JOC Note

Stereoselective Synthesis of (+)-Boronolide

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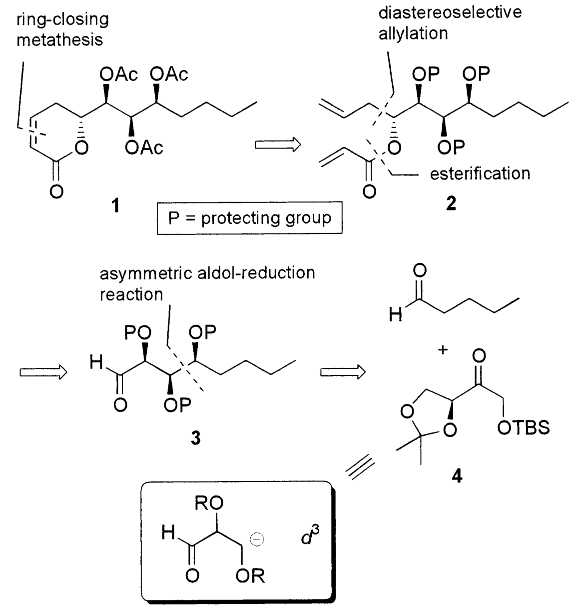
Abstract: The δ-lactone boronolide (+)-**1**, a pharmacologically active, naturally occurring product, has been synthesized in enantiopure form with L-erythrulose as the chiral starting material. The key steps of the synthesis were a highly stereoselective aldol-reduction one-pot sequence, an indium-mediated diastereoselective aldehyde allylation, and a ring-closing metathesis.

Boronolide (+)-**1** was first found in extracts of bark and branches of *Tetradenia fruticosa* Benth.,[1] a shrub belonging to the Lamiaceae family. This shrub grows in Madagascar, where it is named "borona", and has been widely used there for various medicinal purposes. While boronolide was later found again in leaves of *T. barberae*, totally or partially deacetylated derivatives of boronolide have been isolated from *T. riparia*, two additional African *Tetradenia* species used in tribal medicine.[2] Extracts of the roots of these plants were employed by the Zulu as an emetic, while leaf infusions have been reported to be effective against malaria.[2]

Five total syntheses of **1** have been reported in the literature in recent years.[3] One of them used acrolein dimer as the starting material and yielded racemic boronolide,[3a] whereas the remaining ones led to the natural product in enantiopure form. Three of these syntheses made use of precursors from the chiral pool,[3b,d,e] and the other relied upon a Sharpless asymmetric dihydroxylation for the creation of stereogenic centers.[3c] As a part of our current interest in naturally occurring, pharmacologically active δ-lactones,[4] we have performed a total, stereoselective synthesis of boronolide (+)-**1** employing the L-erythrulose derivative **4** (TBS = *tert*-butyldimethylsilyl)[5] as the chiral starting compound.

SCHEME 1



Our retrosynthetic analysis of (+)-**1** is depicted in Scheme 1. The unsaturated lactone moiety was to be built up by means of an olefin ring-closing metathesis (RCM) in acrylate ester **2**, prepared in turn through stereoselective allylation of aldehyde **3** and subsequent acylation with acryloyl chloride (P = protecting group). Aldehyde **3** should be made available through the use of our recently developed boron aldol methodology with erythrulose derivatives.[6] In the proposed synthetic scheme, ketone **4** behaves, as already anticipated,[6a] as a new type of chiral, functionalized d^3 (homoenolate) synthon.[7]

Enolization of **4** with Chx$_2$BCl/Et$_3$N (Chx = cyclohexyl) followed by addition of pentanal generated a boron aldolate intermediate **5**, which was reduced in situ upon treatment with LiBH$_4$.[8] With this one-pot methodology, the all-syn acetonide **6** was obtained as a single stereoisomer in 83% yield (Scheme 2). Compound **6** contains four contiguous stereocenters, three of which possess the absolute configuration present in (+)-**1**.

The oxidative cleavage of the acetonide moiety in **6** requires the protection of the two free hydroxyl functions. Since a TBS group was already present in the vicinal trihydroxyl chain, we decided to protect these hydroxyl functions as the TBS derivatives. However, when the corresponding trisylilated derivative **6** (R = R′ = TBS) was treated with periodic acid hydrate (H$_5$IO$_6$),[9] extensive decomposition of the starting material was observed

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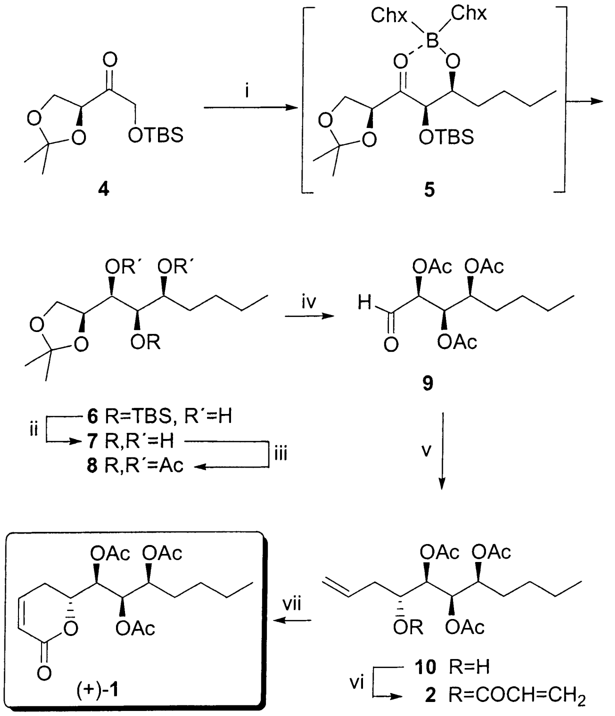
10.1021/jo025813f CCC: $22.00

SCHEME 2[a]



[a] Reagents and conditions: (i) Chx_2BCl, Et_3N, $CH_3(CH_2)_3CHO$, Et_2O, from −78 to 0 °C, 5 h, then $LiBH_4$, 2 h (83%); (ii) TBAF, THF, 15 min (96%); (iii) Ac_2O, Et_3N, cat. DMAP, CH_2Cl_2, rt, 12 h (90%); (iv) H_5IO_6, AcOEt, rt, 1 h (85%); (v) allyl bromide, In powder, THF/H_2O (1:1), rt, 18 h; (vi) acryloyl chloride, Et_3N, cat. DMAP, CH_2Cl_2, rt, 12 h (50% overall of two steps); (vii) $PhCH{=}RuCl_2(Chx_3P)_2$, $Ti(O\textit{i}Pr)_4$, CH_2Cl_2, reflux, 24 h (71%).

under all assayed conditions. Likewise, attempts at hydrolytic cleavage of the acetonide moiety with a range of acid catalysts led only to decomposition or to partial desilylation.[10] In view of this, and with the aim at minimizing the manipulation of protecting groups, we introduced at this stage the required acetate residues (**6** → **7** → **8**) in the hope that they would resist the subsequent reaction conditions. In fact, when compound **8** was treated with H_5IO_6, aldehyde **9** (=**3**, P = Ac, Scheme 1) was obtained in a satisfactory 85% yield after rapid chromatographic purification. The remaining stereocenter was now to be created with its correct configuration through stereoselective allylation of **9** under Felkin−Anh (nonchelation) control.[11] After some experimentation, we found that allylation under Barbier conditions in an aqueous medium was the method of choice. Thus, aldehyde **9** was dissolved in 1:1 THF/H_2O and treated with indium metal and allyl bromide. This provided in 83% yield an inseparable 91:9 mixture of homoallyl alcohol **10**, that expected from a nonchelated transition state, and its epimer (*epi*-**10**) at the newly formed stereogenic carbon. This stereochemical outcome is frequently observed in indium-mediated allylations of O-protected α-hydroxy aldehydes in aqueous media.[12] Acylation of the mixture **10**/*epi*-**10** with acryloyl chloride yielded ester **2**, which was separated at this stage from its diastereomer by crystallization. The absolute configuration of acrylate **2** was secured by means of an X-ray analysis,[13] as well as through its final conversion into boronolide. In the event, RCM of **2** catalyzed by Grubbs ruthenium complex[14] $PhCH{=}RuCl_2(PCy_3)_2$ in the presence of $Ti(O\textit{i}Pr)_4$ yielded boronolide (+)-**1**, identical in physical and spectral data with the natural product.[3a,c] It is worth noting here that a considerable excess of $Ti(O\textit{i}Pr)_4$ (3 equiv) was found necessary to achieve RCM at a reasonable rate. Slow rates in RCM processes where certain donor atoms were present in the vicinity of the reaction center have previously been observed.[15] The phenomenon was attributed to a blockage of the catalytic cycle due to internal complexation of the ruthenium atom by the donor atoms, which would be in the present case the three acetate carbonyls. The Lewis acidic compound $Ti(O\textit{i}Pr)_4$ complexes reversibly with these atoms and prevents the blockage, thus accelerating the reaction.[3d,15]

In summary, we have completed a total, stereoselective synthesis of boronolide that demonstrates the usefulness and applicability of our aldol methodology for the construction of natural molecules containing polyoxygenated chains. Key steps of the synthesis were (a) a highly stereoselective aldol reaction followed by in situ stereoselective reduction of the intermediate boron aldolate, (b) a stereoselective, indium-mediated allylation of a polyfunctionalized aldehyde in an aqueous solvent, and (c) a RCM to create the conjugated lactone moiety. The synthesis has been accomplished with an overall yield of 21% in seven operative steps from L-erythrulose derivative **4**, which behaves here as a functionalized homoenolate synthon. Our synthesis is thus the most efficient route to (+)-**1** reported so far and can be easily adapted to the preparation of analogues of boronolide, as well as of other structurally similar lactones. Efforts in this direction are underway.

Experimental Section

General. NMR spectra were measured at 22 °C. The signals of the deuterated solvent ($CDCl_3$) were taken as the reference. Unambiguous assignments of signals were made with a combination of spin decoupling, DEPT, and HMQC experiments. High-resolution mass spectra were run in all cases by the electron impact mode (EIMS, 70 eV). Samples for IR spectral measurements were prepared as oily films on NaCl plates (oils) or KBr pellets (solids). Optical rotations were measured at 22 °C. Et_2O and THF were freshly distilled under Ar from sodium-benzophe-

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(10) This includes, for example, the following reaction conditions: (i) 80% aq AcOH, 55 °C (acetonide cleavage and partial desilylation; no reaction at room temperature); (ii) PPTS/MeOH, reflux (decomposition); (iii) ethanedithiol, *p*-TsOH, $CHCl_3$, reflux (acetonide cleavage and partial desilylation); (iv) $Zn(NO_3)_2$·hydrate/MeCN, 50 °C; (v) $FeCl_3$·hydrate/CH_2Cl_2, 0 °C; (vi) $CuCl_2$·hydrate/MeOH, reflux (in the last three reaction conditions, acetonide cleavage and selective monodesilylation of the distal TBS group was observed). For pertinent citations, see: Greene, T. W.; Wuts, P. G. M. *Protective Groups in Organic Synthesis*, 3rd ed.; John Wiley and Sons: New York, 1999; pp 207−215.

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none ketyl. Dichloromethane was freshly distilled from CaH$_2$. Tertiary amines were freshly distilled from KOH. Commercially available reagents were used as received. Chx$_2$BCl was generated by hydroboration of cyclohexene with monochloroborane as reported in the literature and used as a neat liquid.[16] Column chromatography (CC) was performed on silica gel Süd-Chemie AG (60−200 μm) with the solvent mixture indicated in each case.

(1*R*,2*R*,3*S*)-2-(*tert*-Butyldimethylsilyloxy)-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]heptane-1,3-diol (6). Chx$_2$BCl (1.2 mL, ca. 5.4 mmol) and Et$_3$N (840 μL, 6 mmol) were dissolved under Ar in anhydrous Et$_2$O (15 mL) at −78 °C. Erythrulose derivative **4**[5] (823 mg, 3 mmol) was dissolved in anhydrous ether (10 mL) and added dropwise via syringe to the reagent solution. After 10 min, the reaction mixture was warmed to 0 °C, stirred for 1 h at this tempperature, and then recooled to −78 °C. After 10 min of stirring, a solution of pentanal (1.6 mL, 15 mmol) in ether (10 mL) was added dropwise. The stirring was continued for 10 min, the reaction mixture was then warmed to 0 °C and further stirred for 5 h. Then, a 2 M solution of LiBH$_4$ in THF (4.5 mL, 9 mmol) was added dropwise, and the reaction mixture was stirred at 0 °C for 2 h. For the workup, phosphate pH 7 buffer solution (20 mL) and MeOH (20 mL) were added at 0 °C, followed by 30% aq H$_2$O$_2$ (10 mL). After stirring for 1 h at room temperature, the mixture was poured onto brine and extracted with Et$_2$O. The organic layer was then dried on anhydrated Na$_2$SO$_4$. Solvent removal in vacuo and column chromatography of the residue on silica gel (hexanes−EtOAc, 9:1) afforded diol **6** (903 mg, 83% yield): $[\alpha]^{22}_{\mathrm{D}}$ −2.1 (*c* 1.5, CHCl$_3$); ^{1}H NMR (400 MHz) δ 4.30 (ddd, 6.7, 6.4, 5.5 Hz, 1H, H-4′), 4.01 (dd, 8.2, 6.4 Hz, 1H, H-5′$_a$), 3.84 (dd, 8.2, 6.7 Hz, 1H, H-5′), 3.67 (m, 1H, H-3), 3.60 (dd, 4.4, 2.2 Hz, 1H, H-2), 3.57 (m, 1H, H-1), 2.50 (br s, 1H, OH), 2.15 (br s, 1H, OH), 1.88 (m, 1H, H-4$_a$), 1.70 (m, 1H, 4$_b$), 1.60−1.20 (br m, 4H, H-5, H-6), 1.42 (s, 3H, acetonide *Me*), 1.35 (s, 3H, acetonide *Me*), 0.91 (s, 9H, *Me*$_3$CSi), 0.90 (t, J = 7 Hz, 3H, H-7), 0.12 (s, 3H, Si*Me*$_2$), 0.10 (s, 3H, Si*Me*$_2$). ^{13}C NMR (100 MHz) δ 109.2 (acetonide *C*), 76.2 (C-4′), 75.5 (C-2), 72.7 (C-1), 70.3 (C-3), 66.4 (C-5′), 34.5 (C-4), 28.2 (C-5), 26.7 (acetonide *Me*), 26.0 (*Me*$_3$CSi), 25.4 (acetonide *Me*), 22.7 (C-6), 18.3 (Me$_3$*C*Si), 14.1 (C-7), −4.1 (Si*Me*$_2$), −4.5 (Si*Me*$_2$). IR $\nu_{\max}$ 3480 (br), 1463, 1380, 1339, 1255, 1217, 1067, 838. 1615 cm^{-1}. HR EIMS *m/z* (% rel intensity) 347.2243 (M$^+$ − Me, 23), 247 (60), 215 (98), 187 (62), 173 (65), 161 (83), 143 (100), 101 (77), 75 (88). Calcd for C$_{18}$H$_{38}$O$_5$Si − Me, 347.2253. Anal. Calcd. for C$_{18}$H$_{38}$O$_5$Si: C, 59.63; H, 10.56. Found: C, 59.41; H, 10.73.

(1*S*,2*R*,3*S*)-1-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-heptane-1,2,3-triol (7). A solution of diol **6** (800 mg, ca. 2.2 mmol) in THF (15 mL) was treated under Ar with solid tetra-*n*-butylammonium fluoride trihydrate (863 mg, 3.3 mmol) and stirred at room temperature for 15 min. After addition of water (0.5 mL), the volatiles were totally eliminated at reduced pressure. Column chromatography of the residue on silica gel (hexanes−EtOAc, 1:1) provided triol **7** (524 mg, 96%) as a colorless oil: $[\alpha]^{22}_{\mathrm{D}}$ −4.2 (*c* 0.8, CHCl$_3$).^{1}H NMR (400 MHz) δ 4.29 (ddd, 6.6, 6.4, 5.2 Hz, 1H, H-4″), 4.06 (dd, 8.4, 6.6 Hz, 1H, H-5′), 3.84 (dd, 8.4, 6.4 Hz, 1H, H-5′$_b$), 3.73 (m, 1H, H-3), 3.62 (m, 1H, H-1), 3.39 (m, 1H, H-2), 3.05 (d, 5 Hz, OH), 3.02 (d, 4 Hz, OH), 2.90 (br s, OH), 1.55−1.30 (br m, 6H), 1.44 (s, 3H, acetonide *Me*), 1.36 (s, 3H, acetonide *Me*), 0.90 (t, 7 Hz, 3H, H-7). ^{13}C NMR (100 MHz) δ 109.9 (acetonide *C*), 76.9 (C-4′), 73.3 (C-2), 73.2 (C-1), 73.0 (C-3), 65.9 (C-5′), 33.3 (C-4), 27.9 (C-5), 26.6 (acetonide *Me*), 25.4 (acetonide *Me*), 22.7 (C-6), 14.1 (C-7). IR $\nu_{\max}$ 3420 (br), 1456, 1372, 1257, 1215, 1071, 855, 797 cm^{-1}. HR EIMS *m/z* (% rel intensity) 233.1382 (M$^+$ − Me, 29), 215 (5), 173 (12), 155 (15), 131 (25), 101 (100), 59 (72). Calcd for C$_{12}$H$_{24}$O$_5$ − Me, 233.1389. Anal. Calcd for C$_{12}$H$_{24}$O$_5$: C, 58.04; H, 9.74. Found: C, 58.00; H, 9.97.

(1*R*,2*R*,3*S*)-2,3-Diacetoxy-1-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]heptyl acetate (8). To a solution of triol **7** (497 mg, 2 mmol), triethylamine (1.7 mL, ca. 12 mmol), and DMAP (12 mg, 0.1 mmol) in dry CH$_2$Cl$_2$ (20 mL) was added dropwise acetic anhydride (0.95 mL, ca. 10 mmol). The mixture was then stirred overnight at room temperature. After this time, the reaction mixture was poured into brine and extracted twice with CH$_2$Cl$_2$. The organic phases were washed with aqueous 1 M HCl and then with brine. The organic layer was then dried on anhydrous Na$_2$SO$_4$, filtered, and evaporated under reduced pressure to afford an oily residue that was chromatographed on silica gel (hexanes−EtOAc, 1:1). This furnished **8** (674 mg, 90%) as a colorless oil: $[\alpha]^{22}_{\mathrm{D}}$ −14.8 (*c* 3.2, CHCl$_3$).^{1}H NMR (400 MHz) δ 5.26 (dd, 6.2, 4.5 Hz, 1H, H-2), 5.13 (dt, 8, 5 Hz, 1H, H-3), 5.04 (dd, 6.2, 4.2 Hz, 1H, H-1), 4.20 (ddd, 6.7, 5.2, 4.2 Hz, 1H, H-4′), 3.97 (dd, 8.8, 6.7, 1H, H-5′), 3.70 (dd, 8.8, 5.2 Hz, 1H, H-5′), 2.08 (s, 3H, acetate *Me*, acetonide), 2.06 (s, 6H, acetate *Me*), 1.55 (m, 2H, H-4), 1.40 (s, 3H, acetonide *Me*), 1.29 (s, 3H, acetonide *Me*), 1.30−1.20 (m, 4H, H-5, H-6), 0.85 (t, 7 Hz, 3H, H-7). ^{13}C NMR (100 MHz) δ 170.5, 170.4, 170.1 (acetate C═O), 110.1 (acetonide *C*), 74.0 (C-4′), 72.2 (C-2), 71.7 (C-3), 71.4 (C-1), 65.7 (C-5′), 30.6 (C-4), 27.1 (C-5), 26.1 (acetonide *Me*), 25.3 (acetonide *Me*), 22.4 (C-6), 21.0, 20.8, 20.7 (acetate *Me*), 13.9. IR $\nu_{\max}$ 1747, 1644, 1558, 1457, 1434, 1372, 1219, 1160, 1126, 1026, 964, 849, 707 cm^{-1}. HR EIMS *m/z* (% rel intensity) 359.1695 (M$^+$ − Me, 71), 137 (56), 101 (100). Calcd for C$_{18}$H$_{30}$O$_8$ − Me, 359.1705. Anal. Calcd for C$_{18}$H$_{30}$O$_8$: C, 57.74; H, 8.08. Found: C, 57.55; H, 7.99.

(2*S*,3*R*,4*S*)-2,3,4-Triacetoxyoctanal (9). Triacetate **8** (562 mg, 1.5 mmol) was dissolved in EtOAc (30 mL) and treated with H$_5$IO$_6$ (684 mg, 3 mmol). After the mixture was stirred at room temperature until total consumption of **8** (1−1.5 h, TLC monitoring!), solid sodium thiosulfate (240 mg, ca. 1.5 mmol) was added. The reaction mixture was stirred for 15 min, filtered through Celite (the Celite was washed with an additional amount of EtOAc), and evaporated under reduced pressure. The oily residue was subjected to rapid chromatography on silica gel (hexanes−EtOAc, 7:3) to yield **9** (385 mg, still impure, 85%) as a colorless oil: ^{1}H NMR (400 MHz) δ 9.50 (s, 1H, H-1), 5.43 (dd, 4.8, 4.2 Hz, 1H, H-3), 5.25 (d, 4.2 Hz, 1H, H-2), 5.20 (m,1H, H-4), 2.21 (s, 3H, acetate *Me*), 2.13 (s, 3H, acetate *Me*), 2.04 (s, 3H, acetate *Me*), 1.80 (m, 2H, H-5), 1.60 (m, 2H, H-6), 1.30 (m, 2H, H-7), 0.89 (t, 6.5 Hz, 3H, H-8). ^{13}C NMR (100 MHz) δ 194.0 (C-1), 170.0, 169.8, 169.6 (acetate C═O), 75.5 (C-2), 71.1 (C-3), 70.9 (C-4), 30.0 (C-5), 27.0 (C-6), 22.4 (C-7), 20.8, 20.5, 20.3 (acetate *Me*), 13.8 (C-8). IR $\nu_{\max}$ 1745, 1644, 1559, 1433, 1372, 1216, 1049, 964, 864, 737, 705 cm^{-1}.

(4*R*,5*R*,6*R*,7*S*)-5,6,7-Triacetoxyundec-1-en-4-ol (10). Allyl bromide (330 μL, 3.75 mmol) and indium powder (290 mg, ca. 2.5 mmol) were added to a vigorously stirred solution of aldehyde **9** (378 mg, 1.25 mmol) in a 1:1 THF/H$_2$O mixture (35 mL). The reaction mixture was stirred overnight at room temperature, then poured onto brine and thoroughly extracted with EtOAc. The organic phases were washed again with brine and dried over anhydrous Na$_2$SO$_4$. Filtration and evaporation of the solvent under reduced pressure gave an oily residue that was chromatographed on silica gel to provide a 91:9 mixture of **10** and its epimer (362 mg, 84%): ^{1}H NMR (400 MHz, signals from the major diastereoisomer) δ 5.80 (m, 1H, H-2), 5.30 (dd, 7.7, 2.5 Hz, 1H, H-6), 5.15−5.05 (m, 2H, H-1$_a$, H-1$_b$), 5.03 (m, 1H, H-7), 4.96 (dd, 8.2, 2.5 Hz, 1H, H-5), 3.54 (m, 1H, H-4), 2.85 (d, 4.5 Hz, 1H, 3-OH), 2.25−2.05 (m, 2H, H-3$_a$, H-3$_b$), 2.12 (s, 3H, acetate *Me*), 2.11 (s, 3H, acetate *Me*), 2.03 (s, 3H, acetate *Me*), 1.70−1.50 (m, 2H, H-8), 1.40−1.20 (m, 4H, H-9, H-10), 0.86 (t, 6.5 Hz, 3H, H-11). ^{13}C NMR (100 MHz) δ 171.6, 170.4, 170.2 (acetate C═O), 133.9 (C-2), 118.4 (C-1), 73.1 (C-5), 72.5 (C-6), 72.0 (C-7), 68.6 (C-4), 37.3 (C-3), 30.1 (C-8), 26.9 (C-9), 22.4 (C-10), 21.0, 20.8 (acetate *Me*), 13.9 (C-11). IR $\nu_{\max}$ 3500 (br), 3078, 1746, 1643, 1434, 1374, 1227, 1030, 922, 863 cm^{-1}. HR EIMS *m/z* (% rel intensity) 345.1900 (M + H$^+$, 1), 243 (63), 171 (66), 141 (100), 115 (88). Calcd for C$_{17}$H$_{29}$O$_7$, 345.1913.

(4*R*,5*R*,6*R*,7*S*)-5,6,7-Triacetoxyundec-1-en-4-yl acrylate (2). Acryloyl chloride (162 μL, 2 mmol) was added dropwise under Ar to a solution of **10** (+ *epi*-**10**, 91:9) (345 mg, 1 mmol), triethylamine (310 μL, 2.2 mmol), and DMAP (6 mg, 0.05 mmol) in dry CH$_2$Cl$_2$ (10 mL). The mixture was stirred overnight at room temperature, then poured into brine and extracted twice with CH$_2$Cl$_2$. The organic phases were washed with 1 M aq HCl and with brine, dried over anhydrous Na$_2$SO$_4$, filtered, and evaporated under reduced pressure. This afforded an oily residue

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that was chromatographed on silica gel (hexanes−EtOAc, 1:1) to give a colorless solid product. Crystallization from hexanes/ether afforded pure **2** (239 mg, 60%) as white cubes: $[\alpha]^{22}_{D}$ +1.8 (*c* 0.3, $CHCl_3$), mp 82.7−83.7 °C. ^1H NMR (400 MHz) δ 6.35 (dd, 17.3, 1.5 Hz, 1H, H-β acrylate), 6.04 (dd, 17.3, 10.3 Hz, 1H, H-α acrylate), 5.82 (dd, 10.5, 1.5 Hz, 1H, H-β' acrylate), 5.70 (m, 1H, H-2), 5.32 (dd, 6, 4.4 Hz, 1H, H-5), 5.23 (dd, 6.3, 4.4 Hz, 1H, H-6), 5.10−5.05 (m, 3H, H-1, H-4), 5.00 (m, 1H, H-7), 2.38 (m, 2H, H-3), 2.10 (s, 3H, acetate *Me*), 2.06 (s, 3H, acetate *Me*), 2.05 (s, 3H, acetate *Me*), 1.55 (m, 2H, H-8), 1.30−1.20 (m, 4H, H-9, H-10), 0.86 (t, 7.0 Hz, 3H, H-11). ^{13}C NMR (100 MHz) δ 170.5, 170.0, 169.9 (acetate C═O), 165.1 (acrylate C═O), 132.5 (C-2), 131.4 (acrylate ═CH), 128.0 (acrylate ═CH_2), 118.6 (C-1), 71.6 (C-7), 71.2 (C-5), 71.0 (C-6), 70.3 (C-4), 34.6 (C-3), 30.1 (C-8), 27.0 (C-9), 22.4 (C-10), 20.9, 20.8, 20.7 (acetate *Me*), 13.9 (C-11). IR ν_{max} 3080, 1748 (br), 1638, 1407, 1373, 1220, 1045, 851, 807 cm^{-1}. HR EIMS *m*/*z* (% rel intensity) 398.1940 (M^+, 1), 327 (15), 224 (55), 169 (100), 127 (48). Calcd for $C_{20}H_{30}O_8$, 398.1941. Anal. Calcd for $C_{20}H_{30}O_8$: C, 60.29; H, 7.59. Found: C, 60.41; H, 7.73.

Boronolide, (+)-1. A solution of acrylate **2** (199 mg, ca. 0.5 mmol), $Ti(OiPr)_4$ (450 μL, ca. 1.5 mmol), and Grubbs catalyst $PhCH{=}RuCl_2(PCy_3)_2$ (41 mg, 0.05 mmol) in dry CH_2Cl_2 (60 mL) was heated at reflux for 24 h. After removal of all volatiles in vacuo, the crude residue was chromatographed on silica gel (hexanes−EtOAc, 7:3, then 1:1) to furnish (+)-**1** (132 mg, 71%) as colorless crystals, mp 88−90 °C (lit.[1] mp 90 °C); $[\alpha]^{22}_{D}$ +25.1 (*c* 0.1, EtOH) (lit.[1] $[\alpha]_{D}^{22}$ +25 (*c* 0.2, EtOH)). ^1H NMR (500 MHz) δ 6.86 (ddd, 9.7, 6.2, 2.5 Hz, 1H), 6.02 (dd, 9.7, 2.5 Hz, 1H), 5.33 (m, 2H), 5.00 (q, 6 Hz, 1H), 4.52 (dt, 12, 4.5 Hz, 1H), 2.52 (ddt, 18, 11.8, 2.5 Hz, 1H), 2.30 (m, 1H), 2.12 (s, 3H, acetate *Me*), 2.08 (s, 3H, acetate *Me*), 2.06 (s, 3H, acetate *Me*), 1.55 (m, 2H), 1.25 (m, 4H), 0.87 (t, 6.5 Hz). ^{13}C NMR (125 MHz) δ 170.5, 169.9, 169.7 (acetate C═O), 162.5, 144.1, 121.5, 75.2, 71.7, 70.8, 70.7, 30.3, 27.1, 25.2, 22.4, 21.0, 20.7, 20.6 (acetate *Me*), 13.9 (C-5). IR ν_{max} 1736 (br), 1374, 1220, 1030, 816 cm^{-1}. HR EIMS *m*/*z* (% rel intensity) 371.1699 (M + H^+, 1), 273 (16), 242 (86), 182 (69), 140 (100), 97 (37). Calcd for $C_{18}H_{27}O_8$, 371.1706.

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