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Total synthesis of brevenal

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ABSTRACT

The convergent total synthesis of brevenal, a non-toxic brevetoxin antagonist, has been achieved. The ABC ring segment and the E ring precursor were connected by the intramolecular allylation followed by ring-closing metathesis to furnish the pentacyclic ether compound. An alternative route to the key synthetic intermediate, a pentacyclic ether core, was also examined. The right- and left-hand side chains were introduced by Wittig and Horner–Wadsworth–Emmons reactions, respectively, to furnish brevenal (**1**).

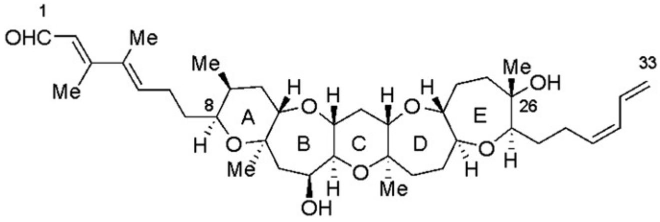
1. Introduction

In recent years there has been an explosion of interest in biologically active natural products of marine origin.[1] Due to their structural novelty and toxicity, polycyclic ethers are particularly attractive targets for synthetic chemists.[2] Brevenal (**1**) was isolated from *Karenia brevis* in 2004, as a new family of marine polycyclic ether (Fig. 1).[3] This compound inhibits the binding of tritiated dihydrobrevetoxin B to voltage-sensitive sodium channels in a concentration dependent manner without showing toxicity.[3] Moreover, a significant improvement of tracheal mucus velocity was observed in an animal model of asthma.[4] The novel biological activities and the unique structural features have attracted attention of synthetic chemists. In 2006, the first total synthesis and structural revision of **1** was reported by Sasaki and co-workers.[5] In this paper, we wish to describe a full detail of our total synthesis of brevenal (**1**).[6]

2. Results and discussion

2.1. First generation retrosynthetic analysis

Our retrosynthetic analysis of **1** is illustrated in Scheme 1. The right- and left-hand side chains would be constructed by Wittig and Horner–Wadsworth–Emmons reactions, respectively, at a later stage. A key synthetic intermediate, the pentacyclic ether core **2**, would be synthesized from **3** via the intramolecular allylation followed by ring-closing metathesis.[7] The substrate **3** was retrosynthetically broken down into the ABC ring segment **4** and the E ring precursor **5**. The tricycle **4** would be prepared from **6** and **7**.



Brevenal (**1**)

Figure 1. Structures of brevenal (**1**).

2.2. Synthesis of the ABC ring segment

Scheme 2 describes the synthesis of the ABC ring. Protection of the known alcohol **8**[8] with TBSCl/imidazole, reductive cleavage of the benzylidene acetal with DIBAL-H, and protection of the resulting primary alcohol with BnBr/KH gave the bis-benzyl ether **9** in 71% yield over three steps. Ozonolysis of the olefin **9** followed by Brown's asymmetric allylboration provided **10** as a single

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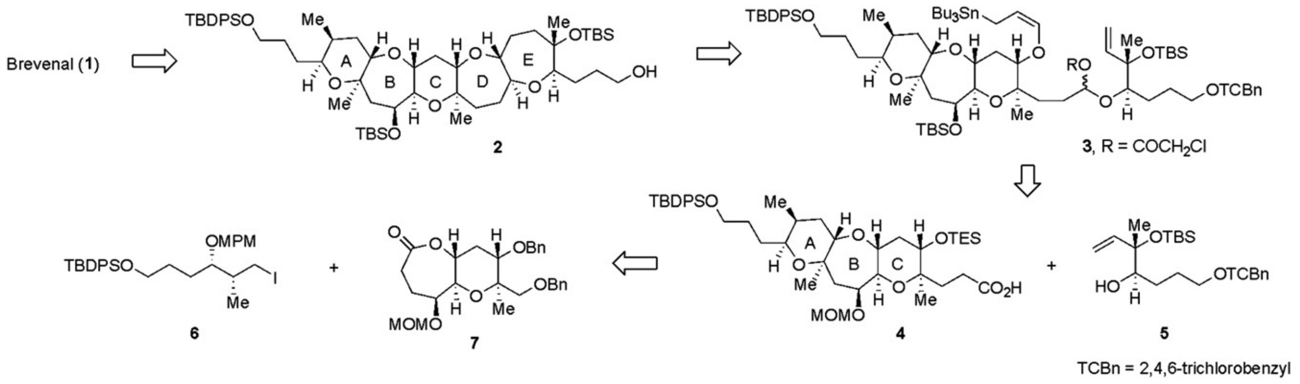
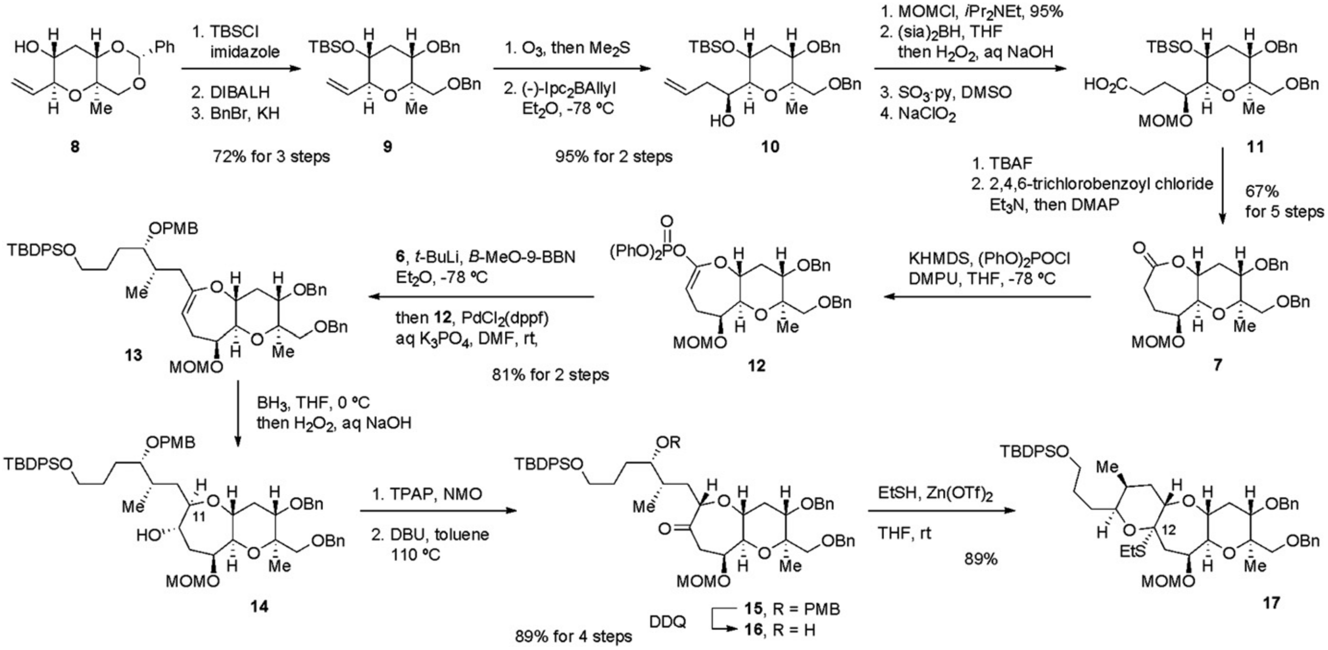


Scheme 1. Retrosynthetic analysis of **1**.



Scheme 2. Synthesis of the mixed thioacetal **17**.

stereoisomer in 95% yield over two steps.[9] Protection of the alcohol **10** with MOMCl/i-Pr_2NEt followed by hydroboration–oxidation afforded the corresponding alcohol. The alcohol obtained was subjected to the stepwise oxidation leading to the carboxylic acid **11**. Removal of the TBS group with TBAF, followed by the Yamaguchi lactonization provided **7** in 64% yield over six steps.[10] The lactone **7** was converted to the enol phosphate **12** with $(PhO)_2POCl$/KHMDS. The Suzuki–Miyaura coupling of **12** and an alkyl borate, prepared from the iodide **6**[5c] by known procedure,[11] was carried out with $PdCl_2$(dppf) to furnish the enol ether **13** in 81% yield over two steps.[12] Unfortunately, hydroboration of **13** with BH_3 followed by oxidative workup gave the undesired stereoisomer **14** as the sole product. Although the detailed conformational analysis of **13** was not carried out, the MOM group at C14 position seems to prevent the reagent approaching from the β-face of the olefin (Fig. 2). Since several attempts failed to obtain the desired product from **13** directly, stereoinversion at the C11 position was carried out. Oxidation of **14** with TPAP/NMO followed by treatment of the resulting ketone with DBU in toluene at 110 °C provided **15** as a single stereoisomer. Deprotection of the PMB group of **15** using DDQ furnished the alcohol **16** in 89% yield over four steps. Treatment of the hydoxy ketone **16** with EtSH/$Zn(OTf)_2$ gave the mixed thioacetal **17** in 89% yield.[5,13]

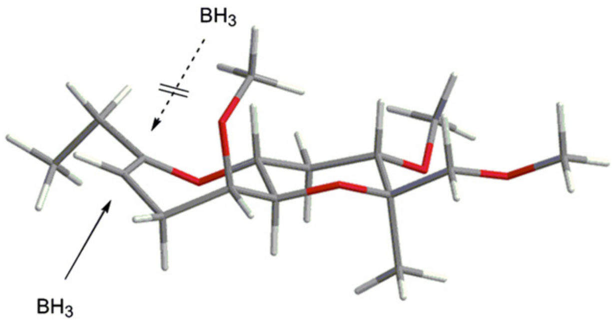
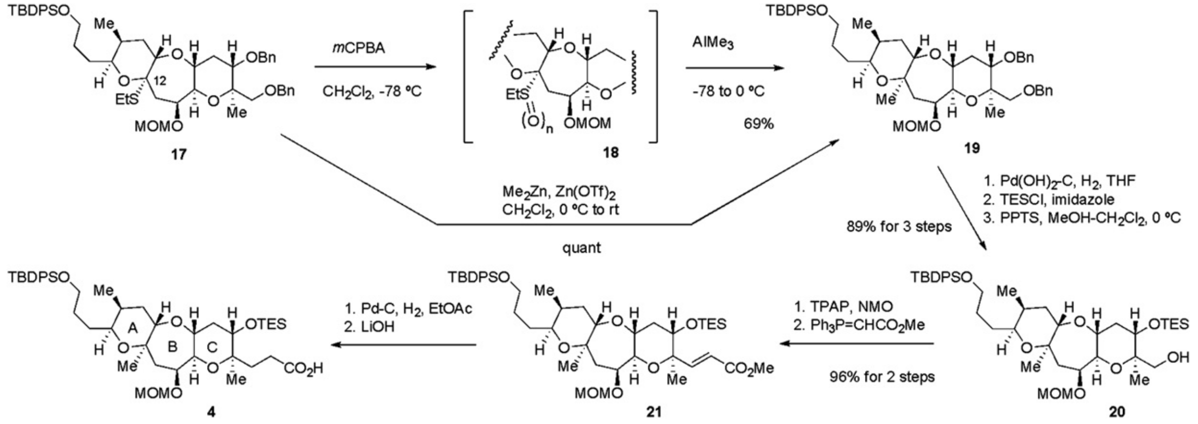


Figure 2. A plausible conformation for **13** composed by Chem 3D. The protective groups and side chain were replaced by methyl and ethyl groups for clarity.

We next examined the construction of an angular methyl group at the C12 position based on a reported procedure (Scheme 3). Thus, oxidation of **17** with m-CPBA followed by treatment of the resulting sulfoxide intermediate **18** with $AlMe_3$ provided **19** as a single stereoisomer in 69% yield.[5,14] Although, the desired product **19** was obtained in a reasonable yield, formation of significant amount of unidentified by-products was observed.

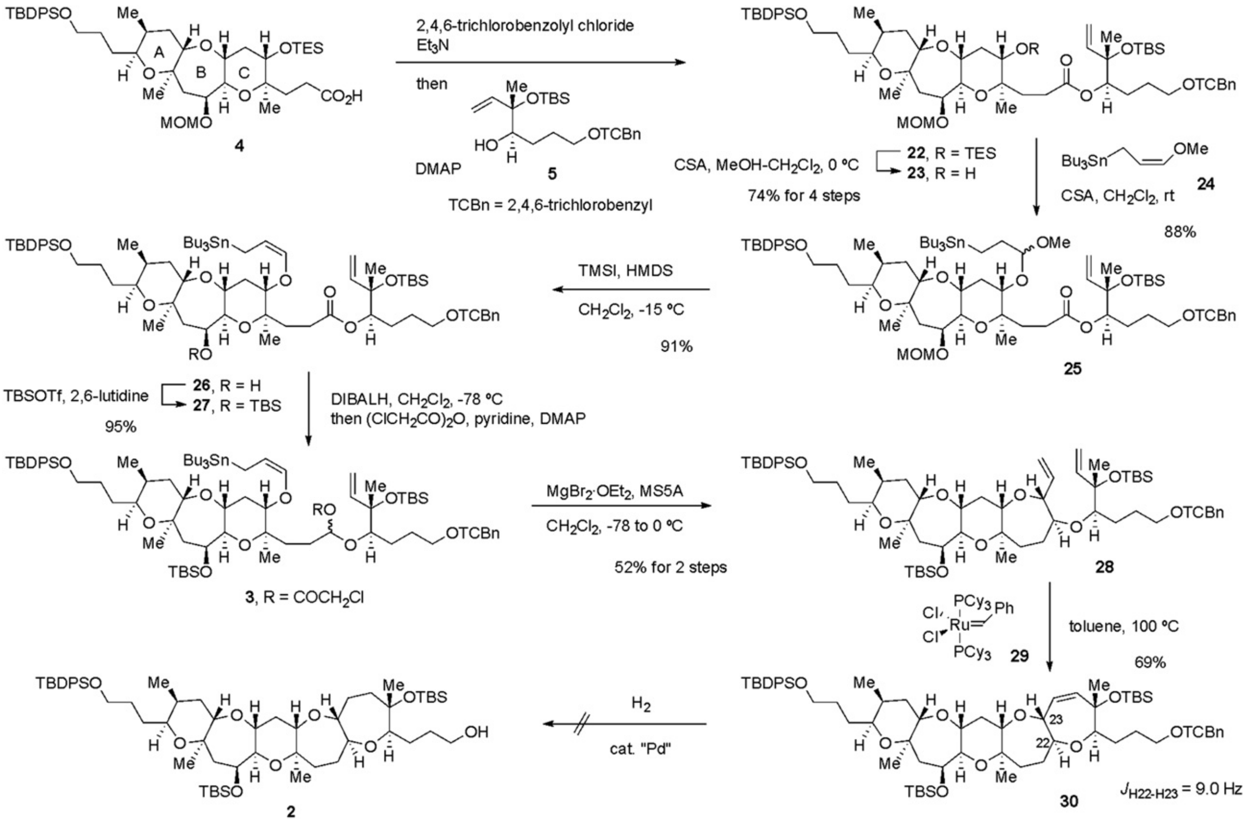


Scheme 3. Synthesis of the ABC ring segment **4**.

Furthermore the reproducibility of this reaction was not satisfactory in large-scale experiments, presumably, because of the low stability of the intermediate **18**. After several examinations, we found that the reaction of **17** with $Me_2Zn/Zn(OTf)_2$ furnished **19**, directly, in quantitative yield. The MOM protection was totally inert under the reaction conditions. Debenzylation of **19** with $H_2/Pd(OH)_2$–C, protection of the resulting diol with TESCl/imidazole, and selective cleavage of the primary TES ether under acidic conditions afforded **20** in 89% yield over three steps. TPAP oxidation of the alcohol **20** followed by Wittig reaction with $Ph_3P{=}CHCO_2Me$ gave the unsaturated ester **21** in 96% yield over two steps. The ester obtained was subjected to hydrogenation and saponification leading to the ABC ring segment **4**, which was used for the next reaction directly.

2.3. Coupling of the segments

We next examined the key segment coupling (Scheme 4). Thus, esterification of the carboxylic acid **4** and the known alcohol **5**[15] under the Yamaguchi conditions gave the ester **22**. The TES protection was cleaved with CSA, selectively, to provide **23** in 74% yield over four steps. Reaction of **23** with γ-methoxyallylstannane **24** in the presence of CSA provided the acetal **25** as a mixture of diastereoisomers in 88% yield. Treatment of **25** with TMSI/HMDS gave allylic stannane **26** in 91% yield.[16] Since the MOM protection was cleaved under the reaction conditions, the resulting hydroxy group of **26** was protected as a TBS ether to furnish **27** in 95% yield. Modified Rychnovsky acetylation of the ester **27** provided the α-chloroacetoxy ether **3**.[17,18] The cyclization precursor **3** was then

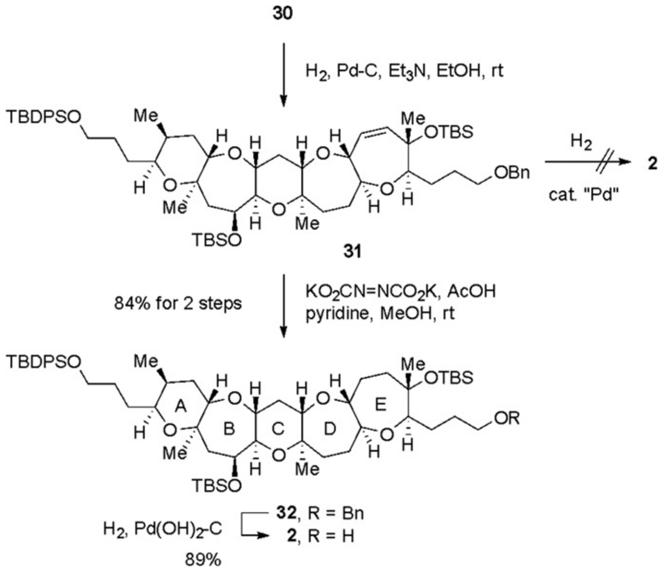


Scheme 4. Coupling of the segments **4** and **5**.

subjected to the intramolecular allylation with $MgBr_2 \cdot OEt_2$ to give **28** as a single stereoisomer in 52% yield over two steps. Ring-closing metathesis of the diene **28** was carried out with the Grubbs' catalyst **29** leading to the pentacyclic ether **30** in 69% yield.[19] At this stage, the trans relationship between H22 and H23 was confirmed by the coupling constant, $J_{H22-H23}$=9.0 Hz. Having synthesized the pentacyclic ether core, we next examined the deprotection of the 2,4,6-trichlorobenzyl (TCBn) group before constructing the left-hand side chain. However, the direct conversion of **30** to the alcohol **2** resulted in failure. Cleavage of the TCBn ether was very slow under the standard hydrogenation conditions such as H_2 and Pd catalysts, and decomposition of the substrate was observed when a prolonged reaction time was employed.[20]

2.4. Removal of the TCBn group

After several attempts, removal of the TCBn group was performed via the Sajiki's dechlorination procedure as shown in Scheme 5. Thus, the reaction of **30** with H_2/Pd–C in the presence of Et_3N afforded the corresponding benzyl ether **31** in quantitative yield.[21] Although the direct conversion to **2** under the hydrogenation conditions was unsatisfactory, reduction of the E ring olefin with diimide proceeded smoothly to furnish **32**, a synthetic intermediate of Sasaki's total synthesis,[5a,b,22] in 84% yield over two steps. Finally, debenzylation of **32** was carried out with H_2/Pd$(OH)_2$–C leading to **2** in 89% yield.



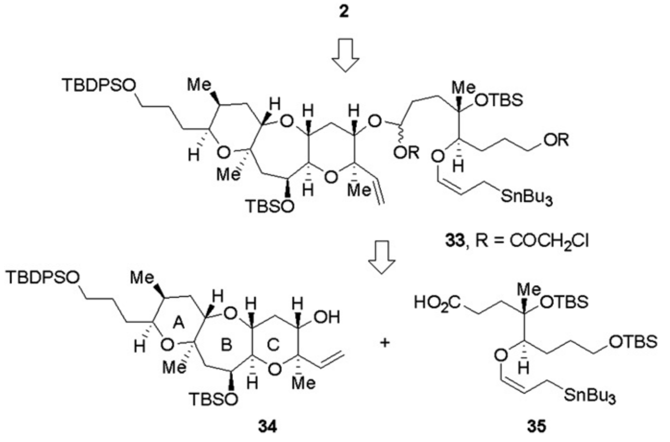
Scheme 5. Synthesis of the key intermediate **2**.

2.5. Second generation retrosynthesis of 2

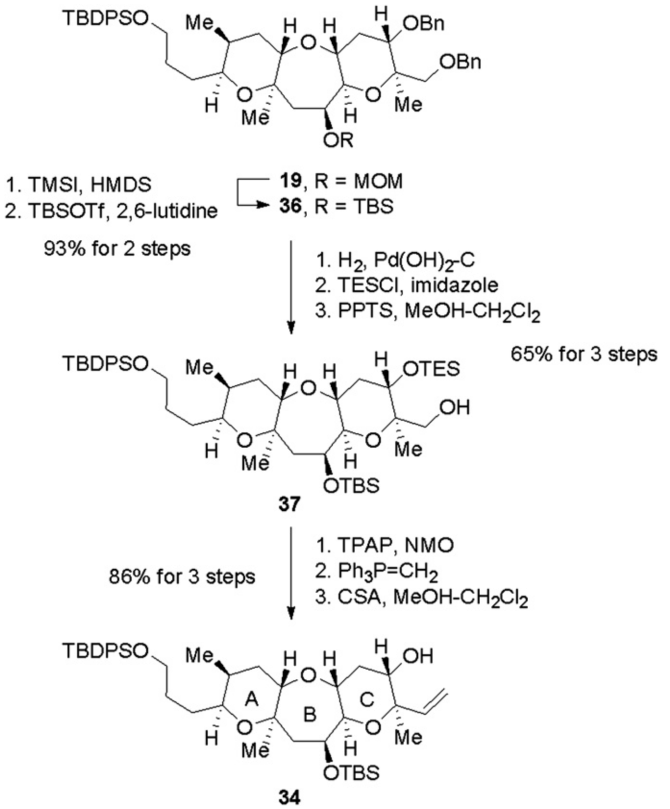
We next examined an alternative, more convergent approach to the key synthetic intermediate **2**. The retrosynthesis for the new strategy is shown in Scheme 6. The intramolecular allylation would be employed for the synthesis of the E ring, and the D ring moiety would be constructed by the ring-closing metathesis. The cyclization precursor **33** was retrosynthetically broken down into the ABC ring segment **34** and the E ring precursor **35**, which has an allylic stannane moiety.

2.6. Preparation of the ABC ring segment

The MOM protection of **19** was removed by TMSI/HMDS, and the resulting alcohol was protected with TBSOTf/2,6-lutidine to give **36** in 93% yield over two steps (Scheme 7). Debenzylation of **36**, followed by protection of the resulting diol with TESCl/imidazole and selective desilylation of the primary TES ether provided **37** in 65% yield over three steps. TPAP oxidation of the alcohol **37**, Wittig reaction, and selective removal of the TES protection furnished the ABC ring segment **34** in 86% yield over three steps.



Scheme 6. Second generation retrosynthesis of **2**.

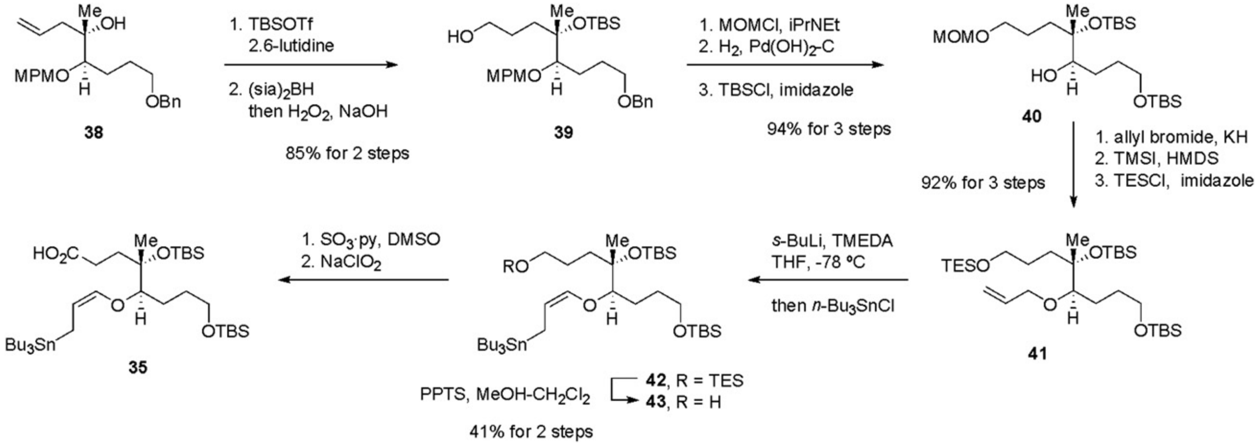


Scheme 7. Synthesis of the ABC ring segment **34**.

2.7. Preparation of the E ring precursor

Scheme 8 describes the synthesis of the E ring precursor **35** having an allylic stannane moiety. Protection of the alcohol **38**, prepared by the known procedure,[15] with TBSOTf/2,6-lutidine followed by hydroboration–oxidation afforded **39** in 85% yield over two steps. Protection of the alcohol **39** with MOMCl/*i*-

Pr_2NEt, deprotection of the Bn and MPM groups with H_2/Pd$(OH)_2$–C, and selective protection of the primary alcohol with TBSCl/imidazole afforded **40** in 94% yield over three steps. Treatment of **40** with allyl bromide/KH followed by deprotection of the MOM group with TMSI/HMDS and protection of the resulting alcohol with TESCl/imidazole provided the allyl ether **41** in 92% yield over three steps. Treatment of **41** with *s*-BuLi/TMEDA followed by trapping the resulting allylic anion with *n*-Bu_3SnCl gave the allylic stannane **42** in 64% yield.[23,24] Selective removal of the TES group with PPTS gave **43** in 65% yield. The primary alcohol **43** was subjected to the two-step oxidation leading to the carboxylic acid **35**, which was used for the next reaction without purification.



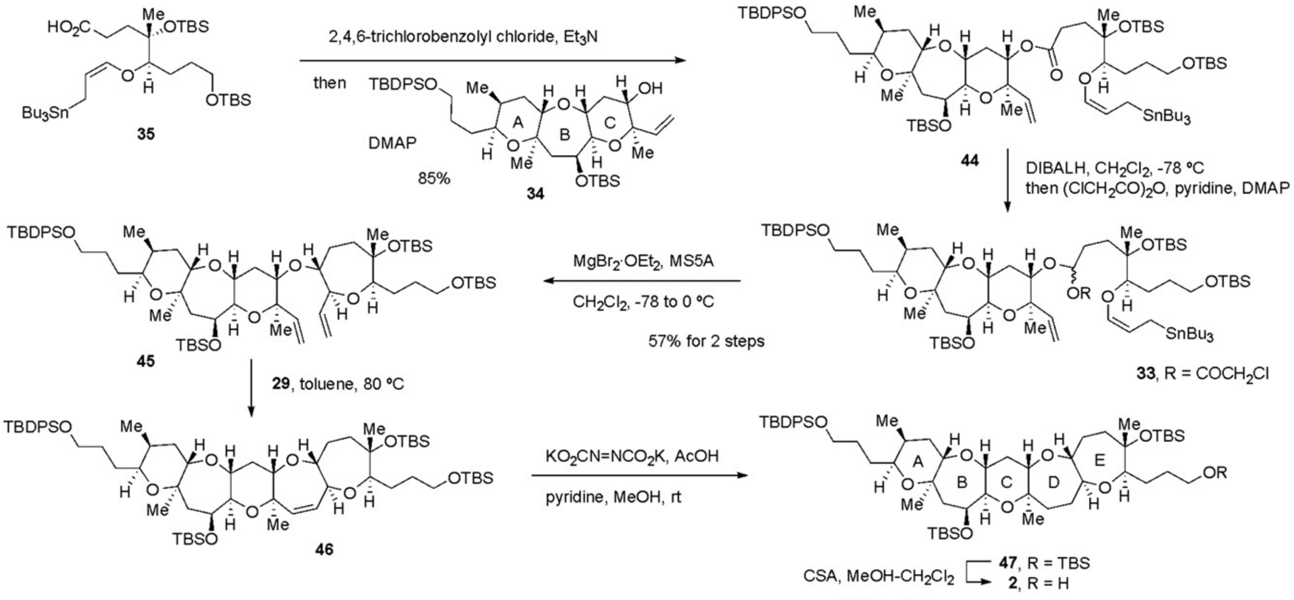
Scheme 8. Synthesis of the E ring precursor **35**.

2.8. Synthesis of the pentacycle 2

Synthesis of the key synthetic intermediate **2** is described in Scheme 9. Esterification of the carboxylic acid **35** and the alcohol **34** under the Yamaguchi conditions gave the ester **44** in 85% yield. Conversion of **44** to the cyclization precursor **33** was performed by the same procedure described in Scheme 4. Intramolecular allylation of **33** was carried out with $MgBr_2 \cdot OEt_2$ to give **45** as a single stereoisomer in 57% yield over two steps. Ring-closing metathesis of the diene **45** with the Grubbs' catalyst **29**, diimide reduction of the resulting olefin **46**, and selective removal of the primary TBS group of **47** with CSA furnished the A–E ring system **2** in 76% yield over three steps.

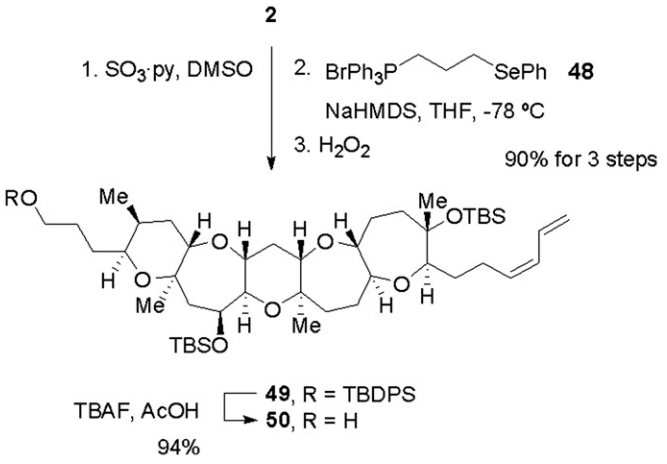
2.9. Construction of the right-hand side chain

Having the pentacyclic ether core **2** in hand, we next examined the synthesis of the diene side chains. Construction of the right-hand (*Z*)-diene moiety was carried out according to the Nicolaou's procedure (Scheme 10).[25] Thus, oxidation of **2** with $SO_3 \cdot py$/DMSO followed by Wittig reaction using a ylide generated from the phosphonium salt **48** and NaHMDS, and subsequent oxidation with H_2O_2 provided **49** as a single



Scheme 9. Coupling of the segments **34** and **35**.

stereoisomer in 90% yield over three steps. Selective removal of the TBDPS group was carried out with TBAF/AcOH to give the alcohol **50** in 94% yield.

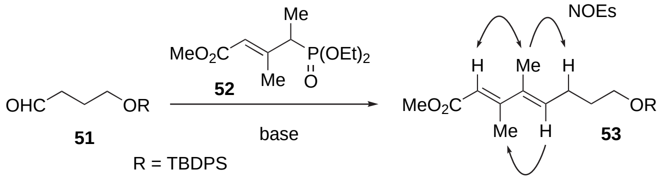


Scheme 10. Construction of the right-hand side chain.

2.10. Model studies for the construction of the (*E*,*E*)-diene side chain

Next task was the synthesis of the left-hand side chain. As well as the synthesis of the pentacyclic ether framework, the stereoselective construction of the left-hand side chain, highly substituted (*E*,*E*)-diene moiety, was one of the challenging problems inherent in the total synthesis of brevenal (**1**). We chose a Horner–Wadsworth–Emmons reaction as a possible route to the diene system, and tested the reaction using aldehyde **51** as a model substrate. Table 1 summarizes the results of the reaction of **51** with the phosphonate **52**[6,26] under various conditions. The best result was obtained from the reaction using *n*-BuLi as a base in the absence of any additives (entry 1). The desired product **53** was obtained in 92% yield as a single stereoisomer. The stereochemistry of **53** was determined by NOE experiments. None of the other olefinic isomer was detected in this reaction. The use of DMPU as an additive decreased the stereoselectivity (entries 2, 4, and 5). The reaction with LiHMDS gave the product in moderate yield although the high stereoselectivity was observed (entry 3). On the other hand, poor selectivity was obtained in the reaction with NaHMDS (entry 6).

Table 1
Horner–Wadsworth–Emmons reaction with phosphonate **52**[a]



Entry	Base	Additive	Solvent	Yield[b] (%)	*E*/*Z*[c]
1	*n*-BuLi	—	THF	92	>95:5
2	*n*-BuLi	DMPU	THF	96	93:7
3	LiHMDS	—	THF	41	>95:5
4	LiHMDS	DMPU	THF	61	93:7
5	LDA	DMPU	THF	87	89:11
6	NaHMDS	DMPU	THF	91	75:25

[a] Reactions were carried out with 5.0 equiv of **52** and 5.0 equiv of base at −78 °C to rt.

[b] Isolated yields.

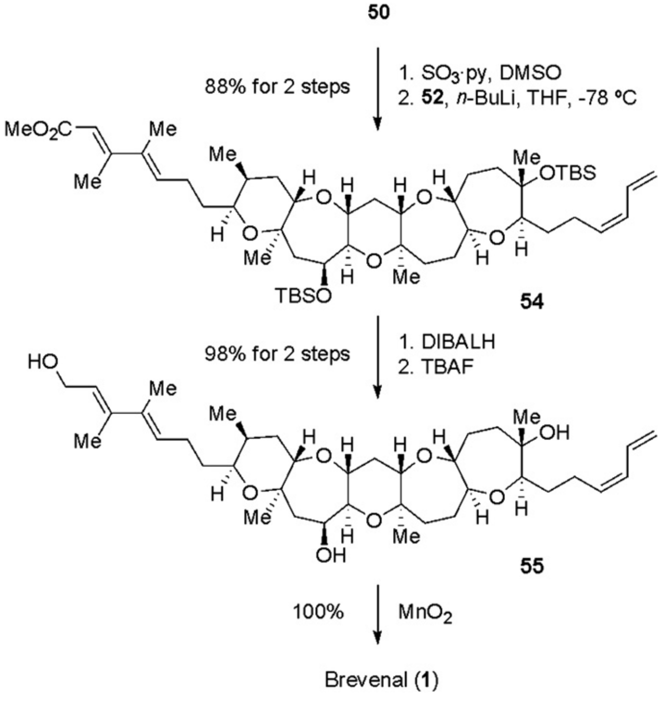
[c] The ratio was determined by ^{1}H NMR analysis.

2.11. Completion of the total synthesis of brevenal

Encouraged by the results obtained above, we faced up to the final stage of the total synthesis. Thus, after oxidation of **50** with $SO_3\cdot$py/DMSO, the resulting aldehyde was treated with the enolate generated from **52** and *n*-BuLi to provide **54** as a single stereoisomer in 88% yield over two steps. Reduction of the ester **54** with DIBAL-H followed by desilylation with TBAF afforded the triol **55** in 98% yield over two steps. Finally, selective oxidation of the allylic alcohol **55** with MnO_2 furnished brevenal (**1**) in quantitative yield. The synthetic **1** exhibited physical and spectroscopic data identical with those reported previously.

3. Conclusion

In conclusion, we have achieved a stereocontrolled total synthesis of brevenal (**1**). Key features of the synthetic strategy included the intramolecular allylation of an α-chloroacetoxy ether and ring-closing metathesis. In the first generation synthesis, the longest linear sequence leading to **1** was 57 steps with 1.2% overall yield. The second generation strategy provided **1** in 1.8% overall yield over 53 steps (the longest liner sequence). Novel methods for the direct methylation of a mixed thioacetal (Scheme 2) and the stereoselective synthesis of the left-hand (*E*,*E*)-diene system (Scheme 11) are also deserving of attention.



Scheme 11. Completion of the total synthesis of brevenal (**1**).

4. Experimental section

4.1. General

All reactions involving air- and/or moisture-sensitive materials were carried out under argon with dry solvents purchased from Wako or Kanto chemicals. On workup, extracts were dried over $MgSO_4$. Reactions were monitored by thin-layer chromatography carried out on 0.25 mm Merck silica gel plates (60F-254). Column chromatography was performed with Kanto Chemical silica gel 60N

(40–100 mesh, spherical, neutral) or Fuji Silysia silica gel BW-300 (200–400 mesh). Yields refer to chromatographically and spectroscopically homogeneous materials. The NMR spectra were recorded on JEOL JNM-AL400 (^{1}H, ^{13}C NMR). Chemical shifts were reported in delta units (δ) relative to chloroform (7.24) or benzene (7.15). IR spectra were recorded on a JASCO FT/IR-460 Plus. Optical rotations were measured by a JASCO DIP-1000. Mass spectra were measured by Micromass LCT (ESI TOF-MS).

4.2. Bis-benzyl ether 9

To a solution of **8** (11.3 g, 40.8 mmol) in DMF (200 mL) at room temperature were added imidazole (5.56 g, 81.6 mmol) and TBSCl (9.24 g, 61.2 mmol). After stirring for 2 h at 50 °C, the reaction mixture was quenched with MeOH. The mixture was diluted with EtOAc, then washed with water and brine. After concentration, the residue was passed through a short silica gel column (hexane/EtOAc, 10:1) to give the crude silyl ether, which was used for the next reaction directly.

To a solution of the crude silyl ether in CH_2Cl_2 (180 mL) at −78 °C was added DIBAL-H (168 mL, 163.3 mmol, 0.97 M solution in hexane). The mixture was allowed to warm to room temperature over 5.5 h. The reaction mixture was quenched with MeOH, filtered through a Celite pad, and concentrated. The residue was purified by chromatography (hexane/EtOAc, 25:1 to 10:1 to 6:1 to 2:1) to give the corresponding primary alcohol (11.6 g, 72% for the 2 steps) and unreacted starting material (3.22 g, 20% recovery): colorless oil; R_f=0.38 (hexane/EtOAc, 4:1); $[\alpha]_D^{28}$ −32.4 (*c* 1.00, $CHCl_3$); IR (neat) 3466, 3033, 1072 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.26 (m, 5H), 5.78 (ddd, *J*=17.1, 10.5, 6.0 Hz, 1H), 5.29 (ddd, *J*=17.1, 1.6, 1.6 Hz, 1H), 5.17 (ddd, *J*=10.5, 1.6, 1.0 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.51 (d, *J*=11.7 Hz, 1H), 3.78 (dd, *J*=9.0, 6.0 Hz, 1H), 3.68 (dd, *J*=12.0, 4.4 Hz, 1H), 3.62–3.48 (m, 2H), 3.25 (ddd, *J*=11.2, 9.3, 4.9 Hz, 1H), 2.17 (ddd, *J*=9.3, 4.6, 4,6 Hz, 1H), 2.02 (dd, *J*=9.5, 3.7 Hzw, 1H), 1.62 (q, *J*=12.0 Hz, 1H), 1.17 (s, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.4 (2C), 136.4, 128.3, 127.6, 127.5 (2C), 116.9, 76.5, 75.7, 73.2, 71.5, 70.8, 67.7, 34.8, 25.8 (3C), 18.1, 13.7, −4.1, −4.4; HRMS (ESI TOF) calcd for $C_{22}H_{36}O_4SiNa$ $(M+Na)^+$ 415.2281, found 415.2275.

To a stirred suspension of KH (5.81 g, 72.4 mmol, 50%, prewashed with hexane) in THF (100 mL) at 0 °C were added a solution of the alcohol (19.0 g, 48.3 mmol) in THF (100 mL) and BnBr (8.6 mL, 72.4 mmol). After stirring for 1 h at room temperature, the reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 100:1 to 50:1) gave **9** (23.1 g, 99%): light yellow oil; R_f=0.53 (hexane/EtOAc, 10:1); $[\alpha]_D^{23}$ −29.6 (*c* 1.00, $CHCl_3$); IR (neat) 3030, 1093 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34–7.23 (m, 10H), 5.85 (ddd, *J*=17.1, 10.5, 6.1 Hz, 1H), 5.31 (ddd, *J*=17.1, 2.0, 2.0 Hz, 1H), 5.16 (ddd, *J*=10.5, 2.0, 1.0 Hz, 1H), 4.64 (d, *J*=12.6 Hz, 1H), 4.54 (d, *J*=12.6 Hz, 1H), 4.53 (d, *J*=11.8 Hz, 1H), 4.43 (d, *J*=11.8 Hz, 1H), 3.77 (dd, *J*=9.0, 6.1 Hz, 1H), 3.72 (dd, *J*=12.2, 4.6 Hz, 1H), 3.55 (d, *J*=10.6 Hz, 1H), 3.44 (d, *J*=10.6 Hz, 1H), 3.30 (ddd, *J*=11.0, 9.2, 4.6 Hz, 1H), 2.15 (ddd, *J*=12.0, 4.9, 4,9 Hz, 1H), 1.62 (q, *J*=12.0 Hz, 1H), 1.17 (s, 3H), 0.85 (s, 9H), 0.01 (s, 3H), −0.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 136.8, 128.2 (2C), 127.6 (2C), 127.5 (2C), 127.4 (2C), 127.3 (2C), 116.8, 77.2, 76.0, 74.7, 73.6, 73.5, 71.4, 70.7, 34.9, 25.9 (3C), 18.1, 13.7, −4.1, −4.4; HRMS (ESI TOF) calcd for $C_{29}H_{42}O_4SiNa$ $(M+Na)^+$ 505.2750, found 505.2739.

4.3. Homoallylic alcohol 10

Ozone was passed through a solution of **9** (2.88 g, 5.96 mmol) in $MeOH/CH_2Cl_2$ (6.0 mL/4.5 mL) at −78 °C until the solution turned to blue. After removal of excess ozone with an oxygen stream, the mixture was treated with Me_2S (1.32 mL, 17.9 mmol) and allowed to warm to room temperature with stirring. Concentration gave the corresponding crude aldehyde, which was used for the next reaction directly.

To a solution of (−)-Ipc_2BOMe (3.77 g, 11.9 mmol) in Et_2O (15 mL) at 0 °C was added allylmagnesium bromide (11.9 mL, 11.9 mmol, 1.0 M solution in Et_2O). After stirring for 70 min at room temperature, the mixture was cooled to −78 °C. To this mixture was added a solution of the crude aldehyde in Et_2O (15 mL). After stirring for 1 h at −78 °C, the reaction mixture was allowed to warm to room temperature over 1.5 h with stirring before quenching with MeOH at 0 °C. To the mixture were added 3 M NaOH (7.0 mL) and 30% H_2O_2 (7.0 mL) at the same temperature, and the reaction mixture was stirred for 40 min at 30 °C. The reaction mixture was quenched with saturated Na_2SO_3 at 0 °C and then stirred for 20 min at room temperature. The mixture was diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 5:1) gave **10** (2.99 g, 95% for the 2 steps) as a single stereoisomer: colorless oil; R_f=0.30 (hexane/EtOAc, 4:1); $[\alpha]_D^{23}$ −36.2 (*c* 1.00, $CHCl_3$); IR (neat) 3492, 2980, 1087 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.25 (m, 10H), 5.92 (dddd, *J*=17.1, 9.8, 7.1, 7.1 Hz, 1H), 5.10 (dd, *J*=17.1, 1.5 Hz, 1H), 5.06 (ddd, *J*=9.8, 1.5, 1.0 Hz, 1H), 4.59 (d, *J*=12.4 Hz, 1H), 4.54 (d, *J*=12.4 Hz, 1H), 4.52 (d, *J*=11.7 Hz, 1H), 4.47 (d, *J*=11.7 Hz, 1H), 3.82 (m, 1H), 3.68 (dd, *J*=12.0, 4.6 Hz, 1H), 3.58–3.52 (m, 1H), 3.53 (d, *J*=10.5 Hz, 1H), 3.40 (d, *J*=10.5 Hz, 1H), 3.36 (dd, *J*=9.0, 5.4 Hz, 1H), 2.41–2.32 (m, 1H), 2.30–2.22 (m, 1H), 2.12 (ddd, *J*=12.0, 4.6, 4.6 Hz, 1H), 1.59 (q, *J*=12.0 Hz, 1H), 1.13 (s, 3H), 0.86 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 138.5, 135.3, 128.2 (4C), 127.5 (2C), 127.4 (2C), 127.3 (2C), 116.8, 77.2, 75.6, 74.6, 73.5, 73.4, 72.2, 71.7, 70.5, 36.6, 35.2, 25.8 (3C), 17.9, 13.6, −3.6, −4.6; HRMS (ESI TOF) calcd for $C_{31}H_{46}O_5SiNa$ $(M+Na)^+$ 549.3012, found 549.2993.

4.4. Lactone 7

To a solution of **10** (7.23 g, 13.7 mmol) in CH_2Cl_2 (60 mL) at room temperature were added diisopropylethylamine (14.1 mL, 82.3 mmol) and MOMCl (4.1 mL, 54.9 mmol). After stirring for 1 h, the reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. Concentration and chromatography (hexane/EtOAc, 20:1 to 10:1 to 5:1) gave the corresponding MOM ether (7.43 g, 95%): colorless oil; R_f=0.60 (hexane/EtOAc, 4:1); $[\alpha]_D^{24}$ −46.9 (*c* 1.00, $CHCl_3$); IR (neat) 3030, 2929, 1641 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.23 (m, 10H), 5.93 (dddd, *J*=17.1, 10.0, 7.1, 7.1 Hz, 1H), 5.07 (dd, *J*=17.1, 2.0 Hz, 1H), 5.01 (dd, *J*=10.0, 2.0 Hz, 1H), 4.71 (d, *J*=6.9 Hz, 1H), 4.63 (d, *J*=12.0 Hz, 1H), 4.61 (d, *J*=6.9 Hz, 1H), 4.55 (d, *J*=11.5 Hz, 1H), 4.52 (d, *J*=12.0 Hz, 1H), 4.49 (d, *J*=11.5 Hz, 1H), 3.87 (ddd, *J*=9.5, 3.7, 1.0 Hz, 1H), 3.72 (dd, *J*=12.0, 4.4 Hz, 1H), 3.60–3.56 (m, 1H), 3.58 (d, *J*=10.5 Hz, 1H), 3.47 (d, *J*=10.5 Hz, 1H), 3.43 (ddd, *J*=9.0, 4.8, 4.8 Hz, 1H), 3.35 (s, 3H), 2.49–2.40 (m, 1H), 2.29–2.20 (m, 1H), 2.12 (ddd, *J*=12.0, 4.6, 4.6 Hz, 1H), 1.57 (q, *J*=12.0 Hz, 1H), 1.14 (s, 3H), 0.86 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.9, 138.7, 136.3, 128.2 (2C), 128.1 (2C), 127.5 (2C), 127.4 (2C), 127.3, 127.2, 116.4, 95.9, 77.2, 76.5, 76.4, 74.7, 73.6, 73.3, 71.6, 67.3, 55.6, 35.1, 33.9, 25.8 (3C), 17.9, 13.3, −3.7, −4.6; HRMS (ESI TOF) calcd for $C_{33}H_{50}O_6SiNa$ $(M+Na)^+$ 593.3275, found 593.3295.

To a solution of 2-methyl-2-butene (0.5 mL, 4.55 mmol) in THF (2 mL) at 0 °C was added $BH_3\cdot SMe_2$ (0.2 mL, 2.28 mmol) and stirred for 15 min at the same temperature. To the mixture was added a solution of the MOM ether (260 mg, 0.455 mmol) in THF (2.5 mL), and the resulting mixture was stirred for 1 h at room temperature. To the mixture were added 3 M NaOH (1 mL) and 30% H_2O_2 (1 mL) at 0 °C, and the reaction mixture was stirred for 10 min at room temperature. To the mixture at 0 °C was added saturated Na_2SO_3, and the stirring was continued for additional 20 min at room temperature. The mixture was diluted with EtOAc, then washed with water and brine. Concentration gave the crude alcohol, which was used for the next reaction directly.

To a solution of the crude alcohol in CH_2Cl_2 (2 mL) and DMSO (0.5 mL) at 0 °C were added Et_3N (0.3 mL, 2.28 mmol) and $SO_3 \cdot py$ (217 mg, 1.37 mmol), and the mixture was stirred for 1 h at room temperature. The mixture was diluted with EtOAc, then washed with saturated NH_4Cl, water, and brine. Concentration gave the crude aldehyde, which was used for the next reaction directly.

To a solution of the crude aldehyde in *t*-BuOH (1.5 mL) and 2-methyl-2-butene (1.5 mL) at 0 °C were added 5% NaH_2PO_4 (3.0 mL) and $NaClO_2$ (412 mg, 4.55 mmol), and the mixture was stirred vigorously at the same temperature for 3 h. The mixture was diluted with Et_2O, then washed with water and brine. Concentration gave the crude carboxylic acid **11**, which was used for the next reaction directly.

To a solution of the crude carboxylic acid **11** was added TBAF (2.3 mL, 2.30 mmol, 1.0 M solution in THF), and the mixture was stirred for 7 h at 50 °C. The mixture was diluted with Et_2O, then washed with saturated NH_4Cl, water, and brine. Concentration gave the crude hydroxy carboxylic acid, which was used for the next reaction directly.

To a solution of the crude hydroxy carboxylic acid in THF (3.0 mL) were added Et_3N (0.13 mL, 0.910 mmol) and 2,4,6-trichlorobenzoyl chloride (0.11 mL, 0.675 mmol). After stirring for 1.5 h at room temperature, the reaction mixture was concentrated under reduced pressure and diluted with toluene (10 mL). To the mixture was added DMAP (111 mg, 0.910 mmol) in toluene (7 mL), and stirred for 40 min at room temperature. The mixture was diluted with EtOAc and filtered through a Celite pad. The filtrate was concentrated, and the residue was purified by chromatography (hexane/EtOAc, 5:1 to 2.5:1) to give **7** (144 mg, 67% for the 5 steps): yellow oil; R_f=0.53 (hexane/EtOAc, 1:1); $[\alpha]_D^{22}$ +3.2 (*c* 1.00, $CHCl_3$); IR (neat) 3031, 1739, 1038 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.32–7.22 (m, 10H), 4.84 (d, *J*=6.6 Hz, 1H), 4.62–4.55 (m, 1H), 4.61 (d, *J*=6.6 Hz, 1H), 4.57 (d, *J*=12.0 Hz, 1H), 4.53 (d, *J*=12.0 Hz, 1H), 4.45 (d, *J*=12.0 Hz, 1H), 4.44 (d, *J*=12.0 Hz, 1H), 4.03–3.98 (m, 1H), 3.72 (dd, *J*=12.0, 4.4 Hz, 1H), 3.57–3.52 (m, 1H), 3.52 (d, *J*=10.5 Hz, 1H), 3.40 (d, *J*=10.5 Hz, 1H), 3.32 (s, 3H), 3.03 (t, *J*=13.0 Hz, 1H), 2.45–2.35 (m, 2H), 2.11–2.02 (m, 1H), 1.90–1.76 (m, 2H), 1.15 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 138.3, 138.2, 128.3 (2C), 128.2 (2C), 127.6 (2C), 127.5 (2C), 127.4 (2C), 97.2, 77.2, 74.6, 74.0, 73.4, 73.2, 72.4, 71.5, 70.0, 55.6, 30.3, 27.6, 27.1, 13.1; HRMS (ESI TOF) calcd for $C_{27}H_{34}O_7Na$ $(M+Na)^+$ 493.2202, found 493.2216.

4.5. Enol ether 13

To a solution of **7** (699 mg, 1.48 mmol), DMPU (0.98 mL, 3.70 mmol), and $(PhO)_2POCl$ (0.55 mL, 2.67 mmol) in THF (10 mL) at −78 °C was added KHMDS (5.9 mL, 2.95 mmol, 0.5 M solution in toluene). After stirring for 0.5 h at −78 °C, the reaction mixture was quenched with a 1:1 mixture of saturated $NaHCO_3$ and MeOH (3 ml), and the resultant mixture was allowed to warm to room temperature. The mixture was diluted with Et_2O, then washed with water and brine, and concentrated. The residue was passed through a short pad of silica gel column (hexane/EtOAc, 2:1) to give the crude enol phosphate **12**, which was used for the next reaction without further purification.

To a solution of **6** (1.63 g, 2.64 mmol) in Et_2O (15 mL) at −78 °C was added *t*-BuLi (4.4 mL, 5.28 mmol, 1.2 M solution in pentane). After stirring for 3 min at −78 °C a mixture of 9-BBN–OMe (6.6 mL, 6.60 mmol, 1.0 M solution in hexane) in THF (12 mL) was introduced, and the mixture was allowed to warm to room temperature over 1.5 h. To the mixture were added 3 M K_3PO_4 (2.2 mL, 6.60 mmol) and a solution of the crude enol phosphate **12** and $PdCl_2(dppf)$ (122 mg, 0.149 mmol) in a 5:1 mixture DMF and THF (18 mL), and the mixture was stirred for 40 min at room temperature. To the reaction mixture were added 3 M NaOH (5 mL) and 30% H_2O_2 (5 mL) at 0 °C, and stirred for 20 min at room temperature. The mixture was quenched with saturated Na_2SO_3 at 0 °C and stirred for 0.5 h at room temperature. The resulting mixture was diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 10:1 to 8:1 containing 0.5% Et_3N) gave **13** (1.13 g, 81% for the 2 steps): yellow oil; R_f=0.34 (hexane/EtOAc, 4:1); $[\alpha]_D^{25}$ +17.5 (*c* 1.00, $CHCl_3$); IR (neat) 3028, 2933, 1109 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.82–7.76 (m, 4H), 7.34–7.03 (m, 18H), 6.81 (d, *J*=8.8 Hz, 2H), 4.94 (d, *J*=6.4 Hz, 1H), 4.73 (dd, *J*=8.3, 3.4 Hz, 1H), 4.71 (d, *J*=6.4 Hz, 1H), 4.52 (d, *J*=12.0 Hz, 1H), 4.49–4.37 (m, 4H), 4.27 (d, *J*=12.0 Hz, 1H), 4.02–3.93 (m, 2H), 3.83 (dd, *J*=12.0, 4.6 Hz, 1H), 3.76–3.66 (m, 2H), 3.57 (d, *J*=10.5 Hz, 1H), 3.53 (dd, *J*=9.5, 2.2 Hz, 1H), 3.42 (d, *J*=10.5 Hz, 1H), 3.35–3.25 (m, 1H), 3.31 (s, 3H), 3.30 (s, 3H), 2.56 (dd, *J*=12.0, 2.7 Hz, 1H), 2.52 (ddd, *J*=11.7, 5.0, 5.0 Hz, 1H), 2.33–2.12 (m, 3H), 1.99–1.61 (m, 6H), 1.18 (s, 9H), 1.18 (s, 3H), 1.13 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 159.5, 158.2 (2C), 139.4, 139.3, 136.0 (4C), 134.5 (4C), 131.9 (2C), 129.9 (2C), 129.4 (2C), 128.5 (2C), 128.4 (2C), 127.9 (4C), 127.6 (2C), 114.0 (2C), 105.2, 96.7, 82.2, 78.3, 77.4, 75.2, 74.1, 73.8, 73.4, 71.8, 71.6, 71.5, 64.5, 55.3, 54.9, 39.8, 33.6, 32.5, 29.6, 28.2, 27.3 (3C), 27.2, 19.6, 15.4, 13.4; HRMS (ESI TOF) calcd for $C_{58}H_{74}O_9SiNa$ $(M+Na)^+$ 965.0000, found 965.0001.

4.6. Hydroxy ketone 16

To a solution of **13** (332 mg, 0.352 mmol) in THF (1.5 mL) at 0 °C was added $BH_3 \cdot THF$ (3.5 mL, 3.50 mmol, 1.0 M solution in THF). After stirring for 40 min at the same temperature, the mixture was quenched with MeOH at 0 °C. The mixture was then treated with 3 M NaOH (2 mL) and 30% H_2O_2 (2 mL), and the resulting mixture was stirred for 20 min at the same temperature. The mixture was quenched with saturated Na_2SO_3 at 0 °C and stirred for 0.5 h at room temperature. The mixture was diluted with EtOAc, then washed with water and brine. Concentration gave the crude alcohol **14**, which was used for the next reaction directly.

To a stirred solution of the crude alcohol **14** and MS4 Å in CH_2Cl_2 (3 mL) at 0 °C were added TPAP (14.1 mg, 40.1 μmol) and NMO (82.5 mg, 0.704 mmol). After stirring for 1.5 h at room temperature, the mixture was filtered through a short silica gel column (hexane/EtOAc, 2:1) to give the crude ketone, which was used for the next reaction directly.

A mixture of the crude ketone and DBU (0.11 mL, 0.704 mmol) in toluene (3 mL) was heated at 110 °C with stirring. After 3 h, the mixture was filtered through a short silica gel column (hexane/EtOAc, 2:1) to give ketone **15**, which was used for the next reaction without further purification.

To a solution of the ketone **15** in CH_2Cl_2 (7.5 mL) and saturated $NaHCO_3$ (1.5 mL) was added DDQ (160 mg, 0.704 mmol). After stirring for 0.5 h at room temperature, the reaction mixture was diluted with CH_2Cl_2, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 7:1 to 4:1 to 2:1) gave **16** (263 mg, 89% for the 4 steps): light yellow oil; R_f=0.33 (hexane/EtOAc, 2:1); $[\alpha]_D^{26}$ −32.8 (*c* 0.97, $CHCl_3$); IR (neat) 3686–3243, 2940, 1715 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.67–7.63 (m, 4H), 7.40–7.20 (m, 16H), 4.74 (d, *J*=6.8 Hz, 1H), 4.57 (d, *J*=11.5 Hz, 1H), 4.57 (d, *J*=6.8 Hz, 1H), 4.53 (d, *J*=12.0 Hz, 1H), 4.45 (d, *J*=12.0 Hz, 1H), 4.40 (d, *J*=11.5 Hz, 1H), 4.09 (br d, *J*=7.8 Hz, 1H), 3.84 (dd, *J*=10.1, 3.4 Hz, 1H), 3.72–3.63 (m, 3H), 3.58 (br d, *J*=3.9 Hz, 2H), 3.53–3.46 (m, 1H), 3.51 (d, *J*=10.3 Hz, 1H), 3.41 (d, *J*=10.3 Hz, 1H), 3.33 (s, 3H), 2.99 (d, *J*=12.9 Hz, 1H), 2.73 (dd, *J*=12.9, 7.8 Hz, 1H), 2.35 (ddd, *J*=11.7, 3.9, 3.9 Hz, 1H), 2.22 (br s, 1H), 1.81–1.40 (m, 8H), 1.17 (s, 3H), 1.03 (s, 9H), 0.90 (d, *J*=6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 212.7, 138.5, 138.4, 135.5 (4C), 133.7 (2C), 129.5 (2C), 128.2 (4C), 127.6 (2C), 127.5

(6C), 127.4 (2C), 96.2, 85.9, 77.5, 77.2, 74.8, 74.7, 74.4, 73.5 (2C), 71.6, 71.3, 64.1, 55.6, 43.7, 36.0, 35.5, 31.7, 30.6, 29.5, 26.9 (3C), 19.3, 13.6, 13.4; HRMS (ESI TOF) calcd for $C_{50}H_{66}O_9SiNa$ $(M+Na)^+$ 861.4374, found 861.4376.

4.7. Mixed thioacetal 17

To a solution of **16** (182 mg, 0.217 mmol) in THF (2 mL) were added EtSH (0.32 mL, 4.35 mmol) and $Zn(OTf)_2$ (115 mg, 0.326 mmol). After stirring for 15 min at room temperature, the mixture was quenched with Et_3N, and the insoluble material was filtered off through a Celite pad. The filtrate was concentrated and purified by chromatography (hexane/EtOAc, 15:1) to give **17** (171 mg, 89%): colorless oil; R_f=0.53 (hexane/EtOAc, 4:1); $[\alpha]_D^{27}$ −38.9 (*c* 1.00, $CHCl_3$); IR (neat) 3030, 2931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.61 (m, 4H), 7.42–7.32 (m, 6H), 7.32–7.20 (m, 10H), 4.72 (d, *J*=6.6 Hz, 1H), 4.65 (d, *J*=6.6 Hz, 1H), 4.57 (d, *J*=11.8 Hz, 1H), 4.54 (d, *J*=12.2 Hz, 1H), 4.48 (d, *J*=12.2 Hz, 1H), 4.39 (d, *J*=11.8 Hz, 1H), 4.15 (dd, *J*=11.8, 5.0 Hz, 1H), 4.00–3.95 (m, 1H), 3.93 (d, *J*=9.5 Hz, 1H), 3.85–3.78 (m, 1H), 3.75–3.57 (m, 4H), 3.48 (d, *J*=10.5 Hz, 1H), 3.41 (d, *J*=10.5 Hz, 1H), 3.33 (s, 3H), 2.68 (dd, *J*=15.8, 5.1 Hz, 1H), 2.41–2.21 (m, 4H), 2.03 (ddd, *J*=12.4, 12.4, 4.5 Hz, 1H), 1.83–1.75 (m, 1H), 1.72–1.35 (m, 6H), 1,19 (t, *J*=7.6 Hz, 3H), 1.16 (s, 3H), 1.02 (s, 9H), 0.90 (d, *J*=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 135.5 (4C), 134.0 (2C), 129.5 (2C), 128.2 (4C), 127.5 (4C), 127.4 (2C), 127.3 (2C), 127.2 (2C), 96.4, 93.0, 77.2, 75.9, 75.1, 74.4, 73.9, 73.7, 73.4 (2C), 72.7, 71.7, 70.9, 63.9, 55.4, 46.0, 35.5, 31.9, 31.6, 29.5, 28.7, 26.9 (3C), 19.3, 14.4, 13.3, 12.9; HRMS (ESI TOF) calcd for $C_{52}H_{70}O_8SSiNa$ $(M+Na)^+$ 905.4459, found 905.4427.

4.8. Tricycle 19

To a solution of **17** (171 mg, 0.194 mmol) in CH_2Cl_2 (2 mL) at 0 °C were added Me_2Zn (1.9 mL, 1.90 mmol, 1.0 M solution in hexane) and $Zn(OTf)_2$ (2.6 mg, 0.58 mmol), and the reaction mixture was allowed to warm to room temperature over 1 h with stirring. After quenching with a 1:1 mixture of MeOH and Et_3N (1 mL), the mixture was diluted with Et_2O and filtered through a Celite pad. Concentration and chromatography (hexane/EtOAc, 10:1) gave **19** (163 mg, quant.): colorless oil; R_f=0.50 (hexane/EtOAc, 4:1); $[\alpha]_D^{24}$ −18.7 (*c* 0.97, $CHCl_3$); IR (neat) 3030, 2931 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J*=7.8, 1.4 Hz, 4H), 7.42–7.32 (m, 6H), 7.32–7.20 (m, 10H), 4.73 (d, *J*=6.6 Hz, 1H), 4.70 (d, *J*=6.6 Hz, 1H), 4.58 (d, *J*=11.7 Hz, 1H), 4.56 (d, *J*=12.2 Hz, 1H), 4.49 (d, *J*=12.2 Hz, 1H), 4.41 (d, *J*=11.7 Hz, 1H), 4.17 (dd, *J*=11.5, 5.1 Hz, 1H), 3.98–3.93 (m, 1H), 3.75–3.57 (m, 4H), 3.50 (d, *J*=10.5 Hz, 1H), 3.43 (d, *J*=10.5 Hz, 1H), 3.36 (s, 3H), 3.46–3.31 (m, 2H), 2.35 (ddd, *J*=11.9, 4.6, 4.6 Hz, 1H), 2.20 (dd, *J*=16.1, 3.7 Hz, 1H), 1.90 (dd, *J*=15.9, 3.9 Hz, 1H), 1.77–1.24 (m, 8H), 1.18 (s, 3H), 1.14 (s, 3H), 1.04 (s, 9H), 0.90 (d, *J*=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 135.5 (4C), 134.0 (4C), 129.4 (2C), 128.2 (4C), 127.5 (4C), 127.4 (2C), 127.3 (2C), 127.2 (2C), 96.0, 77.4, 77.1, 76.5, 76.1, 75.0, 73.9, 73.5, 73.3, 72.9, 71.0, 63.9, 55.3, 46.1, 34.9, 32.7, 31.9, 29.8, 29.2, 29.1, 26.9 (3C), 20.5, 19.3, 13.3, 12.4; HRMS (ESI TOF) calcd for $C_{51}H_{68}O_8SiNa$ $(M+Na)^+$ 859.4581, found 859.4512.

4.9. Alcohol 20

A mixture of **19** (181 mg, 0.216 mmol) and $Pd(OH)_2$–C (60.0 mg) in THF (2 mL) was stirred under H_2 atmosphere at room temperature. After 4 h, the catalyst was filtered off, and the filtrate was concentrated to give the crude diol, which was used for the next reaction directly.

To a solution of the crude diol in DMF (1 mL) were added imidazole (148 mg, 2.18 mmol) and TESCl (0.18 mL, 1.09 mmol), and the mixture was stirred for 30 min at room temperature. The mixture was quenched with MeOH, diluted with Et_2O, then washed with water and brine. Concentration gave the crude bis-silyl ether, which was used for the next reaction directly.

To a solution of the crude bis-silyl ether in MeOH (2 mL) and CH_2Cl_2 (2 mL) at 0 °C was added PPTS (11.0 mg, 43.6 μmol). After stirring for 1 h at the same temperature, the reaction mixture was quenched with Et_3N (0.5 mL). Concentration and chromatography (hexane/EtOAc, 20:1 to 5:1) gave **20** (148 mg, 89% for the 3 steps): colorless oil; R_f=0.37 (hexane/EtOAc, 4:1); $[\alpha]_D^{23}$ −13.7 (*c* 0.97, $CHCl_3$); IR (neat) 3655–3299, 2953, 1087 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=8.0, 1.6 Hz, 4H), 7.42–7.31 (m, 6H), 4.71 (d, *J*=6.7 Hz, 1H), 4.66 (d, *J*=6.7 Hz, 1H), 4.12 (dd, *J*=11.1, 5.0 Hz, 1H), 3.88 (dd, *J*=11.8, 4.8 Hz, 1H), 3.84 (t, *J*=3.7 Hz, 1H), 3.69–3.56 (m, 3H), 3.50–3.34 (m, 3H), 3.37 (s, 3H), 3.28 (d, *J*=9.0 Hz, 1H), 2.56 (dd, *J*=9.8, 2.7 Hz, 1H), 2.18 (dd, *J*=15.9, 3.8 Hz, 1H), 2.08 (ddd, *J*=12.0, 4.6, 4.6 Hz, 1H), 1.91 (dd, *J*=15.9, 3.8 Hz, 1H), 1.79–1.20 (m, 8H), 1.16 (s, 3H), 1.03 (s, 3H), 1.02 (s, 9H), 0.95–0.90 (m, 9H), 0.92 (d, *J*=7.8 Hz, 3H), 0.58 (q, *J*=7.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (4C), 134.0 (2C), 129.4 (2C), 127.5 (4C), 97.3, 79.0, 77.4, 75.7, 73.6, 73.0, 71.0, 67.3, 66.5, 63.9, 55.5, 46.5, 36.0, 34.8, 32.7, 32.6, 29.2, 29.1, 26.9 (3C), 20.5, 19.3, 13.0, 12.4, 6.9 (3C), 5.1 (3C); HRMS (ESI TOF) calcd for $C_{43}H_{70}O_8Si_2Na$ $(M+Na)^+$ 793.4507, found 793.4514.

4.10. Unsaturated ester 21

To a solution of **20** (270 mg, 0.345 mmol) and MS4 Å (30 mg) in CH_2Cl_2 (3.5 mL) at 0 °C were added TPAP (12.1 mg, 34.5 μmol) and NMO (80.8 mg, 0.690 mmol), and the mixture was stirred for 0.5 h at room temperature. The mixture was filtered through a short silica gel column (hexane/EtOAc, 2:1) to give the crude aldehyde, which was used for the next reaction directly.

A mixture of the crude aldehyde and $Ph_3P{=}CHCO_2Me$ (346 mg, 1.04 mmol) in benzene (3.5 mL) was refluxed for 4 h. The mixture was subjected directly to a column chromatography (hexane/EtOAc, 20:1 to 5:1) to give the unsaturated ester **21** (141 mg, 96% for the 2 steps): colorless oil; R_f=0.48 (hexane/EtOAc, 4:1); $[\alpha]_D^{22}$ −21.8 (*c* 0.76, $CHCl_3$); IR (neat) 2952, 1727, 1661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=6.3, 1.6 Hz, 4H), 7.42–7.32 (m, 6H), 7.05 (d, *J*=15.6 Hz, 1H), 5.98 (d, *J*=15.6 Hz, 1H), 4.77 (d, *J*=6.7 Hz, 1H), 4.69 (d, *J*=6.7 Hz, 1H), 4.16 (dd, *J*=11.6, 5.0 Hz, 1H), 3.95 (t, *J*=3.8 Hz, 1H), 3.71–3.57 (m, 3H), 3.71 (s, 3H), 3.50 (dd, *J*=11.6, 4.8 Hz, 1H), 3.45–3.39 (m, 1H), 3.40 (s, 3H), 3.32 (d, *J*=8.8 Hz, 1H), 2.21 (dd, *J*=16.0, 3.8 Hz, 1H), 2.07 (ddd, *J*=12.0, 4.8, 4.8 Hz, 1H), 1.89 (dd, *J*=16.0, 3.8 Hz, 1H), 1.75–1.21 (m, 8H), 1.22 (s, 3H), 1.16 (s, 3H), 1.02 (s, 9H), 0.92 (t, *J*=8.1 Hz, 9H), 0.91 (d, *J*=7.6 Hz, 3H), 0.56 (q, *J*=8.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 152.2, 135.5 (4C), 134.0 (2C), 129.4 (2C), 127.5 (4C), 118.1, 96.3, 77.2, 76.8, 75.9, 73.5, 72.6, 71.5, 71.0, 63.9, 55.5, 51.5, 46.1, 36.2, 34.8, 32.7, 29.2, 29.1, 26.9 (3C), 22.7, 20.5, 19.3, 14.8, 12.4, 6.9 (3C), 5.0 (3C); HRMS (ESI TOF) calcd for $C_{46}H_{72}O_9Si_2Na$ $(M+Na)^+$ 847.4612, found 847.4606.

4.11. Hydroxy ester 23

A mixture of **21** (278 mg, 0.332 mmol) and Pd–C (55.0 mg) in EtOAc (5 mL) was stirred under H_2 atmosphere at room temperature. After 3 h, the catalyst was filtered off through a short silica gel column (EtOAc), and the filtrate was concentrated to give the crude saturated ester, which was used for the next reaction directly.

To a solution of the crude ester in THF (2 mL) and H_2O (2 mL) was added $LiOH{\cdot}H_2O$ (41.8 mg, 0.996 mmol). After stirring for 10 h at 75 °C, an additional amount of $LiOH{\cdot}H_2O$ (41.8 mg, 0.996 mmol) was added, and the reaction mixture was stirred for further 6.5 h. The reaction mixture was cooled to 0 °C, diluted with Et_2O, and then neutralized carefully with 0.5 M HCl. The resulting mixture was diluted with EtOAc, then washed with water and brine. The aqueous layer was extracted with EtOAc (two times). The combined organic layer was concentrated to give the crude carboxylic acid **4**, which was used for next reaction directly.

To a solution of the crude **4** in THF (1.5 mL) were added Et_3N (0.21 mL, 1.49 mmol) and 2,4,6-trichlorobenzoyl chloride (0.13 mL, 0.830 mmol). After stirring for 40 min at room temperature, the mixture was concentrated under reduced pressure, then diluted with toluene (5 mL). To the resulting mixture was added a solution of **5** (310.7 mg, 0.644 mmol) and DMAP (142.0 mg, 1.16 mmol) in toluene (5 mL). After stirring for 1.5 h at room temperature, the mixture was diluted with EtOAc and filtered through a Celite pad. Concentration and chromatography (hexane/EtOAc, 4:1) gave a mixture of ester **22** and unreacted **5**. The mixture was used for the next reaction without further purification.

To a crude mixture of **22** and **5** in MeOH (2 mL) and CH_2Cl_2 (2 mL) at 0 °C was added CSA (15.4 mg, 66.4 μmol). After stirring for 1 h at the same temperature, the reaction mixture was quenched with Et_3N. Concentration and chromatography (hexane/EtOAc, 20:1 to 4:1 to 2:1) gave **23** (281 mg, 74% for the 4 steps): colorless oil; R_f=0.41 (hexane/EtOAc, 2:1); $[\alpha]_D^{25}$ −23.7 (*c* 0.83, $CHCl_3$); IR (neat) 3637–3243, 2929, 1737 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=7.9, 1.6 Hz, 4H), 7.42–7.32 (m, 6H), 7.31 (s, 2H), 5.81 (dd, *J*=17.3, 10.7 Hz, 1H), 5.16 (dd, *J*=17.3, 1.2 Hz, 1H), 5.08 (dd, *J*=10.7, 1.2 Hz, 1H), 4.82–4.76 (m, 1H), 4.70 (d, *J*=6.6 Hz, 1H), 4.63 (d, *J*=6.6 Hz, 1H), 4.65 (s, 2H), 4.11 (dd, *J*=11.5, 4.9 Hz, 1H), 3.88 (t, *J*=3.6 Hz, 1H), 3.69–3.56 (m, 3H), 3.48 (t, *J*=6.1 Hz, 2H), 3.44–3.32 (m, 2H), 3.36 (s, 3H), 3.24 (d, *J*=9.3 Hz, 1H), 2.46 (ddd, *J*=17.4, 7.0, 7.0 Hz, 1H), 2.39 (d, *J*=5.4 Hz, 1H), 2.31 (ddd, *J*=17.4, 7.0, 7.0 Hz, 1H), 2.17 (dd, *J*=16.0, 3.5 Hz, 1H), 2.10 (ddd, *J*=11.7, 4.5, 4.5 Hz, 1H), 1.94–1.84 (m, 3H), 1.83–1.42 (m, 10H), 1.39–1.28 (m, 2H), 1.24 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H), 1.02 (s, 9H), 0.89 (d, *J*=6.8 Hz, 3H), 0.84 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 142.9, 137.2 (2C), 135.5 (4C), 134.6, 134.0 (2C), 132.3, 129.4 (2C), 128.2 (2C), 127.5 (4C), 114.3, 95.9, 78.8, 77.4, 76.9, 76.5, 75.8, 75.6, 73.4, 73.2, 70.9, 70.4, 69.4, 66.5, 63.9, 55.2, 46.0, 34.9, 34.8, 33.9, 32.6, 29.2, 29.1, 27.7, 26.9 (3C), 26.4, 25.9 (3C), 25.6, 22.3, 20.5, 19.3, 18.3, 15.5, 12.4, −2.0 (2C); HRMS (ESI TOF) calcd for $C_{60}H_{89}Cl_3O_{11}Si_2Na$ $(M+Na)^+$ 1171.4899, found 1171.4878.

4.12. Mixed acetal 25

To a mixture of **23** (214 mg, 0.186 mmol) and **24** (0.18 mL, 0.559 mmol) in CH_2Cl_2 (3 mL) was added CSA (8.6 mg, 0.037 mmol). After stirring for 15 min at room temperature, the reaction mixture was quenched with Et_3N. Concentration and chromatography (hexane/EtOAc, 100:1 to 50:1 to 15:1 to 4:1 containing 0.5% Et_3N) gave **25** (245 mg, 88%) and unreacted **23** (25.1 mg, 12% recovery): colorless oil; R_f=0.54 (hexane/EtOAc, 4:1); IR (neat) 2928, 1737, 1101 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.82–7.77 (m, 4H), 7.27–7.09 (m, 6H), 6.94–6.91 (m, 2H), 5.93–5.83 (m, 1H), 5.21–5.11 (m, 2H), 5.04–4.97 (m, 1H), 4.80–4.74 (m, 2H), 4.50–4.34 (m, 4H), 4.02–3.94 (m, 1H), 3.89–3.59 (m, 3H), 3.48–3.10 (m, 11H), 2.80–2.55 (m, 2H), 2.46–2.02 (m, 3H), 2.00–1.46 (m, 18H), 1.45–1.33 (m, 6H), 1.30–1.16 (m, 21H), 1.04–0.84 (m, 30H), 0.18–0.11 (m, 6H).

4.13. Allylic stannane 26

To a mixture of **25** (89.3 mg, 59.1 μmol) in CH_2Cl_2 (4 mL) at −15 °C were added HMDS (0.39 ml, 1.77 mmol) and TMSI (84 μl, 0.59 mmol), and the mixture was stirred for 1.5 h at the same temperature. The reaction mixture was quenched with saturated $NaHCO_3$, diluted with AcOEt, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 100:1 to 20:1 to 10:1 to 8:1 containing 2% Et_3N) gave **26** (76.8 mg, 91%): colorless oil; R_f=0.51 (hexane/EtOAc, 4:1); $[\alpha]_D^{23}$ −8.6 (*c* 0.78, C_6D_6); IR (neat) 3668–3280, 2929, 1736 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.83–7.77 (m, 4H), 7.26–7.21 (m, 6H), 6.93 (s, 2H), 5.84 (dd, *J*=17.4, 10.7 Hz, 1H), 5.17 (dd, *J*=17.4, 1.2 Hz, 1H), 5.08 (dd, *J*=9.9, 2.3 Hz, 1H), 4.98 (dd, *J*=10.7, 1.2 Hz, 1H), 4.68 (ddd, *J*=9.0, 9.0, 6.0 Hz, 1H), 4.44 (s, 2H), 4.14 (dd, *J*=9.6, 7.2 Hz, 1H), 3.97 (br s, 1H), 3.79–3.65 (m, 2H), 3.60 (ddd, *J*=10.7, 10.7, 4.4 Hz, 1H), 3.45–3.25 (m, 5H), 2.54–2.42 (m, 3H), 2.37 (dd, *J*=15.9, 2.9 Hz, 1H), 2.33–2.21 (m, 2H), 2.13–1.99 (m, 2H), 1.97–1.85 (m, 2H), 1.84–1.48 (m, 20H), 1.45–1.33 (m, 8H), 1.29 (s, 3H), 1.20 (s, 3H), 1.19 (s, 9H), 1.01 (s, 9H), 1.01–0.96 (m, 18H), 0.16 (s, 3H), 0.12 (s, 3H); HRMS (ESI TOF) calcd for $C_{73}H_{115}Cl_3O_{10}Si_2SnNa$ $(M+Na)^+$ 1455.6014, found 1455.6338.

4.14. Silyl ether 27

To a solution of **26** (170 mg, 0.119 mmol) in CH_2Cl_2 (3 mL) at 0 °C were added 2,6-lutidine (0.14 mL, 1.19 mmol) and TBSOTf (0.08 mL, 0.348 mmol). After stirring for 0.5 h at 0 °C, an additional amount of TBSOTf (0.04 mL, 0.174 mmol) was added, and the reaction mixture was stirred for 0.5 h. The reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with saturated $NaHCO_3$ and brine. Concentration and chromatography (hexane/EtOAc, 1:0 to 50:1 to 20:1 containing 0.5% Et_3N) gave **27** (175 mg, 95%): colorless oil; R_f=0.56 (hexane/EtOAc, 7:1); $[\alpha]_D^{23}$ −1.6 (*c* 0.75, C_6D_6); IR (neat) 2928, 1738, 1089 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.83–7.76 (m, 4H), 7.28–7.21 (m, 6H), 6.93 (s, 2H), 5.88 (dd, *J*=17.3, 10.7 Hz, 1H), 5.68 (d, *J*=5.9 Hz, 1H), 5.19 (dd, *J*=17.3, 1.5 Hz, 1H), 5.14 (dd, *J*=10.1, 2.1 Hz, 1H), 5.01 (dd, *J*=10.7, 1.2 Hz, 1H), 4.65 (ddd, *J*=9.0, 9.0, 6.0 Hz, 1H), 4.44 (s, 2H), 4.45–4.40 (m, 1H), 3.99 (br s, 1H), 3.88–3.79 (m, 1H), 3.79–3.62 (m, 2H), 3.49–3.32 (m, 4H), 3.23 (d, *J*=9.3 Hz, 1H), 2.76–2.58 (m, 2H), 2.42–2.32 (m, 2H), 2.22 (dd, *J*=16.0, 3.0 Hz, 1H), 2.10–2.01 (m, 1H), 2.01–1.90 (m, 2H), 1.89–1.49 (m, 19H), 1.45–1.33 (m, 6H), 1.31 (s, 3H), 1.23 (s, 3H), 1.22 (s, 3H), 1.19 (s, 9H), 1.09 (s, 9H), 1.05 (d, *J*=7.1 Hz, 3H), 1.02–0.97 (m, 15H), 1.01 (s, 9H), 0.21 (s, 3H), 0.19 (s, 3H), 0.18 (s, 3H), 0.13 (s, 3H); HRMS (ESI TOF) calcd for $C_{79}H_{129}Cl_3O_{10}Si_3SnNa$ $(M+Na)^+$ 1569.6881, found 1569.6549.

4.15. Diene 28

To a stirring solution of **27** (24.6 mg, 15.9 μmol) in CH_2Cl_2 (1.5 mL) at −78 °C was added DIBAL-H (32 μL, 32.6 μmol, 1.02 M solution in hexane). To this mixture, pre-cooled (−40 °C) solutions of pyridine (8 μL, 98.9 μmol) and DMAP (7.8 mg, 63.6 μmol) in CH_2Cl_2 (0.3 mL) and $(ClCH_2CO)_2O$ (22 mg, 0.129 mmol) in CH_2Cl_2 (0.7 mL) were introduced immediately. The reaction mixture was allowed to warm to −10 °C over 1 h with stirring, and quenched with H_2O. The mixture was diluted with Et_2O, then washed with saturated potassium sodium tartrate, saturated $CuSO_4$, water, saturated $NaHCO_3$, and brine. Concentration gave the crude α-chloroacetoxy ether **3**, which was used for the next reaction directly.

To the stirring suspension of $MgBr_2\cdot OEt_2$ (41.1 mg, 0.159 mmol) and MS5 Å (30 mg) in CH_2Cl_2 (1.5 mL) at −78 °C was added a pre-cooled (−40 °C) solution of **3** (dried over MS5 Å) in CH_2Cl_2 (1.5 mL). The mixture was allowed to warm to 0 °C over 50 min, and quenched with Et_3N. The mixture was filtered through a short silica gel column (EtOAc) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 1:0 to 40:1 to 20:1 to 10:1) to give **28** (10.2 mg, 52% for the 2 steps): colorless oil; R_f=0.42 (hexane/EtOAc, 7:1); $[\alpha]_D^{23}$ −8.6 (*c* 0.63, $CHCl_3$); IR (neat) 2929, 1471, 1428, 1081 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=7.4, 1.5 Hz, 4H), 7.42–7.31 (m, 6H), 7.31 (s, 2H), 5.90 (dd, *J*=17.6, 10.7 Hz, 1H), 5.63 (ddd, *J*=17.1, 10.7, 5.1 Hz, 1H), 5.20 (dd, *J*=17.1, 1.5 Hz, 1H), 5.18 (d, *J*=17.6 Hz, 1H), 5.15 (d, *J*=10.7 Hz, 1H), 5.01 (dd, *J*=10.7, 1.5 Hz, 1H), 4.66 (s, 2H), 4.29 (d, *J*=4.6 Hz, 1H), 4.21 (dd, *J*=11.3, 5.0 Hz, 1H), 3.95 (br s, 1H), 3.70–3.36 (m, 8H), 3.17 (d, *J*=9.3 Hz, 1H), 3.07 (dd, *J*=7.1, 2.7 Hz, 1H), 2.05–1.20 (m, 19H), 1.26 (s, 3H), 1.15 (s, 3H), 1.12 (s, 3H), 1.03 (s, 9H), 0.92–0.88 (m, 12H), 0.83 (s, 9H), 0.06 (s, 3H), 0.05 (s, 6H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.6, 137.9, 137.2 (2C), 135.5 (4C), 134.5, 134.1 (2C), 132.4, 129.4 (2C), 128.2 (2C), 127.5 (4C), 114.4, 114.1, 87.3, 82.7, 82.2, 77.6, 77.5, 77.2, 76.2, 75.2, 72.7, 72.5, 71.4, 70.8, 66.6, 64.0 (2C), 49.5, 35.0, 34.9, 34.4, 32.5, 29.3, 29.1, 28.2, 27.5, 26.9 (3C), 26.1 (3C), 26.0 (3C), 23.3, 20.9, 20.2, 19.3, 18.3, 18.2, 15.5, 12.4, −1.9 (2C), −3.9, −5.0; HRMS (ESI TOF) calcd for $C_{67}H_{103}Cl_3O_9Si_3Na$ $(M+Na)^+$ 1265.5868, found 1265.6018.

4.16. Pentacycle 30

To a solution of **28** (10.9 mg, 8.77 μmol) in toluene (2.9 mL) was added the Grubbs' catalyst **29** (22 mg, 26 μmol), and the mixture was stirred at 100 °C. After 15 min, an additional amount of **29** (3.6 mg, 4.37 μmol) was added. After stirring for 15 min at 100 °C, the reaction was quenched with Et_3N at room temperature, diluted with EtOAc, filtered through a short silica gel column (EtOAc). Concentration and chromatography (cH_2Cl_2/EtOAc, 1:0 to 100:1 to 50:1, hexane/EtOAc, 40:1 to 30:1 to 20:1) gave **30** (7.4 mg, 69%): colorless oil; R_f=0.46 (hexane/EtOAc, 7:1); $[\alpha]_D^{24}$ −11.0 (*c* 0.67, $CHCl_3$); IR (neat) 2929, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67−7.61 (m, 4H), 7.42−7.31 (m, 6H), 7.31 (s, 2H), 5.63 (dd, *J*=13.3, 2.3 Hz, 1H), 5.41 (dd, *J*=13.3, 1.5 Hz, 1H), 4.67 (s, 2H), 4.16 (dd, *J*=11.3, 4.8 Hz, 1H), 3.95 (br s, 1H), 3.89 (br d, *J*=9.3 Hz, 1H), 3.75−3.46 (m, 5H), 3.39 (dd, *J*=6.1, 6.1 Hz, 1H), 3.31 (d, *J*=10.7 Hz, 1H), 3.28−3.18 (m, 3H), 2.06 (ddd, *J*=11.5, 4.3, 4.3, 1H), 2.03−1.95 (m, 1H), 1.94−1.21 (m, 17H), 1.17 (s, 3H), 1.14 (s, 3H), 1.11 (s, 3H), 1.02 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=6.6 Hz, 3H), 0.81 (s, 9H), 0.07 (s, 6H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.8, 137.2 (2C), 135.5 (4C), 134.5, 134.1 (2C), 132.4, 129.9, 129.4 (2C), 128.2 (2C), 127.5 (4C), 88.2, 86.3, 83.9, 80.2, 78.3, 77.6, 77.2, 76.0, 75.7, 73.1, 72.6, 71.2, 70.8, 66.6, 64.0, 49.5, 38.1, 35.0, 33.7, 32.6, 30.4, 29.3, 29.1, 27.2, 26.9 (3C), 26.7, 26.0 (3C), 25.8 (3C), 21.9, 20.9, 19.3, 18.3, 18.2, 17.7, 12.3, −1.9, −2.1, −4.1, −4.9; HRMS (ESI TOF) calcd for $C_{65}H_{99}Cl_3O_9Si_3Na$ $(M+Na)^+$ 1237.5554, found 1237.5496.

4.17. Benzyl ether 32

A mixture of **30** (5.7 mg, 4.69 μmol) and Pd−C (5.6 mg) and Et_3N (50 μL) in EtOH (1 mL) was stirred under H_2 atmosphere. After 1.5 h, the catalyst was filtered off through a short silica gel column (EtOAc), and the filtrate was concentrated to give the crude benzyl ether **31**, which was used for the next reaction directly.

To a stirred solution of the crude benzyl ether, pyridine (85 μL, 1.06 mmol) and $KO_2CN{=}NCO_2K$ (68.3 mg, 0.352 mmol) in MeOH (1 mL) at room temperature was added a solution of AcOH (40 μL, 0.704 mmol) in MeOH (0.3 mL) over 75 min via a syringe pomp. The reaction mixture was the quenched with saturated NH_4Cl, diluted with Et_2O. The organic layer was washed with saturated $CuSO_4$, water, saturated $NaHCO_3$, and brine. After concentration, the residue was subjected to the same procedure described above to complete the reaction. The crude product obtained was purified by chromatography (hexane/EtOAc, 40:1 to 20:1 to 15:1) to give **32** (4.4 mg, 84% for the 2 steps): colorless oil; R_f=0.39 (hexane/EtOAc, 7:1); $[\alpha]_D^{24}$ −13.1 (*c* 0.21, $CHCl_3$); IR (neat) 2929, 1090 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=7.8, 1.5 Hz, 4H), 7.41−7.20 (m, 11H), 4.49 (s, 2H), 4.17 (dd, *J*=11.5, 5.1 Hz, 1H), 3.94 (dd, *J*=3.7, 3.7 Hz, 1H), 3.73−3.56 (m, 3H), 3.51−3.43 (m, 2H), 3.42−3.36 (m, 1H), 3.34−3.15 (m, 4H), 3.10 (dd, *J*=12.2, 3.9 Hz, 1H), 2.13−1.20 (m, 23H), 1.14 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 1.02 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=6.3 Hz, 3H), 0.81 (s, 9H), 0.05 (s, 3H), 0.03 (s, 6H), 0.03 (s, 3H); (400 MHz, C_6D_6) δ 7.83−7.73 (m, 4H), 7.33 (d, *J*=7.6 Hz, 2H), 7.26−7.06 (m, 9H), 4.42 (dd, *J*=11.4, 5.7 Hz, 1H), 4.36 (s, 2H), 4.03 (br s, 1H), 3.92 (ddd, *J*=11.7, 9.3, 4.9 Hz, 1H), 3.78−3.60 (m, 2H), 3.59−3.27 (m, 6H), 3.23 (ddd, *J*=8.9, 8.9, 3.7 Hz, 1H), 3.17 (dd, *J*=12.0, 4.0 Hz, 1H), 2.34 (ddd, *J*=12.0, 4.0, 4.0 Hz, 1H), 2.25−2.15 (m, 2H), 2.10−1.65 (m, 13H), 1.65−1.42 (m, 5H), 1.40−1.25 (m, 2H), 1.24 (s, 3H), 1.19 (s, 9H), 1.15 (s, 3H), 1.13 (s, 3H), 1.09 (s, 9H), 1.05 (d, *J*=7.1 Hz, 3H), 0.94 (s, 9H), 0.20 (s, 3H), 0.17 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 135.5 (4C), 134.1 (2C), 129.4 (2C), 128.2 (2C), 127.6 (2C), 127.5 (4C), 127.4, 88.2, 86.6, 85.0, 82.2, 77.6, 77.2, 76.1, 75.5, 73.1, 72.9, 72.8, 72.6, 70.8, 70.7, 64.0, 49.5, 37.8, 37.7, 35.0, 33.9, 32.6, 29.6, 29.5, 29.3, 29.1, 28.9, 27.3, 27.0 (3C), 26.0 (3C), 25.8 (3C), 24.0, 20.9, 19.3, 18.3, 18.1, 16.2, 12.4, −2.0, −2.2, −4.2, −4.8; (100 MHz, C_6D_6) δ 139.5, 136.0 (4C), 134.5 (2C), 129.9 (2C), 128.5(2C), 127.9 (4C), 127.5 (3C), 88.7, 86.6, 85.0, 83.0, 78.1, 77.7, 76.6, 76.2, 73.8, 73.4, 73.3, 73.1, 71.2, 71.0, 64.4, 50.0, 38.1 (2C), 35.6, 34.8, 33.3, 30.3, 30.0, 29.6, 29.5, 27.9 (2C), 27.3 (3C), 26.5 (3C), 26.2 (3C), 24.1, 21.4, 19.6, 18.7, 18.5, 16.1, 13.0, −1.8, −1.9, −3.8, −4.6; HRMS (ESI TOF) calcd for $C_{65}H_{104}O_9Si_3Na$ $(M+Na)^+$ 1135.6886, found 1135.6899.

4.18. Alcohol 2

A mixture of **32** (5.6 mg, 5.03 μmol) and $Pd(OH)_2$−C (7.2 mg) in EtOAc (1.2 mL) was stirred under H_2 atmosphere at room temperature. After 45 min, the catalyst was filtered off through a short silica gel column (EtOAc) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 10:1 to 7:1 to 4:1) to give **2** (4.6 mg, 89%): colorless oil; R_f=0.20 (hexane/EtOAc, 4:1); $[\alpha]_D^{22}$ −9.1 (*c* 0.87, $CHCl_3$); IR (neat) 3606−3144, 2928, 1731, 1085 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.61 (m, 4H), 7.41−7.31 (m, 6H), 4.17 (dd, *J*=11.6, 5.0 Hz, 1H), 3.94 (dd, *J*=3.7, 3.7 Hz, 1H), 3.73−3.56 (m, 5H), 3.41−3.22 (m, 3H), 3.22−3.16 (m, 2H), 3.10 (dd, *J*=12.1, 3.7 Hz, 1H), 2.17−1.20 (m, 23H), 1.14 (s, 3H), 1.12 (s, 3H), 1.08 (s, 3H), 1.02 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=6.3 Hz, 3H), 0.81 (s, 9H), 0.06 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (4C), 134.1 (2C), 129.4 (2C), 127.5 (4C), 88.3, 86.5, 84.8, 82.3, 77.6, 77.2, 76.0, 75.5, 73.1, 72.9, 72.5, 70.8, 64.0, 63.0, 49.5, 37.7, 37.5, 35.0, 33.9, 32.5, 30.3, 29.8, 29.6, 29.3, 28.8, 26.9 (3C), 26.5, 26.0 (3C), 25.8 (3C), 24.0, 20.9, 19.3, 18.3, 18.1, 16.1, 12.4, −2.0, −2.2, −4.2, −4.8; HRMS (ESI TOF) calcd for $C_{58}H_{98}O_9Si_3Na$ $(M+Na)^+$ 1045.6416, found 1045.6412.

4.19. TBS ether 36

To a stirred solution of **18** (215 mg, 0.257 mmol) in CH_2Cl_2 (7.0 mL) were added HMDS (0.86 mL, 5.14 mmol) and TMSI (0.36 mL, 2.53 mmol) at 0 °C. After 30 min, the reaction mixture was quenched with saturated $NaHCO_3$, and diluted with Et_2O. The organic layer was washed with water and brine. After concentration, the residue was dissolved in MeOH (4.0 mL) and CH_2Cl_2 (4.0 mL). To this solution at 0 °C was added CSA (26 mg, 0.112 mmol), and the mixture was stirred for 40 min at the same temperature. The reaction mixture was quenched with Et_3N, diluted with EtOAc, then washed with water and brine. Concentration gave the crude alcohol, which was used for the next reaction directly.

To a stirred solution of the alcohol in CH_2Cl_2 (5.0 mL) at 0 °C were added 2,6-lutidine (0.15 mL, 1.28 mmol) and TBSOTf (0.14 mL, 0.789 mmol). After stirring for 1 h at room temperature, the reaction mixture was cooled to 0 °C, and quenched with MeOH. The mixture was diluted with Et_2O, and washed with water and brine. Concentration and chromatography (hexane/EtOAc, 50:1 to 30:1) gave **36** (218 mg, 93% for the 2 steps): colorless oil; R_f=0.70 (hexane/EtOAc, 4:1); $[\alpha]_D^{27}$ −10.2 (*c* 0.95, $CHCl_3$); IR (neat) 3434, 3069, 1079 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=7.8, 1.7 Hz, 4H), 7.42−7.31 (m, 6H), 7.31−7.19 (m, 10H), 4.56 (d, *J*=12.0 Hz, 1H), 4.48 (s, 2H), 4.36 (d, *J*=12.0 Hz, 1H), 4.25 (dd, *J*=11.3, 5.0 Hz, 1H), 4.04−3.97 (m, 1H), 3.73−3.57 (m, 2H), 3.48 (d, *J*=7.1 Hz, 1H), 3.47−3.35 (m, 3H), 3.44 (d, *J*=7.1 Hz, 1H), 3.25 (d, *J*=9.5 Hz, 1H), 2.34 (ddd, *J*=12.2, 4.1, 4.1 Hz, 1H), 2.01 (dd, *J*=14.8, 3.6 Hz, 1H), 1.90 (dd, *J*=15.6, 3.9 Hz, 1H), 1.74−1.44 (m, 5H), 1.38−1.22 (m, 3H), 1.16 (s, 3H), 1.15 (s, 3H), 1.03 (s, 9H), 0.90−0.84 (m, 12H), 0.06 (s, 3H), 0.03

(s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7, 138.6, 135.5 (4C), 134.1 (2C), 129.4 (2C), 128.1 (4C), 127.6 (2C), 127.5 (4C), 127.3 (2C), 127.2 (2C), 77.6, 76.7, 75.9, 75.0, 73.5, 72.6, 72.1, 71.0, 70.8, 65.8, 64.0, 49.4, 35.1, 32.6, 31.8, 29.3, 29.1, 27.0 (3C), 26.0 (3C), 20.9, 19.3, 18.2, 15.3, 13.1, 12.4, −4.4, −4.9; HRMS (ESI) calcd for $C_{55}H_{78}O_7Si_2Na$ $(M+Na)^+$ 929.5184, found 929.5189.

4.20. Alcohol 37

A mixture of **36** (218 mg, 0.240 mmol) and $Pd(OH)_2$–C (75.0 mg) in THF (4.0 mL) was stirred vigorously under hydrogen atmosphere. After 4 h, the catalyst was filtered off through a short silica gel column (EtOAc). The filtrate was concentrated to give the corresponding diol, which was used for next reaction directly.

To a solution of the crude diol in DMF (7.0 mL) at room temperature were added imidazole (163 mg, 2.39 mmol) and TESCl (0.20 mL, 1.19 mmol). After stirring for 20 min, the reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with water and brine. Concentration gave the crude bis-TES ether, which was used for the next reaction directly.

To a stirred solution of the bis-TES ether in CH_2Cl_2 (2.4 mL) and MeOH (2.4 mL) at 0 °C was added PPTS (12.0 mg, 47.8 μmol). After 25 min, the reaction mixture was quenched with Et_3N, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 20:1 to 10:1) gave **37** (135 mg, 67% for the 3 steps): colorless oil; R_f=0.45 (hexane/EtOAc, 10:1); $[\alpha]_D^{27}$ −20.9 (*c* 0.63, $CHCl_3$); IR (neat) 3553–3273, 2953, 1087 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J*=7.8, 1.5 Hz, 4H), 7.42–7.22 (m, 6H), 4.22 (dd, *J*=11.5, 8.1 Hz, 1H), 4.01–3.97 (m, 1H), 3.75 (dd, *J*=11.8, 4.6 Hz, 1H), 3.71–3.57 (m, 4H), 3.48–3.37 (m, 3H), 3.23 (d, *J*=9.3 Hz, 1H), 2.07 (ddd, *J*=12.0, 4.7, 4.7 Hz, 1H), 2.03 (dd, *J*=15.3, 3.4 Hz, 1H), 1.94–1.86 (m, 2H), 1.76–1.20 (m, 7H), 1.16 (s, 3H), 1.06 (s, 3H), 1.03 (s, 9H), 0.96–0.88 (m, 21H), 0.58 (q, *J*=7.9 Hz, 6H), 0.07 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (4C), 134.1 (2C), 129.4 (2C), 127.5 (4C), 77.5, 77.2, 75.9, 72.9, 72.6, 72.2, 70.9, 68.1, 67.5, 64.0, 49.3, 36.1, 34.9, 32.6, 29.3, 29.1, 27.0 (3C), 25.9 (3C), 20.8, 19.3, 18.2, 12.7, 12.5, 6.9 (3C), 5.1 (3C), −4.4, −4.6; HRMS (ESI) calcd for $C_{47}H_{80}O_7Si_3Na$ $(M+Na)^+$ 863.5110, found 863.5104.

4.21. Alcohol 34

To a mixture of **37** (135 mg, 0.160 mmol) and MS4 Å (16 mg) in CH_2Cl_2 (3.2 mL) at room temperature were added TPAP (16.0 mg, 45.5 μmol) and NMO (112 mg, 0.956 mmol). After stirring for 2.5 h, the mixture was filtered through a short silica gel column (hexane/EtOAc, 4:1) to give the corresponding aldehyde, which was used for the next reaction directly.

To a suspension of $Ph_3P^+CH_3Br^-$ (340 mg, 0.952 mmol) in THF (2.0 mL) at 0 °C was added NaHMDS (0.80 mL, 0.80 mmol, 1.0 M solution in THF), and the mixture was stirred for 10 min. A solution of the crude aldehyde in THF (2.0 mL) was introduced, and the mixture was allowed to warm to room temperature. After 1.5 h, the reaction mixture was quenched with H_2O, diluted with EtOAc, then washed with water and brine. After concentration, the crude product was used for next reaction directly.

To a stirred solution of the olefin in CH_2Cl_2 (1.6 mL) and MeOH (1.6 mL) at 0 °C was added CSA (11.0 mg, 47.4 μmol). After 25 min, the reaction mixture was quenched with Et_3N. Concentration and chromatography (hexane/EtOAc, 10:1 to 8:1) gave **34** (99.8 mg, 86% for the 3 steps): amorphous; R_f=0.20 (hexane/EtOAc, 4:1); $[\alpha]_D^{24}$ −31.5 (*c* 1.00, $CHCl_3$); IR (neat) 3564–3145, 2931, 1071 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (dd, *J*=7.8, 1.5 Hz, 4H), 7.43–7.32 (m, 6H), 5.89 (dd, *J*=17.7, 11.0 Hz, 1H), 5.27 (dd, *J*=17.7, 1.2 Hz, 1H), 5.15 (dd, *J*=11.0, 1.2 Hz, 1H), 4.24 (dd, *J*=11.3, 5.3 Hz, 1H), 4.06–4.00 (m, 1H), 3.79 (ddd, *J*=11.7, 9.3, 4.9 Hz, 1H), 3.69–3.57 (m, 2H), 3.46–3.37 (m, 2H), 3.29 (d, *J*=9.3 Hz, 1H), 2.18 (ddd, *J*=11.7, 4.6, 4.6 Hz, 1H), 2.03 (dd, *J*=16.6, 3.4 Hz, 1H), 1.92 (dd, *J*=16.6, 4.2 Hz, 1H), 1.77–1.45 (m, 5H), 1.43–1.18 (m, 3H), 1.23 (s, 3H), 1.17 (s, 3H), 1.03 (s, 9H), 0.92–0.87 (m, 12H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.0, 135.5 (4C), 134.1 (2C), 129.4 (2C), 127.5 (4C), 114.2, 77.6, 76.7, 75.6, 72.8, 72.6, 72.2, 70.8 (2C), 64.0, 49.4, 35.0, 34.7, 32.6, 29.3, 29.1, 26.9 (3C), 26.0 (3C), 20.9, 19.3, 18.2, 13.4, 12.4, −4.3, −4.7; HRMS (ESI) calcd for $C_{42}H_{66}O_6Si_2Na$ $(M+Na)^+$ 745.4296, found 745.4297.

4.22. Alcohol 39

To a mixture of **38** (678 mg, 1.76 mmol) in CH_2Cl_2 (12 mL) at 0 °C were added 2,6-lutidine (0.62 mL, 5.29 mmol) and TBSOTf (0.81 mL, 3.53 mmol), and the mixture was stirred for 2.5 h at room temperature. The reaction mixture was quenched with MeOH at 0 °C, diluted with Et_2O, then washed with saturated $NaHCO_3$ and brine. Concentration gave the corresponding silyl ether, which was used for next reaction directly.

To a stirred solution of 2-methyl-2-butene (1.87 mL, 17.6 mmol) in THF (15 mL) at −15 °C was added $BH_3\cdot SMe_2$ (0.84 mL, 8.82 mmol), and the mixture was stirred for 0.5 h at the same temperature. To this mixture at −15 °C was introduced a solution of the silyl ether in THF (20 mL). After stirring for 1 h at the same temperature, the reaction mixture was quenched with MeOH, then 3 M NaOH (5.0 mL) and 30% H_2O_2 (5.0 mL), and was stirred for 0.5 h at room temperature. The mixture was quenched with saturated Na_2SO_3, diluted with Et_2O, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 6:1 to 4:1) gave **39** (774 mg, 85% for the 2 steps): colorless oil; R_f=0.16 (hexane/EtOAc, 4:1); $[\alpha]_D^{25}$ +6.4 (*c* 1.14, $CHCl_3$); IR (neat) 3730–3141, 2953, 2855 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36–7.19 (m, 7H), 6.85 (d, *J*=8.8 Hz, 2H), 4.55 (d, *J*=10.7 Hz, 1H), 4.51 (d, *J*=10.7 Hz, 1H), 4.49 (s, 2H), 3.78 (s, 3H), 3.57 (t, *J*=6.3 Hz, 2H), 3.53–3.42 (m, 2H), 3.25 (dd, *J*=8.7, 2.6 Hz, 1H), 1.95–1.30 (m, 9H), 1,21 (s, 3H), 0.86 (s, 9H), 0.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.9, 138.6, 131.2, 128.9 (2C), 128.2 (2C), 127.5 (2C), 127.4, 113.6 (2C), 84.2, 78.1, 73.6, 72.8, 70.8, 63.6, 55.3, 36.5, 27.9, 27.2, 27.1, 26.1 (3C), 23.6, 18.5, −1.7, −1.8; HRMS (ESI) calcd for $C_{30}H_{48}O_5SiNa$ $(M+Na)^+$ 539.3169, found 539.3166.

4.23. Alcohol 40

To a solution of **39** (384 mg, 0.742 mmol) in CH_2Cl_2 (7.4 mL) at room temperature were added diisopropylethylamine (1.30 mL, 7.42 mmol) and MOMCl (0.28 mL, 3.71 mmol). After stirring for 1 h, the reaction mixture was quenched with MeOH at 0 °C, diluted with EtOAc, then washed with saturated NH_4Cl, saturated $NaHCO_3$, and brine. Concentration gave the crude MOM ether, which was used for next reaction directly.

A mixture of the MOM ether and $Pd(OH)_2$–C (112 mg) in THF (7.4 mL) was stirred under hydrogen atmosphere. After 1 h, the catalyst was filtered off, and concentrated. The crude diol obtained was used for next reaction directly.

To a mixture of the diol in DMF (7.4 mL) at −15 °C were added imidazole (253 mg, 3.72 mmol) and TBSCl (340 mg, 2.26 mmol), and the mixture was stirred for 0.5 h at the same temperature. The reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 10:1 to 6:1) gave **40** (324 mg, 94% for the 3 steps): colorless oil; R_f=0.41 (hexane/EtOAc, 4:1); $[\alpha]_D^{24}$ +12.9 (*c* 1.09, $CHCl_3$); IR (neat) 3735–3102, 2954, 1109 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.58 (s, 2H), 3.70–3.57 (m, 2H), 3.47 (ddd, *J*=6.3, 6.3, 2.5 Hz, 2H), 3.38–3.31 (m, 1H), 3.32 (s, 3H), 2.58 (d, *J*=3.9 Hz, 1H), 1.84–1.50 (m, 6H), 1.48–1.34 (m, 1H), 1.34–1.24 (m, 1H), 1,19 (s, 3H), 0.86 (s, 9H), 0.85 (s, 9H), 0.09 (s, 6H), 0.02 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 96.3, 78.3, 77.5, 68.3, 63.2, 55.1, 34.7, 30.3, 27.8, 26.0 (6C), 24.1, 23.9, 18.4 (2C), −1.9 (2C), −5.2 (2C); HRMS (ESI) calcd for $C_{23}H_{52}O_5Si_2$ $(M+Na)^+$ 487.3251, found 487.3257.

4.24. Allyl ether 41

To a stirred suspension of KH (475 mg, 3.55 mmol, 30%, prewashed with hexane) in THF (7 mL) at 0 °C were added allyl bromide (0.30 mL, 3.54 mmol) and a solution of **40** (329 mg, 708 mmol) in THF (7 mL), and the mixture was stirred for 1 h at room temperature. The reaction mixture was cooled to 0 °C, and quenched with MeOH, diluted with Et_2O, then washed with water and brine. Concentration gave the crude allylic ether, which was used for next reaction directly.

To a mixture of the allylic ether in CH_2Cl_2 (7 mL) at 0 °C were added HMDS (1.48 mL, 7.08 mmol) and TMSI (0.50 mL, 3.54 mmol). After stirring for 1 h, the reaction mixture was quenched with MeOH (7 mL), and stirred with K_2CO_3 (300 mg) for 1 h at room temperature. The reaction mixture was diluted with EtOAc, then washed with water and brine. Concentration gave the crude alcohol, which was used for next reaction directly.

To a mixture of the alcohol in DMF (7 mL) were added imidazole (243 mg, 3.56 mmol) and TESCl (0.36 mL, 2.12 mmol). After stirring for 20 min at room temperature, the reaction mixture was quenched with MeOH, diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 200:1 to 40:1) gave **41** (373 mg, 92% for the 3 steps): colorless oil; R_f=0.31 (hexane/EtOAc, 20:1); $[\alpha]_D^{25}$ +5.6 (*c* 1.35, $CHCl_3$); IR (neat) 3081, 1098 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 (dddd, *J*=17.1, 10.5, 5.4, 5.4 Hz, 1H), 5.22 (dd, *J*=17.1, 1.2 Hz, 1H), 5.08 (dd, *J*=10.5, 1.2 Hz, 1H), 4.11–4.01 (m, 2H), 3.67–3.50 (m, 4H), 3.10 (dd, *J*=8.8, 1.7 Hz, 1H), 1.90–1.29 (m, 8H), 1,17 (s, 3H), 0.94 (t, *J*=7.9 Hz, 9H), 0.88 (s, 9H), 0.85 (s, 9H), 0.58 (q, *J*=7.9 Hz, 6H), 0.08 (s, 6H), 0.03 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.4, 115.6, 84.6, 78.1, 73.2, 63.8, 63.4, 36.8, 31.0, 27.3, 27.0, 26.1 (6C), 23.5, 18.5 (2C), 6.9 (3C), 4.5 (3C), −1.7, −1.8, −5.2 (2C); HRMS (ESI) calcd for $C_{30}H_{66}O_4Si_3Na$ $(M+Na)^+$ 597.4167, found 597.4169.

4.25. Allyl stannane 43

To a stirred solution of **41** (164 mg, 0.285 mmol) in THF (2.8 mL) at −78 °C was added *s*-BuLi (1.35 mL, 1.43 mmol. 1.06 M solution in hexane), and the mixture was stirred for 3 h at the same temperature. To the resulting yellow solution was added Bu_3SnCl (0.39 mL, 1.44 mmol), and the mixture was allowed to warm to 0 °C with stirring. The reaction mixture was diluted with Et_2O, then washed with water and brine. Concentration gave the crude allylic stannane **42**, which was used for next reaction directly.

To a mixture of **42** in CH_2Cl_2 (1.5 mL) and MeOH (3.0 mL) at −15 °C was added PPTS (13.4 mg, 53.3 μmol), and the mixture was stirred for 0.5 h, at the same temperature. The reaction mixture was quenched with Et_3N, diluted with Et_2O, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 40:1 to 30:1 to 20:1, containing 0.5% Et_3N) gave **43** (88.4 mg, 41% for the 2 steps): colorless oil; R_f=0.26 (hexane/EtOAc, 7:1); $[\alpha]_D^{23}$ −36.9 (*c* 1.41, $CHCl_3$); IR (neat) 3599–3114, 2955, 1098 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 5.86 (d, *J*=6.1 Hz, 1H), 4.49 (ddd, *J*=8.9, 8.9, 6.1 Hz, 1H), 3.76–3.62 (m, 2H), 3.49–3.37 (m, 3H), 2.09–1.96 (m, 2H), 1.96–1.49 (m, 14H), 1.42 (sex, *J*=7.3 Hz, 6H), 1.31 (s, 3H), 1.05–0.95 (m, 15H), 1.02 (s, 9H), 1.00 (s, 9H), 0.19 (s, 3H), 0.16 (s, 3H), 0.10 (s, 6H); HRMS (ESI) calcd for $C_{36}H_{78}O_4Si_2SnNa$ $(M+Na)^+$ 773.4365, found 773.4362.

4.26. Ester 44

To a mixture of **43** (126 mg, 0.168 mmol), DMSO (1.1 mL), and Et_3N (0.23 mL, 1.68 mmol) in CH_2Cl_2 (4.4 mL) at 0 °C was added $SO_3 \cdot py$ (242 mg, 0.846 mmol), and the mixture was stirred at room temperature. After 2 h, the mixture was diluted with EtOAc, then washed with saturated NH_4Cl, water, and brine. Concentration gave the crude aldehyde, which was used for the next reaction directly.

To a mixture of the aldehyde in *t*-BuOH (2.2 mL), 5% NaH_2PO_4 (2.2 mL), and 2-methyl-2-butene (3.3 mL) was added $NaClO_2$ (46.5 mg, 0.514 mmol) at 0 °C. After stirring at same temperature for 0.5 h, the mixture was diluted with EtOAc, then washed with water and brine. Concentration gave the crude carboxylic acid **35**, which was used for the next reaction directly.

To a solution of the crude **35** in THF (1 mL) were added Et_3N (0.11 mL, 0.756 mmol) and 2,4,6-trichlorobenzoyl chloride (66 μL, 0.422 mmol). After stirring for 2.5 h at room temperature, the mixture was concentrated under reduced pressure, then diluted with toluene (0.6 mL). To the resulting mixture was added a solution of **34** (29.4 mg, 54.5 μmol) and DMAP (73.3 mg, 0.594 mmol) in toluene (1.2 mL). After stirring for 2.5 h at room temperature, the mixture was diluted with EtOAc and filtered through a Celite pad. Concentration and chromatography (hexane/EtOAc, 80:1 to 40:1 to 15:1, containing 0.5% Et_3N) gave **44** (68.0 mg, 85%): colorless oil; R_f=0.60 (hexane/EtOAc, 7:1); $[\alpha]_D^{23}$ −39.7 (*c* 1.46, $CHCl_3$); IR (neat), 2955, 1743, 1102 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.82–7.75 (m, 4H), 7.27–7.21 (m, 6H), 6.06 (dd, *J*=17.5, 11.0 Hz, 1H), 5.81 (d, *J*=6.1 Hz, 1H), 5.41 (dd, *J*=17.5, 1.2 Hz, 1H), 5.12 (dd, *J*=11.0, 1.2 Hz, 1H), 5.12–5.02 (m, 1H), 4.52 (ddd, *J*=8.8, 8.8, 6.2 Hz, 1H), 4.39 (dd, 11.7, 5.4 Hz, 1H), 4.12–4.06 (m, 1H), 4.06–3.96 (m, 1H), 3.80–3.55 (m, 4H), 3.43 (d, *J*=9.3 Hz, 1H), 3.37–3.25 (m, 2H), 2.68–2.40 (m, 3H), 2.27–2.13 (m, 2H), 2.13–1.47 (m, 22H), 1.47–1.37 (m, 6H), 1.27 (s, 3H), 1.23 (s, 3H), 1.18 (s, 9H), 1.06–0.93 (m, 48H), 0.28 (s, 3H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.10 (s, 6H); HRMS (ESI) calcd for $C_{78}H_{140}O_{10}Si_4SnNa$ $(M+Na)^+$ 1491.8462, found 1491.8472.

4.27. Diene 45

To a stirring solution of **44** (22.1 mg, 15.0 μmol) in CH_2Cl_2 (2 mL) at −78 °C was added DIBAL-H (30 μL, 31 μmol, 1.02 M solution in hexane). To this mixture, pre-cooled (−40 °C) solutions of pyridine (10 μL, 120 μmol) and DMAP (15.0 mg, 123 μmol) in CH_2Cl_2 (0.5 mL), and $(clCH_2CO)_2O$ (31 mg, 181 μmol) in CH_2Cl_2 (0.5 mL) were introduced immediately. The reaction mixture was allowed to warm to 0 °C over 1 h with stirring, and quenched with H_2O. The mixture was diluted with Et_2O, then washed with saturated potassium sodium tartrate, saturated $CuSO_4$, water, saturated $NaHCO_3$, and brine. Concentration gave the crude α-chloroacetoxy ether **33**, which was used for the next reaction directly.

To the stirring suspension of $MgBr_2 \cdot OEt_2$ (102 mg, 395 μmol) and MS5 Å (50 mg) in CH_2Cl_2 (1.5 mL) at −78 °C was added a precooled (−40 °C) solution of **33** (dried over MS5 Å) in CH_2Cl_2 (2.5 mL). The mixture was allowed to warm to 0 °C over 1 h, and quenched with Et_3N. The mixture was filtered through a short silica gel column (EtOAc) and concentrated. The residue was purified by chromatography (hexane/EtOAc, 50:1 to 30:1, containing 0.5% Et_3N) to give **45** (10.0 mg, 57% for the 2 steps): colorless oil; R_f=0.20 (hexane/EtOAc, 20:1); $[\alpha]_D^{27}$ −13.7 (*c* 0.73, $CHCl_3$); IR (neat), 3071, 2851, 1086 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.83–7.75 (m, 4H), 7.27–7.21 (m, 6H), 6.21 (dd, *J*=17.4, 10.9 Hz, 1H), 5.97 (ddd, *J*=17.2, 10.6, 5.1 Hz, 1H), 5.51 (dd, *J*=17.4, 1.7 Hz, 1H), 5.46 (ddd, *J*=17.2, 1.7, 1.7 Hz, 1H), 5.17 (dd, *J*=10.9, 1.8 Hz, 1H), 5.10 (dd, *J*=10.6, 1.8 Hz, 1H), 4.52 (dd, *J*=11.5, 5.4 Hz, 1H), 4.14–4.08 (m, 1H), 3.99 (ddd, *J*=11.7, 9.3, 4.6 Hz, 1H), 3.89 (dd, *J*=6.6, 5.4 Hz, 1H), 3.76–3.55 (m, 4H), 3.45–3.24 (m, 5H), 2.36 (ddd, *J*=12.2, 4.6, 4.6 Hz, 1H), 2.24 (dd, *J*=15.7, 3.0 Hz, 1H), 1.98–1.68 (m, 9H), 1.68–1.43 (m, 8H), 1.34 (s, 3H), 1.25 (s, 3H), 1.10 (s, 12H), 1.07 (s, 9H), 1.06 (d, *J*=7.1 Hz, 3H), 1.00 (s, 9H), 0.99 (s, 9H), 0.22 (s, 3H), 0.18 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.01 (s, 6H); ^{13}C NMR (100 MHz, C_6D_6) δ 143.6, 138.5, 136.0 (4C), 134.5 (2C), 129.9 (2C), 127.9 (4C), 114.7, 113.3, 88.1, 86.3, 83.2, 79.1, 78.1, 77.7, 76.6, 76.4, 73.4, 73.1, 72.6, 71.2, 64.4, 63.9, 49.9, 37.7, 35.7, 34.8, 33.3, 30.8, 30.0, 29.6, 27.7, 27.3 (3C), 27.2, 26.4 (6C), 26.3 (3C), 23.3, 21.3, 19.6, 18.7, 18.6, 18.5, 15.7, 13.1, −1.6, −1.7, −4.0, −4.4, −4.9 (2C); HRMS (ESI) calcd for $C_{66}H_{114}O_9Si_4Na$ $(M+Na)^+$ 1185.7438, found 1185.7432.

4.28. Pentacycle 2

To a mixture of **45** (6.9 mg, 5.9 μmol) in toluene (1.0 mL) was added the Grubbs' catalyst **29** (4.8 mg, 5.8 μmol). After stirring for 45 min at 80 °C, an additional amount of **29** (16.1 mg, 19.6 μmol) was added. After stirring for 1 h at 80 °C, the reaction mixture was quenched with Et_3N at room temperature, diluted with EtOAc, filtered through a short silica gel column (hexane/EtOAc, 2:1, containing 0.5% Et_3N). The filtrate was concentrated to give the crude **46**, which was used for next reaction without further purification.

To a stirred solution of the crude **46**, pyridine (0.16 mL, 1.98 mmol) and $KO_2CN{=}NCO_2K$ (126 mg, 0.646 mmol) in MeOH (1 mL) at room temperature was added a solution of AcOH (74 μL, 1.29 mmol) in MeOH (0.3 mL) over 1 h via a syringe pump. The reaction mixture was quenched with saturated NH_4Cl, diluted with Et_2O. The organic layer was washed with saturated $CuSO_4$, water, saturated $NaHCO_3$, and brine. After concentration, the residue was filtered through a short silica gel column (hexane/Et_2O, 10:1) to give the crude **47**, which was used for next reaction without further purification.

To a stirred mixture of the crude TBS ether **47** in CH_2Cl_2 (0.4 mL) and MeOH (0.80 mL) at 0 °C was added CSA (2.4 mg, 10 μmol). After stirring for 1 h at the same temperature, the reaction mixture was quenched with Et_3N. Concentration and chromatography (hexane/EtOAc, 20:1 to 10:1 to 5:1) gave **2** (4.6 mg, 76% for the 3 steps).

4.29. (*Z*)-Diene 49

To a mixture of **2** (4.8 mg, 4.69 μmol) in CH_2Cl_2 (0.4 mL) and DMSO (0.1 mL) at 0 °C was added Et_3N (65 μL, 0.469 mmol) and $SO_3 \cdot py$ (37.3 mg, 0.235 mmol). After stirring for 1 h at room temperature, the mixture was diluted with EtOAc, then washed with saturated NH_4Cl, water, and brine. Concentration gave the crude aldehyde, which was used for the next reaction directly.

To a stirring suspension of **48** (126.7 mg, 0.235 mmol) in THF (0.3 mL) at −30 °C was added NaHMDS (0.19 mL, 0.190 mmol, 1.0 M solution in THF). After stirring for 15 min at the same temperature, the mixture was cooled to −78 °C. To this solution was added a precooled (−78 °C) solution of the crude aldehyde in THF (0.7 mL), and the mixture was allowed to warm to room temperature over 1 h with stirring. The reaction mixture was quenched with saturated $NaHCO_3$, diluted with EtOAc, then washed with water and brine. After concentration, the residue was filtered through a short silica gel column (hexane/EtOAc, 10:1) to give the crude phenylselenide, which was used for next reaction without further purification.

To a mixture of the crude phenylselenide in THF (0.6 mL) at room temperature were added $NaHCO_3$ (7.9 mg, 93.8 μL) and 30% H_2O_2 (0.2 mL), and the mixture was stirred for 21 h at 30 °C. The reaction mixture was quenched with saturated Na_2SO_3 at 0 °C, then diluted with EtOAc, washed with water and brine. Concentration and chromatography (hexane/EtOAc, 100:1 to 70:1 to 40:1 to 20:1) gave **49** (4.4 mg, 90% for the 3 steps): colorless oil; R_f=0.38 (hexane/EtOAc, 10:1); $[\alpha]_D^{24}$ −14.3 (*c* 0.20, $CHCl_3$); IR (neat) 2930, 1737, 1643, 1087 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, *J*=7.8, 1.5 Hz, 4H), 7.41–7.31 (m, 6H), 6.63 (ddd, *J*=16.8, 11.1, 10.0 Hz, 1H), 6.01 (dd, *J*=11.1, 10.0 Hz, 1H), 5.41 (ddd, *J*=10.0, 6.6, 6.6 Hz, 1H), 5.18 (d, *J*=16.8 Hz, 1H), 5.07 (d, *J*=10.0 Hz, 1H), 4.17 (dd, *J*=11.6, 5.0 Hz, 1H), 3.94 (dd, *J*=3.7, 3.7 Hz, 1H), 3.74–3.56 (m, 3H), 3.39 (dd, *J*=6.8, 6.8, 1H), 3.30–3.15 (m, 4H), 3.11 (dd, *J*=12.1, 3.8 Hz, 1H), 2.36–2.19 (m, 2H), 2.19–1.20 (m, 21H), 1.14 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 1.02 (s, 9H), 0.89 (s, 9H), 0.88 (d, *J*=6.3 Hz, 3H), 0.82 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.5 (4C), 134.1 (2C), 132.7, 132.1, 129.6, 129.4 (2C), 127.5 (4C), 117.0, 86.9, 86.3, 85.2, 82.1, 77.6, 77.2, 76.1, 75.5, 73.1, 72.9, 72.6, 70.8, 64.0, 49.5, 37.8, 37.7, 35.0, 34.0, 32.6, 30.2, 29.8, 29.3, 29.1, 28.8, 27.0 (3C), 25.9 (3C), 25.8 (3C), 24.8, 24.1, 20.9, 19.3, 18.3, 18.1, 16.3, 12.4, −2.0, −2.2, −4.2, −4.8; HRMS (ESI TOF) calcd for $C_{61}H_{100}O_8Si_3Na$ $(M+Na)^+$ 1067.6624, found 1067.6631.

4.30. Alcohol 50

To a mixture of **49** (3.3 mg, 3.16 μmol) in THF (0.1 mL) at room temperature was added a solution of TBAF/AcOH (0.1 mL, prepared from 0.5 mL of TBAF (1.0 M solution in THF) and 30 μL of AcOH). After stirring for 11 h, the mixture was diluted with EtOAc, then washed with saturated $NaHCO_3$, water, and brine. Concentration and chromatography (hexane/EtOAc, 7:1 to 4:1 to 3:1) gave **50** (2.4 mg, 94%): colorless oil; R_f=0.10 (hexane/EtOAc, 4:1); $[\alpha]_D^{23}$ −22.3 (*c* 0.12, $CHCl_3$); IR (neat) 3661–3120, 2928, 1737, 1643, 1089 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.63 (ddd, *J*=16.8, 11.0, 9.8 Hz, 1H), 6.01 (dd, *J*=11.0, 10.2 Hz, 1H), 5.41 (ddd, *J*=10.2, 7.1, 7.1 Hz, 1H), 5.17 (d, *J*=16.8 Hz, 1H), 5.07 (d, *J*=9.8 Hz, 1H), 4.22 (dd, *J*=11.6, 5.0 Hz, 1H), 3.95 (dd, *J*=3.7, 3.7 Hz, 1H), 3.74–3.59 (m, 2H), 3.59–3.46 (m, 2H), 3.30–3.14 (m, 4H), 3.11 (dd, *J*=12.2, 3.9 Hz, 1H), 2.92 (br s, 1H), 2.38–2.20 (m, 2H), 2.18–1.95 (m, 3H), 1.91–1.20 (m, 18H), 1.23 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 0.93 (d, *J*=6.8 Hz, 3H), 0.90 (s, 9H), 0.82 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.7, 132.1, 129.6, 117.0, 86.9, 86.3, 85.2, 82.0, 78.5, 77.2, 76.2, 75.5, 73.2, 72.6, 72.5, 72.3, 62.8, 49.3, 37.8, 37.7, 34.9, 33.9, 33.6, 30.6, 30.5, 30.1, 29.8, 28.8, 26.0 (3C), 25.8 (3C), 24.8, 24.0, 20.7, 18.3, 18.1, 16.3, 12.6, −2.0, −2.2, −4.2, −4.8; HRMS (ESI TOF) calcd for $C_{45}H_{82}O_8Si_2Na$ $(M+Na)^+$ 829.5446, found 829.5440.

4.31. Reaction of 51 and 52

To a mixture of phosphate **52** (120 mg, 0.46 mmol) in THF (1.2 mL) −78 °C was added *n*-BuLi (0.22 mL, 0.37 mmol, 1.65 M solution in hexane), and the mixture was stirred for 10 min at the same temperature. After stirring for additional 50 min at 0 °C, the mixture was cooled to −78 °C. To this mixture was added a precooled (−78 °C) solution of the aldehyde **51** (30 mg, 0.0191 mmol) in THF (0.8 mL). The reaction mixture was allowed to warm to room temperature over 1 h with stirring. The reaction was quenched with saturated NH_4Cl, diluted with EtOAc, and washed with water and brine. Concentration and chromatography (hexane/EtOAc, 100:1 to 70:1 to 40:1 to 20:1) gave **53** (37 mg, 92%): colorless oil; R_f=0.72 (hexane/EtOAc, 4:1); IR (neat) 3071, 2931, 1609 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.66–7.63 (m, 4H), 7.42–7.33 (m, 6H), 5.88 (t, *J*=7.2 Hz, 1H), 5.83 (s, 1H), 3.70 (s, 3H), 3.66 (t, *J*=6.3 Hz, 2H), 2.28 (s, 3H), 2.27–2.23 (m, 2H), 1.79 (s, 3H), 1.68–1.61 (m, 2H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.5, 135.5 (4C), 135.4, 133.8 (2C), 132.9, 129.5, 129.4 (2C), 127.5 (4C), 113.9, 63.2, 50.9, 32.2, 26.9 (3C), 25.3, 19.3, 15.5, 14.1; HRMS (ESI TOF) calcd for $C_{27}H_{36}O_3SiNa$ $(M+Na)^+$ 459.2332, found 459.2312.

4.32. Unsaturated ester 54

To a solution of **50** (2.4 mg, 2.97 μmol) in CH_2Cl_2 (0.3 mL) and DMSO (0.1 mL) at 0 °C were added Et_3N (41 μL, 0.297 mmol) and $SO_3 \cdot py$ (23.6 mg, 0.149 mmol), and the mixture was stirred for 45 min at room temperature. The mixture was diluted with EtOAc, then washed with saturated NH_4Cl, water, and brine. After concentration, the residue was filtered through a short silica gel column (Et_2O) to give the crude aldehyde, which was used for the next reaction directly.

To a solution of **52** (92.3 mg, 0.349 mmol) in THF (0.2 mL) −78 °C was added *n*-BuLi (0.19 mL, 0.297 mmol, 1.59 M solution in hexane), and the mixture was stirred for 10 min at the same temperature. After stirring for additional 50 min at 0 °C, the mixture was cooled to −78 °C. To this mixture was added a pre-cooled (−78 °C) solution of the crude aldehyde in THF (0.7 mL). The reaction mixture was allowed to warm to room temperature over 1 h with stirring. After stirring the mixture for additional 26 h at room temperature, the reaction mixture was quenched with saturated NH_4Cl, diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 100:1 to 70:1 to 40:1 to 20:1) gave **54** (2.4 mg, 88% for the 2 steps): colorless oil; R_f=0.59 (hexane/EtOAc, 4:1); $[\alpha]_D^{23}$ −22.4 (*c* 0.12, $CHCl_3$); IR (neat) 2929, 1719, 1609, 1086 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.63 (ddd, *J*=17.1, 10.9, 10.2 Hz, 1H), 6.01 (dd, *J*=10.9, 10.0 Hz, 1H), 5.93 (t, *J*=7.1 Hz, 1H), 5.82 (s, 1H), 5.41 (ddd, *J*=10.0, 7.3, 7.3 Hz, 1H), 5.18 (d, *J*=17.1 Hz, 1H), 5.07 (d, *J*=10.2 Hz, 1H), 4.19 (dd, *J*=11.5, 5.1 Hz, 1H), 3.95 (dd, *J*=3.4, 3.4 Hz, 1H), 3.74–3.62 (m, 1H), 3.69 (s, 3H), 3.45–3.39 (m, 1H), 3.30–3.15 (m, 4H), 3.11 (dd, *J*=12.2, 4.1 Hz, 1H), 2.37–1.20 (m, 23H), 2.29 (s, 3H), 1.78 (s, 3H), 1.17 (s, 3H), 1.10 (s, 3H), 1.06 (s, 3H), 0.91 (d, *J*=7.1 Hz, 3H), 0.90 (s, 9H), 0.82 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 135.8, 133.5, 132.7, 132.1, 129.6 (2C), 117.0, 113.8, 86.9, 86.3, 85.2, 82.1, 77.7, 77.2, 76.1, 75.5, 73.1, 72.8, 72.6, 70.7, 50.9, 49.5, 37.8, 37.7, 35.0, 34.0, 32.9, 32.5, 30.2, 29.8 (2C), 28.8, 25.9 (3C), 25.8 (3C), 24.8, 24.0, 20.9, 18.3, 18.1, 16.3, 15.5, 14.1, 12.6, −2.0, −2.2, −4.2, −4.8; HRMS (ESI TOF) calcd for $C_{52}H_{90}O_9Si_2Na$ $(M+Na)^+$ 937.6021, found 937.6024.

4.33. Triol 55

To a solution of **54** (2.4 mg, 2.62 μmol) in CH_2Cl_2 (0.7 mL) at −78 °C was added DIBAL-H (10 μL, 10.2 μmol, 1.02 M solution in hexane). After stirring for 15 min, the reaction mixture was quenched with MeOH, diluted with Et_2O, then filtered through a short silica gel column (Et_2O to EtOAc). Concentration gave the crude alcohol, which was used for the next reaction directly.

A mixture of the crude alcohol obtained and TBAF (0.2 mL, 0.2 mmol, 1.0 M solution in THF) was stirred for 32 h at 75 °C in a sealed tube. The mixture was diluted with EtOAc, then washed with water and brine. Concentration and chromatography (hexane/EtOAc, 1:1 to 1:2 to 0:1) gave **55** (1.7 mg, 98% for the 2 steps): colorless oil; R_f=0.19 (hexane/EtOAc, 1:1); $[\alpha]_D^{25}$ −22.4 (*c* 0.08, benzene); IR (neat) 3649–3114, 2929, 1643, 1087 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 6.76 (ddd, *J*=16.8, 10.9, 10.5 Hz, 1H), 6.08 (dd, *J*=10.9, 10.5 Hz, 1H), 5.70 (t, *J*=6.3 Hz, 1H), 5.65 (t, *J*=7.3 Hz, 1H), 5.45 (ddd, *J*=10.5, 7.3, 7.3 Hz, 1H), 5.16 (d, *J*=16.8 Hz, 1H), 5.06 (d, *J*=10.5 Hz, 1H), 4.10–4.05 (m, 3H), 4.01 (dd, *J*=11.4, 5.5 Hz, 1H), 3.70 (ddd, *J*=11.2, 9.7, 5.2 Hz, 1H), 3.45 (dd, *J*=9.6, 2.8 Hz, 1H), 3.44–3.39 (m, 1H), 3.34 (ddd, *J*=8.4, 8.4, 7.5 Hz, 1H), 3.20–3.12 (m, 2H), 2.93 (dd, *J*=12.3, 4.0 Hz, 1H), 2.39–2.07 (m, 9H), 1.95–1.23 (m, 17H), 1.81 (s, 3H), 1.71 (s, 3H), 1.22 (s, 3H), 1.12 (s, 3H), 0.99 (d, *J*=7.1 Hz, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, C_6D_6) δ 138.2, 136.1, 132.9, 132.6, 130.1, 127.5, 125.5, 117.2, 87.4, 86.2, 84.7, 82.0, 77.3, 77.2, 76.7, 75.1, 74.1, 73.7, 70.8, 69.9, 60.1, 48.0, 38.6, 37.8, 35.5, 34.6, 33.6, 33.4, 30.8, 30.0, 29.4, 26.1, 25.3, 23.7, 19.4, 16.3, 14.4, 14.3, 13.0; HRMS (ESI TOF) calcd for $C_{39}H_{62}O_8Na$ $(M+Na)^+$ 681.4343, found 681.4343.

4.34. Brevenal (1)

To a mixture of **55** (1.0 mg, 1.52 μmol) in CH_2Cl_2 (0.2 mL) at room temperature was added MnO_2 (4.0 mg, 46.0 μmol). After stirring for 1 h, the mixture was filtered through a short silica gel column (EtOAc), and the filtrate was concentrated. The residue was purified by chromatography (hexane/EtOAc, 2:1 to 1:1 to 1:2) to give **1** (1.0 mg, quant.): colorless oil; R_f=0.30 (hexane/EtOAc, 1:1); $[\alpha]_D^{23}$ −27.7 (*c* 0.05, benzene); IR (neat) 3655–3163, 2935, 1657, 1619, 1087 cm^{-1}; ^{1}H NMR (400 MHz, C_6D_6) δ 10.08 (d, *J*=7.6 Hz, 1H), 6.76 (ddd, *J*=16.8, 10.2, 10.0 Hz, 1H), 6.14 (d, *J*=7.6 Hz, 1H), 6.08 (dd, *J*=10.7, 10.2 Hz, 1H), 5.81 (t, *J*=7.2 Hz, 1H), 5.45 (ddd, *J*=10.7, 7.8, 7.8 Hz, 1H), 5.16 (d, *J*=16.8 Hz, 1H), 5.06 (d, *J*=10.0 Hz, 1H), 4.10–4.04 (m, 1H), 4.01 (dd, *J*=10.7, 6.3 Hz, 1H), 3.71 (ddd, *J*=10.5, 9.5, 5.1 Hz, 1H), 3.45 (dd, *J*=9.5, 2.4 Hz, 1H), 3.39–3.31 (m, 1H), 3.28 (ddd, *J*=9.0, 2.9, 2.9 Hz, 1H), 3.21–3.13 (m, 2H), 2.94 (dd, *J*=12.3, 4.0 Hz, 1H), 2.38–1.97 (m, 9H), 1.97–1.38 (m, 14H), 1.79 (s, 3H), 1.55 (s, 3H), 1.18 (s, 3H), 1.14 (s, 3H), 1.13–1.06 (m, 1H), 0.97 (s, 3H), 0.96 (d, *J*=7.3 Hz, 3H), 0.55 (br s, 1H); ^{13}C NMR (100 MHz, C_6D_6) δ 190.5, 156.1, 135.9, 134.5, 132.9, 132.6, 130.1, 126.0, 117.2, 87.4, 86.2, 84.8, 82.0, 77.3, 76.8, 76.5, 75.1, 74.0, 73.3, 70.9, 70.0, 47.5, 38.6, 37.8, 35.4, 34.6, 33.6, 32.8, 30.8, 30.0, 29.5, 26.6, 25.3, 23.7, 19.4, 16.3, 14.0, 13.9, 12.9; HRMS (ESI TOF) calcd for $C_{39}H_{60}O_8Na$ $(M+Na)^+$ 679.4186, found 679.4190.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.05.069. These data include MOL files and InChIKeys of the most important compounds described in this article.

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