dihydroxylation of (*Z*)-Olefin



entry	substrate	oxidant	product (yield, %)	
1	**5** (R^1 = H)	AD-mix-β[a]	**12A** (53)[c]	**13A** (25)[c]
2	**5** (R^1 = H)	AD-mix-α[a]	**12A** (27)[c]	**13A** (41)[c]
3	**5** (R^1 = H)	OsO_4−NMO[b]	**12A** (46)[c]	**13A** (45)[c]
4	**10** (R^1 = Ac)	OsO_4−NMO[b]	**12B** (46)[c]	**13B** (42)[c]
5	**11** (R^1 = CMe_2)	OsO_4−NMO[b]	**12C** (19)	**13C** (74)

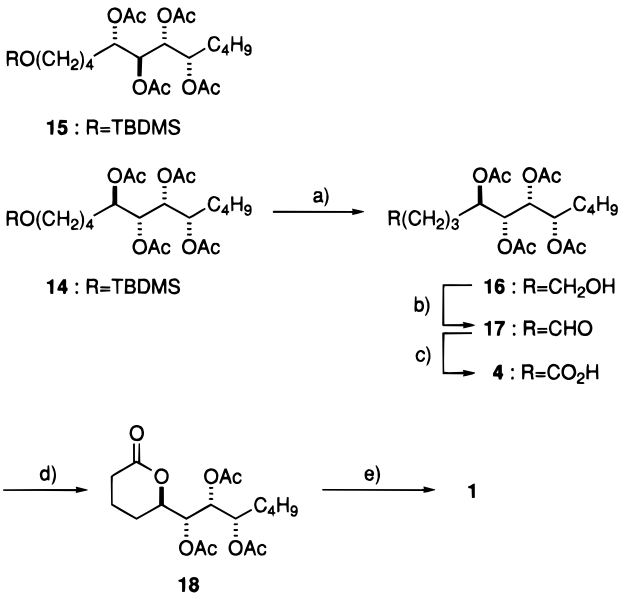
[a] AD-mix reagent (14 g/mmol of substrate) was used in 50% aqueous *t*-BuOH (50 mL/mmol of substrate). [b] OsO_4 (35 mol %), 4-methylmorpholine *N*-oxide (NMO) (3 mol equiv) in 75% aqueous *t*-BuOH (30 mL/mmol of substrate). [c] Yield was that of the corresponding tetraacetate after treatment with acetic anhydride in pyridine.

Diacetate **10** was hydrolyzed with potassium carbonate in MeOH to give diol **5**, and acetonide formation then afforded cyclic acetal **11** (Scheme 2).

These substrates, **5**, **10**, and **11**, were subjected to the second dihydroxylation reaction under the conditions shown in Table 1.

Dihydroxylation of protected diols **10** and **11** using AD-mix reagents was sluggish and gave only trace amounts of the desired products even with a large excess of reagents. Without a chiral ligand (Table 1, entries 4 and 5), the reactions proceeded smoothly to afford diols with different diastereoselectivity depending on the substrate used.[11] Dihydroxylation of diacetate **10** gave **12B** and **13B** in a ratio of *ca.* 1:1 (Table 1, entry 4); however, cyclic acetal **11** gave undesired isomer **13C** as the major product (Table 1, entry 5). A similar reaction of diol **5** with AD-mix-β under the standard conditions[7,8a,12] was also sluggish, but the starting material was consumed within 24 h when excess reagent was used to give tetrols **12A** and **13A** as an inseparable mixture. After acetylation, column chromatography on silica gel gave the desired product **14** in 53% yield together with **15** in 25% yield (Table 1, entry 1). The use of AD-mix-α showed a converse diastereoselectivity (Table 1, entry 2), and no diastereoselectivity was observed in the absence of chiral ligand in this reaction (Table 1, entry 3). Although the absolute stereochemistries of the acetoxylated carbons in compound **14** could not be determined at this stage, a 5*R*,6*R*,7*R*,8*S* configuration was assumed on the basis of the empirical rule[7] and was unambiguously determined by conversion of **14** into the natural product, (+)-boronolide, as shown in Scheme 3.

Scheme 3[a]



[a] Reagents and conditions: (a) AcOH−H_2O−THF (3:1:1), rt (97%); (b) PCC, AcONa, rt (76%); (c) $NaClO_2$, 2-methyl-2-butene, *t*-BuOH−H_2O, rt (95%); (d) NaOMe, MeOH, rt, then 2N HCl; *p*-TsOH, benzene−THF, reflux; Ac_2O, Py, rt (79%); (e) $[PhSe(O)]_2O$, chlorobenzene, reflux (63%).

Hydrolysis of the TBDMS group of **14** with aqueous acetic acid gave alcohol **16**, which on sequential oxidation with PCC and sodium chlorite yielded acid **4**. Methanolysis of the acetyl groups in **4** with sodium methoxide, followed by neutralization with 2N hydrochloric acid gave a tetrol−acid, which, without purification, was treated with *p*-toluenesulfonic acid in benzene−THF to provide a trihydroxy lactone. Finally, acetylation with acetic anhydride in pyridine furnished triacetate **18**, $[\alpha]^{25}_D$ −19.5 (*c* 0.36, EtOH) [lit.[6] $[\alpha]^{24}_D$ −19.3 (*c* 0.55, EtOH); lit.[1] $[\alpha]_D$ −10 (EtOH)], in 79% yield. Following the reported procedure,[5] lactone **18** was dehydrogenated with benzeneseleninic anhydride to give (+)-boronolide **1**, mp 89.5−90.5 °C (lit.[1] mp 90 °C; lit.[2] mp 89−90 °C; lit.[6] mp 89.4−90.5 °C), $[\alpha]^{25}_D$ +25.1 (*c* 0.2, EtOH) [lit.[1] $[\alpha]_D$ +25 (EtOH); lit.[2] $[\alpha]^{26}_D$ +28 (*c* 0.08, EtOH); lit.[6] $[\alpha]_D$ +25.7 (*c* 0.54, EtOH)], in 63% yield.

In summary, we have presented a concise enantioselective synthesis of (+)-boronolide **1**, in high ee (essentially enantiomerically pure) and chemical yield (11 steps in 16.5% overall yield), by means of the Sharpless catalytic asymmetric dihydroxylation reaction. This strategy should also be applicable to the synthesis of other stereoisomers of boronolide **1**.

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Experimental Section

General Procedures. Melting points are uncorrected. IR spectra were recorded in $CHCl_3$. ^1H and ^{13}C NMR spectra were obtained for solutions in $CDCl_3$ using TMS as internal standard.

(*E*)-1-(*tert*-Butyldimethylsiloxy)-7-dodecen-5-yne (6). To a stirred solution of (*E*)-1-iodo-1-hexene (6 g, 28.6 mmol), bis(triphenylphosphine)palladium(II) dichloride (771 mg, 1.1 mmol), and copper(I) iodide (419 mg, 2.2 mmol) in diethylamine (47 mL) was added dropwise a solution of alkyne **7** (4 g, 22.0 mmol) in diethylamine (31 mL), and the resulting mixture was stirred for 20 h at rt under Ar. Evaporation of the solvent gave a residue that was dissolved in EtOAc. The solution was washed with saturated aqueous NH_4Cl solution and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (19:1, v/v) as eluent to afford the coupling product **6** (5.51 g, 95%) as a colorless oil: ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.88 (t, 3H, J = 6.7 Hz, Me), 0.89 (s, 9H, *t*-Bu), 1.3−1.5 (m, 8H, 2-, 3-, 10-, and 11-H_2), 2.09 (m, 2H, 9-H_2), 2.30 (dt, 2H, J = 1.8, 6.7 Hz, 4-H_2), 3.62 (t, 2H, J = 6.1 Hz, 1-H_2), 5.43 (dt, 1H, J = 1.2, 15.8 Hz, 7-H), 6.03 (dt, 1H, J = 6.7, 15.8 Hz, 8-H); HRMS calcd for $C_{14}H_{25}OSi$ (M^+ − 57) 237.1674, found 237.1674. Anal. Calcd for $C_{18}H_{34}OSi$: C, 73.40; H, 11.64. Found: C, 73.12; H, 11.55.

(7*R*,8*S*)-1-(*tert*-Butyldimethylsiloxy)-7,8-dihydroxydodec-5-yne (8). To a stirred solution of AD-mix-α (3.6 g) in *t*-BuOH (6.5 mL) and water (13 mL) were added methanesulfonamide (245 mg, 2.57 mmol) and a solution of olefin **6** (756 mg, 2.57 mmol) in *t*-BuOH (6.5 mL) at 0 °C, and the resulting mixture was stirred for 27 h at the same temperature. While the mixture was being stirred at 0 °C, sodium sulfite (3.86 g) was added and the mixture was allowed to warm to rt and stirred for 1 h. Evaporation of the solvent left an oily product that was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (3:1, v/v) as eluent to afford diol **8** (808 mg, 96%) as a colorless oil: $[\alpha]^{27}_D$ −9.3 (*c* 1.0, $CHCl_3$); IR 3450 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6H, $SiMe_2$), 0.89 (s, 9H, *t*-Bu), 0.91 (t, 3H, J = 6.7 Hz, Me), 1.25−1.67 (m, 10H, 2-, 3-, 9-, 10-, and 11-H_2), 2.25 (dt, 1H, J = 1.8, 6.7 Hz, 4-H), 2.53 and 2.55 (each br s, each 1H, each OH), 3.56−3.63 (m, 1H, 8-H), 3.63 (t, 2H, J = 6.1 Hz, 1-H_2), 4.10−4.13 (m, 1H, 7-H); ^{13}C NMR (270 MHz) δ −5.44, 13.87, 18.16, 18.39, 22.53, 24.89, 25.81, 27.57, 31.77, 32.09, 62.46, 66.28, 75.08, 78.84, 86.55. Anal. Calcd for $C_{18}H_{36}O_3Si \cdot 1/10H_2O$: C, 65.44; H, 11.05. Found: C, 65.27; H, 11.03. The ee of the bisbenzoyl esters of **8** was determined to be 94% by HPLC analysis on a Chiralcel OD column (Daicel Chemical Industries, Ltd.) using hexane−2-propanol (99:1, v/v) as eluent.

(7*R*,8*S*)-1-(*tert*-Butyldimethylsiloxy)-7,8-diacetoxydodec-5-yne (9). To a stirred solution of diol **8** (2.0 g, 6.1 mmol) in pyridine (20 mL) was added acetic anhydride (10 mL), and the resulting mixture was stirred for 20 h at rt. After addition of saturated aqueous $KHSO_4$ solution, the mixture was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (19:1, v/v) as eluent to afford diacetate **9** (2.48 g, 99%) as a colorless oil: $[\alpha]^{25}_D$ +34.5 (*c* 1.09, $CHCl_3$); IR 1735 cm^{-1}; ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.89 (s, 9H, *t*-Bu), 0.90 (t, 3H, J = 6.7 Hz, Me), 1.25−1.82 (m, 10H, 2-, 3-, 9-, 10-, and 11-H_2), 2.07 and 2.08 (each s, each 3H, each Ac), 2.23 (dt, 2H, J = 1.8, 6.7 Hz, 4-H_2), 3.61 (t, 2H, J = 6.1 Hz, 1-H_2), 5.07 (ddd, 1H, J = 4.3, 6.7, 8.6 Hz, 8-H), 5.42 (dt, 1H, J = 1.8, 6.7 Hz, 7-H); HRMS calcd for $C_{18}H_{31}O_5Si$ (M^+ − 57) 355.1941, found 355.1942. Anal. Calcd for $C_{22}H_{40}O_5Si$: C, 64.04; H, 9.77. Found: C, 63.87; H, 9.86.

(7*S*,8*S*)-(*Z*)-1-(*tert*-Butyldimethylsiloxy)-7,8-diacetoxy-5-dodecene (10). A mixture of alkyne **9** (2.48 g, 6.02 mmol) and Pd−$CaCO_3$ (Lindlar catalyst) (500 mg) in EtOAc (25 mL) was stirred for 40 min at rt under an atmospheric pressure of hydrogen. After filtration of the catalyst, the filtrate was concentrated to leave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (19:1, v/v) as eluent to afford *cis*-olefin **10** (2.48g, 99.6%) as a colorless oil: $[\alpha]^{24}_D$ −24.3 (*c* 0.89, $CHCl_3$); IR 1730 cm^{-1}; ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.88 (t, 3H, J = 6.7 Hz, Me), 0.89 (s, 9H, *t*-Bu), 1.18−1.65 (m, 10H, 2-, 3-, 9-, 10-, and 11-H_2), 2.02 and 2.06 (each s, each 3H, each Ac), 2.15−2.30 (m, 2H, 4-H_2), 3.61 (t, 2H, J = 6.1 Hz, 1-H_2), 5.01 (ddd, 1H, J = 4.3, 6.7, 8.6 Hz, 8-H), 5.28 (ddt, 1H, J = 1.2, 8.6, 10.1 Hz, 6-H), 5.59−5.70 (m, 2H, 5- and 7-H); ^{13}C NMR (500 MHz) −5.32, 13.87, 18.31, 20.93, 21.02, 22.43, 25.63, 25.94, 27.24, 27.87, 30.03, 32.43, 62.92, 70.54, 74.19, 123.88, 136.69, 169.87, 170.49; HRMS calcd for $C_{18}H_{33}O_5Si$ (M^+ − 57) 357.2095, found 357.2094. Anal. Calcd for $C_{22}H_{42}O_5Si$: C, 63.73; H, 10.21. Found: C, 63.51; H, 10.21.

(7*S*,8*S*)-(*Z*)-1-(*tert*-Butyldimethylsiloxy)-7,8-dihydroxy-5-dodecene (5). To a stirred solution of diacetate **10** (130 mg, 0.31 mmol) in MeOH (3 mL) was added potassium carbonate (130 mg, 0.94 mmol) at 0 °C, and the resulting mixture was stirred for 1 h at rt. After addition of saturated aqueous NH_4Cl solution, the organic solvent was evaporated to leave an oily product that was extracted with EtOAc. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (3:1, v/v) as eluent to afford diol **5** (103 mg, 99%) as a colorless oil: $[\alpha]^{26}_D$ +2.3 (*c* 1.08, $CHCl_3$); IR 3440 and 3580 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6H, $SiMe_2$), 0.89 (s, 9H, *t*-Bu), 0.90 (t, 3H, J = 6.7 Hz, Me), 1.25−1.60 (m, 10H, 2-, 3-, 9-, 10-, and 11-H_2), 2.04−2.25 (m, 2H, 4-H_2), 2.43 and 2.61 (each br s, each 1H, each OH), 3.42 (br s, 1H, 8-H), 3.61 (t, 2H, J = 6.1 Hz, 1-H_2), 4.19 (t, 1H, J = 8.6 Hz, 7-H), 5.38 (ddt, 1H, J = 1.2, 8.6, 11.0 Hz, 6-H), 5.61 (dt, 1H, J = 6.7, 11.0 Hz, 5-H); ^{13}C NMR (270 MHz) −5.24, −5.20, 14.08, 18.42, 22.76, 25.89, 26.02, 27.85, 27.94, 32.43, 32.52, 63.06, 71.15, 75.09, 128.86, 134.82. Anal. Calcd for $C_{18}H_{38}O_3Si$: C, 65.40; H, 11.59. Found: C, 65.08; H, 11.25.

(7*S*,8*S*)-(*Z*)-1-(*tert*-Butyldimethylsiloxy)-7,8-*O*-(isopropylidenedioxy)-5-dodecene (11). To a stirred solution of diol **5** (250 mg, 0.76 mmol) in CH_2Cl_2 (3 mL) were added 2,2-dimethoxypropane (0.47 mL, 3.8 mmol) and PPTS (0.15 mmol), and the resulting mixture was stirred for 5 h at rt under Ar. After addition of saturated aqueous $NaHCO_3$ solution, the mixture was extracted with CH_2Cl_2. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (40:1, v/v) as eluent to afford cyclic acetal **11** (241 mg, 86%) as a colorless oil: $[\alpha]^{24}_D$ −1.16 (*c* 0.74, $CHCl_3$); ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.88 (t, 3H, J = 6.7 Hz, Me), 0.89 (s, 9H, *t*-Bu), 1.25−1.65 (m, 10H, 2-, 3-, 9-, 10-, and 11-H_2), 1.40 and 1.41 (each s, each 3H, CMe_2), 2.04−2.27 (m, 2H, 4-H_2), 3.61 (t, 2H, J = 6.1 Hz, 1-H_2), 3.60−3.67 (m, 1H, 8-H), 4.35 (t, 1H, J = 8.6 Hz, 7-H), 5.35 (ddt, 1H, J = 1.2, 8.6, 11.0 Hz, 6-H), 5.67 (dt, 1H, J = 7.3, 11.0 Hz, 5-H); ^{13}C NMR (270 MHz) −5.20, 14.04, 18.43, 22.88, 26.05, 27.22, 27.42, 27.73, 28.25, 31.51, 32.50, 63.02, 76.80, 81.00, 108.31, 126.70, 136.08; HRMS calcd for $C_{20}H_{39}O_3Si$ (M^+ − 15) 355.2666, found 355.2664. Anal. Calcd for $C_{21}H_{42}O_3Si$: C, 68.05; H, 11.42. Found: C, 68.15; H, 11.63.

General Procedure for Dihydroxylation of *cis*-Olefins 5, 10, and 11 with OsO_4−NMO. To a stirred solution of *cis*-olefin (1 mmol) in *t*-BuOH (3.3 mL/mmol of substrate) and water (7.8 mL/mmol of substrate) were added 4-methylmorpholine *N*-oxide (NMO) and a solution of OsO_4 in *t*-BuOH (5 mg of OsO4 in 1 mL of *t*-BuOH) (0.35 mol equiv), and the resulting solution was stirred for 5 h at rt. After addition of sodium hydrogen sulfate (5 mol equiv), the mixture was further stirred for 30 min at the same temperature. Evaporation of the organic solvent left an oily product that was extracted with EtOAc. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue. In the case of entry 5 (Table 1), the crude product was purified by column chromatography on silica gel using hexane−EtOAc (7:1, v/v) as eluent. The first fraction gave (5*R*,6*R*,7*R*,8*S*)-1-(*tert*-butyldimethylsiloxy)-5,6-dihydroxy-7,8-

O-(isopropylidenedioxy)dodecane (**12C**) as a colorless oil: IR 3550 cm^{-1}; ^1H NMR (270MHz) δ 0.05 (s, 6H, $SiMe_2$), 0.90 (s, 9H, *t*-Bu), 0.91 (t, 3H, J = 6.7 Hz, Me), 1.25−1.8 (m, 12H, 2-, 3-, 4-, 9-, 10-, and 11-H_2), 1.40 and 1.41 (each s, each 3H, CMe_2), 2.27 (br s, 1H, OH), 2.64 (br s, 1H, OH), 3.37 (br s, 1H, 6-H), 3.63 (t, 2H, J = 6.1 Hz, 1-H_2), 3.5−3.7 (m, 1H, 8-H), 3.80 (dd, 1H, J = 1.2, 8.5 Hz, 7-H), 4.11 (ddd, 1H, J = 4.9, 6.7, 8.6 Hz, 5-H); HRMS calcd for $C_{20}H_{41}O_5Si$ (M^+ − 15) 389.2723, found 389.2723. The second fraction gave (5*S*,6*S*,7*R*,8*S*)-1-(*tert*-butyldimethylsiloxy)-5,6-dihydroxy-7,8-*O*-(isopropylidenedioxy)dodecane (**13C**) as a colorless oil: $[\alpha]^{24}_D$ −18.2 (*c* 1.0, $CHCl_3$); IR 3480 cm^{-1}; ^1H NMR (270 MHz) δ 0.05 (s, 6H, $SiMe_2$), 0.89 (t, 3H, J = 6.7 Hz, Me), 0.90 (s, 9H, *t*-Bu), 1.25−1.85 (m, 12H, 2-, 3-, 4-, 9-, 10-, and 11-H_2), 1.38 and 1.40 (each s, each 3H, CMe_2), 2.22 (br d, 1H, J = 4.3 Hz, OH), 2.44 (br s, 1H, OH), 3.55−3.67 (m, 3H, 6-, 7-, and 8-H), 3.72 (t, 2H, J = 6.7 Hz, 1-H_2), 4.03 (ddd, 1H, J = 3.1, 7.3, 8.5 Hz, 5-H); HRMS calcd for $C_{20}H_{41}O_5Si$ (M^+ − 15) 389.2723, found 389.2723. In the cases of entries 3 and 4 (Table 1), the crude product was treated with acetic anhydride (1.5 mL/mmol of substrate) in pyridine (3 mL/mmol of substrate) for 10 h at rt. After addition of saturated aqueous $KHSO_4$ solution, the mixture was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (8:1, v/v) as eluent. The first fraction gave (5*S*,6*S*,7*R*,8*S*)-1-(*tert*-butyldimethylsiloxy)-5,6,7,8-tetraacetoxydodecane (**15**) as a colorless oil: $[\alpha]^{26}_D$ −30.6 (*c* 0.99, $CHCl_3$); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.88 (t, 3H, J = 6.7 Hz, Me), 0.89 (s, 9H, *t*-Bu), 1.18−1.72 (m, 12H, 2-, 3-, 4-, 9-, 10-, and 11-H_2), 2.02, 2.03, 2.04, and 2.16 (each s, each 3H, each Ac), 3.59 (t, 2H, J = 6.1 Hz, 1-H_2), 4.89 and 5.12 (each br t, each 1H, J = 6.7 Hz, 5- and 8-H), 5.19 (br s, 2H, 6- and 7-H); ^{13}C NMR (500 MHz) −5.36, 13.82, 18.26, 20.70, 20.78, 20.86, 21.82, 22.42, 25.89, 27.24, 28.01, 30.39, 32.33, 62.73, 70.07, 70.58, 70.76, 72.34, 169.74, 170.06, 170.49, 170.53; HRMS calcd for $C_{22}H_{39}O_9Si$ (M^+ − 57) 475.2363, found 475.2363. Anal. Calcd for $C_{26}H_{48}O_9Si$: C, 58.62; H, 9.08. Found: C, 58.51; H, 9.22. The second fraction gave (5*R*,6*R*,7*R*,8*S*)-1-(*tert*-butyldimethylsiloxy)-5,6,7,8-tetraacetoxydodecane (**14**) as a colorless oil: $[\alpha]^{26}_D$ +7.0 (*c* 0.99, $CHCl_3$); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.04 (s, 6H, $SiMe_2$), 0.88 (t, 3H, J = 6.7 Hz, Me), 0.89 (s, 9H, *t*-Bu), 1.14−1.76 (m, 12H, 2-, 3-, 4-, 9-, 10-, and 11-H_2), 2.00, 2.06, 2.09, and 2.10 (each s, each 3H, each Ac), 3.59 (t, 2H, J = 6.1 Hz, 1-H_2), 4.91 (ddd, 1H, J = 3.1, 5.5, 9.8 Hz, 5-H), 4.99 (dt, 1H, J = 5.5, 6.1 Hz, 8-H), 5.21 (t, 1H, J = 5.5 Hz, 7-H), 5.29 (t, 1H, J = 5.5 Hz, 6-H); ^{13}C NMR (500 MHz) −5.35, 13.80, 18.29, 20.61, 20.73, 20.80, 20.86, 21.54, 22.33, 25.90, 26.98, 29.17, 30.13, 32.42, 62.67, 70.87, 71.08, 71.42, 71.54, 170.03, 170.24, 170.46; HRMS calcd for $C_{22}H_{39}O_9Si$ (M^+ − 57) 475.2362, found 475.2362. Anal. Calcd for $C_{26}H_{48}O_9Si$: C, 58.62; H, 9.08. Found: C, 58.52; H, 9.23.

Genaral Procedure for Dihydroxylation of *cis*-Olefin (5) with AD-mix Reagent. To a stirred solution of AD-mix reagent (14 g/mmol of substrate) in 50% aqueous *t*-BuOH (50 mL/mmol of substrate) were added methanesulfonamide (1 mol equiv) and *cis*-olefin **5** (1 mmol) at 0 °C, and the resulting mixture was stirred for 24 h at rt. Sodium sulfite (15 g/mmol of substrate) was added at 0 °C, and the mixture was allowed to warm to rt and stirred for 1 h. Evaporation of the solvent left an oily product that was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that, without purification, was treated with acetic anhydride (1.5 mL/mmol of substrate) in pyridine (3 mL/mmol of substrate) for 10 h at rt. After addition of saturated aqueous $KHSO_4$ solution, the mixture was extracted with EtOAc. The extract was washed with saturated aqueous $NaHCO_3$ solution and brine and dried over Na_2SO_4. Removal of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (8:1, v/v) as eluent to afford tetraacetates **14** and **15**.

(5*R*,6*R*,7*R*,8*S*)-5,6,7,8-Tetraacetoxydodecan-1-ol (16). A solution of ether **14** (252 mg, 0.47 mmol) in AcOH−H_2O−THF (6 mL, 3:1:1) was stirred for 3 h at rt. After addition of saturated aqueous $NaHCO_3$ solution, the mixture was extracted with EtOAc. The extract was washed with brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (1:1, v/v) as eluent to afford alcohol **16** (473 mg, 97%) as a colorless oil: $[\alpha]^{26}_D$ +9.4 (*c* 1.01, $CHCl_3$); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.88 (t, 3H, J = 6.7 Hz, Me), 1.18−1.82 (m, 12H, 2-, 3-, 4-, 9-, 10-, and 11-H_2), 2.02, 2.07, 2.10, and 2.11 (each s, each 3H, each Ac), 3.62 (t, 2H, J = 6.1 Hz, 1-H_2), 4.93 (ddd, 1H, J = 2.4, 5.5, 9.8 Hz, 5-H), 5.00 (dt, 1H, J = 5.5, 6.1 Hz, 8-H), 5.22 (t, 1H, J = 5.5 Hz, 7-H), 5.30 (t, 1H, J = 5.5 Hz, 6-H). Anal. Calcd for $C_{20}H_{34}O_9$: C, 57.40; H, 8.19. Found: C, 57.15; H, 8.30.

(5*R*,6*R*,7*R*,8*S*)-5,6,7,8-Tetraacetoxydodecan-1-al (17). To a stirred suspension of PCC (309 mg, 1.44 mmol), Celite (309 mg), and anhydrous sodium acetate (118 mg, 1.44 mmol) in CH_2Cl_2 (2 mL) was added a solution of alcohol **16** (200 mg, 0.48 mmol) in CH_2Cl_2 (2 mL), and the resulting mixture was stirred for 40 min at rt under Ar. The reaction mixture was diluted with Et_2O (20 mL) and stirred for 20 min. The organic layer was decanted and evaporated to give a residue that was purified by column chromatography on silica gel using hexane−EtOAc (2:1, v/v) as eluent to afford aldehyde **17** (151 mg, 76%) as a colorless oil: $[\alpha]^{26}_D$ +8.6 (*c* 1.1, $CHCl_3$); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.88 (t, 3H, J = 6.7 Hz, Me), 1.18−1.81 (m, 10H, 3-, 4-, 9-, 10-, and 11-H_2), 2.02, 2.07, 2.10, and 2.11 (each s, each 3H, each Ac), 2.45−2.49 (m, 2H, 2-H_2), 4.91 (ddd, 1H, J = 2.4, 5.5, 9.8 Hz, 5-H), 4.99 (dt, 1H, J = 5.5, 6.1 Hz, 8-H), 5.20 (t, 1H, J = 5.5 Hz, 7-H), 5.30 (t, 1H, J = 5.5 Hz, 6-H), 9.76 (t, 1H, J = 1.8 Hz, CHO). Anal. Calcd for $C_{20}H_{32}O_9$: C, 57.68; H, 7.74. Found: C, 57.73; H, 7.94.

(5*R*,6*R*,7*R*,8*S*)-5,6,7,8-Tetraacetoxy-1-dodecanoic Acid (4). To a stirred solution of aldehyde **17** (34 mg, 0.08 mmol), a 2 M THF solution of 2-methyl-2-butene (0.18 mL, 0.37 mmol), and sodium dihydrogen phosphate (13 mg, 0.08 mmol) in *t*-BuOH (3 mL) and water (0.8 mL) was added portionwise sodium chlorite (22 mg, 0.25 mmol), and the resulting mixture was stirred for 1 h at rt. Evaporation of the organic solvent left an oily product, and the aqueous layer was acidified with 2 N HCl solution and extracted with $CHCl_3$. The extract was washed with brine and dried over Na_2SO_4. Removal of the solvent gave a residue that was purified by column chromatography on silica gel using $CHCl_3$−MeOH (96:4, v/v) as eluent to afford acid **4** (33.5 mg, 95%) as a colorless oil: $[\alpha]^{26}_D$ +9.9 (*c* 0.62, $CHCl_3$); IR 1735 and 3500 cm^{-1}; ^1H NMR (270 MHz) δ 0.88 (t, 3H, J = 6.7 Hz, Me), 1.18−1.80 (m, 10H, 3-, 4-, 9-, 10-, and 11-H_2), 2.02, 2.06, 2.09, and 2.11 (each s, each 3H, each Ac), 2.37 (br t, 2H, J = 6.7 Hz, 2-H_2), 4.91 (ddd, 1H, J = 2.4, 5.5, 9.8 Hz, 5-H), 5.00 (dt, 1H, J = 5.5, 6.1 Hz, 8-H), 5.21 (t, 1H, J = 5.5 Hz, 7-H), 5.30 (t, 1H, J = 5.5 Hz, 6-H); ^{13}C NMR (270 MHz) 13.91, 20.72, 20.85, 20.96, 20.99, 21.44, 22.43, 27.08, 29.07, 30.27, 32.25, 62.58, 70.74, 71.20, 71.52, 71.58, 170.17, 170.24, 170.45, 170.69; HRMS calcd for $C_{18}H_{29}O_8$ (M^+ − 43) 373.1862, found 373.1862.

(6*R*)-6-[(1*R*,2*R*,3S)-Triacetoxyheptyl]-5,6-dihydro-2*H*-pyran-2-one (18). To a stirred solution of acid **4** (68 mg, 0.16 mmol) in MeOH (2 mL) was added dropwise a 28% methanolic solution of sodium methoxide (0.3 mL, 1.57 mmol), and the mixture was stirred for 1 h at rt. The mixture was neutralized with 2 N HCl solution and concentrated to leave a residue that was dissolved in benzene (4 mL) and THF (1 mL). To this solution was added *p*-toluenesulfonic acid monohydrate (6 mg, 0.03 mmol), and the mixture was heated at reflux under a Dean−Stark trap for 1 h under Ar. After neutralization with saturated aqueous $NaHCO_3$ solution, the solvent was evaporated to leave a residue that was treated with acetic anhydride (1 mL) in pyridine (1.5 mL) for 10 h at rt. The mixture was diluted with EtOAc and washed with saturated aqueous $KHSO_4$ solution, saturated aqueous $NaHCO_3$ solution, and brine and dried over Na_2SO_4. Evaporation of the solvent gave a residue that was purified by column chromatography on silica gel using hexane−EtOAc (1:1, v/v) as eluent to afford lactone **18** (46 mg, 79%) as a colorless oil: $[\alpha]^{25}_D$ −19.5 (*c* 0.36, EtOH); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.88 (t, 3H, J = 6.7 Hz, Me), 1.20−2.22 (m, 10H, 4-, 5-, 4′-, 5′-, and 6′-H_2), 2.08, 2.10, and 2.13 (each s, each 3H, each Ac), 2.3−2.66 (m, 2H,

3-H_2), 4.42 (ddd, 1H, J = 3.1, 5.5, 11.0 Hz, 6-H), 5.02 (dt, 1H, J = 5.5, 6.1 Hz, 3′-H), 5.20 (dd, 1H, J = 4.3, 5.5 Hz, 2′-H), 5.36 (dd, 1H, J = 4.3, 5.5 Hz, 1′-H); HRMS calcd for $C_{13}H_{21}O_6$ ($M^+ - 99$) 273.1336, found 273.1335, HRMS calcd for $C_{16}H_{25}O_6$ ($M^+ - 59$) 313.1650, found 313.1645, HRMS calcd for $C_{14}H_{19}O_8$ ($M^+ - 57$) 315.1080, found 315.1081. These data were identical with those reported.[5,6]

(+)-Boronolide (1). A solution of lactone **18** (29 mg, 0.08 mmol) and benzeneseleninic anhydride (48mg, 0.09 mmol) in dry chlorobenzene (3 mL) was heated at 130 °C for 74 h. After cooling, the solvent was evaporated to leave a residue that was purified by column chromatography on silica gel using benzene−Et_2O (1:1, v/v) as eluent to afford (+)-boronolide **1** (18 mg, 63%) as colorless needles: $[\alpha]^{25}_D$ +25.1 (*c* 0.2, EtOH); mp 89.5−90.5 °C (benzene−hexane); IR 1740 cm^{-1}; ^1H NMR (270 MHz) δ 0.88 (t, 3H, J = 7.3 Hz, Me), 1.2−1.7 (m, 6H, 4′-, 5′-, and 6′-H_2), 2.08, 2.10, and 2.14 (each s, each 3H, each Ac), 2.26−2.60 (m, 2H, 5-H_2), 4.54 (ddd, 1H, J = 4.3, 5.5, 11.6 Hz, 6-H), 5.02 (dt, 1H, J = 5.5, 6.1 Hz, 3′-H), 5.3−5.37 (m, 2H, 1′- and 2′-H), 6.04 (ddd, 1H, J = 1.2, 2.4, 9.8 Hz, 3-H), 6.87 (ddd, 1H, J = 2.4, 6.1, 9.8 Hz, 4-H); HRMS calcd for $C_{14}H_{17}O_8$ ($M^+ - 57$) 313.0923, found 313.0928. These data were identical with those reported.[2,5,6]

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