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Synthesis and Biological Activity of the C′D′E′F′ Ring System of Maitotoxin

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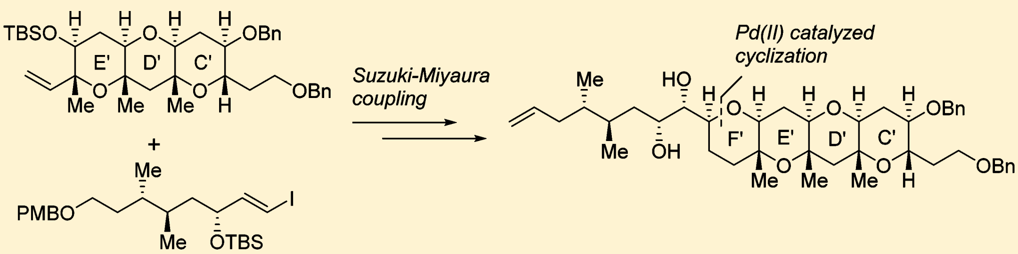
Supporting Information



ABSTRACT: Stereoselective synthesis of the C′D′E′F′ ring system of maitotoxin was achieved starting from the E′ ring through successive formation of the D′ and C′ rings based on SmI_2-mediated reductive cyclization. Construction of the F′ ring was accomplished via Suzuki−Miyaura cross-coupling with a side chain fragment and Pd(II)-catalyzed cyclization of an allylic alcohol. The C′D′E′F′ ring system inhibited maitotoxin-induced Ca^{2+} influx in rat glioma C6 cells with an IC_{50} value of 59 μM.

INTRODUCTION

Maitotoxin (MTX, **1**), produced by epiphytic dinoflagellate *Gambierdiscus toxicus*, is suspected as one of the causative toxins associated with seafood poisoning (Figure 1).[1] MTX is one of the largest molecules among the nonpeptide secondary metabolites[2] whose structures have been elucidated.[3] Because of its unique molecular structure possessing 32 cyclic ethers and 98 stereogenic centers,[4,5] MTX has attracted considerable attention from the synthetic community.[6,7] MTX exhibits remarkable biological activities at extremely low concentrations, i.e., hemolytic activity at 15 nM[8] and Ca^{2+} influx activity at 0.3 nM.[9] The gigantic molecule can be divided into two parts, the hydrophobic part (the P−F′ ring system) and the hydrophilic part (the A−O ring system).[2e] During the course of structure−activity relationship studies to develop inhibitors against biological activities induced by MTX, we have designed and synthesized the W−C′ ring system of MTX (**2**)[10] corresponding to a partial structure of the hydrophobic part of the molecule, based on the hypothesis that the hydrophobic portion would be an interacting motif against its target membrane proteins.[11] We found that compound **2** inhibited hemolytic activity induced by MTX by 80% at a concentration of 10 μM,[10] while its inhibitory activity against MTX-induced Ca^{2+} influx was comparable to that of brevetoxin B (IC_{50} = 30 μM).[11] These results prompted us to examine the biological activities of the rest of the hydrophobic moiety of MTX. Herein, we describe a stereoselective synthesis of the C′D′E′F′ ring system (**3**) and its inhibitory activity against MTX-induced Ca^{2+} influx.

RESULTS AND DISCUSSION

Although synthesis of the C′D′E′F′ ring system of MTX was reported by Nakata[6c] and that lacking its side chain on the F′ ring by Nicolaou,[7a] we envisaged an alternative synthetic route as shown in Scheme 1. The C′D′E′F′ ring system **3** would be synthesized through Pd(II)-catalyzed cyclization reported by Uenishi[12] for the construction of the F′ ring from diol **4**, which was to be derived from *trans*-iodoolefin **5** and terminal olefin **6** via Suzuki-Miyaura cross coupling reaction.[13] For the construction of the C′D′E′ ring system **7**, SmI_2-mediated reductive cyclization[14] developed by Nakata, was to be utilized iteratively starting from the known compound **8**[15] corresponding to the E′ ring.

Synthesis of the C′D′E′ ring system is shown in Scheme 2. Hydroboration of the known terminal olefin **8**[15] with disiamylborane gave primary alcohol **11** in 95% yield after oxidative work up. TEMPO oxidation[16] of **11** gave an aldehyde, followed by treatment with methylmagnesium bromide and 2-azaadamantane-*N*-oxyl (AZADO) oxidation[17] of the resulting secondary alcohol to furnish ketone **12**. Removal of the TBS group of **12** with TBAF at room temperature for 1 h gave secondary alcohol **13** in 75% yield

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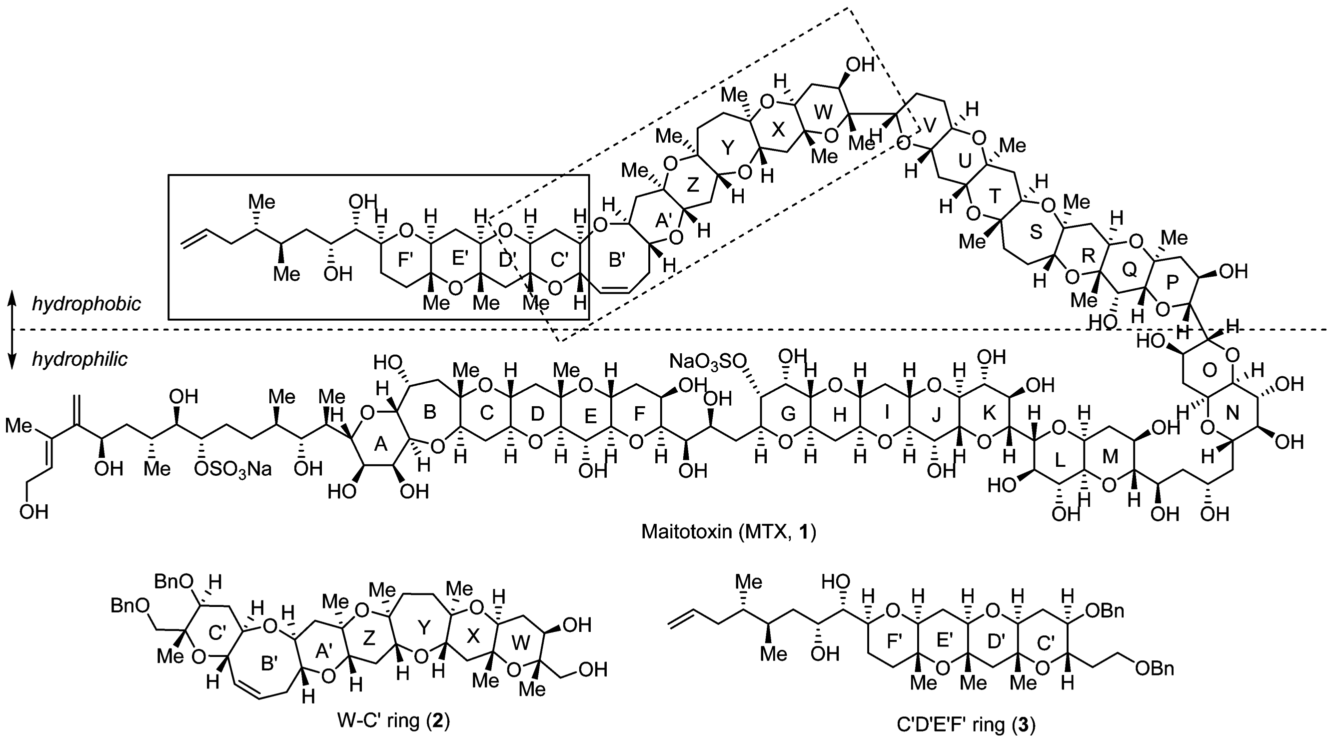
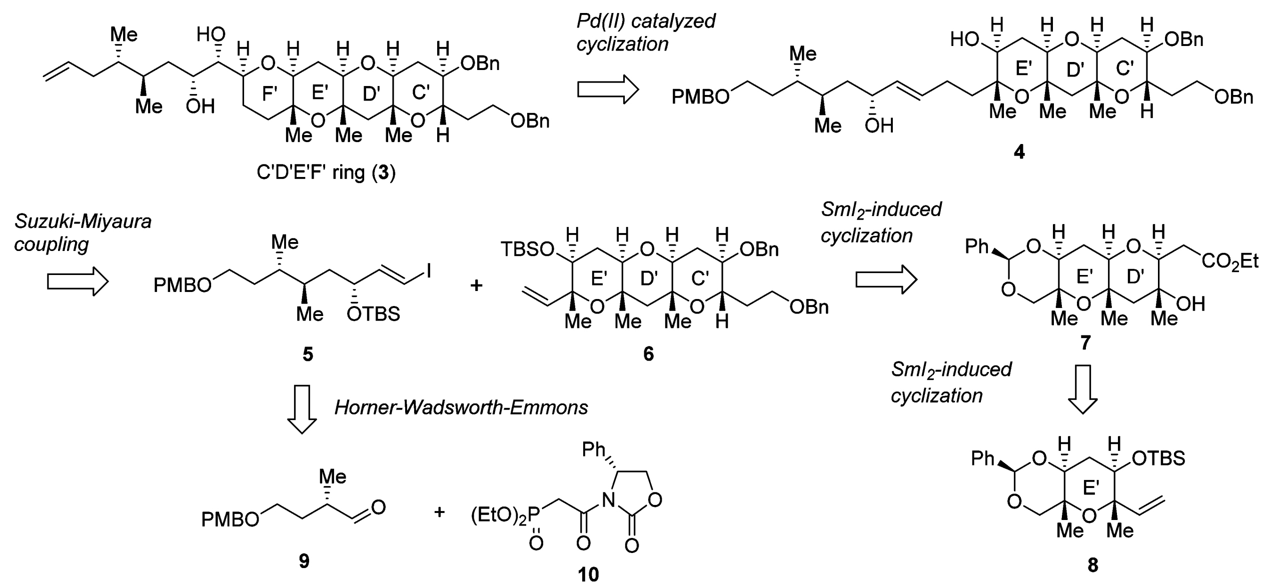


Figure 1. Structures of maitotoxin (MTX, **1**), the W–C′ ring system (**2**), and the C′D′E′F′ ring system (**3**).

Scheme 1. Retrosynthetic Analysis of the C′D′E′F′ Ring System (3) of MTX



with recovery of **12** (18%), but prolonged reaction time resulted in the formation of byproducts.[18] Oxa-Michael addition of the secondary alcohol **13** by treatment with ethyl propiolate in the presence of *N*-methylmorpholine (NMM) resulted in the formation of *trans-β*-alkoxyacrylate **14** in 89% yield, which was subjected to SmI_2-mediated reductive cyclization[14] to afford the D′E′ ring system **7** in 86% yield as a single isomer. The structure of **7** was unambiguously determined by NOE experiments. Treatment of the ester **7** with $LiAlH_4$ formed diol **15**, followed by selective protection of the primary alcohol **15** as an acetate to furnish **16** in 99% yield over two steps. The second oxa-Michael addition of the tertiary alcohol **16** was problematic because of the low reactivity of the tertiary alcohol. After considerable experimentation, we found that desired product **17** was obtained by adding methyl propiolate (3 equiv) to a solution of **16** and trimethylphosphine (5 equiv) at room temperature in 83% yield.[19] Methanolysis of acetate **17** with K_2CO_3 gave primary alcohol **18** (92%), which was oxidized under Parikh-Doering conditions.[20] The resulting aldehyde was subjected to the second SmI_2-mediated reductive cyclization[14] to afford the C′D′E′ ring system **19** as a single isomer in 77% yield for two steps, and the structure was confirmed by NOE experiments. Reduction of the ester **19** with $LiAlH_4$ followed by protection of the resulting diol **20** as benzyl ethers by treatment with BnBr and NaH furnished **21** in 77% yield for two steps.

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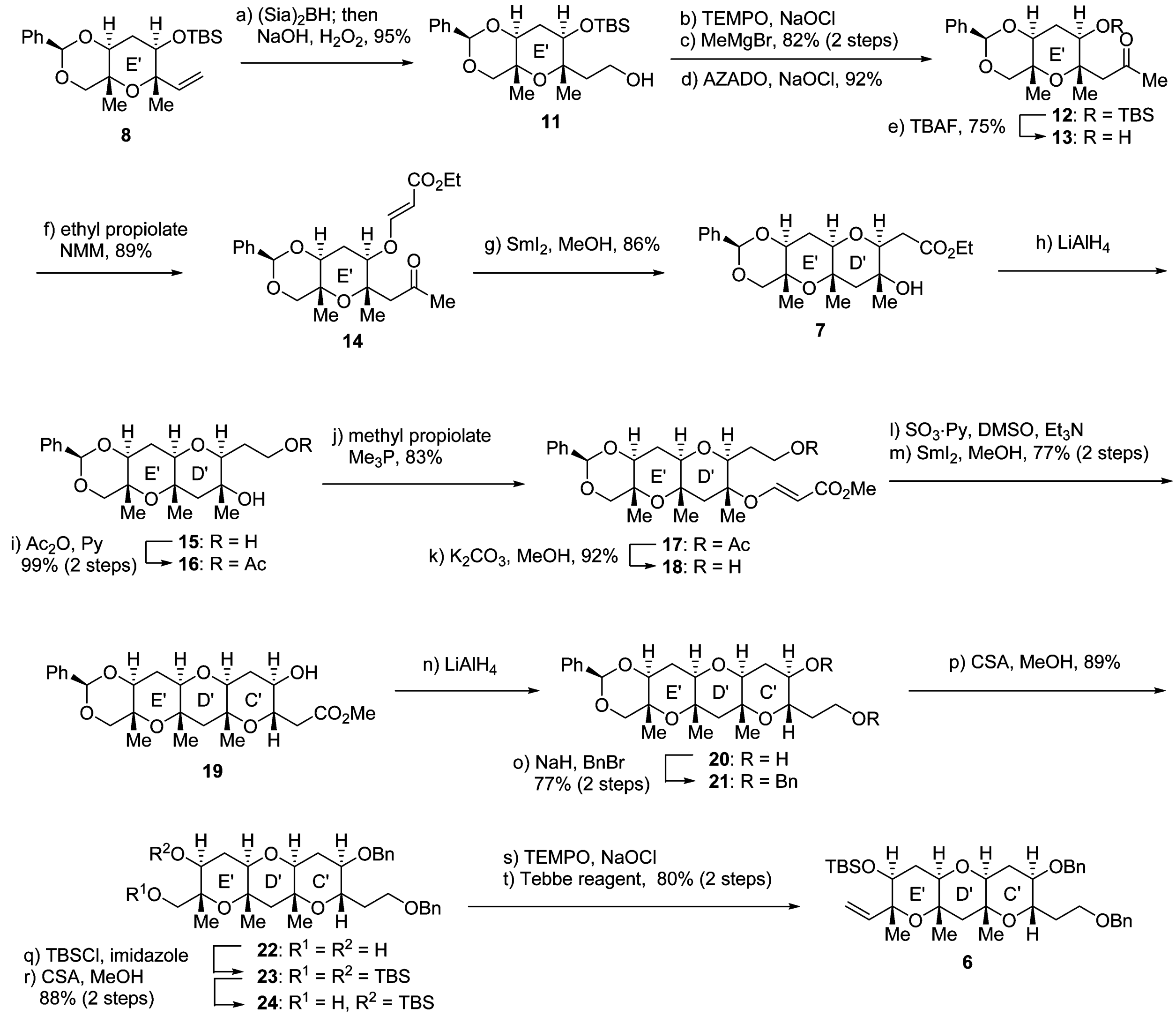
Scheme 2. Synthesis of the C′D′E′ Ring Fragment (6) of MTX[a]

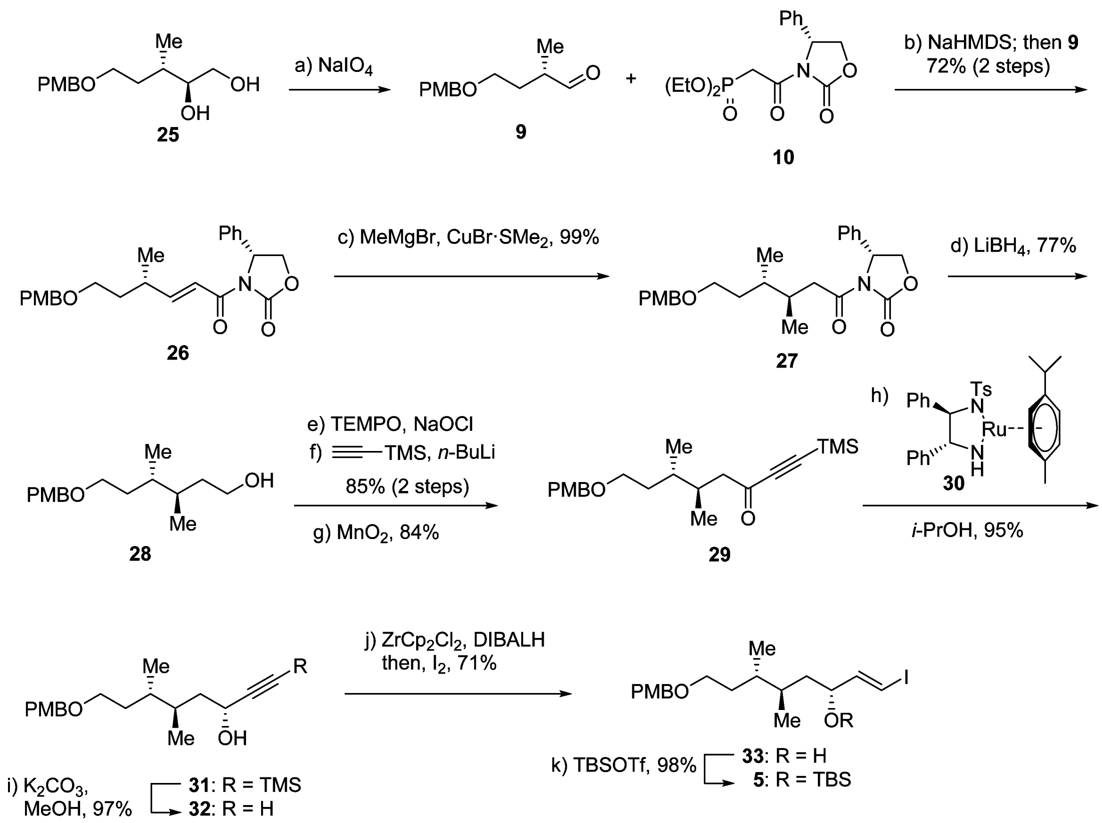


[a](a) $(Sia)_2BH$, rt, 1 h; then, NaOH, H_2O_2, rt, 1 h, 95% (b) TEMPO, KBr, NaOCl, $NaHCO_3$, CH_2Cl_2, 0 °C, 30 min; (c) MeMgBr, THF, 0 °C, 20 min, 82% (2 steps); (d) AZADO, KBr, NaOCl, $NaHCO_3$, CH_2Cl_2, 0 °C, 25 min, 92%; (e) TBAF, THF, rt, 1 h, 75%; (f) $HC{\equiv}CCO_2Et$, NMM, CH_2Cl_2, rt, 5 h 45 min, 89%; (g) SmI_2, MeOH, THF, 0 °C, 50 min, 86%; (h) $LiAlH_4$, THF, −15 °C, 2 h; (i) Ac_2O, pyridine, rt, 2 h, 99% (2 steps); (j) $HC{\equiv}CCO_2Me$, Me_3P, THF, rt, 40 min, 83%; (k) K_2CO_3, MeOH, rt, 4 h 20 min, 92%; (l) $SO_3{\cdot}Py$, DMSO, Et_3N, CH_2Cl_2, rt, 2 h; (m) SmI_2, MeOH, THF, 0 °C, 40 min, 77% (2 steps); (n) $LiAlH_4$, THF, −15 °C, 2 h 15 min; (o) BnBr, NaH, THF, DMF, 20 h, 77% (2 steps); (p) CSA, THF, MeOH, rt, 3 h 10 min, 89%; (q) TBSCl, imidazole, DMF, rt, 38 h; (r) CSA, CH_2Cl_2, MeOH, rt, 3 h, 88% (2 steps); (s) TEMPO, KBr, NaOCl, $NaHCO_3$, CH_2Cl_2, 0 °C, 1 h 10 min; (t) Tebbe reagent, THF, 0 °C, 20 min, 80% (2 steps).

Removal of the benzylidene acetal with CSA in methanol gave diol **22**, followed by protection of the resulting diol as TBS ethers **23**. Selective deprotection with CSA in methanol resulted in the formation of primary alcohol **24** in 88% yield for two steps. TEMPO oxidation of **24** gave an aldehyde, which was converted to the terminal olefin **6** by treatment with Tebbe reagent[21] in 80% yield for two steps.

Next, synthesis of the *trans*-iodoolefin **5** commenced with Horner–Wadsworth–Emmons reaction of the known aldehyde **9**[22] derived from diol **25** by oxidative cleavage with $NaIO_4$ in an analogous sequence reported by Nakata[6c] (Scheme 3). Treatment of the known phosphonate **10**[23] possessing a chiral auxiliary with NaHMDS, followed by addition of the aldehyde, resulted in the formation of olefin **26** in 72% yield over two steps as a single isomer. Subsequent conjugate addition of methylcuprate proceeded stereoselectively to afford **27** in 99% yield in *a* > 30:1 ratio.[6c,24] Reductive removal of the chiral auxiliary with $LiBH_4$ gave primary alcohol **28** in 77% yield. TEMPO oxidation of **28** followed by treatment of the resulting aldehyde with lithium trimethylsilylacetylide resulted in the formation of a propargylic alcohol in 85% yield over two steps as a mixture of diastereomers, which was converted to ketone **29** by oxidation with MnO_2 in 84% yield. Noyori asymmetric hydrogen transfer using catalyst **30**[25] afforded alcohol **31** as a single isomer in 95% yield. The TMS group was removed with K_2CO_3 in methanol to give terminal alkyne **32** in 97% yield. The terminal alkyne was subjected to a hydrozirconation-iodination sequence[26] by treatment with Schwartz reagent prepared from Cp_2ZrCl_2 and DIBALH in situ followed by iodine to afford iodoolefin **33** in 71% yield.

Scheme 3. Synthesis of the *trans*-Iodoolefin (5)[a]



[a](a) $NaIO_4$, THF, H_2O, rt, 10 min; (b) NaHMDS, rt, 30 min; then, **9**, 0 °C, 16 h, 72%; (c) $CuBr·SMe_2$, MeMgBr, Me_2S, THF, −66 to 0 °C, 65 min; then **26**, THF, CH_2Cl_2, −65 to −30 °C, 1.5 h, 99%; (d) $LiBH_4$, MeOH, Et_2O, 0 °C, 15 min, 77%; (e) TEMPO, KBr, NaOCl, $NaHCO_3$, CH_2Cl_2, 0 °C, 40 min; (f) TMS acetylene, *n*-BuLi, −70 °C, 25 min, 85% (2 steps); (g) MnO_2, CH_2Cl_2, rt, 37 h, 84%; (h) **30**, *i*-PrOH, rt, 100 h, 95%; (i) K_2CO_3, MeOH, rt, 15.5 h, 97%; (j) Cp_2ZrCl_2, DIBALH, THF, 0 °C, 35 min; then, **32**, THF, rt, 40 min; then, I_2, THF, −71 to 0 °C, 10 min, 71%; (k) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 15 min, 98%.

Protection of the secondary alcohol as a TBS ether furnished **5** in 98% yield.

Having synthesized the C′D′E′ ring fragment **6** and the *trans*-iodoolefin **5**, we moved onto the synthesis of the C′D′E′F′ ring system **3** (Scheme 4). Suzuki-Miyaura coupling[13] via hydroboration of the terminal olefin **6** with 9-BBN followed by treatment with the iodoolefin **5** (1.25 equiv) in the presence of $PdCl_2(dppf)·CH_2Cl_2$ and K_3PO_4 in THF/DMF at 35 °C for 5 h proceeded smoothly to afford coupling product **34** in 98% yield. Removal of the TBS groups with TBAF furnished diol **4** in 96% yield, which is the precursor for the key reaction for the construction of the F′ ring system. As expected, treatment of the allylic alcohol **4** with $PdCl_2(CH_3CN)_2$ resulted in the formation of **35** in 93% yield as a single isomer.[12] The structure of **35** was unambiguously determined by NOE experiments. Stereoselective dihydroxylation of the olefin **35** was achieved by Sharpless asymmetric dihydroxylation[27] using $(DHQD)_2AQN$ as a ligand to afford α-diol **36** as a mixture of the β-diol in a 10:1 ratio in 96% yield. It is interesting to note that the use of *t*-BuOMe as a cosolvent was essential to obtaining high diastereoselectivity,[5a] and the reaction rate was faster than that using $(DHQD)_2PHAL$. The diol **36** was protected as a TBS ether to give **37** (92%), and the PMB group of **37** was removed with DDQ to afford primary alcohol **38** (88%), which was separated from the other diastereomer derived from the β-diol. Dess-Martin oxidation[28] of the primary alcohol **38**, followed by Wittig olefination of the resulting aldehyde, gave terminal olefin **39** in 77% yield for two steps. Finally, removal of the TBS groups of **39** with TBAF afforded the C′D′E′F′ ring system **3** in quantitative yield. The longest linear sequence is 29 steps from the E′ ring **8**, and the total yield is 5.9% with 90% average yield.

Differences in the proton (600 MHz) and carbon (150 MHz) NMR chemical shifts in 1:1 C_5D_5N-CD_3OD between the synthetic C′D′E′F′ ring system **3** and MTX are shown in Figure 2.[29] The ^1H and ^{13}C NMR chemical shifts of **3** were in good accordance with those of MTX, supporting the proposed structure, but those at the C′ terminus deviated since the structure was different from MTX.

The biological activity of the synthetic C′D′E′F′ ring system **3** was then evaluated. MTX induced Ca^{2+} influx in rat glioma C6 cells at 1 nM, and this value was taken as 100%. The C′D′E′F′ ring system **3** blocked this Ca^{2+} influx activity in a dose-dependent manner as shown in Figure 3, and the IC_{50} value was estimated to be 59 μM. Although this value is higher than that of the W−C′ ring system **2**[10] (IC_{50} = 30 μM), it is interesting to note that the tetracyclic system (**3**) elicited inhibitory activity in comparable magnitude with the heptacyclic system (**2**).[30−32] To improve the inhibitory activity against MTX-induced Ca^{2+} influx, design and synthesis of a decacyclic system corresponding to the W−F′ ring portion of MTX is in progress in our laboratory.

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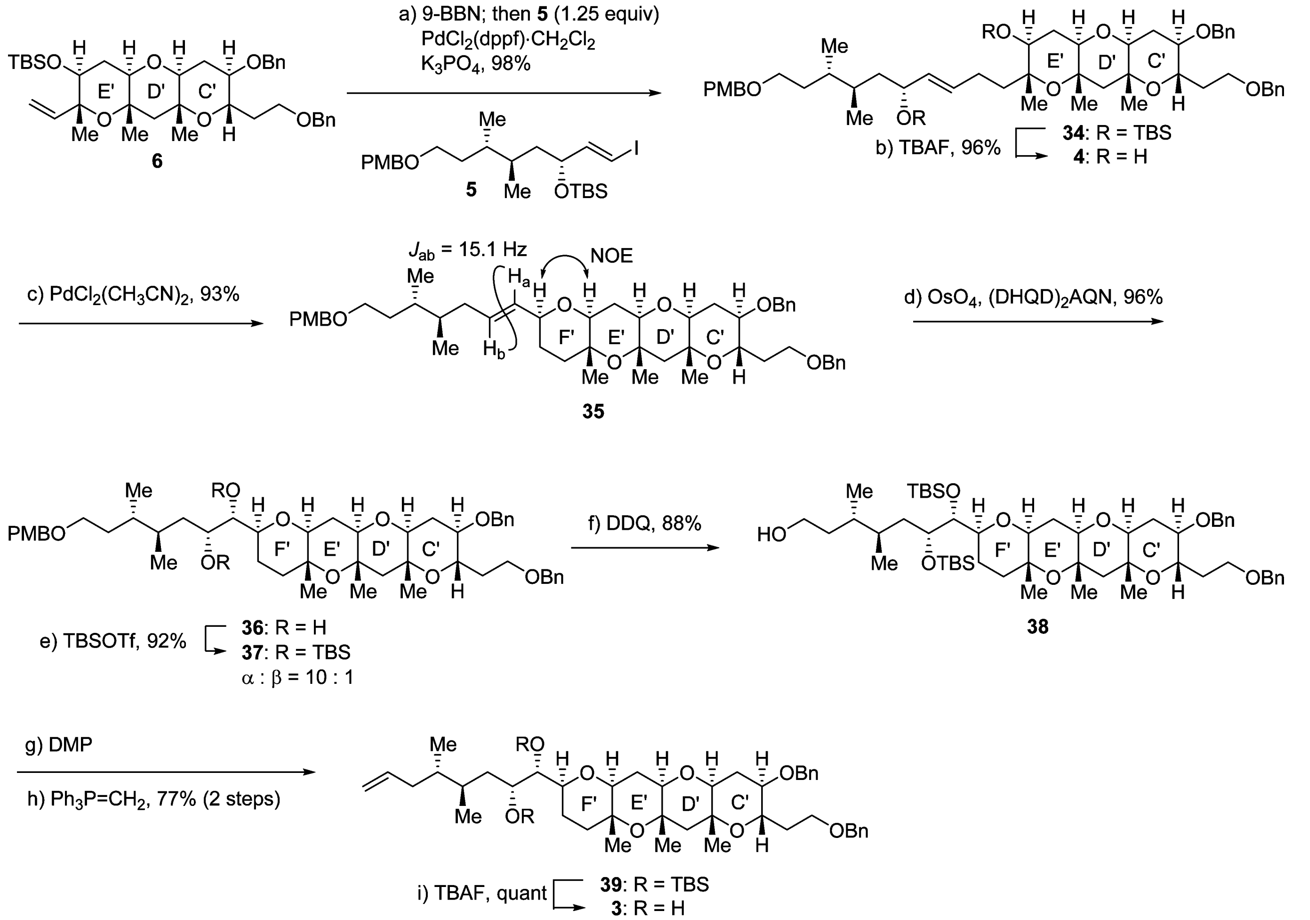
Scheme 4. Synthesis of the C′D′E′F′ Ring System (3) of MTX[a]



[a](a) 9-BBN, THF, rt, 1.5 h; H_2O; then **5** (1.25 equiv), $Pd(dppf)Cl_2{\cdot}CH_2Cl_2$, K_3PO_4, THF, DMF, 35 °C, 5 h, 98%; (b) TBAF, THF, reflux, 13 h, 96%; (c) $PdCl_2(CH_3CN)_2$, THF, 0 °C, 2 h, 93%; (d) $K_2OsO_4{\cdot}2H_2O$, $(DHQD)_2AQN$, K_2CO_3, $MeSO_2NH_2$; $K_3Fe(CN)_6$, *t*-BuOMe, *t*-BuOH, H_2O, 0 °C, 24 h, 96%; (e) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 50 min, 92%; (f) DDQ, pH 6.9 buffer, CH_2Cl_2, rt, 50 min, 88%; (g) DMP, CH_2Cl_2, rt, 2 h; (h) $PPh_3^+CH_3Br^-$, NaHMDS, THF, 0 °C, 40 min, 77%; (i) TBAF, THF, 50 °C, 12 h, quant.

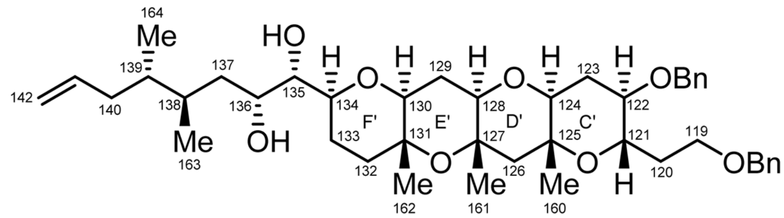
■ CONCLUSION

In conclusion, the stereoselective synthesis of the C′D′E′F′-ring system of MTX containing the side chain was achieved. The key reactions are (i) SmI_2-mediated reductive cyclization for the construction of the C′ and D′ rings, (ii) Suzuki-Miyaura cross coupling for introduction of the side chain, and (iii) Pd(II)-catalyzed cyclization for the construction of the F′ ring. The C′D′E′F′ ring system inhibited MTX-induced Ca^{2+} influx into rat glioma C6 cells (IC_{50} = 59 μM). Further structure−activity relationship studies based on the chemical synthesis of partial structures of MTX are currently in progress in our laboratory.

■ EXPERIMENTAL SECTION

General Methods for Organic Synthesis. All reactions sensitive to air or moisture were performed under argon atmosphere with dry glassware unless otherwise noted in particular. The dehydrated solvents, CH_2Cl_2, tetrahydrofuran (THF), toluene, and *N*,*N*-dimethylformamide (DMF) were used without further dehydration. NMM and BnBr were distilled before using. Molecular sieves (MS4A) were preactivated by heating *in vacuo*. All other chemicals were obtained from local venders and used as supplied unless otherwise stated. Thin-layer chromatography (TLC) was performed using precoated TLC glass plates (silica gel 60 F_{254}, 0.25 mm thickness) for the reaction analyses. For column chromatography, silica gel was used for column chromatography (spherical, neutral, 100−210 μm) or for flash chromatography (40−50 μm). Optical rotations were recorded on a polarimeter. IR spectra were recorded on a FT/IR equipment. ^{1}H NMR spectra were recorded at 600 or 400 MHz, and ^{13}C NMR spectra were recorded at 150 or 100 MHz. Chemical shifts are reported in ppm from tetramethylsilane (TMS) with reference to internal residual solvent [^{1}H NMR, $CHCl_3$ (7.26), CD_2HOD (3.31); ^{13}C NMR, $CDCl_3$ (77.16), CD_3OD (48.94)]. The following abbreviations are used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, brs = broad singlet. High resolution mass spectra (HRMS) were recorded on ESI-TOF equipment.

2-((2*R*,4a*R*,6*S*,7*R*,8a*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-4a,6-dimethyl-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-6-yl)-ethanol (11). 2-Methyl-2-butene (23.0 mL, 217 mmol) was added to a solution of $BH_3{\cdot}SMe_2$ (10.3 mL, 109 mmol) in dry THF (161 g) at 0 °C. After the mixture was stirred at room temperature for 1 h, a solution of olefin **8** (33.0 g, 81.6 mmol) in dry THF (60.4 g + 5.0 mL × three rinses) was added via cannula to the reaction mixture at 0 °C. After the mixture was stirred at room temperature for 1 h, a solution of NaOH (3 M in H_2O, 163 mL, 489 mmol) and H_2O_2 (30% in H_2O, 84 mL, 0.82 mol) was added to the reaction mixture. After the mixture was stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7/1 → 5/1 → 3/1 → 2/1) to give primary alcohol **11** (32.8 g, 77.5 mmol, 95%) as colorless solid.



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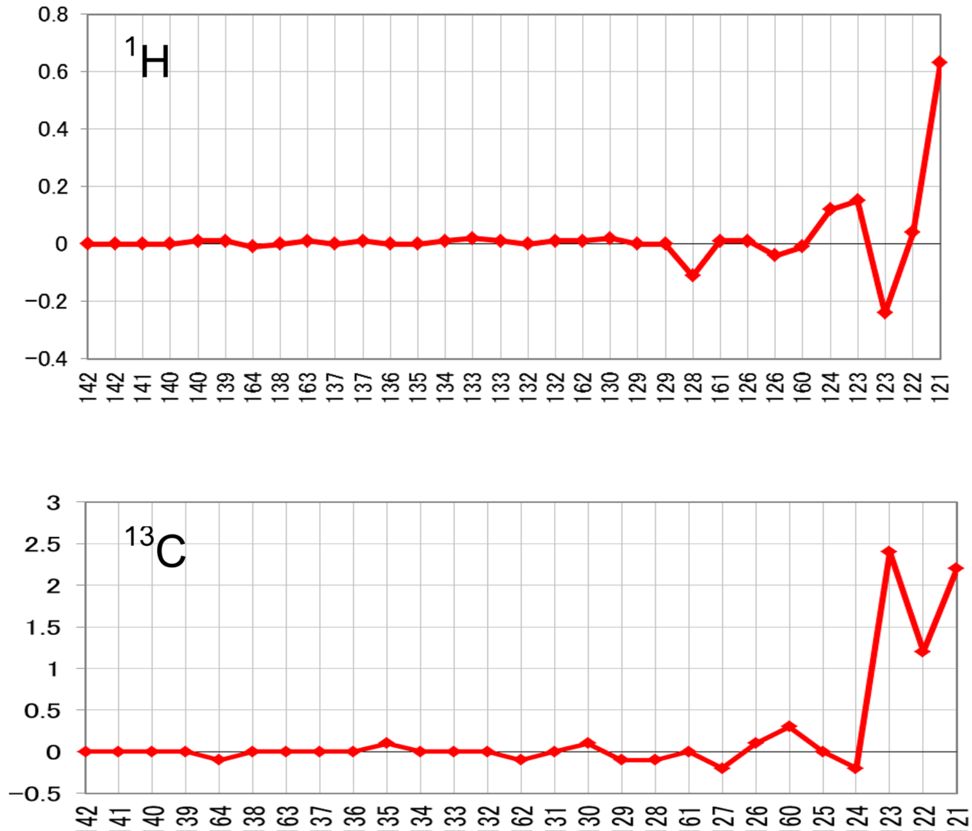

Figure 2. Differences in ^{1}H- and ^{13}C NMR (150 MHz, 1:1 C_5D_5N/CD_3OD, 25 °C) chemical shifts between MTX and the synthetic fragment **3**. The *x*- and *y*-axes represent carbon number and $\Delta\delta$ ($\Delta\delta = \delta$MTX − δsynthetic **3** in ppm), respectively.

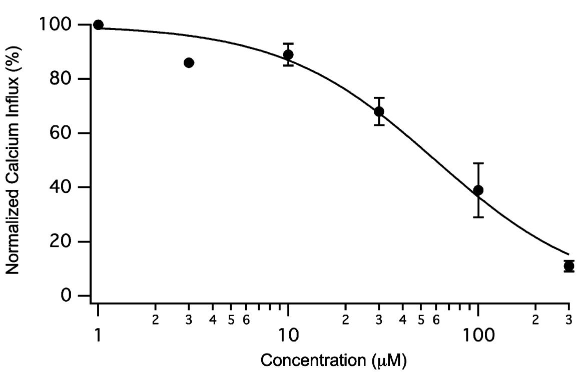

Figure 3. Inhibition of MTX-induced Ca^{2+} influx by the C′D′E′F′ ring (**3**). The level of Ca^{2+} influx induced by 1 nM MTX was defined as 100%.

$[\alpha]_D^{24}$ −27.5 (*c* 1.33, $CHCl_3$); IR (neat) 3453, 2953, 2857, 1471, 1374, 1254, 1090, 836, 775 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48−7.47 (m, 2H), 7.38−7.35 (m, 3H), 5.56 (s, 1H), 3.85 (d, *J* = 9.6 Hz, 1H), 3.84−3.79 (m, 3H), 3.60 (dd, *J* = 12.4, 3.5 Hz, 1H), 3.53 (d, *J* = 9.6 Hz, 1H), 2.03 (ddd, *J* = 11.0, 4.1, 3.4 Hz, 1H), 1.97 (ddd, *J* = 11.7, 11.7, 11.6 Hz, 1H), 1.85 (ddd, *J* = 14.5, 6.2, 2.8 Hz, 1H), 1.75 (ddd, *J* = 14.5, 8.3, 3.5 Hz, 1H), 1.55 (s, 3H), 1.35 (s, 3H), 0.87 (s, 9H), 0.09 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 137.5, 129.3, 128.5 (2C), 126.4 (2C), 103.2, 81.8, 80.3, 76.9, 74.0, 69.7, 59.5, 43.1, 31.0, 25.8 (3C), 22.1, 19.0, 17.9, −3.7, −4.9; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{38}O_5SiNa$ 445.2386; Found 445.2387.

1-((2*R*,4a*R*,6*S*,7*R*,8a*S*)-7-((*tert*-Butyldimethylsilyl)oxy)-4a,6-dimethyl-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-6-yl)-propan-2-one (12). TEMPO (124 mg, 790 μmol) and KBr (0.5 M in H_2O, 15.5 mL, 7.75 mmol) were added to a solution of alcohol **11** (32.8 g, 77.5 mmol) in CH_2Cl_2 (150 mL) at 0 °C, and then a mixture of a solution of NaOCl (1.73 M in H_2O, 49.5 mL, 85.6 mmol) and saturated aqueous solution of $NaHCO_3$ (49.5 mL) was added dropwise to the reaction mixture over 6 min. After being stirred at 0 °C for 30 min, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde (32.3 g) as pale brown amorphous. The material was used directly in the next reaction without further purification.

A solution of MeMgBr (1 M in THF, 92.5 mL, 92.5 mmol) was added dropwise to a solution of aldehyde described above in dry THF (200 g) at 0 °C over 17 min. After being stirred at room temperature for 20 min, the reaction mixture was quenched with a saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with a saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1 → 7/1 → 5/1 → 3/1) to give secondary alcohol (27.8 g, 63.7 mmol, 82% yield from alcohol **11**) as colorless amorphous.

AZADO (1.5 mg, 9.9 μmol) and KBr (0.5 M in H_2O, 380 μL, 190 μmol) were added to a solution of the alcohol (737 mg, 1.69 mmol) in CH_2Cl_2 (10 mL) at 0 °C, and then a mixture of NaOCl (1.73 M in H_2O, 1.17 mL, 2.02 mmol) and saturated aqueous solution of $NaHCO_3$ (1.17 mL) was added dropwise to the reaction mixture. After being stirred at 0 °C for 15 min, a mixture of NaOCl (1.73 M in H_2O, 0.585 mL, 1.01 mmol) and saturated aqueous solution of $NaHCO_3$ (0.59 mL) was added dropwise to the reaction mixture. After being stirred at 0 °C for 10 min, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 30/1 → 20/1 → 14/1 → 10/1 → 7/1 → 5/1 → 3/1) to give ketone **12** (677 mg, 1.56 mmol, 92%) as a colorless solid.

$[\alpha]_D^{22}$ −25.6 (*c* 0.990, $CHCl_3$); IR (neat) 2954, 2929, 2857, 2363, 1707, 1471, 1373, 1254, 1093, 837 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48−7.46 (m, 2H), 7.38−7.34 (m, 3H), 5.54 (s, 1H), 4.13 (dd, *J* = 11.0, 4.8 Hz, 1H), 3.83 (d, *J* = 9.6 Hz, 1H), 3.54 (dd, *J* = 12.4, 3.4 Hz, 1H), 3.49 (d, *J* = 9.6 Hz, 1H), 2.65 (d, *J* = 13.1 Hz, 1H), 2.43 (d, *J* = 13.0 Hz, 1H), 2.18 (s, 3H), 2.00 (ddd, *J* = 12.4, 4.8, 4.1 Hz, 1H), 1.92 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.52 (s, 3H), 1.31 (s, 3H), 0.87 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 208.5, 137.7, 129.3, 128.5 (2C), 126.5 (2C), 103.1, 80.2, 79.3, 76.8, 71.8, 69.3, 52.9, 33.6, 31.0, 25.8 (3C), 23.3, 19.0, 18.0, −3.9, −4.8; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{24}H_{38}O_5SiNa$ 457.2386; Found 457.2385.

1-((2*R*,4a*R*,6*S*,7*R*,8a*S*)-7-Hydroxy-4a,6-dimethyl-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-6-yl)propan-2-one (13). A solution of TBAF (1.0 M in THF, 57.0 mL, 57.0 mmol) was added to a solution of **12** (16.6 g, 38.1 mmol) in dry THF (160 g) at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 30/1 → 20/1 → 10/1 → 7/1 → 3/1 → 1/1 → 1/3) to give alcohol **13** (9.12 g, 28.5 mmol, 75%) as colorless amorphous and recovery of ketone **12** (2.91 g, 6.70 mmol, 18%).

$[\alpha]_D^{27}$ +9.83 (*c* 1.37, $CHCl_3$); IR (neat) 3444, 2960, 2866, 2360, 1670, 1376, 1112, 1069, 1015, 757, 699 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.40−7.34 (m, 3H), 5.55 (s, 1H), 3.94 (dd, *J* = 11.5, 4.3 Hz, 1H), 3.84 (d, *J* = 9.6 Hz, 1H), 3.80 (d, *J* = 3.7 Hz, 1H), 3.55 (dd, *J* = 12.8, 3.7 Hz, 1H), 3.50 (d, *J* = 9.6 Hz, 1H), 2.85 (d, *J* = 15.6 Hz, 1H), 2.69 (d, *J* = 16.0 Hz, 1H), 2.22 (s, 3H), 2.14 (ddd, *J* = 12.4, 4.4, 4.3 Hz, 1H), 1.93 (ddd, *J* = 12.4, 12.4, 11.5 Hz, 1H), 1.53 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.2, 137.5, 129.2, 128.5 (2C), 126.4 (2C), 103.0, 80.4, 78.3, 76.7, 72.0, 69.2, 55.5, 32.7, 29.9, 22.2, 18.9; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{18}H_{24}O_5Na$ 343.1521; Found 343.1520.

(*E*)-Ethyl-3-(((2*R*,4a*R*,6*S*,7*R*,8a*S*)-4a,6-dimethyl-6-(2-oxopropyl)-2-phenylhexahydropyrano[3,2-*d*][1,3]dioxin-7-yl)oxy)acrylate (14). NMM (10.5 mL, 95.5 mmol) and ethyl propiolate (4.86 mL, 47.9 mmol) were added sequentially to a solution of alcohol **13** (10.2 g, 31.9 mmol) in dry CH_2Cl_2 (233 g) at 0 °C. After being stirred at room temperature for 5 h 45 min, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 10/1 → 7/1 → 5/1 → 3/1 → 2/1) to give β-alkoxyacrylate **14** (11.9 g, 28.5 mmol, 89%) as yellow amorphous.

$[\alpha]_D^{23}$ −41.7 (*c* 1.74, $CHCl_3$); IR (neat) 2983, 2867, 2348, 1706, 1643, 1624, 1469, 1372, 1126, 1010, 838 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 12.4 Hz, 1H), 7.48−7.45 (m, 2H), 7.40−7.35 (m, 3H), 5.55 (s, 1H), 5.36 (d, *J* = 12.4 Hz, 1H), 4.34 (dd, *J* = 11.4, 4.6 Hz, 1H), 4.16 (dq, *J* = 7.3, 1.8 Hz, 2H), 3.85 (d, *J* = 9.6 Hz, 1H), 3.57 (dd, *J* = 12.8, 3.6 Hz, 1H), 3.49 (d, *J* = 11.0 Hz, 1H), 2.74 (d, *J* = 13.3 Hz, 1H), 2.35 (d, *J* = 13.3 Hz, 1H), 2.25 (ddd, *J* = 11.9, 4.2, 4.1 Hz, 1H), 2.18 (s, 3H), 2.01 (d, *J* = 12.4 Hz, 1H), 1.54 (s, 3H), 1.38 (s, 3H), 1.27 (t, *J* = 7.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.7, 167.5, 161.0, 137.3, 129.3, 128.4 (2C), 126.3 (2C), 103.0, 99.1, 80.0, 79.5, 77.2, 76.3, 69.5, 59.9, 51.7, 33.6, 27.1, 23.8, 18.8, 14.4; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{23}H_{30}O_7Na$ 441.1884; Found 441.1886.

Ethyl-2-((2*R*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-hydroxy-4a,5a,7-trimethyl-2-phenyloctahydro-4*H*-pyrano[2′,3′:5,6]pyrano[3,2-*d*]-[1,3]dioxin-8-yl)acetate (7). A solution of freshly prepared SmI_2 (0.080 M in THF, 634 mL, 50.8 mmol) was added to a solution of β-alkoxyacrylate **14** (8.55 g, 20.4 mmol) and dry MeOH (3.10 mL, 76.6 mmol) in dry THF (191 g) via cannula at 0 °C. After being stirred at 0 °C for 50 min, the reaction mixture was quenched with a 1:1 mixture of saturated aqueous solution of $Na_2S_2O_3$ and saturated aqueous solution of $NaHCO_3$, and the resulting cake was removed by filtration through a pad of Celite. The filtrate was concentrated to a half volume under reduced pressure and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 2/1 → 1/1 → 1/2 → 1/3) to give ester **7** (7.40 g, 17.6 mmol, 86%) as colorless solid.

$[\alpha]_D^{24}$ −31.5 (*c* 0.930, $CHCl_3$); IR (neat) 3482, 2957, 2863, 1774, 1456, 1124, 1092, 1049, 919 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48−7.47 (m, 2H), 7.38−7.34 (m, 3H), 5.57 (s, 1H), 4.18 (dq, *J* = 6.9, 2.1 Hz, 2H), 3.84 (d, *J* = 9.7 Hz, 1H), 3.82 (dd, *J* = 8.9, 4.1 Hz, 1H), 3.67 (dd, *J* = 12.4, 3.4 Hz, 1H), 3.54 (d, *J* = 9.7 Hz, 1H), 3.36 (dd, *J* = 11.7, 2.8 Hz, 1H), 2.67 (dd, *J* = 15.1, 4.1 Hz, 1H), 2.49 (dd, *J* = 15.8, 8.9 Hz, 1H), 2.13−2.10 (m, 1H), 2.10 (d, *J* = 12.4 Hz, 1H), 1.97 (ddd, *J* = 12.4, 11.7, 11.6, Hz, 1H), 1.83 (brs, 1H), 1.73 (d, *J* = 12.4 Hz, 1H), 1.61 (s, 3H), 1.40 (s, 3H), 1.33 (s, 3H), 1.27 (t, *J* = 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 137.5, 129.3, 128.5 (2C), 126.4 (2C), 103.3, 85.0, 83.5, 83.2, 76.9, 74.4, 70.6, 70.4, 61.0, 55.0, 35.1, 27.3, 25.1, 21.3, 20.6, 14.3; HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ Calcd for $C_{23}H_{32}O_7Na$ 443.2040; Found 443.2043.

(2*R*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-8-(2-Hydroxyethyl)-4a,5a,7-trimethyl-2-phenyloctahydro-4*H*-pyrano[2′,3′:5,6]pyrano[3,2-*d*]-[1,3]dioxin-7-ol (15). $LiAlH_4$ (746 mL, 19.7 mmol) was added to a solution of ester **7** (6.31 g, 15.0 mmol) in dry THF (110 g) at −15 °C. After being stirred at −15 °C for 2 h, the reaction mixture was diluted with Et_2O (300 mL) and quenched with H_2O (1.20 mL). The reaction mixture was allowed to warm to room temperature, and H_2O (8.35 mL) was added to the reaction mixture. The resulting cake was removed by filtration through a pad of Celite. The filtrate was concentrated under reduced pressure to give crude diol **15** (6.24 g) as colorless amorphous. The material was used directly in the next reaction without further purification.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49−7.47 (m, 2H), 7.38−7.36 (m, 3H), 5.57 (s, 1H), 3.90−3.78 (m, 3H), 3.67 (dd, *J* = 11.9, 3.2 Hz, 1H), 3.54 (d, *J* = 11.0 Hz, 1H), 3.51 (dd, *J* = 9.2, 4.2 Hz, 1H), 3.36 (dd, *J* = 11.9, 2.3 Hz, 1H), 2.14−1.88 (m, 2H), 1.79−1.70 (m, 2H), 1.62 (s, 3H), 1.42 (s, 3H), 1.36 (s, 3H)

2-((2*R*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-Hydroxy-4a,5a,7-trimethyl-2-phenyloctahydro-4*H*-pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]-dioxin-8-yl)ethyl acetate (16). Ac_2O (14.2 mL, 150 mmol) was added to a solution of the diol **15** described above in pyridine (66.0 mL, 823 mmol) at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of $KHSO_4$, saturated aqueous solution of $NaHCO_3$, and saturated aqueous solution of NaCl sequentially, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 2/1 → 1/1 → 1/2 → 1/3) to give acetate **16** (6.26 g, 14.9 mmol, 99% yield from ester **7**) as colorless solid.

$[\alpha]_D^{24}$ −56.0 (*c* 1.14, $CHCl_3$); IR (neat) 3479, 2960, 2863, 1737, 1456, 1382, 1247, 1091, 753 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.48−7.47 (m, 2H), 7.39−7.34 (m, 3H), 5.57 (s, 1H), 4.32 (ddd, *J* = 11.7, 6.2, 5.5 Hz, 1H), 4.18 (ddd, *J* = 13.7, 8.2, 5.5 Hz, 1H), 3.84 (d, *J* = 9.6 Hz, 1H), 3.67 (dd, *J* = 12.4, 3.4 Hz, 1H), 3.53 (d, *J* = 9.6 Hz, 1H), 3.37 (dd, *J* = 11.0, 2.0 Hz, 1H), 3.29 (dd, *J* = 11.7, 2.8 Hz, 1H), 2.12 (ddd, *J* = 11.0, 3.5, 3.4 Hz, 1H), 2.08 (d, *J* = 12.4 Hz, 1H), 2.07 (s, 3H), 2.00−1.94 (m, 1H), 1.97 (d, *J* = 11.7 Hz, 1H), 1.74−1.68 (m, 1H), 1.71 (d, *J* = 13.7 Hz, 1H), 1.61 (s, 3H), 1.41 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.3, 137.5, 129.3, 128.5 (2C), 126.4 (2C), 103.3, 85.4, 83.5, 83.3, 77.0, 74.4, 71.0, 70.4, 62.1, 51.2, 28.4, 27.3, 25.1, 21.3, 21.2, 20.6; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{23}H_{32}O_7Na$ 443.2040; Found 443.2041.

(*E*)-Methyl-3-(((2*R*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-8-(2-acetoxyethyl)-4a,5a,7-trimethyl-2-phenyloctahydro-4*H*-pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]dioxin-7-yl)oxy)acrylate (17). Methyl propiolate (3.50 mL, 42.9 mmol) was added dropwise to a mixture of tertiary alcohol **16** (6.05 g, 14.4 mmol) and a solution of Me_3P (1.0 M, 71.9 mL, 71.9 mmol) at room temperature over 6 min. After being stirred at room temperature for 40 min, the reaction mixture was quenched with H_2O and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10/1 → 7/1 → 5/1 → 3/1 → 2/1 → 1/1 → 1/2 → 1/3) to give β-alkoxyacrylate **17** (6.04 g, 12.0 mmol, 83%) as colorless solid and recovery of tertiary alcohol **16** (974 mg, 2.32 mmol).

$[\alpha]_D^{23}$ −83.1 (*c* 1.20, $CHCl_3$); IR (neat) 2952, 2857, 1738, 1713, 1638, 1385, 1247, 1131, 1042, 837 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 11.9 Hz, 1H), 7.49−7.46 (m, 2H), 7.40−7.35 (m, 3H), 5.56 (s, 1H), 5.35 (d, *J* = 11.9 Hz, 1H), 4.32 (ddd, *J* = 11.4, 6.9, 5.0 Hz, 1H), 4.17 (ddd, *J* = 11.0, 8.3, 6.0 Hz, 1H), 3.83 (d, *J* = 9.6 Hz, 1H), 3.69 (s, 3H), 3.67 (dd, *J* = 11.9, 1.4 Hz, 1H), 3.57 (dd, *J* = 10.5, 1.84 Hz, 1H), 3.52 (d, *J* = 9.6 Hz, 1H), 3.32 (dd, *J* = 11.9, 3.2 Hz, 1H), 2.26 (d, *J* = 12.4 Hz, 1H), 2.14 (ddd, *J* = 11.4, 3.6, 3.2 Hz, 1H), 2.07 (s, 3H), 1.97 (ddd, *J* = 11.9, 11.9, 11.4 Hz, 1H), 1.94−1.88 (m, 1H), 1.82 (d, *J* = 11.9 Hz, 1H), 1.76−1.67 (m, 1H), 1.61 (s, 3H), 1.47 (s, 3H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 168.0, 156.3, 137.4, 129.2, 128.4 (2C), 126.3 (2C), 103.2, 100.4, 83.3, 82.92, 82.87, 80.0, 76.7, 74.0, 70.5, 61.4, 51.3, 51.2, 28.4, 27.1, 22.8, 21.2, 21.1, 20.8; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{27}H_{36}O_9Na$ 527.2257; Found 527.2257.

(*E*)-Methyl-3-(((2*R*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-8-(2-hydroxyethyl)-4a,5a,7-trimethyl-2-phenyloctahydro-4*H*-pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]dioxin-7-yl)oxy)acrylate (18). K_2CO_3 (793 mg, 5.74 mmol) was added to a solution of β-alkoxyacrylate **17** (7.22 g, 14.3 mmol) in MeOH (140 mL) at 0 °C. After being stirred at room temperature for 4 h 20 min, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 2/1 → 1/1 → 1/2 → 1/3 → 0/1) to give alcohol **18** (6.08 g, 13.1 mmol, 92%) as colorless solid.

$[\alpha]_D^{22}$ −89.1 (*c* 0.735, $CHCl_3$); IR (neat) 3473, 2951, 2873, 1710, 1637, 1385, 1131, 756 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 11.7 Hz, 1H), 7.47−7.46 (m, 2H), 7.38−7.33 (m, 3H), 5.54 (s, 1H), 5.35 (d, *J* = 12.4 Hz, 1H), 3.81 (d, *J* = 9.6 Hz, 1H), 3.81−3.75 (m, 2H), 3.69 (dd, *J* = 11.7, 2.0 Hz, 1H), 3.67 (s, 3H), 3.64 (dd, *J* = 11.7, 3.4 Hz, 1H), 3.51 (d, *J* = 9.6 Hz, 1H), 3.37 (dd, *J* = 11.6, 3.42 Hz, 1H), 2.29−2.26 (m, 1H), 2.25 (d, *J* = 12.4 Hz, 1H), 2.12 (ddd, *J* = 11.7, 3.4, 3.4 Hz, 1H), 1.97 (ddd, *J* = 11.7, 11.7, 11.6 Hz, 1H), 1.81 (d, *J* = 11.7 Hz, 1H), 1.82−1.78 (m, 1H), 1.72−1.66 (m, 1H), 1.59 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.1, 156.4, 137.4, 129.3, 128.5 (2C), 126.3 (2C), 103.3, 100.4, 85.0, 83.3, 83.0, 80.1, 76.7, 74.0, 70.6, 60.8, 51.5, 51.2, 31.5, 27.3, 23.0, 21.2, 20.7; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{25}H_{34}O_8Na$ 485.2146; Found 485.2145.

Methyl-2-((2*R*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-hydroxy-4a,5a,6a,8-tetramethyl-2-phenyldodecahydropyrano-[2″,3″:5′,6′]pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]dioxin-8-yl)-acetate (19). Dry DMSO (7.26 mL, 102 mmol) and Et_3N (7.11 mL, 51.2 mmol) and SO_3·Py (4.08 g, 25.6 mmol) were added sequentially to a solution of **18** (5.91 g, 12.8 mmol) in dry CH_2Cl_2 (100 mL) at 0 °C. After the mixture was stirred at room temperature for 1 h, Et_3N (3.55 mL, 25.5 mmol) and SO_3·Py (2.06 g, 12.9 mmol) were added sequentially to the reaction mixture at 0 °C. After being stirred at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was roughly purified by silica gel column chromatography to give aldehyde (5.01 g) as colorless solid. The material was used directly in the next reaction without further purification.

A solution of freshly prepared SmI_2 (0.096 M in THF, 356 mL, 34.2 mmol) was added to a solution of the aldehyde described above and dry MeOH (1.81 mL, 44.7 mmol) in dry THF (52.1 g) via cannula at 0 °C. After being stirred at 0 °C for 40 min, the reaction mixture was quenched with a 1:1 mixture of saturated aqueous solution of $Na_2S_2O_3$ and saturated aqueous solution of $NaHCO_3$, and the resulting cake was removed by filtration through a pad of Celite. The filtrate was concentrated to a half volume under reduced pressure and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 3/1 → 2/1 → 1/1 → 1/2 → 1/3) to give ester **19** (4.58 g, 9.90 mmol, 77% yield from alcohol **18**) as pale yellow solid.

$[\alpha]_D^{23}$ −55.5 (*c* 0.755, $CHCl_3$); IR (neat) 3460, 2952, 2858, 1738, 1383, 1112, 1027, 755 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.48−7.47 (m, 2H), 7.39−7.34 (m, 3H), 5.56 (s, 1H), 3.90 (ddd, *J* = 9.6, 6.2, 5.5 Hz, 1H), 3.83 (d, *J* = 9.6 Hz, 1H), 3.69 (s, 3H), 3.66 (dd, *J* = 12.4, 4.1 Hz, 1H), 3.57−3.50 (m, 1H), 3.51 (d, *J* = 10.3 Hz, 1H), 3.38 (dd, *J* = 12.4, 2.8 Hz, 1H), 3.23 (dd, *J* = 13.1, 2.8 Hz, 1H), 2.72 (dd, *J* = 15.1, 4.8 Hz, 1H), 2.55 (d, *J* = 6.2 Hz, 1H), 2.52 (dd, *J* = 15.1, 6.2 Hz, 1H), 2.23 (ddd, *J* = 11.7, 5.5, 2.7 Hz, 1H), 2.14 (ddd, *J* = 12.4, 4.1, 4.1 Hz, 1H), 2.03 (dd, *J* = 12.4, 8.3 Hz, 1H), 2.00 (d, *J* = 12.4 Hz, 1H), 1.73−1.67 (m, 2H), 1.63 (s, 3H), 1.59 (d, *J* = 12.4 Hz, 1H), 1.48 (s, 3H), 1.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.7, 137.5, 129.4, 128.5 (2C), 126.4 (2C), 103.4, 86.0, 83.8, 83.5, 77.1, 75.4, 73.2, 71.3, 70.8, 70.6, 52.4, 52.0, 38.8, 33.7, 27.5, 22.0, 21.7, 18.1; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{25}H_{34}O_8Na$ 485.2145.

(2*R*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-8-(2-Hydroxyethyl)-4a,5a,6a,8-tetramethyl-2-phenyldodecahydropyrano-[2″,3″:5′,6′]pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]dioxin-9-ol (20). $LiAlH_4$ (489 mg, 12.9 mmol) was added to a solution of ester **19** (4.58 g, 9.90 mmol) in dry THF (100 mL) at −10 °C. After being stirred at −10 °C for 2.25 h, the reaction mixture was diluted with THF (300 mL) and quenched with H_2O (2.00 mL). The reaction mixture was allowed to warm to room temperature, and H_2O (7.16 mL) was added to the reaction mixture. The resulting cake was removed by filtration through a pad of Celite. The filtrate was concentrated under reduced pressure to give crude diol **20** (4.86 g) as a pale yellow solid. The material was used directly in the next reaction without further purification.

(2*R*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a,8-tetramethyl-2-phenyldodecahydropyrano[2″,3″:5′,6′]pyrano[2′,3′:5,6]pyrano[3,2-*d*][1,3]-dioxine (21). NaH (60% in mineral oil, 1.28 g, 32.0 mmol) and BnBr (2.82 mL, 23.8 mmol) were sequentially added to a solution of **20** described above in dry THF (80 mL) and dry DMF (15 mL) at 0 °C. After the mixture was stirred at room temperature for 14 h, NaH (60% in mineral oil, 0.64 g, 16 mmol) and BnBr (1.41 mL, 11.9 mmol) were sequentially added to the reaction mixture. After being stirred at room temperature for 5.5 h, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10/1 → 7/1 → 5/1 → 3/1 → 2/1 → 1/1 → 1/2) to give benzyl ether **21** (4.66 g, 7.59 mmol, 77% yield from ester **19**) as pale yellow amorphous.

$[\alpha]_D^{24}$ −68.7 (*c* 1.57, $CHCl_3$); IR (neat) 2952, 2863, 1455, 1382, 1110, 927 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.52−7.50 (m, 2H), 7.41−7.29 (m, 13H), 5.58 (s, 1H), 4.66 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.49 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.6 Hz, 1H), 3.87 (d, *J* = 9.7 Hz, 1H), 3.76 (ddd, *J* = 8.9, 8.9, 3.1 Hz, 1H), 3.68 (dd, *J* = 11.7, 3.4 Hz, 1H), 3.62−3.56 (m, 2H), 3.53 (d, *J* = 9.6 Hz, 1H), 3.39 (dd, *J* = 12.4, 2.8 Hz, 1H), 3.29 (ddd, *J* = 9.7, 9.7, 5.5 Hz, 1H), 3.18 (dd, *J* = 13.1, 2.8 Hz, 1H), 2.39−2.36 (m, 1H), 2.24−2.19 (m, 1H), 2.16 (d, *J* = 11.7 Hz, 1H), 2.07 (dd, *J* = 11.7, 11.7 Hz, 1H), 2.01 (d, *J* = 12.4 Hz, 1H), 1.73−1.66 (m, 2H), 1.67 (s, 3H), 1.60 (d, *J* = 12.4 Hz, 1H), 1.51 (s, 3H), 1.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.0, 137.5, 129.3, 128.55, 128.50, 128.4, 128.0, 127.9, 127.7, 127.5, 126.4, 103.4, 85.9, 83.8, 83.7, 77.4, 77.1, 75.4, 72.9, 72.6, 71.0, 69.2, 67.0, 60.5, 52.6, 33.1, 30.2, 27.6, 21.9, 21.7, 18.3; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{38}H_{46}O_7Na$ 637.3136; Found 637.3137.

(2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-2-(hydroxymethyl)-2,8,9a,10a-tetramethyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-3-ol (22). CSA (519 mg, 1.61 mmol) was added to a solution of **21** (4.95 g, 8.05 mmol) in THF (40 mL) and MeOH (20 mL) at 0 °C. After being stirred at room temperature for 3 h 10 min, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 3/1 → 2/1 → 1/1 → 1/2 → 1/3 → 0/1) to give alcohol **22** (3.77 g, 7.16 mmol, 89%) as colorless amorphous.

$[\alpha]_D^{24}$ −51.5 (*c* 1.67, $CHCl_3$); IR (neat) 3431, 2952, 2870, 1455, 1386, 1091, 1041, 838 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.27 (m, 10H), 4.63 (d, *J* = 11.6 Hz, 1H), 4.52 (d, *J* = 11.6 Hz, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.05−4.01 (m, 1H), 3.72 (ddd, *J* = 8.9, 8.9, 2.0 Hz, 1H), 3.60−3.56 (m, 2H), 3.38−3.31 (m, 2H), 3.25 (ddd, *J* = 10.3, 10.3, 5.5 Hz, 1H), 3.13 (dd, *J* = 13.0, 2.0 Hz, 2H), 2.39−2.33 (m, 2H), 2.22−2.17 (m, 1H), 2.07−2.05 (m, 1H), 1.97 (d, *J* = 11.7 Hz, 1H), 1.84 (ddd, *J* = 12.4, 11.7, 11.6 Hz, 1H), 1.69−1.60 (m, 2H), 1.50 (d, *J* = 12.4 Hz, 1H), 1.41 (s, 3H), 1.30 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.8, 138.0, 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.6, 83.6, 82.8, 77.9 (2C), 73.7, 72.9, 72.5, 71.0, 69.2, 69.1, 68.1, 66.9, 52.8, 33.1, 30.5, 30.2, 21.1, 20.8, 17.7; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{31}H_{42}O_7Na$ 549.2828; Found 549.2829.

(((2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-2-(((*tert*-butyldimethylsilyl)oxy)methyl)-2,8,9a,10a-tetramethyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-3-yl)oxy)(*tert*-butyl)dimethylsilane (23). Imidazole (1.64 g, 24.1 mmol) and TBSCl (2.40 g, 15.9 mmol) were added sequentially to a solution of alcohol **22** (3.52 g, 6.69 mmoL) in dry DMF (10 mL) at 0 °C. After the mixture was stirred at room temperature for 15 h, dry DMF (10 mL) was added to the reaction mixture. After being stirred at room temperature for 22.5 h, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with a 4:1 mixuture of hexane and EtOAc. The organic layer was washed with H_2O and saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give TBS ether **23** (5.36 g) as colorless amorphous. The material was used directly in the next reaction without further purification.

((2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-3-((*tert*-butyldimethylsilyl)oxy)-2,8,9a,10a-tetramethyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-2-yl)methanol (24). CSA (1.87 g, 8.05 mmol) was added to a solution of TBS ether **23** described above in CH_2Cl_2 (40 mL) and MeOH (20 mL) at 0 °C. After being stirred at room temperature for 3 h, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 14/1 → 10/1 → 7/1 → 5/1 → 3/1 → 2/1) to give alcohol **24** (3.77 g, 5.88 mmol, 88% yield from diol **22**) as colorless amorphous.

$[\alpha]_D^{22}$ −42.6 (*c* 1.07, $CHCl_3$); IR (neat) 3500, 2953, 2928, 2857, 2366, 2356, 2335, 1728, 1471, 1456, 1386, 1255, 1104, 1049, 864, 837, 776, 736, 697; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.27 (m, 10H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 12.4 Hz, 1H), 4.47−4.44 (m, 2H), 4.02 (dd, *J* = 11.0, 5.5 Hz, 1H), 3.71 (dt, *J* = 8.9, 2.8 Hz, 1H), 3.59−3.53 (m, 2H), 3.28−3.22 (m, 3H), 3.44−3.40 (m, 1H), 3.11 (ddd, *J* = 12.4, 8.9, 3.4 Hz, 1H), 2.35−2.31 (m, 1H), 2.21−2.16 (m, 1H), 2.03 (dd, *J* = 10.3, 2.8 Hz, 1H), 1.98−0.95 (m, 2H), 1.84 (q, *J* = 11.6 Hz, 1H), 1.67−1.58 (m, 2H), 1.47 (d, *J* = 12.4 Hz, 1H), 1.40 (s, 3H), 1.29 (s, 3H), 1.15 (s, 3H), 0.86 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.7, 138.0, 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.5, 83.3, 82.7, 78.7, 77.9, 73.4, 72.9, 72.4, 71.0, 69.2, 68.9, 67.2, 66.9, 52.8, 33.0, 31.1, 30.1, 25.7 (3C), 21.4, 21.1, 17.9, 17.6, −3.9, −5.1; HRMS (ESI-TOF) *m/z*: $[M + Na]^+$ Calcd for $C_{37}H_{56}O_7SiNa$ 663.3688; Found 663.3688.

(((2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-2,8,9a,10a-tetramethyl-2-vinyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-3-yl)oxy)(*tert*-butyl)dimethylsilane (6). TEMPO (42.1 mg, 269 μmol) and KBr (0.5 M in H_2O, 1.18 mL, 590 μmol) were added to a solution of alcohol **24** (3.75 g, 5.85 mmol) in CH_2Cl_2 (60 mL) at 0 °C, and then a mixture of NaOCl (1.61 M in H_2O, 4.15 mL, 6.60 mmol) and saturated aqueous solution of $NaHCO_3$ (4.15 mL) was added dropwise to the reaction mixture. After the mixture was stirred at 0 °C for 50 min, a mixture of NaOCl (1.61 M in H_2O, 364 μL, 578 μmol) and saturated aqueous solution of $NaHCO_3$ (364 μL) was added dropwise to the reaction mixture. After being stirred at 0 °C for 20 min, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde (3.85 g) as pale brown amorphous. The material was used directly in the next reaction without further purification.

A solution of Tebbe reagent (0.5 M in toluene, 14.0 mL, 7.00 mmol) was added dropwise to a solution of the aldehyde described above in dry THF (93 g) at 0 °C. After being stirred at 0 °C for 20 min, the reaction mixture was diluted with Et_2O and quenched with a solution of NaOH (1.5 M in H_2O, 5.62 mL). After stirring 1 h 10 min, and the resulting cake was removed by filtration through a pad of Celite and anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography to (hexane/ethyl acetate = 1/0 → 20/1 → 15/1 → 10/1 → 7/1) give olefin **6** (3.00 g, 4.71 mol, 80% yield from alcohol **24**) as pale brown amorphous.

$[\alpha]_D^{23}$ −42.0 (*c* 1.04, $CHCl_3$); IR (neat) 2953, 2857, 2341, 1471, 1386, 1255, 1110, 837, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.34−7.23 (m, 10H), 5.86 (dd, *J* = 17.2, 10.3 Hz, 1H), 5.25 (d, *J* = 17.2 Hz, 1H), 4.99 (d, *J* = 10.9 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.52 (d, *J* = 11.7 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.45 (d, *J* = 11.6 Hz, 1H), 3.73−3.69 (m, 2H), 3.60−3.53 (m, 2H), 3.34 (dd, *J* = 12.4, 3.42 Hz, 1H), 3.23 (dt, *J* = 9.6, 5.52 Hz, 1H), 3.11 (dd, *J* = 13.1, 3.5 Hz, 1H), 2.32−2.30 (m, 1H), 2.22−2.16 (m, 1H), 2.03−2.01 (m, 2H), 1.82 (dt, *J* = 12.4, 8.94 Hz, 1H), 1.67−1.60 (m, 3H), 1.45 (s, 3H), 1.30 (s, 3H), 1.29 (s, 3H), 0.88 (s, 9H), 0.07 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (600 MHz, $CDCl_3$) δ 145.9, 138.8, 138.1, 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.5, 112.1, 82.5, 82.3, 78.2, 77.9, 74.9, 73.1, 72.9, 72.5, 70.9, 69.1, 67.0, 53.2, 33.1, 32.0, 30.2, 25.8 (3C), 24.0, 21.6, 18.0, 17.5, −4.1, −4.9; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{38}H_{56}O_6SiNa$ 659.3738; Found 659.3735.

(*R*)-3-((*S*,*E*)-6-((4-Methoxybenzyl)oxy)-4-methylhex-2-enoyl)-4-phenyloxazolidin-2-one (26). A solution of diol **25** (5.92 g, 23.3 mmol) in THF (15 mL + 5.0 mL × three rinses) was added to a solution of sodium periodate (5.98 g, 28.0 mmol) in THF (30 mL) and H_2O (30 mL) at 0 °C. After being stirred at room temperature for 10 min, the reaction mixture was diluted with EtOAc and quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde **9** (5.50 g) as pale yellow oil. The material was used directly in the next reaction without further purification.

A solution of NaHMDS (1.9 M in THF, 20.8 mL, 39.5 mmol) was added dropwise to a solution of pohosphonate **10** (15.9 g, 46.6 mmol) in dry THF (180 g) over 2 min at 0 °C. After being stirred for 30 min, the mixture was cooled to 0 °C, and a solution of aldehyde **9** described above in dry THF (39.9 g + 3.0 mL × three rinses) was added via cannula. After being stirred at 0 °C for 15.5 h, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate =7/1 → 5/1 → 3/1 → 2/1 → 1/1) to give olefin **26** (6.89 g, 16.8 mmol, 72% yield from alcohol **25**) as yellow syrup.

$[\alpha]_D^{26}$ −24.2 (c 0.965, $CHCl_3$); IR (neat) 2929, 2859, 2359, 1775, 1685, 1633, 1513, 1326, 1246, 1194, 1099, 760 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.39−7.37 (m, 2H), 7.34−7.31 (m, 3H), 7.24−7.20 (m, 3H), 6.98 (dd, J = 15.1, 7.6 Hz, 1H), 6.88−6.85 (m, 2H), 5.48 (dd, J = 8.22, 3.4 Hz, 1H), 4.70 (t, J = 8.6 Hz, 1H), 4.39 (s, 2H), 4.28 (dd, J = 8.9, 3.4 Hz, 1H), 3.80 (s, 3H), 3.45−3.39 (m, 2H), 2.62−2.57 (m, 1H), 1.71−1.62 (m, 2H), 1.06 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 164.7, 159.1, 156.4, 153.7, 139.2, 130.5, 129.3 (2C), 129.1 (2C), 128.6, 126.0 (2C), 118.9, 113.8 (2C), 72.6, 69.9, 67.5, 57.7, 55.2, 35.7, 33.8, 19.3; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{27}NO_5Na$ 432.1787; Found 432.1787.

(*R*)-3-((3*R*,4*S*)-6-((4-Methoxybenzyl)oxy)-3,4-dimethylhexanoyl)-4-phenyloxazolidin-2-one (27). A solution of methylmagnesium bromide (1.0 M in THF, 95 mL, 95 mmol) was added dropwise to a solution of copper(I) bromide dimethyl sulfide complex (13.8 g, 67.3 mmol) in dry THF (150 g) and dry dimethyl sulfide (80 mL) over 23 min at −66 °C. After being stirred at −66 °C for 40 min, the mixture was allowed to warm to 0 °C. After being stirred for 25 min, the mixture was cooled to −70 °C. The mixture was added to a solution of olefin **26** (10.9 g, 26.7 mmol) in dry THF (128 g) and dry CH_2Cl_2 (137 g) at −65 °C via cannula over 10 min, and then the reaction mixture was allowed to warm to −30 °C over 60 min. After being stirred at −30 °C for 20 min, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7/1 → 5/1 → 3/1 → 2/1 → 1/1) to give amide **27** (11.3 g, 26.5 mmol, 99%, dr > 30:1) as colorless solid.

$[\alpha]_D^{25}$ −42.1 (c 1.05, $CHCl_3$); IR (neat) 2958, 2872, 1779, 1704, 1512, 1384, 1246, 1093, 820, 769 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.22 (m, 7H), 6.88−6.85 (m, 2H), 5.38 (dd, J = 8.72, 4.12 Hz, 1H), 4.62 (t, J = 8.9 Hz, 1H), 4.42 (d, J = 11.4 Hz, 1H), 4.38 (d, J = 11.5 Hz, 1H), 4.24 (dd, J = 8.7, 3.7 Hz, 1H), 3.80 (s, 3H), 3.49−3.37 (m, 2H), 2.91 (dd, J = 16.0, 5.5 Hz, 1H), 2.78 (dd, J = 16.0, 8.7 Hz, 1H), 2.08−1.98 (m, 1H), 1.72−1.64 (m, 1H), 1.61−1.55 (m, 1H), 1.36−1.26 (m, 1H), 0.85 (d, J = 6.9 Hz, 3H), 0.81 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 159.2, 153.8, 139.3, 130.9, 129.3 (2C), 129.2 (2C), 128.7, 126.0 (2C), 113.8 (2C), 72.6, 69.9, 68.7, 57.8, 55.4, 38.9, 34.3, 34.0, 32.7, 16.6, 16.4; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{25}H_{31}NO_5Na$ 448.2094; Found 448.2096.

(3*R*,4*S*)-6-((4-Methoxybenzyl)oxy)-3,4-dimethylhexan-1-ol (28). $LiBH_4$ (703 mg, 32.3 mmol) was added to a solution of amide **27** (11.3 g, 26.5 mmol) and dry MeOH (1.30 mL, 32.1 mmol) in dry Et_2O (250 mL) at 0 °C. After being stirred at 0 °C for 15 min, the reaction mixture was quenched with a solution of NaOH (3.0 M in H_2O). After being stirred at room temperature for 3 h, the reaction mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 2/1 → 1/1) to give alcohol **28** (5.44 g, 20.4 mmol, 77%) as pale yellow oil.

$[\alpha]_D^{21}$ −3.50 (c 1.06, $CHCl_3$); IR (neat) 3396, 2955, 2871, 1612, 1513, 1246, 1091, 1036, 821 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26−7.25 (m, 2H), 6.88−6.87 (m, 2H), 4.44 (d, J = 11.0 Hz, 1H), 4.42 (d, J = 11.7 Hz, 1H), 3.80 (s, 3H), 3.70 (ddd, J = 10.3, 6.8, 5.5 Hz, 1H), 3.62 (ddd, J = 9.6, 6.9, 6.8 Hz, 1H), 3.50 (ddd, J = 9.6, 7.6, 5.5 Hz, 1H), 3.44 (ddd, J = 9.6, 7.6, 6.9 Hz, 1H), 1.71−1.66 (m, 1H), 1.63−1.52 (m, 3H), 1.39−1.30 (m, 2H), 0.86 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 130.7, 129.32 (2C), 113.8 (2C), 72.6, 68.9, 61.6, 55.3, 35.9, 34.5, 34.1, 32.8, 16.41, 16.37; HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{26}O_3Na$ 289.1774; Found 289.1774.

(5*R*,6*S*)-8-((4-Methoxybenzyl)oxy)-5,6-dimethyl-1-(trimethylsilyl)oct-1-yn-3-one (29). TEMPO (31.5 mg, 202 μmol) and KBr (0.5 M in H_2O, 4.08 mL, 2.04 mmol) were added to a solution of alcohol **28** (5.44 g, 20.4 mmol) in CH_2Cl_2 (100 mL) at 0 °C, and then a mixture of NaOCl (1.95 M in H_2O, 11.5 mL, 22.4 mmol) and saturated aqueous solution of $NaHCO_3$ (11.5 mL) was added dropwise to the reaction mixture over 1.5 min. After being stirred at 0 °C for 20 min, a mixture of NaOCl (1.95 M in H_2O, 1.05 mL, 2.04 mmol) and saturated aqueous solution of $NaHCO_3$ (1.05 mL) was added dropwise to the reaction mixture over 2 min. After being stirred at 0 °C for 20 min, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde (5.66 g) as pale brown oil. The material was used directly in the next reaction without further purification.

A solution of n-BuLi (1.6 M in hexane, 19.0 mL, 30.6 mmol) was added to a solution of trimethylsilylacetylene (5.41 mL, 38.3 mmol) in dry THF (91.2 g) at 0 °C. After being stirred for 40 min at 0 °C, the mixture was cooled to −70 °C, and a solution of the aldehyde described above in dry THF (15 mL + 3.0 mL x 3 rinse) was added via cannula over 5 min. After being stirred at −70 °C for 25 min, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 14/1 → 10/1 → 7/1 → 5/1 → 3/1) to give alcohol (6.32 g, 17.4 mmol, 85% yield from alcohol **28**) as brown oil.

MnO_2 (44.7 g, 515 mmol) was added to a solution of the alcohol (6.22 g, 17.2 mmol) in dry CH_2Cl_2 (174 g) at room temperature. After being stirred at room temperature for 13 h, MnO_2 (7.05 g, 81.1 mmol) was added to the reaction mixture. After being stirred at room temperature for 8.5 h, MnO_2 (16.4 g, 189 mmol) was added to the reaction mixture. After being stirred at room temperature for 15.5 h, the reaction mixture was filtered through a pad of Celite, and the filterate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 50/1 → 30/1 → 20/1 → 14/1 → 10/1) to give alcohol **29** (5.20 g, 14.4 mmol, 84%) as a pale yellow oil.

$[\alpha]_D^{27}$ −6.43 (c 1.30, $CHCl_3$); IR (neat) 2959, 2366, 1675, 1613, 1249, 1092, 846 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26−7.25 (m, 2H), 6.88−6.87 (m, 2H), 4.44 (d, J = 11.7 Hz, 1H), 4.41 (d, J = 11.6 Hz, 1H), 3.80 (s, 3H), 3.50 (ddd, J = 8.94, 7.56, 5.5 Hz, 1H), 3.44 (ddd, J = 8.94, 6.9, 6.8 Hz, 1H), 2.56 (dd, J = 15.8, 4.8 Hz, 1H), 2.32 (dd, J = 15.8, 9.5 Hz, 1H), 2.17–2.11 (m, 1H), 1.70–1.59 (m, 2H), 1.40–1.34 (m, 1H), 0.90 (d, J = 6.9 Hz, 3H), 0.85 (d, J = 6.8 Hz, 3H), 0.24 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.8, 159.2, 130.7, 129.2 (2C), 113.8 (2C), 102.3, 97.3, 72.6, 68.5, 55.2, 49.0, 34.3, 34.0, 33.2, 16.7, 16.1, −0.7 (3C); HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{32}O_3SiNa$ 383.2013; Found 383.2017.

(3*R*,5*R*,6*S*)-8-((4-Methoxybenzyl)oxy)-5,6-dimethyl-1-(trimethylsilyl)oct-1-yn-3-ol (31). (*R*,*R*)-Ru catalyst **30** (83.7 mg, 140 mmol) was added to a solution of ketone **29** (5.06 g, 14.0 mmol) in *i*-PrOH (150 mL), and the resulting mixture was stirred at room temperature for 98.5 h. During the period, additional (*R*, *R*)-Ru catalyst **30** was added portion wise after 48 h (50.6 mg, 84.4 mmol), after 7 h (85.0 mg, 142 mmol), after 15 h (41.3 mg, 68.9 mmol), and after 8.5 h (43.5 mg, 72.5 mmol). The solvent was evaporated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 7/1) to give alcohol **31** (4.81 g, 13.3 mmol, 95%) as a yellow oil.

$[\alpha]_D^{26}$ +17.5 (c 1.27, $CHCl_3$); IR (neat) 3425, 2956, 2858, 2170, 1612, 1513, 1249, 1093, 1037, 841 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.25 (m, 2H), 6.88 (d, J = 8.9 Hz, 2H) 4.42 (dd, J = 17.2, 11.7 Hz, 2H), 4.38 (m, 1H), 3.80 (s, 3H), 3.50 (m, 1H), 3.43 (m, 1H) 1.79 (d, J = 5.5 Hz, 1H), 1.77–1.72 (m, 2H), 1.68 (m, 1H), 1.60 (m, 1H), 1.45 (m, 1H), 1.36 (m, 1H), 0.89 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H), 0.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 130.7, 129.4 (2C), 113.8 (2C), 107.7, 88.8, 72.6, 68.9, 61.2, 55.4, 41.3, 34.6, 33.5, 32.7, 16.3, 16.2, 0.00 (3C); HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{21}H_{34}O_3SiNa$ 385.2175; Found 385.2174.

(3*R*,5*R*,6*S*)-8-((4-Methoxybenzyl)oxy)-5,6-dimethyloct-1-yn-3-ol (32). K_2CO_3 (361 mg, 2.61 mmol) was added to a solution of **31** (4.72 g, 13.0 mmol) in MeOH (65 mL) at 0 °C. After being stirred at room temperature for 15.5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 14/1 → 10/1 → 7/1 → 5/1 → 3/1 → 2/1) to give alcohol **32** (3.65 g, 12.6 mmol, 97%) as pale yellow oil.

$[\alpha]_D^{26}$ +17.0 (c 0.995, $CHCl_3$); IR (neat) 3411, 3289, 2956, 2872, 2359, 1612, 1513, 1246, 1034, 821 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.25 (m, 2H), 6.88–6.87 (m, 2H), 4.44 (d, J = 11.7 Hz, 1H), 4.41 (d, J = 11.7 Hz, 1H), 4.39 (ddd, J = 10.3, 8.3, 2.7 Hz, 1H), 3.81 (s, 3H), 3.50 (ddd, J = 8.9, 6.9, 5.5 Hz, 1H), 3.43 (ddd, J = 8.9, 7.6, 6.9 Hz, 1H), 2.45 (d, J = 2.4 Hz, 1H), 1.83 (d, J = 6.2 Hz, 1H), 1.80–1.75 (m, 2H), 1.70–1.65 (m, 1H), 1.62–1.58 (m, 1H), 1.46 (ddd, J = 14.5, 10.3, 4.1 Hz, 1H), 1.36 (ddd, J = 14.4, 8.9, 6.2 Hz, 1H), 0.90 (d, J = 6.2 Hz, 3H), 0.84 (d, J = 6.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 130.7 (2C), 129.4 (2C), 113.9, 85.8, 72.6, 72.5, 68.8, 60.5, 55.3, 42.9, 34.5, 33.4, 32.7, 16.3, 16.1; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{26}O_3Na$ 313.1774; Found 313.1779.

(3*R*,5*R*,6*S*,*E*)-1-Iodo-8-((4-methoxybenzyl)oxy)-5,6-dimethyl-oct-1-en-3-ol-(33). A solution of DIBALH (1.0 M in toluene, 18.6 mL, 18.6 mmol) was added dropwise to a solution of zirconocene dichloride (5.71 g, 19.5 mmol) in dry THF (74.4 g) at 0 °C over 4 min. After stirring at 0 °C for 35 min, a solution of alkyne **32** (2.39 g, 8.21 mmol) in dry THF (12.1 g + 5.0 mL × 2 rinse) was added via cannula to the reaction mixture at 0 °C over 3 min. The reaction mixture was allowed to warm to room temperature. After being stirred at room temperature for 40 min, the reaction mixture was cooled to −71 °C, and then a solution I_2 (1.0 M in THF, 22.0 mL, 22.0 mmol) was added to the reaction mixture at −71 °C over 8 min; the reaction mixture was allowed to warm to 0 °C. After being stirred at 0 °C for 10 min, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ and sodium potassium tartrate, and the reaction mixture was allowed to warm to room temperature. After being stirred at room temperature for 2 days 15.5 h, the mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 10/1 → 7/1 → 5/1 → 3/1 → 2/1) to give iodoolefin **33** (2.44 g, 5.84 mmol, 71%, *trans*:*gem* > 20:1) as a brown oil.

$[\alpha]_D^{22}$ +15.3 (c 1.37, $CHCl_2$); IR (neat) 3412, 2955, 2871, 2359, 2341, 1611, 1512, 1246, 1083, 1034, 820, 772 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.25 (m, 2H), 6.89–6.87 (m, 2H), 6.57 (dd, J = 14.5, 6.9 Hz, 1H), 6.31 (dd, J = 14.4, 1.0 Hz, 1H), 4.43 (d, J = 11.6 Hz, 1H), 4.41 (d, J = 11.6 Hz, 1H), 4.14–4.10 (m, 1H), 3.81 (s, 3H), 3.52–3.48 (m, 1H), 3.45–3.41 (m, 1H), 1.80 (d, J = 4.8 Hz, 1H), 1.75–1.69 (m, 1H), 1.69–1.63 (m, 1H), 1.61–1.58 (m, 1H), 1.50 (ddd, J = 13.7, 9.6, 3.4 Hz, 1H), 1.39–1.33 (m, 1H), 1.23 (ddd, J = 14.4, 10.3, 4.1 Hz, 1H), 0.88 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 149.5, 130.6, 129.4 (2C), 113.8 (2C), 76.6, 72.7 (2C), 68.9, 55.4, 39.8, 35.0, 33.1, 32.9, 16.4, 16.2; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{18}H_{27}IO_3Na$ 441.0897, found 441.0888.

***tert*-Butyl(((3*R*,5*R*,6*S*,*E*)-1-iodo-8-((4-methoxybenzyl)oxy)-5,6-dimethyloct-1-en-3-yl)oxy)dimethylsilane (5).** 2,6-Lutidine (1.63 mL, 14.0 mmol) and TBSOTf (1.61 mL, 7.00 mmol) were added sequentially to a solution of alcohol **33** (2.44 g, 5.84 mmoL) in dry CH_2Cl_2 (75.8 g) at 0 °C. After being stirred at 0 °C for 15 min, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The organic layer was washed sequentially with saturated aqueous solution of $NaHCO_3$, $KHSO_4$, and NaCl, and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 50/1 → 30/1 → 20/1 → 14/1) to give TBS ether **5** (3.50 g, 5.73 mmol, 98%) as a pale yellow oil.

$[\alpha]_D^{22}$ +42.7 (c 1.11, $CHCl_3$); IR (neat) 2953, 2928, 2855, 2359, 2341, 1611, 1513, 1247, 1086, 835, 774, 678 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.26–7.25 (m, 2H), 6.87 (d, J = 8.9 Hz, 2H), 6.50 (dd, J = 14.4, 6.8 Hz, 1H), 6.19 (d, J = 14.5 Hz, 1H), 4.43 (d, J = 11.7 Hz, 1H), 4.41 (d, J = 11.0 Hz, 1H), 4.11–4.08 (m, 1H), 3.80 (s, 3H), 3.48–3.42 (m, 2H), 1.65–1.61 (m, 2H), 1.49 (ddd, J = 12.4, 8.9, 3.5 Hz, 1H), 1.39–1.33 (m, 1H), 1.25 (s, 1H), 1.12 (ddd, J = 13.7, 10.3, 4.1 Hz, 1H), 0.88 (s, 9H), 0.84 (d, J = 6.9 Hz, 3H), 0.80 (d, J = 6.9 Hz, 3H), 0.03 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 150.1, 130.9, 129.3 (2C), 113.8 (2C), 75.6, 73.6, 72.7, 68.8, 55.4, 40.8, 34.7, 33.2, 32.8, 26.0 (3C), 18.2, 16.6, 16.0, −4.2, −4.8; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{24}H_{41}IO_3SiNa$ 555.1762, found 555.1751.

(((2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-2-((5*R*,7*R*,8*S*,*E*)-5-((*tert*-butyldimethylsilyl)-oxy)-10-((4-methoxybenzyl)oxy)-7,8-dimethyldec-3-en-1-yl)-2,9a,10a-trimethyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-3-yl)oxy)(*tert*-butyl)dimethylsilane (34). Olefin **6** (2.32 g, 3.65 mmol) was azeotroped with toluene and then dried over MS4A (21 granule) in dry THF (9.04 g) for 40 min. The dried olefin **6** in dry THF (9.04 g + 1.5 mL × three rinses) was added via cannula to a suspension of 9-BBN dimer (2.23 g, 9.12 mmol) in dry THF (5.5 mL) at 0 °C. After being stirred at room temperature for 1.5 h, H_2O (987 μL, 54.8 mmol) was added to the reaction mixture at 0 °C. After being stirred at room temperature for 25 min, the reaction mixture in THF (9.04 g + 10.0 mL + 2.5 mL × two rinses) was added via cannula to the 100 mL Schlenk flask in which $PdCl_2(dppf)\cdot CH_2Cl_2$ (498 mg, 609 μmol) and K_3PO_4 (2.60 g, 12.2 mmol) in freshly distilled DMF (17.0 mL) were stirred at 35 °C. Iodoolefin **5** (2.42 g, 4.55 mmol) in freshly distilled DMF (6.0 mL + 2.0 mL rinse) was added via cannula to the reaction mixture at 35 °C. After being stirred at 35 °C for 5 h, the reaction mixture was quenched with $NaBO_3\cdot 4H_2O$ (9.37 g, 60.9 mmol) and H_2O (15 mL) at room temperature. After being stirred at room temperature for 13.8 h, saturated aqueous solution of $Na_2S_2O_3$ was added to the reaction mixture. After being stirred at room temperature for 3 h, the reaction mixture extracted with a 4:1 mixture of hexane and EtOAc. The organic layer was washed with H_2O and saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 20/1 → 14/1 → 10/1 → 7/1 → 5/1) to give coupling product **34** (3.75 g, 3.59 mmol, 98%) as yellow amorphous.

$[\alpha]^{22}_{D}$ −13.5 (*c* 1.29, $CHCl_3$); IR (neat) 2953, 2928, 2856, 2360, 2336, 1462, 1613, 1249, 1102, 836 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.34−7.25 (m, 12H), 6.87 (d, *J* = 8.2 Hz, 2H), 5.59 (dt, *J* = 15.7, 6.2 Hz, 1H), 5.44 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 12.3 Hz, 1H), 4.47−4.42 (m, 4H), 4.08 (bs, 1H), 3.80 (s, 3H), 3.72−3.69 (m, 2H), 3.57−3.54 (m, 2H), 3.52−3.48 (m, 1H), 3.46−3.42 (m, 1H), 3.25−3.21 (m, 1H), 3.10 (ddd, *J* = 15.8, 13.0, 3.4 Hz, 1H), 2.32−2.30 (m, 1H), 2.20−2.04 (m, 3H), 1.93 (d, *J* = 12.4 Hz, 1H), 1.81 (q, *J* = 11.6 Hz, 1H), 1.70−1.60 (m, 5H), 1.52−1.47 (m, 3H), 1.45−1.40 (m, 1H), 1.38−1.33 (m, 4H), 1.28 (s, 3H), 1.23 (s, 3H), 1.18 (ddd, *J* = 13.4, 9.6, 4.1 Hz, 1H), 0.88−0.85 (m, 12H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.08 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 138.9, 138.1, 134.5, 131.0, 130.1, 129.3 (2C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.8 (2C), 127.6, 113.9 (2C), 83.7, 82.7, 78.0, 77.9, 73.5, 73.0, 72.8, 72.7, 72.6, 72.0, 71.0, 69.2, 69.1, 67.1, 55.4, 53.0, 42.2, 41.7, 34.7, 33.21, 33.18, 32.0, 31.6, 30.2, 26.1 (4C), 25.8 (3C), 24.7, 21.0, 18.3, 18.0, 17.7, 16.6, 16.2, −3.6, −3.7, −4.6, −4.9; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{62}H_{98}O_9Si_2$ 1065.6642, found 1065.6643.

(2*R*,3*S*,4a*R*,5a*S*,7*R*,8*S*,9a*R*,10a*S*)-7-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-2-((5*R*,7*R*,8*S*,*E*)-5-hydroxy-10-((4-methoxybenzyl)oxy)-7,8-dimethyldec-3-en-1-yl)-2,9a,10a-trimethyldecahydro-2*H*-dipyrano[3,2-*b*:2′,3′-*e*]pyran-3-ol (4). A solution of TBAF (1.0 M in THF, 11.0 mL, 11.0 mmol) was added dropwise to a solution TBS ether **34** (4.78 g, 4.58 mmol) in dry THF (34.0 mL) at room temperature. After being stirred under reflux for 13 h, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl at room temperature. The mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 3/1 → 2/1 → 1/1 → 1/2 → 1/3) to give diol **4** (3.57 g, 4.38 mmol, 96%) as pale brown amorphous.

$[\alpha]^{22}_{D}$ −31.6 (*c* 0.93, $CHCl_3$); IR (neat) 3437, 2953, 2928, 2871, 2369, 2328, 1612, 1513, 1248, 1092, 1040, 772 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.33−7.25 (m, 12H), 6.88−6.87 (m, 2H), 5.60 (dt, *J* = 14.4, 6.2 Hz, 1H), 5.46 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.62 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 12.4 Hz, 1H), 4.47−4.40 (m, 4H), 4.08 (bs, 1H), 3.80 (s, 3H), 3.73−3.70 (m, 2H), 3.57−3.53 (m, 2H), 3.52−3.48 (m, 1H), 3.45−3.41 (m, 1H), 3.23 (dt, *J* = 15.1, 4.7 Hz, 1H), 3.12 (dt, *J* = 13.4, 2.8 Hz, 2H), 2.33−2.30 (m, 1H), 2.20−2.16 (m, 2H), 2.10 (q, *J* = 6.8 Hz, 2H), 2.07−2.03 (m, 1H), 1.94 (d, *J* = 12.4 Hz, 1H), 1.82 (q, *J* = 11.0 Hz, 1H), 1.70−1.47 (m, 6H), 1.38−1.33 (m, 4H), 1.28 (s, 6H), 1.19 (ddd, *J* = 6.5, 4.3, 1.7 Hz, 1H), 0.87 (d, *J* = 11.4 Hz, 3H), 0.86 (d, *J* = 11.0 Hz, 3H), 0.83 (d, *J* = 1.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 138.8, 138.1, 133.7, 131.5, 130.8, 129.4 (2C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.5, 113.9 (2C), 83.8, 82.8, 78.0, 73.3 (2C), 73.0, 72.9, 72.7, 72.5, 71.1, 71.0, 69.2, 69.1, 67.0, 55.4, 52.9, 42.3, 40.8, 34.8, 33.5, 33.1, 32.8, 31.1, 30.2, 26.0, 23.7, 21.0, 17.7, 16.38, 16.37; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{50}H_{70}O_9Na$ 837.4912; Found 837.4912.

(2*S*,3*R*,4a*S*,5a*R*,6a*S*,8*S*,10a*R*,11a*S*,12a*R*)-3-(Benzyloxy)-2-(2-(benzyloxy)ethyl)-8-((4*R*,5*S*,*E*)-7-((4-methoxybenzyl)oxy)-4,5-dimethylhept-1-en-1-yl)-10a,11a,12a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran (35). $PdCl_2(CH_3CN)_2$ (322 mg, 1.24 mmol) was added to a solution of diol **3** (3.37 g, 4.14 mmol) in dry THF (51.9 g) at 0 °C. After being stirred at 0 °C for 2 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 7/1 → 5/1 → 3/1 → 2/1 → 1/1) to give olefin **35** (3.07 g, 3.85 mmol, 93%) as colorless amorphous.

$[\alpha]^{23}_{D}$ −68.4 (*c* 1.04, $CHCl_3$); IR (neat) 2952, 2930, 2857, 2360, 2340, 2211, 1671, 1612, 1512, 1248, 1105, 775 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.23 (m, 12H), 6.88−6.87 (m, 2H), 5.63 (dt, *J* = 15.1, 6.8 Hz, 1H), 5.44 (dd, *J* = 15.8, 6.8 Hz, 1H), 4.62 (d, *J* = 11.6 Hz, 1H), 4.51 (d, *J* = 12.4 Hz, 1H), 4.47−4.40 (m, 4H), 3.92−3.89 (m, 1H), 3.80 (s, 3H), 3.70 (dd, *J* = 8.94, 2.8 Hz, 1H), 3.59−3.52 (m, 2H), 3.50−3.46 (m, 1H), 3.44−3.40 (m, 1H), 3.28 (dd, *J* = 12.4, 3.4 Hz, 1H), 3.25 (dt, *J* = 15.1, 5.5 Hz, 2H), 3.19 (dd, *J* = 11.7, 3.4 Hz, 1H), 3.13 (dd, *J* = 13.1, 2.8 Hz, 1H), 2.35−2.32 (m, 1H), 2.19−2.15 (m, 1H), 2.11−2.06 (m, 1H), 2.03−2.00 (m, 1H), 1.97 (d, *J* = 12.4 Hz, 1H), 1.88 (q, *J* = 12.4 Hz, 1H), 1.81−1.74 (m, 2H), 1.71−1.60 (m, 5H), 1.57−1.51 (m, 2H), 1.50−1.43 (m, 4H), 1.37−1.31 (m, 7H), 0.83 (d, *J* = 6.8 Hz, 3H), 0.81 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 138.9, 138.1, 132.6, 131.3, 130.9, 129.3 (2C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.6, 113.9 (2C), 86.2, 83.5, 83.3, 80.3, 78.1, 74.6, 73.7, 72.9, 72.69, 72.65, 71.0, 69.2, 69.0, 67.0, 55.4, 53.0, 38.8, 37.9, 36.2, 34.3, 33.2, 32.9, 30.6, 30.2, 28.1, 21.7, 21.5, 18.3, 16.6, 16.2; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{50}H_{68}O_8Na$ 819.4806, found. 819.4808

(1*S*,2*R*,4*R*,5*S*)-1-((2*S*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran-2-yl)-7-((4-methoxybenzyl)oxy)-4,5-dimethylheptane-1,2-diol (36). A mixture of $K_2OsO_4·2H_2O$ (106 mg, 286 μmol), $(DHQD)_2AQN$ (541 mg, 631 μmol), $K_3Fe(CN)_6$ (2.83 g, 8.60 mmol), K_2CO_3 (1.19 g, 8.61 mmol), and $MeSO_2NH_2$ (818 mg, 8.60 mmol) in *t*-BuOH (14.5 mL) and H_2O (14.5 mL) was stirred at room temperature for 30 min, *t*-BuOMe (18.0 mL) was added to this suspension. A solution of olefin **35** (2.28 g, 2.86 mmol) in *t*-BuOMe (5.0 mL + 2.0 mL × three rinses) was added to this suspension at 0 °C. After being stirred at 0 °C for 24 h, the reaction mixture was quenched with saturated aqueous solution of $Na_2S_2O_3$ (70 mL) and allowed to warm to room temperature, and EtOAc (30 mL) and H_2O (50 mL) were added to the reaction mixture. After being stirred at room temperature for 62.5 h, the organic layer was separated, and the aqueous layer was extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 3/1 → 2/1 → 1/1 → 1/3) to give diol **36** (2.30 g, 2.76 mmol, 96%, α/β = 10:1) as colorless amorphous.

^1H NMR (600 MHz, $CDCl_3$) δ 7.35−7.23 (m, 12H), 6.88−6.87 (m, 2H), 4.63 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.47−4.40 (m, 4H), 3.80 (s, 3H), 3.75−3.69 (m, 2H), 3.62 (ddd, *J* = 11.6, 3.4, 3.4 Hz, 1H), 3.59−3.42 (m, 4H), 3.28−3.18 (m, 4H), 3.13 (dd, *J* = 12.0, 2.8 Hz, 1H), 2.59 (d, *J* = 4.8 Hz, 1H), 2.54 (d, *J* = 6.9 Hz, 1H), 2.32 (ddd, *J* = 11.0, 4.8, 3.4 Hz, 1H), 2.17 (dddq, *J* = 5.5, 5.5, 2.7, 2.0 Hz, 1H), 2.01−1.94 (m, 2H), 1.89−1.84 (m, 2H), 1.72−1.52 (m, 9H), 1.47 (ddd, *J* = 13.0, 12.4, 4.8 Hz, 1H), 1.43 (s, 3H), 1.40−1.38 (m, 1H), 1.34 (s, 3H), 1.31 (s, 3H), 1.15−1.11 (m, 1H), 0.87 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 138.8, 138.0, 130.8, 129.4 (2C), 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.7 (2C), 127.5, 113.9 (2C), 85.9, 83.6, 83.4, 81.3, 78.0, 75.8, 74.7, 73.6, 72.9, 72.7, 72.6, 71.0, 70.4, 69.1, 69.0, 67.0, 55.4, 53.0, 43.5, 38.1, 37.2, 35.0, 33.3, 33.1, 32.9, 27.9, 25.6, 21.6, 21.2, 18.3, 16.4, 16.1; HRMS (ESI-TOF) *m*/*z*: [M + Na]$^+$ Calcd for $C_{50}H_{70}O_{10}Na$ 853.4861; Found 853.4862.

(5*R*,6*R*)-5-((2*S*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran-2-yl)-6-((2*R*,3*S*)-5-((4-methoxybenzyl)oxy)-2,3-dimethylpentyl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (37). 2,6-Lutidine (1.95 mL, 16.8 mmol) and TBSOTf (1.93 mL, 8.40 mmol) were added sequentially to a solution of alcohol **36** (3.17 g, 3.82 mmoL) in dry CH_2Cl_2 (87.3 g) at 0 °C. After being stirred at 0 °C for 50 min, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and extracted with EtOAc. The organic layer was washed sequentially with saturated aqueous solution of $NaHCO_3$, $KHSO_4$, and NaCl, and dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 15/1 → 10/1 → 7/1 → 5/1) to give TBS ether **37** (3.73 g, 3.52 mmol, 92%, α/β = 10:1) as colorless amorphous.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.26 (m, 12H), 6.89−6.88 (m, 2H), 4.62 (d, J = 11.7 Hz, 1H), 4.51 (d, J = 11.7 Hz, 1H), 4.47−4.44 (m, 4H), 3.80 (s, 3H), 3.71 (ddd, J = 8.9, 8.9, 2.0 Hz, 1H), 3.67 (ddd, J = 9.6, 3.4, 2.8 Hz, 1H), 3.59−3.54 (m, 2H), 3.50−3.41 (m, 4H), 3.28 (dd, J = 12.4, 2.0 Hz, 1H), 3.24 (ddd, J = 9.6, 9.6, 4.8 Hz, 1H), 3.14−3.09 (m, 2H), 2.33 (ddd, J = 11.0, 4.1, 4.1 Hz, 1H), 2.17 (dddq, J = 6.2, 4.9, 2.7, 2.0 Hz, 1H), 2.00 (ddd, J = 11.7, 3.4, 2.8 Hz, 1H), 1.97 (d, J = 12.4 Hz, 1H), 1.83 (ddd, J = 11.7, 11.7, 11.6 Hz, 1H), 1.77 (ddd, J = 12.4, 3.4, 3.4 Hz, 1H), 1.71−1.59 (m, 6H), 1.55−1.51 (m, 3H), 1.45−1.34 (m, 4H), 1.43 (s, 3H), 1.31 (s, 6H), 0.885 (s, 3H), 0.878 (s, 3H), 0.82 (d, J = 7.6 Hz, 3H), 0.81 (d, J = 6.2 Hz, 3H), 0.054 (s, 6H), 0.050 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 138.9, 138.1, 130.9, 129.4 (2C), 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.8 (2C), 127.5, 113.9 (2C), 86.1, 83.4, 83.2, 79.7, 78.1, 77.1, 74.5, 73.8, 73.2, 72.9, 72.74, 72.66, 71.0, 69.18, 69.16, 67.0, 55.4, 53.1, 38.8, 35.4, 34.4, 33.5, 33.4, 33.2, 30.2, 28.0, 27.0, 26.1 (6C), 21.7, 21.5, 18.4, 18.3, 18.2, 16.2, 16.1, −3.5, −3.9, −4.5, −4.6; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{62}H_{98}O_{10}Si_2Na$ 1081.6591; Found 1081.6590.

(3*S*,4*R*,6*R*,7*R*)-7-((2*S*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran-2-yl)-6,7-bis((*tert*-butyldimethylsilyl)oxy)-3,4-dimethylheptan-1-ol (38). DDQ (15.3 mg, 67.4 μmol) was added to a solution of **37** (50.7 mg, 47.8 μmol) in CH_2Cl_2 (1.0 mL) and pH 6.86 buffer (0.5 mL) at 0 °C. After the mixture was stirred at room temperature for 40 min, DDQ (6.0 mg, 26 μmol) was added to the reaction mixture at 0 °C. After being stirred at room temperature for 10 min, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and saturated aqueous solution of $Na_2S_2O_3$. The reaction mixture was extracted with EtOAc and washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate =10/1 → 7/1 → 5/1 → 4/1) to give alcohol **38** (39.6 mg, 42.2 μmol, 88%) as colorless amorphous.

$[\alpha]^{23}_D$ −22 (c 0.48, $CHCl_3$); IR (neat) 3475, 2953, 2856, 2357, 1471, 1384, 1252, 1098, 835, 774 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34−7.25 (m, 10H), 4.62 (d, J = 11.7 Hz, 1H), 4.51 (d, J = 12.4 Hz, 1H), 4.46−4.44 (m, 2H), 3.73−3.62 (m, 4H), 3.59−3.48 (m, 3H), 3.42 (dd, J = 6.2, 4.1 Hz, 1H), 3.28 (dd, J = 12.4, 2.8 Hz, 1H), 3.24 (dt, J = 10.3, 5.5 Hz, 1H), 3.12 (ddd, J = 15.1, 12.4, 3.5 Hz, 2H), 2.35−2.32 (m, 1H), 2.19−2.14 (m, 1H), 2.00−1.96 (m, 2H), 1.84 (q, J = 11.7 Hz, 1H), 1.77 (dt, J = 11.7, 3.4 Hz, 1H), 1.69−1.59 (m, 6H), 1.55−1.53 (m, 3H), 1.45−1.34 (m, 7H), 1.31 (s, 6H), 0.883 (s, 9H), 0.878 (s, 9H), 0.85 (d, J = 6.9 Hz, 3H), 0.82 (d, J = 6.8 Hz, 3H), 0.06 (s, 6H), 0.05 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.1, 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.8 (2C), 127.6, 86.2, 83.5, 83.2, 79.6, 78.1, 77.1, 74.6, 73.9, 73.2, 72.9, 72.7, 71.0, 69.2, 67.0, 61.9, 53.1, 38.8, 36.6, 35.2, 34.4, 33.4, 33.2, 30.2, 28.0, 27.0, 26.1 (7C), 21.7, 21.5, 18.4, 18.3, 18.2, 16.2, −3.5, −3.9, −4.49, −4.54; HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{54}H_{90}O_9Si_2Na$ 961.6016; Found 961.6061.

(5*R*,6*R*)-5-((2*S*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran-2-yl)-6-((2*R*,3*S*)-2,3-dimethylhex-5-en-1-yl)-2,2,3,3,8,8,9,9-octamethyl-4,7-dioxa-3,8-disiladecane (39). DMP (8.6 mg, 20 μmol) was added to a solution of **38** (9.6 mg, 10 μmol) in CH_2Cl_2 (1.0 mL) at 0 °C. After being stirred at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous solution of $NaHCO_3$ and saturated aqueous solution of $Na_2S_2O_3$. The reaction mixture was extracted with EtOAc and washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde as colorless amorphous. The material was used directly in the next reaction without further purification.

A solution of NaHMDS (0.6 M in toluene, 85 μL, 51 μmol) was added to a solution methyltriphenylphosphonium bromide (36.5 mg, 102 μmol) in dry THF (0.3 mL) at 0 °C. After the mixture was stirred at 0 °C for 30 min, a solution of **51** (10.4 mg, 10.2 μmol, crude) in dry THF (0.2 mL × three rinses) was added to the reaction mixture via cannula. After being stirred at 0 °C for 40 min, the reaction mixture was quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 1/0 → 30/1 → 20/1 → 14/1 → 10/1 → 7/1) to give olefin **39** (7.4 mg, 7.9 μmol, 77% from alcohol **38**) as colorless amorphous.

$[\alpha]^{23}_D$ −19 (c 0.37, $CHCl_3$); IR (neat) 2953, 2857, 2349, 1558, 1457, 1253, 1101, 835, 697 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34−7.25 (m, 10H), 5.82−5.75 (m, 1H), 5.01−4.96 (m, 2H), 4.62 (d, J = 11.6 Hz, 1H), 4.51 (d, J = 12.4 Hz, 1H), 4.46−4.44 (m, 2H), 3.72−3.66 (m, 2H), 3.58−3.54 (m, 2H), 3.52−3.48 (m, 1H), 3.42 (dd, J = 6.2, 3.4 Hz, 1H), 3.29−3.22 (m, 2H), 3.12 (ddd, J = 12.4, 8.9, 2.8 Hz, 2H), 2.35−2.31 (m, 1H), 2.19−2.14 (m, 1H), 2.10 (dt, J = 13.0, 5.5 Hz, 1H), 2.00−1.96 (m, 2H), 1.86−1.81 (m, 2H), 1.77 (dt, J = 11.7, 3.5 Hz, 1H), 1.66−1.52 (m, 6H), 1.47−1.38 (m, 7H), 1.33−1.25 (m, 7H), 0.88 (s, 9H), 0.87 (s, 9H), 0.83−0.81 (m, 6H), 0.05−0.04 (s, 12H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.5, 138.1, 128.6 (2C), 128.4 (2C), 128.0 (2C), 127.9, 127.8 (2C), 127.6, 115.4, 86.2, 83.5, 83.2, 79.8, 78.1, 77.21, 74.6, 73.9, 73.1, 72.9, 72.7, 71.0, 69.2, 67.0, 53.1, 38.8, 38.7, 38.2, 33.2 (2C), 30.2, 28.0, 27.0, 26.1 (7C), 21.7, 21.5, 18.4, 18.3, 18.2, 16.3, 16.1, −3.5, −3.9, −4.5 (2C); HRMS (ESI-TOF) m/z: [M + Na]$^+$ Calcd for $C_{55}H_{90}O_8Si_2Na$ 957.6066; Found 957.6066.

(1*S*,2*R*,4*R*,5*S*)-1-((2*S*,4a*R*,5a*S*,6a*R*,8*S*,9*R*,10a*S*,11a*R*,12a*S*)-9-(Benzyloxy)-8-(2-(benzyloxy)ethyl)-4a,5a,6a-trimethyltetradecahydropyrano[3,2-*b*]pyrano[2′,3′:5,6]pyrano[2,3-*e*]pyran-2-yl)-4,5-dimethyloct-7-ene-1,2-diol (3). A solution of TBAF (1.0 M in THF, 230 μL, 230 μmol) was added to a solution of **39** (21.8 mg, 23.3 μmol) in dry THF (0.8 mL) at room temperature. The reaction mixture was stirred at 50 °C for 11.5 h. The reaction mixture was cooled to room temperature and quenched with saturated aqueous solution of NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous solution of NaCl, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 2/1 → 1/1 → 1/2) to give C′D′E′F′ ring system **3** (17.0 mg, 23.3 μmol, quant) as colorless amorphous.

$[\alpha]^{23}_D$ −45.8 (c 0.82, $CHCl_3$); IR (neat) 3481, 2953, 2871, 2368, 1636, 1456, 1384, 1219, 1107, 772, 699 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.35−7.26 (m, 10H), 5.81−5.74 (m, 1H), 5.02−4.97 (m, 2H), 4.63 (d, J = 11.6 Hz, 1H), 4.51 (d, J = 12.4 Hz, 1H), 4.46−4.44 (m, 2H), 3.75−3.74 (m, 1H), 3.70 (dt, J = 8.9, 2.8 Hz, 1H), 3.65 (dt, J = 11.7, 3.4 Hz, 1H), 3.58−3.52 (m, 4H), 3.12 (dd, J = 13.1, 3.4 Hz, 1H), 2.58−2.55 (m, 2H), 2.33−2.30 (m, 1H), 2.20−2.10 (m, 2H), 2.03−1.96 (m, 3H), 1.89−1.84 (m, 3H), 1.76−1.70 (m, 2H), 1.68−1.45 (m, 7H), 1.43 (s, 3H), 1.34 (s, 3H), 1.31 (s, 3H), 1.12 (ddd, J = 13.4, 11.0, 3.4 Hz, 1H), 0.89 (d, J = 6.9 Hz, 3H), 0.84 (d, J = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 138.9, 138.4, 138.1, 128.6 (2C), 128.4 (2C), 128.0 (2C), 128.0, 127.8 (2C), 127.6, 115.5, 85.9, 83.7, 83.5, 81.6, 78.1, 75.8, 74.7, 73.6, 73.0, 72.6, 71.1, 70.5, 69.2, 67.0, 53.0, 38.25, 38.18, 38.0, 37.2, 33.2, 33.0, 30.2, 28.0, 25.6, 21.7, 21.2, 18.3, 16.4, 16.0; HRMS (ESI) calcd. $C_{43}H_{62}O_8Na$ For (M + Na$^+$) 729.4337, found. 729.4336.

^{1}H NMR (600 MHz, C_5D_5N-CD_3OD = 1:1, ref CHD_2OD: 3.310 ppm) δ 7.32−7.31 (m, 2H), 7.28−7.16 (m, 8H), 5.74−5.67 (m, 1H), 4.93−4.90 (m, 1H), 4.89−4.87 (m, 1H), 4.60 (d, J = 11.6 Hz, 1H), 4.41 (d, J = 13.7 Hz, 2H), 4.36 (d, J = 12.4 Hz, 1H), 3.85 (dt, J = 10.3, 3.4 Hz, 1H), 3.78 (dt, J = 11.7, 3.5 Hz, 1H), 3.73 (dt, J = 8.9, 2.1 Hz, 1H), 3.56−3.50 (m, 2H), 3.36 (d, J = 4.8 Hz, 1H), 3.29–3.21 (m, 3H), 3.10 (dd, J = 13.0, 2.7 Hz, 1H), 2.34–2.30 (m, 1H), 2.19–2.15 (m, 1H), 2.09–2.06 (m, 1H), 1.94–1.92 (m, 3H), 1.86–1.83 (m, 2H), 1.78–1.71 (m, 3H), 1.65–1.61 (m, 2H), 1.56–1.50 (m, 3H), 1.42–1.38 (m, 1H), 1.34 (s, 3H), 1.30 (s, 3H), 1.27–1.23 (m, 1H), 1.21 (s, 3H), 0.86 (d, J = 6.9 Hz, 3H), 0.75 (d, J = 6.8 Hz, 3H); ^{13}C NMR (150 MHz, C_5D_5N-CD_3OD = 1:1, ref CHD_2OD: 48.94 ppm) δ 140.0, 139.7, 139.3, 129.3 (2C), 129.2 (2C), 128.8 (2C), 128.5 (3C), 128.3, 115.8, 86.8, 84.3 (2C), 81.6, 79.1, 77.8, 75.4, 74.8, 73.5, 73.4, 71.4, 70.2, 69.9, 67.6, 54.1, 39.4 (2C), 38.8, 37.8, 34.13, 34.09, 31.0, 28.8, 26.5, 22.2, 21.9, 18.6, 16.7, 16.4.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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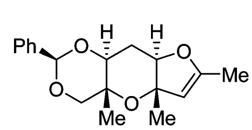

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