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Towards the Synthesis of (–)-Callipeltoside A: Stereoselective Synthesis of the C1–C14 Macrolactone Core

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A highly stereoselective synthesis of the C1–C14 macrolactone core of the cytotoxic macrolide (–)-callipeltoside A has been achieved by utilizing an *anti*-selective aldol reaction and Wittig olefination to introduce an (*E*)-trisubstituted alkene, chemoselective diisobutylaluminum hydride (DIBAL-H) reduction of the 2,3-epoxy tosylate to install the C13 stereocenter, and intramolecular trapping of the acyl-ketene intermediate by the C13 hydroxy group as key steps.

Introduction

In 1996, Minale and co-workers reported the isolation of three macrocyclic lactones, callipeltosides A–C, of the same aglycon skeleton appended with dissimilar sugar subunits, from the shallow-water lithistid sponge *callipelta sp*, collected off the east coast of New Caledonia.[1] In preliminary biological investigations of (–)-callipeltoside A (**1**) it was found to inhibit in vitro proliferation of P388 cells (IC_{50} = 15.26 μg/mL) and NSCLC-N6 human bronchopulmunary non-small-cell-lung carcinoma (IC_{50} = 11.26 μg/mL). The results indicate that this activity is cell-cycle-dependent, blocking cell proliferation in the G1 phase and thereby establishing callipeltoside A (**1**) as an interesting mechanism-based lead.[1] Further biological evaluation was restricted owing to the low natural abundance of callipeltoside A (obtained in 1.4×10^{-4}% yield).[1] The appealing structural aspects of callipeltoside A (Figure 1) were ascertained to be a 14-membered macrolactone linked glycosidically through C5 to a highly functionalized deoxyamino sugar, and a dienyne-*trans*-chlorocyclopropane chain appended at C13. An encapsulated six-membered hemiketal pyran ring, an (*E*)-trisubstituted olefin, and a dipropionate backbone consisting of five contiguous stereocenters with a total of seven stereocenters are among the notable features of the macrolactone core of callipeltoside A (Figure 1). The low natural abundance, incomplete biological evaluation, initial stereochemical ambiguities, integrated with challenging molecular architecture attracted and prompted the synthetic community to produce a number of successful synthetic efforts toward callipeltoside A.[2] In a continuation of the synthesis of complex natural products, we herein disclose our stereoselective synthesis of the C1–C14 macrolactone core segment **2** of callipeltoside A.

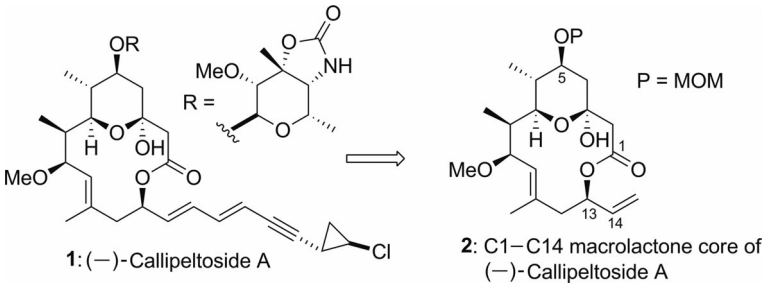

Figure 1. Structures of (–)-callipelltoside A (**1**) and the C1–C14 macrolactone core **2** of callipeltoside A.

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Retrosynthetic analysis, summarized in Figure 2, involved cleavage of the hemiketal pyran portion at the C4–C5 bond as well as the ester linkage of macrolactone **2** to give aldehyde **3**, bearing five stereogenic centers with an (*E*)-trisubstituted olefin and dienyl silyl ether **4**. Aldehyde **3** could be obtained from chemoselective reduction of 2,3-epoxy tosylate **5**, which, in turn, could be derived from alde-

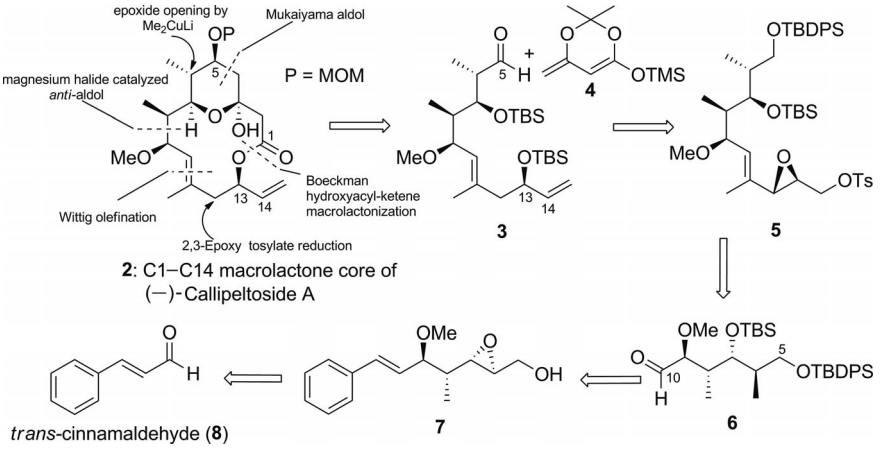


Figure 2. Retrosynthetic analysis of **2**.

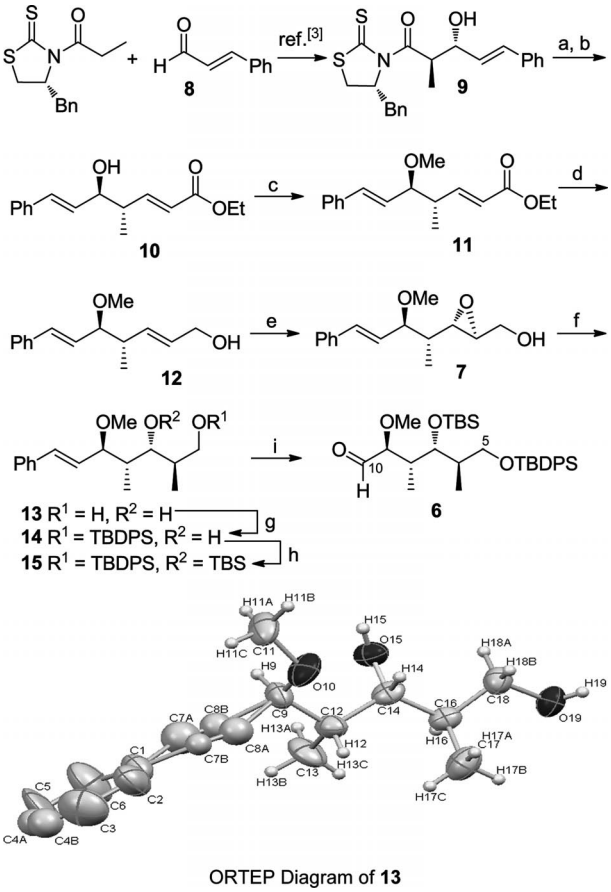
hyde **6** through Wittig reactions and Katsuki–Sharpless asymmetric epoxidation to install the (*E*)-trisubstituted olefin and the requisite stereochemistry at the C13 stereocenter. As outlined in Figure 2, the C8 and C9 stereocenters in aldehyde **6** could be established through a magnesium halide catalyzed aldol reaction, and C6 and C7 through epoxide opening with Me_2CuLi by starting from *trans*-cinnamaldehyde.

Results and Discussion

Synthesis of Aldehyde 6

The synthesis began with an aldol reaction between chiral *N*-acylthiazolidinethiones and *trans*-cinnamaldehyde (**8**) in the presence of $MgBr_2{\cdot}OEt_2$[3] as catalyst to afford the known *anti*-aldol adduct **9** (Scheme 1).

Reduction of **9** with diisobutylaluminum hydride (DIBAL-H) (2.5 equiv.) at –78 °C in tetrahydrofuran (THF) furnished the corresponding aldehyde.[4] The following Wittig olefination reaction with $Ph_3P{=}CHCO_2Et$ in benzene afforded α,β-unsaturated ester **10** (65% yield over two steps). The allylic hydroxy group present in **10** was converted into its methyl ether with Ag_2O and MeI to obtain **11** in quantitative yield. Reduction of ester **11** with DIBAL-H in THF furnished allyl alcohol **12** (98%), which was then subjected to Katsuki–Sharpless asymmetric epoxidation[5] reaction conditions to obtain α-epoxy alcohol **7** (α/β ≥ 24:1) in 92% yield. Epoxide opening proceeded smoothly with high regioselectivity after treatment of α-epoxy alcohol **7** with Me_2CuLi[6] to give diol **13** in good yield; the latter compound possesses *anti-syn-anti* stereochemistry concerning the four contiguous stereocenters. The assignments of the stereocenters of diol **13** were further supported by its X-ray crystal structure (Scheme 1).[7] Diol **13** was then transformed into aldehyde **6** by a three-step, high-yielding reaction sequence (Scheme 1). Selective protection of the primary alcohol functionality as its TBDPS ether with TBDPSCl, imidazole, and 4-(dimethylamino)pyridine



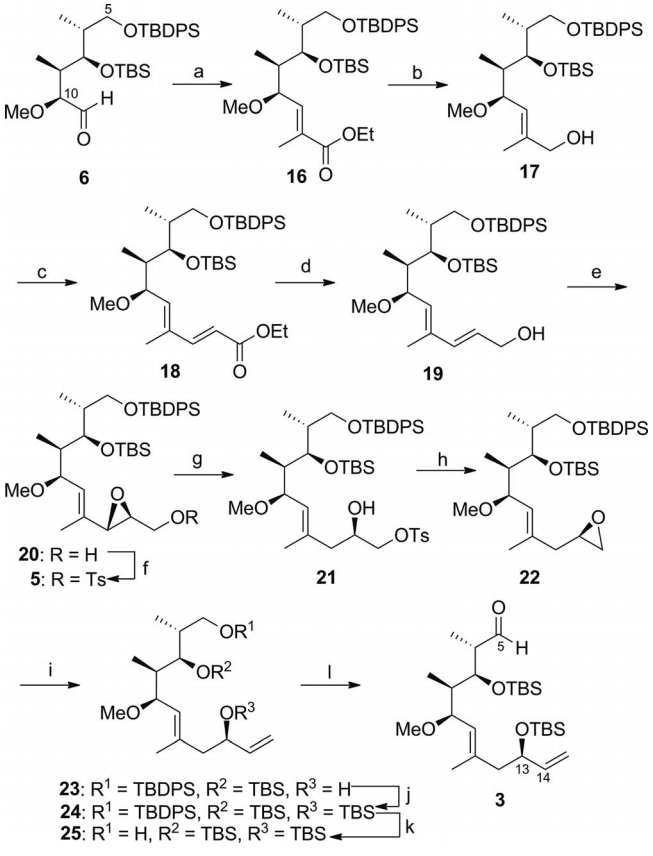
Scheme 1. Reagents and conditions: (a) DIBAL-H, THF, –78 °C, 20 min; (b) $Ph_3P{=}CHCO_2Et$, benzene, 80 °C, 4 h, 2 steps, 65%; (c) Ag_2O, CH_3I, 40 °C, 36 h, quantitative; (d) DIBAL-H, THF, 0 °C, 30 min, 98%; (e) $Ti(OiPr)_4$, (+)-L-DIPT, TBHP, MS (4 Å), CH_2Cl_2, –23 °C, 18 h, 92%; (f) Me_2CuLi, Et_2O, –45 °C, 90 min, 80%; (g) TBDPSCl, imidazole, DMAP, CH_2Cl_2, –5 °C, 1 h, 94%; (h) TBSOTf, 2,6-lutidine, CH_2Cl_2, 30 min, –50 °C, 96%; (i) OsO_4, NMO, THF/acetone, pH 7 buffer, room temp., 14 h, then $NaIO_4$, THF, pH 7 buffer, room temp., 3 h.

(DMAP) at –5 °C afforded compound **14** in 94% yield. The secondary alcohol functionality of **14** was then protected as its TBS ether with *tert*-butyldimethylsilyl trifluoromethane-

sulfonate (TBSOTf) and 2,6-lutidine to obtain **15** (96%); subsequent oxidative cleavage of the double bond present in **15** under standard reaction conditions [OsO_4, *N*-methylmorpholine *N*-oxide (NMO), then $NaIO_4$] furnished aldehyde **6** as an unpurified mixture with coproduct benzaldehyde.

Synthesis of Aldehyde 3

With the C5–C10 dipropionate chain in hand, we focused on the conversion of **6** into the C5–C14 segment **3** (Scheme 2). Freshly prepared, unpurified aldehyde **6** was first converted into α,β-unsaturated ester **16** by a Wittig reaction with $Ph_3P{=}C(CH_3)CO_2Et$ in toluene (91% overall yield from **15**) to install the requisite (*E*)-trisubstituted alkene with complete control over the geometry of the double bond. DIBAL-H mediated reduction of ester **16** in THF furnished trisubstituted allylic alcohol **17** (98%), which, upon Swern oxidation[8] followed by Wittig olefination with $Ph_3P{=}CH_2CO_2Et$, resulted in the formation of (2*E*,4*E*)-dienyl ester **18** [(2*E*)/(2*Z*) ≥ 5:1, as an inseparable mixture] in 93% yield from **17**. Reduction of **18** with DIBAL-H afforded the corresponding (2*E*,4*E*)-dienyl allylic alcohol **19** (81%), which was easily purified by silica gel column chromatography as a single isomer.



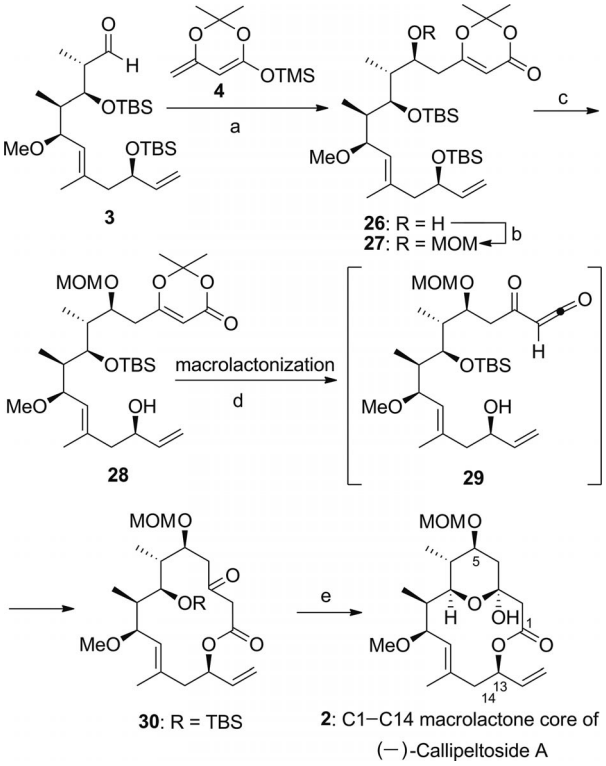
Scheme 2. Reagents and conditions: (a) $Ph_3P{=}C(CH_3)CO_2Et$, toluene, 90 °C, 18 h, 91% from **15**; (b) DIBAL-H, THF, 30 min, 98%; (c) (1) $(COCl)_2$, DMSO, Et_3N, –78 °C, 90 min, (2) $Ph_3P{=}CHCO_2Et$, benzene, 80 °C, 12 h, 2 steps, 93%; (d) DIBAL-H, THF, 30 min, 81%; (e) $Ti(OiPr)_4$, (+)-L-DIPT, TBHP, MS (4 Å), CH_2Cl_2, –23 °C, 22 h, 89%; (f) TsCl, Et_3N, DMAP, CH_2Cl_2, 18 h, 94%; (g) DIBAL-H (3 equiv.), CH_2Cl_2, –40 °C, 3 h, 91%; (h) NaH, THF, 0 °C, 30 min, 97%; (i) $Me_3S^+I^-$, *n*BuLi, THF, –10 °C to 0 °C to room temp., 2 h, 92%; (j) TBSOTf, 2,6-lutidine, CH_2Cl_2, –50 °C, 30 min, 95%; (k) NH_4F, MeOH, 50 °C, 4 h, 89%; (l) Dess–Martin periodinane, pyridine, wet CH_2Cl_2, 2 h.

Dienyl allylic alcohol **19** was subjected to Katsuki–Sharpless asymmetric epoxidation[5] [with near stoichiometric amounts of $Ti(OiPr)_4$ and L-(+)-DIPT] reaction conditions to afford β-epoxy alcohol **20** (α/β ≥ 1:52) in 89% yield. Epoxy alcohol **20** was derivatized as the corresponding 2,3-epoxy tosylate **5** with TsCl and Et_3N in 94% yield. The key reduction step of **5** with DIBAL-H (3 equiv.) occurred chemoselectively in CH_2Cl_2 at –40 °C to furnish the requisite 1-tosyloxy-2-alkanol **21** in excellent yield and selectivity.[9] Formation of the terminal epoxide **22** proceeded smoothly after treatment of **21** with NaH in THF (97%). The terminal epoxide **22** was transformed into one-carbon-homologated allylic alcohol **23** in 92% yield by treatment with an excess of dimethylsulfonium methylide.[10] Having all the requisite stereogenic centers in place, we employed the remaining synthetic operations to arrive at aldehyde **3** from the terminal olefin **23**. Protection of the allylic hydroxy group in **23** as its TBS ether to afford **24** in 95% yield and subsequent selective deprotection of the primary TBDPS ether present in **24** with NH_4F in methanol at 50 °C furnished **25** in 89% yield. The primary alcohol **25** was smoothly converted into aldehyde **3** under Dess–Martin periodinane oxidation conditions.[11]

Synthesis of the C1–C14 Segment of (–)-Callipeltoside A

With aldehyde **3** in hand, we proceeded to install the C5 stereogenic center along with the requisite carbon–oxygen framework to construct the 14-membered macrolactone **2** embedded with the hemiketal pyran ring. As illustrated in Scheme 3, by employing a diastereoselective aldol addition from the C5–C14 aldehyde segment **3** and dienyl silyl ether **4** afforded Felkin–Anh-type adduct **26** as the only product in 85% yield from **25**.[12]

The resultant hydroxy group in **26** was protected as its MOM ether by using standard conditions to obtain **27**. At this juncture, initially we decided to adopt the Hoye[2i] protocol for dual macrolactonization/pyran-hemiketal formation via acyl-ketenes. Several efforts to liberate both C7 and C13 hydroxy groups from **27** were found to be unsuccessful with HF·Py in MeOH, $Et_3N{\cdot}3HF$ in CH_3CN, and TASF in *N*,*N*-dimethylformamide (DMF)/H_2O. Use of these reaction conditions liberated only the C13 hydroxy group, with the C7 TBS ether remaining intact, giving the TBS-protected product **28** in excellent yield; as a result, the dihydroxy dioxinone precursor for the Hoye protocol could not be attained. With compound **28** in hand, we designed our synthetic operations in a stepwise fashion to implement first Boeckman macrolactonization[13] via monohydroxy acyl-ketene intermediate **29** and subsequent hemiketal py-



Scheme 3. Reagents and conditions: (a) $BF_3{\cdot}OEt_2$, CH_2Cl_2, –78 °C, 1 h, 85% from **25**; (b) MOMCl, $i Pr_2EtN$, CH_2Cl_2, 0 °C, 90 min, 97%; (c) HF·Py, MeOH, 0 °C to room temp., 6 h, quantitative; (d) toluene, 110 °C, 1 h, 84%; (e) HF·Py, MeOH, 0 °C, 2 h, 96%.

ran formation as elaborated in Trost's[2d] synthesis of this natural product. Thus, heating of a dilute solution of hydroxy dioxinone **28** in refluxing toluene induced the loss of acetone through thermal decomposition to evolve the acylketene intermediate **29**, which was then trapped intramolecularly by the pendant secondary hydroxy group at C13 to generate the 14-membered lactone **30** in an impressive yield of 84%. The final synthetic operation was carried out by using HF·Py in methanol to transform the macrolacone **30** into the C1–C14 segment **2** of (–)-callipeltoside A by removal of the silyl protecting group through in situ participation of the free hydroxy group at C7 and the carbonyl functionality at C3 to form the requisite tetrahydropyran/hemiketal ring.[2b]

Compound **2** was extensively characterized by using ^1H NMR spectroscopy. Analysis of the ^1H NMR coupling constants (Figure 3) of the tetrahydropyran/hemiketal ring protons, specifically the large coupling constants $J_{Hb/Hc}$ = 11.0 Hz, $J_{Hc/Hd}$ = 10.5 Hz, $J_{He/Hd}$ = 10.3 Hz, together with the small coupling constant $J_{Ha/Hc}$ = 4.7 Hz unambiguously established that H_b, H_c, H_d and H_e are all axially disposed in a six-membered ring. Hence, we have illustrated a straightforward and highly stereoselective approach to complete the synthesis of the C1–C14 segment **2** of (–)-callipeltoside A through acyclic stereocontrol in 26 steps (longest linear sequence) with 11% overall yield from the known intermediate **9**.

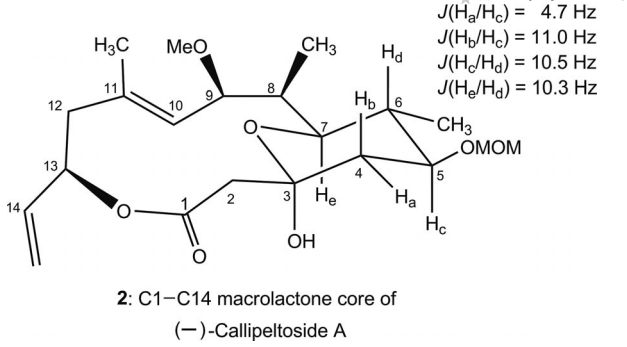


Figure 3. Tetrahydropyran/hemiketal ring stereochemistry of macrolactone **2**.

Conclusions

By utilizing high-yielding chemical transformations, we have accomplished a highly convergent and stereoselective linear synthesis of the macrolactone core segment of callipeltoside A, a potent cytotoxic macrolide. The notable feature of the synthesis is the construction of the C5–C14 segment (aldehyde **3**) consisting of five stereogenic centers with an (*E*)-trisubstituted olefin in a highly concise and stereoselective manner. The C8 and C9 stereocenters of the dipropionate portion were introduced by employing the Evans *anti*-aldol method. Katsuki–Sharpless asymmetric epoxidation and regioselective epoxide opening with Me_2-CuLi installed the stereocenters at C6 and C7. A straightforward and useful access to the (*E*)-trisubstituted olefin along with the C13 stereocenter has been illustrated efficiently through Wittig olefination and chemoselective DIBAL-H reduction of the 2,3-epoxy tosylate. The installation of the C5 stereocenter and penultimate macrolactonization were performed by a Mukaiyama aldol addition and intramolecular trapping of acyl-ketene intermediate by the pendant secondary hydroxy group at C13.

Experimental Section

General Methods: All reactions requiring anhydrous conditions were conducted in flame-dried glass apparatus under nitrogen. THF and Et_2O were freshly distilled from sodium benzophenone ketyl prior to use. CH_2Cl_2 was freshly distilled from CaH_2; toluene and benzene were dried azeotropically by using a Dean–Stark apparatus. Anhydrous methanol was obtained by distillation from magnesium alkoxide and stored under nitrogen over activated 4 Å molecular sieves. Reactions were monitored by TLC analysis using silica plates with fluorescent indicator (254 nm). All commercially available reagents were purchased and typically used as supplied. ^1H and ^{13}C NMR spectra were recorded in Fourier transform mode at the field strength specified (300, 400, 500, or 600 MHz for ^1H and 75 or 150 MHz for ^{13}C). Chemical shifts (δ) are reported in ppm referenced to $CDCl_3$ (δ = 7.26 ppm) or C_6D_6 (δ = 7.16 ppm) for ^1H and $CDCl_3$ (δ = 77.16 ppm) or C_6D_6 (δ = 128.06 ppm) for ^{13}C. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br. = broad, ABq = AB quartet), coupling constant (Hz), and integra-

tion. Ratios of diastereomers (*dr*) were obtained from ^{1}H NMR (300 MHz) spectra obtained with a signal/noise ratio > 200:1. Infrared spectra were recorded with an FTIR instrument, and the values are reported in terms of frequency of absorption (cm^{-1}). Melting points were recorded with an uncorrected melting point instrument. Optical rotations were measured with a polarimeter fitted with a sodium lamp (589 nm, D-line) by using a 1 dm, 1 mL quartz sample cell and are reported as $[\alpha]_D$ (concentration in g/100 mL solvent). For high-resolution mass spectra (HRMS), ion mass/charge (*m*/*z*) ratios are reported as values in atomic mass units.

Ethyl (2*E*,4*S*,5*R*,6*E*)-5-Hydroxy-4-methyl-7-phenyl-2,6-heptadienoate (10): To a stirred solution of aldol adduct **9** (2.2 g, 5.54 mmol) in THF (100 mL), DIBAL-H (1.5 M in toluene, 9.23 mL, 13.85 mmol) was added dropwise at –78 °C by using a syringe. The reaction was monitored by TLC and quenched by the dropwise addition of MeOH (1.5 mL). After warming to room temperature, saturated aqueous sodium potassium tartrate (25 mL) was added, and the mixture was stirred for 30 min. The mixture was poured into brine (20 mL) and extracted with ethyl acetate (3 × 50 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified through a short plug of silica gel (SiO_2; ethyl acetate/hexane, 20–30%) to obtain the corresponding aldehyde, which was immediately used for the next reaction. A 100 mL round-bottomed flask fitted with a cold-finger condenser was charged with the above crude aldehyde [predried by coevaporation from benzene (2 × 10 mL)] and benzene (50 mL). Ethyl triphenylphosphorylideneacetate (3.8 g, 11.0 mmol) was added in a single portion, and the resulting suspension was heated to 80 °C for 12 h. After being cooled to room temperature, the reaction mixture was diluted with hexane, filtered, and concentrated to remove Ph_3PO and unreacted ethyl triphenylphosphorylideneacetate. The crude product was purified by flash chromatography (SiO_2; ethyl acetae/hexane, 15%) to afford α,β-unsaturated ester **10** (936 mg, 65% from **9**) as a colorless liquid. $[\alpha]_D^{27}$ = –22.6 (*c* = 1.88, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3447, 2974, 1709, 1651, 1369, 1272, 1180, 1029, 970 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.17 (m, 5 H), 6.96 (dd, *J* = 15.9, 7.8 Hz, 1 H), 6.58 (d, *J* = 15.9 Hz, 1 H), 6.15 (dd, *J* = 15.9, 6.9 Hz, 1 H), 5.87 (dd, *J* = 15.9, 1.2 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.17 (m, 1 H), 2.54 (m, 1 H), 1.63–1.56 (br. s, 1 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.12 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.7, 150.3, 136.5, 132.3, 129.8, 128.7, 128.0, 126.7, 122.4, 76.2, 60.5, 43.1, 15.7, 14.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{20}O_3Na^+$ [M + Na]$^+$ 283.1310; found 283.1309.

Ethyl (2*E*,4*S*,5*R*,6*E*)-5-Methoxy-4-methyl-7-phenyl-2,6-heptadienoate (11): A 50 mL round-bottomed flask fitted with a cold-finger condenser was charged with free hydroxy compound **10** (690 mg, 2.65 mmol) and MeI (30 mL). Ag_2O (1.84 g, 7.95 mmol) was added in a single portion, and the resulting suspension was heated to 50 °C whilst stirring in the dark for 36 h. After being cooled to room temperature, the reaction mixture was filtered and concentrated. The product was purified by flash chromatography (SiO_2; ethyl acetate/hexane, 10%) to afford methyl ether **11** (726 mg, quantitative) as a yellow liquid. $[\alpha]_D^{25}$ = –11.5 (*c* = 2.22, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2979, 2933, 1719, 1652, 1452, 1368, 1266, 1180, 1090, 1037, 973 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.17 (m, 5 H), 6.96 (dd, *J* = 15.9, 7.8 Hz, 1 H), 6.51 (d, *J* = 15.9 Hz, 1 H), 5.98 (dd, *J* = 15.9, 8.4 Hz, 1 H), 5.81 (dd, *J* = 15.9, 1.2 Hz, 1 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 3.56 (ddd, *J* = 8.4, 6.6, 0.9 Hz, 1 H), 3.28 (s, 3 H), 2.55 (m, 1 H), 1.30 (t, *J* = 7.2 Hz, 3 H), 1.08 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.8, 151.0, 136.4, 134.2, 128.8, 128.0, 127.9, 126.7, 121.5, 86.0, 60.4, 56.8, 41.8, 15.8, 14.4 ppm. HRMS (ESI): calcd. for $C_{17}H_{22}O_3Na^+$ [M + Na]$^+$ 297.1466; found 297.1461.

{(2*S*,3*S*)-3-[(1*R*,2*R*,3*E*)-2-Methoxy-1-methyl-4-phenyl-3-butenyl]-oxiran-2-yl}methanol (12): To a stirred solution of α,β-unsaturated ester **11** (1.10 g, 4.0 mmol) in THF (25 mL) was added DIBAL-H (1.5 M in toluene, 5.9 mL, 8.8 mmol) at 0 °C. After stirring for 30 min, the reaction was quenched with saturated aqueous potassium sodium tartrate (20 mL). The heterogeneous mixture was warmed to room temperature and stirred vigorously for 2 h. The organic layer was washed with brine (10 mL), and the aqueous layer was back-extracted with Et_2O (3 × 20 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by flash chromatography (SiO_2; ethyl acetate/hexane, 20%) to furnish allylic alcohol **12** (910 mg, 98%) as a colorless liquid. $[\alpha]_D^{25}$ = –7.1 (*c* = 2.14, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3423, 2971, 2930, 1690, 1453, 1087, 972 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.15 (m, 5 H), 6.48 (d, *J* = 15.9 Hz, 1 H), 6.00 (dd, *J* = 15.9, 8.1 Hz, 1 H), 5.76–5.58 (m, 2 H), 4.09 (dd, *J* = 4.5, 0.9 Hz, 2 H), 3.49 (ddd, *J* = 8.1, 6.0, 0.9 Hz, 1 H), 3.28 (s, 3 H), 2.41 (m, 1 H), 1.47-1.33 (br. m, 1 H), 1.03 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.6, 134.8, 133.5, 129.5, 128.7, 128.4, 127.9, 126.6, 86.6, 63.8, 56.7, 41.5, 16.5 ppm. HRMS (ESI): calcd. for $C_{15}H_{20}O_2Na^+$ [M + Na]$^+$ 255.1360; found 255.1356.

{(2*S*,3*S*)-3-[(1*R*,2*R*,3*E*)-2-Methoxy-1-methyl-4-phenyl-3-butenyl]-oxiran-2-yl}methanol (7): To a stirred suspension of activated powdered 4 Å molecular sieves (1.40 g) in CH_2Cl_2 (30 mL), was added titanium(IV) isopropoxide (0.42 mL, 1.43 mmol) followed by (+)-L-diisopropyl tartrate (0.30 mL, 1.43 mmol) at –23 °C. After stirring for 10 min, a solution of allylic alcohol **12** (1.66 g, 7.15 mmol) in CH_2Cl_2 (15 mL) was added to the reaction mixture. After stirring for 30 min, *tert*-butyl hydroperoxide (TBHP; 2 M in toluene, 8.6 mL, 17.1 mmol) was added, and the mixture was stirred at –23 °C for 18 h. The reaction was then quenched with water (20 mL) and 30% NaOH solution saturated with aqueous NaCl (20 mL). The mixture was stirred vigorously at room temperature for 2 h, then the reaction mixture was filtered through a plug of Celite, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 25%) to furnish epoxy alcohol **7** (α/β ≥ 24:1, 1.63 g, 92%) as a colorless liquid. $[\alpha]_D^{25}$ = –44.5 (*c* = 2.24, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3629, 2925, 2854, 1463, 1253, 1087, 833 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.16 (m, 5 H), 6.52 (d, *J* = 15.9 Hz, 1 H), 5.99 (dd, *J* = 15.9, 8.1 Hz, 1 H), 3.84 (dt, *J* = 12.3, 3.9 Hz, 1 H), 3.64 (dd, *J* = 6.3, 3.9 Hz 1 H), 3.56 (ddd, *J* = 8.1, 7.5, 0.6 Hz, 1 H), 3.30 (s, 3 H), 2.98 (dt, *J* = 4.2, 2.4 Hz, 1 H), 2.91 (dd, *J* = 7.2, 2.4 Hz, 1 H), 1.73 (m, 1 H), 1.57 (m, 1 H), 1.01 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.4, 133.8, 128.8, 128.2, 128.0, 126.6, 85.2, 62.0, 59.1, 58.3, 56.7, 41.0, 13.4 ppm. HRMS (ESI): calcd. for $C_{15}H_{20}O_3Na^+$ [M + Na]$^+$ 271.1310; found 271.1299.

(2*R*,3*R*,4*S*,5*R*,6*E*)-5-Methoxy-2,4-dimethyl-7-phenyl-6-heptene-1,3-diol (13): To a stirred solution of Me_2CuLi [prepared from CuI (2.66 g, 14 mmol) and MeLi (1.4 M in Et_2O, 20 mL, 28 mmol) in Et_2O (30 mL) at –23 °C] was added a solution of epoxy alcohol **7** (694 mg, 2.8 mmol) in Et_2O (10 mL) at –45 °C. After stirring for 90 min, the reaction mixture was quenched with a mixture of saturated NH_4Cl and 28% aqueous NH_3 (2:1, 25 mL). The organic layer was separated, and the aqueous layers were extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried with

Na_2SO_4 and concentrated. The residue was dissolved in 60% aqueous acetonitrile (25 mL) followed by slow addition of $NaIO_4$ (1.2 g, 5.6 mmol) at 0 °C. After stirring at room temperature for 1 h, acetonitrile was removed under reduced pressure, and the aqueous layer was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (40 mL), dried with Na_2SO_4, and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 40%) to afford diol **13** (591 mg, 80%) as a solid, which, upon crystallization from ethyl acetate/hexane, gave colorless crystals. M.p. 64–65 °C. $[\alpha]_D^{26}$ = –6.5 (*c* = 1.35, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3338, 2925, 2854, 1450, 1384, 1079, 975 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.18 (m, 5 H), 6.55 (d, *J* = 15.9 Hz, 1 H), 6.14 (dd, *J* = 15.9, 7.8 Hz, 1 H), 3.92 (dd, *J* = 9.6, 1.5 Hz, 1 H), 3.79 (ddd, *J* = 7.8, 4.8, 0.6 Hz, 1 H), 3.69-3.52 (m, 2 H), 3.49-3.37 (br. m, 2 H), 3.35 (s, 3 H), 1.93–1.71 (m, 2 H), 1.04 (d, *J* = 7.1 Hz, 3 H), 0.72 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.4, 133.3, 128.7, 128.5, 127.9, 126.6, 86.6, 76.6, 69.1, 57.3, 40.0, 37.4, 13.4, 10.3 ppm. HRMS (ESI): calcd. for $C_{16}H_{24}O_3Na^+$ $[M + Na]^+$ 287.1623; found 287.1616.

(2*R*,3*R*,4*S*,5*R*,6*E*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-5-methoxy-2,4-dimethyl-7-phenyl-6-hepten-3-ol (14): To a stirred solution of the diol **13** (219 mg, 0.83 mmol) in CH_2Cl_2 (8 mL), was added imidazole (75 mg, 1.08 mmol), *tert*-butyldiphenylsilyl chloride (TBDPSCl; 0.24 mL, 0.90 mmol) and 4-(dimethylamino)pyridine (DMAP; catalytic) at –5 °C, and stirring was continued for 1 h. The reaction mixture was partitioned between CH_2Cl_2 (20 mL) and H_2O (10 mL), and the organic layer was washed with brine (10 mL), dried with Na_2SO_4, and concentrated. The crude product was purified by flash chromatography (SiO_2; ethyl acetate/hexane, 10%) to obtain alcohol **14** (390 mg, 94%) as a white solid. M.p. 72–73 °C. $[\alpha]_D^{25}$ = –20.2 (*c* = 2.17, $CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3505, 2959, 2929, 2857, 1462, 1428, 1112, 1086, 969, 822 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.73–7.64 (m, 4 H), 7.45–7.17 (m, 11 H), 6.54 (d, *J* = 15.9 Hz, 1 H), 6.04 (dd, *J* = 15.9, 8.1 Hz, 1 H), 3.99 (dt, *J* = 9.6, 1.8 Hz, 1 H), 3.79–3.70 (m, 3 H), 3.38 (br. d, *J* = 1.8 Hz, 1 H), 3.35 (s, 3 H), 1.89–1.66 (m, 2 H), 1.07 (s, 9 H), 0.89 (d, *J* = 7.0 Hz, 3 H), 0.77 (d, *J* = 6.9 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 135.8, 134.9, 133.4, 129.9, 129.8, 129.5, 128.7, 127.9, 126.6, 84.9, 73.7, 69.3, 56.9, 40.1, 38.1, 27.0, 19.3, 13.4, 9.5 ppm. HRMS (ESI): calcd. for $C_{32}H_{42}O_3NaSi^+$ $[M + Na]^+$ 525.2800; found 525.2822.

***tert*-Butyl{[(1*R*,2*R*,3*R*,4*E*)-1-{(1*R*)-2-[(*tert*-butyldiphenylsilyl)oxy]-1-methylethyl}-3-methoxy-2-methyl-5-phenyl-4-pentenyl]oxy}dimethylsilane (15):** A stirred solution of alcohol **14** (595 mg, 1.18 mmol) in CH_2Cl_2 (15 mL) at –50 °C was treated with 2,6-lutidine (0.27 mL, 2.36 mmol) and TBSOTf (0.41 mL, 1.77 mmol). After 30 min, saturated $NaHCO_3$ (10 mL) was added. The organic layer was separated and the aqueous layer extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by flash column chromatography (SiO_2; ethyl acetate/hexane, 5%) to afford compound **15** (698 mg, 96%) as a yellow liquid. $[\alpha]_D^{25}$ = +15.0 (*c* = 1.08, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2956, 2929, 2857, 1461, 1388, 1252, 1106, 1086, 1029, 968, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 7.72–7.62 (m, 4 H), 7.44–7.17 (m, 11 H), 6.44 (d, *J* = 15.9 Hz, 1 H), 5.90 (dd, *J* = 15.9, 8.7 Hz, 1 H), 4.14 (br. d, *J* = 6.3 Hz, 1 H), 3.76 (dd, *J* = 9.6, 5.7 Hz, 1 H), 3.45 (dd, *J* = 9.0, 8.7 Hz, 1 H), 3.39 (dd, *J* = 9.6, 7.5 Hz, 1 H), 3.23 (s, 3 H), 1.92 (m, 1 H), 1.78 (m, 1 H), 1.08 (s, 9 H), 0.94 (d, *J* = 6.9 Hz, 3 H), 0.84 (s, 9 H), 0.77 (d, *J* = 6.9 Hz, 3 H), 0.03 (s, 3 H), –0.10 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.8, 135.9, 134.2, 133.8, 129.8, 129.6, 128.7, 127.8, 127.7, 126.6, 84.2, 71.7, 66.9, 55.9, 41.8, 40.5, 27.1, 26.3, 19.4, 18.6, 13.9, 10.8, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{38}H_{56}O_3NaSi_2^+$ $[M + Na]^+$ 639.3665; found 639.3636.

Ethyl (*E*,4*R*,5*R*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(*tert*-butyldiphenylsilyl)oxy]-4-methoxy-2,5,7-trimethyl-2-octenoate (16): To a stirred solution of **15** (387 mg, 0.63 mmol) in THF (3 mL), acetone (3 mL) and pH 7 buffer (3 mL), was added NMO (105 mg, 0.9 mmol) and OsO_4 (0.2 M in toluene, 96 μL, 0.019 mmol). The mixture was stirred at room temperature for 14 h, then diluted with ethyl acetate (30 mL). The reaction mixture was cooled to 0 °C, and saturated aqueous $NaHSO_3$ (6 mL) was added. The ice bath was removed, and the mixture was stirred for an additional 30 min and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (50 mL), dried with Na_2SO_4, and concentrated. The crude diol was used for the next reaction without further purification. A stirred biphasic solution of the crude diol in THF (8 mL) and pH 7 buffer (4 mL) was treated with $NaIO_4$ (270 mg, 1.26 mmol) and stirred at 23 °C for 3 h. The reaction mixture was diluted with Et_2O (30 mL) and filtered through a plug of Celite. The filtrate was washed with saturated aqueous $NaHCO_3$ (20 mL), then dried with Na_2SO_4 and concentrated to give crude aldehyde **6** as an inseparable mixture with coproduct benzaldehyde. The crude aldehyde **6** was directly used for the Wittig reaction. A 50 mL round-bottomed flask fitted with a cold-finger condenser was charged with crude aldehyde **6** [predried by coevaporation from benzene (2 × 8 mL)] and toluene (25 mL). [1-(Ethoxycarbonyl)ethylidene]triphenylphosphorane (1.14 g, 3.15 mmol) was added in a single portion, and the resulting suspension was heated to vigorous reflux for 18 h. After having been cooled to room temperature, the reaction mixture was diluted with hexane, filtered, and concentrated to remove Ph_3PO and unreacted [1-(ethoxycarbonyl)-ethylidene]triphenylphosphorane. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 6%) to obtain α,β-unsaturated ester **16** (360 mg, 91% from **15**) as a yellow liquid. $[\alpha]_D^{25}$ = +14.4 (*c* = 1.35, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2929, 2857, 1715, 1650, 1465, 1385, 1258, 1225, 1106, 1080, 1029, 832 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.61 (m, 4 H), 7.44–7.31 (m, 6 H), 6.42 (dd, *J* = 10.0, 1.2 Hz, 1 H), 4.22 (q, *J* = 7.2 Hz, 2 H), 4.16 (dd, *J* = 6.8, 1.0 Hz, 1 H), 3.81 (dd, *J* = 10.0, 9.6 Hz, 1 H), 3.72 (dd, *J* = 9.8, 5.6 Hz, 1 H), 3.36 (dd, *J* = 9.8, 7.8 Hz, 1 H), 3.18 (s, 3 H), 1.90 (m, 1 H), 1.87 (d, *J* = 0.8 Hz, 3 H), 1.74 (m, 1 H), 1.34 (t, *J* = 7.2 Hz, 3 H), 1.07 (s, 9 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.83 (s, 9 H), 0.69 (d, *J* = 6.9 Hz, 3 H), 0.04 (s, 3 H), –0.11 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 141.4, 135.8, 134.1, 131.7, 129.6, 127.7, 78.1, 71.0, 66.9, 60.9, 56.0, 41.7, 40.1, 27.0, 26.2, 19.4, 18.5, 14.4, 13.8, 13.4, 9.8, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{36}H_{58}O_5NaSi_2^+$ $[M + Na]^+$ 649.3720; found 649.3700.

(*E*,4*R*,5*R*,6*R*,7*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-8-[(*tert*-butyldiphenylsilyl)oxy]-4-methoxy-2,5,7-trimethyl-2-octen-1-ol (17): To a stirred solution of α,β-unsaturated ester **16** (334 mg, 0.534 mmol) in THF (10 mL), was added DIBAL-H (1.5 M in toluene, 0.75 mL, 1.12 mmol) at 0 °C. After stirring for 30 min, the reaction was quenched with saturated aqueous potassium sodium tartrate (10 mL). The heterogeneous mixture was warmed to room temperature and stirred vigorously for 2 h. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by chromatography (SiO_2; ethyl acetate/hexane, 15%) to furnish allylic alcohol **17** (306 mg, 98%) as a colorless liquid. $[\alpha]_D^{26}$ = –5.0 (*c* = 0.7, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3429, 3070, 2959, 2931, 2856, 1681, 1463, 1428, 1384, 1111, 1006, 855 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 7.69–7.71 (m, 4 H), 7.42–7.31 (m, 6 H), 5.17 (dq, *J* = 9.5, 1.5 Hz, 1 H), 4.12 (dd, *J* = 7.0, 1.0 Hz, 1 H), 4.05 (s, 2 H), 3.74 (dd, *J* = 10.0, 5.5 Hz, 1

H), 3.72 (dd, *J* = 10.0, 9.5 Hz, 1 H), 3.35 (dd, *J* = 10.0, 7.9 Hz, 1 H), 3.15 (s, 3 H), 1.88 (m, 1 H), 1.70 (d, *J* = 1.0 Hz, 3 H), 1.64 (m, 1 H), 1.07 (s, 9 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.82 (s, 9 H), 0.69 (d, *J* = 6.9 Hz, 3 H), 0.04 (s, 3 H), –0.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.9, 135.9, 134.2, 129.6, 127.7, 125.7, 77.6, 71.5, 68.4, 67.0, 55.3, 41.7, 40.5, 27.0, 26.2, 19.4, 18.5, 14.6, 14.0, 10.0, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{34}H_{56}O_4NaSi_2^+$ [M + Na]$^+$ 607.3614; found 607.3625.

Ethyl (2*E*,4*E*,6*R*,7*R*,8*R*,9*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-10-[(*tert*-butyldiphenylsilyl)oxy]-6-methoxy-4,7,9-trimethyl-2,4-decadienoate (18): A solution of anhydrous DMSO (0.12 mL, 1.64 mmol) in CH_2Cl_2 (10 mL) was treated with oxalyl chloride (0.11 mL, 1.23 mmol) and stirred at –78 °C for 15 min. A solution of allylic alcohol **17** (480 mg, 0.822 mmol) in CH_2Cl_2 (5 mL) was added dropwise to the reaction mixture. The solution was stirred at –78 °C for 30 min, Et_3N (0.34 mL, 2.47 mmol) was added, and the cloudy reaction mixture was warmed to 0 °C over 30 min and stirred at 0 °C for an additional 10 min. The white suspension was diluted with pentane (100 mL), and the reaction mixture was filtered to remove the majority of the Et_3N salt. The filtrate was washed with H_2O (2 × 15 mL), and the combined organic layers were washed with saturated aqueous $NaHCO_3$ (15 mL), dried with Na_2SO_4, and concentrated. The crude aldehyde was directly used in the next reaction without further purification. A 50 mL round-bottomed flask fitted with a cold-finger condenser was charged with unpurified aldehyde obtained from Swern oxidation [predried by coevaporation from benzene (2 × 10 mL)] and benzene (25 mL). Ethyl triphenylphosphorylideneacetate (860 mg, 2.47 mmol) was added in a single portion, and the resulting suspension was heated to 80 °C for 12 h. After having been cooled to room temperature, the reaction mixture was diluted with hexane, filtered and concentrated to remove Ph_3PO and unreacted ethyl triphenylphosphorylideneacetate. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 7%) to afford (2*E*,4*E*)-dienyl ester **18** [(2*E*)/(2*Z*) ≥ 5:1, 500 mg, 93%] as a yellow liquid. $[\alpha]_D^{25}$ = +19.9 (*c* = 1.54, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3069, 2931, 2857, 2893, 1715, 1624, 1466, 1429, 1388, 1299, 1256, 1170, 1106, 1082, 1031, 836 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.58 (m, 4 H), 7.43–7.28 (m, 7 H), 5.84 (d, *J* = 15.6 Hz, 1 H), 5.61 (d, *J* = 9.6 Hz, 1 H), 4.21 (q, *J* = 7.0 Hz, 2 H), 4.14 (d, *J* = 6.8 Hz, 1 H), 3.84 (dd, *J* = 9.6, 9.6 Hz, 1 H), 3.72 (dd, *J* = 9.9, 5.7 Hz, 1 H), 3.36 (dd, *J* = 9.9, 7.8 Hz, 1 H), 3.15 (s, 3 H), 1.89 (m, 1 H), 1.83 (d, *J* = 0.9 Hz, 3 H), 1.69 (m, 1 H), 1.32 (t, *J* = 7.0 Hz, 3 H), 1.06 (s, 9 H), 0.91 (d, *J* = 6.9 Hz, 3 H), 0.83 (s, 9 H), 0.68 (d, *J* = 6.9 Hz, 3 H), 0.04 (s, 3 H), –0.11 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.4, 148.7, 141.3, 136.4, 135.8, 134.2, 129.6, 127.7, 117.7, 77.9, 71.2, 66.9, 60.5, 55.8, 41.7, 40.4, 27.0, 26.2, 19.4, 18.5, 14.5, 13.8, 13.2, 9.9, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{38}H_{60}O_5NaSi_2^+$ [M + Na]$^+$ 675.3877; found 675.3853.

(2*E*,4*E*,6*R*,7*R*,8*R*,9*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-10-[(*tert*-butyldiphenylsilyl)oxy]-6-methoxy-4,7,9-trimethyl-2,4-decadien-1-ol (19): To a stirred solution of dienyl ester **18** (208 mg, 0.318 mmol) in THF (5 mL) was added DIBAL-H (1.5 M in toluene, 0.48 mL, 0.70 mmol) at 0 °C. After stirring for 30 min, the reaction was quenched with saturated potassium sodium tartrate solution (4 mL). The heterogeneous mixture was warmed to room temperature and stirred vigorously for 2 h. The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 6 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 15%) to obtain pure (2*E*,4*E*)-dienyl allylic alcohol **19** (157 mg, 81%) as a colorless liquid. $[\alpha]_D^{25}$ = +8.6 (*c* = 1.95, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3422, 3068, 2932, 2858, 2891, 1717, 1465, 1428, 1386, 1254, 1108, 832 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.72–7.60 (m, 4 H), 7.44–7.30 (m, 6 H), 6.30 (dtd, *J* = 15.6, 1.5, 0.6 Hz, 1 H), 5.80 (dt, *J* = 15.6, 6.0 Hz, 1 H), 5.21 (dd, *J* = 9.6, 0.9 Hz, 1 H), 4.21 (br. d, *J* = 6.0 Hz, 2 H), 4.12 (dd, *J* = 6.9, 1.2 Hz, 1 H), 3.81 (dd, *J* = 9.6, 9.6 Hz, 1 H), 3.75 (dd, *J* = 9.8, 5.6 Hz, 1 H), 3.36 (dd, *J* = 9.8, 7.9 Hz, 1 H), 3.15 (s, 3 H), 1.89 (m, 1 H), 1.80 (d, *J* = 0.9 Hz, 3 H), 1.66 (m, 1 H), 1.06 (s, 9 H), 0.93 (d, *J* = 6.9 Hz, 3 H), 0.83 (s, 9 H), 0.68 (d, *J* = 6.9 Hz, 3 H), 0.04 (s, 3 H), –0.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 137.0, 136.0, 135.9, 134.2, 133.3, 129.6, 127.7, 127.3, 77.9, 71.5, 67.0, 63.9, 55.5, 41.7, 40.7, 27.0, 26.2, 19.4, 18.5, 14.0, 13.4, 10.0, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{36}H_{58}O_4NaSi_2^+$ [M + Na]$^+$ 633.3771; found 633.3766.

[(2*S*,3*S*)-3-{(*E*,3*R*,4*R*,5*R*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(*tert*-butyldiphenylsilyl)oxy]-3-methoxy-1,4,6-trimethyl-1-heptenyl}-oxiran-2-yl]methanol (20): To a stirred suspension of powdered activated 4 Å molecular sieves (125 mg) in CH_2Cl_2 (10 mL), was added titanium(IV) isopropoxide (0.11 mL, 0.35 mmol) followed by (+)-L-diisopropyl tartrate (85 μL, 0.40 mmol) at –23 °C. After stirring for 10 min, a solution of dienyl allylic alcohol **19** (385 mg, 0.625 mmol) in CH_2Cl_2 (5 mL) was added to the mixture. After stirring for 30 min, *tert*-butyl hydroperoxide (2 M in toluene, 0.75 mL, 1.5 mmol) was added, and the mixture was stirred at –23 °C for 22 h. The reaction was then quenched with water (5 mL) and 30% NaOH solution saturated with aqueous NaCl (5 mL) and stirred vigorously at room temperature for another 2 h. The reaction mixture was filtered through a plug of Celite, and the organic layer was separated. The aqueous layer was extracted with CH_2Cl_2 (3 × 15 mL), and the combined organic layers were washed with brine (25 mL), dried with Na_2SO_4, and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 20%) to furnish β-epoxy alcohol **20** (α/β ≥ 1:52, 350 mg, 89%) as a colorless liquid. $[\alpha]_D^{25}$ = +1.1 (*c* = 2.98, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3428, 3070, 2931, 2857, 2891, 1655, 1465, 1428, 1386, 1252, 1082, 1027, 834 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.71–7.60 (m, 4 H), 7.44–7.29 (m, 6 H), 5.35 (d, *J* = 9.6 Hz, 1 H), 4.11 (dd, *J* = 6.9, 0.9 Hz, 1 H), 3.96 (ddd, *J* = 13.2, 4.8, 2.7 Hz 1 H), 3.74 (dd, *J* = 9.6, 9.6 Hz, 1 H), 3.73 (dd, *J* = 9.9, 5.4 Hz, 1 H), 3.65 (dd, *J* = 7.5, 4.2 Hz, 1 H), 3.39 (br. d, *J* = 2.4 Hz, 1 H), 3.35 (dd, *J* = 9.9, 7.8 Hz, 1 H), 3.15 (s, 3 H), 3.10 (dt, *J* = 3.9, 2.4 Hz, 1 H), 1.86 (m, 1 H), 1.66 (m, 1 H), 1.58 (d, *J* = 1.3 Hz, 3 H), 1.06 (s, 9 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.82 (s, 9 H), 0.70 (d, *J* = 6.9 Hz, 3 H), 0.03 (s, 3 H), –0.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.8, 135.6, 134.2, 130.2, 129.6, 127.7, 77.5, 71.4, 67.0, 61.6, 58.9, 57.8, 55.5, 41.7, 40.4, 27.0, 26.2, 19.4, 18.5, 13.9, 12.0, 10.0, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{36}H_{58}O_5NaSi_2^+$ [M + Na]$^+$ 649.3720; found 649.3691.

[(2*S*,3*S*)-3-{(*E*,3*R*,4*R*,5*R*,6*R*)-5-[(*tert*-Butyldimethylsilyl)oxy]-7-[(*tert*-butyldiphenylsilyl)oxy]-3-methoxy-1,4,6-trimethyl-1-heptenyl}-oxiran-2-yl]methyl 4-Methyl-1-benzenesulfonate (5): To a stirred solution of epoxy alcohol **20** (192 mg, 0.306 mmol) in CH_2Cl_2 (12 mL) were added triethylamine (0.14 mL, 1.02 mmol), 4-(dimethylamino)pyridine (catalytic), and toluenesulfonyl chloride (100 mg, 0.51 mmol), and the reaction mixture was stirred at 0 °C for 18 h. The reaction was quenched with saturated aqueous NH_4Cl (10 mL), the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 10%) to afford 2,3-epoxy tosylate **5** (225 mg, 94%) as a colorless liquid. $[\alpha]_D^{25}$ = –8.2 (*c* = 0.745, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2925, 2855, 1638, 1463, 1367, 1253, 1180, 1085, 1026, 966, 825 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.4 Hz, 2

H), 7.69–7.59 (m, 4 H), 7.42–7.29 (m, 8 H), 5.30 (d, J = 9.6 Hz, 1 H), 4.22 (dd, J = 11.4, 3.9 Hz, 1 H), 4.10 (dd, J = 6.9, 0.9 Hz, 1 H), 4.03 (dd, J = 11.4, 5.7 Hz, 1 H), 3.71 (dd, J = 9.6, 9.6 Hz, 1 H), 3.70 (dd, J = 9.9, 3.3 Hz, 1 H), 3.35 (dd, J = 9.9, 7.8 Hz, 1 H), 3.19 (br. d, J = 1.5 Hz, 1 H), 3.15 (dd, J = 3.6, 1.8 Hz, 1 H), 3.13 (s, 3 H), 2.47 (s, 3 H), 1.86 (m, 1 H), 1.64 (m, 1 H), 1.52 (d, J = 0.9 Hz 3 H), 1.06 (s, 9 H), 0.91 (d, J = 6.9 Hz, 3 H), 0.81 (s, 9 H), 0.66 (d, J = 6.9 Hz, 3 H), 0.01 (s, 3 H), –0.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.1, 135.6, 134.3, 133.9, 132.5, 130.9, 129.9, 129.4, 127.9, 127.4, 76.5, 71.0, 69.7, 66.7, 59.4, 55.3, 53.9, 41.4, 40.1, 26.8, 26.0, 21.6, 19.2, 18.2, 13.6, 11.6, 9.7, –4.1, –4.3 ppm. HRMS (ESI): calcd. for $C_{43}H_{64}O_7NaSi_2S^+$ [M + Na]$^+$ 803.3809; found 803.3794.

(2*R*,4*E*,6*R*,7*R*,8*R*,9*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-10-[(*tert*-butyldiphenylsilyl)oxy]-2-hydroxy-6-methoxy-4,7,9-trimethyl-4-decenyl 4-Methyl-1-benzenesulfonate (21): A stirred solution of 2,3-epoxy tosylate **5** (132 mg, 0.168 mmol) in CH_2Cl_2 (2 mL) at –78 °C was treated with DIBAL-H (1.5 M in toluene, 0.34 mL, 0.51 mmol). The reaction mixture was stirred at –78 °C for 5 min, then warmed to –40 °C and stirred at that temperature for 3 h. The reaction mixture was diluted with CH_2Cl_2 (10 mL), then quenched with a saturated solution of potassium sodium tartrate (5 mL) and warmed to room temperature. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 15%) to furnish 1-tosyloxy-2-alkanol **21** (120 mg, 91%) as a colorless liquid. $[\alpha]_D^{29}$ = +4.74 (c = 1.18, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3480, 2924, 2854, 1464, 1362, 1180, 1085, 1026, 975, 832 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80 (d, J = 8.5 Hz, 2 H), 7.70–7.63 (m, 4 H), 7.44–7.31 (m, 8 H), 4.95 (d, J = 9.5 Hz, 1 H), 4.06 (dd, J = 6.5, 0.5 Hz, 1 H 1 H), 4.06 (dd, J = 10.0, 3.5 Hz, 1 H), 4.00 (m, 1 H), 3.92 (dd, J = 10.0, 6.5 Hz 1 H), 3.76 (dd, J = 10.0, 5.5 Hz, 1 H), 3.68 (dd, J = 9.5, 9.5 Hz, 1 H), 3.36 (dd, J = 10.0, 8.0, Hz, 1 H), 3.11 (s, 3 H), 2.44 (s, 3 H), 2.27-2.18 (m, 2 H), 2.02 (d, J = 3.5 Hz, 1 H), 1.88 (m, 1 H), 1.67 (d, J = 1.3 Hz, 3 H), 1.60 (m, 1 H), 1.06 (s, 9 H), 0.91 (d, J = 6.9 Hz, 3 H), 0.81 (s, 9 H), 0.65 (d, J = 6.9 Hz, 3 H), 0.02 (s, 3 H), –0.13 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.2, 135.8, 135.7, 134.2, 132.8, 130.1, 129.8, 129.6, 128.1, 127.7, 77.7, 73.6, 71.4, 67.5, 67.0, 55.3, 43.5, 41.6, 40.4, 27.0, 26.2, 21.8, 19.4, 18.5, 17.2, 14.0, 10.1, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{43}H_{66}O_7NaSi_2S^+$ [M + Na]$^+$ 805.3965; found 805.3945.

***tert*-Butyl({(2*R*,3*R*,4*R*,5*R*,6*E*)-3-[(*tert*-butyldimethylsilyl)oxy]-5-methoxy-2,4,7-trimethyl-8-[(2*R*)-oxiran-2-yl]-6-octenyl}oxy)diphenylsilane (22):** A stirred solution of 1-tosyloxy-2-alkanol **21** (108 mg, 0.138 mmol) in THF (2 mL) at 0 °C was treated with NaH (4 mg, 0152 mmol). After 30 min, the reaction was quenched with water (2 mL), and the aqueous layer was extracted with Et_2O (3 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 7%) to obtain terminal epoxide **22** (82 mg, 97%) as a colorless liquid. $[\alpha]_D^{25}$ = +0.55 (c = 3.5, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2930, 2857, 1630, 1466, 1385, 1253, 1082, 1026, 833 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.70–7.60 (m, 4 H), 7.44–7.28 (m, 6 H), 5.01 (d, J = 9.6 Hz, 1 H), 4.10 (dd, J = 6.9, 0.9 Hz, 1 H), 3.74 (dd, J = 9.9, 5.1 Hz, 1 H), 3.69 (dd, J = 9.9, 9.6 Hz, 1 H), 3.34 (dd, J = 9.9, 7.8 Hz, 1 H), 3.15 (s, 3 H), 2.96 (m, 1 H), 2.74 (dd, J = 5.1, 3.9 Hz, 1 H), 2.45 (dd, J = 5.1, 2.7 Hz, 1 H), 2.26 (br. d, J = 6.0 Hz, 2 H), 1.88 (m, 1 H), 1.74 (d, J = 0.9 Hz, 3 H), 1.62 (m, 1 H), 1.06 (s, 9 H), 0.92 (d, J = 6.9 Hz, 3 H), 0.81 (s, 9 H), 0.70 (d, J = 6.9 Hz, 3 H), 0.03 (s, 3 H), –0.13 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.7, 135.9, 134.3, 129.6, 127.9, 127.7, 77.8, 71.6, 67.0, 55.2, 51.6, 47.0, 42.9, 41.7, 40.6, 27.1, 26.2, 19.4, 18.5, 17.8, 14.0, 10.1, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{36}H_{58}O_4NaSi_2^+$ [M + Na]$^+$ 633.3771; found 633.3766.

(3*R*,5*E*,7*R*,8*R*,9*R*,10*R*)-9-[(*tert*-Butyldimethylsilyl)oxy]-11-[(*tert*-butyldiphenylsilyl)oxy]-7-methoxy-5,8,10-trimethyl-1,5-undecadien-3-ol (23): A stirred suspension of trimethylsulfonium iodide (70 mg, 0.35 mmol) in THF (2 mL) at –10 °C was treated with *n*BuLi (1.6 M in hexane, 0.2 mL, 0.33 mmol). After 30 min, terminal epoxide **22** (35 mg, 0.057 mmol) in THF (1 mL) was added, generating a milky suspension. The reaction mixture was warmed to 0 °C over 30 min and then stirred at room temperature for 2 h. The reaction was quenched with water at 0 °C, the mixture extracted with Et_2O (3 × 10 mL), and the combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 15%) to furnish terminal olefin **23** (33 mg, 92%) as a colorless liquid. $[\alpha]_D^{25}$ = +9.0 (c = 1.2, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3478, 2925, 2854, 1463, 1428, 1384, 1255, 1111, 1083, 1028, 834 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69–7.59 (m, 4 H), 7.43–7.28 (m, 6 H), 5.86 (ddd, J = 15.9, 10.5, 5.7 Hz, 1 H), 5.25 (dt, J = 17.1, 1.5 Hz, 1 H), 5.10 (dt, J = 10.5, 1.5 Hz, 1 H), 4.99 (d, J = 9.6 Hz, 1 H), 4.23 (m, 1 H), 4.10 (d, J = 6.6 Hz, 1 H), 3.76 (dd, J = 9.6, 5.7 Hz, 1 H), 3.68 (dd, J = 9.6, 9.3 Hz, 1 H), 3.34 (dd, J = 9.6, 8.1 Hz, 1 H), 3.14 (s, 3 H), 2.36–2.14 (m, 2 H), 1.87 (m, 1 H), 1.71 (d, J = 0.9 Hz, 3 H), 1.61 (m, 1 H), 1.06 (s, 9 H), 0.92 (d, J = 6.9 Hz, 3 H), 0.81 (s, 9 H), 0.70 (d, J = 6.9 Hz, 3 H), 0.02 (s, 3 H), –0.13 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.7, 136.7, 135.9, 134.3, 129.6, 129.4, 127.7, 114.9, 77.8, 71.6, 70.8, 67.0, 55.2, 48.2, 41.7, 40.5, 27.1, 26.2, 19.4, 18.5, 17.4, 14.1, 10.3, –3.8, –4.0 ppm. HRMS (ESI): calcd. for $C_{37}H_{60}O_4NaSi_2^+$ [M + Na]$^+$ 647.3927; found 647.3912.

***tert*-Butyl{[(1*R*,2*R*,3*R*,4*E*,7*R*)-7-[(*tert*-butyldimethylsilyl)oxy]-1-{(1*R*)-2-[(*tert*-butyldiphenylsilyl)oxy]-1-methylethyl}-3-methoxy-2,5-dimethyl-4,8-nonadienyl]oxy}dimethylsilane (24):** To a stirred solution of allylic alcohol **23** (56 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) was added 2,6-lutidine (22 μL, 0.18 mmol) and TBSOTf (32 μL, 0.136 mmol) at –50 °C. After 30 min, saturated aqueous $NaHCO_3$ (2 mL) was added. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 5%) to afford **24** (64 mg, 95%) as a yellow liquid. $[\alpha]_D^{27}$ = +8.37 (c = 0.95, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2930, 2857, 1639, 1464, 1383, 1253, 1081, 1023, 834 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69–7.61 (m, 4 H), 7.42–7.29 (m, 6 H), 5.79 (ddd, J = 16.8, 10.3, 6.2 Hz, 1 H), 5.12 (ddd, J = 17.1, 1.8, 1.2 Hz, 1 H), 5.02 (ddd, J = 10.5, 1.8, 1.2 Hz, 1 H), 4.90 (d, J = 9.7 Hz, 1 H), 4.25 (m, 1 H), 4.08 (dd, J = 6.9, 1.2 Hz, 1 H), 3.74 (dd, J = 9.9, 5.4 Hz, 1 H), 3.64 (dd, J = 9.6, 9.3 Hz, 1 H), 3.33 (dd, J = 9.9, 8.1 Hz, 1 H), 3.11 (s, 3 H), 2.34 (dd, J = 13.3, 5.3 Hz, 1 H), 2.22 (dd, J = 13.3, 7.4 Hz, 1 H), 1.86 (m, 1 H), 1.68 (d, J = 0.9 Hz, 3 H), 1.58 (m, 1 H), 1.06 (s, 9 H), 0.92 (d, J = 6.9 Hz, 3 H), 0.90 (s, 9 H), 0.81 (s, 9 H), 0.68 (d, J = 6.9 Hz, 3 H), 0.06 (s, 3 H), 0.04 (s, 3 H), 0.01 (s, 3 H), –0.14 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.3, 137.0, 135.9, 134.3, 129.6, 128.5, 127.7, 114.1, 77.7, 73.3, 71.6, 67.1, 55.2, 49.1, 41.6, 40.7, 27.0, 26.2, 26.0, 19.4, 18.5, 18.4, 18.0, 14.1, 10.1, –3.8, –4.0, –4.2, –4.7 ppm. HRMS (ESI): calcd. for $C_{43}H_{74}O_4NaSi_3^+$ [M + Na]$^+$ 761.4792; found 761.4793.

(2*R*,3*R*,4*R*,5*R*,6*E*,9*R*)-3,9-Bis[(*tert*-butyldimethylsilyl)oxy]-5-methoxy-2,4,7-trimethyl-6,10-undecadien-1-ol (25): To a stirred solution of **24** (28.2 mg, 0.038 mmol) in MeOH (1.5 mL) was added NH_4F

(9 mg, 0.24 mmol). The mixture was warmed to 50 °C and stirred for 4 h before quenching with saturated aqueous $NaHCO_3$ (1 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 15%) to obtain alcohol **25** (18 mg, 89%) as a colorless liquid: $[a]_D^{27}$ = –11.67 (*c* = 0.75, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3449, 2932, 2859, 1646, 1463, 1253, 1079, 1028, 836 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.79 (ddd, *J* = 16.9, 10.3, 6.3 Hz, 1 H), 5.12 (ddd, *J* = 17.1, 1.8, 1.2 Hz, 1 H), 5.02 (ddd, *J* = 10.2, 1.8, 1.2 Hz, 1 H), 4.91 (dq, *J* = 9.9, 1.2 Hz, 1 H), 4.26 (m, 1 H), 4.15 (dd, *J* = 5.4, 1.3 Hz, 1 H), 3.65 (dd, *J* = 9.9, 9.6 Hz, 1 H), 3.56–3.43 (m, 2 H), 3.19 (s, 3 H), 2.35 (ddd, *J* = 13.5, 5.7, 0.9 Hz, 1 H), 2.23 (ddd, *J* = 13.5, 7.2, 0.6 Hz, 1 H), 1.87 (m, 1 H), 1.70 (d, *J* = 1.5 Hz, 3 H), 1.60 (m, 1 H), 0.93 (s, 9 H), 0.90 (s, 9 H), 0.83 (d, *J* = 6.9 Hz, 3 H), 0.74 (d, *J* = 6.9 Hz, 3 H), 0.12 (s, 3 H), 0.11 (s, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 141.2, 137.7, 127.7, 114.2, 79.6, 73.2, 72.7, 66.0, 55.6, 49.0, 41.5, 39.8, 26.2, 26.0, 18.5, 18.4, 18.0, 12.7, 11.3, –4.0, –4.2, –4.2, –4.7 ppm. HRMS (ESI): calcd. for $C_{27}H_{56}O_4NaSi_2^+$ $[M + Na]^+$ 523.3614; found 523.3635.

6-{(2*S*,3*R*,4*R*,5*R*,6*R*,7*E*,10*R*)-4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-2-hydroxy-6-methoxy-3,5,8-trimethyl-7,11-dodecadienyl}-2,2-dimethyl-4*H*-1,3-dioxin-4-one (26): To a stirred solution of alcohol **25** (44.1 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) and pyridine (36 μL, 0.45 mmol) at 23 °C was added Dess–Martin periodinane reagent (51 mg, 0.12 mmol). A solution of wet CH_2Cl_2 (1 mL, prepared by vigorously mixing 10 mL CH_2Cl_2 and 10 μL of water) was then added dropwise over 30 min. The resulting solution was diluted with Et_2O (20 mL) and washed successively with saturated aqueous $Na_2S_2O_3$ (5 mL), saturated aqueous $NaHCO_3$ (5 mL), and water (5 mL). The combined aqueous layers were extracted with Et_2O (2 × 15 mL), and the combined organic layers were washed with saturated NaCl (20 mL), dried with Na_2SO_4, and concentrated. The crude oil was dissolved in pentane and filtered through a plug of Celite. The solvent was removed under reduced pressure to give aldehyde **3** as a yellow liquid, which was used in the next step without further purification. The crude aldehyde **3** was dissolved in CH_2Cl_2 (3 mL) and cooled to –78 °C. Sequentially, dienyl silyl ether **4** (96 mg, 0.45 mmol), and $BF_3{\cdot}OEt_2$ (36 μL, 0.27 mmol) were added whilst stirring. The reaction was continued at –78 °C for 1 h and quenched with pH 7.0 phosphate buffer (3 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 40%) to obtain aldol adduct **26** (48 mg, 85% 2 steps) as a yellow liquid. $[a]_D^{28}$ = –2.93 (*c* = 0.57, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3484, 2930, 2857, 1730, 1634, 1462, 1390, 1274, 1253, 1205, 1081, 1016, 835 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ = 5.79 (ddd, *J* = 16.8, 10.3, 6.4 Hz, 1 H), 5.35 (s, 1 H), 5.13 (ddd, *J* = 16.8, 1.8, 1.2 Hz, 1 H), 5.03 (ddd, *J* = 10.2, 1.8, 0.9 Hz, 1 H), 4.89 (dd, *J* = 9.6, 0.9 Hz, 1 H), 4.31 (m, 1 H), 4.27 (m, 1 H), 4.11 (dd, *J* = 4.2, 2.4 Hz, 1 H), 3.67 (dd, *J* = 9.6, 9.3 Hz, 1 H), 3.18 (s, 3 H), 2.45 (dd, *J* = 14.4, 9.0 Hz, 1 H), 2.36 (dd, *J* = 14.4, 5.4 Hz, 1 H), 2.24 (dd, *J* = 13.2, 7.2 Hz, 1 H), 2.22 (dd, *J* = 13.2, 4.8 Hz, 1 H), 1.72 (m, 1 H), 1.70 (d, *J* = 0.6 Hz, 3 H), 1.69 (s, 6 H), 1.51 (m, 1 H), 0.97 (d, *J* = 7 Hz, 3 H), 0.92 (s, 9 H), 0.89 (s, 9 H), 0.80 (d, *J* = 7 Hz, 3 H), 0.12 (s, 6 H), 0.06 (s, 3 H), 0.05 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.8, 161.4, 141.2, 137.9, 127.6, 114.2, 106.6, 95.0, 79.3, 75.7, 73.2, 68.4, 55.6, 49.0, 43.5, 41.9, 39.8, 26.3, 26.0, 25.5, 24.9, 18.5, 18.4, 18.1, 11.5, 10.4, –3.6, –4.0, –4.2, –4.7 ppm. HRMS (ESI): calcd. for $C_{34}H_{64}O_7NaSi_2^+$ $[M + Na]^+$ 663.4088; found 663.4080.

6-{(2*S*,3*R*,4*S*,5*R*,6*R*,7*E*,10*R*)-4,10-Bis[(*tert*-butyldimethylsilyl)oxy]-6-methoxy-2-(methoxymethoxy)-3,5,8-trimethyl-7,11-dodecadienyl}-2,2-dimethyl-4*H*-1,3-dioxin-4-one (27): To a stirred solution of aldol adduct **26** (27 mg, 0.042 mmol) and *i*Pr_2NEt (44 μL, 0.252 mmol) in CH_2Cl_2 (1 mL) at 0 °C, was added MOMCl (20 μL, 0.244 mmol). After 90 min at 0 °C, the reaction mixture was diluted with saturated aqueous NaCl (1 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried with Na_2SO_4 and concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 30%) to furnish MOM ether **27** (28 mg, 97%) as a light-yellow liquid. $[a]_D^{25}$ = –17.4 (*c* = 0.39, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2926, 2854, 1738, 1635, 1463, 1389, 1252, 1081, 1036, 835 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.79 (ddd, *J* = 16.9, 10.3, 6.3 Hz, 1 H), 5.28 (s, 1 H), 5.13 (ddd, *J* = 16.8, 1.8, 1.2 Hz, 1 H), 5.02 (ddd, *J* = 10.5, 1.8, 1.2 Hz, 1 H), 4.86 (d, *J* = 9.6 Hz 1 H), 4.64, 4.63 (ABq, *J* = 7.2 Hz, 2 H), 4.26 (m, 1 H), 4.22 (dd, *J* = 6.9, 0.6 Hz, 1 H), 3.88 (td, *J* = 6.3, 4.2 Hz, 1 H), 3.66 (dd, *J* = 9.9, 9.6 Hz, 1 H), 3.35 (s, 3 H), 3.15 (s, 3 H), 2.64 (dd, *J* = 14.4, 6.4 Hz, 1 H), 2.45 (dd, *J* = 14.4, 6.3 Hz, 1 H), 2.35 (dd, *J* = 13.2, 5.4 Hz, 1 H), 2.22 (dd, *J* = 13.2, 6.9 Hz, 1 H), 1.68 (m, 1 H), 1.70 (d, *J* = 0.6 Hz, 3 H), 1.69 (s, 6 H), 1.54 (m, 1 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.92 (s, 9 H), 0.90 (s, 9 H), 0.70 (d, *J* = 6.9 Hz, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.6, 161.3, 141.2, 137.5, 128.3, 114.2, 106.6, 96.9, 95.2, 78.0, 76.9, 73.2, 71.0, 55.9, 55.3, 49.1, 43.3, 40.2, 38.3, 26.4, 26.0, 25.4, 25.1, 18.7, 18.4, 18.0, 10.6, 10.1, –3.5, –4.1, –4.2, –4.7 ppm. HRMS (ESI): calcd. for $C_{36}H_{68}O_8NaSi_2^+$ $[M + Na]^+$ 707.4350; found 707.4367.

6-{(2*S*,3*R*,4*S*,5*R*,6*R*,7*E*,10*R*)-4-[1*tert*-Butyldimethylsilyl)oxy]-10-hydroxy-6-methoxy-2-(methoxymethoxy)-3,5,8-trimethyl-7,11-dodecadienyl}-2,2-dimethyl-4*H*-1,3-dioxin-4-one (28): In a 5 mL round-bottom plastic tube, a stirred solution of **27** (12 mg, 0.018 mmol) in MeOH (1 mL) was cooled to 0 °C, and a solution of HF·Py (0.3 mL in 0.7 mL of MeOH) was added. The reaction mixture was stirred at room temperature for 6 h, then quenched at 0 °C by pouring into a solution of saturated aqueous $NaHCO_3$ (10 mL). The product was extracted with ethyl acetate (3 × 15 mL), and the combined organic extracts were washed with saturated aqueous $CuSO_4$ (10 mL) and water (10 mL), and dried with $MgSO_4$. After concentration of the organic extracts, the crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 40%) to afford hydroxy dioxinone **28** (10 mg, quantitative) as a colorless liquid. $[a]_D^{27}$ = +5.6 (*c* = 0.45, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3316, 2928, 2851, 1714, 1385, 1256, 1199, 1083, 1035 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.89 (ddd, *J* = 17, 10.5, 6.0 Hz, 1 H), 5.32 (s, 1 H), 5.27 (dt, *J* = 17, 1.5 Hz, 1 H), 5.12 (dt, *J* = 10.5, 1.5 Hz, 1 H), 4.97 (dq, *J* = 9.5, 1.0 Hz, 1 H), 4.67, 4.65 (ABq, *J* = 7.0 Hz, 2 H), 4.26 (m, 1 H), 4.24 (dd, *J* = 6.5, 0.7 Hz, 1 H), 3.92 (td, *J* = 6.5, 4.5 Hz, 1 H), 3.72 (dd, *J* = 10.0, 9.5 Hz, 1 H), 3.36 (s, 3 H), 3.19 (s, 3 H), 2.65 (dd, *J* = 14.5, 6.5 Hz, 1 H), 2.49 (dd, *J* = 14.5, 6.1 Hz, 1 H), 2.32 (dd, *J* = 13.2, 5.3 Hz, 1 H), 2.28 (dd, *J* = 13.2, 8.2 Hz, 1 H), 1.72 (d, *J* = 1.5 Hz, 3 H), 1.70 (m, 1 H), 1.69 (s, 3 H), 1.68 (s, 3 H), 1.59 (m, 1 H), 0.93 (d, *J* = 7.0 Hz, 3 H), 0.92 (s, 9 H), 0.73 (d, *J* = 7.0 Hz, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 169.5, 161.4, 140.5, 137.1, 129.1, 115.1, 106.6, 96.9, 95.1, 77.9, 76.7, 70.9, 70.8, 55.9, 55.4, 48.1, 43.1, 40.0, 38.3, 26.4, 25.4, 25.1, 18.7, 17.3, 10.5, 10.1, –3.5, –4.1 ppm. HRMS (ESI): calcd. for $C_{30}H_{54}O_8NaSi^+$ $[M + Na]^+$ 593.3485; found 593.3477.

(6*S*,7*R*,8*S*,9*R*,10*R*,14*R*)-8-[(*tert*-Butyldimethylsilyl)oxy]-10-methoxy-6-(methoxymethoxy)-7,9,12-trimethyl-14-vinyl-1-oxa-11-cyclotetradecene-2,4-dione (30): A solution of hydroxy dioxinone **28**

(8 mg, 0.014 mmol) in freshly azeotropically dried toluene (20 mL) was added by using a cannula to stirred azeotropically dried toluene (60 mL) at reflux over 45 min. The reaction mixture was stirred at 110 °C for 1 h and then concentrated. The crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 15%) to obtain macrolactone **30** (6 mg, 84%) as a colorless liquid. $[a]_D^{26}$ = –24.3 (*c* = 0.3, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 2927, 2857, 1716, 1629, 1463, 1251, 1096, 1038, 834 cm^{-1}. ^1H NMR (600 MHz, C_6D_6): δ = 5.60 (ddd, *J* = 16.8, 10.8, 6.0 Hz, 1 H), 5.56 (m, 1 H), 5.41 (br. d, *J* = 9.0 Hz, 1 H), 5.15 (dd, *J* = 16.8, 1.2 Hz, 1 H), 4.96 (dd, *J* = 10.2, 1.2 Hz, 1 H), 4.68 (d, *J* = 6.5 Hz, 1 H), 4.59 (d, *J* = 6.5 Hz, 1 H), 4.29 (m, 1 H), 4.06–3.97 (br. m, 1 H), 3.74 (dd, *J* = 9.0, 1.0 Hz, 1 H), 3.21 (d, *J* = 15.6 Hz, 1 H), 3.15 (s, 3 H), 3.13 (d, *J* = 15.6 Hz, 1 H), 3.07 (s, 3 H), 2.84 (dd, *J* = 15.6, 8.4 Hz, 1 H), 2.57 (dd, *J* = 15.6, 4.8 Hz, 1 H), 2.26 (dd, *J* = 14.4, 11.7 Hz, 1 H), 2.05 (d, *J* = 14.4 Hz, 1 H), 2.02 (m, 1 H), 1.69 (m. 1 H), 1.55 (s, 3 H), 1.23 (d, *J* = 7.2 Hz, 3 H), 1.07 (s, 9 H), 1.03 (d, *J* = 7.2 Hz, 3 H), 0.27 (s, 3 H), 0.20 (s, 3 H) ppm. ^{13}C NMR (150 MHz, C_6D_6): δ = 200.4, 166.1, 136.7, 135.1, 129.5, 116.5, 97.5, 82.4, 77.0, 72.2, 69.9, 56.0, 55.6, 50.3, 46.1, 45.8, 45.6, 40.8, 26.4, 18.8, 15.5, 15.2, 12.2, –4.1 ppm. HRMS (ESI): calcd. for $C_{27}H_{48}O_7NaSi^+$ $[M + Na]^+$ 535.3067; found 535.3063.

C1–C14 Macrolactone Core 2 of (–)-Callipeltoside A: In a 5 mL round-bottom plastic tube a stirred solution of macrolactone **30** (5.4 mg, 0.011 mmol) in MeOH (0.7 mL) was cooled to 0 °C, and a solution of HF·Py (0.2 mL in 0.5 mL of MeOH) was added dropwise. The reaction mixture was stirred for 2 h and quenched at 0 °C by slow dropwise addition of saturated aqueous sodium hydrogen carbonate solution (1 mL) to the reaction vessel by using a syringe. After transferring the mixture to a larger vessel, another 7 mL of saturated aqueous $NaHCO_3$ solution was added. The product was extracted with ethyl acetate (3 × 15 mL), and the combined organic extracts were washed with aqueous $CuSO_4$ solution (10 mL) and water (10 mL) and dried with Na_2SO_4. After concentration of the organic extracts, the crude product was purified by column chromatography (SiO_2; ethyl acetate/hexane, 20%) to furnish **2** (4 mg, 96%) as a colorless liquid. $[a]_D^{24}$ = –17.0 (*c* = 0.18, $CHCl_3$). IR (neat): $\tilde{\nu}$ = 3457, 2925, 2854, 1704, 1464, 1228, 1177, 1154, 1086, 1034, 897 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 5.88 (ddd, *J* = 17.0, 10.5, 6.0 Hz, 1 H), 5.78 (m, 1 H), 5.31 (d, *J* = 10.0 Hz, 1 H), 5.30 (dt, *J* = 17.0, 1.3 Hz, 1 H), 5.19 (dt, *J* = 10.5, 1.0 Hz, 1 H), 5.03 (d, *J* = 2.5 Hz, 1 H), 4.73 (d, *J* = 6.8 Hz, 1 H), 4.63 (d, *J* = 6.8 Hz, 1 H), 3.81 (dd, *J* = 9.5, 2.5 Hz, 1 H), 3.67 (ddd, *J* = 11.0, 10.5, 4.7 Hz, 1 H), 3.65 (dd, *J* = 10.3, 2.5 Hz,1 H), 3.38 (s, 3 H), 3.24 (s, 3 H), 2.55 (d, *J* = 12.9 Hz, 1 H), 2.44 (d, *J* = 12.9 Hz, 1 H), 2.32–2.27 (m, 2 H), 2.22 (m, 1 H), 2.22 (dd, *J* = 12.0, 4.7 Hz, 1 H), 1.75 (d, *J* = 1.3 Hz, 3 H), 1.50 (m, 1 H), 1.30 (ddd, *J* = 12.0, 11.0, 2.5 Hz, 1 H), 0.99 (d, *J* = 7.0 Hz, 3 H), 0.96 (d, *J* = 6.5 Hz, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.1, 136.3, 132.7, 127.7, 116.7, 96.1, 95.4, 80.0, 76.2, 75.2, 72.3, 55.7, 55.4, 46.9, 44.9, 41.6, 38.3, 37.1, 16.3, 12.4, 6.6 ppm. HRMS (ESI): calcd. for $C_{21}H_{34}O_7Na^+$ $[M + Na]^+$ 421.2202; found 421.2203.

Supporting Information (see footnote on the first page of this article): Copies of ^1H and ^{13}C NMR spectra for all new compounds.

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