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Total Syntheses of (−)- and (+)-Boronolide and Their Plant Growth-Inhibitory Activity

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Optically pure (+)- and (−)-boronolides were stereoselectively synthesized from yeast reductive products which had been obtained by yeast reduction of one common racemic substrate. The lactone structure of boronolide was constructed by Baeyer-Villiger oxidation. The stereochemistry of the yeast reduction products was studied to obtain the stereocenters at 5 positions of the dodecanolides of (+)- and (−)-boronolides. The stereochemistry of the 6 and 7 positions was obtained by AD-mix-*α* or *β* oxidation. The chiral center at the 8 position was constructed by employing (*R*)-(+)- or (*S*)-(−)-2-methyl-CBS-oxazaborolidine reduction or the Mitsunobu reaction. The plant growth-inhibitory activity against *Echinochloa crusgalli* L. of naturally occurring (+)-boronolide was higher than that of the (−)-boronolide.

Key words: boronolide; plant growth-inhibitory activity; 6-substituted 5,6-dihydro-*α*-pyrone; yeast reduction

(+)-Boronolide (**1**),[1,2] which has been synthesized by many research groups,[3–6] comprises 6-substituted 5,6-dihydro-*α*-pyrone bearing a polyacetoxy side chain (Fig. 1). Many compounds bearing a similar structure have been reported and characterized as having wide-ranging biological activity.[7] Although the extracts containing (+)-boronolide has been used as a folk medicine, the biological activity of (+)-boronolide has not been elucidated. Neither the isolation nor synthetic study of (−)-boronolide (**2**) has been reported. Stimulated by the apparent biological activity, total syntheses of (+)- and (−)-boronolides and a biological study were the objectives of this project. This article describes a new synthetic route to (+)-boronolide, the first synthesis of (−)-boronolide, and their plant growth-regulatory activity. The plant growth-regulatory activity of one of the enantiomers of parasorbic acid, psilotin, and cryptocaryalactone (Fig. 1) have been identified in the course of biological research into 6-substituted 5,6-dihydro-*α*-pyron.[7] However, the optical purity of the isolated 6-substituted 5,6-dihydro-*α*-pyrone has not been reported. This present study is the first attempt to clarify the biological activity of both enantiomers by using the optically pure 6-substituted 5,6-dihydro-*α*-pyrone compound.

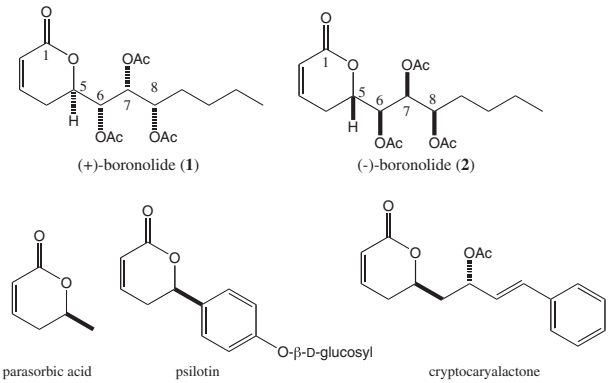

Fig. 1. (+)- and (−)-Boronolides and Plant Growth-Inhibiting 6-Substituted 5,6-Dihydro-*α*-pyrone Compounds.

The retrosynthetic analysis is outlined in Scheme 1. The chiral carbons at the 5-positions of (+)- and (−)-boronolides could respectively be converted from the 1 and 5 positions of yeast reductive products **3** and **4**,[8] which were obtained from a common racemate. The lactone rings could be constructed by Baeyer-Villiger oxidation to cyclopentanone derivatives which could be obtained from **5** and **6**. The stereochemistry of the 6 and 7 positions could respectively be constructed by AD-mix-*β* and *α* oxidations[9] to olefins **5** and **6**. The 8 positions would then be obtained by respective alkylation to aldehydes **7** and **8**. Aldehyde **7** could then be transformed from diol **9** which had previously been obtained from yeast reductive product **3** in our laboratory.[10] The Aldehyde **8** could be obtained from **10** which had also previously been prepared from yeast reductive product **4**.[10] The *α*,*β*-unsaturated olefin of **7** would be introduced by the Wittig reaction to the aldehyde derived from primary alcohol **9**, using $ClPh_3CH_2OCH_3$ followed by elimination. Aldehyde **8** could also be obtained after converting **10** to the enantiomer of **9**.

Results and Discussion

The development of diol **9** is depicted in Scheme 2. After selectively protecting the primary hydroxy group as a trityl ether, the secondary hydroxy group was converted to a triisopropylsilyl ether. Selective cleavage

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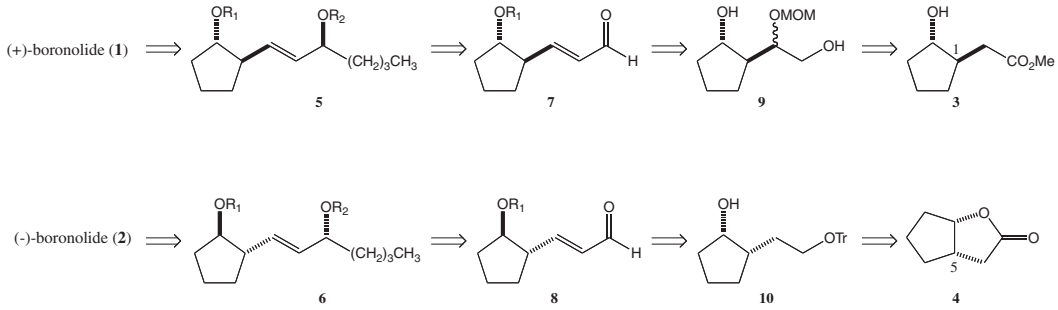
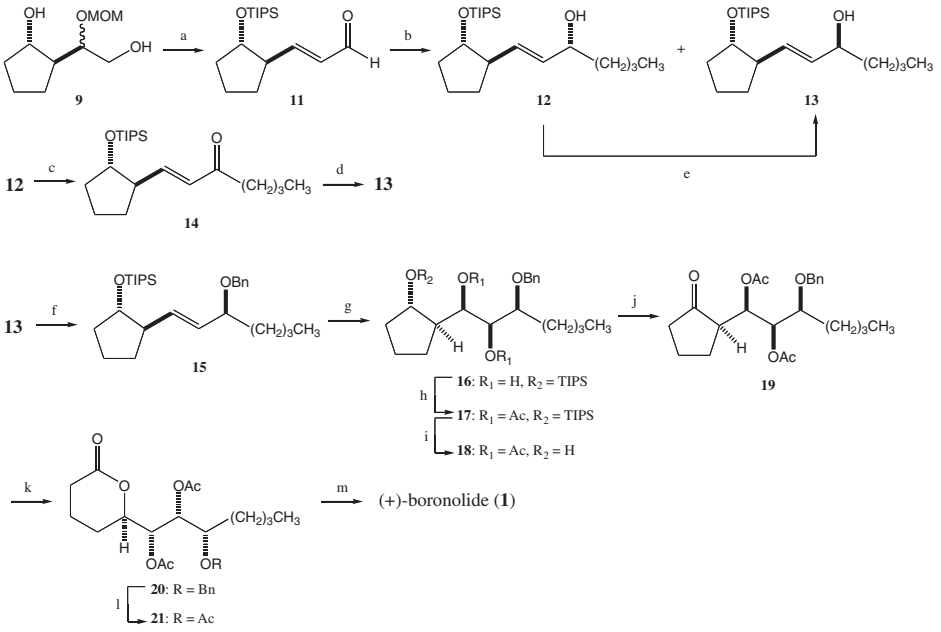


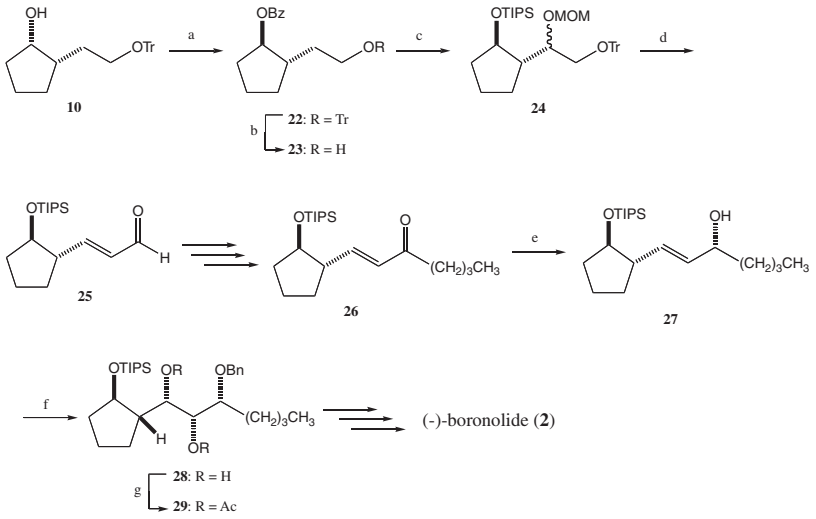
Scheme 1. Retrosynthetic Analysis of (+)- and (−)-Boronolides.



Scheme 2. Synthesis of (+)-Boronolide.

(a) (1) TrCl, pyridine, r.t., 2 h, 73% yield; (2) TIPSOTf, 2,6-lutidine, CH_2Cl_2, r.t., 2 h, 84% yield; (3) HCO_2H, ether, −5 °C, 15 min, 71% yield; (4) PCC, MS 4A, CH_2Cl_2, r.t., 16 h, 88% yield; (5) $ClPh_3PCH_2OCH_3$, KHMDS, −70 °C, 30 min, and then r.t., 1 h, 92% yield; (6) 50% CH_3CO_2H in THF, r.t., 110 h, 99% yield. (b) *n*-BuLi, THF, −70 °C, 1 h, **12**: 63% yield, **13**: 27% yield. (c) PCC, MS 4A, CH_2Cl_2, r.t., 12 h, 91% yield. (d) (*R*)-(+)-2-methyl-CBS-oxazaborolidine, catecholborane, −70 °C, 1 h, 61% yield (recovery of **14**, 30%). (e) (1) Ph_3P, *p*-nitrobenzoic acid, DEAD, THF, r.t., 4 h; (2) 1 M aq. NaOH, EtOH, r.t., 3 h, 60% yield (2 steps). (f) MgO, 2-benzyloxymethylpyridinium triflate, benzotrifluoride, 85 °C, 72 h, 60% yield (recovery of **13**, 38%). (g) AD-mix-β, methanesulfonamide, aq. *tert*-BuOH, r.t., 76 h, 75% yield. (h) Ac_2O, DMAP, pyridine, r.t., 18 h, 91% yield. (i) HF-pyridine, THF, r.t., 22 h, 93% yield. (j) PCC, MS 4A, CH_2Cl_2, r.t., 16 h, 85% yield. (k) MCPBA, Na_2HPO_4–NaH_2PO_4 buffer, $CHCl_3$, r.t., 16 h, 50% yield (recovery of **19**, 42%). (l) (1) H_2, 20% $Pd(OH)_2$/C, EtOAc, ambient temperature, 7 h; (2) pyridine, Ac_2O, DMAP, r.t., 8 h, 96% yield. (m) reference 14.

of the trityl group and subsequent oxidation by pyridinium chlorochromate of the resulting primary hydroxy group gave the corresponding aldehyde. This aldehyde was subjected to the Wittig reaction by using $ClPh_3CH_2OCH_3$ and potassium bis(trimethylsilyl)amide, and then the resulting enol ether was treated with acetic acid to give *trans*-α,β-unsaturated aldehyde **11** as a single isomer. The reaction of this aldehyde **11** with *n*-butyl lithium gave undesired *R*-alcohol **12** (63%) and desired *S*-alcohol **13** (27%). Applying the *R*- and *S*-Mosher reagent to **12** and **13** were ineffective to determine their stereochemistry. However, the stereochemistry of **12** and **13** could be assumed by the (*R*)- and (*S*)-CBS reduction. After converting alcohol **12** to ketone **14** by oxidation, the resulting ketone was exposed to (*R*)-(+)-2-methyl-CBS-oxazaborolidine,[11] giving the same product as **13** as a single stereoisomer in 61% yield. On the other hand, treating ketone **14** with (*S*)-(−)-2-methyl-CBS-oxazaborolidine gave the same product as **12** as a single stereoisomer in 80% yield. Undesired *R*-alcohol **12** was converted to desired *S*-alcohol **13** by employing the Mitsunobu reaction followed by hydrolysis in 60% yield. Benzylation of the secondary hydroxy group of **13** under the basic or Lewis acid condition was troublesome due to decomposition, however, benzyl ether **15** was obtained in the moderate yield under the neutral condition using 2-benzyloxymethylpyridinium triflate.[12] This intermediate was then carried through the stage where the two chiral centers were constructed. The exposure of **15** to AD-mix-β gave desired glycol **16** in 75% yield, together with an undesired glycol (17%). The desilylation of **17** was then attempted after acetylation. The application of HF/pyridine allowed clean deprotection of the triisopropylsilyl group without any by-products, which were caused by treating with tetra-*n*-butylammonium fluoride. Resulting cyclopentanol derivative **18** was oxidized to cyclopentanone derivative **19** by using pyridinium chlorochromate. The oxygen atom of the lactone was introduced by Baeyer-Villiger oxidation, employing



Scheme 3. Synthesis of (−)-Boronolide (**2**).

(a) (1) MsCl, Et_3N, CH_2Cl_2, r.t., 1 h; (2) BzONa, DMSO, 60 °C, 30 h, 50% yield (2 steps). (b) PPTS, MeOH, reflux, 4 h, 75% yield. (c) (1) PCC, MS 4A, CH_2Cl_2, r.t., 16 h, 76% yield; (2) TIPSOTf, DBU, DMAP, CH_2Cl_2, r.t., 3 h, 100% yield; (3) OsO_4, NMO, aq. acetone, *tert*-BuOH, r.t., 20 h; $NaBH_4$, EtOH, r.t., 4 h, 71% yield (2 steps); (4) TrCl, pyridine, r.t., 16 h, 94% yield; (5) MOMCl, *iso*-Pr_2NEt, CH_2Cl_2, r.t., 16 h; (6) 1 M aq. NaOH, EtOH, 60 °C, 12 h; (7) TIPSOTf, 2,6-lutidine, r.t., 2 h, 85% yield (3 steps). (d) see Scheme 2. (e) (*S*)-(−)-2-methyl-CBS-oxazaborolidine, catecholborane, −70 °C, 1 h, 63% yield. (f) (1) MgO, 2-benzyloxymethylpyridinium triflate, benzotrifluoride, 85 °C, 72 h, 65% yield; (2) AD-mix-α, methanesulfonamide, aq. *tert*-BuOH, r.t., 76 h, 81% yield. (g) Ac_2O, DMAP, pyridine, r.t., 18 h, 89% yield.

m-chloroperbenzoic acid, giving lactone **20**. Baeyer-Villiger oxidation did not proceed when the cyclopentanone derivative bearing a triacetoxy side chain was used as a substrate. Benzyl ether was selected as one of the protective groups for this reason. The hydrogenolysis of **20** by using $Pd(OH)_2/C$ under H_2 gas and subsequent acetylation led to known intermediate **21**. Intermediate **21** synthesized in this study exhibited ^1H- and ^{13}C-NMR spectra indistinguishable from those previously reported for **21**.[13] Finally, an α,β-unsaturated double bond was introduced to lactone **21** by reacting with $[PhSe(O)]_2O$[14] to give **1**. The NMR data and optical rotation value of our synthetic **1** were in agreement with those of natural **1**.[5]

As depicted Scheme 3, the synthesis of (−)-boronolide began with converting **10**,[10] which had been prepared from another yeast reductive product, to α,β-unsaturated aldehyde **25**. After converting the secondary hydroxy group of **10** to a mesylate, treating with sodium benzoate afforded a benzoate with inversion of the configuration. The *cis*-cyclopentane isomer of **29** was obtained from **10** without inverting the configuration. Many by-products were observed due to migration of the acetyl group by applying the *cis*-cyclopentane derivative at the stage of desilylation to give a cyclopentanol derivative. Faced with this problem, configuration inversion was achieved at the first stage to give **22**. Cleavage of the trityl ether and subsequent oxidation gave the corresponding aldehyde. This aldehyde was transformed to a glycol by α-hydroxylation and subsequent reduction. Protections of the respective primary and secondary hydroxy groups as a trityl ether and methoxymethyl ether, and subsequent hydrolysis and silylation gave corresponding fully protected compound **24**. After deprotecting the primary hydroxy group, the resulting alcohol was converted to **25** by the same method as that described for the preparation of **11**, and then the (−)-boronolide was obtained from **25** according to the synthetic method described for the (+)-boronolide. (*S*)-(−)-2-Methyl-CBS-oxazaborolidine reduction was applied to **26** to construct the stereochemistry at the 8-position of the (−)-boronolide, giving **27**. AD-mix-α was employed to olefin **27** after benzylation to obtain **28**. The enantiomeric excess of both the (+)- and (−)-boronolides was determined as more than 99% by using a chiral column. The enantiomeric excess of the synthesized (+)-boronolide had not been described in the previous reports.

Table 1. Plant Growth-Inhibitory Activity of (+)- and (−)-Boronolide at 1 mM (growth %)

		(+)-Boronolide	(−)-Boronolide
Lolium multiflorum Lam.:	Shoot	80% ± 12	109% ± 7.66
wase-fudo	Root	52% ± 9.3	78% ± 9.4
Lactuca sativa L.:	Shoot	100% ± 7.3	125% ± 9.63
green-wave	Root	102% ± 8.4	121% ± 8.11

The plant growth-regulatory activity of the (+)- and (−)-boronolides was next evaluated (Table 1). (+)-Boronolide, which is a natural component, depressed the root growth of Italian ryegrass (*Lolium multiflorum* Lam.) at 1 mM. The activity of the unnatural (−)-boronolide was weaker than that of the (+)-boronolide. Weak activity of (+)-boronolide against shoot growth was also observed. Although the plant growth-inhibitory activity of some other 6-substituted 5,6-dihydro-α-pyrones has been reported (Fig. 1), the activity of their enantiomers has not previously been reported. The plant growth inhibitory activity of (+)-boronolide against plant growth was therefore discovered for the first time, and the activity was compared with its enantiomer from this present study. Neither the (+)- nor (−)-boronolide affected the growth of *Lactuca sativa* L.

In summary, a new synthetic route to optically pure (+)-boronolide was developed, and the first synthesis of optically pure (−)-boronolide was achieved by employing two yeast reduction products from one common racemic compound. This enabled us to compare the

biological activity of both enantiomers, revealing the plant growth-inhibitory activity of the (+)-boronolide. This result is valuable information in the field of chemical ecology.

Experimental

General experimental procedures. Optical rotations values were measured with a Horiba SEPA-200 instrument, and IR data were measured with a Horiba FT-720 instrument. NMR data were obtained with a JNM-EX400 spectrometer, and EI and FABMS data were measured with a JMS-MS700V spectrometer. The silica gel used was Wakogel C-300 (Wako, 200–300 mesh). HPLC analyses were performed with Shimadzu LC-6AD and SPD-6AV instruments.

E-*3-[(1*R,2S*)-2-(Triisopropylsilyloxy)cyclopent-1-yl]propenal (**11**).* A solution of diol **9** (8.80 g, 46.3 mmol) and TrCl (12.9 g, 46.3 mmol) in pyridine (14 mL) was stirred at room temperature for 2 h before additions of H_2O and EtOAc. The organic solution was separated, washed with sat. aq. $CuSO_4$, sat. aq. $NaHCO_3$, and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/6) gave hydroxy trityl ether as a mixture of diastereomers (14.6 g, 33.8 mmol, 73%). *Anal.* Found: C, 77.38; H, 7.43%. Calcd. for $C_{28}H_{32}O_4$: C, 77.75; H, 7.46. To an ice-cooled solution of hydroxy trityl ether (14.6 g, 33.8 mmol) and 2,6-lutidine (10.8 mL, 92.4 mmol) in CH_2Cl_2 (100 mL) was added TIPSOTf (9.50 mL, 35.3 mmol). The reaction solution was stirred at room temperature for 2 h before addition of sat. aq. $NaHCO_3$ solution. The organic solution was separated, washed with sat. aq. $CuSO_4$ and sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/6) gave silyloxy trityl ether as a mixture of diastereomers (16.8 g, 28.5 mmol, 84%). *Anal.* Found: C, 75.17; H, 8.82%. Calcd. for $C_{37}H_{52}O_4Si$: C, 75.46; H, 8.90%. To a solution of trityl ether (16.8 g, 28.5 mmol) in ether (830 mL) was added HCO_2H (760 mL) at −5 °C. The reaction solution was stirred at −5 °C for 15 min before additions of $CHCl_3$ and H_2O. The organic solution was separated, washed with sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5%EtOAc/hexane) gave silyl ether as a mixture of diastereomers (7.02 g, 20.3 mmol, 71%). *Anal.* Found: C, 61.98; H, 10.72%. Calcd. for $C_{18}H_{38}O_4Si$: C, 62.38; H, 11.05. A reaction mixture of alcohol (7.02 g, 20.3 mmol), PCC (6.50 g, 30.2 mmol), and MS 4A (3 g) in CH_2Cl_2 (150 mL) was stirred at room temperature for 16 h before addition of ether. The mixture was filtered, and then the filtrate was concentrated. The residue was applied to silica gel column chromatography (10% EtOAc/hexane) to give unstable aldehyde as a mixture of diastereomers (6.14 g, 17.8 mmol, 88%). *Anal.* Found: C, 62.44; H, 10.26%. Calcd. for $C_{18}H_{36}O_4Si$: C, 62.74; H, 10.53. To a suspension of $ClPh_3PCH_2OCH_3$ (18.5 g, 54.0 mmol) in THF (300 mL) was added KHMDS (53.0 mL, 0.5 M in toluene, 26.5 mmol) at −70 °C. After the mixture was stirred at −70 °C for 30 min, aldehyde (6.14 g, 17.8 mmol) in THF (30 mL) was added. The reaction mixture was stirred at −70 °C for 30 min and then at room temperature for 1 h. After addition of hexane, the mixture was filtered. The filtrate was concentrated, and then the residue was applied to silica gel column chromatography (1% EtOAc/hexane and EtOAc/hexane = 1/8) to give isomeric mixture of enol ether (6.08 g, 16.3 mmol, 92%). *Anal.* Found: C, 64.37; H, 10.78%. Calcd. for $C_{20}H_{40}O_4Si$: C, 64.47; H, 10.82. A reaction solution of enol ether (2.43 g, 6.52 mmol) and 50% CH_3CO_2H (140 mL) in THF (140 mL) was stood at room temperature for 110 h before additions of sat. aq. $NaHCO_3$ and $CHCl_3$. The organic solution was separated and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc in hexane) gave aldehyde **11** (1.93 g, 6.51 mmol, 99%) as a colorless oil, $[\alpha]^{20}_D$ +53 (*c* 1.3, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.80–0.95 (3H, m), 1.04 (18H, s), 1.49 (1H, m), 1.63–1.75 (2H, m), 1.85 (1H, m), 1.92 (1H, m), 2.02 (1H, m), 2.73 (1H, m), 4.13 (1H, ddd, J = 5.9, 5.9, 5.9 Hz), 6.13 (1H, dd, J = 15.6, 5.9 Hz), 6.79 (1H, dd, J = 15.6, 8.0 Hz), 9.50 (1H, d, J = 8.0 Hz). ^{13}C-NMR ($CDCl_3$) δ: 12.2, 18.0, 21.8, 29.0, 35.3, 52.3, 78.9, 132.4, 160.7, 194.0. IR ν_{max} ($CHCl_3$): 2962, 2944, 2867, 1685, 1367, 1238, 1215, 1126, 1012 cm^{-1}. HRFABMS m/z $(M+H)^+$: calcd. for $C_{17}H_{33}O_2Si$, 297.2250; found, 297.2252.

*(1*R,2S*)-2-(2-Trityloxyeth-1-yl)cyclopentyl benzoate (**22**).* To an ice-cooled solution of alcohol **10** (20.2 g, 54.2 mmol) and Et_3N (8.30 mL, 59.5 mmol) in CH_2Cl_2 (20 mL) was added MsCl (4.60 mL, 59.4 mmol). The reaction mixture was stirred at room temperature for 1 h before addition of H_2O. The organic solution was separated, and dried (Na_2SO_4). After concentration of the solvent, the residue was dissolved in DMSO (400 mL). To this solution was added BzONa (39.2 g, 272 mmol), and then the reaction mixture was stirred at 60 °C for 30 h before additions of H_2O and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc in hexane) gave benzoate **22** (12.9 g, 27.1 mmol, 50%, 2 steps) as a colorless oil, $[\alpha]^{20}_D$ −31 (*c* 0.6, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.20 (1H, m), 1.56 (1H, m), 1.62–1.77 (3H, m), 1.84–1.94 (2H, m), 2.05 (1H, m), 2.22 (1H, m), 3.07–3.18 (2H, m), 4.98 (1H, m), 7.16–7.27 (11H, m), 7.40–7.43 (6H, m), 7.54 (1H, m), 7.99 (2H, d, J = 8.8 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.6, 30.1, 31.8, 33.8, 42.5, 62.4, 82.0, 86.5, 126.8, 127.7, 128.2, 128.6, 129.5, 130.7, 132.7, 144.4, 166.3; IR ν_{max} ($CHCl_3$): 2960, 1709 cm^{-1}. *Anal.* Found: C, 83.06; H, 6.85%. Calcd. for $C_{33}H_{32}O_3$: C, 83.16; H, 6.77%.

*(1*R,2S*)-2-(2-Hydroxyeth-1-yl)cyclopentyl benzoate (**23**).* A reaction solution of trityl ether **22** (23.8 g, 49.9 mmol) and PPTS (17 mg, 0.068 mmol) in MeOH (150 mL) was heated under refluxing for 4 h before addition of a few drops of Et_3N. After concentration, the residue was applied to silica gel column chromatography (EtOAc/hexane = 1/5) to give alcohol **23** (8.76 g, 37.4 mmol, 75%) as a colorless oil, $[\alpha]^{20}_D$ −48 (*c* 0.7, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.28 (1H, m), 1.58 (1H, m), 1.68–1.87 (4H, m), 1.98–2.09 (2H, m), 2.23 (1H, m), 2.43 (1H, br. s), 3.71 (1H, ddd, J = 11.0, 5.5, 5.5 Hz), 3.80 (1H, ddd, J = 11.0, 6.4, 6.4 Hz), 5.11 (1H, ddd, J = 5.9, 3.5, 3.5 Hz), 7.41–7.45 (2H, m), 7.55 (1H, m), 7.98–8.03 (2H, m). ^{13}C-NMR ($CDCl_3$) δ: 22.9, 30.7, 31.6, 36.6, 42.5, 61.5, 81.8, 128.3, 129.5, 130.5, 132.9, 166.8; IR ν_{max} ($CHCl_3$): 3500, 2950, 1709 cm^{-1}. *Anal.* Found: C, 71.80; H, 7.69%. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74%.

E-*3-[(1*S,2R*)-2-(Triisopropylsilyloxy)cyclopent-1-yl]-3-propenal (**25**).* A reaction mixture of alcohol **23** (8.76 g, 37.4 mmol), PCC (9.67 g, 44.9 mmol), and MS 4A (0.60 g) in CH_2Cl_2 (100 mL) was stirred at room temperature for 16 h before addition of ether. After the mixture was filtered, the filtrate was concentrated, and then the residue was applied to silica gel column chromatography (EtOAc/hexane = 1/9) to give unstable aldehyde (6.59 g, 28.4 mmol, 76%) as a colorless oil, $[\alpha]^{20}_D$ −51 (*c* 2.2, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.30 (1H, m), 1.74–1.88 (3H, m), 2.06–2.16 (2H, m), 2.47 (1H, ddd, J = 16.5, 8.9, 1.8 Hz), 2.58 (1H, m), 2.76 (1H, ddd, J = 16.5, 5.1, 1.4 Hz), 5.04 (1H, m), 7.42–7.45 (2H, m), 7.55 (1H, m), 8.01–8.07 (2H, m), 9.79 (1H, dd, J = 1.8, 1.4 Hz). ^{13}C-NMR ($CDCl_3$) δ: 22.5, 30.1, 31.3, 39.8, 47.4, 81.0, 128.2, 129.4, 130.2, 132.8, 166.3, 201.3. A reaction mixture of unstable aldehyde (6.59 g, 28.4 mmol), TIPSOTf (8.40 mL, 31.2 mmol), DBU (9.30 mL, 62.2 mmol), and DMAP (3.10 g, 25.4 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature for 3 h before addition of sat. aq. $NaHCO_3$ solution. The organic solution was separated, washed with sat. aq. $CuSO_4$ solution and sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (1% EtOAc/hexane) gave unstable isomeric mixture of silyl enol ether (11.0 g, 28.4 mmol, 100%). A reaction mixture of silyl enol ether (11.0 g, 28.4 mmol), NMO (4.40 g, 37.6 mmol), and 2% aq. OsO_4 solution in acetone (117 mL), *tert*-BuOH (29 mL), and H_2O (29 mL) was stirred at room temperature for 20 h before addition of sat. aq. $Na_2S_2O_3$ solution. After concentration of the mixture, the residue was dissolved in EtOAc and H_2O. The organic solution was separated and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/2) gave polymer of α-hydroxy aldehyde (6.54 g). To an ice-cooled solution of this polymer (6.54 g) in EtOH (20 mL) was added $NaBH_4$ (1.00 g, 26.4 mmol). The resulting reaction mixture was stirred at room temperature for 4 h before addition of 1 M aq. HCl solution. After neutralization with sat. aq. $NaHCO_3$ solution, the mixture was concentrated. The residue was dissolved in EtOAc and H_2O. The EtOAc solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/2) gave a diastereomeric mixture of glycol (5.03 g,

20.1 mmol, 71%, 2 steps) as a colorless oil. *Anal*. Found: C, 66.91; H, 7.40%. Calcd. for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25%. A reaction solution of glycol (5.03 g, 20.1 mmol) and trityl chloride (6.20 g, 22.2 mmol) in pyridine (20 mL) was stirred at room temperature for 16 h before additions of H_2O and EtOAc. The organic solution was separated, washed with sat. aq. $CuSO_4$ solution, sat. aq. $NaHCO_3$ solution, and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/9) gave a diastereomeric mixture of hydroxy trityl ether (9.26 g, 18.8 mmol, 94%) as a colorless oil. *Anal*. Found: C, 80.53; H, 6.65%. Calcd. for $C_{33}H_{32}O_4$: C, 80.46; H, 6.55%. To a solution of hydroxy trityl ether (9.26 g, 18.8 mmol) and *iso*-Pr_2NEt (27.5 mL, 158 mmol) in CH_2Cl_2 (25 mL) was added MOMCl (6.10 mL, 80.3 mmol). The reaction mixture was stirred at room temperature for 16 h before additions of MeOH and H_2O. The organic solution was separated, washed with 1 M aq. HCl solution and sat. aq. $NaHCO_3$ solution, and dried. Concentration gave crude benzoyloxy MOM ether. A reaction solution of crude benzoate in 1 M aq. NaOH solution (166 mL) and EtOH (470 mL) was stirred at 60 °C for 12 h before addition of $CHCl_3$. The organic solution was separated and dried (Na_2SO_4). Concentration gave crude alcohol. To an ice-cooled solution of crude alcohol and 2,6-lutidine (4.00 mL, 34.2 mmol) in CH_2Cl_2 (25 mL) was added TIPSOTf (5.60 mL, 20.8 mmol). The resulting reaction solution was stirred at room temperature for 2 h before addition of sat. aq. $NaHCO_3$ solution. The organic solution was separated, washed with sat. aq. $CuCO_4$ solution and sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (1% EtOAc/hexane) gave diastereomeric mixture of silyl ether **24** (9.40 g, 16.0 mmol, 85%, 3 steps). This resulting silyl ether **24** was converted to (1*S*,2*R*)-propenal **25** by the same method as that described for the synthesis of (1*R*,2*S*)-propenal **11**. $[\alpha]^{20}_D$ −54 (*c* 0.7, $CHCl_3$).

*(*E*,3*S*)-1-[(1*R*,2*S*)-2-(Triisopropylsilyloxy)cyclopent-1-yl]-1-hepten-3-ol (**13**).* To a solution of *n*-BuLi (15.2 mL, 2.60 M in hexane, 39.5 mmol) in THF (20 mL) was added a solution of aldehyde **11** (3.10 g, 10.5 mmol) in THF (10 mL) at −70 °C. After the reaction solution was stirred at −70 °C for 1 h, sat. aq. NH_4Cl solution and EtOAc were added. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (1% EtOAc in hexane) gave 3*R*-alcohol **12** (2.34 g, 6.60 mmol, 63%, R*f*: 0.28) as a colorless oil and 3*S*-alcohol **13** (1.02 g, 2.88 mmol, 27%, R*f*: 0.20) as a colorless oil. 3*R*-alcohol **12**: $[\alpha]^{20}_D$ +40 (*c* 1.2, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) *δ*: 0.91 (3H, t, *J* = 7.1 Hz), 0.92–1.09 (3H, m), 1.05 (18H, s), 1.20–1.40 (5H, m), 1.47 (1H, m), 1.50–1.61 (3H, m), 1.76 (1H, m), 1.80–1.94 (2H, m), 2.43 (1H, m), 3.99 (1H, ddd, *J* = 5.6, 5.6, 5.6 Hz), 4.03 (1H, ddd, *J* = 6.5, 6.5, 6.5 Hz), 5.48 (1H, dd, *J* = 15.5, 6.8 Hz), 5.58 (1H, dd, *J* = 15.5, 7.4 Hz). ^{13}C-NMR ($CDCl_3$) *δ*: 12.2, 14.0, 18.0, 18.1, 21.7, 22.6, 27.7, 29.5, 34.9, 36.9, 51.4, 73.1, 79.3, 132.7, 134.0. *Anal*. Found: C, 70.81; H, 11.82%. Calcd. for $C_{21}H_{42}O_2Si$: C, 71.12; H, 11.94%. 3*S*-alcohol **13**: $[\alpha]^{20}_D$ +35 (*c* 1.2, $CHCl_3$); ^{1}H-NMR ($CDCl_3$) *δ*: 0.90 (3H, t, *J* = 7.1 Hz), 0.97–1.08 (21H, m), 1.21–1.39 (5H, m), 1.40–1.50 (2H, m), 1.50–1.60 (2H, m), 1.74 (1H, m), 1.84 (1H, m), 1.89 (1H, m), 2.43 (1H, m), 3.98 (1H, ddd, *J* = 5.5, 5.5, 5.5 Hz), 4.03 (1H, ddd, *J* = 6.4, 6.4, 6.4 Hz), 5.45–5.61 (2H, m). ^{13}C-NMR ($CDCl_3$) *δ*: 12.3, 14.0, 18.0, 18.1, 21.9, 22.7, 27.6, 29.7, 35.1, 37.0, 51.6, 73.2, 79.4, 132.8, 134.3. IR ν_{max}($CHCl_3$) 3610, 2947, 1651, 1056 cm^{-1}. EIMS *m*/*z* (%) 354 (M^+, 6), 337 (100). *Anal*. Found: C, 70.77%; H, 11.92%. Calcd. for $C_{21}H_{42}O_2Si$: C, 71.12%; H, 11.94%. ***27***: $[\alpha]^{20}_D$ −33 (*c* 1.2, $CHCl_3$).

E*-1-[(1*R*,2*S*)-2-(Triisopropylsilyloxy)cyclopent-1-yl]-1-hepten-3-one (**14**).* A reaction mixture of 3*R*-alcohol **12** (0.12 g, 0.34 mmol), PCC (88 mg, 0.41 mmol), and MS 4A (0.5 g) in CH_2Cl_2 (20 mL) was stirred at room temperature for 12 h before addition of ether. After the mixture was filtered, the filtrate was concentrated. The residue was applied to silica gel column chromatography (5% EtOAc in hexane) to give ketone **14** (0.11 g, 0.31 mmol, 91%) as a colorless oil. $[\alpha]^{20}_D$ +64 (*c* 1.4, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) *δ*: 0.92 (3H, t, *J* = 7.4 Hz), 1.00–1.10 (3H, m), 1.04 (18H, s), 1.33 (2H, m), 1.47 (1H, m), 1.60 (2H, m), 1.60–1.70 (2H, m), 1.80 (1H, m), 1.83–2.00 (2H, m), 2.52 (2H, t, *J* = 7.4 Hz), 2.57 (1H, m), 4.08 (1H, ddd, *J* = 5.9, 5.9, 5.9 Hz), 6.11 (1H, d, *J* = 16.0 Hz), 6.75 (1H, dd, *J* = 16.0, 8.4 Hz). ^{13}C-NMR ($CDCl_3$) *δ*: 12.2, 13.8, 18.0, 21.8, 22.4, 26.4, 29.1, 35.2, 39.9, 51.9, 79.0, 129.8, 149.0, 200.7. HRFABMS *m*/*z* $(M + H)^+$: calcd. for $C_{21}H_{41}O_2Si$ 353.2876; found, 353.2877. *Ketone **26***: $[\alpha]^{20}_D$ −63 (*c* 1.0, $CHCl_3$).

*Stereoselective reduction of ketone **14**.* To a solution of ketone **14** (0.11 g, 0.31 mmol) in toluene (4 mL) was added a solution of (*R*)-(+)-2-methyl-CBS-oxazaborolidine (0.36 g, 1.30 mmol) in toluene (1 mL) and catecholborane (0.13 mL, 1.22 mmol) in toluene (3 mL) at −70 °C. After the reaction mixture was stirred at −70 °C for 1 h, MeOH was added, and then the mixture was filtered. The filtrate was concentrated. The resulting residue was applied to silica gel column chromatography (1% EtOAc in hexane) to give 3*S*-alcohol **13** (69 mg, 0.19 mmol, 61%). Ketone **14** (33 mg, 0.094 mmol, 30%) was recovered. Alcohol **27** was obtained from **26** by employing (*S*)-(−)-2-methyl-CBS-oxazaborolidine.

*Isomerization of 3*R*-alcohol **12** to 3*S*-alcohol **13**.* A reaction solution of 3*R*-alcohol **12** (0.59 g, 1.66 mmol), Ph_3P (0.88 g, 3.36 mmol), *p*-nitrobenzoic acid (0.56 g, 3.35 mmol), and DEAD (1.53 mL, 40% in toluene, 3.36 mmol) in THF (5 mL) was stirred at room temperature for 4 h before additions of H_2O and EtOAc. The organic solution was separated, washed with sat. aq. $NaHCO_3$ solution and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (hexane/toluene = 3/1) gave *p*-nitrobenzoate (0.53 g). A reaction solution of *p*-nitrobenzoate (0.53 g) in 1 M aq. NaOH solution (25 mL) and EtOH (100 mL) was stirred at room temperature for 3 h before additions of $CHCl_3$ and H_2O. The organic solution was separated and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (3% EtOAc in hexane) gave 3*S*-alcohol **13** (0.35 g, 0.99 mmol, 60%, 2 steps).

*(3*S*)-3-Benzyloxy1-[(1*R*,2*S*)-2-(triisopropylsilyloxy)cyclopent-1-yl]-heptane (**15**).* A reaction mixture of alcohol **13** (3.74 g, 10.5 mmol), vacuum-dried MgO (0.58 g, 14.4 mmol), and 2-benzyloxymethylpyridinium triflate (7.40 g, 21.1 mmol) in benzotrifluoride (22 mL) was stirred at 85 °C for 72 h before filtration with EtOAc. The filtrate was concentrated, and then the residue was applied to silica gel column chromatography (10% EtOAc/hexane) to give benzyl ether **15** (2.80 g, 6.30 mmol, 60%) as a colorless oil together with recovered alcohol **13** (1.43 g, 4.03 mmol, 38%). $[\alpha]^{20}_D$ +11 (*c* 0.6, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) *δ*: 0.88 (3H, t, *J* = 7.2 Hz), 1.00–1.20 (3H, m), 1.05 (18H, s), 1.27–1.34 (3H, m), 1.34–1.50 (3H, m), 1.55–1.70 (3H, m), 1.77 (1H, m), 1.85 (1H, m), 1.95 (1H, m), 2.49 (1H, m), 3.66 (1H, m), 4.01 (1H, m), 4.31 (1H, d, *J* = 12.0 Hz), 4.55 (1H, d, *J* = 12.0 Hz), 5.35 (1H, dd, *J* = 15.6, 8.2 Hz), 5.53 (1H, dd, *J* = 15.6, 7.8 Hz), 7.26 (1H, m), 7.31–7.37 (4H, m). ^{13}C-NMR ($CDCl_3$) *δ*: 12.3, 14.0, 18.10, 18.12, 22.0, 22.7, 27.7, 30.0, 35.2, 35.6, 51.6, 69.7, 79.4, 80.3, 127.3, 127.7, 127.8, 128.3, 128.4, 130.4, 136.5, 139.1. IR ν_{max}($CHCl_3$) 2947, 2337, 1466, 1272, 1095 cm^{-1}. EIMS *m*/*z* (%) 444 (M^+, 7), 309 (100). *Anal*. Found: C, 75.62%; H, 10.68%. Calcd. for $C_{28}H_{48}O_2Si$: C, 75.61%; H, 10.88%. *(3*R*)-1-[(1*S*,2*R*)]-**15***: $[\alpha]^{20}_D$ −11 (*c* 0.3, $CHCl_3$).

*(1*R*,2*S*,3*S*)-3-Benzyloxy-1-[(1*R*,2*S*)-2-(triisopropylsilyloxy)cyclopent-1-yl]-1,2-heptanediol (**16**).* To an ice-cooled suspension of AD-mix-*β* (11.6 g) and methanesulfonamide (0.79 g, 8.31 mmol) in *tert*-BuOH (30 mL) and H_2O (40 mL) was added a solution of alkene **15** (3.67 g, 8.25 mmol) in *tert*-BuOH (10 mL). The resulting reaction mixture was stirred at room temperature for 76 h before additions of sat. aq. $Na_2S_2O_3$ solution and EtOAc. The organic solution was separated, washed with brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc in hexane) gave (1*R*,2*S*)-glycol **16** (2.96 g, 6.18 mmol, R*f*: 0.18, 75%) as a colorless oil and (1*S*,2*R*)-glycol isomer (0.69 g, 1.44 mmol, R*f*: 0.34, 17%) as a colorless oil. (1*R*,2*S*)-glycol **16**: $[\alpha]^{20}_D$ +48 (*c* 0.4, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) *δ*: 0.91 (3H, t, *J* = 6.8 Hz), 0.98–1.10 (3H, m), 1.06 (18H, s), 1.26–1.40 (4H, m), 1.50–1.60 (4H, m), 1.60–1.78 (3H, m), 1.78–1.95 (2H, m), 2.58 (1H, d, *J* = 7.0 Hz), 2.73 (1H, d, *J* = 3.7 Hz), 3.45–3.53 (2H, m), 3.84 (1H, m), 4.22 (1H, m), 4.48 (1H, d, *J* = 11.2 Hz), 4.62 (1H, d, *J* = 11.2 Hz), 7.26–7.36 (5H, m). ^{13}C-NMR ($CDCl_3$) *δ*: 12.5, 14.0, 18.1, 18.2, 21.8, 22.7, 23.0, 27.5, 30.1, 35.2, 51.7, 71.1, 72.1, 74.1, 76.0, 80.2, 127.9, 128.5, 138.0. IR ν_{max}($CHCl_3$) 3740, 2946, 2337, 1519, 1049 cm^{-1}. *Anal*. Found: C, 70.45%; H, 10.71%. Calcd. for $C_{28}H_{50}O_4Si$: C, 70.24%; H, 10.53%. (1*S*,2*R*)-glycol: $[\alpha]^{20}_D$ +50

(*c* 0.6, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.90 (3H, t, $J = 7.0$ Hz), 1.00–1.20 (3H, m), 1.09 (18H, s), 1.20–1.40 (4H, m), 1.45 (1H, m), 1.50–1.65 (3H, m), 1.65–1.90 (3H, m), 1.91 (1H, m), 2.05 (1H, m), 2.59 (1H, d, $J = 9.6$ Hz), 3.31 (1H, m), 3.54 (1H, m), 3.76 (1H, m), 3.82 (1H, d, $J = 9.1$ Hz), 4.22 (1H, m), 4.61 (2H, s), 7.26–7.40 (5H, m). ^{13}C-NMR ($CDCl_3$) δ: 12.6, 14.1, 18.05, 18.14, 20.4, 23.0, 24.7, 27.3, 31.1, 34.3, 49.1, 73.1, 73.2, 73.7, 79.4, 80.3, 127.6, 127.9, 128.4, 138.8. EIMS *m/z* (%) 477 ($M^+ - 1$, 4), 355 (100). *Anal*. Found: C, 70.42; H, 10.62%. Calcd. for $C_{28}H_{50}O_4Si$: C, 70.24; H, 10.53%. *Glycol* ***28***: AD-mix-α was employed to give the desired compound in 81% yield, $[\alpha]^{20}_D$ −48 (*c* 2.5, $CHCl_3$).

*(1*R*,2*R*)-1-[(1*S*)-1-Benzyloxypent-1-yl]-2-[(1*R*,2*S*)-2-(triisopropylsilyloxy)cyclopent-1-yl]ethylene diacetate (**17**).* A reaction solution of glycol **16** (1.48 g, 3.09 mmol) and DMAP (0.20 g, 1.64 mmol) in pyridine (15 mL) and Ac_2O (15 mL) was stirred at room temperature for 18 h before addition of ice. After 6 h at room temperature, EtOAc was added. The organic solution was separated, washed with sat. aq. $NaHCO_3$ solution and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (5% EtOAc in hexane) gave diacetate **17** (1.59 g, 2.82 mmol, 91%) as a colorless oil; $[\alpha]^{20}_D$ +22 (*c* 0.5, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.86 (3H, t, $J = 7.0$ Hz), 0.92–1.12 (3H, m), 1.04 (18H, s), 1.20–1.32 (3H, m), 1.34 (1H, m), 1.54–1.70 (8H, m), 2.02 (3H, s), 2.03 (3H, s), 2.20 (1H, m), 3.45 (1H, m), 3.98 (1H, m), 4.57 (1H, d, $J = 11.8$ Hz), 4.65 (1H, d, $J = 11.8$ Hz), 5.12 (1H, dd, $J = 7.7$, 3.8 Hz), 5.61 (1H, dd, $J = 7.7$, 1.4 Hz), 7.26–7.35 (5H, m). ^{13}C-NMR ($CDCl_3$) δ: 12.4, 14.0, 18.1, 18.2, 20.9, 21.0, 22.4, 22.6, 23.2, 27.8, 29.5, 35.5, 49.5, 71.6, 71.9, 74.2, 76.2, 77.7, 127.5, 127.8, 128.3, 138.2, 170.1, 170.4. IR ν_{max} ($CHCl_3$) 2954, 2337, 1743, 1519, 1319, 1049 cm^{-1}. EIMS *m/z* (%) 563 ($M^+ + 1$, 0.4), 173 (100). *Anal*. Found: C, 68.34; H, 9.74%. Calcd. for $C_{32}H_{54}O_6Si$: C, 68.28; H, 9.67%. *Diaceate-**29***: $[\alpha]^{20}_D$ −22 (*c* 2.9, $CHCl_3$).

*(1*R*,2*R*)-1-[(1*S*)-1-Benzyloxypent-1-yl]-2-[(1*S*,2*S*)-2-hydroxycyclopent-1-yl]ethylene diacetate (**18**).* To a solution of silyl ether **17** (0.52 g, 0.92 mmol) in THF (30 mL) was added HF-pyridine (4.90 mL, 70%, 189 mmol). The resulting reaction mixture was stirred at room temperature for 22 h before additions of sat. aq. $NaHCO_3$ and EtOAc. The organic solution was separated, washed with sat. aq. Cu_2SO_4, sat. aq. $NaHCO_3$ solution, and brine, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/5) gave alcohol **18** (0.35 g, 0.86 mmol, 93%) as a colorless oil, $[\alpha]^{20}_D$ +17 (*c* 1.0, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, $J = 7.0$ Hz), 1.24–1.38 (4H, m), 1.43 (1H, m), 1.50–1.70 (6H, m), 1.80–1.94 (2H, m), 2.06 (3H, s), 2.07 (3H, s), 2.52 (1H, s), 3.47 (1H, m), 3.70 (1H, m), 4.55 (1H, d, $J = 11.5$ Hz), 4.62 (1H, d, $J = 11.5$ Hz), 5.19 (1H, dd, $J = 4.9$, 4.9 Hz), 5.35 (1H, dd, $J = 4.9$, 4.9 Hz), 7.27–7.30 (2H, m), 7.34–7.35 (3H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.0, 20.8, 21.0, 21.2, 22.7, 24.2, 27.4, 29.4, 33.2, 48.8, 72.0, 72.1, 73.9, 74.5, 77.3, 127.8, 128.0, 128.4, 138.0, 170.9, 171.3. IR ν_{max}($CHCl_3$) 3730, 2954, 2337, 1735, 1519, 1241, 1049 cm^{-1}. EIMS *m/z* (%) 407 ($M^+ + 1$, 10), 180 (100). *Anal*. Found: C, 67.96%; H, 8.46%. Calcd. for $C_{23}H_{34}O_6$: C, 67.96%; H, 8.43%. *(1*S*,2*S*)-1-[(1*R*)]-2-[(1*R*,2*R*)]-**18***: $[\alpha]^{20}_D$ −17 (*c* 2.4, $CHCl_3$).

*(1*R*,2*R*)-[(1*S*)-1-Benzyloxypent-1-yl]-2-[(1*R*)-2-oxocyclopent-1-yl]-ethylene diacetate (**19**).* A reaction mixture of alcohol **18** (0.73 g, 1.80 mmol), PCC (0.42 g, 1.95 mmol), and MS 4A (1 g) in CH_2Cl_2 (50 mL) was stirred at room temperature for 16 h before addition of ether and filtration. The filtrate was concentrated, and then the residue was applied to silica gel column chromatography (EtOAc/hexane = 1/3) to give ketone **19** (0.62 g, 1.53 mmol, 85%) as a colorless oil, $[\alpha]^{20}_D$ +52 (*c* 0.5, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, $J = 7.0$ Hz), 1.22–1.40 (4H, m), 1.49–1.80 (4H, m), 1.80–2.05 (3H, m), 1.96 (3H, s), 2.05 (3H, s), 2.17–2.32 (2H, m), 3.42 (1H, m), 4.56 (1H, d, $J = 11.7$ Hz), 4.63 (1H, d, $J = 11.7$ Hz), 5.19 (1H, dd, $J = 7.5$, 4.0 Hz), 5.70 (1H, dd, $J = 7.5$, 3.0 Hz), 7.27–7.35 (5H, m). ^{13}C-NMR ($CDCl_3$) δ: 14.0, 20.6, 20.7, 20.9, 22.6, 24.1, 27.8, 29.2, 37.9, 49.7, 69.5, 71.8, 73.3, 127.8, 128.2, 128.5, 137.9, 169.3, 170.4, 216.2. IR ν_{max}($CHCl_3$) 3031, 2962, 2870, 1743, 1241 cm^{-1}. HRFABMS *m/z* ($M + H)^+$: calcd. for $C_{23}H_{33}O_6$, 405.2277; found, 405.2273. *(1*S*,2*S*)-[(1*R*)]-2-[(1*S*)]-**19***: $[\alpha]^{20}_D$ −52 (*c* 2.1, $CHCl_3$).

*(5*R*,6*R*,7*R*,8*S*)-8-Benzyloxy-6,7-diacetoxy-5-dodecanolide (**20**).* A reaction mixture of ketone **19** (0.62 g, 1.53 mmol) and MCPBA (1.51 g, 70%, 6.13 mmol) in $CHCl_3$ (15 mL) and Na_2HPO_4–NaH_2PO_4 buffer (pH 8, 15 mL) was stirred at room temperature for 16 h. After addition of sat. aq. $Na_2S_2O_3$ solution, the organic solution was separated, washed with sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/2) gave lactone **20** (0.32 g, 0.76 mmol, 50%) as a colorless oil. Ketone **19** (0.26 g, 0.64 mmol, 42%) was recovered. $[\alpha]^{20}_D$ +9 (*c* 0.9, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (3H, t, $J = 7.1$ Hz), 1.22–1.32 (3H, m), 1.39 (1H, m), 1.56–1.79 (5H, m), 1.85 (1H, m), 2.062 (3H, s), 2.064 (3H, s), 2.38 (1H, ddd, $J = 18.1$, 9.3, 7.1 Hz), 2.50 (1H, ddd, $J = 18.1$, 6.0, 6.0 Hz), 3.47 (1H, m), 4.41 (1H, m), 4.56 (1H, d, $J = 11.6$ Hz), 4.61 (1H, d, $J = 11.6$ Hz), 5.28 (1H, dd, $J = 5.6$, 5.6 Hz), 5.39 (1H, dd, $J = 5.6$, 4.5 Hz), 7.26–7.35 (5H, m). ^{13}C-NMR ($CDCl_3$) δ: 13.9, 18.1, 20.8, 20.9, 22.6, 22.9, 27.8, 29.5, 29.6, 70.6, 71.4, 72.4, 77.7, 78.3, 127.9, 128.0, 128.5, 137.9, 169.6, 170.3. IR ν_{max}($CHCl_3$) 2962, 2360, 1735, 1519, 1241, 1049. HRFABMS *m/z* ($M + H)^+$: calcd for $C_{23}H_{33}O_7$, 421.2226; found, 421.2224. *(5*S*,6*S*,7*S*,8*R*)-**20***: $[\alpha]^{20}_D$ −9 (*c* 0.8, $CHCl_3$).

*(5*R*,6*R*,7*R*,8*S*)-6,7,8-Triacetoxy-5-dodecanolide (**21**).* A reaction mixture of benzyl ether (0.32 g, 0.76 mmol) and 20% $Pd(OH)_2/C$ (0.3 g) in EtOAc (20 mL) was stirred under H_2 gas at the ambient temperature for 7 h before filtration. The filtrate was concentrated. A reaction solution of the residue, Ac_2O (0.93 mL, 9.84 mmol), pyridine (1.59 mL, 19.7 mmol), and DMAP (1 mg, 0.0082 mmol) in CH_2Cl_2 (15 mL) was stirred at room temperature for 8 h before addition of H_2O. The organic solution was separated, washed with 1 M aq. HCl solution and sat. aq. $NaHCO_3$ solution, and dried (Na_2SO_4). Concentration followed by silica gel column chromatography (EtOAc/hexane = 1/1) gave triacetate (0.27 g, 0.73 mmol, 96%) as a colorless oil, $[\alpha]^{20}_D$ −25 (*c* 1.0, EtOH), $[\alpha]^{20}_D$ −20 (*c* 1.25, EtOH) in the literature. The NMR data agreed with those in the literature.[13] *(5*S*,6*S*,7*S*,8*R*)-**21**: $[\alpha]^{20}_D$ +25 (*c* 1.0, EtOH).

*(+)-Boronolide (**1**).* Lactone **21** was converted to (+)-boronolide (**1**) by the same method as that described in the literature,[14] $[\alpha]^{20}_D$ +23 (*c* 0.5, EtOH), $[\alpha]^{20}_D$ +26 (*c* 0.7, EtOH) in the literature. The NMR data agreed with those in the literature.[5] ≫99%ee (Chiralpak AD-H, 250 mm × 4.6 mm i.d., 5 μm, *iso*-PrOH/hexane = 5/95, 1 mL/min, 210 nm, t_R 18 min). *(−)-Boronolide (**2**)*: $[\alpha]^{20}_D$ −25 (*c* 0.1, EtOH). ≫99%ee (t_R 23 min).

Evaluation of the plant growth-inhibitory activity. The plant growth-inhibitory activities of (+)- and (−)-boronolides were evaluated by using lettuce (*Lactuca sativa* L.: green-wave (Takii Seed Co., Kyoto, Japan)) and Italian ryegrass (*Lolium multiflorum* Lam.: wasefudo (Takii Seed Co., Kyoto, Japan)). A sheet of filter paper (90 mm or 40 mm in diameter) was placed in a 90 mm or 40 mm Petri dish and wetted with 500 μL or 160 μL of the test sample solution dissolved in acetone at a concentration of 6.0 mM. After drying the filter paper, 3 mL or 1 mL of water was poured into the dish to adjust the concentration to 1.0 mM. Thirty seeds of each plant were then placed on the filter paper, and after the Petri dishes were sealed with Parafilm, they were incubated in the dark at 20 °C. After 3 and 5 d for lettuce and barnyard grass, respectively, the lengths of their roots and shoots were measured with a ruler. The respective root and shoot lengths of the control were *ca.* 3 cm and 1 cm for lettuce, and 4 cm and 3 cm for grass. The experiments were performed in triplicate or more for each sample (n = 3).

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