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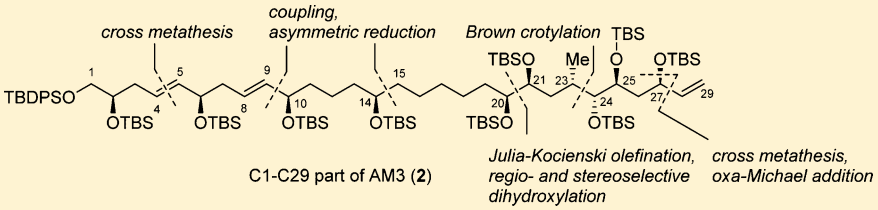
Stereoselective Synthesis of the C1−C29 Part of Amphidinol 3

Takeshi Tsuruda, Makoto Ebine, Aya Umeda, and Tohru Oishi*

Department of Chemistry, Faculty and Graduate School of Sciences, Kyushu University, 6-10-1 Hakozaki, Higashi-ku, Fukuoka 812-8581, Japan

Supporting Information



ABSTRACT: Stereoselective synthesis of the C1−C29 part of amphidinol 3 (AM3) was achieved. The C1−C20 part was assembled from three building blocks via regioselective cross metathesis to form the C4−C5 double bond and addition of an alkenyllithium and a lithium acetylide to two Weinreb amides followed by asymmetric reduction to form the C9−C10 and C14−C15 bonds, respectively. The C21−C29 part was synthesized via successive cross metathesis and oxa-Michael addition sequence to construct the 1,3-diol system at C25 and C27 and Brown asymmetric crotylation to introduce the stereogenic centers at C23 and C24. Coupling of the C1−C20 and C21−C29 parts was achieved by Julia−Kocienski olefination and regio- and stereoselective dihydroxylation of the C20−C21 double bond in the presence of the C4−C5 and C8−C9 double bonds to afford the C1−C29 part of AM3.

INTRODUCTION

Amphidinol 3 (AM3, **1**, Figure 1), a marine natural product produced by the dinoflagellate *Amphidinium klebsii*, shows antifungal and hemolytic activity.[1] The biological activity of AM3 can be accounted for by the formation of ion-permeable pores in a sterol-dependent manner.[2] A number of congeners of amphidinol[3] have been isolated to date, including luteophanol,[4a,b,e] lingshuiol,[4c,d] karatungiol,[4f] karlotoxin,[4g,i] carteraol,[4h] and amdigenol.[4j] Although it has been difficult to determine the molecular structure of AM3 due to the limited availability of the natural product and the presence of a number of stereogenic centers on the long acyclic carbon chain, the stereochemistry of AM3 was determined in 1999 by the *J*-based configuration analysis (JBCA) method,[5] the modified Mosher method,[6] and degradation of the natural product. During the course of our studies confirming the structure of AM3 based on chemical synthesis, the absolute configuration at C45 was confirmed to be *R*,[7] while those at C2 and C51 were revised as *R* and *S*, respectively.[8,9] Therefore, total synthesis of AM3 is necessary to confirm the complete stereochemistry. Herein, we report the stereoselective synthesis of the C1−C29 part (**2**) corresponding to the polyol moiety of AM3 (Figure 1).

RESULTS AND DISCUSSION

The striking structural features of AM3, represented by the presence of a long hydrophilic polyol chain, highly substituted tetrahydropyran ring systems, and a hydrophobic polyene unit, have attracted considerable attention in the synthetic community,[10] and a number of synthetic studies of AM3 have been reported by Cossy,[11] Paquette,[12] Roush,[13] Rychnovsky,[14] Markó,[15] Crimmins,[16] and our groups.[8,9,17] Although synthesis of the polyol moiety of AM3 has been reported, we envisaged an alternative synthetic route based on the revised structure of AM3 as shown in Scheme 1. The C1−C29 part (**2**) was to be synthesized through Julia−Kocienski olefination[18,19] from aldehyde **3** and sulfone **4**, followed by regio- and stereoselective dihydroxylation[20] of the C20−C21 double bond. The C1−C20 part (**3**) would be derived from terminal olefins **5** and **6** via cross metathesis,[8,21] and **6** would be derived from Weinreb amide **8**[22] through the formation of the C9−C10 and C14−C15 bonds via the addition of an alkenyllithium derived from iodoalkene **7** and a lithium acetylide derived from **9**, respectively, followed by asymmetric reduction. Sulfone **4**, corresponding to the C21−C29 part, was to be synthesized from α,β-unsaturated aldehyde **10** derived from the terminal olefin **11** via cross metathesis with acrolein **12**,[11a] followed by acid-catalyzed oxa-Michael addition reported by Evans[23] to construct the 1,3-diol system at C25 and C27 and Brown asymmetric crotylation[24] to induce the stereogenic centers at C23 and C24. In this strategy, it was a challenging task to construct the C20−C21 diol moiety by dihydroxylation of the C20−C21 double bond in the presence of the C4−C5 and the C8−C9 double bonds. There was also the question of whether the cross metathesis of **5** and **6**, also a key step, would proceed efficiently, although we have reported a similar coupling strategy.[8]

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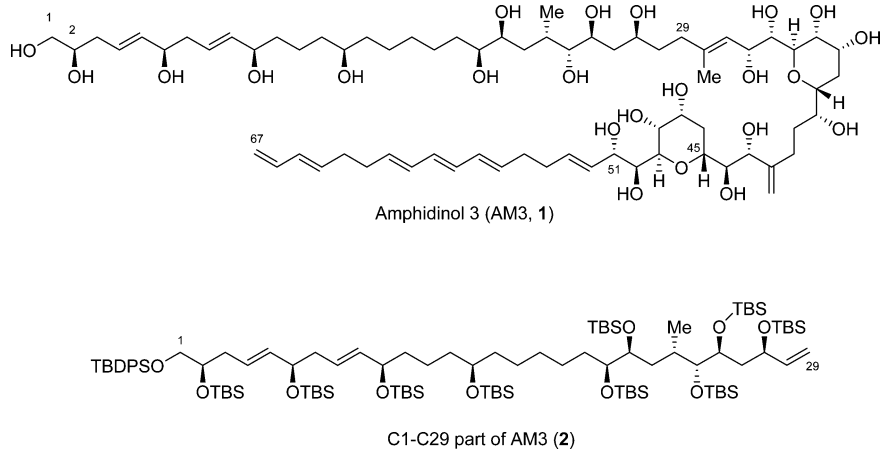
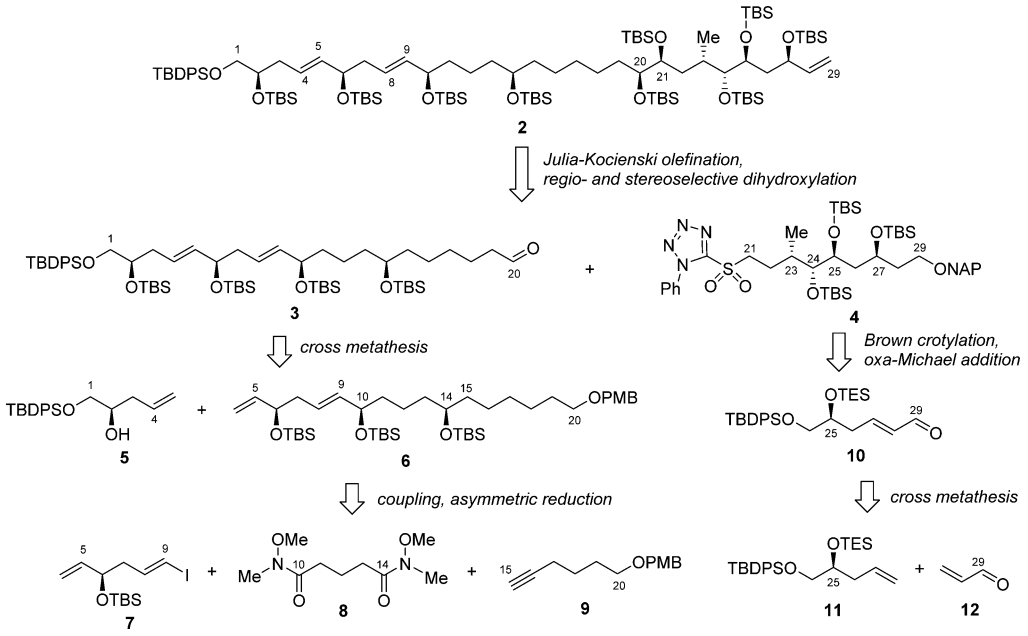


Figure 1. Structures of amphidinol 3 (AM3, **1**) and the C1−C29 part of AM3 (**2**).

Scheme 1. Retrosynthetic Analysis of the C1−C29 Part (2) of AM3



The synthetic route for the C1−C20 part (**3**) of AM3 is shown in Scheme 2. Racemic alcohol **14** was prepared from acrolein **12** and an organozinc reagent derived from propargyl bromide **13** in 68% yield after distillation.[25] Hydrostannylation[26] of the terminal alkyne **14** with Bu_3SnH and $Pd_2(dba)_3\cdot CHCl_3$ (dba = dibenzylideneacetone) resulted in the formation of stannane **15** (58%), which was subjected to tin−halogen exchange reaction to furnish iodoalkene **16** (95%). Sharpless kinetic resolution[27] of racemic alcohol **16** using L-(+)-dicyclohexyltartrate (DCHT) furnished allylic alcohol **17** in 39% yield and with >99% ee. The enantiomeric excess was determined by HPLC analysis using a chiral column, and the absolute configuration was determined by the modified Mosher method (see the Supporting Information). Protection of the secondary alcohol as a TBS ether gave **7** (97%). Next, the known Weinreb amide **8**[22] was treated with 1.2 equiv of the lithium acetylide derived from alkyne **9**[28] by treatment with *n*-BuLi to afford ketone **18** in 81% yield. Noyori asymmetric hydrogen transfer to **18** with catalyst **19**[29] proceeded smoothly to give propargylic alcohol **20** in 90% yield and with 94% ee. The enantiomeric excess was determined by conversion to MTPA esters, and the absolute configuration was determined by the modified Mosher method (see the Supporting Information). Hydrogenation of alkyne **20** with Pd/C(en)[30] (89%) was followed by protection of the secondary alcohol **21** as a TBS ether to furnish **22** (99%), corresponding to the C6−C20 part. Treatment of the Weinreb amide **22** with alkenyllithium derived from iodoolefin **7** by treatment with *n*-BuLi resulted in the formation of enone **23** (99%), which was subjected to CBS reduction using **24**[31] to afford allylic alcohol **25** in 99% yield and with 95:5 selectivity. The diastereomeric ratio was determined by conversion to MTPA esters, and the absolute configuration was determined by the modified Mosher method (see the Supporting Information). After protection of the secondary alcohol **25** as TBS ether **6** (99%), one of the crucial steps of the present synthesis, a cross metathesis reaction with the known olefin **5**[32] was carried out (Table 1). There are two problems in conducting cross metathesis: (i) competitive formation of homodimers and (ii) isolation of the products from a complex mixture of starting materials and possible homodimers. To overcome the latter problem, we carried out the cross metathesis using a combination of a polar substrate (alcohol

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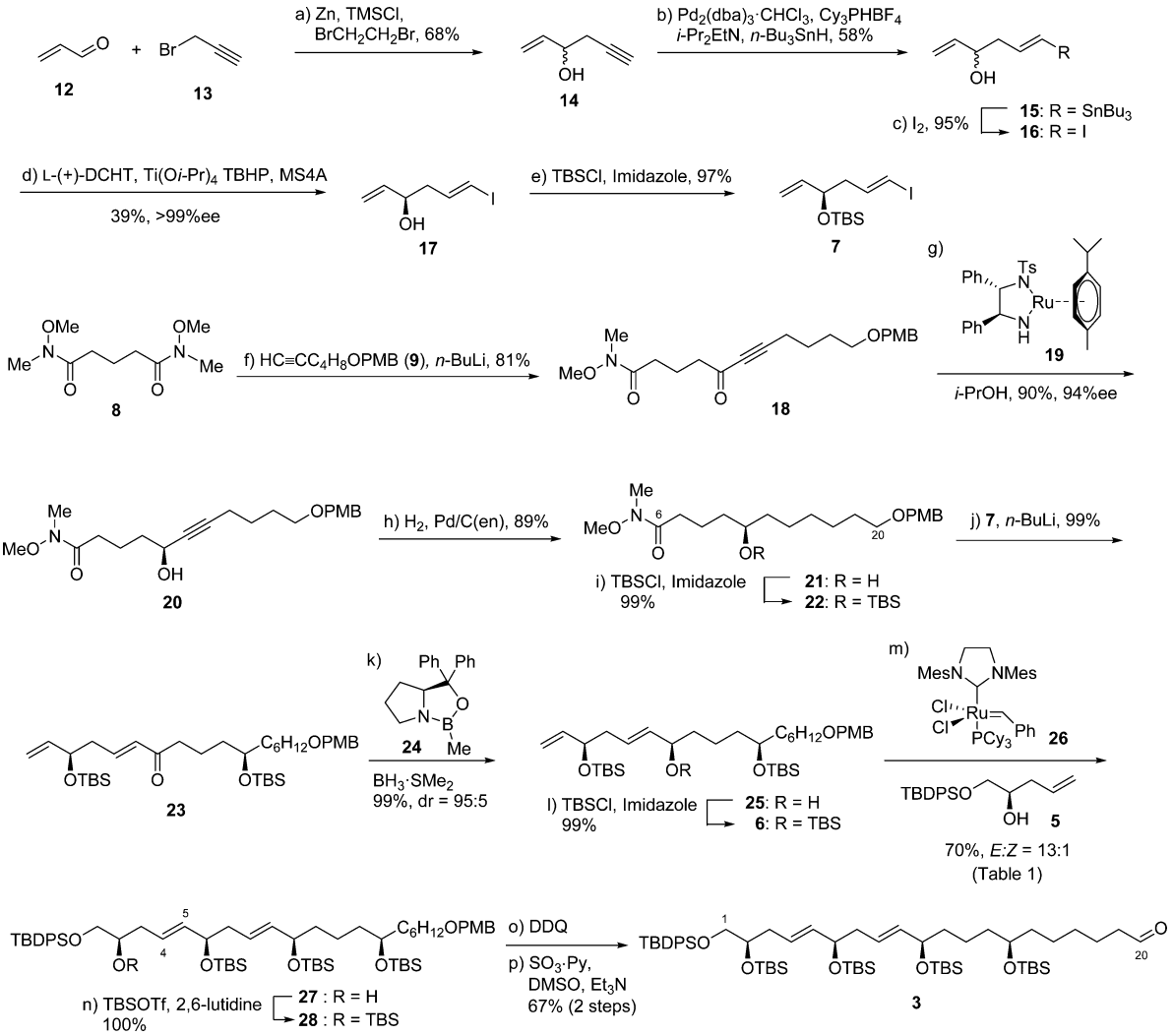
Scheme 2. Synthesis of the C1−C20 (3) Part of AM3[a]



[a]Key: (a) **13**, Zn, 1,2-dibromoethane, TMSCl, THF, rt, 20 min; then **12**, THF, −78 to 0 °C, 12 h, 68%; (b) $Pd_2(dba)_3·CHCl_3$, Cy_3PHBF_4, *i*-Pr_2EtN, *n*-Bu_3SnH, CH_2Cl_2, 0 °C to rt, 1 h, 58%; (c) I_2, CH_2Cl_2, 0 °C, 10 min, 95%; (d) L-(+)-DCHT, Ti(O*i*-Pr)$_4$, TBHP, MS4A (molecular sieves 4A), −20 °C, 9 days, 39% (> 99%ee); (e) TBSCl, imidazole, DMF, 0 °C, 2 h, 97%; (f) *n*-BuLi, HC≡CC_4H_8OPMB (**9**), −78 to −20 °C, THF, 1 h, 81%; (g) **19**, *i*-PrOH, rt, 2 h, 90%, 94%ee; (h) H_2, Pd/C(en), rt, 24 h, 89%; (i) TBSCl, imidazole, DMF, 0 °C, 4 h, 99%; (j) **7**, *n*-BuLi, THF, −78 °C, 10 min; then **22**, THF, −50 °C, 8 min, 99%; (k) **24**, $BH_3·SMe_2$, toluene, −78 to −30 °C, 2 h, 99% (dr = 95:5); (l) TBSCl, imidazole, DMF, 0 °C, 4 h, 99%; (m) **5**, Grubbs second-generation catalyst (**26**), CH_2Cl_2, 45 °C, 3 h, 70%, *E*/*Z* = 13:1, 70%; (n) TBSOTf, 2,6-lutidine, 0 °C, 10 min, 100%; (o) DDQ, pH 7 buffer, CH_2Cl_2, rt, 1 h; (p) SO_3·Py, DMSO, Et_3N, 0 °C to rt, 3 h, 67% (two steps).

5) and a less polar substrate (TBS ether **6**) because the polarity of the product **27** is between those of **5** and **6**, while the homodimer derived from **6** would be less polar than **6** and that derived from **5** would be more polar than **5**. Thus, a solution of olefin **5** and **6** in a 3:1 ratio in CH_2Cl_2 was treated with the second-generation Grubbs catalyst **26**[33] under reflux to afford the coupling product **27** in 38% yield in an *E*/*Z* ratio of 13:1 with 56% recovery of **6** (entry 1). As a byproduct, the dimeric compound **30** was formed in 31% yield, which corresponds to a 62% yield based on the monomer unit. When **26** was replaced with Zhan 1B catalyst (**29**),[34] the yield of **27** dropped to 26%, with recovery of **6** at 72% and the formation of dimer **30** in 34% yield (68% based on the monomer unit) (entry 2). As the reason for the low yield of **27** was the competitive formation of homodimer **30** derived from **5**, because the free hydroxy group accelerated coordination to the Ru catalyst, the ratio of **6** was increased (**5**:**6** = 1:1.3), and the yield of **27** increased slightly to 40% (entry 3). When the ratio was increased to **5**:**6** = 1:3, the yield of the desired product improved dramatically to afford **27** in 70% yield with 70% recovery of **6** (entry 4). The homodimer **30** was formed in 20% yield as a byproduct, but a possible dimer derived from **6** was not detectable, and the desired product **27** was easily separated from the starting material **6** and the homodimer **30** by silica gel column chromatography.

Having obtained the coupling product **27**, we moved on to the synthesis of the C1−C20 part. Protection of the secondary alcohol as a TBS ether **28** (100%) followed by removal of the PMB group with DDQ and Parikh−Doering oxidation[35] of the resulting primary alcohol gave aldehyde **3** (67%, two steps), corresponding to the C1−C20 part of AM3.

Next, synthesis of the C21−C29 part (**4**) commenced with protection of the known alcohol **31**[36] as TES ether **11** (99%), as shown in Scheme 3. Cross metathesis of the terminal olefin **11** and acrolein **12** using Hoveyda−Grubbs second-generation catalyst **32**[37] afforded **10** in 72% yield, while the reaction using Grubbs second-generation catalyst **26** resulted in a low yield of

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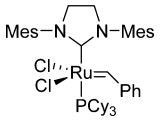
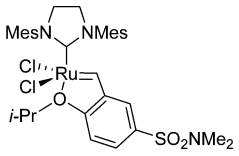
Table 1. Cross-Metathesis Reaction of 5 and 6

entry[a]	catalyst[b]	substrate/ratio 5	substrate/ratio 6	yield of 27 (%)	recovery of 6 (%)	yield of 30[c] (%)
1	Grubbs second (**26**)	3	1	38	56	31 (62)
2	Zhan 1B (**29**)	3	1	26	72	34 (68)
3	Grubbs second (**26**)	1	1.3	40	61	ND[d]
4	Grubbs second (**26**)	1	3	70	70	

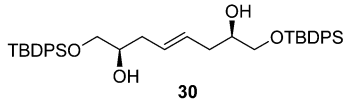
[a]All reactions were carried out under reflux in CH_2Cl_2. [b]10 mol % catalyst was used in each reaction. [c]The number in parentheses is the yield based on the monomer unit. [d]Not determined.



Grubbs 2nd (**26**)



Zhan 1B (**29**)



10 (19%). The α,β-unsaturated aldehyde **10** was subjected to oxa-Michael reaction as reported by Evans,[23] using acetaldehyde and $Bi(NO_3)_3{\cdot}5H_2O$ to furnish acetal **33**, and the resulting aldehyde was reduced with $NaBH_4$ to yield primary alcohol **34** in 87% yield for two steps. Protection of the primary alcohol **34** as the NAP (2-naphthylmethyl) ether **35** with NAPBr and NaH (82%) and removal of the TBS group with TBAF gave alcohol **36** (96%). Oxidation of the primary alcohol with Dess–Martin periodinane (DMP)[38] gave aldehyde **37** followed by Brown asymmetric crotylation using **38**[24] to afford **39** as a single isomer in 61% yield over two steps. The absolute configuration of alcohol **39** was determined by the modified Mosher method (see the Supporting Information). Hydrolysis of acetal **39** with p-TsOH·H_2O in THF/MeOH/H_2O at 60 °C for 20 h gave triol **40** in 42% yield, with recovery of **39** at 53% (89% yield based on recovered starting material); this was followed by protection of the resulting triol **40** as a TBS ether to yield **41** (98%). Hydroboration of the terminal olefin **41** with dicyclohexylborane followed by oxidative workup gave primary alcohol **42** in 91% yield. Treatment of **42** with 1-phenyl-1*H*-tetrazole-5-thiol **43** in the presence of Ph_3P and diisopropyl azodicarboxylate (DIAD) furnished sulfide **44** in 91% yield. Although oxidation of lipophilic sulfide **44** with $Mo_7(NH_4)_6O_{24}{\cdot}4H_2O$ and H_2O_2 was sluggish under the two-phase reaction conditions to obtain sulfone **4** in 78% yield after 6 days, that with *m*-chloroperbenzoic acid (MCPBA) proceeded more rapidly to afford **4** in 86% yield.

Having synthesized the C1–C20 part **3** and the C21–C29 part **4**, we moved on to the synthesis of the C1–C29 part **2** (Scheme 4). Julia–Kocienski olefination[19] of aldehyde **3** with sulfone **4** using KHMDS as a base at −78 °C to room temperature for 22 h proceeded smoothly to afford the coupling product **45** in 86% yield in an E/Z = 20:1 ratio. The next task was the crucial step of the present synthesis: dihydroxylation of the C20–C21 double bond in the presence of the C4–C5 and the C8–C9 double bonds. Fortunately, regio- and stereoselective dihydroxylation of olefin **45** at the less-hindered site was achieved by Sharpless asymmetric dihydroxylation[20] using $(DHQ)_2PHAL$ as a ligand to afford β-diol **46** along with the corresponding α-diol in a 4.8:1 ratio in 62% yield. The diastereoselectivity was improved by using monomeric ligand DHQ-MEQ (dihydroquinine 4-methyl-2-quinolyl ether)[39] to furnish **46** along with the corresponding α-diol in 13:1 ratio in 65% yield. The diol **46** was separated from the corresponding α-diol by silica gel column chromatography and protected as a TBS ether to give **47** (93%), and the NAP group of **47** was removed with DDQ to afford alcohol **48** (83%). Finally, the primary alcohol was converted to terminal olefin **2** by the Nishizawa–Grieco method[40] using 2-nitrophenyl selenocyanate and Me_3P followed by treatment with H_2O_2 to afford the C1–C29 part **2** in 97% yield. The longest linear sequence was 21 steps from acrolein **12**, and the total yield was 1.7%, with an 82% average yield.

■ CONCLUSION

In conclusion, stereoselective synthesis of the C1–C29 part of AM3 was achieved. The C1–20 part was constructed via regioselective cross metathesis to form the C4–C5 double bond, addition of lithium acetylide to a Weinreb amide followed by asymmetric reduction (C14–C15 bond formation), and addition of an alkenyllithium to a Weinreb amide followed by asymmetric reduction (C9–C10 bond formation). The C21–C29 part was synthesized via successive cross metathesis, oxa-Michael addition, and Brown asymmetric crotylation followed by coupling of the C1–C20 aldehyde and the C21–C29 sulfone by Julia–Kocienski olefination and then regio- and stereoselective dihydroxylation of the C20–C21 double bond in the presence of the C4–C5 and C8–C9 double bonds. Further studies toward the total synthesis of AM3 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*-

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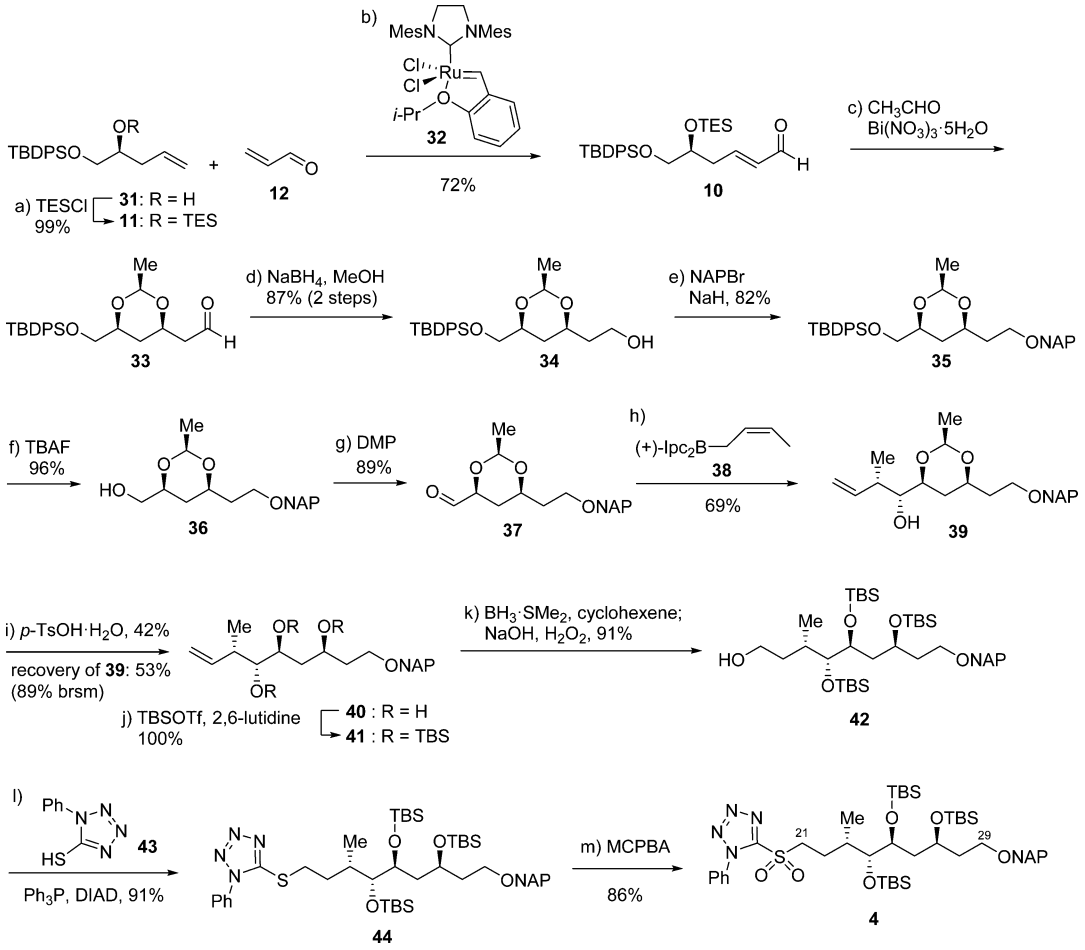
Scheme 3. Synthesis of the C21−C29 (4) Part of AM3[a]



[a](a) TESCl, imidazole, DMF, 0 °C to rt, 30 min, 99%; (b) Hoveyda−Grubbs second-generation cat. (**32**), CH_2Cl_2, 35 °C, 5 h, 72%; (c) CH_3CHO, $Bi(NO_3)_3·5H_2O$, CH_2Cl_2, 30 °C, 67 h; (d) $NaBH_4$, MeOH, 0 °C, 10 min, 87% (2 steps); (e) NAPBr, NaH, DMF, 0 °C, 80 min, 82%; (f) TBAF, THF, rt, 40 min, 96%; (g) DMP, CH_2Cl_2, rt, 2.5 h, 89%; (h) **38** (Ipc = isopinocampheyl), THF, −78 °C to rt, 8.5 h, 69%; (i) *p*-TsOH·H_2O, THF, MeOH, H_2O, 60 °C, 20 h, 42%, recovery of **39** 53% (89% brsm); (j) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 30 min, 98%; (k) $BH_3·SMe_2$, cyclohexene, THF, 0 °C to rt, 30 min; then aq NaOH, H_2O_2, rt, 2 h, 91%; (l) **43**, PPh_3, DIAD, THF, 0 °C, 10 min, 91%; (m) MCPBA, CH_2Cl_2, 0 °C, 39 h, 86%.

dimethylformamide (DMF) were used without further dehydration. Propargyl bromide, Bu_3SnH, and Et_3N were distilled before use. Molecular sieves 4A (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. 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 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 were reported in ppm from tetramethylsilane (TMS) with reference to internal residual solvent [^{1}H NMR: $CHCl_3$ (7.26), C_6D_5H (7.16); ^{13}C NMR: $CDCl_3$ (77.16), C_6D_6 (128.0)]. 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 or APCI-TOF equipment.

Hex-1-en-5-yn-3-ol (14). To a suspension of zinc powder (47.0 g, 718 mmol) in THF (650 mL) was added 1,2-dibromoethane (6.2 mL, 72 mmol) and the mixture heated to 65 °C for 10 min. After the mixture was allowed to cool to 25 °C and stirred for 20 min, chlorotrimethylsilane (9.1 mL, 72 mmol) was added dropwise via syringe. The mixture was stirred vigorously for 20 min and then cooled to −10 °C. To this mixture was added a solution of propargyl bromide **13** (54.4 mL, 718 mmol) in THF (78 mL) slowly via cannula. The mixture was stirred for 1 h below −10 °C and then cooled to −78 °C. To the mixture was added a solution of freshly distilled acrolein **12** (24.0 mL, 359 mmol) in THF (600 mL) over 1 h via dropping funnel. The resulting mixture was gradually warmed to 0 °C over 12 h and quenched with saturated aqueous NH_4Cl (200 mL). The mixture was extracted with Et_2O, and the combined 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 remove THF and Et_2O. The residue was purified by distillation (56 °C/20 mmHg) to give known alcohol **14**[25] (23.6 g, 246 mmol, 68%) as a colorless oil.

***(E)*-6-(Tributylstannyl)hexa-1,5-dien-3-ol (15).** A mixture of $Pd_2(dba)_3·CHCl_3$ (538 mg, 0.520 mmol), tricyclohexylphosphonium tetrafluoroborate (766 mg, 2.08 mmol), and *i*-Pr_2NEt (0.75 mL, 4.2 mmol) in CH_2Cl_2 (1 L) was stirred at room temperature for 10 min. To this mixture was added a solution of alcohol **14** (10.0 g, 104 mmol) in CH_2Cl_2 (75 mL + 2 × 5 mL rinse) at room temperature. The reaction mixture was cooled to −10 °C, and a solution of Bu_3SnH (35.0 mL, 130 mmol) in CH_2Cl_2 (115 mL) was added via dropping funnel over 10 min. The resultant solution was stirred at 0 °C for 30 min and then warmed to room temperature. After 30 min, the reaction mixture was concentrated and purified by silica gel column chromatography (hexane/ethyl acetate = 70/1 → 50/1 with addition

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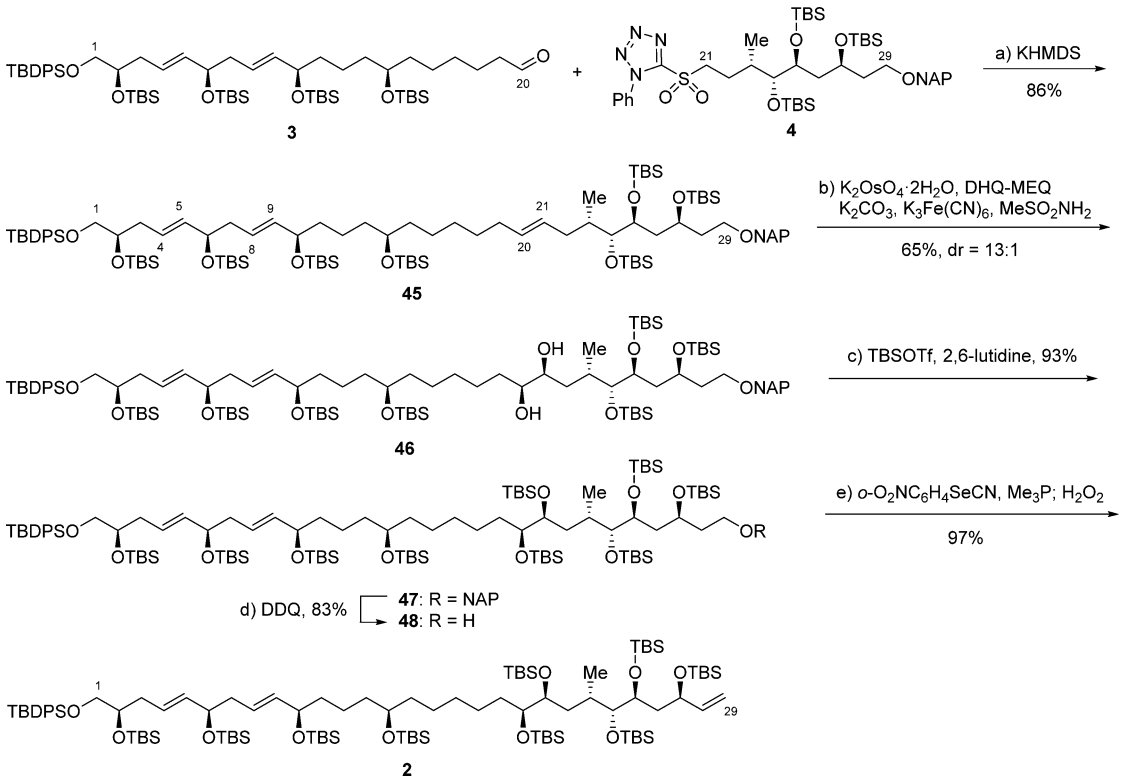
Scheme 4. Synthesis of the C1−C29 (2) Part of AM3[a]



[a](a) KHMDS, THF, −78 °C, 4 h then rt, 18 h, 86%; (b) $K_2OsO_4·2H_2O$, DHQ-MEQ, K_2CO_3, $K_3Fe(CN)_6$, $MeSO_2NH_2$, *t*-BuOH, *t*-BuOMe, H_2O, 0 °C, 69 h, 65%, dr =13:1; (c) TBSOTf, 2,6-lutidine, CH_2Cl_2, 0 °C, 10 min, 93%; (d) DDQ, pH 7 buffer, CH_2Cl_2, 0 °C, 1 h, then $NaBH_4$, MeOH, THF, 0 °C, 10 min, 83%; (e) *o*-$O_2NC_6H_4SeCN$, Me_3P, MS4A, THF, rt, 30 min; then aq H_2O_2, rt, 2.5 h, 97%.

of 1 v/v% Et_3N) to afford vinylstannane **15** (23.4 g, 60.5 mmol, 58%) as a colorless oil: R_f = 0.48 (hexane/ethyl acetate = 6/1); IR (neat) 3727, 3353, 2955, 2925, 1599, 1463, 921 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.07 (d, J = 18.6 Hz, 1H), 5.93 (dt, J = 18.6, 6.6 Hz, 1H), 5.90 (ddd, J = 17.4, 10.2, 6.6 Hz, 1H), 5.25 (ddd, J = 17.4, 1.2, 1.2 Hz, 1H), 5.12 (ddd, J = 10.2, 1.2, 1.2 Hz, 1H), 4.20−4.17 (m, 1H), 2.47−2.43 (m, 1H), 2.38−2.33 (m, 1H), 1.71−1.70 (m, 1H), 1.54−1.42 (m, 6H), 1.33−1.26 (m, 6H), 0.93−0.82 (m, 15H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.3, 140.5, 133.4, 114.7, 71.7, 46.0, 29.3 (3C), 27.4 (3C), 13.8 (3C), 9.6 (3C); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{18}H_{36}OSnNa$ 411.1680, found 411.1663.

(*E*)-6-Iodohexa-1,5-dien-3-ol (16). To a solution of vinylstannane **15** (23.4 g, 60.5 mmol) in CH_2Cl_2 (302 mL) was added a solution of I_2 (23.0 g, 90.7 mmol) in CH_2Cl_2 (450 mL) via cannula at 0 °C. After 10 min, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. The separated organic layer was washed with saturated aqueous 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 = 50/1→10/1) to give iodoolefin **16** (12.9 g, 57.5 mmol, 95%) as a colorless oil: R_f = 0.53 (hexane/ethyl acetate = 2/1); IR (neat) 3360, 2904, 1605, 1423, 1218, 990, 926 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.55 (dt, J = 14.4, 7.8 Hz, 1H), 6.16 (d, J = 14.4 Hz, 1H), 5.87 (ddd, J = 17.4, 10.8, 6.0 Hz, 1H), 5.27 (d, J = 17.4 Hz, 1H), 5.17 (d, J = 10.8 Hz, 1H), 4.21−4.18 (m, 1H), 2.35−2.26 (m, 2H), 1.60 (d, J = 4.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 139.8, 115.6, 77.9, 71.5, 43.5; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for C_6H_9IONa 246.9590, found 246.9591.

(*R*,*E*)-6-Iodohexa-1,5-dien-3-ol (17). A solution of L-(+)-DCHT (6.31 g, 20.1 mmol) and iodoolefin **16** (6.00 g, 26.8 mmol) in CH_2Cl_2 (125 mL + 3 × 2 mL rinse) was added to a suspension of activated powdered MS4A (3.0 g) in CH_2Cl_2 (3 mL). The mixture was cooled to −20 °C and stirred for 30 min. To this mixture was added Ti(O-*i*-Pr)$_4$ (4.0 mL, 13 mmol) with stirring for 30 min followed by addition of TBHP (3.2 M in CH_2Cl_2, 5.9 mL, 19 mmol) via syringe over 10 min. After the mixture was stirred for 165.5 h, TBHP (3.2 M in CH_2Cl_2, 4.2 mL, 13 mmol) was added. After 47 h, the reaction was quenched with ice-cold $FeSO_4$/citric acid solution (39 g of $FeSO_4$ heptahydrate and 12.2 g of citric acid monohydrate in 118 mL water) at −20 °C. The mixture was warmed to room temperature and stirred for 30 min before filtering through a pad of Celite. The filtrate was extracted with ethyl acetate. The organic layer was washed with water and saturated aqueous 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 → 4/1 → 1/1) to give allylic alcohol **17** (2.36 g, 10.5 mmol, 39%, er = 99.97:0.03) as a yellow oil. The enantiomeric ratio of alcohol **17** was determined by HPLC using chiral column (CHIRALPAK AD, ϕ 4.6 × 250 mm, eluted with 5% *i*-PrOH in hexane, 0.5 mL/min, detected at 260 nm), t_R = 16.3 min ((*R*)-**17**), t_R = 26.1 min ((*S*)-**17**): R_f = 0.47 (hexane/ethyl acetate = 3/1); $[\alpha]^{24}_D$ +4.3 (*c* 1.0, $CHCl_3$); IR (neat) 3734, 3357, 2902, 1636, 1606, 1473, 990 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.55 (dt, J = 15.0, 7.2 Hz, 1H), 6.16 (dt, J = 15.0, 1.2 Hz, 1H), 5.87 (ddd, J = 16.8, 10.4, 6.0 Hz, 1H), 5.27 (dt, J = 16.8, 1.2 Hz, 1H), 5.17 (dt, J = 10.4, 1.2 Hz, 1H), 4.22−4.17 (m, 1H), 2.37−2.25 (m, 2H), 1.60 (d, J = 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 139.8, 115.7, 77.8, 71.6, 43.6; HRMS (APCI-TOF) m/z [M + H]$^+$ calcd for $C_6H_{10}IO$ 224.9771, found 224.9773.

(*R*,*E*)-*tert*-Butyl((6-iodohexa-1,5-dien-3-yl)oxy)dimethylsilane (7). To a solution of alcohol **17** (1.93 g, 8.63 mmol) in DMF (12.3 mL) were added imidazole (1.76 g, 25.9 mmol) and TBSCl (1.95 g, 13.0 mmol) at 0 °C. After the mixture was stirred for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 100/1) afforded TBS ether **7** (2.84 g, 8.39 mmol, 97%) as a colorless oil: R_f = 0.83 (hexane/ethyl

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acetate =7/1); $[\alpha]^{23}_{D}$ −4.5 (*c* 1.0, $CHCl_3$); IR (neat) 3709, 3628, 1652, 1558, 983, 771 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 6.50 (ddd, *J* = 14.4, 7.8, 7.8 Hz, 1H), 6.04 (d, *J* = 14.4 Hz, 1H), 5.78 (ddd, *J* = 17.4, 10.8, 5.4 Hz, 1H), 5.18 (d, *J* = 17.4 Hz, 1H), 5.07 (d, *J* = 10.8 Hz, 1H), 4.15−4.12 (m, 1H), 2.24−2.20 (m, 2H), 0.90 (s, 9H), 0.06 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 143.0, 140.7, 114.5, 77.4, 72.7, 44.7, 26.0 (3C), 18.4, −4.4, −4.7; HRMS (APCI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{12}H_{24}IOSi$ 339.0636, found 339.0616.

N-Methoxy-11-((4-methoxybenzyl)oxy)-N-methyl-5-oxoundec-6-ynamide (18). To a solution of alkyne **9** (2.85 g, 13.1 mmol) in THF (120 mL) at −78 °C was added *n*-BuLi (1.6 M in hexane, 6.8 mL, 10.8 mmol) dropwise. After the mixture was stirred at 0 °C for 30 min, the mixture was added dropwise to a solution of amide **8** (4.75 g, 21.8 mmol) in THF (78 mL) at −20 °C and stirred for 30 min. The reaction was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 3/1 → 2/1 → 1/1) afforded ynone **18** (3.30 g, 8.79 mmol, 81%) as a yellow oil: R_f = 0.23 (hexane/ethyl acetate =1/1); IR (neat) 2935, 2857, 2209, 1666, 1612, 1511, 1457, 1244, 1100, 1032, 820 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.25 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 4.43 (s, 2H), 3.81 (s, 3H), 3.67 (s, 3H), 3.46 (t, *J* = 6.0 Hz, 2H), 3.17 (s, 3H), 2.63 (t, *J* = 7.2 Hz, 2H), 2.46 (t, *J* = 7.2 Hz, 2H), 2.38 (t, *J* = 6.6 Hz, 2H), 1.99 (q, *J* = 7.2 Hz, 2H), 1.73−1.65 (m, 4H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.7, 173.8, 159.3, 130.6, 129.3 (2C), 113.9 (2C), 94.2, 81.0, 72.7, 69.3, 61.3, 55.4, 44.7, 32.2, 30.7, 29.0, 24.7, 18.92, 18.85; HRMS (APCI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{21}H_{30}NO_5$ 376.2119, found 376.2119.

(S)-5-Hydroxy-N-methoxy-11-((4-methoxybenzyl)oxy)-N-methylundec-6-ynamide (20). To a solution of ynone **18** (3.30 g, 8.79 mmol) in *i*-PrOH (80 mL) at room temperature was added Ru[(*S*,*S*)-Tsdpen](*p*-cymene) **19** (52.7 mg, 87.9 μmol). After 1 h, catalyst **19** (52.7 mg, 87.9 μmol) was again added, and the reaction mixture was stirred for another 1 h. The organic solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography (hexane/ethyl acetate = 2/1→1/3) to give alcohol **20** (2.98 g, 7.89 mmol, 90%) as a brown oil: R_f = 0.28 (hexane/ethyl acetate = 1/2); $[\alpha]^{24}_{D}$ −2.3 (*c* 0.53, $CHCl_3$); IR (neat) 3408, 2935, 2857, 1644, 1586, 1513, 1456, 1100, 1033, 822 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.0 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 4.43 (s, 2H), 4.36 (t, *J* = 6.0 Hz, 1H), 3.81 (s, 3H), 3.68 (s, 3H), 3.45 (t, *J* = 6.0 Hz, 2H), 3.18 (s, 3H), 2.49−2.48 (m, 2H), 2.22 (dt, *J* = 7.2, 1.8 Hz, 2H), 1.84−1.66 (m, 6H), 1.60−1.55 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.6, 159.3, 130.8, 129.4 (2C), 113.9 (2C), 85.3, 81.5, 72.7, 69.6, 62.4, 61.3, 55.4, 37.9, 32.3, 31.5, 29.0, 25.5, 20.2, 18.7; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{31}NO_5Na$ 400.2094, found 400.2083.

(R)-5-Hydroxy-N-methoxy-11-((4-methoxybenzyl)oxy)-N-methylundecanamide (21). To a solution of alcohol **20** (2.98 g, 7.89 mmol) in THF (72 mL) was added 4.3% Pd/C(en) (303 mg) and the mixture stirred under a hydrogen atmosphere (balloon) at room temperature for 24 h. The reaction mixture was filtered through Celite and concentrated under reduced pressure. The residue was purified by column chromatography (hexane/ethyl acetate =1/1→1/2) to give alcohol **21** (2.67 g, 7.00 mmol, 89%) as a colorless oil: R_f = 0.17 (hexane/ethyl acetate = 1/2); $[\alpha]^{22}_{D}$ −1.1 (*c* 0.42, $CHCl_3$); IR (neat) 3431, 2930, 2855, 1655, 1511, 1460, 1385, 1301, 1246, 1173, 1096, 992, 821, 774 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.0 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 4.42 (s, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 3.58−3.56 (m, 1H), 3.42 (t, *J* = 6.0 Hz, 2H), 3.18 (s, 3H), 2.46 (brs, 2H), 1.80−1.71 (m, 2H), 1.69−1.57 (m, 2H), 1.54−1.26 (m, 10H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.8, 159.2, 130.9, 129.4 (2C), 113.9 (2C), 72.6, 71.4, 70.3, 61.3, 55.4, 37.5, 37.2, 32.3, 31.7, 29.8, 29.7, 26.3, 25.8, 20.4; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{21}H_{35}NO_5Na$ 404.2407, found 404.2403.

(R)-5-((*tert*-Butyldimethylsilyl)oxy)-N-methoxy-11-((4-methoxybenzyl)oxy)-N-methylundecanamide (22). To a solution of alcohol **21** (2.67 g, 7.00 mmol) in DMF (8.8 mL) were added imidazole (1.14 g, 16.8 mmol) and TBSCl (1.27 g, 8.40 mmol) at 0 °C. After the mixture was stirred for 4 h, the reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1→2/1) afforded TBS ether **22** (3.45 g, 6.97 mmol, 99%) as a colorless oil: R_f = 0.55 (hexane/ethyl acetate =1/1); $[\alpha]^{23}_{D}$ −0.38 (*c* 1.0, $CHCl_3$); IR (neat) 3727, 3626, 2931, 2855, 1669, 1512, 1248, 1096, 1037, 1003, 835 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.0 Hz, 2H), 6.87 (d, *J* = 9.0 Hz, 2H), 4.43 (s, 2H), 3.80 (s, 3H), 3.67 (s, 3H), 3.65 (q, *J* = 6.0 Hz, 1H), 3.43 (t, *J* = 6.0 Hz, 2H), 3.17 (s, 3H), 2.45−2.40 (m, 2H), 1.72−1.57 (m, 4H), 1.50−1.39 (m, 4H), 1.37−1.25 (m, 6H), 0.88 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.8, 159.2, 131.0, 129.3 (2C), 113.9 (2C), 72.6, 72.3, 70.3, 61.3, 55.4, 37.1, 36.9, 32.3 (2C), 29.89, 29.86, 26.4, 26.1, 25.4 (3C), 20.7, 18.3, −4.3 (2C); HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{49}NO_5SiNa$ 518.3272, found 518.3267.

(5*R*,13*R*,*E*)-13-(6-((4-Methoxybenzyl)oxy)hexyl)-2,2,3,3,15,15,16,16-octamethyl-5-vinyl-4,14-dioxa-3,15-disilaheptadec-7-en-9-one (23). To a solution of iodoolefin 7 (2.70 g, 8.00 mmol) in THF (80 mL) at −78 °C was added *n*-BuLi (1.6 M in hexane, 4.6 mL, 7.4 mmol) via syringe and the mixture stirred at −78 °C for 10 min. To this mixture was added a solution of compound **22** (3.04 g, 6.14 mmol) in THF (8.8 mL + 2 × 1.0 mL rinse) through a cannula and the mixture stirred at −50 °C for 8 min. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. 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→10/1) to give enone **23** (3.93 g, 6.08 mmol, 99%) as a colorless oil: R_f = 0.42 (hexane/ethyl acetate = 7/1); $[\alpha]^{22}_{D}$ −4.3 (*c* 1.0, $CHCl_3$); IR (neat) 3727, 2929, 2855, 1698, 1676, 1586, 1248, 1173, 1092, 1006, 938, 835, 774 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.79 (ddd, *J* = 15.6, 7.2, 7.2 Hz, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 5.80 (ddd, *J* = 16.8, 10.8, 7.2 Hz, 1H), 5.19 (d, *J* = 16.8 Hz, 1H), 5.08 (d, *J* = 10.8 Hz, 1H), 4.43 (s, 2H), 4.24 (ddd, *J* = 7.2, 7.2, 7.2 Hz, 1H), 3.80 (s, 3H), 3.63 (dddd, *J* = 6.0, 6.0, 6.0, 6.0 Hz, 1H), 3.43 (t, *J* = 7.2 Hz, 2H), 2.54−2.52 (m, 2H), 2.40 (dd, *J* = 7.2, 7.2 Hz, 2H), 1.69−1.57 (m, 4H), 1.46−1.38 (m, 4H), 1.38−1.25 (m, 6H), 0.89 (s, 9H), 0.88 (s, 9H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.5, 159.2, 143.3, 140.7, 132.6, 131.0, 129.3 (2C), 114.7, 113.9 (2C), 72.8, 72.6, 72.2, 70.3, 55.4, 41.4, 40.2, 37.1, 36.7, 29.89, 29.87, 26.4, 26.1 (3C), 25.9 (3C), 25.4, 20.2, 18.33, 18.27, −4.3 (2C), −4.7 (2C); HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{37}H_{66}O_5Si_2Na$ 669.4341, found 669.4333.

(5*R*,9*R*,13*R*,*E*)-13-(6-((4-Methoxybenzyl)oxy)hexyl)-2,2,3,3,15,15,16,16-octamethyl-5-vinyl-4,14-dioxa-3,15-disilaheptadec-7-en-9-ol (25). To a solution of enone **23** (3.50 g, 5.41 mmol) and (*S*)-Me-CBS reagent **24** (3.00 g, 10.8 mmol) in toluene (54 mL) at −78 °C was added $BH_3{\cdot}SMe_2$ (1.00 mL, 10.8 mmol) via syringe over a period of 3 min. After the mixture was stirred at −30 °C for 2 h, the reaction was quenched by sequential addition of MeOH followed by saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 6/1) afforded allylic alcohol **25** (3.49 g, 5.38 mmol, 99% dr = 95:5) as a yellow oil: R_f = 0.23 (hexane/ethyl acetate = 5/1); $[\alpha]^{24}_{D}$ −5.7 (*c* 1.0, $CHCl_3$); IR (neat) 3441, 2929, 2856, 1613, 1512, 1463, 1249, 1082, 1038, 834, 774 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9.0 Hz, 2H), 6.88 (d, *J* = 9.0 Hz, 2H), 5.80 (ddd, *J* = 16.8, 10.8, 6.0 Hz, 1H), 5.62 (ddd, *J* = 14.4, 6.6, 6.6 Hz, 1H), 5.48 (dd, *J* = 14.4, 7.2 Hz, 1H), 5.15 (d, *J* = 16.8 Hz, 1H), 5.04 (d, *J* = 10.8 Hz, 1H), 4.43 (s, 2H), 4.13 (ddd, *J* = 6.0, 6.0, 6.0 Hz, 1H), 4.04 (ddd, *J* = 7.2, 7.2, 7.2 Hz, 1H), 3.80 (s, 3H), 3.63−3.59 (m, 1H), 3.43 (t, *J* = 6.0 Hz, 2H), 2.28−2.18 (m, 2H), 1.61−1.57 (m, 2H), 1.44−1.25 (m, 14H), 0.89 (s, 9H), 0.88 (s, 9H), 0.05 (s, 3H), 0.03 (s, 3H), 0.02 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 141.2, 135.7, 131.0, 129.4

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(2C), 128.0, 114.0, 113.9 (2C), 73.7, 73.3, 72.7, 72.3, 70.4, 55.4, 41.3, 37.6, 37.2, 37.1, 29.9 (2C), 26.4, 26.1 (3C), 26.0 (3C), 25.5, 21.4, 18.4, 18.3, −4.2 (2C), −4.3, −4.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{37}H_{68}O_5Si_2Na$ 671.4503, found 671.4481.

(5*R*,9*R*,13*R*,*E*)-9-((*tert*-Butyldimethylsilyl)oxy)-13-(6-((4-methoxybenzyl)oxy)hexyl)-2,2,3,3,15,15,16,16-octamethyl-5-vinyl-4,14-dioxa-3,15-disilaheptadec-7-ene (6). To a solution of allylic alcohol **25** (3.49 g, 5.38 mmol) in DMF (7.2 mL) were added imidazole (1.12 g, 16.2 mmol) and TBSCl (1.20 g, 8.08 mmol) at 0 °C. After the mixture was stirred at 0 °C for 4 h, the reaction was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 60/1→20/1) afforded TBS ether **6** (4.05 g, 5.30 mmol, 99%) as a colorless oil: R_f = 0.53 (hexane/ethyl acetate = 6/1); $[\alpha]^{24}_D$ −6.1 (*c* 1.0, $CHCl_3$); IR (neat) 3728, 2928, 2855, 1613, 1512, 1463, 1249, 1081, 1039, 834, 773 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.26 (d, J = 9.0 Hz, 2H), 6.88 (d, J = 9.0 Hz, 2H), 5.79 (ddd, J = 17.4, 10.2, 6.0 Hz, 1H), 5.49 (ddd, J = 15.6, 7.2, 7.2 Hz, 1H), 5.42 (dd, J = 15.6, 7.2 Hz, 1H), 5.14 (d, J = 17.4 Hz, 1H), 5.03 (d, J = 10.2 Hz, 1H), 4.43 (s, 2H), 4.11 (dd, J = 6.0, 6.0 Hz, 1H), 4.01−3.99 (m, 1H), 3.80 (s, 3H), 3.61−3,58 (m, 1H), 3.43 (t, J = 7.2 Hz, 2H), 2.28−2.17 (m, 2H), 1.62−1.57 (m, 2H), 1.49−1.25 (m, 14H), 0.89 (s, 9H), 0.88 (s, 18H), 0.05 (s, 3H), 0.032 (s, 3H), 0.030 (s, 3H), 0.02 (s, 6H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.2, 141.2, 136.4, 131.0, 129.3 (2C), 125.9, 114.0, 113.9 (2C), 73.83, 73.77, 72.7, 72.4, 70.4, 55.4, 41.3, 38.9, 37.33, 37.26, 29.9 (2C), 26.4, 26.1 (6C), 26.0 (3C), 25.5, 21.3, 18.4 (2C), 18.3, −4.0, −4.2 (2C), −4.4, −4.5, −4.6; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{43}H_{82}O_5Si_3Na$ 785.5362, found 785.5364.

(6*R*,8*E*,10*R*,12*E*,14*R*,18*R*)-10,14-Bis((*tert*-butyldimethylsilyl)-oxy)-18-(6-((4-methoxybenzyl)oxy)hexyl)-2,2,20,20,21,21-hexamethyl-3,3-diphenyl-4,19-dioxa-3,20-disiladocosa-8,12-dien-6-ol (27). To a solution of terminal olefin **6** (1.01 g, 1.32 mmol) and homoallylic alcohol **5** (149 mg, 0.483 mmol) in CH_2Cl_2 (2.2 mL) under reflux was added a solution of Grubbs second-generation catalyst **26** (37 mg, 44 μmol) in CH_2Cl_2 (1.4 mL + 2 × 0.2 mL rinse). After the mixture was stirred under reflux for 3 h, the reaction was quenched with Et_3N at 0 °C and stirred for 1 h at room temperature. The solution was concentrated under reduced pressure and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 50/1, 30/1, 20/1, 1/1) to give alcohol **27** (329 mg, 0.306 mmol, 70%) as a brown oil, with recovery of olefin **6** (758 mg, 0.993 mmol, 75%): R_f = 0.50 (hexane/ethyl acetate = 5/1); $[\alpha]^{22}_D$ −0.29 (*c* 0.99, $CHCl_3$); IR (neat) 3734, 2929, 2856, 1653, 1588, 1513, 1463, 1249, 1112, 1077, 834, 774, 702 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 7.76−7.75 (m, 4H), 7.27 (d, J = 8.4 Hz, 2H), 7.25−7.24 (m, 6H), 6.83 (d, J = 8.4 Hz, 2H), 5.77 (ddd, J = 15.0, 7.2, 7.2 Hz, 1H), 5.70 (ddd, J = 15.0, 7.8, 7.8 Hz, 1H), 5.61 (dd, J = 15.0, 7.2 Hz, 1H), 5.55 (dd, J = 15.0, 6.0 Hz, 1H), 4.38 (s, 2H), 4.20−4.18 (m, 1H), 4.15 (dd, J = 6.0, 6.0 Hz, 1H), 3.80−3.75 (m, 1H), 3.74−3.71 (m, 1H), 3.66 (dd, J = 10.2, 3.6 Hz, 1H), 3.59 (dd, J = 7.8, 7.2 Hz, 1H), 3.38 (t, J = 7.2 Hz, 2H), 3.32 (s, 3H), 2.36−2.27 (m, 2H), 2.25−2.16 (m, 3H), 1.71−1.62 (m, 4H), 1.60−1.50 (m, 4H), 1.46−1.41 (m, 4H), 1.41−1.31 (m, 4H), 1.13 (s, 9H), 1.06 (s, 9H), 1.04 (s, 9H), 1.03 (s, 9H), 0.17 (s, 6H), 0.15 (s, 3H), 0.13 (s, 6H), 0.10 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 159.7, 136.7, 136.3, 136.0 (4C), 133.8 (2C), 131.6, 130.2 (4C), 129.3 (2C), 128.3 (2C), 126.7, 126.5, 114.1 (2C), 74.2, 73.9, 72.8, 72.7, 71.9, 70.3, 68.2, 54.8, 42.0, 39.4, 37.8, 37.7, 36.5, 30.4, 30.3, 27.1 (3C), 26.8, 26.3 (6C), 26.2 (3C), 25.8, 21.7, 19.5, 18.53, 18.51, 18.4, −3.7, −3.9, −4.05, −4.08, −4.4, −4.5; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{62}H_{106}O_7Si_4Na$ 1097.6908, found 1097.6878.

(6*R*,8*E*,10*R*,12*E*,14*R*,18*R*)-6,10,14-Tris((*tert*-butyldimethylsilyl)oxy)-18-(6-((4-methoxybenzyl)oxy)hexyl)-2,2,20,20,21,21-hexamethyl-3,3-diphenyl-4,19-dioxa-3,20-disiladocosa-8,12-diene (28). To a solution of alcohol **27** (568 mg, 0.528 mmol) in CH_2Cl_2 (4.2 mL) at 0 °C were added 2,6-lutidine (0.15 mL, 1.3 mmol) and TBSOTf (0.15 mL, 0.63 mmol). After the mixture was stirred at 0 °C for 10 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 100/1 → 40/1) afforded TBS ether **28** (627 mg, 0.527 mmol, 100%) as a colorless oil: R_f = 0.58 (hexane/ethyl acetate =10/1); $[\alpha]^{23}_D$ −0.08 (*c* 1.00, $CHCl_3$); IR (neat) 3734, 2928, 2856, 1653, 1616, 1508, 1472, 1250, 1113, 835, 774, 701 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 7.84−7.82 (m, 4H), 7.30−7.25 (m, 8H), 6.83 (d, J = 8.4 Hz, 2H), 5.82 (ddd, J = 15.6, 7.2, 7.2 Hz, 1H), 5.81 (ddd, J = 15.6, 7.2, 7.2 Hz, 1H), 5.68 (dd, J = 15.6, 6.6 Hz, 1H), 5.64 (dd, J = 15.6, 6.6 Hz, 1H), 4.38 (s, 2H), 4.22 (ddd, J = 6.6, 6.6, 6.6 Hz, 1H), 4.21 (ddd, J = 6.6, 6.6, 6.6 Hz, 1H), 3.94−3.91 (m, 1H), 3.80−3.75 (m, 2H), 3.74−3.70 (m, 1H), 3.38 (t, J = 7.2 Hz, 2H), 3.32 (s, 3H), 2.57−2.44 (m, 2H), 2.42−2.33 (m, 2H), 1.75−1.62 (m, 4H), 1.61−1.49 (m, 4H), 1.47−1.42 (m, 4H), 1.41−1.30 (m, 4H), 1.21 (s, 9H), 1.07 (s, 9H), 1.05 (s, 9H), 1.04 (s, 9H), 0.99 (s, 9H), 0.19 (s, 3H), 0.18 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 159.7, 136.7, 136.3, 136.1 (4C), 134.1 134.0, 131.6, 130.1 (4C), 129.3 (2C), 128.3 (2C), 126.6, 126.5, 114.1 (2C), 74.3, 74.0, 73.3, 72.8, 72.7, 70.3, 67.6, 54.8, 42.1, 39.5, 37.8, 37.7, 37.6, 30.4, 30.3, 27.2 (3C), 26.9, 26.3 (6C), 26.24 (3C), 26.18 (3C), 25.8, 21.8, 19.5, 18.54, 18.52, 18.44, 18.37, −3.6, −3.9, −4.0, −4.1, −4.2, −4.37, −4.39, −4.5; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{68}H_{120}O_7Si_5Na$ 1211.7773, found 1211.7775.

(7*R*,11*R*,12*E*,15*R*,16*E*,19*R*)-7,11,15,19-Tetrakis((*tert*-butyldimethylsilyl)oxy)-20-((*tert*-butyldiphenylsilyl)oxy)icosa-12,16-dienal (3). To a solution of PMB ether **28** (115 mg, 96.6 μmol) in CH_2Cl_2/pH 7 buffer (v/v = 3:1, 1.6 mL) at 0 °C was added DDQ (28.5 mg, 0.126 mmol). The resultant mixture was stirred at room temperature for 2 h before being quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ at 0 °C. The mixture was extracted with ethyl acetate, and the organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 15/1→10/1) afforded mixture of alcohol and anisaldehyde (110 mg). The mixture was used in next reaction without further purification.

To a solution of crude alcohol in CH_2Cl_2 (0.96 mL) at 0 °C were added DMSO (0.10 mL, 1.4 mmol), Et_3N (0.10 mL, 0.72 mmol), and SO_3·py (69.2 mg, 0.435 mmol). After the mixture was stirred at room temperature for 3 h, the reaction was quenched with saturated aqueous NH_4Cl at 0 °C and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 50/1→20/1) gave aldehyde **3** (69.2 mg, 64.8 μmol, 67% for the two steps) as a colorless viscous oil: R_f = 0.52 (hexane/ethyl acetate = 10/1); $[\alpha]^{26}_D$ +0.97 (*c* 0.49, $CHCl_3$); IR (neat) 3839, 3073, 2928, 2856, 2710, 1731, 1653, 1472, 1462, 1234, 1112, 1074, 971, 834, 774, 702 cm^{-1}; ^1H NMR (600 MHz, C_6D_6) δ 9.34 (s, 1H), 7.83−7.82 (m, 4H), 7.30−7.25 (m, 6H), 5.81 (ddd, J = 15.6, 6.6, 6.6 Hz, 2H), 5.68 (dd, J = 15.6, 6.0 Hz, 1H), 5.64 (dd, J = 15.6, 6.6 Hz, 1H), 4.24−4.19 (m, 2H), 3.94−3.89 (m, 1H), 3.79−3.75 (m, 2H), 3.72−3.67 (m, 1H), 2.56−2.43 (m, 2H), 2.42−2.33 (m, 2H), 1.84 (t, J = 7.2 Hz, 2H), 1.73−1.42 (m, 8H), 1.39−1.21 (m, 4H), 1.21 (s, 9H), 1.14−1.08 (m, 2H), 1.07 (s, 9H), 1.05 (s, 9H), 1.03 (s, 9H), 0.99 (s, 9H), 0.19 (s, 3H), 0.18 (s, 3H), 0.151 (s, 3H), 0.145 (s, 3H), 0.12 (s, 6H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 136.7, 136.3, 136.1 (4C), 134.1 134.0, 131.6, 130.1 (4C), 128.3 (2C), 126.7, 126.5, 74.3, 74.0, 73.3, 72.6, 67.6, 43.8, 42.1, 39.5, 37.8, 37.7, 37.6, 37.4, 29.7 (2C), 27.2 (3C), 26.28 (3C), 26.25 (6C), 26.2, 25.4, 22.3, 21.7, 19.5, 18.53, 18.52, 18.42, 18.37, −3.6, −3.9, −4.0, −4.1, −4.2, −4.37, −4.40, −4.5; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{60}H_{110}O_6Si_5Na$ 1089.7041, found 1089.7047.

(*S*)-6-Allyl-8,8-diethyl-2,2-dimethyl-3,3-diphenyl-4,7-dioxa-3,8-disiladecane (11). To a solution of alcohol **31** (7.90 g, 17.0 mmol) and imidazole (2.20 g, 33.0 mmol) in DMF (72 mL) was added TESCl (4.30 mL, 26.0 mmol) at 0 °C. After the mixture was stirred at room temperature for 30 min, the reaction was quenched

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with saturated aqueous $NaHCO_3$ at 0 °C and extracted with Et_2O. The organic layer was washed saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 50/1→35/1→20/1) afforded TES ether **11** (7.60 g, 17.0 mmol, 99%) as a colorless oil: R_f = 0.49 (hexane/ethyl acetate = 20/1); $[\alpha]^{26}_D$ −5.2 (*c* 1.2, $CHCl_3$); IR (neat) 3072, 2954, 2932, 2875, 2359, 2341, 1462, 1428, 1390, 1362, 1239, 1110, 1005, 961, 913, 856, 822, 738, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68−7.66 (m, 4H), 7.44−7.36 (m, 6H), 5.84 (ddt, *J* = 17.2, 10.3, 6.9 Hz, 1H), 5.07 (dd, *J* = 17.2, 2.0 Hz, 1H), 5.03 (dd, *J* = 10.3, 2.0 Hz, 1H), 3.78−3.73 (m, 1H), 3.56 (dd, *J* = 9.6, 4.8 Hz, 1H), 3.50 (dd, *J* = 9.6, 6.8 Hz, 1H), 2.49−2.44 (m, 1H), 2.27−2.22 (m, 1H), 1.05 (s, 9H), 0.89 (t, *J* = 8.3 Hz, 9H), 0.52 (q, *J* = 8.3 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.8 (2C), 135.7 (2C), 135.3, 133.9, 133.8, 129.7 (2C), 127.8 (4C), 117.0, 72.8, 67.4, 39.2, 27.0 (3C), 19.3, 7.0 (3C), 5.0 (3C); HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{27}H_{42}O_2Si_2Na$ 477.2616, found 477.2608.

(*S*,*E*)-6-((*tert*-Butyldiphenylsilyl)oxy)-5-((triethylsilyl)oxy)hex-2-enal (10). To a solution of olefin **11** (522 mg, 1.15 mmol) and acrolein **12** (0.25 mL, 3.4 mmol) in CH_2Cl_2 (7.7 mL) was added Hoveyda−Grubbs second-generation catalyst **32** (36 mg, 57 μmol). After the mixture was stirred at 35 °C for 3.4 h, acrolein (0.17 mL, 2.3 mmol) and Hoveyda−Grubbs second-generation catalyst (7.0 mg, 12 μmol) were added. After the mixture was stirred at 35 °C for 1.6 h, the solution was filtered through a pad of silica gel and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane/ethyl acetate = 40/1→30/1→25/1) to give aldehyde **10** (400 mg, 0.828 mmol, 72%) as a colorless oil: R_f = 0.18 (hexane/ethyl acetate = 20/1); $[\alpha]^{26}_D$ −4.1 (*c* 1.8, $CHCl_3$); IR (neat) 3071, 2954, 2932, 2875, 2359, 1694, 1589, 1462, 1427, 1390, 1362, 1239, 1189, 1112, 1006, 978, 822, 739, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.47 (d, *J* = 8.2 Hz, 1H), 7.66−7.63 (m, 4H), 7.45−7.37 (m, 6H), 6.88 (dt, *J* = 15.8, 7.6 Hz, 1H), 6.17 (dd, *J* = 15.8, 8.2 Hz, 1H), 3.88−3.84 (m, 1H), 3.59 (dd, *J* = 10.1, 4.6 Hz, 1H), 3.46 (dd, *J* = 10.1, 8.3 Hz, 1H), 2.74−2.69 (m, 1H), 2.61−2.53 (m, 1H), 1.05 (s, 9H), 0.86 (t, *J* = 7.8 Hz, 9H), 0.49 (q, *J* = 7.8 Hz, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.0, 155.4, 135.7 (2C), 135.7 (2C), 135.1, 133.5, 133.4, 130.0 (2C), 127.9 (4C), 71.6, 67.2, 38.0, 27.0 (3C), 19.4, 6.9 (3C), 4.9 (3C); HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{28}H_{42}O_3Si_2Na$ 505.2565, found 505.2556.

(2*S*,4*S*,6*S*)-6-(((*tert*-Butyldiphenylsilyl)oxy)methyl)-2-methyl-1,3-dioxan-4-yl)ethan-1-ol (34). To a solution of aldehyde **10** (396 mg, 0.820 mmol) and acetaldehyde (1.0 mL, 16 mmol) in CH_2Cl_2 (8.2 mL) at 0 °C was added $Bi(NO_3)_3{\cdot}5H_2O$ (40 mg, 82 μmol). After the mixture was stirred at 30 °C for 67 h, the reaction was quenched with saturated aqueous $NaHCO_3$ at 0 °C and extracted with CH_2Cl_2. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde **33** as a colorless oil. This material was used in the next reaction without further purification.

To a solution of crude aldehyde **33** in MeOH (8.2 mL) at 0 °C was added $NaBH_4$ (31 mg, 0.82 mmol). After the mixture was stirred at 0 °C for 10 min, the reaction was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 10/1 → 5/1→2/1) afforded alcohol **34** (296 mg, 0.714 mmol, 87% for two steps) as a colorless syrup: R_f = 0.15 (hexane/ethyl acetate = 3/1); $[\alpha]_D^{25}$ −11.8 (*c* 1.5, $CHCl_3$); IR (neat) 3380, 3070, 3050, 2930, 2857, 2360, 2341, 1632, 1589, 1488, 1472, 1445, 1428, 1415, 1389, 1362, 1341, 1305, 1240, 1188, 1144, 1110, 1050, 998, 949, 893, 854, 823, 801, 741, 701 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.68−7.66 (m, 4H), 7.44−7.35 (m, 6H), 4.71 (q, *J* = 4.8 Hz, 1H), 3.91−3.86 (m, 1H), 3.83−3.75 (m, 4H), 3.59 (dd, *J* = 10.3, 5.5 Hz, 1H), 2.28−2.26 (m, 1H), 1.84−1.73 (m, 2H), 1.58 (dt, *J* = 13.1, 2.1 Hz, 1H), 1.41−1.35 (m, 1H), 1.30 (d, *J* = 4.8 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 135.80 (2C), 135.77 (2C), 133.7, 129.8 (2C), 127.8 (5C), 98.5, 76.7, 75.8, 66.9, 60.7, 38.1, 33.5, 27.0 (3C), 21.2, 19.4; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{24}H_{34}O_4SiNa$ 437.2119, found 437.2115.

***tert*-Butyl(((2*S*,4*S*,6*S*)-2-methyl-6-(2-(naphthalen-2-ylmethoxy)ethyl)-1,3-dioxan-4-yl)methoxy)diphenylsilane (35).** To a solution of alcohol **34** (3.50 g, 8.44 mmol) and 2-naphthylmethyl bromide (2.13 g, 10.1 mmol) in DMF (84 mL) at 0 °C was added NaH (ca. 60% dispersion in mineral oil, 372 mg, 9.28 mmol). After the mixture was stirred for 2.5 h at 0 °C, 2-naphthylmethyl bromide (1.07 g, 5.01 mmol) and NaH (ca. 60% dispersion in mineral oil, 169 mg, 4.22 mmol) were added, and the mixture was stirred for 1 h. The resultant mixture was quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The organic layer was washed with saturated aqueous 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 = 15/1 → 10/1 → 5/1→1/1) to give NAP ether **35** (3.82 g, 6.89 mmol, 82%) as a colorless oil with recovery of starting material **34** (0.52 g, 1.25 mmol, 15%): R_f = 0.41 (hexane/ethyl acetate = 10/1); $[\alpha]^{26}_D$ −9.3 (*c* 1.4, $CHCl_3$); IR (neat) 3050, 2929, 2857, 2359, 1589, 1508, 1472, 1428, 1378, 1340, 1145, 1106, 1057, 998, 948, 905, 854, 821, 773, 741, 702 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.85−7.67 (m, 8H), 7.49−7.35 (m, 9H), 4.70−4.65 (m, 3H), 3.85−3.80 (m, 1H), 3.79−3.74 (m, 2H), 3.69−3.65 (m, 1H), 3.61−3.56 (m, 2H), 1.89−1.78 (m, 2H), 1.61 (ddd, *J* = 13.0, 2.1, 2.1 Hz, 1H), 1.31−1.24 (m, 1H), 1.26 (d, *J* = 4.8 Hz, 3H), 1.05 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.2, 135.81 (2C), 135.79 (2C), 133.8, 133.5, 133.1, 129.8, 129.7, 128.3, 128.0, 127.8, 127.7 (5C), 126.5, 126.2, 126.0, 125.9, 98.5, 76.7, 73.2 (2C), 67.0, 66.3, 36.4, 33.8, 27.0 (3C), 21.1, 19.4; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{35}H_{42}O_4SiNa$ 577.2745, found 577.2721.

((2*S*,4*S*,6*S*)-2-Methyl-6-(2-(naphthalen-2-ylmethoxy)ethyl)-1,3-dioxan-4-yl)methanol (36). To a solution of TBDPS ether **35** (783 mg, 1.41 mmol) in THF (14 mL) at 0 °C was added TBAF (1 M in THF, 1.7 mL, 1.7 mmol). After the mixture was stirred at room temperature for 40 min, the reaction was quenched with saturated aqueous NH_4Cl at 0 °C and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 1/1) afforded alcohol **36** (429 mg, 1.35 mmol, 96%) as a colorless oil: R_f = 0.35 (hexane/ethyl acetate = 1/1); $[\alpha]^{26}_D$ −12.2 (*c* 0.75, $CHCl_3$); IR (neat) 3444, 3053, 2990, 2918, 2865, 2360, 2341, 1602, 1509, 1412, 1378, 1340, 1236, 1166, 1140, 1097, 1039, 967, 943, 903, 854, 820, 770, 752 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.85−7.76 (m, 4H), 7.50−7.45 (m, 3H), 4.72 (q, *J* = 4.8 Hz, 1H), 4.68 (d, *J* = 12.4 Hz, 1H), 4.65 (d, *J* = 12.4 Hz, 1H), 3.87−3.82 (m, 1H), 3.79−3.75 (m, 1H), 3.69−3.65 (m, 1H), 3.63−3.59 (m, 2H), 3.58−3.53 (m, 1H), 1.97 (brs, 1H), 1.91−1.85 (m, 1H), 1.83−1.77 (m, 1H), 1.44−1.34 (m, 2H), 1.30 (d, *J* = 4.8 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.1, 133.4, 133.1, 128.3, 128.0, 127.8, 126.5, 126.2, 126.0, 125.9, 98.7, 76.7, 73.2, 73.1, 66.1, 65.8, 36.3, 32.4, 21.1; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{24}O_4Na$ 339.1567, found 339.1582.

(2*S*,4*S*,6*S*)-2-Methyl-6-(2-(naphthalen-2-ylmethoxy)ethyl)-1,3-dioxane-4-carbaldehyde (37). To a solution of alcohol **36** (280 mg, 0.885 mmol) in CH_2Cl_2 (8.5 mL) at 0 °C was added Dess−Martin periodinane (940 mg, 2.22 mmol). After the mixture was stirred at room temperature for 2.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ at 0 °C and was extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to give crude aldehyde **37** as a colorless oil. Purification of the residue by silica gel column chromatography (hexane/ethyl acetate = 3/1→1/1) afforded aldehyde **37** (247 mg, 0.786 mmol, 89%) as a colorless oil: R_f = 0.33 (hexane/ethyl acetate = 1/1); $[\alpha]^{25}_D$ −23.1 (*c* 1.6, $CHCl_3$); IR (neat) 3054, 2989, 2920, 2866, 1737, 16031509, 1435, 1411, 1376, 1338, 1219, 1093, 963, 901, 853, 818, 772 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.62 (s, 1H), 7.86−7.80 (m, 3H), 7.77 (s, 1H), 7.52−7.43 (m, 3H), 4.76 (q, *J* = 5.0 Hz, 1H), 4.69 (d, *J* = 11.9 Hz, 1H), 4.65 (d, *J* = 11.9 Hz, 1H), 4.15−4.09 (m, 1H), 3.93−3.84 (m, 1H), 3.67 (ddd, *J* = 9.2, 7.8, 5.0 Hz, 1H), 3.59

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(ddd, J = 9.2, 5.5, 5.5 Hz, 1H), 1.94−1.75 (m, 3H), 1.47−1.36 (m, 1H), 1.35 (d, J = 5.5 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 200.5, 135.9, 133.4, 133.1, 128.3, 128.0, 127.8, 126.6, 126.3, 126.0, 125.9, 98.8, 80.1, 73.3, 73.1, 65.8, 36.1, 31.2, 21.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{19}H_{22}O_4Na$ 337.1410, found 337.1411.

(1*R*,2*S*)-2-Methyl-1-((2*S*,4*S*,6*S*)-2-methyl-6-(2-(naphthalen-2-ylmethoxy)ethyl)-1,3-dioxan-4-yl)but-3-en-1-ol (39). To a suspension of *t*-BuOK (dried at 80 °C under vacuum for 18 h, 530 mg, 4.72 mmol) in freshly distilled THF (4.0 mL) at −78 °C was added liquid *cis*-2-butene (0.42 mL, 4.7 mmol) followed by *n*-BuLi (1.6 M in *n*-hexane, 2.6 mL, 4.2 mmol). The mixture was stirred at −45 °C for 15 min and then cooled to −78 °C. To this mixture was added a solution of (+)-Ipc$_2$BOMe (1.49 g, 4.71 mmol) in THF (2.5 mL) via cannula, and after 30 min, BF_3·Et_2O (0.52 mL, 4.2 mmol) and a solution of aldehyde **37** (294 mg, 0.935 mmol) in THF (2.5 mL, dried over MS4A) were sequentially added. After the mixture was stirred at −78 °C for 6.5 h, the reaction was quenched with 3 M aqueous NaOH (4.0 mL) followed by 30% H_2O_2 (1.9 mL) and then stirred at room temperature for 2 h. The organic layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic layers were washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 7/1→5/1→3/1→1/1) afforded homoallylic alcohol **39** (240 mg, 0.648 mmol, 69%) as a colorless oil: R_f = 0.40 (hexane/ethyl acetate = 3/1); $[\alpha]^{23}_D$ −37.7 (c 0.64, $CHCl_3$); IR (neat) 3478, 3055, 2958, 2924, 2867, 2360, 2341, 1640, 1603, 1509, 1442, 1412, 1378, 1337, 1272, 1236, 1125, 1092, 1031, 997, 954, 914, 854, 817, 770, 751 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86−7.80 (m, 3H), 7.78 (s, 1H), 7.50−7.44 (m, 3H), 5.70 (ddd, J = 17.2, 10.3, 7.6 Hz, 1H), 5.04 (d, J = 17.2 Hz, 1H), 5.03 (d, J = 10.3 Hz, 1H), 4.71 (q, J = 5.5 Hz, 1H), 4.68 (d, J = 12.4 Hz, 1H), 4.66 (d, J = 12.4 Hz, 1H), 3.83−3.77 (m, 1H), 3.70−3.65 (m, 2H), 3.63−3.58 (m, 1H), 3.53 (dd, J = 7.6, 4.1 Hz, 1H), 2.37−2.29 (m, 1H), 2.11 (brs, 1H, OH), 1.91−1.79 (m, 2H), 1.56−1.51 (m, 2H), 1.28 (d, J = 4.8 Hz, 3H), 1.10 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.4, 136.1, 133.4, 133.1, 128.3, 128.0, 127.8, 126.5, 126.2, 126.0, 125.9, 115.4, 98.6, 76.8, 75.9, 73.2, 73.1, 66.2, 39.4, 36.4, 29.8, 21.2, 16.1; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{23}H_{30}O_4Na$ 393.2036, found 393.2038.

(3*S*,5*S*,6*R*,7*S*)-7-Methyl-1-(naphthalen-2-ylmethoxy)non-8-ene-3,5,6-triol (40). To a solution of alcohol **39** (83.0 mg, 0.224 mmol) in MeOH (0.7 mL), H_2O (0.7 mL) and THF (0.7 mL) at 0 °C was added *p*-TsOH·H_2O (130 mg, 0.686 mmol). After the mixture was stirred at 60 °C for 20 h, the reaction was quenched with saturated aqueous $NaHCO_3$ at 0 °C and was extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 5/1 → 3/1 → 1/2) afforded triol **40** (32 mg, 0.094 mmol, 42%, 89% brsm) as a colorless syrup, and alcohol **39** (44.0 mg, 0.119 mmol, 53%) was recovered: R_f = 0.16 (hexane/ethyl acetate = 1/1); $[\alpha]^{24}_D$ −6.6 (c 0.63, $CHCl_3$); IR (neat) 3392, 3057, 2921, 2866, 2366, 2357, 1639, 1603, 1509, 1420, 1369, 1341, 1272, 1172, 1123, 1089, 999, 916, 855, 817, 751 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86−7.76 (m, 4H), 7.51−7.42 (m, 3H), 5.72 (ddd, J = 17.2, 10.3, 7.6 Hz, 1H), 5.05−5.01 (m, 2H), 4.69 (s, 2H), 4.15−4.11 (m, 1H), 3.89−3.86 (m, 1H), 3.81−3.78 (m, 1H), 3.74−3.70 (m, 1H), 3.42 (dd, J = 7.6, 4.9 Hz, 1H), 2.37 (q, J = 6.9 Hz, 1H), 1.91−1.84 (m, 1H), 1.78−1.73 (m, 1H), 1.70−1.68 (m, 2H), 1.11 (d, J = 6.9 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 140.9, 135.1, 133.4, 133.2, 128.6, 128.0, 127.9, 126.8, 126.4, 126.2, 125.7, 115.1, 77.1, 73.8, 72.9, 72.5, 69.5, 40.2, 37.1, 36.8, 16.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{21}H_{28}O_4Na$ 367.1880, found 367.1885.

(5*R*,6*S*,8*S*)-5-((*S*)-But-3-en-2-yl)-6-((*tert*-butyldimethylsilyl)-oxy)-2,2,3,3,10,10,11,11-octamethyl-8-(2-(naphthalen-2-yl-methoxy)ethyl)-4,9-dioxa-3,10-disiladodecane (41). To a solution of triol **40** (145 mg, 0.421 mmol) and 2,6-lutidine (0.44 mL, 3.8 mmol) in CH_2Cl_2 (4.2 mL) at 0 °C was added TBSOTf (0.58 mL, 2.5 mmol). After the mixture was stirred at 0 °C for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with hexane. The organic layer was washed with saturated aqueous $KHSO_4$, $NaHCO_3$, and NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 50/1→40/1) afforded TBS ether **41** (304 mg, 0.413 mmol, 98%) as a colorless oil: R_f = 0.24 (hexane/ethyl acetate = 50/1); $[\alpha]^{23}_D$ −32.9 (c 0.54, $CHCl_3$); IR (neat) 2955, 2928, 2886, 2856, 2359, 2342, 1472, 1462, 1407, 1387, 1361, 1342, 1254, 1124, 1095, 1047, 1024, 1005, 947, 868, 835, 810, 774, 749 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83−7.76 (m, 4H), 7.48−7.43 (m, 3H), 5.68 (ddd, J = 17.8, 8.9, 8.9 Hz, 1H), 5.01−4.98 (m, 2H), 4.66 (d, J = 12.4 Hz, 1H), 4.62 (d, J = 12.4 Hz, 1H), 3.98−3.93 (m, 1H), 3.75−3.73 (m, 1H), 3.65−3.58 (m, 2H), 3.44−3.42 (m, 1H), 2.16 (q, J = 6.9 Hz, 1H), 1.93−1.87 (m, 1H), 1.85−1.80 (m, 1H), 1.57−1.51 (m, 2H), 0.99 (d, J = 6.9 Hz, 3H), 0.90 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.05 (s, 6H), 0.04 (s, 3H), 0.02 (s, 3H), 0.01 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 141.9, 136.4, 133.5, 133.1, 128.1, 128.0, 127.8, 126.5, 126.1, 126.0, 125.8, 114.9, 81.6, 73.3, 72.4, 67.5, 67.2, 43.1, 40.5, 36.4, 26.3 (6C), 26.0 (3C), 18.6, 18.23, 18.19, 17.8, −3.01, −3.04, −4.1, −4.3, −4.6, −4.8; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{39}H_{70}O_4Si_3Na$ 709.4474, found 709.4484.

(3*S*,4*R*,5*S*,7*S*)-4,5,7-Tris((*tert*-butyldimethylsilyl)oxy)-3-methyl-9-(naphthalen-2-ylmethoxy)nonan-1-ol (42). To a solution of BH_3·SMe_2 (0.13 mL, 1.3 mmol) in THF (0.2 mL) was added cyclohexene (0.27 mL, 2.6 mmol) at 0 °C. After the mixture was stirred at 0 °C for 15 min, the reaction mixture was allowed to warm to room temperature. After 1 h, the solution was cooled to 0 °C, and a solution of olefin **41** (302 mg, 0.439 mmol) in THF (1.2 mL + 2 × 0.6 mL rinse) was added via cannula. After the mixture was stirred at room temperature for 25 min, the reaction was cooled to 0 °C and treated with 3 M aqueous NaOH (3.2 mL) and 30% H_2O_2 (1.1 mL). After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ at 0 °C and was extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by silica gel column chromatography (hexane/ethyl acetate = 7/1→5/1) afforded alcohol **42** (283 mg, 0.399 mmol, 91%) as a colorless syrup: R_f = 0.31 (hexane/ethyl acetate = 5/1); $[\alpha]^{23}_D$ −26.2 (c 0.43, $CHCl_3$); IR (neat) 3420, 2953, 2928, 2885, 2856, 1472, 1361, 1254, 1095, 1005, 939, 835, 774, 749, 678, 666 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83−7.78 (m, 4H), 7.47−7.43 (m, 3H), 4.66 (d, J = 12.4 Hz, 1H), 4.62 (d, J = 12.4 Hz, 1H), 4.01−3.96 (m, 1H), 3.69−3.58 (m, 4H), 3.55−3.51 (m, 1H), 3.50−3.49 (m, 1H), 1.95−1.90 (m, 1H), 1.82−1.77 (m, 1H), 1.71−1.60 (m, 4H), 1.30−1.24 (m, 1H), 0.90 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.84 (d, J = 6.9 Hz, 3H), 0.12 (s, 3H), 0.05 (s, 3H × 3), 0.03 (s, 3H), 0.01 (s, 3H), one −OH proton is missing; ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.2, 133.5, 133.1, 128.2, 128.0, 127.8, 126.6, 126.1 (2C), 125.9, 81.6, 73.4, 72.8, 67.4, 67.3, 61.4, 41.6, 37.3, 36.2, 34.6, 26.2 (6C), 26.0 (3C), 18.6, 18.19, 18.16, 15.8, −3.19, −3.23, −4.1, −4.3, −4.6, −4.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{39}H_{72}O_5Si_3Na$ 727.4580, found 727.4585.

1-Phenyl-5-(((3*S*,4*R*,5*S*,7*S*)-4,5,7-tris((*tert*-butyldimethylsilyl)-oxy)-3-methyl-9-(naphthalen-2-ylmethoxy)nonyl)thio)-1*H*-tetrazole (44). To a solution of alcohol **42** (627 mg, 0.889 mmol), PPh_3 (317 mg, 1.78 mmol), and 5-mercapto-1-phenyl-1*H*-tetrazole **43** (466 mg, 1.78 mmol) in THF (8.9 mL) at 0 °C was added DIAD (1.9 M in toluene, 0.94 mL, 1.8 mmol) via syringe. The reaction was stirred at 0 °C for 10 min before being quenched with saturated aqueous NH_4Cl. The mixture was extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 15/1→5/1) gave sulfide **44** (698 mg, 0.806 mmol, 91%) as a colorless syrup: R_f = 0.57 (hexane/ethyl acetate = 7/1); $[\alpha]^{26}_D$ −29.0 (c 0.95, $CHCl_3$); IR (neat) 3734, 3628, 3056, 2954, 2928, 2856, 1599, 1500, 1472, 1387, 1252, 1092, 1044, 939, 835, 740 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82−7.79 (m, 4H), 7.57−7.50 (m, 5H), 7.47−7.41 (m, 3H), 4.63 (ddd, J = 6.0, 6.0, 6.0 Hz, 2H), 3.96−3.95 (m, 1H), 3.64−3.56 (m, 3H), 3.52−3.47 (m, 2H), 3.28−3.24 (m, 1H), 1.97−1.89 (m, 2H),

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1.82−1.78 (m, 1H), 1.73−1.67 (m, 1H), 1.60−1.51 (m, 3H), 0.92 (d, J = 6.6 Hz, 3H), 0.88 (s, 9H), 0.848 (s, 9H), 0.846 (s, 9H), 0.11 (s, 3H), 0.034 (s, 3H), 0.030 (s, 3H), 0.027 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.4, 136.3, 133.9, 133.4, 133.1, 130.2, 129.9 (2C), 128.2, 128.0, 127.8, 126.5, 126.1, 126.0, 125.8, 123.9 (2C), 81.1, 73.3, 72.9, 67.4, 67.1, 42.0, 37.1, 36.5, 33.2, 31.8, 26.2 (6C), 26.0 (3C), 18.5, 18.2 (2C), 14.5, −3.2, −3.3, −4.1, −4.3, −4.6 (2C); HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{46}H_{76}N_4O_4SSi_3Na$ 887.4787, found 887.4824.

1-Phenyl-5-(((3*S*,4*R*,5*S*,7*S*)-4,5,7-tris((*tert*-butyldimethylsilyl)oxy)-3-methyl-9-(naphthalen-2-ylmethoxy)nonyl)sulfonyl)-1*H*-tetrazole (4). To a solution of sulfide **44** (622 mg, 0.719 mmol) in CH_2Cl_2 (9.6 mL) at 0 °C was added m-CPBA (989 mg, 3.96 mmol). After the mixture was stirred at 0 °C for 39 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$. The mixture was extracted with ethyl acetate, washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filteredm and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 10/1→3/1) gave sulfone **4** (555 mg, 0.619 mmol, 86%) as a colorless viscous syrup: R_f = 0.5 (hexane/ethyl acetate = 7/1 × 2); $[\alpha]^{25}_D$ −25.6 (c 0.93, $CHCl_3$); IR (neat) 3734, 3628, 2954, 2928, 2856, 1596, 1558, 1497, 1472, 1340, 1254, 1093, 939, 835, 774 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83−7.77 (m, 4H), 7.69−7.67 (m, 2H), 7.63−7.54 (m, 3H), 7.47−7.44 (m, 3H), 4.66−4.60 (m, 2H), 4.00−3.97 (m, 1H), 3.76−3.71 (m, 1H), 3.65−3.57 (m, 4H), 3.53−3.52 (m, 1H), 2.09−2.05 (m, 1H), 1.93−1.89 (m, 1H), 1.81−1.77 (m, 1H), 1.73−1.68 (m, 2H), 1.62−1.54 (m, 2H), 0.91 (d, J = 4.8 Hz, 3H), 0.89 (s, 9H), 0.86 (s, 9H), 0.85 (s, 9H), 0.13 (s, 3H), 0.051 (s, 6H), 0.046 (s, 3H), 0.019 (s, 3H), 0.015 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 153.6, 136.3, 133.5, 133.2, 133.1, 131.6, 129.9 (2C), 128.1, 128.0, 127.8, 126.5, 126.12, 126.08, 125.9, 125.2 (2C), 80.9, 73.3, 73.1, 67.2, 67.0, 54.9, 42.1, 36.9, 36.4, 26.3, 26.2 (6C), 26.0 (3C), 18.5, 18.2 (2C), 14.8, −3.20, −3.27, −4.1, −4.3, −4.6, −4.7; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{46}H_{76}N_4O_6SSi_3Na$ 919.4686, found 919.4662.

(6*R*,8*E*,10*R*,12*E*,14*R*,18*R*,24*E*,27*S*,28*R*,29*S*,31*S*)-6,10,14,18,28,29-Hexakis((*tert*-butyldimethylsilyl)oxy)-2,2,27,33,33,34,34-heptamethyl-31-(2-(naphthalen-2-ylmethoxy)ethyl)-3,3-diphenyl-4,32-dioxa-3,33-disilapentatriaconta-8,12,24-triene (45). To a solution of aldehyde **3** (411 mg, 0.385 mmol) and sulfone **4** (554 mg, 0.617 mmol) in THF (12 mL) at −78 °C was added KHMDS (0.5 M in THF, 1.2 mL, 0.6 mmol). After the mixture was stirred at −78 °C for 4 h, the reaction was allowed to warm to room temperature and stirred for 18 h. The reaction was quenched with saturated aqueous NH_4Cl at 0 °C and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 80/1 → 30/1 → 15/1) gave triene **45** (576 mg, 0.331 mmol, 86%) as a colorless viscous syrup: R_f = 0.78 (hexane/ethyl acetate = 10/1); $[\alpha]^{25}_D$ −12.0 (c 1.29, $CHCl_3$); IR (neat) 3734, 2953, 2928, 2856, 1716, 1653, 1636, 1507, 1462, 1362, 1254, 1091, 1005, 835, 774, 740 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ 7.83−7.65 (m, 8H), 7.49−7.47 (m, 1H), 7.32−7.25 (m, 8H), 5.81 (ddd, J = 16.2, 6.6, 6.6 Hz, 1H), 5.80 (ddd, J = 15.0, 6.6, 6.6 Hz, 1H), 5.69 (dd, J = 15.0, 6.0 Hz, 1H), 5.63 (dd, J = 16.2, 6.6 Hz, 1H), 5.53 (ddd, J = 16.2, 6.0, 6.0 Hz, 1H), 5.46 (ddd, J = 16.2, 6.0, 6.0 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.30−4.27 (m, 1H), 4.24−4.21 (m, 2H), 3.93−3.89 (m, 1H), 3.86−3.85 (m, 1H), 3.79−3.75 (m, 3H), 3.75−3.72 (m, 1H), 3.70−3.69 (m, 1H), 3.67−3.64 (m, 1H), 2.56−2.42 (m, 2H), 2.42−2.29 (m, 3H), 2.14−2.11 (m, 2H), 2.10−2.06 (m, 2H), 1.94−1.89 (m, 1H), 1.87−1.83 (m, 1H), 1.74−1.30 (m, 16H), 1.20 (s, 9H), 1.08 (s, 9H), 1.07 (s, 9H), 1.05 (s, 9H), 1.04 (s, 9H), 1.03 (s, 9H), 1.03 (d, J = 8.4 Hz, 3H), 1.01 (s, 9H), 0.99 (s, 9H), 0.33 (s, 3H), 0.28 (s, 3H), 0.21 (s, 3H), 0.192 (s, 3H), 0.187 (s, 3H), 0.18 (s, 3H), 0.17 (s, 6H), 0.16 (s, 3H), 0.14 (s, 6H), 0.12 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 136.8, 136.7, 136.3, 136.1 (4C), 134.1, 134.0 (2C), 133.6, 132.6, 130.1 (4C), 129.1, 128.3 (2C), 128.0 (3C), 126.8, 126.6, 126.5, 126.3 (2C), 126.0, 81.6, 74.3, 74.0, 73.7, 73.5, 73.2, 72.7, 67.5, 67.34, 67.26, 42.15, 42.12, 39.5, 38.5, 38.1, 37.8, 37.7, 37.6, 37.2, 33.2, 30.2, 30.0, 27.2 (3C), 26.5 (6C), 26.31 (3C), 26.29 (3C), 26.25 (3C), 26.21 (3C), 26.19 (3C), 25.7, 21.8, 19.5, 18.8, 18.6, 18.53, 18.45, 18.38 (2C), 18.36, 15.9, −2.8, −3.0, −3.6, −3.7, −3.9, −4.0, −4.06, −4.13, −4.2, −4.37, −4.40 (3C), −4.46; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{99}H_{180}O_9Si_8Na$ 1760.1674, found 1760.1686.

(6*R*,8*E*,10*R*,12*E*,14*R*,18*R*,24*S*,25*S*,27*S*,28*R*,29*S*,31*S*)-6,10,14,18,28,29-Hexakis((*tert*-butyldimethylsilyl)oxy)-2,2,27,33,33,34,34-heptamethyl-31-(2-(naphthalen-2-ylmethoxy)ethyl)-3,3-diphenyl-4,32-dioxa-3,33-disilapentatriaconta-8,12-diene-24,25-diol (46). A mixture of $K_2OsO_4{\cdot}2H_2O$ (4.9 mg, 13 μmol), DHQ-MEQ (49.9 mg, 107 μmol), $K_3Fe(CN)_6$ (263 mg, 800 μmol), K_2CO_3 (111 mg, 800 μmol), and $MeSO_2NH_2$ (76.1 mg, 800 μmol) in t-BuOH/H_2O (v/v = 1:1, 4.4 mL) was stirred at room temperature for 30 min. To this suspension at 0 °C was added a solution of olefin **45** (464 mg, 0.267 mmol) in t-BuOMe (3.2 mL + 3 × 0.4 mL rinse) via cannula. After the mixture was stirred at 0 °C for 69 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and stirred at 0 °C for 30 min. The mixture was extracted with ethyl acetate. The organic layer was washed with saturated aqueous 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 → 12/1 → 10/1) to afford diol **46** as a mixture of diastereoisomers (308 mg, 0.174 mmol, 65%, dr =13:1) as a colorless viscous syrup: R_f = 0.16 (hexane/ethyl acetate = 10/1); $[\alpha]^{25}_D$ −14.3 (c 1.10, $CHCl_3$); IR (neat) 3734, 3649, 3178, 2952, 2928, 2856, 1716, 1653, 1636, 1472, 1461, 1362, 1252, 1070, 1005, 833, 772, 701 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ 7.83−7.65 (m, 8H), 7.46−7.44 (m, 1H), 7.32−7.26 (m, 8H), 5.813 (ddd, J = 15.0, 6.6, 6.6 Hz, 1H), 5.807 (ddd, J = 15.0, 6.6, 6.6 Hz, 1H), 5.68 (dd, J = 15.0, 6.6 Hz, 1H), 5.64 (dd, J = 15.0, 7.2 Hz, 1H), 4.51 (d, J = 11.4 Hz, 1H), 4.47 (d, J = 11.4 Hz, 1H), 4.31−4.28 (m, 1H), 4.24−4.20 (m, 2H), 3.96−3.90 (m, 2H), 3.80−3.72 (m, 5H), 3.62 (d, J = 6.6 Hz, 1H), 3.25−3.20 (m, 1H), 3.19−3.15 (m, 1H), 2.57−2.43 (m, 2H), 2.43−2.33 (m, 2H), 2.12−2.07 (m, 2H), 2.03−1.99 (m, 1H), 1.90−1.83 (m, 2H), 1.76−1.28 (m, 17H), 1.23−1.18 (m, 1H), 1.21 (s, 9H), 1.10 (s, 9H), 1.07 (s, 9H), 1.06 (s, 9H), 1.041 (s, 9H), 1.035 (s, 9H), 1.02 (s, 9H), 0.99 (s, 9H), 0.95 (d, J = 7.2 Hz, 3H), 0.34 (s, 3H), 0.28 (s, 3H), 0.21 (s, 3H), 0.20 (s, 3H), 0.190 (s, 3H), 0.187 (s, 9H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 136.7, 136.4, 136.3, 136.1 (4C), 134.1, 133.99, 133.96, 133.6, 130.1 (4C), 128.5 (2C), 128.0 (2C), 127.3, 126.7, 126.6, 126.5, 126.3 (2C), 126.1, 82.9, 75.3, 74.3, 74.0, 73.7, 73.3 (2C), 72.7, 72.6, 67.61, 67.56, 67.2, 42.1, 41.7, 39.5 (2C), 37.79, 37.77, 37.6, 36.4, 34.22, 34.15, 30.6 (2C), 27.2 (3C), 26.52 (3C), 26.46 (3C), 26.30 (6C), 26.25 (3C), 26.21 (3C), 26.18 (3C), 25.9, 21.8, 19.5, 18.9, 18.6, 18.52, 18.46, 18.40, 18.37 (2C), 16.3, −2.9, −3.0, −3.6, −3.8, −3.9, −4.01, −4.03, −4.1, −4.2, −4.36, −4.39 (3C), −4.5; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{99}H_{182}O_{11}Si_8Na$ 1794.1729, found 1794.1726.

(6*R*,8*E*,10*R*,12*E*,14*R*,18*R*,24*S*,25*S*,27*S*,28*R*,29*S*,31*S*)-6,10,14,18,24,25,28,29-Octakis((*tert*-butyldimethylsilyl)oxy)-2,2,27,33,33,34,34-heptamethyl-31-(2-(naphthalen-2-ylmethoxy)ethyl)-3,3-diphenyl-4,32-dioxa-3,33-disilapentatriaconta-8,12-diene (47). To a solution of diol **46** (308 mg, 0.174 mmol) in CH_2Cl_2 (3.4 mL) were added 2,6-lutidine (0.16 mL, 1.4 mmol) and TBSOTf (0.16, 0.70 mmol) at 0 °C. After being stirred at 0 °C for 10 min, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and extracted with ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 150/1→15/1) afforded TBS ether **47** (323 mg, 0.162 mmol, 93%) as a colorless viscous syrup: R_f = 0.73 (hexane/ethyl acetate = 10/1); $[\alpha]^{25}_D$ −24.5 (c 1.01, $CHCl_3$); IR (neat) 3750, 3734, 3676, 2953, 2928, 2856, 1716, 1653, 1636, 1522, 1472, 1459, 1362, 1254, 1086, 1005, 835, 773, 701 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ 7.83−7.66 (m, 8H), 7.49−7.48 (m, 1H), 7.32−7.26 (m, 8H), 5.81 (ddd, J = 15.0, 7.2, 7.2 Hz, 1H), 5.80 (ddd, J = 15.0, 7.2, 7.2 Hz, 1H), 5.68 (dd, J = 15.0, 6.6 Hz, 1H), 5.63 (dd, J = 15.0, 6.6 Hz, 1H), 4.59 (d, J = 11.4 Hz, 1H), 4.52 (d, J = 11.4 Hz, 1H),

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4.35−4.31 (m, 1H), 4.24−4.19 (m, 2H), 3.97−3.86 (m, 3H), 3.84−3.64 (m, 7H), 2.57−2.43 (m, 2H), 2.43−2.32 (m, 2H), 2.26−2.14 (m, 2H), 2.05−1.89 (m, 3H), 1.83−1.34 (m, 18H), 1.21 (s, 9H), 1.12 (s, 9H), 1.13−1.11 (m, 3H), 1.07 (s, 9H), 1.05 (s, 18H), 1.04 (s, 18H), 1.03 (s, 9H), 1.01 (s, 9H), 0.99 (s, 9H), 0.36 (s, 3H), 0.30 (s, 3H), 0.25 (s, 3H), 0.24 (s, 3H), 0.23 (s, 3H), 0.22 (s, 3H), 0.19 (s, 3H), 0.182 (s, 6H), 0.175 (s, 3H), 0.17 (s, 3H), 0.16 (s, 3H), 0.15 (s, 9H), 0.13 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 136.8, 136.7, 136.3, 136.1 (4C), 134.1, 134.0 (2C), 133.6, 130.1 (4C), 128.3 (2C), 128.2, 128.0 (2C), 126.8, 126.6, 126.5, 126.34, 126.27, 126.0, 83.7, 75.8, 74.7, 74.3, 74.0, 73.5, 73.3, 72.8, 72.7, 67.6, 67.3 (2C), 42.8, 42.1, 39.5, 37.8 (2C), 37.6, 37.4, 36.0, 34.3, 30.71, 30.69, 27.7, 27.2 (3C), 26.6 (3C), 26.4 (3C), 26.31 (6C), 26.25 (6C), 26.23 (3C), 26.18 (6C), 26.0, 21.8, 19.5, 18.8, 18.6, 18.5, 18.45, 18.38 (2C), 18.34, 18.31, 18.29, 14.0, −2.9, −3.0, −3.62, −3.64 (2C), −3.8, −3.9, −4.0 (2C), −4.1, −4.2, −4.26, −4.28, −4.31, −4.35, −4.39 (2C), −4.5; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{111}H_{210}O_{11}Si_{10}Na$ 2022.3458, found 2022.3477.

(3*S*,5*S*,6*R*,7*S*,9*S*,10*S*,16*R*,20*R*,21*E*,24*R*,25*E*,28*R*)-3,5,6,9,10,16,20,24,28-Nonakis((*tert*-butyldimethylsilyl)oxy)-29-((*tert*-butyldiphenylsilyl)oxy)-7-methylnonacosa-21,25-dien-1-ol (48). To a solution of NAP ether **47** (321 mg, 0.160 mmol) in CH_2Cl_2/pH 7 buffer (v/v = 3:1, 2.1 mL) at 0 °C was added DDQ (72.8 mg, 0.322 mmol). After the mixture was stirred for 1 h at 0 °C, the reaction was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$. The mixture was extracted with ethyl acetate, and the organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was dissolved in MeOH/THF (v/v = 1:1, 1.6 mL) and cooled to 0 °C. $NaBH_4$ (60.6 mg, 1.60 mmol) was added to the mixture and stirred for 10 min. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. Purification by flash silica gel column chromatography (hexane/ethyl acetate = 80/1 → 50/1 → 9/1) afforded alcohol **48** (247 mg, 0.133 mmol, 83%) as a colorless viscous syrup: R_f = 0.48 (hexane/ethyl acetate = 12/1); $[\alpha]^{25}_D$ −22.6 (c 0.90, $CHCl_3$); IR (neat) 3727, 3624, 3492, 2954, 2929, 2894, 2857, 1723, 1665, 1584, 1472, 1425, 1361, 1254, 1083, 1005, 835, 773, 702 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ 7.83−7.80 (m, 4H), 7.31−7.26 (m, 6H), 5.81 (ddd, J = 15.6, 7.2, 7.2 Hz, 1H), 5.80 (ddd, J = 15.6, 7.2, 7.2 Hz, 1H), 5.68 (dd, J = 15.6, 6.6 Hz, 1H), 5.63 (dd, J = 15.6, 7.2 Hz, 1H), 4.31−4.27 (m, 1H), 4.24−4.19 (m, 2H), 3.94−3.86 (m, 4H), 3.82−3.73 (m, 6H), 2.57−2.43 (m, 2H), 2.43−2.33 (m, 2H), 2.17−2.12 (m, 1H), 2.03−1.92 (m, 4H), 1.82−1.35 (m, 18H), 1.21 (s, 9H), 1.12−1.10 (m, 3H), 1.12 (s, 9H), 1.07 (s, 9H), 1.06 (s, 9H), 1.05 (s, 9H), 1.042 (s, 9H), 1.038 (s, 9H), 1.03 (s, 18H), 0.99 (s, 9H), 0.35 (s, 3H), 0.28 (s, 3H), 0.25 (s, 3H), 0.218 (s, 3H), 0.215 (s, 3H), 0.194 (s, 3H), 0.191 (s, 3H), 0.186 (s, 6H), 0.18 (s, 3H), 0.17 (s, 3H), 0.162 (s, 3H), 0.156 (s, 3H), 0.154 (s, 3H), 0.151 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 136.7, 136.3, 136.1 (4C), 134.1, 134.0, 130.1 (4C), 128.3 (2C), 126.6, 126.5, 83.6, 75.8, 74.7, 74.3, 74.0, 73.3, 72.8, 72.7, 69.0, 67.6, 60.0, 42.1, 41.9, 39.5, 38.6, 37.8 (2C), 37.6, 35.9, 34.2, 30.72, 30.69, 27.7, 27.2 (3C), 26.6 (3C), 26.4 (3C), 26.31 (9C), 26.25 (6C), 26.2 (6C), 25.9, 21.8, 19.5, 18.8, 18.6, 18.5, 18.45, 18.42, 18.38, 18.32, 18.30, 18.27, 14.2, −2.9, −3.0, −3.6, −3.7, −3.77, −3.80, −3.9, −4.0 (2C), −4.1, −4.2, −4.26, −4.34 (3C), −4.4, −4.46, −4.47; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{100}H_{202}O_{11}Si_{10}Na$ 1882.2832, found 1882.2858.

(5*R*,7*S*,8*R*,9*S*,11*S*,12*S*,18*R*,22*R*,23*E*,26*R*,27*E*,30*R*)-7,8,11,12,18,22,26,30-Octakis((*tert*-butyldimethylsilyl)oxy)-2,2,3,3,9,34,34-heptamethyl-33,33-diphenyl-5-vinyl-4,32-dioxa-3,33-disilapentatriaconta-23,27-diene (2). To a mixture of alcohol **48** (244 mg, 0.131 mmol), o-O_2NPhSeCN (149 mg, 0.655 mmol), and activated powdered MS4A (110 mg) in THF (0.5 mL) at 55 °C was added Me_3P (1.0 M in THF, 2.6 mL, 2.6 mmol) via syringe at once. After the mixture was stirred at room temperature for 30 min, 30% H_2O_2 (595 μL, 5.24 mmol) was added. The resultant mixture was stirred for 3 h before the reaction was quenched with saturated aqueous $NaHCO_3$ and $Na_2S_2O_3$ at 0 °C. After being diluted with Et_2O, the mixture was filtered through cotton and extracted with Et_2O. The organic layer was washed with saturated aqueous 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 = 100/1 → 20/1) to afford triene **2** (235 mg, 0.127 mmol, 97%) as a yellow viscous syrup: R_f = 0.43 (hexane/ethyl acetate = 20/1); $[\alpha]^{25}_D$ −19.7 (c 1.03, $CHCl_3$); IR (neat) 3727, 3621, 2954, 2929, 2890, 2857, 1732, 1593, 1506, 1472, 1428, 1362, 1254, 1085, 972, 835, 773, 701 cm^{-1}; ^{1}H NMR (600 MHz, C_6D_6) δ 7.83−7.80 (m, 4H), 7.30−7.25 (m, 6H), 6.02 (ddd, J = 16.8, 10.8, 6.6 Hz, 1H), 5.81 (ddd, J = 15.0, 7.8, 7.8 Hz, 1H), 5.80 (ddd, J = 15.0, 7.2, 7.2 Hz, 1H), 5.69 (dd, J = 15.0, 6.0 Hz, 1H), 5.64 (dd, J = 15.0, 6.6 Hz, 1H), 5.37 (d, J = 16.8 Hz, 1H), 5.14 (d, J = 10.8 Hz, 1H), 4.51−4.48 (m, 1H), 4.24−4.19 (m, 2H), 3.94−3.86 (m, 3H), 3.80−3.73 (m, 5H), 2.57−2.43 (m, 2H), 2.43−2.32 (m, 2H), 2.18−2.13 (m, 1H), 2.06−1.91 (m, 3H), 1.82−1.36 (m, 17H), 1.20 (s, 9H), 1.12−1.11 (m, 3H), 1.11 (s, 9H), 1.07 (s, 9H), 1.058 (s, 9H), 1.056 (s, 18H), 1.039 (s, 9H), 1.036 (s, 18H), 0.99 (s, 9H), 0.33 (s, 3H), 0.243 (s, 3H), 0.239 (s, 3H), 0.23 (s, 3H), 0.20 (s, 6H), 0.19 (s, 3H), 0.18 (s, 6H), 0.171 (s, 3H), 0.165 (s, 3H), 0.158 (s, 3H), 0.156 (s, 3H), 0.154 (s, 3H), 0.148 (s, 3H), 0.12 (s, 3H), 0.10 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (150 MHz, C_6D_6) δ 141.8, 136.7, 136.3, 136.1 (4C), 134.1, 134.0, 130.1 (4C), 128.3 (2C), 126.6, 126.5, 115.1, 83.3, 75.8, 74.5, 74.3, 74.0, 73.3, 72.9, 72.7, 72.3, 67.5, 43.1, 42.1, 39.5, 37.8 (2C), 37.6, 36.2, 33.6, 30.74, 30.70, 27.7, 27.2 (3C), 26.6 (3C), 26.4 (3C), 26.31 (6C), 26.26 (6C), 26.21 (3C), 26.18 (6C), 25.9, 21.8, 19.5, 18.8, 18.6 (2C), 18.53, 18.45 (2C), 18.38, 18.32, 18.30, 14.1, −2.8, −3.0, −3.6, −3.7, −3.8, −3.9, −4.03 (2C), −4.05, −4.19, −4.23 (3C), −4.27, −4.34, −4.36, −4.39, −4.5; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{100}H_{200}O_{10}Si_{10}Na$ 1864.2726, found 1864.2778.

■ 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.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: oishi@chem.kyushu-univ.jp.

Notes

The authors declare no competing financial interest.

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