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Synthesis of the Acyclic Carbon Skeleton of Filipin III

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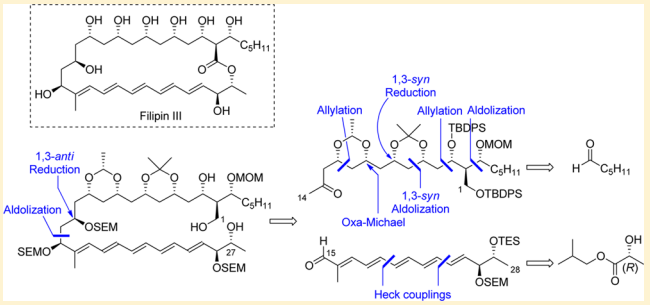
Supporting Information

ABSTRACT: The synthesis of the carbon skeleton of filipin III, a polyenic macrolactone possessing 11 stereogenic centers, was achieved using a convergent strategy with the longest linear sequence of 19 steps starting from hexanal. Construction of the polyene was realized using two successive Heck couplings as the key steps. Control of the stereogenic centers of the polyol fragment was performed by utilizing an Evans aldolization, a 1,3-*syn* aldolization, enantio- and diastereoselective allylations, a hemiacetalization/oxa-Michael sequence, and a 1,3-*syn* reduction. The polyol and polyenic fragments were coupled using a 1,5-*anti* diastereoselective aldolization followed by a 1,3-*anti* reduction.



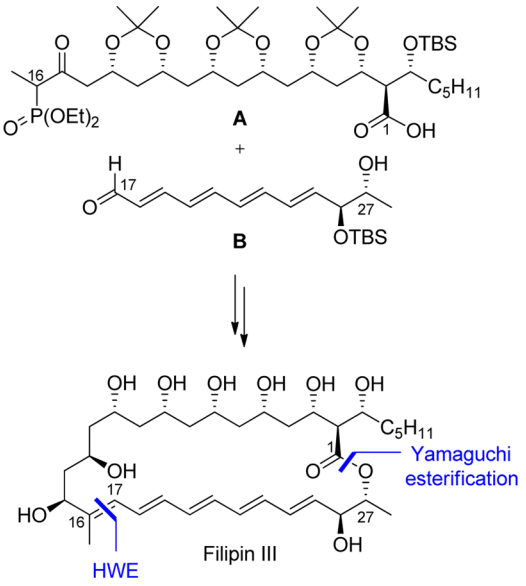
INTRODUCTION

Filipins were isolated from the cell culture filtrates of *Streptomyces filipensis*, which were collected in the Philippine Islands.[1] A mixture of at least eight compounds was found in these filtrates, and four fractions were separated: filipin I (4%), filipin II (25%), filipin III (53%), and filipin IV (18%).[2] The structure of the major compound, filipin III, was determined by degradation studies,[3] and its relative and absolute stereochemistry were determined by synthesis.[4] Filipin III is a polyenic macrocycle which possesses antibiotic properties[5] but is too toxic to have therapeutic applications. However, filipin III has been widely used as a histochemical stain for cholesterol to study its distribution and quantify it in cell membranes.[6] This strong interaction between cholesterol and filipin III has been used clinically in the study and diagnosis of type C Niemann-Pick disease.[7] Moreover, filipin III was shown to prevent pathological accumulation of the membrane-bound prion protein, whose expression is a key event in the pathogenesis of transmissible spongiform encephalopathies.[8]

The synthesis of the C1−C15 polyol fragment of filipin III was published by Kiyooka et al.,[9] and synthesis of the C1−C10 fragment of the enantiomer of filipin III was realized by Brückner and Walleser;[10] however, it is worth noting that only one total synthesis of filipin III was reported to date by Rychnovsky et al.[11] This synthesis is convergent and was achieved from a polyol fragment **A** and a polyenic fragment **B**, which were coupled using first a Yamaguchi esterification and then an intramolecular Horner-Wadsworth-Emmons (HWE) reaction to construct the macrocycle (Scheme 1).

In the context of our program concerning the synthesis of natural products[12] and the study of their biological mechanism of action, we became interested in the synthesis of filipin III to access several analogues to modulate its biological activity.

Scheme 1. Synthesis of Filipin III by Rychnovsky et al.



Here, we report our efforts toward the synthesis of the carbon skeleton of filipin III.

From a retrosynthetic analysis, we planned to access filipin III from two fragments: a polyol fragment **C** and a polyenic fragment **D**. The assembly of the two fragments would be achieved using a diastereoselective aldolization to form the C14−C15 bond, and the final step would be a macrolactonization to form the C1−O29 bond (Scheme 2).

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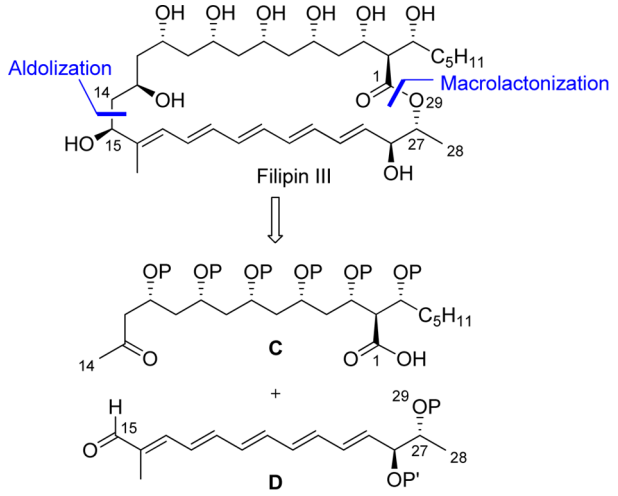
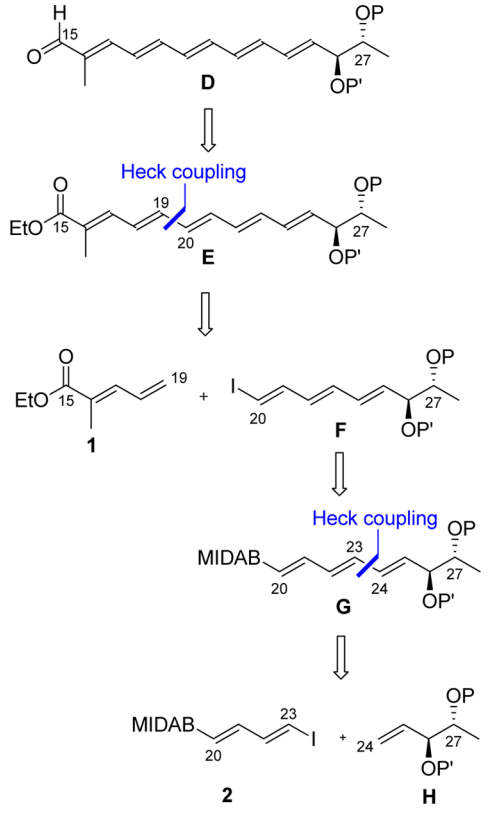
Scheme 2. Retrosynthesis



Scheme 3. Retrosynthesis of the C15−C28 Fragment



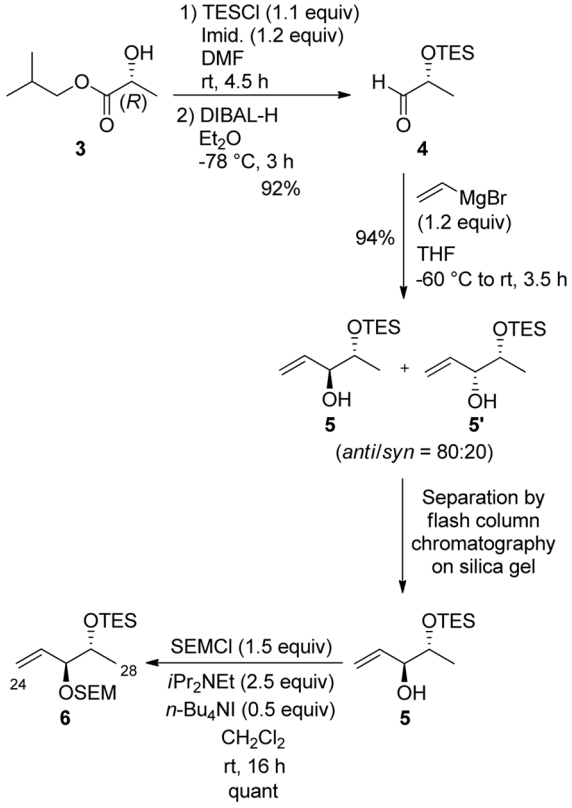
RESULTS AND DISCUSSION

Synthesis of the C15−C28 Fragment (Fragment D). The C15−C28 fragment of filipin III is a conjugated pentaenic aldehyde possessing a 1,2-*anti*-diol unit. The aldehyde function would allow the formation of the C14−C15 bond by performing an aldol condensation.

Our retrosynthetic analysis of the polyenic fragment is based on a method developed by Burke and co-workers to synthesize polyenes using successive chemoselective palladium-catalyzed cross-couplings involving alkenyl boronic esters derived from *N*-methyliminodiacetic acid (MIDA),[13] which was recently extended by our group to more complex polyenes and applied to the synthesis of the polyenic fragment of mirabaline.[14] On the basis of this strategy, two Heck couplings were envisaged to build up the polyenic fragment: one to form the C19−C20 bond, and the second one to form the C23−C24 bond (Scheme 3). For these two Heck couplings, the conjugated iodo-triene **F** and iodo-diene **2** have to be synthesized and then respectively coupled with the conjugated dienic ester **1** and the allylic 1,2-diol **H**.

The synthesis of the α,β-unsaturated 1,2-diol **H** was realized in four steps, starting from the commercially available (*R*)-isobutyl lactate **3** (Scheme 4). After protection of the alcohol (TESCl, imidazole, DMF) and reduction of the ester (DIBAL-H, Et_2O, −78 °C), lactate **3** was transformed to aldehyde **4**[15] (92%), which was then treated with vinylmagnesium bromide (THF, −60 °C to rt) to furnish a mixture of the two diastereomeric alcohols **5** and **5′** in 94% yield in a ratio of 80:20 in favor of the *anti*-isomer **5** which corresponds to the expected Felkin-Anh adduct. These two diastereomers were separated by column chromatography on silica gel to afford the pure desired 1,2-*anti*-diol **5**. As planned in our retrosynthesis, a Yamaguchi macrolactonization was envisioned to access filipin III, and a selective deprotection of the hydroxyl present at C27 was thus required. Therefore, to protect the hydroxyl group present at C26, an orthogonal protecting group to the TES group present at C27 had to be used, and a SEM group was chosen to this end. After treatment of **5** with SEMCl (iPr_2NEt, n-Bu_4NI, CH_2Cl_2, rt, 16 h), the protected diol **6** was isolated in quantitative yield (Scheme 4).

Scheme 4. Synthesis of the 1,2-Diol 6



The synthesis of the iodo-diene **2**[14] was then achieved (Scheme 5). The synthesis started with the hydrostannylation followed by the iodo-destannylation of alkyne **7** to produce **8** (Bu_3SnH and AIBN then I_2, THF, −78 °C to rt, 72%) (Scheme 5). The obtained vinyl iodide **8** was then involved in a Heck coupling with vinyltrimethylsilane [$Pd(OAc)_2$, AgOAc, MeCN,

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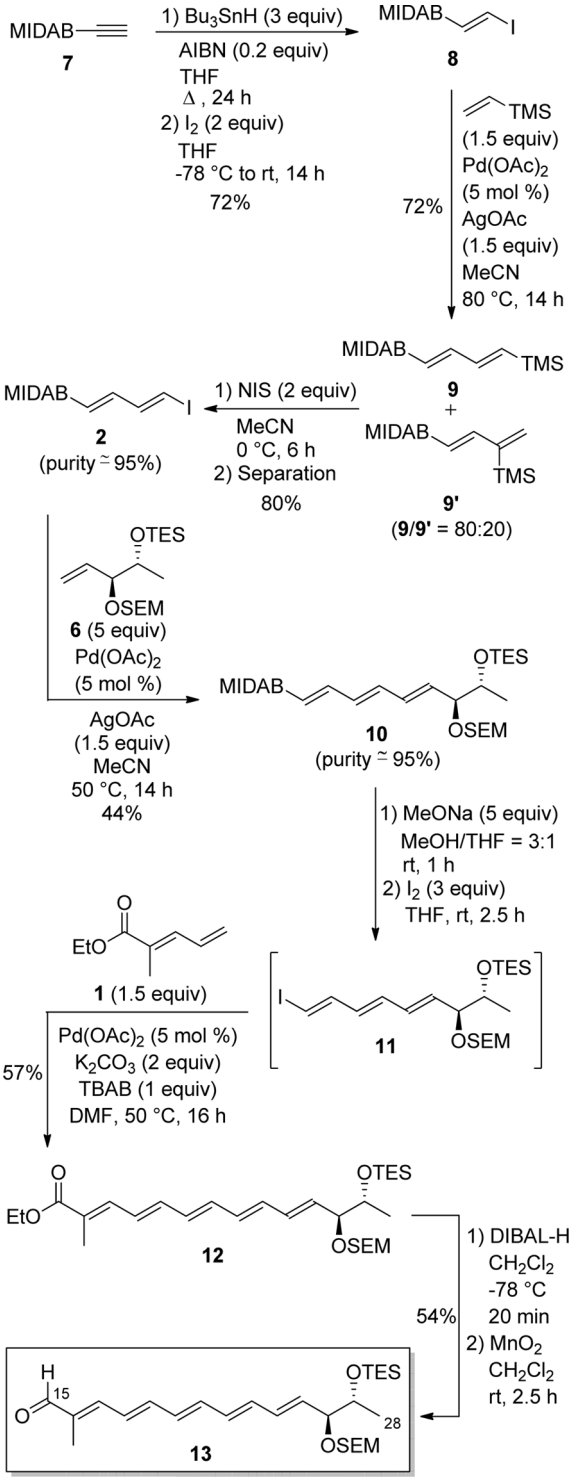
Scheme 5. Synthesis of the Pentaenic Aldehyde 13



80 °C], leading to a mixture of the desired diene **9** and the branched diene **9′** in a ratio of 80:20 (72%) which, at this stage, could not be separated. However, after iodo-desilylation using NIS at 0 °C (MeCN, 6 h) and purification by column chromatography on silica gel, the two iodo-isomers were separated, and the desired linear iodo-diene **2** was isolated in 80% yield (Scheme 5).[16] With **2** and **6** in hand, the second Heck coupling was examined. When iodo-diene **2** was treated with 1.5 equiv of diol **6** in the presence of $Pd(OAc)_2$ (5 mol %) and AgOAc (1.5 equiv) in MeCN for 14 h at 80 °C using previously described conditions,[14] only 15% of the desired coupling product **10** was obtained (Table 1, entry 1). A decrease in the temperature to 50 °C did not increase the yield of **10** (16%) (Table 1, entry 2). On the contrary, when the reaction was performed at 50 °C using 5 equiv of 1,2-diol **6**, the yield of **10** increased to 44% (Table 1, entry 3).[17]

To access pentadiene **E**, compound **10** has to be transformed into an iodo-triene of type **F**. Thus, the MIDA boronate **10** was hydrolyzed using sodium methylate (MeONa, MeOH/THF = 3:1, rt, 1 h), and the resulting boronic acid was involved in an iodo-deborylation (I_2, THF, rt, 2.5 h) to produce iodo-triene **11**, which was not purified but directly involved in a Heck coupling with the dienic ester **1**[18] utilizing Jeffery's conditions[19] [$Pd(OAc)_2$, K_2CO_3, TBAB, DMF, 50 °C, 16 h], providing the desired conjugated pentaenic ester **12** in 57% yield over the three steps. After reduction of the ester (DIBAL-H, −78 °C), the resulting alcohol was not purified but directly oxidized by MnO_2 to produce the desired aldehyde **13** in 54% yield over the two steps (Scheme 5). It is worth mentioning that aldehyde **13** is prone to degradation, therefore it must be synthesized and used rapidly after its preparation. The pentaenic fragment **13** was thus synthesized in 10 steps from (*R*)-isobutyl lactate **3** with a global yield of 12% (Scheme 5).

The synthesis of the C1−C14 Fragment (Fragment C). The synthesis of the polyol fragment **C** was envisaged from enone **I** which would be prepared from the *α,β*-unsaturated ketone **J** and the *β*-hydroxy aldehyde **K** (Scheme 6). Control of the stereogenic centers at C2 and C3′ in **K** would be achieved using an Evans aldol condensation. The C3 and C11 stereogenic centers in **K** and **J** would be introduced using, respectively, a diastereoselective and an enantioselective allylation of the corresponding aldehydes. An aldol condensation between **J** and **K** would allow the control of the stereogenic center at C5 according to a 1,3-*syn* control. The stereogenic center at C9 would be introduced using a hemiacetalization/oxa-Michael addition sequence applied to enone **I**, and finally, control of the C7 stereogenic center would be achieved by a 1,3-*syn* diastereoselective reduction of the resulting *β*-hydroxy ketone (Scheme 6).

The synthesis of the C1−C5 fragment, compound **21**, started with the unsaturated oxazolidinone **15** prepared by acylation of the (*S*)-4-isopropyl-5,5-dimethyloxazolidin-2-one **14**.[20−22] After treatment of **15** under Evans conditions [*n*-Bu_2BOTf (1.1 equiv), Et_3N (1.4 equiv), CH_2Cl_2, −78 °C],[23] the enol borinate was condensed with hexanal which, after oxidative treatment (H_2O_2, pH 7 buffer), led to the aldol product **16** as a single detectable diastereomer (by ^1H NMR) in 94% yield. After protection of the hydroxyl group [MOMCl (4 equiv), *i*Pr_2NEt, CH_2Cl_2, rt, 18 h], the resulting MOM ether **17** was ozonolyzed, and the obtained aldehyde **18** was directly treated with allylmagnesium chloride in the presence of $ZnCl_2$[24] to produce the homoallylic alcohol **19** as a single detectable diastereomer in 73% yield (from **17**).[25] The homoallylic alcohol **19** was then transformed in three steps into aldehyde **21**. After cleavage of the chiral auxiliary by $LiAlH_4$ (toluene, −30 °C to −10 °C),[26] the resulting diol was directly protected (TBDPSOTf, 2,6-lutidine, CH_2Cl_2) to furnish compound **20** (63% over the 2 steps) which, after ozonolysis, led to the desired aldehyde **21** (O_3, CH_2Cl_2, −78 °C then PPh_3, 95%). The C1−C5 fragment was thus obtained from hexanal in 7 steps for the longest linear sequence with an overall yield of 39% (Scheme 7).

Methyl ketone **26**, which represents the C6−C13 fragment, was obtained in 4 steps from 1,3-propanediol **22**. The diol was

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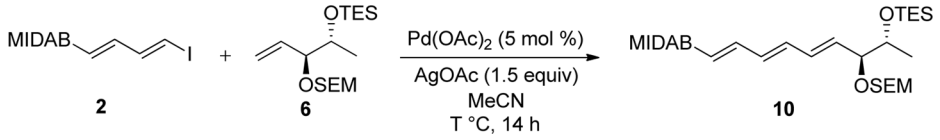
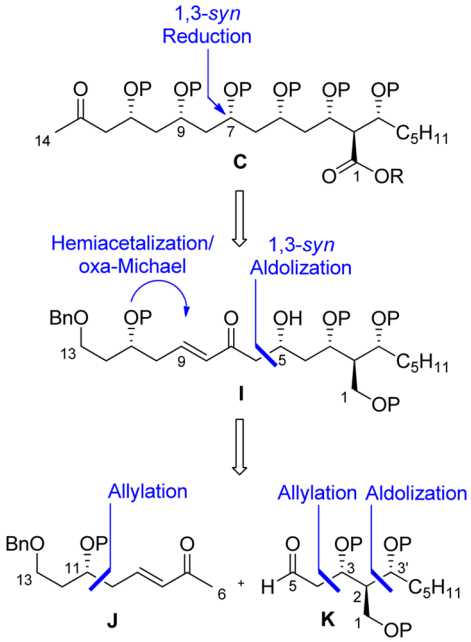
Table 1. Optimization of the Second Heck Coupling



	6 (equiv)	T (°C)	yield (%)[a]
1	1.5	80	15
2	1.5	50	16
3	5.0	50	44

[a]Isolated yield.

Scheme 6. Retrosynthesis of the C1−C14 Fragment



first monobenzylated to produce **23**[27] and, after a catalytic enantioselective allylation using the conditions developed by Krische et al.,[28] the homoallylic alcohol **24** was isolated in 72% yield with an enantiomeric excess of 94%.[29] After protection of the alcohol, the resulting silyl ether **25**[30] was involved in a cross-metathesis with methyl vinyl ketone [5.1 equiv, **HG-II** (2 mol %), CH_2Cl_2, 45 °C, 2 h], and the α,β-unsaturated ketone **26** was isolated in 98% yield (Scheme 8).

Having methyl ketone **26** and aldehyde **21** in hand, a diastereoselective aldol condensation has to be performed to access the C1−C13 fragment of filipin III. As the stereogenic center at C5 has to be introduced in a stereocontrolled manner, we took advantage of the preexisting hydroxyl group present at C3 in compound **21**, and Paterson's conditions were chosen to control the diastereoselectivity.[31]

Different dialkyl borane reagents were tried to favor 1,3-*syn* control between the hydroxyl groups at C3 and C5 during the aldolization. When methyl ketone enol borinate was prepared using chlorodicyclohexylborane [2.6 equiv in the presence of Et_3N (3.0 equiv) in Et_2O at 0 °C] and condensed with aldehyde **21**, two diastereomers, **27** and **27′**, were obtained in 50% yield[32] in a ratio of 60:40 in favor of the 1,3-*syn* product **27** (Scheme 9, eq 1).[31] The diastereoselectivity in favor of **27** was improved when the methyl ketone enol borinate was prepared with (+)-chlorodiisopinocampheylborane [(+)-DIPCl][33] using the same reaction conditions as before, and the ratio of **27**/**27′** was improved to 90:10. After separation of the two diastereomers by flash column chromatography on silica gel, **27** was isolated with a yield of 67% (from aldehyde **21**) (Scheme 9, eq 2). We have to point out that the 1,3-*syn* stereoselectivity was later verified on compound **29** (vide infra).

Two stereogenic centers remained to be controlled in fragment C1−C13. At first, the stereogenic center at C9 was introduced using a hemiacetalization/1,4-addition sequence applied to the α,β-unsaturated ketone **27** in the presence of acetaldehyde and catalyzed by $Bi(NO_3)_3{\cdot}5H_2O$ (0.1 equiv) (CH_2Cl_2, rt, 15 h).[34] It was not necessary to cleave the triethylsilyl group because, under these conditions, the acetal **28** was directly obtained in 56% yield as a single detectable diastereomer. The last stereogenic center at C7 was controlled by realizing a 1,3-*syn* diastereoselective reduction of the β-hydroxyketone **28** (Et_2BOMe, $NaBH_4$, MeOH/THF = 1:4, −78 to 0 °C)[35] to afford the 1,3-*syn* diol **29** in 73% yield, again as a single detectable diastereomer. The transformation of **29** to methyl ketone **31** was finally realized in 5 steps. After protection of the diol (dimethoxypropane, PPTS, rt) and deprotection of the benzyl alcohol (Pd/C, H_2, MeOH, rt), compound **30** was isolated in 77% yield. After oxidation (DMP, $NaHCO_3$), addition of methylmagnesium bromide (Et_2O, 0 °C), and another oxidation (DMP, $NaHCO_3$), the desired methyl ketone **31** was isolated in 86% yield over 3 steps (Scheme 10).

It is worth noting that compound **29** was also transformed into the 1,3,5-deprotected triol **32** to confirm the relative stereochemistry between the hydroxyl groups present at C3, C5, and C7 using Kishi's ^{13}C NMR database.[36] Treatment of **29** with TBAF (THF, 0 °C) gave tetraol **32** in 74% yield, and the analysis of its ^{13}C NMR spectrum in deuterated methanol showed a chemical shift at 70.8 ppm for C5, which is in accordance with a *syn*/*syn* relative stereochemistry between the hydroxyl groups at C3, C5, and C7 (Scheme 11).

Synthesis of the Carbon Skeleton of Filipin III. With the C1−C14 and C15−C28 fragments in hand, a 1,5-*anti* diastereoselective aldol condensation had to be performed to access the carbon skeleton of filipin III and to introduce the stereogenic center at C15.

Methyl ketone **31** was thus involved in an aldol condensation with aldehyde **13** under Paterson's conditions (Cy_2BCl, Et_3N, Et_2O, −78 °C to −20 °C, 14 h) to produce the β-hydroxyketone **34** in 91% yield as a single detectable diastereomer resulting from a 1,5-*anti* control from the acetal at C11.[37] The obtained β-hydroxyketone was stereoselectively reduced using $Me_4NBH(OAc)_3$ (10 equiv, MeCN/AcOH = 10:1, −20 °C, 14 h)[38] to produce the 1,3-*anti* diol **35** again as a single detectable diastereomer (80%). After a SEM protection of the C13 and C15 hydroxyl groups (SEMCl, iPr_2NEt,

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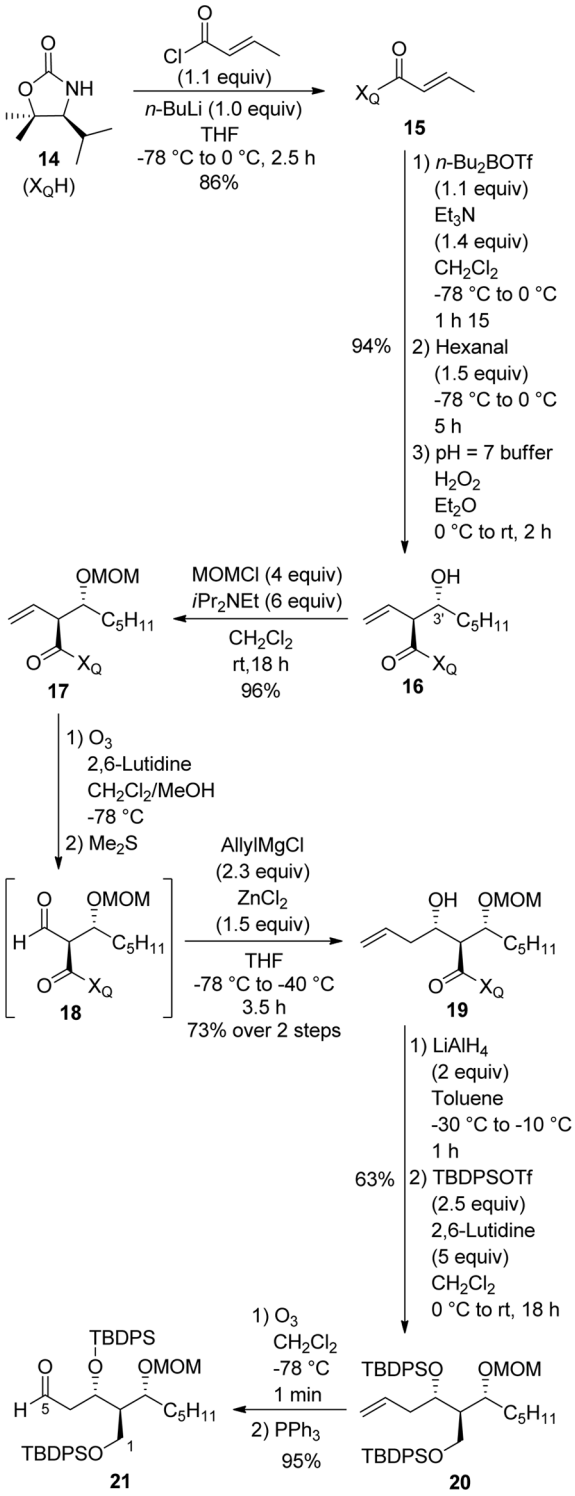
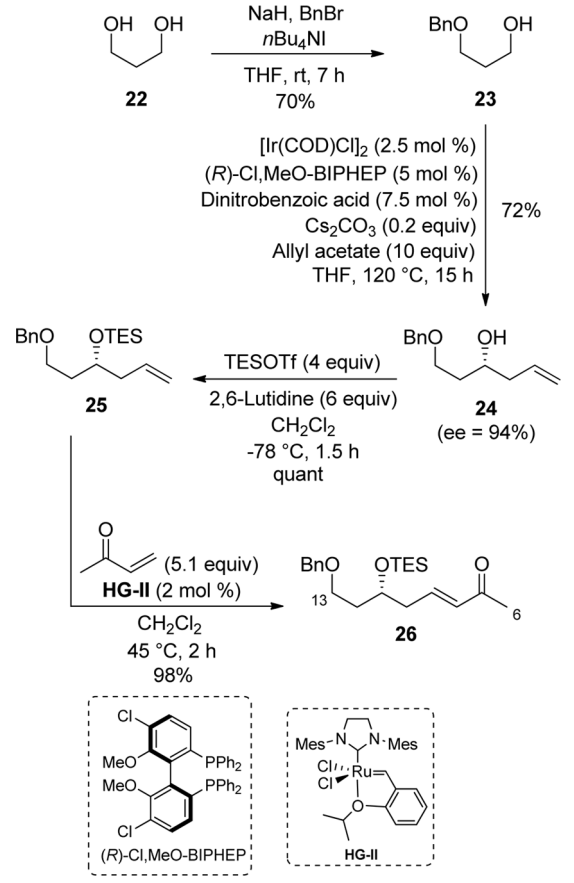
Scheme 7. Synthesis of the C1−C5 Fragment



Scheme 8. Synthesis of the C6−C13 Fragment



CH_2Cl_2, rt) followed by cleavage of the silyl ethers (TBAF, THF, rt), we were able to isolate compound **36** (79%), which corresponds to the carbon skeleton of filipin III with all the stereogenic centers in place (Scheme 12).

Unfortunately, if the primary alcohol at C1 was selectively oxidized to the corresponding aldehyde using TEMPO in the presence of a catalytic amount of [bis(acetoxy)-iodo]benzene (BAIB),[39] it was not possible to oxidize this aldehyde to the corresponding acid, which would have allowed the formation of the macrolactone. Even under the mild Pinnick-Lindgren oxidation conditions ($NaClO_2$, NaH_2PO_4, 2-methylbut-2-ene), which proved to be efficient in several syntheses of polyenic natural products,[40] the aldehyde was transformed to a complex mixture due to the degradation of the polyenic moiety under these oxidative conditions. In addition, direct selective oxidation of the primary alcohol to the corresponding acid using Epp and Widlanski conditions [TEMPO, $PhI(OAc)_2$, $MeCN/H_2O$ = 1:1],[41] which were also used in several total syntheses of complex molecules,[42] led to the decomposition of compound **36**, and we were never able to obtain the desired carboxylic acid.

CONCLUSION

The strategy which was envisioned to construct the macrocyclic core of filipin III, even if reported to be successful in the syntheses of several polyenic natural products,[40,42] proved to be inefficient in our case, probably due to the instability of the polyenic moiety during the last steps. Due to our previous failures in the synthesis of wortmannilactone (concomitantly realized to the synthesis of filipin III),[43] we would like to stress avoiding the use of an oxidation/macrolactonization sequence at the last crucial step to access polyenic macrolactones. One piece of advice would be to favor a Horner-Wadsworth-Emmons reaction to construct one of the olefins of the polyene and to access the macrocycle, a strategy which was successfully used by Rychnovsky et al. for the synthesis of filipin III[11] as well as in our final successful attempt to access wortmannilactone.[12b,43] A cross-coupling reaction would be another alternative

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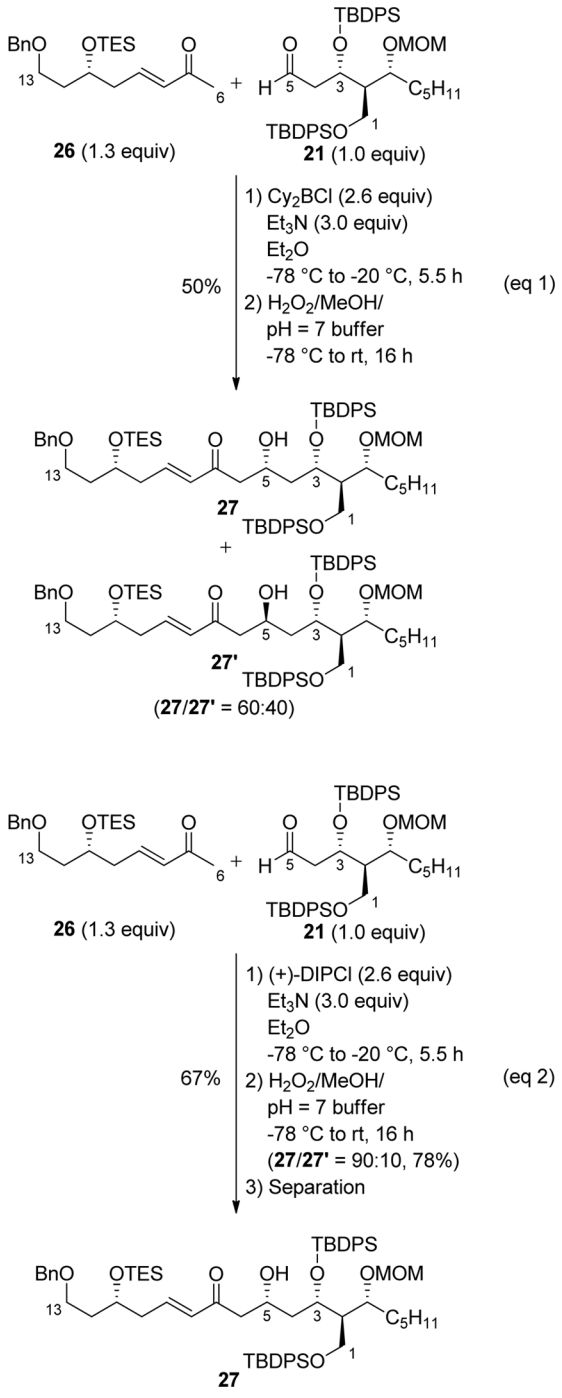
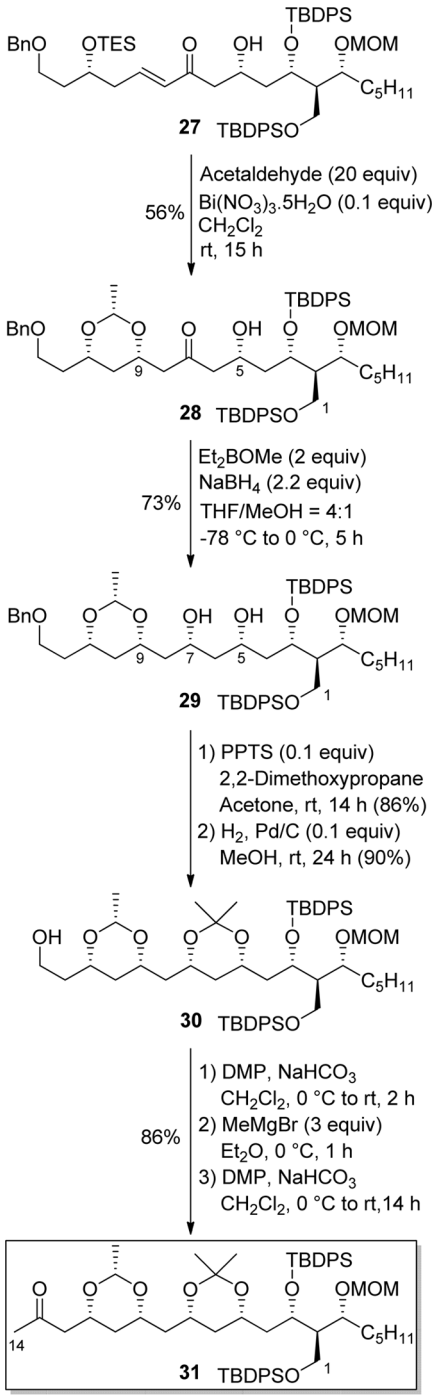
Scheme 9. Synthesis of the C1−C13 Fragment



Scheme 10. Synthesis of the C1−C14 Methyl Ketone



to install the sensitive polyene moiety in one of the last steps of the synthesis.

EXPERIMENTAL SECTION

General Experimental Methods. All reactions were carried out under anhydrous conditions using flame-dried glassware under an argon atmosphere. CH_2Cl_2, Et_3N, and iPr_2NEt were distilled from CaH_2; Et_2O and THF were distilled from Na/benzophenone. Other reagents were obtained from commercial suppliers and used as received. TLC was performed on silica gel plates with UV and *p*-anisaldehyde or $KMnO_4$ stain visualization. Flash chromatography was performed on silica gel (230−400 mesh). Optical rotations were measured using a polarimeter with a 1 dm path length. IR spectra were recorded on an ATR plate; wave numbers are indicated in cm^{-1}. ^1H NMR spectra were recorded at 400 MHz in $CDCl_3$, acetone-d6, C_6D_6, or CD_3OD, and data are reported as follows: chemical shift in ppm from tetramethylsilane or residual solvent signals ($CHCl_3$: 7.26 ppm, acetone-d5: 2.05 ppm, C_6D_5H: 7.16 ppm, MeOD-d3: 3.31 ppm) as an internal standard, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, hept = heptuplet, m = multiplet or overlap of nonequivalent resonances, br = broad), coupling constant in Hz, and integration. ^{13}C NMR spectra were recorded at 100 MHz in $CDCl_3$, acetone-d6, C_6D_6, or CD_3OD, and data are reported as follows: chemical shift in ppm from tetramethylsilane with the solvent as an internal indicator ($CDCl_3$: 77.16 ppm, acetone-d6: 29.84 and 206.26 ppm, C_6D_6: 128.06 ppm, MeOD-d4: 49.00 ppm). Mass spectra were realized with a gas chromatograph−mass spectrometer by

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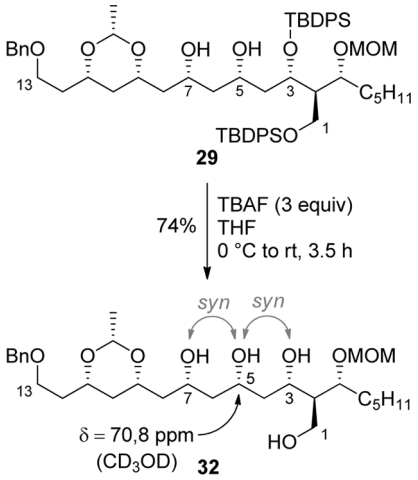
Scheme 11. Determination of the Relative Stereochemistry of 29

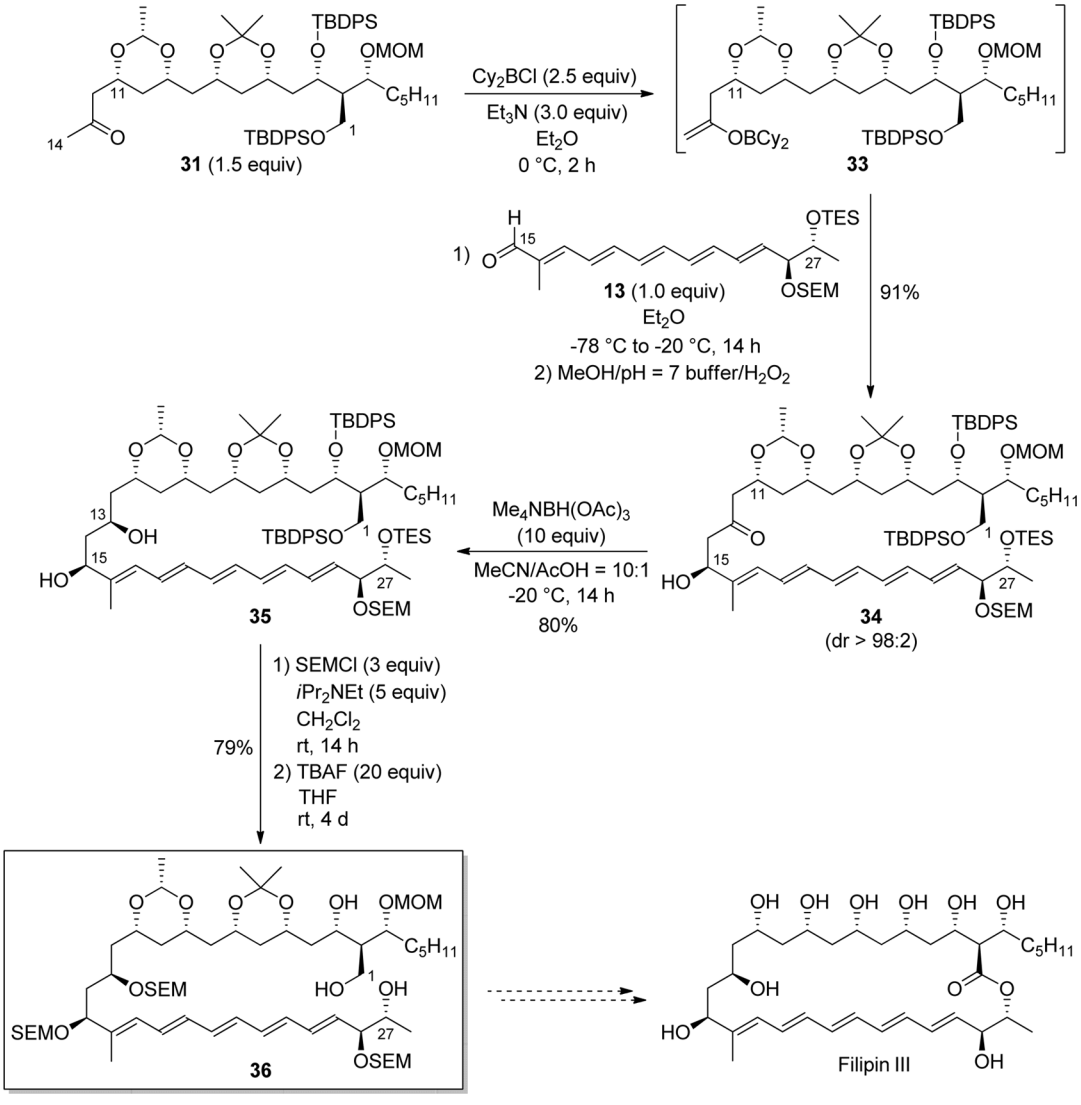


electronic impact. High-resolution mass spectra (HRMS) were performed with an orbitrap mass analyzer by electrospray ionization.

*(E)-Ethyl 2-methylpenta-2,4-dienoate (**1**).*[18] To a solution of (carboethoxyethylidene)triphenylphosphorane (2 g, 5.5 mmol, 1.0 equiv) in dry CH_2Cl_2 (16 mL) was added acrolein (0.37 mL, 5.5 mmol, 1.0 equiv) dropwise. The mixture was stirred at rt for 1 h and then heated at 38 °C for 3.5 h. The solution was cooled to rt and concentrated under vacuum, and then pentane was added (20 mL). The suspension was filtered over Celite, and the filtrate was concentrated under vacuum. Purification of the crude material by flash column chromatography on silica gel (pentane/Et_2O = 98:2) afforded the dienic ester **1** (517 mg, 3.69 mmol, 67%) as a colorless oil. The spectral data are in agreement with those reported in the literature.[18] IR: ν 3091, 2982, 2933, 1705, 1633, 1596, 1446, 1421, 1392, 1367, 1341, 1244, 1195, 1176, 1100, 1034, 1008, 990, 928 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.17 (br d, J = 11.4 Hz, 1H), 6.66 (ddd, J = 16.8, J = 11.3 and J = 10.1 Hz, 1H), 5.57 (br d, J = 16.8 Hz, 1H), 5.45 (br d, J = 10.0 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.96 (br d, J = 1.3 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 168.5, 138.4, 132.4, 128.3, 124.2, 60.8, 14.4, 12.8; MS (EI) m/z: 140 (M^+, 25), 112 (36), 111 [$(M\text{-}Et)^+$, 23], 97 (16), 96 (11), 95 [$(M\text{-}EtO)^+$, 57], 69 (15), 67 (100), 66 (31), 65 (36), 56 (12), 55 (13).

*[(1E,3E)-4-Iodobuta-1,3-dien-1-yl]boronic Acid MIDA Ester (**2**).*[14] To a solution of vinyl trimethylsilane **9** used as an 80:20 mixture with **9′** (500 mg, 1.78 mmol, 1.0 equiv) in anhydrous MeCN (17.8 mL) cooled to 0 °C was added NIS (800 mg, 3.56 mmol, 2.0 equiv). The

Scheme 12. Construction of the Carbon Skeleton of Filipin III



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mixture was stirred at 0 °C in the absence of light for 6 h and then quenched by the addition of a saturated aqueous solution of $Na_2S_2O_3$ (20 mL). EtOAc (20 mL) was added; the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (Et_2O/acetone = 8:2 to 7:3) to afford iododiene **2** (476 mg, 1.42 mmol, 80%) as a yellow viscous foam. The spectral data are in agreement with those reported in the literature.[14] IR: ν 3007, 2958, 1753, 1698, 1616, 1458, 1336, 1285, 1247, 1154, 1119, 1083, 1023, 997, 954, 890, 872, 835 cm^{-1}; ^1H NMR (acetone-d6, 400 MHz): δ 7.15 (ddd, J = 14.4, J = 10.4 and J = 0.8 Hz, 1H), 6.67 (br d, J = 14.4 Hz, 1H), 6.53 (dd, J = 17.4 and J = 10.5 Hz, 1H), 5.77 (d, J = 17.4 Hz, 1H), 4.23 ($d_{AB\ syst}$, J = 16.8 Hz, 2H), 4.05 ($d_{AB\ syst}$, J = 16.8 Hz, 2H), 3.02 (s, 3H); ^{13}C NMR (acetone-d6, 100 MHz): δ 169.0 (2C), 148.3, 142.5, 82.1, 62.2 (2C), 47.4, C-B not visible.[44]

Synthesis of 4. *(R)-Isobutyl 2-(triethylsilyloxy)propanoate (3′).*[15] To a solution of (*R*)-isobutyl lactate **3** (7.1 g, 48.6 mmol, 1.0 equiv) in DMF (50 mL) were added imidazole (3.9 g, 57.3 mmol, 1.2 equiv) and TESCl (8.5 mL, 50 mmol, 1.1 equiv). The mixture was stirred at rt for 4.5 h and then quenched by addition of H_2O (20 mL). Et_2O (50 mL) was added; the layers were separated, and the aqueous layer was extracted with Et_2O (4 × 50 mL). The combined organic layers were washed with brine (2 × 10 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/Et_2O = 95:5) to afford the silyl ether **3′** (12.62 g, 48.5 mmol, quant) as a colorless oil. The spectral data are in agreement with those reported in the literature.[15] $[\alpha]_D^{20}$ 25.3 (*c* 0.04, $CHCl_3$); IR: ν 2956, 2877, 1756, 1459, 1141, 1002 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 4.32 (q, J = 6.7 Hz, 1H), 3.92 ($dd_{AB\ syst}$, J = 10.6 and J = 6.8 Hz, 1H), 3.87 ($dd_{AB\ syst}$, J = 10.6 and J = 6.7 Hz, 1H), 1.95 (hept, J = 6.7 Hz, 1H), 1.40 (d, J = 6.7 Hz, 3H), 0.98−0.90 (m, 15H), 0.62 (q, J = 8.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 174.2, 70.8, 68.1, 27.8, 21.6, 19.09, 19.07, 6.7 (3C), 4.6 (3C); MS (EI) *m*/*z*: 231 [(M-Et)$^+$, 3], 203 [(M-*i*Bu)$^+$, 11], 176 (14), 175 (100), 159 (40), 147 (22), 131 (TESO$^+$, 21), 119 (28), 115 (TES$^+$, 25), 103 (62), 87 (25), 75 (27), 59 (22), 58 (11), 57 (*i*Bu$^+$, 27).

(R)-2-(Triethylsilyloxy)propanal (4).[15] To a solution of previously synthesized ester **3′** (2.6 g, 10 mmol, 1.0 equiv) in dry Et_2O (40 mL) cooled to −78 °C was added dropwise a solution of DIBAL-H (15 mL, 1 M in hexanes, 15 mmol, 1.5 equiv) over a period of 20 min. The mixture was stirred for 3 h at −78 °C then quenched by the addition of H_2O (20 mL) and warmed to rt. The gel formed was dissolved by the addition of an aqueous solution of HCl (10% in weight). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/Et_2O = 95:5) to afford aldehyde **4** (1.74 g, 9.2 mmol, 92%) as a colorless oil. The spectral data are in agreement with those reported in the literature.[15] $[\alpha]_D^{20}$ 10 (*c* 1.56, $CHCl_3$) {for *ent*-**4**, $[\alpha]_D^{20}{}_{lit}$ −11.5 (*c* 1.55, $CHCl_3$)}[15b] IR: ν 2956, 2878, 1739, 1459, 1375, 1239, 1135, 1096, 1006 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.62 (d, J = 1.4 Hz, 1H), 4.08 (qd, J = 6.8 and J = 1.4 Hz, 1H), 1.29 (d, J = 6.8 Hz, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.64 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 204.3, 73.5, 18.6, 6.7 (3C), 4.7 (3C); MS (EI) *m*/*z*: 159 [(M-CHO)$^+$, 98], 131 (100), 115 (49), 103 (29), 87 (75), 75 (25), 59 (41).

(3S,4R)-4-(Triethylsilyloxy)pent-1-en-3-ol (5). To a solution of vinylmagnesium bromide (10.8 mL, 1 M in THF, 10.8 mmol, 1.2 equiv) in dry THF (15 mL) cooled to −60 °C was cannulated a solution of aldehyde **4** (1.7 g, 9.0 mmol, 1.0 equiv) in dry THF (10 mL). The mixture was stirred at −60 °C for 30 min then warmed to rt and stirred for 3 h. The reaction mixture was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL) and H_2O (20 mL). Et_2O (30 mL) was added; the layers were separated, and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 98:2) to afford the alcohols **5** and **5′** as a mixture of diastereomers in an 80:20 ratio (1.84 g, 8.5 mmol, 94%) as a colorless oil. The spectral data are in agreement with those reported in the literature.[15a] Separation of the two diastereomers by flash column chromatography on silica gel (CH_2Cl_2) afforded pure **5**. $[\alpha]_D^{20}$ −21.7 (*c* 1.02, $CHCl_3$); IR: ν 3462, 3080, 2956, 2912, 2878, 1459, 1416, 1379, 1239, 1130, 1093, 1005, 972, 933 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.82 (ddd, J = 17.3, J = 10.5 and J = 6.1 Hz, 1H), 5.30 (dt_{app}, J = 17.3 and J = 1.6 Hz, 1H), 5.19 (dt_{app}, J = 10.5 and J = 1.5 Hz, 1H), 4.05 (m, 1H), 3.86 (qd, J = 6.3 and J = 3.6 Hz, 1H), 2.36 (br d, J = 4.0 Hz, 1H, OH), 1.09 (d, J = 6.3 Hz, 3H), 0.97 (t, J = 7.9 Hz, 9H), 0.62 (q, J = 7.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.6, 116.5, 76.7, 71.1, 17.5, 6.9 (3C), 4.9 (3C); MS (EI) *m*/*z*: 198 [(M-H_2O)$^+$, 1], 187 [(M-Et)$^+$, 32], 159 (30), 131 (26), 115 (51), 103 (100), 87 (54), 75 (77), 59 (24).

(3S,4R)-4-(Triethylsilyloxy)-3-[(trimethylsilylethoxy)methyloxy]-pent-1-ene (6). To a solution of alcohol **5** (1.25 g, 5.77 mmol, 1.0 equiv) in dry CH_2Cl_2 (24 mL) were added *i*Pr_2NEt (2.4 mL, 14.5 mmol, 2.5 equiv), *n*-Bu_4NI (1.07 g, 2.9 mmol, 0.5 equiv), and SEMCl (1.53 mL, 8.64 mmol, 1.5 equiv). The mixture was stirred at rt for 16 h and then quenched by the addition of H_2O (30 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 45 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/Et_2O = 99:1) to afford acetal **6** (2.0 g, 5.77 mmol, quant) as a colorless oil. $[\alpha]_D^{20}$ 51.4 (*c* 1.04, $CHCl_3$); IR: ν 3079, 2955, 2878, 1684, 1459, 1416, 1377, 1249, 1107, 1031, 1010, 925, 860 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.73 (ddd, J = 16.8, J = 11.1 and J = 7.5 Hz, 1H), 5.26−5.19 (m, 2H), 4.69 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.64 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 3.87−3.78 (m, 2H), 3.74−3.50 (m, 2H), 1.15 (d, J = 6.1 Hz, 3H), 0.94 (t, J = 7.9 Hz, 9H), 0.98−0.88 (m, 2H), 0.58 (q, J = 7.9 Hz, 6H), 0.01 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 135.8, 118.7, 92.4, 81.7, 70.8, 65.2, 20.0, 18.2, 7.0 (3C), 5.1 (3C), −1.3 (3C); MS (EI) *m*/*z*: 309 (1), 287 (1), 273 [(M-TMS)$^+$, 1], 259 (10), 215 (8), 199 (20), 175 (10), 159 (67), 147 (10), 131 (40), 115 (63), 103 (32), 87 (35), 73 (100), 59 (17); HRMS (ESI): calculated for $C_{17}H_{38}O_3Si_2Na$ [M + Na]$^+$: 369.2252, found: 369.2251.

(E)-(2-Iodovinyl)boronic Acid MIDA Ester (8).[14] To a suspension of alkyne **7** (2.5 g, 13.8 mmol, 1.0 equiv) in dry THF (60 mL) were added AIBN (227 mg, 1.38 mmol, 0.1 equiv) and Bu_3SnH (5.6 mL, 20.8 mmol, 1.5 equiv). The mixture was heated at reflux for 16 h, and then AIBN (227 mg, 1.38 mmol, 0.1 equiv) and Bu_3SnH (5.6 mL, 20.8 mmol, 1.5 equiv) were added again. After 8 h of reflux, the solution was cooled to −78 °C, and a solution of I_2 (7.0 g, 27.6 mmol, 2.0 equiv) in dry THF (40 mL) was added dropwise over 1 h. The mixture was stirred at −78 °C, progressively warmed to rt overnight, and then quenched by the addition of a saturated aqueous solution of $Na_2S_2O_3$ (40 mL). EtOAc (50 mL) was added; the layers were separated, and the aqueous layer was extracted with EtOAc (2 × 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The resulting solid was suspended in Et_2O, filtered, and washed with additional Et_2O to give the vinyl iodide **8** (3.07 g, 9.9 mmol, 72%) as a white solid. The spectral data are in agreement with those reported in the literature.[14] Mp: 163−165 °C (lit.:[14] 145 °C); IR: ν 3005, 2961, 1745, 1708, 1569, 1451, 1336, 1283, 1184, 1154, 1104, 1077, 1022, 1005, 965, 952, 893 cm^{-1}; ^1H NMR (acetone-d6, 400 MHz): δ 6.91 (d, J = 15.6 Hz, 1H), 6.82 (d, J = 15.6 Hz, 1H), 4.27 ($d_{AB\ syst}$, J = 16.9 Hz, 2H), 4.11 ($d_{AB\ syst}$, J = 16.9 Hz, 2H), 3.08 (s, 3H); ^{13}C NMR (acetone-d6, 100 MHz): δ 168.6 (2C), 90.2, 62.6 (2C), 47.6, C-B not visible.[44]

[(1E,3E)-4-(Trimethylsilyl)buta-1,3-dien-1-yl]boronic Acid MIDA Ester (9).[14] To a solution of vinyl iodide **8** (1.0 g, 3.24 mmol, 1.0 equiv) in anhydrous MeCN (22 mL) in a vial were added AgOAc (810 mg, 4.85 mmol, 1.5 equiv), $Pd(OAc)_2$ (36 mg, 0.16 mmol, 0.05 equiv), and vinyltrimethylsilane (0.71 mL, 4.82 mmol, 1.5 equiv). The vial was sealed, and the mixture was heated at 80 °C for 14 h. The mixture was then cooled to rt, transferred into a flask containing Celite using

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acetone, and concentrated under vacuum to give a gray powder. Purification of the crude material by flash column chromatography on silica gel (solid loading, Et_2O/acetone = 10:0 to 8:2) afforded the desired diene **9** as an unseparable mixture with the branched isomer **9′** in an 8:2 ratio (660 mg, 2.35 mmol, 72%) as a beige solid. The spectral data are in agreement with those reported in the literature.[14] Mp: 205−207 °C (lit.:[14] 210 °C); IR (mixture of isomers): ν 3016, 2956, 2899, 1753, 1624, 1572, 1462, 1333, 1294, 1246, 1175, 1155, 1118, 1083, 1000, 966, 952, 851 cm^{-1}; ^1H NMR (acetone-d6, 400 MHz, major isomer): δ 6.66−6.52 (m, 2H), 5.92 (d, J = 17.9 Hz, 1H), 5.74 (d, J = 17.0 Hz, 1H), 4.22 ($d_{AB\ syst}$, J = 16.8 Hz, 2H), 4.04 ($d_{AB\ syst}$, J = 16.8 Hz, 2H), 3.01 (s, 3H), 0.08 (s, 9H); ^{13}C NMR (acetone-d6, 100 MHz, major isomer): δ 169.0 (2C), 147.3, 145.9, 135.1, 62.3 (2C), 47.4, −1.3 (3C), C-B not visible.[44]

*{(1E,3E,5E,7S,8R)-8-(Triethylsilyloxy)-7-{[2-(trimethylsilyl)ethoxy]-methoxy}nona-1,3,5-trien-1-yl}boronic Acid MIDA Ester (**10**).* To a solution of vinyl iodide **2** (330 mg, 0.98 mmol, 1.0 equiv) in anhydrous MeCN (11.2 mL) in a vial were added the protected allylic alcohol **6** (1.70 g, 4.9 mmol, 5.0 equiv), AgOAc (246 mg, 1.48 mmol, 1.5 equiv), and $Pd(OAc)_2$ (11 mg, 0.05 mmol, 0.05 equiv). The vial was sealed, and the mixture was heated at 50 °C for 14 h. The mixture was then cooled to rt, diluted with acetone, transferred into a flask containing Celite, and concentrated under vacuum to give a gray powder. Purification of the crude material by flash column chromatography on silica gel (solid loading, Et_2O/acetone = 10:0 to 8:2) afforded the desired triene **10** contamined with traces of another unidentified isomer (95% purity, 238 mg, 0.43 mmol, 44%) as a yellow oil. $[\alpha]_D^{20}$ 78.9 (c 1.0, acetone); IR: ν 2956, 2879, 1769, 1623, 1586, 1461, 1379, 1340, 1299, 1250, 1196, 1110, 1028, 990, 959, 863, 838 cm^{-1}; ^1H NMR (acetone-d6, 400 MHz): δ 6.62 (br dd, J = 17.3 and J = 9.4 Hz, 1H), 6.40−6.25 (m, 3H), 5.74 (m, 1H), 5.73 (d, J = 17.4 Hz, 1H), 4.64 (br s, 2H), 4.21 ($d_{AB\ syst}$, J = 16.9 Hz, 2H), 4.03 ($dd_{AB\ syst}$, J = 16.9 and J = 1.4 Hz, 2H), 3.94−3.87 (m, 2H), 3.73 (td, J = 9.5 and J = 7.4 Hz, 1H), 3.57 (td, J = 9.1 and J = 7.4 Hz, 1H), 2.99 (s, 3H), 1.13 (d, J = 6.0 Hz, 3H), 0.96 (t, J = 8.0 Hz, 9H), 0.98−0.89 (m, 2H), 0.61 (q, J = 8.0 Hz, 6H), 0.03 (s, 9H); ^{13}C NMR (acetone-d6, 100 MHz): δ 169.0 (2C), 143.2, 135.8, 134.6, 133.7, 132.8, 92.8, 81.4, 71.6, 65.4, 62.3 (2C), 47.3, 20.5, 18.5, 7.2 (3C), 5.5 (3C), −1.3 (3C), C-B not visible;[44] HRMS (ESI): calculated for $C_{26}H_{48}BNO_7Si_2Na$ $[M + Na]^+$: 576.2955, found: 576.2952.

*(2E,4E,6E,8E,10E,12S,13R)-Ethyl-2-methyl-13-(triethylsilyloxy)-12-{[2-(trimethylsilyl) ethoxy]-methoxy}tetradeca-2,4,6,8,10-pentaenoate (**12**).* To a solution of triene **10** (160 mg, 0.29 mmol, 1.0 equiv) in a mixture of THF (2.1 mL) and MeOH (0.7 mL) was added MeONa (78 mg, 1.44 mmol, 5.0 equiv). The mixture was stirred at rt in the dark for 1 h, and then a solution of I_2 (220 mg, 0.87 mmol, 3.0 equiv) in dry THF (2.1 mL) was added. The mixture was stirred at rt in the dark for 2.5 h, and then a pH 7 buffer (5 mL) was added. The mixture was diluted with Et_2O (5 mL); the layers were separated, and the organic layer was washed with a saturated aqueous solution of $Na_2S_2O_3$ (5 mL). The aqueous layer was then extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the iodotriene **11**, which was not purified but directly involved in the next step.

To the unpurified iodotriene **11** were added K_2CO_3 (80 mg, 0.58 mmol, 2.0 equiv), $Pd(OAc)_2$ (3.3 mg, 0.015 mmol, 0.05 equiv), and n-Bu_4Br (93 mg, 0.29 mmol, 1.0 equiv). The mixture was degassed under vacuum and refilled with argon three times. The ester **1** (61 mg, 0.435 mmol, 1.5 equiv) and DMF (3 mL) were then added, and the mixture was stirred in the dark, heated at 50 °C for 16 h, and then cooled to rt. Et_2O (5 mL) was added followed by a saturated aqueous solution of NaCl (5 mL). The layers were separated, and the aqueous layer was then extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification of the crude material by flash column chromatography on silica gel (pentane/Et_2O = 95:5) afforded the pentaenic ester **12** (89 mg, 0.166 mmol, 57%) as a bright yellow oil. $[\alpha]_D^{20}$ 112.6 (c 1.0, $CHCl_3$); IR: ν 3022, 2954, 2877, 1702, 1620, 1577, 1458, 1415, 1367, 1241, 1219, 1162, 1140, 1101, 1028, 1003, 937, 920, 860, 836 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 7.51 (dq, J = 11.0 and J = 1.4 Hz, 1H), 6.42−6.08 (m, 7H), 5.85 (dd, J = 15.3 and J = 7.9 Hz, 1H), 4.85 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.72 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.14 (br dd, J = 7.9 and J = 4.8 Hz, 1H), 4.10 (q, J = 7.1 Hz, 2H), 4.01 (qd, J = 6.2 and J = 4.6 Hz, 1H), 3.86 (m, 1H), 3.61 (m, 1H), 1.98 (d, J = 1.3 Hz, 3H), 1.30 (d, J = 6.2 Hz, 3H), 1.07 (t, J = 8.0 Hz, 9H), 1.08−0.98 (m, 2H), 1.03 (t, J = 7.1 Hz, 3H), 0.68 (q, J = 8.2 Hz, 6H), 0.03 (s, 9H); ^{13}C NMR (C_6D_6, 100 MHz): δ 167.9, 139.5, 138.3, 136.3, 134.6, 134.4, 133.3, 132.9, 128.5 (2C), 127.7, 92.6, 81.2, 71.4, 65.3, 60.5, 20.7, 18.3, 14.4, 13.1, 7.2 (3C), 5.5 (3C), −1.3 (3C); HRMS (ESI): calculated for $C_{29}H_{52}O_5Si_2Na$ $[M + Na]^+$: 559.3246, found: 559.3238.

*(2E,4E,6E,8E,10E,12S,13R)-2-Methyl-13-(triethylsilyloxy)-12-{[2-(trimethylsilyl)ethoxy] methoxy}tetradeca-2,4,6,8,10-pentaenal (**13**).* To a solution of ester **12** (69 mg, 128 μmol, 1.0 equiv) in dry CH_2Cl_2 (2.4 mL) cooled to −78 °C was added DIBAL-H (0.39 mL, 1 M in toluene, 0.39 mmol, 3.0 equiv) dropwise. The mixture was stirred at −78 °C in the dark for 20 min, and then MeOH (1 mL) was added. The mixture was poured into a saturated aqueous solution of Rochelle's salt (20 mL) and stirred at rt in the dark for 2 h. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the allylic alcohol, which was not purified but directly engaged in the next step.

To a solution of crude allylic alcohol in dry CH_2Cl_2 (4.5 mL) was added freshly prepared MnO_2 (110 mg, 1.27 mmol, 10 equiv). The mixture was stirred at rt in the dark for 2.5 h and then filtered through a pad of Celite. The filtrate was concentrated under vacuum and then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 95:5) to afford the pentaenic aldehyde **13** (34 mg, 69 μmol, 54%) as a bright yellow oil. $[\alpha]_D^{20}$ 129.6 (c 1.0, CH_3CN); IR: ν 2953, 2877, 1678, 1667, 1618, 1573, 1459, 1408, 1378, 1361, 1248, 1198, 1177, 1097, 1003, 937, 859, 835 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 9.39 (s, 1H), 6.42−6.12 (m, 7H), 6.05 (dd, J = 14.2 and J = 10.1 Hz, 1H), 5.88 (dd, J = 15.1 and J = 7.9 Hz, 1H), 4.84 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.71 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.13 (dd, J = 7.7 and J = 4.6 Hz, 1H), 3.99 (qd, J = 6.2 and J = 4.7 Hz, 1H), 3.84 (m, 1H), 3.61 (m, 1H), 1.77 (br s, 3H), 1.29 (d, J = 6.2 Hz, 3H), 1.06 (t, J = 8.0 Hz, 9H), 0.99 (t_{app}, J = 8.0 Hz, 2H), 0.67 (q, J = 8.0 Hz, 6H), 0.02 (s, 9H); ^{13}C NMR (C_6D_6, 100 MHz): δ 193.3, 147.2, 140.7, 137.9, 137.5, 135.2, 134.4, 133.7, 133.0, 132.9, 127.9, 92.7, 81.1, 71.4, 65.4, 20.7, 18.3, 9.7, 7.2 (3C), 5.5 (3C), −1.3 (3C); HRMS (ESI): calculated for $C_{27}H_{48}O_4Si_2Na$ $[M + Na]^+$: 515.2983, found: 515.2981.

*(E)-(S)-3-(But-2-enoyl)-4-isopropyl-5,5-dimethyloxazolidin-2-one (**15**).*[27] To a solution of oxazolidinone **14** (2.0 g, 12.7 mmol, 1.0 equiv) in dry THF (40 mL) cooled to −78 °C was added n-BuLi (5.08 mL, 2.5 M in hexanes, 12.7 mmol, 1.0 equiv). The mixture was stirred at −78 °C for 15 min, and then crotonyl chloride (1.34 mL, 14.0 mmol, 1.1 equiv) was added dropwise. The mixture was stirred at −78 °C for 1 h, then at 0 °C for 1.5 h, and quenched by the addition of a saturated aqueous solution of NH_4Cl (40 mL). Et_2O (40 mL) was added, and the layers were separated. The organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and then with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether:EtOAc = 90:10) to afford acyloxazolidonone **15** (2.46 g, 10.9 mmol, 86%) as a white solid. The spectral data are in agreement with those reported in the literature.[21] Mp: 66−68 °C (lit.:[21] 69−70 °C); $[\alpha]_D^{20}$ 58.2 (c 1.0, $CHCl_3$); $[\alpha]_D^{20}{}_{lit}$ 52 (c 1.0, $CHCl_3$);[21c] IR: ν 2971, 2935, 2880, 1753, 1686, 1633, 1447, 1390, 1375, 1361, 1336, 1314, 1298, 1279, 1219, 1174, 1126, 1072, 1032, 974, 924, 832 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.32 (br d, J = 15.3 Hz, 1H), 7.15 (m, 1H), 4.22 (br d, J = 3.4 Hz, 1H), 2.16 (m, 1H), 1.96 (br d, J = 6.8 Hz, 3H), 1.52 (s, 3H), 1.39 (s, 3H), 1.04 (d, J = 7.0 Hz, 3H), 0.96 (d, J = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 165.8, 153.7, 146.7, 122.1, 82.9, 66.4, 29.8, 28.9, 21.6, 21.5, 18.6, 17.2; MS (EI) m/z: 225 ($M^{+\cdot}$, 2), 210 [(M-Me)$^+$, 2], 182 (9), 70 (7), 69 (100).

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*(S)-3-[(2S,3R)-3-Hydroxy-2-vinyloctanoyl]-4-isopropyl-5,5-dimethyloxazolidin-2-one (**16**).* To a solution of acyloxazolidinone **15** (2.04 g, 9.06 mmol, 1.0 equiv) in dry CH_2Cl_2 (36 mL) cooled to −78 °C was added Bu_2BOTf (10 mL, 1 M in CH_2Cl_2, 10 mmol, 1.1 equiv). The mixture was stirred at −78 °C for 5 min, and then Et_3N (1.76 mL, 12.66 mmol, 1.4 equiv) was added. After being stirred for 1 h at −78 °C, the temperature was raised to 0 °C for 15 min and finally cooled to −78 °C. Hexanal (1.67 mL, 13.59 mmol, 1.5 equiv) was added, and the mixture was stirred at −78 °C, progressively warmed to 0 °C over a period of 5 h, and then quenched by addition of an aqueous solution of NH_4Cl (125 mL). A 1:1 mixture of petroleum ether and EtOAc (125 mL) was added, and the layers were separated. The organic layer was washed with brine and then concentrated under vacuum. The residue was dissolved in Et_2O (75 mL) and cooled to 0 °C. A pH 7 buffer solution (20 mL) and H_2O_2 (30% in weight, 20 mL) were added. The mixture was progressively warmed to rt and stirred for 2 h. H_2O (200 mL) was then added followed by the addition of a 1:1 mixture of petroleum ether and EtOAc (200 mL). The layers were separated, and the organic layer was washed with a saturated aqueous solution of $NaHCO_3$ and then with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:10) to afford aldol **16** (2.76 g, 8.48 mmol, 94%) as a single diastereomer and as a colorless oil. $[\alpha]_D^{20}$ −28.2 (*c* 1.0, $CHCl_3$); IR: ν 3505, 2959, 2933, 2861, 1771, 1691, 1634, 1466, 1394, 1363, 1312, 1279, 1217, 1172, 1119, 1069, 996, 963, 929 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.99 (ddd, *J* = 17.2, *J* = 10.2 and *J* = 9.1 Hz, 1H), 5.47 (br d, *J* = 17.2 Hz, 1H), 5.38 (dd, *J* = 10.2 and *J* = 1.5 Hz, 1H), 4.64 (dd, *J* = 9.0 and *J* = 3.7 Hz, 1H), 4.21 (d, *J* = 3.1 Hz, 1H), 3.95 (m, 1H), 3.08 (br d, *J* = 1.7 Hz, 1H, OH), 2.13 (heptd, *J* = 6.9 Hz, *J* = 3.1 Hz, 1H), 1.52 (s, 3H), 1.54−1.40 (m, 2H), 1.41 (s, 3H), 1.38−1.24 (m, 6H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.88 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.2, 153.2, 131.9, 121.7, 82.9, 71.7, 66.1, 52.2, 34.1, 31.9, 30.0, 28.9, 25.4, 22.7, 21.6, 21.4, 16.8, 14.2; MS (EI) *m*/*z*: 225 (2), 210 (1), 182 (4), 181 (3), 114 (33), 98 (6), 97 (9), 96 (10), 88 (9), 70 (37), 69 (100), 68 (28), 55 (20); HRMS (ESI): calculated for $C_{18}H_{31}NO_4Na$ $[M + Na]^+$: 348.2145, found: 348.2143.

*(S)-4-Isopropyl-3-[(2S,3R)-3-(methoxymethoxy)-2-vinyloctanoyl]-5,5-dimethyloxazolidin-2-one (**17**).* To a solution of alcohol **16** (1.2 g, 3.69 mmol, 1.0 equiv) in dry CH_2Cl_2 (40 mL) were added iPr_2NEt (3.7 mL, 22.3 mmol, 6.0 equiv) and MOMCl (1.1 mL, 14.9 mmol, 4.0 equiv) dropwise. The mixture was stirred at rt for 18 h and then quenched by the addition of H_2O (20 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 90:10) to afford the protected alcohol **17** (1.31 g, 35.4 mmol, 96%) as a colorless oil. $[\alpha]_D^{20}$ 53.6 (*c* 1.01, $CHCl_3$); IR: ν 2932, 1771, 1695, 1637, 1466, 1394, 1362, 1312, 1278, 1217, 1170, 1118, 1096, 1068, 1035, 998, 964, 919, 859 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 6.02 (ddd, *J* = 17.3, *J* = 10.1 and *J* = 9.0 Hz, 1H), 5.33 (br d, *J* = 17.3 Hz, 1H), 5.27 (dd, *J* = 10.1 and *J* = 1.5 Hz, 1H), 4.83 (dd, *J* = 8.9 and *J* = 5.8 Hz, 1H), 4.65 ($d_{AB\ syst}$, *J* = 7.1 Hz, 1H), 4.57 ($d_{AB\ syst}$, *J* = 7.1 Hz, 1H), 4.15 (d, *J* = 3.3 Hz, 1H), 3.88 (m, 1H), 3.34 (s, 3H), 2.15 (heptd, *J* = 6.9 and *J* = 3.2 Hz, 1H), 1.58−1.50 (m, 2H), 1.51 (s, 3H), 1.42 (s, 3H), 1.36−1.21 (m, 6H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.8, 153.5, 134.0, 119.7, 96.6, 82.8, 79.4, 66.7, 56.1, 51.6, 32.9, 32.0, 29.8, 28.6, 25.2, 22.7, 21.58, 21.53, 17.1, 14.2; MS (EI) *m*/*z*: 279 (17), 278 (78), 277 (7), 202 (18), 201 (100), 200 (25), 199 (44), 181 (15), 155 (15), 154 (98), 153 (9), 152 (16), 149 (6), 124 (6), 123 (8), 77 (8), 51 (14); HRMS (ESI): calculated for $C_{20}H_{35}NO_5Na$ $[M + Na]^+$: 392.2407, found: 392.2409.

*(S)-3-{(2S,3R)-2-[(S)-1-Hydroxybut-3-en-1-yl]-3-(methoxymethoxy)octanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one (**19**).* To a solution of alkene **17** (1.06 g, 2.87 mmol, 1.0 equiv) in a mixture of dry CH_2Cl_2 (14 mL) and anhydrous MeOH (14 mL) were added 2,6-lutidine (0.17 mL, 1.46 mmol, 0.5 equiv) and a trace of Sudan III dye. Ozone was bubbled through the pink solution, cooled to −78 °C until the color of the dye faded. The reaction mixture was replaced under oxygen and then under an argon atmosphere. Me_2S (2.1 mL, 28.4 mmol, 10 equiv) was added, and the mixture was warmed to rt and stirred for 1.25 h. Petroleum ether (15 mL) and H_2O (15 mL) were added, and the layers were separated. The organic layer was washed with a saturated aqueous solution of $CuSO_4$, then with H_2O, and then with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford aldehyde **18**, which was not purified but directly engaged in the next step.

To a suspension of $ZnCl_2$ (586 mg, 4.30 mmol, 1.5 equiv) in dry THF (14 mL) cooled to 0 °C was added allylmagnesium chloride (3.3 mL, 2 M in THF, 6.6 mmol, 2.3 equiv). The mixture was stirred at 0 °C for 5 min, then at rt for 30 min, then cooled to −78 °C, and a solution of crude aldehyde **18** in dry THF (15 mL) was cannulated. The mixture was stirred at −78 °C, progressively warmed to −40 °C over 1 h, and stirred at this temperature for 2.5 h. The reaction mixture was quenched by the addition of a saturated aqueous solution of NH_4Cl (30 mL), warmed to rt, and diluted with EtOAc (30 mL) and H_2O (20 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 98:2 to 90:10) to afford the homoallylic alcohol **19** (870 mg, 2.10 mmol, 73%) as a single diastereomer and a white solid. Mp: 75−77 °C; $[\alpha]_D^{20}$ 75.7 (*c* 1.05, $CHCl_3$); IR: ν 3669, 3477, 2958, 2931, 1774, 1691, 1642, 1467, 1395, 1377, 1362, 1312, 1278, 1217, 1172, 1119, 1068, 1022, 968, 915, 859 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.90 (m, 1H), 5.20−5.14 (m, 2H), 4.68 ($d_{AB\ syst}$, *J* = 7.1 Hz, 1H), 4.50 ($d_{AB\ syst}$, *J* = 7.1 Hz, 1H), 4.49 (dd, *J* = 7.9 and *J* = 6.1 Hz, 1H), 4.15 (d, *J* = 3.1 Hz, 1H), 4.14−4.07 (m, 2H), 3.37 (s, 3H), 2.46 (d, *J* = 4.3 Hz, 1H, OH), 2.40 (m, 1H), 2.28 (m, 1H), 2.15 (heptd, *J* = 6.8 and *J* = 3.1 Hz, 1H), 1.71 (m, 1H), 1.51 (s, 3H), 1.47−1.37 (m, 2H), 1.41 (s, 3H), 1.35−1.20 (m, 5H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.9, 154.0, 134.4, 118.9, 96.2, 83.0, 77.5, 70.2, 67.2, 56.3, 50.5, 39.5, 32.0, 31.9, 29.8, 28.3, 25.5, 22.8, 21.8, 21.5, 17.2, 14.2; MS (EI) *m*/*z*: 281 (2), 238 (3), 210 (4), 199 (3), 158 (6), 126 (8), 125 (89), 124 (10), 114 (7), 97 (15), 81 (14), 68 (16), 55 (100); HRMS (ESI): calculated for $C_{22}H_{39}NO_6Na$ $[M + Na]^+$: 436.2670, found: 436.2670.

*(S)-3-{(2R,3R)-3-Hydroxy-2-[(S)-1-hydroxybut-3-en-1-yl]-octanoyl}-4-isopropyl-5,5-dimethyloxazolidin-2-one (**19′**).* To a solution of ether **19** (60 mg, 0.144 mmol, 1 equiv) in dry CH_2Cl_2 (6 mL) cooled to −30 °C was added TMSBr (75 μL, 0.57 mmol, 4.0 equiv). The mixture was stirred at −30 °C, progressively warmed to −20 °C, and stirred for 1 h. A saturated aqueous solution of $NaHCO_3$ (5 mL) was added; the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification of the crude material by flash column chromatography on silica gel (petroleum ether/EtOAc = 80:20) afforded the corresponding diol **19′** (42 mg, 0.114 mmol, 79%) as a colorless oil. $[\alpha]_D^{20}$ 36.3 (*c* 1.1, $CHCl_3$); IR: ν 3447, 2958, 2933, 2873, 1770, 1688, 1643, 1466, 1394, 1363, 1314, 1278, 1217, 1174, 1121, 1072, 996, 964, 915, 860 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.90 (m, 1H), 5.21−5.15 (m, 2H), 4.32 (t_{app}, *J* = 7.4 Hz, 1H), 4.21 (m, 1H), 4.20 (d, *J* = 2.7 Hz, 1H), 4.13 (m, 1H), 3.25 (br s, 1H, OH), 3.04 (br s, 1H, OH), 2.41 (m, 1H), 2.34 (m, 1H), 2.16 (heptd, *J* = 7.1 and *J* = 2.7 Hz, 1H), 1.53 (s, 3H), 1.50−1.42 (m, 2H), 1.40 (s, 3H), 1.38−1.20 (m, 6H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.4, 154.0, 134.2, 119.0, 83.0, 73.3, 72.6, 66.9, 53.4, 39.8, 34.8, 31.8, 29.9, 28.8, 25.5, 22.7, 21.7, 21.5, 17.1, 14.1; MS (EI) *m*/*z*: 251 (1), 210 (16), 114 (16), 97 (18), 96 (10), 95 (100), 94 (16), 70 (11), 67 (56), 66 (20), 65 (11), 55 (18); HRMS (ESI): calculated for $C_{20}H_{35}NO_5Na$ $[M + Na]^+$: 392.2407, found: 392.2408.

*(S)-3-[(4S,5R,6R)-4-Allyl-2,2-dimethyl-6-pentyl-1,3-dioxane-5-carbonyl]-4-isopropyl-5,5-dimethyloxazolidin-2-one (**19″**).* To a solution of diol **19′** (32 mg, 0.087 mmol, 1 equiv) in a mixture of acetone

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(1 mL) and 2,2-dimethoxypropane (0.5 mL) was added PPTS (2.2 mg, 8.8 μmol, 0.1 equiv). The mixture was stirred at rt for 4 h and then quenched by addition of one drop of Et_3N. Evaporation of the solvents and purification of the crude material by flash column chromatography (petroleum ether/EtOAc = 95:5) afforded acetonide **19″** (33 mg, 0.081 mmol, 93%) as a colorless oil. $[\alpha]_D^{20}$ 27.6 (*c* 1.0, $CHCl_3$); IR: ν 3077, 2933, 1774, 1685, 1643, 1465, 1429, 1392, 1362, 1310, 1276, 1217, 1201, 1170, 1120, 1068, 1019, 999, 963, 947, 912, 865 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.89 (m, 1H), 5.05 (br d, *J* = 17.1 Hz, 1H), 5.04 (br d, *J* = 11.2 Hz, 1H), 4.20 (d, *J* = 2.4 Hz, 1H), 4.15 (td_{app}, *J* = 9.0 and *J* = 2.4 Hz, 1H), 4.07−3.99 (m, 2H), 2.40 (m, 1H), 2.26−2.14 (m, 2H), 1.53 (s, 3H), 1.49 (s, 3H), 1.47 (m, 1H), 1.41 (s, 3H), 1.38 (s, 3H), 1.30−1.16 (m, 7H), 1.04 (d, *J* = 7.0 Hz, 3H), 0.99 (d, *J* = 6.9 Hz, 3H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 173.3, 153.1, 134.5, 116.9, 98.8, 82.5, 72.3, 71.7, 66.7, 49.1, 38.7, 34.4, 31.8, 30.0, 29.9, 28.9, 24.8, 22.6, 21.8, 21.5, 19.7, 17.1, 14.2; MS (EI) *m*/*z*: 394 [(M-Me)$^+$, 15], 334 (5), 310 (13), 290 (8), 252 (11), 251 (10), 210 (17), 158 (42), 125 (31), 114 (27), 98 (10), 97 (42), 96 (11), 95 (55), 94 (15), 88 (29), 83 (14), 82 (14), 81 (20), 79 (13), 71 (20), 70 (24), 69 (19), 68 (11), 67 (56), 66 (11), 59 (24), 58 (29), 57 (29), 56 (27), 55 (100), 54 (18), 53 (10); HRMS (ESI): calculated for $C_{23}H_{39}NO_5Na$ [M + Na]$^+$: 432.2720, found: 432.2722.

*(4S,5R,6R)-4-(tert-Butyldiphenylsilyloxy)-5-[(tert-butyldiphenylsilyloxy)methyl]-6-(methoxymethoxy)undec-1-ene (**20**).* To a solution of carbamate **19** (0.7 g, 1.69 mmol, 1.0 equiv) in toluene (30 mL) cooled to −30 °C was added $LiAlH_4$ (3.4 mL, 1 M in THF, 3.4 mmol, 2.0 equiv). The mixture was stirred at −30 °C and progressively warmed to −10 °C. After 1 h, a saturated aqueous solution of Rochelle's salt (30 mL) was added. The mixture was warmed to rt; Et_2O (30 mL) was added, and the mixture was stirred at rt for 3 h. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the corresponding diol, which was not purified but directly engaged in the next step.

To a solution of crude diol in dry CH_2Cl_2 (30 mL) cooled to 0 °C were added 2,6-lutidine (1.0 mL, 8.6 mmol, 5.0 equiv) and TBDPSOTf (1.67 g, 4.3 mmol, 2.5 equiv) dropwise. The mixture was warmed to rt, stirred for 18 h, and then quenched by the addition of H_2O (15 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 99:1 to 98:2) to afford the silyl ether **20** (0.79 g, 1.07 mmol, 63%) as a viscous colorless oil.

$[\alpha]_D^{20}$ 43.5 (*c* 2.0, $CHCl_3$); IR: ν 3072, 2955, 2930, 2891, 2857, 1640, 1590, 1472, 1428, 1390, 1361, 1261, 1217, 1190, 1106, 1036, 999, 917, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.73−7.66 (m, 4H), 7.64−7.60 (m, 4H), 7.43−7.30 (m, 12H), 5.45 (ddt, *J* = 17.2, *J* = 10.2 and *J* = 7.1 Hz, 1H), 4.81 (br d, *J* = 10.2 Hz, 1H), 4.73 (br d, *J* = 17.3 Hz, 1H), 4.38 ($d_{AB\ syst}$, *J* = 6.9 Hz, 1H), 4.29 (m, 1H), 4.27 ($d_{AB\ syst}$, *J* = 6.9 Hz, 1H), 4.02 (dd, *J* = 10.1 and *J* = 7.6 Hz, 1H), 3.89−3.83 (m, 2H), 3.23 (s, 3H), 2.35 (m, 1H), 2.14 (m, 1H), 1.85 (m, 1H), 1.73 (m, 1H), 1.37−1.12 (m, 7H), 1.05 (s, 9H), 1.01 (s, 9H), 0.85 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.23 (2C), 136.18 (2C), 135.9 (2C), 135.8 (2C), 135.4, 134.6, 133.9 (2C), 133.7, 129.8, 129.7, 129.64, 129.58, 127.72 (2C), 127.70 (2C), 127.69 (2C), 127.5 (2C), 116.9, 95.3, 75.8, 71.4, 60.0, 55.7, 47.1, 39.3, 32.2, 32.1, 27.3 (3C), 27.1 (3C), 26.1, 22.9, 19.6, 19.3, 14.3; HRMS (ESI): calculated for $C_{46}H_{64}O_4Si_2Na$ [M + Na]$^+$: 759.4235, found: 759.4237.

*(3S,4R,5R)-3-(tert-Butyldiphenylsilyloxy)-4-[(tert-butyldiphenylsilyloxy)methyl]-5-(methoxymethoxy)decanal (**21**).* To a solution of alkene **20** (188 mg, 0.255 mmol, 1.0 equiv) in dry CH_2Cl_2 (11 mL) was added a trace of Sudan III dye. Ozone was bubbled through the pink solution that was cooled to −78 °C until the color of the dye faded. The reaction mixture was placed under oxygen and then under an argon atmosphere. PPh_3 (100 mg, 0.381 mmol, 1.5 equiv) was added, and the mixture was progressively warmed to rt overnight. The reaction mixture was dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 95:5) to afford aldehyde **21** (178 mg, 0.241 mmol, 95%) as a pink oil. $[\alpha]_D^{20}$ −12.8 (*c* 1.01, $CHCl_3$); IR: ν 3071, 3049, 2955, 2931, 2892, 2858, 2717, 1728, 1590, 1472, 1428, 1390, 1362, 1261, 1212, 1147, 1110, 1035, 920, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 9.29 (dd, *J* = 2.6 and *J* = 1.9 Hz, 1H), 7.68−7.59 (m, 8H), 7.45−7.31 (m, 12H), 4.65 (m, 1H), 4.40 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.38 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 3.90 (br d, *J* = 5.5 Hz, 2H), 3.79 (td, *J* = 5.9 and *J* = 5.3 Hz, 1H), 3.13 (s, 3H), 2.69 ($ddd_{AB\ syst}$, *J* = 16.5, *J* = 4.2 and *J* = 1.8 Hz, 1H), 2.51 ($ddd_{AB\ syst}$, *J* = 16.5, *J* = 7.6 and *J* = 2.9 Hz, 1H), 2.01 (m, 1H), 1.34−1.27 (m, 2H), 1.22−1.15 (m, 2H), 1.12−1.02 (m, 4H), 1.06 (s, 9H), 1.00 (s, 9H), 0.84 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 202.3, 136.19 (2C), 136.16 (2C), 135.9 (4C), 133.6, 133.5 (2C), 133.4, 130.0 (2C), 129.86, 129.84, 127.84 (2C), 127.83 (2C), 127.78 (4C), 96.4, 76.5, 67.2, 59.8, 55.8, 49.3, 48.8, 32.02, 31.98, 27.1 (6C), 25.2, 22.8, 19.4, 19.3, 14.2; HRMS (ESI): calculated for $C_{45}H_{62}O_5Si_2Na$ [M + Na]$^+$: 761.4028, found: 761.4032.

*3-(Benzyloxy)propan-1-ol (**23**).*[27] To a suspension of sodium hydride (60% in oil, 1.6 g, 40 mmol, 1 equiv) in dry THF (80 mL) was added dropwise 1,3-propanediol **22** (2.9 mL, 40 mmol, 1 equiv). The mixture was stirred at rt for 45 min. *n*-Bu_4NI was then added (7.4 g, 20 mmol, 0.5 equiv), and benzyl bromide (4.8 mL, 40 mmol, 1 equiv) was added dropwise. The reaction mixture was stirred for 7 h and quenched by the addition of H_2O (80 mL). The phases were separated, and the aqueous layer was extracted three times with Et_2O (3 × 80 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 8:2) to afford 3-(benzyloxy)-propan-1-ol **23** (4.67 g, 28.1 mmol, 70%) as a yellow oil. The spectral data match those reported in the literature.[27] IR: ν 3375, 3030, 2943, 2863, 1496, 1454, 1365, 1205, 1073, 1026, 972, 910 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.26 (m, 5H), 4.53 (s, 2H), 3.79 (t, *J* = 5.7 Hz, 2H), 3.67 (t, *J* = 5.7 Hz, 2H), 2.27 (br s, 1H, OH), 1.87 ($quint_{app}$, *J* = 5.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.1, 128.5 (2C), 127.73, 127.69 (2C), 73.2, 69.1, 61.5, 32.2; MS (EI) *m*/*z*: 166 ($M^{+\cdot}$, 2), 147 (3), 130 (1), 120 (3), 107 (BnO^+, 97), 91 (Bn^+, 100), 79 (29), 77 (Ph^+, 13), 65 (19), 51 (7).

*(R)-1-(Benzyloxy)hex-5-en-3-ol (**24**).*[28] To a solution of alcohol **23** (396 mg, 2.39 mmol, 1 equiv) in dry THF (12 mL) in a vial were added $[Ir(COD)Cl]_2$ (41 mg, 0.06 mmol 2.5 mol %), (*R*)-BIPHEP (78 mg, 0.12 mmol, 5 mol %), Cs_2CO_3 (156 mg, 0.48 mmol, 0.2 equiv), 3,4-dinitrobenzoic acid (38 mg, 0.18 mmol, 7.5 mol %), and allyl acetate (2.58 mL, 23.9 mmol, 10 equiv). The vial was sealed and heated at 120 °C. After 15 h, the mixture was cooled to rt, transferred into a flask containing Celite, and concentrated under vacuum. The crude material was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 9:1 to 85:15) to afford the alcohol **24** (354 mg, 1.72 mmol, 72%, ee = 94%) as a yellow oil. The spectral data are in agreement with those reported in the literature.[28] $[\alpha]_D^{20}$ 4.5 (*c* 1.01, $CHCl_3$); IR: ν 3421, 3067, 3031, 2918, 2861, 1641, 1496, 1454, 1419, 1364, 1309, 1205, 1077, 1027, 996, 913 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.26 (m, 5H), 5.83 (ddt, *J* = 16.9, *J* = 10.3 and *J* = 7.1 Hz, 1H), 5.14−5.07 (m, 2H), 4.53 (s, 2H), 3.88 (m, 1H), 3.72 ($dt_{AB\ syst}$, *J* = 9.4 and *J* = 5.1 Hz, 1H), 3.65 (m, 1H), 2.88 (br s, 1H, OH), 2.27−2.23 (m, 2H), 1.79−1.74 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.0, 134.9, 128.5 (2C), 127.8, 127.7 (2C), 117.6, 73.3, 70.4, 69.0, 41.9, 35.9; MS (EI) *m*/*z*: 129 [(M-Ph)$^+$, 1], 107 (BnO^+, 26), 92 (11), 91 (Bn^+, 100), 79 (19), 77 (Ph^+, 15), 65 (16), 51 (11).

*(R)-{[1-(Benzyloxy)hex-5-en-3-yl]oxy}triethylsilane (**25**).*[30] To a solution of alcohol **24** (320 mg, 1.55 mmol, 1 equiv) in dry CH_2Cl_2 (15.5 mL) cooled to −78 °C were added 2,6-lutidine (1.08 mL, 9.27 mmol, 6 equiv) and TESOTf (1.4 mL, 6.14 mmol, 4 equiv). The reaction mixture was stirred at −78 °C for 1.5 h; H_2O (15 mL) was added, and the mixture was warmed to rt. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc

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= 99:1) to afford the silylated alcohol **25** (496 mg, 1.55 mmol, quant) as a colorless oil. The spectral data match those reported in the literature.[30] $[\alpha]_D^{20}$ −16.2 (*c* 1.5, $CHCl_3$); IR: ν 3068, 3031, 2953, 2912, 2876, 1641, 1496, 1455, 1365, 1238, 1094, 1047, 1004, 911 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.33 (m, 4H), 7.29 (m, 1H), 5.83 (m, 1H), 5.08−5.02 (m, 2H), 4.52 ($d_{AB\ syst}$, J = 11.9 Hz, 1H), 4.47 ($d_{AB\ syst}$, J = 11.9 Hz, 1H), 3.93 (m, 1H), 3.60−3.51 (m, 2H), 2.30−2.19 (m, 2H), 1.82 (m, 1H), 1.71 (m, 1H), 0.96 (t, J = 8.1 Hz, 9H), 0.60 (q, J = 8.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.6, 134.9, 128.4 (2C), 127.7 (2C), 127.5, 117.1, 73.0, 69.0, 67.1, 42.4, 36.8, 6.9 (3C), 5.0 (3C); MS (EI) *m*/*z*: 291 [$(M\text{-}Et)^+$, 1], 173 (10), 131 ($TESO^+$, 3), 129 (3), 115 (TES^+, 6), 91 (Bn^+, 100).

*(R,E)-8-(Benzyloxy)-6-(triethylsilyloxy)oct-3-en-2-one (**26**).* To a solution of alkene **25** (334 mg, 1.04 mmol, 1 equiv) in dry CH_2Cl_2 (9 mL) were added methyl vinylketone (0.44 mL, 5.29 mmol, 5.1 equiv) and Hoveyda-Grubbs second generation catalyst (13 mg, 0.021 mmol, 0.02 equiv). The mixture was heated at reflux for 2 h and then cooled to rt and concentrated under vacuum. The crude material was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 95:5 to 92:8) to afford methyl ketone **26** (370 mg, 1.02 mmol, 98%) as a colorless oil. $[\alpha]_D^{20}$ −11.5 (*c* 1.02, $CHCl_3$); IR: ν 2953, 2912, 2876, 1699, 1676, 1629, 1455, 1416, 1360, 1252, 1203, 1173, 1095, 1045, 1005, 982 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37−7.26 (m, 5H), 6.81 (dt, J = 16.0 and J = 7.4 Hz, 1H), 6.07 (dt, J = 16.0 and J = 1.2 Hz, 1H), 4.51 ($d_{AB\ syst}$, J = 11.8 Hz, 1H), 4.46 ($d_{AB\ syst}$, J = 11.8 Hz, 1H), 4.03 (m, 1H), 3.58−3.49 (m, 2H), 2.47−2.32 (m, 2H), 2.24 (s, 3H), 1.78−1.73 (m, 2H), 0.95 (t, J = 7.9 Hz, 9H), 0.60 (q, J = 8.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 198.5, 144.7, 138.3, 133.5, 128.4 (2C), 127.7 (2C), 127.6, 73.1, 68.4, 66.7, 40.8, 37.4, 26.7, 6.9 (3C), 5.0 (3C); MS (EI) *m*/*z*: 279 (1), 173 (7), 115 (TES^+, 5), 107 (BnO^+, 3), 103 (18), 91 (Bn^+, 100), 75 (24); HRMS (ESI): calculated for $C_{21}H_{34}O_3SiNa$ $[M + Na]^+$: 385.2169, found: 385.2175.

*(5R,6R,7S,9R,15R,E)-15-[2-(Benzyloxy)ethyl]-7-(tert-butyldiphenylsilyloxy)-6-[(tert-butyldiphenylsilyloxy)methyl]-17,17-diethyl-9-hydroxy-5-pentyl-2,4,16-trioxa-17-silanonadec-12-en-11-one (**27**).* To a solution of (+)-DIPCl (103 mg, 0.32 mmol, 2.6 equiv) in dry Et_2O (1 mL) cooled to 0 °C were added Et_3N (50 μL, 0.36 mmol, 3.0 equiv) and a solution of enone **26** (59 mg, 0.16 mmol, 1.3 equiv) in dry Et_2O (2 mL). The mixture was stirred at 0 °C for 2 h and then cooled to −78 °C. A solution of aldehyde **21** (90 mg, 0.122 mmol, 1.0 equiv) in dry Et_2O (1.8 mL) was cannulated, and the mixture was progressively warmed to −20 °C and stirred at this temperature. After 5.5 h, the reaction was quenched by the addition of a mixture of MeOH/pH 7 buffer/35% aqueous H_2O_2 = 1:1:1 (5 mL), and the solution was progressively warmed to rt overnight. The mixture was cooled to 0 °C, and a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) was added dropwise over a period of 30 min. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to afford a mixture of diastereomers **27** and **27′** in a 90:10 ratio. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 92:8 to 90:10), and the diastereomers were separated to afford **27** (90 mg, 0.082 mmol, 67%) as a colorless oil. $[\alpha]_D^{20}$ 4.2 (*c* 1.0, $CHCl_3$); IR: ν 3498, 3070, 2954, 2932, 2877, 2858, 1737, 1665, 1628, 1589, 1456, 1428, 1378, 1257, 1188, 1111, 1037, 916, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.68−7.62 (m, 8H), 7.44−7.25 (m, 17H), 6.64 (dt, J = 15.8 and J = 7.3 Hz, 1H), 5.87 (d, J = 15.9 Hz, 1H), 4.51 ($d_{AB\ syst}$, J = 11.8 Hz, 1H), 4.46 ($d_{AB\ syst}$, J = 11.9 Hz, 1H), 4.42 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.34 ($d_{AB\ syst}$, J = 6.7 Hz, 1H), 4.24 (m, 1H), 4.05−3.93 (m, 3H), 3.88 ($dd_{AB\ syst}$, J = 9.9 and J = 6.2 Hz, 1H), 3.81 (m, 1H), 3.57−3.48 (m, 2H), 3.20 (s, 3H), 3.04 (br d, J = 2.2 Hz, 1H, OH), 2.42−2.25 (m, 2H), 2.19 (dd, J = 17.6 and J = 9.0 Hz, 1H), 2.06 (m, 1H), 1.92 (dd, J = 17.8 and J = 2.2 Hz, 1H), 1.82−1.60 (m, 4H), 1.53 (m, 1H), 1.37−1.10 (m, 7H), 1.06 (s, 9H), 1.02 (s, 9H), 0.94 (t, J = 7.9 Hz, 9H), 0.83 (t, J = 6.5 Hz, 3H), 0.58 (q, J = 7.8 Hz, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 200.2, 143.9, 138.5, 136.3 (2C), 136.2 (2C), 135.9 (2C), 135.8 (2C), 134.0, 133.9, 133.8 (2C), 132.6, 129.8 (3C), 129.7, 128.5 (2C), 127.84 (2C), 127.76 (7C), 127.65 (2C), 96.1, 76.5, 73.2, 69.2, 68.4, 66.7, 65.4, 60.1, 55.7, 48.5, 45.5, 41.0, 40.8, 37.3, 32.5, 32.0, 27.2 (3C), 27.1 (3C), 25.6, 22.8, 19.5, 19.4, 14.2, 7.0 (3C), 5.1 (3C); HRMS (ESI): calculated for $C_{66}H_{96}O_8Si_3Na$ $[M + Na]^+$: 1123.6305, found: 1123.6300.

*(4R,6S,7R,8R)-1-{(2S,4S,6S)-6-[2-(Benzyloxy)ethyl]-2-methyl-1,3-dioxan-4-yl}-6-(tert-butyldiphenylsilyloxy)-7-[(tert-butyldiphenylsilyloxy)methyl]-4-hydroxy-8-(methoxymethoxy)tridecan-2-one (**28**).* To a solution of silyl ether **27** (775 mg, 0.70 mmol, 1.0 equiv) in dry CH_2Cl_2 (35 mL) were added acetaldehyde (0.78 mL, 14 mmol, 20 equiv) and $Bi(NO_3)_3{\cdot}5H_2O$ (35 mg, 0.072 mmol, 0.1 equiv). The mixture was stirred at rt for 15 h and then quenched by the addition of a saturated aqueous solution of $NaHCO_3$ (35 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by column chromatography on silica gel (petroleum ether/EtOAc = 80:20) to afford β-hydroxyketone **28** (407 mg, 0.39 mmol, 56%) as a yellow oil. $[\alpha]_D^{20}$ 3.3 (*c* 1.0, $CHCl_3$); IR: ν 3501, 3071, 2930, 2857, 1711, 1589, 1472, 1428, 1378, 1363, 1110, 1035, 918, 823 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.68−7.60 (m, 8H), 7.44−7.27 (m, 17H), 4.64 (q, J = 5.2 Hz, 1H), 4.53 ($d_{AB\ syst}$, J = 12.1 Hz, 1H), 4.48 ($d_{AB\ syst}$, J = 12.0 Hz, 1H), 4.42 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.36 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.23 (m, 1H), 4.01−3.85 (m, 4H), 3.83−3.75 (m, 2H), 3.64−3.52 (m, 2H), 3.20 (s, 3H), 2.85 (br d, J = 3.1 Hz, 1H, OH), 2.49 (dd, J = 16.2 and J = 7.2 Hz, 1H), 2.17 (dd, J = 16.2 and J = 5.3 Hz, 1H), 2.14 (dd, J = 18.0 and J = 9.2 Hz, 1H), 2.05 (m, 1H), 1.85−1.71 (m, 4H), 1.64 (m, 1H), 1.52 (m, 1H), 1.33−1.23 (m, 2H), 1.23 (d, J = 5.1 Hz, 3H), 1.18−1.10 (m, 7H), 1.06 (s, 9H), 1.02 (s, 9H), 0.83 (t, J = 6.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.1, 138.6, 136.3 (2C), 136.2 (2C), 135.9 (2C), 135.8 (2C), 134.0, 133.8, 133.71, 133.68, 129.83, 129.78 (2C), 129.74, 128.5 (2C), 127.8 (9C), 127.7 (2C), 98.7, 96.1, 76.5, 73.2, 73.1, 72.1, 69.4, 66.1, 65.5, 60.0, 55.7, 49.6, 49.1, 48.6, 40.8, 36.8, 36.2, 32.4, 32.0, 27.2 (3C), 27.1 (3C), 25.4, 22.8, 21.1, 19.5, 19.4, 14.2; HRMS (ESI): calculated for $C_{62}H_{86}O_9Si_2Na$ $[M + Na]^+$: 1053.5703, found: 1053.5695.

*(2R,4S,6S,7R,8R)-1-{(2S,4R,6S)-6-[2-(Benzyloxy)ethyl]-2-methyl-1,3-dioxan-4-yl}-6-(tert-butyldiphenylsilyloxy)-7-[(tert-butyldiphenylsilyloxy)methyl]-8-(methoxymethoxy)tridecane-2,4-diol (**29**).* To a solution of β-hydroxyketone **28** (350 mg, 0.34 mmol, 1 equiv) in a mixture of dry THF (6 mL) and anhydrous MeOH (1.5 mL) cooled to −78 °C was added Et_2BOMe (0.68 mL, 1 M in THF, 0.68 mmol, 2.0 equiv). The mixture was stirred at −78 °C for 1 h. $NaBH_4$ (28 mg, 0.74 mmol, 2.2 equiv) was added, and the mixture was progressively warmed to 0 °C over a period of 5 h. Glacial acetic acid (2.3 mL) and EtOAc (10 mL) were then added, and the solution was warmed to rt. A saturated aqueous solution of $NaHCO_3$ (5 mL) was added, the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was coevaporated with MeOH to realize the hydrolysis of the boronate until no more boronate was visible by TLC. The residual mixture was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 8:2 to 75:25) to afford diol **29** (255 mg, 0.25 mmol, 73%) as a pale yellow oil. $[\alpha]_D^{20}$ 4.6 (*c* 0.9, $CHCl_3$); IR: ν 3484, 3071, 2931, 2857, 1472, 1428, 1379, 1363, 1341, 1310, 1263, 1145, 1105, 1036, 918, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz): δ 7.70−7.61 (m, 8H), 7.44−7.26 (m, 17H), 4.69 (q, J = 5.1 Hz, 1H), 4.54 ($d_{AB\ syst}$, J = 12.2 Hz, 1H), 4.50 ($d_{AB\ syst}$, J = 12.1 Hz, 1H), 4.42 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.33 ($d_{AB\ syst}$, J = 6.8 Hz, 1H), 4.30 (m, 1H), 3.97 ($dd_{AB\ syst}$, J = 10.1 and J = 6.0 Hz, 1H), 3.89 ($dd_{AB\ syst}$, J = 9.8 and J = 5.9 Hz, 1H), 3.85−3.76 (m, 3H), 3.71 (m, 1H), 3.66−3.53 (m, 3H), 3.33 (br s, 1H, OH), 3.20 (s, 3H), 2.05 (m, 1H), 1.87−1.73 (m, 3H), 1.63 (m, 1H), 1.56−1.47 (m, 3H), 1.30 (m, 1H), 1.28 (d, J = 5.0 Hz, 3H), 1.21−1.11 (m, 9H), 1.06 (s, 9H), 1.02 (s, 9H), 0.88 (m, 1H), 0.83 (t, J = 6.7 Hz, 3H), one OH not visible; ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.6, 136.28 (2C), 136.25 (2C), 135.91 (2C), 135.86 (2C), 134.2, 134.0, 133.70, 133.68, 129.8 (2C), 129.74, 129.68, 128.5 (2C), 127.80 (2C), 127.78 (4C), 127.76, 127.67 (2C), 127.66 (2C), 98.6, 96.0, 76.6, 76.2, 73.3, 73.1, 71.3, 70.1, 69.9, 66.1, 60.1, 55.7, 48.6, 43.0, 42.7, 41.9, 37.0, 36.2, 32.3, 32.0, 27.2 (3C), 27.1 (3C), 25.4, 22.8,

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21.2, 19.5, 19.4, 14.2; HRMS (ESI): calculated for $C_{62}H_{88}O_9Si_2Na$ [M + Na]$^+$: 1055.5859, found: 1055.5849.

Synthesis of 30. *(5R,6R,7S)-7-{[(4S,6S)-6-{[(2S,4S,6S)-6-[2-(Benzyloxy)ethyl]-2-methyl-1,3-dioxan-4-yl]methyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-6-[(tert-butyldiphenylsilyloxy)methyl]-10,10-dimethyl-5-pentyl-9,9-diphenyl-2,4,8-trioxa-9-silaundecane (**30′**).* To a solution of diol **29** (253 mg, 0.245 mmol, 1 equiv) in a mixture of acetone (8.4 mL) and 2,2-dimethoxypropane (4.2 mL) was added PPTS (6 mg, 0.024 mmol, 0.1 equiv). The mixture was stirred at rt for 14 h and then quenched by the addition of a few drops of Et_3N. After evaporation of the solvents under vacuum, the crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 9:1 to 88:12) to afford the corresponding acetonide **30′** (227 mg, 0.211 mmol, 86%) as a colorless oil. $[\alpha]_D^{20}$ 4.4 (*c* 1.3, $CHCl_3$); IR: ν 3071, 2992, 2931, 2858, 1590, 1472, 1428, 1379, 1363, 1263, 1201, 1125, 1036, 823 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72−7.63 (m, 8H), 7.42−7.27 (m, 17H), 4.65 (q, *J* = 5.0 Hz, 1H), 4.55 ($d_{AB\ syst}$, *J* = 12.1 Hz, 1H), 4.51 ($d_{AB\ syst}$, *J* = 12.0 Hz, 1H), 4.43 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.36 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.19−4.11 (m, 2H), 3.89−3.73 (m, 3H), 3.71−3.49 (m, 4H), 3.27 (m, 1H), 3.20 (s, 3H), 2.10 (m, 1H), 1.92−1.78 (m, 2H), 1.63−1.52 (m, 4H), 1.49−1.43 (m, 2H), 1.29 (d, *J* = 5.0 Hz, 3H), 1.25−1.10 (m, 8H), 1.19 (s, 3H), 1.07 (s, 9H), 1.01 (s, 12H), 0.85 (t, *J* = 6.9 Hz, 3H), 0.62 (q, *J* = 11.9 Hz, 1H), 0.35 (br d, *J* = 12.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.6, 136.2 (2C), 136.1 (2C), 135.84 (2C), 135.81 (2C), 134.2, 133.9 (2C), 133.7, 129.9, 129.74 (2C), 129.69, 128.5 (2C), 127.82 (2C), 127.77 (8C), 127.7, 98.6, 98.1, 96.4, 76.9, 73.23, 73.21, 72.5, 67.3, 66.4, 66.3, 64.7, 60.0, 55.6, 49.7, 42.1, 41.7, 36.5, 36.4, 36.1, 32.7, 32.0, 30.1, 27.1 (3C), 27.0 (3C), 25.8, 22.8, 21.3, 19.6, 19.5, 19.4, 14.2; HRMS (ESI): calculated for $C_{65}H_{92}O_9Si_2Na$ [M + Na]$^+$: 1095.6172, found: 1095.6164.

*2-[(2S,4S,6S)-6-{[(4S,6S)-6-{(2S,3R,4R)-2-(tert-Butyldiphenylsilyloxy)-3-[(tert-butyldiphenylsilyloxy)methyl]-4-(methoxymethoxy)nonyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2-methyl-1,3-dioxan-4-yl]ethanol (**30**).* To a solution of acetonide **30′** (225 mg, 0.210 mmol, 1 equiv) in anhydrous MeOH (15 mL) was added Pd/C (45 mg, 5% in weight, 0.021 mmol, 0.1 equiv). The mixture was degassed and stirred at rt for 24 h under 1 atm of H_2. The mixture was then replaced under argon, filtered through a pad of Celite, and concentrated under vacuum. The crude material was then purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 7:3) to afford alcohol **30** (185 mg, 0.188 mmol, 90%) as a colorless viscous oil. $[\alpha]_D^{20}$ 7.4 (*c* 1.0, $CHCl_3$); IR: ν 3484, 3071, 3049, 2993, 2932, 2858, 1590, 1472, 1428, 1379, 1341, 1263, 1201, 1134, 1110, 1037, 953, 851, 823 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72−7.63 (m, 8H), 7.45−7.28 (m, 12H), 4.69 (q, *J* = 5.1 Hz, 1H), 4.43 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.36 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.19−4.12 (m, 2H), 3.89−3.81 (m, 5H), 3.69 (m, 1H), 3.54 (m, 1H), 3.30 (m, 1H), 3.21 (s, 3H), 2.36 (br s, 1H, OH), 2.11 (m, 1H), 1.89−1.74 (m, 2H), 1.64−1.56 (m, 4H), 1.50−1.41 (m, 2H), 1.31 (d, *J* = 5.0 Hz, 3H), 1.33−1.11 (m, 8H), 1.20 (s, 3H), 1.07 (s, 9H), 1.01 (s, 12H), 0.85 (t, *J* = 6.7 Hz, 3H), 0.63 (q_{app}, *J* = 11.9 Hz, 1H), 0.36 (br d, *J* = 12.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 136.22 (2C), 136.15 (2C), 135.84 (2C), 135.82 (2C), 134.3, 133.9 (2C), 133.7, 129.9, 129.74 (2C), 129.70, 127.8 (6C), 127.7 (2C), 98.6, 98.2, 96.4, 76.9, 76.0, 72.6, 67.4, 66.4, 64.7, 60.8, 60.0, 55.6, 49.7, 41.9, 41.7, 38.1, 36.2, 36.1, 32.7, 32.1, 30.1, 27.2 (3C), 27.1 (3C), 25.8, 22.8, 21.3, 19.63, 19.55, 19.4, 14.2; HRMS (ESI): calculated for $C_{58}H_{86}O_9Si_2Na$ [M + Na]$^+$: 1005.5703, found: 1005.5693.

*1-[(2S,4S,6S)-6-{[(4S,6S)-6-{(2S,3R,4R)-2-(tert-Butyldiphenylsilyloxy)-3-[(tert-butyldiphenylsilyloxy)methyl]-4-(methoxymethoxy)nonyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2-methyl-1,3-dioxan-4-yl)propan-2-one (**31**).* To a solution of alcohol **30** (82 mg, 84 μmol, 1.0 equiv) in dry CH_2Cl_2 (2.7 mL) was added $NaHCO_3$ (14 mg, 0.17 mmol, 2.0 equiv). The solution was cooled to 0 °C, and DMP (106 mg, 0.25 mmol, 3.0 equiv) was added. The mixture was progressively warmed to rt and stirred for 2 h. A saturated aqueous solution of $NaHCO_3$ (2.5 mL) was added followed by the addition of Et_2O (5 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the aldehyde, which was not purified but directly engaged in the next step.

To a solution of the crude aldehyde in dry Et_2O (2.7 mL) at 0 °C was added MeMgBr (0.08 mL, 3 M in Et_2O, 0.24 mmol, 3.0 equiv). After 1 h, the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (3 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum to afford the desired secondary alcohol as a mixture of diastereomers, which were not purified but directly engaged in the next oxidation step.

To a solution of crude alcohol in dry CH_2Cl_2 (3.6 mL) was added $NaHCO_3$ (14 mg, 0.17 mmol, 2.0 equiv). The solution was cooled to 0 °C, and DMP (106 mg, 0.25 mmol, 3.0 equiv) was added to the mixture, which was progressively warmed to rt. After 14 h, a saturated aqueous solution of $NaHCO_3$ (5 mL) was added followed by the addition of Et_2O (10 mL). After 15 min, the layers were separated, and the aqueous layer was extracted with Et_2O (3 × 5 mL). The combined organic layers were washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum. Purification of the crude material by flash column chromatography on silica gel (petroleum ether/EtOAc = 85:15) afforded methylketone **31** (72 mg, 72 μmol, 86%) as a colorless viscous oil. $[\alpha]_D^{20}$ 12.4 (*c* 0.95, $CHCl_3$); IR: ν 3072, 2993, 2932, 2858, 1719, 1589, 1472, 1428, 1379, 1361, 1260, 1200, 1111, 1037, 944, 823 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.72−7.63 (m, 8H), 7.45−7.28 (m, 12H), 4.68 (q, *J* = 5.2 Hz, 1H), 4.43 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.36 ($d_{AB\ syst}$, *J* = 6.7 Hz, 1H), 4.19−4.13 (m, 2H), 4.07 (m, 1H), 3.87 (dd, *J* = 9.8 and *J* = 7.3 Hz, 1H), 3.83 (m, 1H), 3.69 (m, 1H), 3.54 (m, 1H), 3.30 (m, 1H), 3.20 (s, 3H), 2.80 ($dd_{AB\ syst}$, *J* = 16.0 and *J* = 7.3 Hz, 1H), 2.51 ($dd_{AB\ syst}$, *J* = 16.0 and *J* = 5.1 Hz, 1H), 2.22 (s, 3H), 2.10 (m, 1H), 1.64−1.44 (m, 6H), 1.28 (d, *J* = 5.1 Hz, 3H), 1.25−1.10 (m, 8H), 1.20 (s, 3H), 1.07 (s, 9H), 1.01 (s, 3H), 1.00 (s, 9H), 0.85 (t, *J* = 6.8 Hz, 3H), 0.62 (q_{app}, *J* = 12.4 Hz, 1H), 0.37 (br d, *J* = 12.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 206.9, 136.2 (2C), 136.1 (2C), 135.84 (2C), 135.81 (2C), 134.3, 133.9 (2C), 133.7, 129.8, 129.74 (2C), 129.69, 127.8 (6C), 127.7 (2C), 98.7, 98.2, 96.4, 76.9, 72.4 (2C), 67.4, 66.4, 64.7, 60.0, 55.6, 49.7, 49.6, 42.0, 41.7, 36.1 (2C), 32.7, 32.1, 31.4, 30.1, 27.2 (3C), 27.1 (3C), 25.8, 22.8, 21.2, 19.62, 19.55, 19.4, 14.2; HRMS (ESI): calculated for $C_{59}H_{86}O_9Si_2Na$ [M + Na]$^+$: 1017.5703, found: 1017.5692.

*(2S,3S,5S,7R)-8-{(2S,4R,6S)-6-[2-(Benzyloxy)ethyl]-2-methyl-1,3-dioxan-4-yl}-2-[(R)-1-(methoxymethoxy)hexyl]octane-1,3,5,7-tetraol (**32**).* To a solution of silyl ether **29** (20 mg, 0.019 mmol, 1 equiv) in dry THF (2 mL) cooled to 0 °C was added TBAF (58 μL, 1 M in THF, 0.058 mmol, 3.0 equiv). The mixture was stirred at rt for 3.5 h and then quenched by the addition of H_2O (2 mL). After addition of EtOAc (5 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (4 × 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (CH_2Cl_2/MeOH = 98:2) to afford tetraol **32** (8 mg, 0.014 mmol, 74%) as a colorless oil. $[\alpha]_D^{20}$ −13.1 (*c* 0.4, $CHCl_3$); IR: ν 3420, 2925, 2857, 1454, 1378, 1340, 1143, 1099, 1035, 918, 848 cm^{-1}; ^{1}H NMR (CD_3OD, 400 MHz): δ 7.36−7.25 (m, 5H), 4.71 (q, *J* = 5.0 Hz, 1H), 4.68 ($d_{AB\ syst}$, *J* = 6.9 Hz, 1H), 4.62 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.51 ($d_{AB\ syst}$, *J* = 12.0 Hz, 1H), 4.47 ($d_{AB\ syst}$, *J* = 12.0 Hz, 1H), 4.05−3.92 (m, 3H), 3.89−3.78 (m, 3H), 3.77−3.66 (m, 2H), 3.65−3.52 (m, 2H), 3.37 (s, 3H), 1.91−1.83 (m, 2H), 1.79−1.72 (m, 2H), 1.70 (m, 1H), 1.68−1.56 (m, 5H), 1.52−1.44 (m, 2H), 1.37−1.27 (m, 6H), 1.24 (d, *J* = 5.3 Hz, 3H), 1.20 (m, 1H), 0.92 (t, *J* = 6.7 Hz, 3H), four OH not visible; ^{13}C NMR (CD_3OD, 100 MHz): δ 139.8, 129.4 (2C), 128.9 (2C), 128.7, 99.7, 97.4, 78.6, 75.4, 74.7, 73.9, 71.1, 70.9, 68.3, 67.1, 60.1, 56.1, 50.6, 45.1, 44.3, 42.2, 38.0, 37.1, 33.1, 32.8, 26.8, 23.7, 21.4, 14.4; HRMS (ESI): calculated for $C_{30}H_{52}O_9Na$ [M + Na]$^+$: 579.3504, found: 579.3493.

(4S,5E,7E,9E,11E,13E,15S,16R)-1-{[(2R,4R,6S)-6-{[(4S,6S)-6-{(2S,3R,4R)-2-(tert-Butyldiphenylsilyloxy)-3-[(tert-butyldiphenylsilyloxy)methyl]-4-(methoxymethoxy)nonyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2-methyl-1,3-dioxan-4-yl]-4-hydroxy-5-methyl-16-(triethylsilyloxy)-15-[(2-(trimethylsilyl)ethoxy]methoxy}heptadeca-

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*5,7,9,11,13-pentaen-2-one (**34**).* To a solution of ketone **31** (67 mg, 0.067 mmol, 1.5 equiv) in dry Et_2O (3 mL) cooled to 0 °C were added Et_3N (19 μL, 0.137 mmol, 3.0 equiv) and chlorodicyclohexylborane (0.11 mL, 1 M in hexanes, 0.11 mmol, 2.5 equiv). The mixture was stirred at 0 °C for 2 h and then cooled to −78 °C. A solution of aldehyde **13** (22 mg, 0.045 mmol, 1.0 equiv) in dry Et_2O (5 mL) was added to the boronate **33**, and the mixture was progressively warmed to −20 °C and stirred at this temperature. After 14 h, the reaction was quenched by the addition of a mixture of MeOH/pH 7 buffer/35% aqueous H_2O_2 = 1:1:1 (6 mL), and the solution was progressively warmed to rt and stirred for 2 h. The mixture was cooled to 0 °C, and a saturated aqueous solution of $Na_2S_2O_3$ (5 mL) was added dropwise over a period of 30 min. The layers were separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (petroleum ether/EtOAc = 85:15 to 75:25) to afford **34** (61 mg, 0.041 mmol, 91%) as a single diastereomer and yellow oil. $[\alpha]_D^{20}$ 40.4 (*c* 1.0, CH_3CN); IR: ν 3449, 3071, 2953, 2931, 2876, 2858, 1715, 1617, 1589, 1461, 1428, 1378, 1331, 1249, 1199, 1105, 1035, 1002, 949, 920, 859, 834 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 7.89−7.80 (m, 8H), 7.32−7.22 (m, 12H), 6.48−6.36 (m, 2H), 6.30−6.16 (m, 6H), 5.81 (dd, *J* = 15.2 and *J* = 8.1 Hz, 1H), 4.86 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.72 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.60−4.50 (m, 3H), 4.56 ($d_{AB\ syst}$, *J* = 6.7 Hz, 1H), 4.43 (dd, *J* = 9.8 and *J* = 6.0 Hz, 1H), 4.39 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.23 (dd, *J* = 9.7 and *J* = 6.4 Hz, 1H), 4.14 (dd, *J* = 7.8 and *J* = 4.6 Hz, 1H), 4.12 (m, 1H), 4.04−3.97 (m, 2H), 3.92−3.82 (m, 2H), 3.76 (m, 1H), 3.70−3.57 (m, 2H), 3.12 (s, 3H), 2.75 (br s, 1H, OH), 2.56 (dd, *J* = 15.8 and *J* = 7.4 Hz, 1H), 2.49 (dd, *J* = 16.5 and *J* = 9.5 Hz, 1H), 2.42 (m, 1H), 2.32 (dd, *J* = 16.5 and *J* = 2.8 Hz, 1H), 2.19 (dd, *J* = 15.8 and *J* = 5.0 Hz, 1H), 2.09−1.96 (m, 2H), 1.94−1.79 (m, 2H), 1.64 (s, 3H), 1.64 (m, 1H), 1.51−1.40 (m, 3H), 1.47 (s, 3H), 1.33 (d, *J* = 5.0 Hz, 3H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.26 (s, 3H), 1.25−1.15 (m, 6H), 1.22 (s, 9H), 1.18 (s, 9H), 1.06 (t, *J* = 8.0 Hz, 9H), 1.05−0.95 (m, 2H), 0.93 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.67 (m, 1H), 0.67 (q, *J* = 8.2 Hz, 6H), 0.03 (s, 9H); ^{13}C NMR (C_6D_6, 100 MHz): δ 207.9, 139.6, 136.6 (2C), 136.5 (2C), 136.22 (2C), 136.17 (2C), 135.0, 134.8, 134.3, 134.2 (3C), 133.8, 133.6, 133.2, 132.6, 131.6, 130.2, 130.0 (3C), 129.4, 128.16 (2C), 128.13 (2C), 128.11 (2C), 128.06 (2C), 125.7, 98.8, 98.4, 96.5, 92.5, 81.2, 76.8, 72.7, 72.60, 72.55, 71.5, 68.3, 66.7, 65.31, 65.28, 60.6, 55.5, 49.7, 49.65, 49.54, 42.7, 42.1, 36.8, 36.6, 33.0, 32.4, 30.5, 27.35 (3C), 27.32 (3C), 26.2, 23.1, 21.4, 20.7, 20.0, 19.8, 19.6, 18.3, 14.4, 13.1, 7.3 (3C), 5.5 (3C), −1.2 (3C); HRMS (ESI): calculated for $C_{86}H_{134}O_{13}Si_4Na$ $[M + Na]^+$: 1509.8794, found: 1509.8774.

*(2S,4S,5E,7E,9E,11E,13E,15S,16R)-1-[(2S,4S,6S)-6-{[(4S,6S)-6-{(2S,3R,4R)-2-(tert-Butyldiphenylsilyloxy)-3-[(tert-butyldiphenylsilyloxy)methyl]-4-(methoxymethoxy)nonyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2-methyl-1,3-dioxan-4-yl]-5-methyl-16-(triethylsilyloxy)-15-{[2-(trimethylsilyl)ethoxy]methoxy}heptadeca-5,7,9,11,13-pentaene-2,4-diol (**35**).* To a solution of $Me_4NBH(OAc)_3$ (80 mg, 0.305 mmol, 10 equiv) in anhydrous CH_3CN (0.9 mL) was added glacial acetic acid (0.9 mL) dropwise. The mixture was stirred until it became clear and then cooled to −20 °C. A solution of β-hydroxyketone **34** (45 mg, 0.030 mmol, 1.0 equiv) in CH_3CN (8.1 mL) was cannulated, and the resulting solution was stirred at −20 °C for 14 h. The reaction mixture was then poured into a 1:1 mixture of a saturated aqueous solution of Rochelle's salt and a saturated aqueous solution of $NaHCO_3$ cooled to 0 °C and stirred at rt for 3 h. EtOAc (10 mL) was added; the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with a saturated aqueous solution of $NaHCO_3$ (20 mL) and then with brine (20 mL), dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (pentane/EtOAc = 75:25 to 7:3) to afford diol **35** (36 mg, 0.024 mmol, 80%) as a yellow oil. $[\alpha]_D^{20}$ 38.4 (*c* 1.0, CH_3CN); IR: ν 3455, 3071, 2952, 2933, 2877, 2858, 1589, 1472, 1428, 1378, 1249, 1200, 1110, 1036, 1002, 947, 859, 834 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 7.88−7.80 (m, 8H), 7.30−7.20 (m, 12H), 6.60−6.47 (m, 2H), 6.40 (br dd, *J* = 15.0 and *J* = 9.5 Hz, 1H), 6.34−6.26 (m, 2H), 6.26−6.16 (m, 3H), 5.80 (dd, *J* = 15.2 and *J* = 8.0 Hz, 1H), 4.87 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.72 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.60−4.48 (m, 3H), 4.45−4.37 (m, 3H), 4.25−4.06 (m, 4H), 4.00 (m, 1H), 3.92−3.82 (m, 2H), 3.72 (m, 1H), 3.65−3.57 (m, 2H), 3.45 (m, 1H), 3.11 (s, 3H), 2.42 (m, 1H), 2.08−1.97 (m, 2H), 1.91−1.77 (m, 3H), 1.76 (s, 3H), 1.76−1.60 (m, 3H), 1.47 (s, 3H), 1.43−1.15 (m, 16H), 1.23 (s, 9H), 1.18 (s, 12H), 1.07 (t, *J* = 8.0 Hz, 9H), 1.06−0.95 (m, 2H), 0.93−0.88 (m, 4H), 0.68 (q, *J* = 7.8 Hz, 6H), 0.65 (m, 1H), 0.03 (s, 9H), two OH not visible; ^{13}C NMR (C_6D_6, 100 MHz): δ 141.8, 136.6 (2C), 136.5 (2C), 136.23 (2C), 136.17 (2C), 135.0, 134.8, 134.4, 134.3, 134.2 (2C), 134.0, 133.1, 132.8, 132.4, 131.3, 130.2, 130.0 (3C), 129.8, 128.15 (2C), 128.12 (2C), 128.08 (2C), 128.05 (2C), 125.0, 98.6, 98.4, 96.5, 92.5, 81.3, 77.2, 76.9, 74.1, 72.7, 71.5, 69.6, 68.3, 66.7, 65.27, 65.25, 60.6, 55.5, 49.7, 43.1, 42.6, 42.1 (2C), 36.8 (2C), 33.0, 32.4, 30.5, 27.35 (3C), 27.32 (3C), 26.1, 23.1, 21.3, 20.6, 20.0, 19.8, 19.6, 18.3, 14.4, 13.6, 7.2 (3C), 5.5 (3C), −1.2 (3C); HRMS (ESI): calculated for $C_{86}H_{136}O_{13}Si_4Na$ $[M + Na]^+$: 1511.8950, found: 1511.8916.

Synthesis of 36. *(8S,9E,11E,13E,15E,17E,19S,21R)-21-{[(2S,4S,6S)-6-{[(4S,6S)-6-{(2S,3R,4R)-2-(tert-Butyldiphenylsilyloxy)-3-[(tert-butyldiphenylsilyloxy)methyl]-4-(methoxymethoxy)nonyl}-2,2-dimethyl-1,3-dioxan-4-yl]methyl}-2-methyl-1,3-dioxan-4-yl]methyl}-2,2,18,27,27-pentamethyl-8-[(R)-1-(triethylsilyloxy)ethyl]-19-{[2-(trimethylsilyl)ethoxy]methoxy}-5,7,22,24-tetraoxa-2,27-disilaoctacosa-9,11,13,15,17-pentaene (**36′**).* To a solution of diol **35** (36 mg, 0.024 mmol, 1.0 equiv) in dry CH_2Cl_2 (1 mL) were added iPr_2NEt (24 μL, 0.145 mmol, 6 equiv) and SEMCl (17 μL, 0.096 mmol, 4 equiv) dropwise. The mixture was stirred at rt for 14 h and then quenched by addition of H_2O (1 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (pentane/EtOAc = 9:1) to afford the corresponding ether **36′** (39 mg, 0.022 mmol, 92%). $[\alpha]_D^{20}$ 13.3 (*c* 1.0, CH_3CN); IR: ν 3071, 2953, 2877, 1650, 1589, 1463, 1428, 1378, 1249, 1200, 1105, 1034, 1005, 939, 920, 860, 836 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 7.89−7.80 (m, 8H), 7.33−7.22 (m, 12H), 6.49 (dd, *J* = 13.5 and *J* = 11.4 Hz, 1H), 6.39 (m, 1H), 6.31 (br d, *J* = 11.4 Hz, 1H), 6.27−6.17 (m, 5H), 5.81 (dd, *J* = 15.2 and *J* = 8.0 Hz, 1H), 4.93 ($d_{AB\ syst}$, *J* = 7.0 Hz, 1H), 4.89 ($d_{AB\ syst}$, *J* = 7.0 Hz, 1H), 4.86 ($d_{AB\ syst}$, *J* = 6.8 Hz, 1H), 4.77 ($d_{AB\ syst}$, *J* = 6.7 Hz, 1H), 4.73−4.68 (m, 2H), 4.64 (q, *J* = 5.1 Hz, 1H), 4.59−4.51 (m, 3H), 4.42 (dd, *J* = 9.8 and *J* = 6.0 Hz, 1H), 4.39 (d, *J* = 6.8 Hz, 1H), 4.27−4.17 (m, 2H), 4.16−4.05 (m, 2H), 4.00 (m, 1H), 3.94−3.56 (m, 10H), 3.12 (s, 3H), 2.42 (m, 1H), 2.28 (m, 1H), 2.13 (m, 1H), 2.06−1.90 (m, 4H), 1.89−1.76 (m, 6H), 1.65 (m, 1H), 1.58 (m, 1H), 1.47 (s, 3H), 1.42 (d, *J* = 5.0 Hz, 3H), 1.37−1.15 (m, 7H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.28 (s, 3H), 1.22 (s, 9H), 1.19 (s, 9H), 1.07 (t, *J* = 8.0 Hz, 9H), 1.05−0.95 (m, 6H), 0.93−0.88 (m, 4H), 0.71 (m, 1H), 0.68 (q, *J* = 8.1 Hz, 6H), 0.05 (s, 9H), 0.04 (s, 9H), 0.03 (s, 9H); ^{13}C NMR (C_6D_6, 100 MHz): δ 138.8, 136.6 (2C), 136.5 (2C), 136.23 (2C), 136.17 (2C), 135.0, 134.8, 134.26, 134.24, 134.19, 134.12, 133.8 (2C), 133.3, 132.7, 131.6, 130.14, 130.08, 130.0 (2C), 129.2, 128.4 (2C), 128.3, 128.2 (2C), 128.1 (2C), 128.0 (2C), 98.8, 98.4, 96.5, 95.2, 93.0, 92.5, 81.2, 79.0, 76.9, 73.4, 73.3, 72.8, 71.5, 68.3, 66.7, 65.8, 65.6, 65.4, 65.3, 60.6, 55.5, 49.6, 42.9, 42.6, 42.1, 40.8, 37.4, 36.9, 33.0, 32.4, 30.6, 27.4 (6C), 26.2, 23.1, 21.7, 20.7, 20.0, 19.8, 19.6, 18.43, 18.36, 18.3, 14.4, 12.5, 7.3 (3C), 5.5 (3C), −1.17 (3C), −1.18 (3C), −1.24 (3C); HRMS (ESI): calculated for $C_{98}H_{164}O_{15}Si_6Na$ $[M + Na]^+$: 1772.0578, found: 1772.0565.

*(2S,3S)-4-{(4R,6S)-6-[{(2S,4S,6S)-6-[(2R,4S,5E,7E,9E,11E,13E,-15S,16R)-16-Hydroxy-5-methyl-2,4,15-tris{[2-(trimethylsilyl)ethoxy]methoxy}heptadeca-5,7,9,11,13-pentaen-1-yl]-2-methyl-1,3-dioxan-4-yl}methyl]-2,2-dimethyl-1,3-dioxan-4-yl}-2-[(R)-1-(methoxymethoxy)hexyl]butane-1,3-diol (**36**).* To a solution of silyl ether **36′** (38 mg, 0.022 mmol, 1 equiv) in dry THF (1.5 mL) was added TBAF (0.22 mL, 1 M in THF, 0.22 mmol, 10 equiv). The mixture was stirred at rt for 2 days; TBAF (0.22 mL, 1 M in THF, 0.22 mmol, 10 equiv) was added, and the mixture was stirred at rt for 2 days. The reaction was quenched by the addition of H_2O (2 mL).

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EtOAc (5 mL) was added; the layers were separated, and the aqueous layer was extracted with EtOAc (3 × 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated under vacuum. The crude material was purified by flash column chromatography on silica gel (pentane/EtOAc = 5:5 to 4:6) to afford triol **36** (22 mg, 0.019 mmol, 86%) as a yellow oil. $[\alpha]_D^{20}$ 15.3 (*c* 0.65, CH_3CN); IR: ν 3481, 2952, 2925, 1379, 1249, 1200, 1131, 1099, 1028, 938, 921, 860, 836 cm^{-1}; ^1H NMR (C_6D_6, 400 MHz): δ 6.46 (dd, J = 14.3 and J = 11.3 Hz, 1H), 6.37 (dd, J = 15.1 and J = 9.8 Hz, 1H), 6.30−6.13 (m, 6H), 5.68 (dd, J = 15.0 and J = 7.9 Hz, 1H), 4.87 ($d_{AB\ syst}$, J = 7.0 Hz, 1H), 4.81 ($d_{AB\ syst}$, J = 7.0 Hz, 1H), 4.76 ($d_{AB\ syst}$, J = 5.2 Hz, 1H), 4.75 ($d_{AB\ syst}$, J = 5.2 Hz, 1H), 4.67 (m, 1H), 4.67 ($d_{AB\ syst}$, J = 6.0 Hz, 1H), 4.61 ($d_{AB\ syst}$, J = 6.4 Hz, 1H), 4.59 ($d_{AB\ syst}$, J = 6.2 Hz, 1H), 4.54 ($d_{AB\ syst}$, J = 6.7 Hz, 1H), 4.48 (m, 1H), 4.17 (m, 1H), 4.13−3.84 (m, 11H), 3.81−3.75 (m, 2H), 3.72 (m, 1H), 3.61 (m, 1H), 3.50 (m, 1H), 3.22 (s, 3H), 2.85 (br s, 1H, OH), 2.42 (br s, 1H, OH), 2.27−2.16 (m, 2H), 2.15−2.00 (m, 5H), 1.82 (s, 3H), 1.89−1.65 (m, 4H), 1.60−1.50 (m, 2H), 1.44 (d, J = 5.0 Hz, 3H), 1.37 (s, 3H), 1.36−1.26 (m, 7H), 1.25 (s, 3H), 1.22 (d, J = 6.4 Hz, 3H), 1.17 (m, 1H), 1.05−0.95 (m, 6H), 0.92−0.88 (m, 3H), 0.04 (s, 9H), 0.02 (s, 9H), 0.00 (s, 9H), one OH not visible; ^{13}C NMR (C_6D_6, 100 MHz): δ 138.5, 135.2, 134.2, 134.0, 133.8, 133.4, 132.7, 130.3, 129.1, 128.7, 98.9, 98.8, 96.7, 94.9, 92.9, 92.8, 81.8, 79.1, 78.7, 73.5, 72.8, 72.6, 71.9, 71.1, 70.0, 65.7, 65.6, 65.52, 65.46, 61.7, 55.7, 49.3, 42.8, 42.3, 41.3, 40.3, 37.5, 37.2, 32.4, 32.2, 30.4, 26.2, 23.1, 21.7, 19.9, 18.51, 18.45, 18.36, 18.3, 14.4, 12.1, −1.19 (3C), −1.23 (3C), −1.3 (3C); HRMS (ESI): calculated for $C_{60}H_{114}O_{15}Si_3Na$ $[M + Na]^+$: 1181.7358, found: 1181.7338.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01166.

Copies of ^1H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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