Unified Total Synthesis, Stereostructural Elucidation, and Biological Evaluation of Sarcophytonolides
Hiroyoshi Takamura,*1 Takahiro Kikuchi,1 Kohei Iwamoto,1 Eiji Nakao,1 Naoki Harada,1 Taichi Otsu,1 Noriyuki Endo,2 Yuji Fukuda,2 Osamu Ohno,3 Kiyotake Suenaga,4 Yue-Wei Guo,5 and Isao Kadota1
1Department of Chemistry, Graduate School of Natural Science and Technology, Okayama University, 3-1-1 Tsushimanaka, Kita-ku, Okayama 700-8530, Japan
2Himeji EcoTech Co., Ltd., 841-49 Koh, Shirahama-cho, Himeji 672-8023, Japan
3Department of Chemistry and Life Science, School of Advanced Engineering, Kogakuin University, 2665-1 Nakano, Hachioji 192-0015, Japan
4Department of Chemistry, Faculty of Science and Technology, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223-8522, Japan
5Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zu Chong Zhi Road, Zhangjiang Hi-Tech Park, Shanghai 201203, China
takamura@cc.okayama-u.ac.jp

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Abstract
Sarcophytonolides are cembranolide diterpenes isolated from the soft corals of genus Sarcophyton. Unified total synthesis of sarcophytonolides C, E, F, G, H, and J and isosarcophytonolide D was achieved. The synthetic routes feature NaHMDS- or SmI2-mediated fragment coupling, alkoxycarbonylallylation, macrolactonization, and transannular ring-closing metathesis. These total syntheses led to the absolute configurational confirmation of sarcophytonolide H, elucidation of sarcophytonolides C, E, F, and G, and revision of sarcophytonolide J and isosarcophytonolide D. We also evaluated the antifouling activity and toxicity of the synthetic sarcophytonolides H and J and their analogues as well as the cytotoxicity of the synthetic sarcophytonolides and the key synthetic intermediates.

Introduction
Corals are an important group of marine invertebrates and have proven to be a rich source of secondary metabolites with a diversity of the chemical structure and biological activity.1 Among natural products isolated from soft corals, cembranolide diterpenes2 exhibit a variety of biological activities such as antibacterial,3 antifouling,4 antiviral,5 cytotoxic,6 ichthyotoxic,7 and protein tyrosine phosphatase 1B inhibitory activities.8 In addition, it has been reported that cembranoid diterpenes are implicated in defense of soft corals against predators and
competition between soft corals and hard corals.\textsuperscript{1a,9}

Guo and co-workers have isolated sarcophytonolides, cembranolide diterpenes, from the soft corals of the genus \textit{Sarcophyton} collected at Hainan Province in China since 2005.\textsuperscript{8,10} These natural products have a 14-membered carbon skeleton and butenolide unit as common structures as described in Figure 1. The gross structure of sarcophytonolide C (1) was determined by the 2D NMR analysis and comparison of its NMR data with those of brassicolide (5), of which the relative configuration was assigned by X-ray crystallographic analysis.\textsuperscript{6b,10a} Although the relative stereochemistries at the C1 and C2 positions of 1 were elucidated by NOE observations between H-2 and H-15, the configuration at the C8 position, which is a chiral center remote from the C1 and C2 positions, could not be determined. The relative configurations at the C6 and C8 positions of sarcophytonolide E (2) were assigned by NOE correlations of H-6/H3-19 and analysis of coupling constants and splitting patterns of H2-5 in the model wherein a hydrogen bond between the hydroxy and the carbonyl groups is formed.\textsuperscript{10b} The relative configurations of sarcophytonolides F (3) and G (4), which have the C7/C8 trisubstituted alkenes and the C6 stereoisomeric relationship, were revealed by NOE experiments and analysis of their coupling constants of H2-5.\textsuperscript{10b} The relative stereochemistry of sarcophytonolide H (6) was clarified by the similarity of \textsuperscript{1}H and \textsuperscript{13}C NMR data between 6 and 3 and NOE observations such as those of H-2/H-14 and H-2/H-15.\textsuperscript{10b} The absolute configuration of 6 was determined by applying the modified Mosher method.\textsuperscript{11} The relative stereochemistry of sarcophytonolide D (7) possessing the \(\alpha\)-oriented acetoxy group at the C14 position was elucidated by NOE experiments.\textsuperscript{10a,12} The relative stereochemistries at the C1, C2, and C14 positions of sarcophytonolides I (8),\textsuperscript{10c} J (9),\textsuperscript{10c} and isosarcophytonolide D (10)\textsuperscript{10d} were assigned by the analogy of their \textsuperscript{1}H and \textsuperscript{13}C NMR data to those of sarcophytonolide D (7), whereas the C8 stereochemistry of 9 has remained to be clarified as in the case of sarcophytonolide C (1). Among these sarcophytonolides, sarcophytonolides H (6) and J (9) display the antifouling activity against the cypris larvae of the barnacle \textit{Balanus (Amphibalanus) amphitrite} with EC\textsubscript{50} values of 5.98\textsuperscript{13} and 7.50 \(\mu\text{g/mL},\textsuperscript{14} respectively. Interestingly, there is also a report wherein sarcophytonolide J (9) has no inhibitory activity against the larval settlement of the same barnacle.\textsuperscript{13} In 2013, as a preliminary communication, we reported the total synthesis of two possible diastereomers of sarcophytonolide C (1), which resulted in the absolute configurational determination of this natural product.\textsuperscript{15a,16} In 2016, we also reported the total synthesis of sarcophytonolide H (6) and isosarcophytonolide D (10, proposed structure), which culminated in the absolute stereochemical confirmation of 6 and revision of 10.\textsuperscript{15b} In this full paper, we disclose the unified total synthesis of sarcophytonolides C, E, F, G, H, and J and isosarcophytonolide D by using NaHMDS- or SmI\textsubscript{2}-mediated fragment coupling, alkoxy carbonylation, macrolactonization, and transannular ring-closing metathesis (RCM) as key steps. These total syntheses culminated in the absolute stereochemical confirmation of sarcophytonolide H, determination of sarcophytonolides C, E, F, and G, and revision of sarcophytonolide J and isosarcophytonolide
D. Furthermore, we report the cytotoxicity of the synthetic sarcophytonolides and the key synthetic intermediates, and the antifouling activity and toxicity of the synthetic sarcophytonolides H and J and their analogues.

Figure 1. Structures of selected sarcophytonolides and brassicolide.

Results and Discussion

Retrosynthetic Analysis of 1a and 1b. Toward the absolute configurational determination of natural sarcophytonolide C (1), we decided to synthesize 1a and 1b (Scheme 1), which are two possible diastereomers of this natural product. In the retrosynthetic analysis, we designed hydroxycarboxylic acids 11a and 11b as the key synthetic intermediates to construct the cembranolide frameworks of 1a and its C8 epimer 1b by macrolactonization\textsuperscript{17} and subsequent transannular RCM\textsuperscript{18}, respectively.\textsuperscript{19} We hypothesized that the macrolactonization precursors 11a,b could possibly supplied by the connection of sulfone 12, allylic bromides 13a and 13b, and 2-alkoxycarbonyl allylic metal reagent 14. The chiral pool synthesis starting from (S)- and (R)-citronellols could provide the allylic bromides 13a,b, respectively. We envisioned that this retrosynthetic bond-disconnection could be also applied to the synthesis of C6 hydroxylated and/or C14 acetoxylated sarcophytonolides. Moreover, the use of geraniol and nerol instead of citronellol as starting materials would potentially lead to the total synthesis of
sarcophytonolides bearing the C7/C8 trisubstituted alkene moieties.

**Scheme 1. Retrosynthetic Analysis of 1a and 1b**

![Scheme 1](image)

**Total Synthesis of Two Possible Diastereomers 1a and 1b of Sarcophytonolide C (1).** First, we investigated the enantioselective synthesis of sulfone 20 (Scheme 2). Monosilylation of cis-2-butene-1,4-diol with tert-butyldimethylsilyl chloride (TBSCl) followed by Sharpless asymmetric epoxidation\(^\text{20}\) with (+)-diethyl tartrate (DET) gave epoxy alcohol 15 in 86% yield. The enantiomeric ratio of 17:1 was assigned by the \(^1\)H NMR spectra of (S)- and (R)-α-methoxy-β-(trifluoromethyl)phenylacetyl (MTPA) esters prepared from 15. The epoxide 15 reacted with isopropenylmagnesium bromide in the presence of CuBr-SMe\(^\text{21}\) to provide 1,3-diol 16, regioselectively.\(^\text{22}\) Hydrogenation of the alkene 16 with (Ph\(_3\)P)\(_3\)RhCl and subsequent selective thioetherification of diol 17\(^\text{23}\) with (PhS\(_2\))/n-Bu\(_3\)P afforded sulfide 18. After the alcohol 18 was protected as the TBS ether, sulfide 19 was oxidized to furnish the sulfone 20.\(^\text{24}\)

**Scheme 2. Synthesis of Sulfone 20**

![Scheme 2](image)
Next, connection of the sulfone 20 and allylic bromides 21a and 21b, which were synthesized from (S)- and (R)-citronellols,\textsuperscript{25} was examined (Scheme 3). Thus, the anion derived from 20 with sodium hexamethyldisilazide (NaHMDS) was treated with the optically active 21a and 21b to produce the coupling products 22a and 22b in 88% and 91% yields, respectively. Reductive removal of the sulfonyl groups of 22a,b under Birch conditions,\textsuperscript{26} wherein the pivaloyl (Piv) groups were partially removed,\textsuperscript{27} and protection of the resulting alcohols afforded the corresponding pivalates. The primary TBS ethers were selectively deprotected with camphorsulfonic acid (CSA) to give alcohols 23a and 23b. Oxidation of 23a,b with 2,2,6,6-tetramethylpiperidinyloxyl (TEMPO)/PhI(OAc)\textsuperscript{28} and subsequent Wittig reaction yielded alkenes 24a and 24b. Reductive deprotection of the pivalates 24a,b was carried out with diisobutylaluminum hydride (DIBAL-H) to provide alcohols 25a and 25b.

\textbf{Scheme 3. Synthesis of Alcohols 25a and 25b}
We next tried to synthesize the macrolactonization precursors 30a and 30b as shown in Scheme 4. The alcohols 25a,b were oxidized with TEMPO/PhI(OAc)$_2$\cite{28} and the resulting aldehydes were treated with ethyl (2-bromomethyl)acrylate (26)/Zn dust in THF/aqueous NH$_4$Cl\cite{29} to furnish the desired homoallylic alcohols 27a and 27b in 79% and 93% yields in two steps as 1:1 diastereomeric mixtures, respectively. After the resulting hydroxy groups of 27a,b were protected as the methoxymethyl (MOM) ethers, the TBS moieties of 28a and 28b were removed with tetrabutylammonium fluoride (TBAF) to give alcohols 29a and 29b. Alkaline hydrolysis of the ethyl esters 29a,b with LiOH-H$_2$O afforded hydroxycarboxylic acids 30a and 30b.

Scheme 4. Synthesis of Hydroxycarboxylic Acids 30a and 30b
Scheme 5. Completion of the Total Synthesis of 1a and 1b

With the macrolactonization precursors 30a and 30b in hand, we next investigated the construction of the cembranolide framework and completion of the total synthesis. Thus, the hydroxycarboxylic acids 30a,b were subjected to the Shiina macrolactonization conditions with 2-methyl-6-nitrobenzoic anhydride (MNBA)\textsuperscript{17,30} to give 15-membered macrolactones 31a and 31b in 85% and 78% yields, respectively (Scheme 5). After the MOM ethers 31a,b were deprotected with BF\textsubscript{3} \cdot OEt\textsubscript{2}/Me\textsubscript{2}S,\textsuperscript{31} transannular RCM\textsuperscript{18} of 32a and 32b was conducted by using the second-generation Hoveyda–Grubbs catalyst (33)\textsuperscript{32} to produce butenolides 34a.
and 34b. In these reactions, the prolonged reaction time caused the formation of byproducts, therefore the starting materials 32a and 32b were recovered in 38% and 37% yields, respectively. Finally, TPAP (tetra-n-propylammonium perruthenate) oxidation of 34a,b provided the target molecules 1a and 1b in 27% (43% based on recovered 32a) and 30% (48% based on recovered 32b) in two steps, respectively.

Absolute Configuration of Sarcophytonolide C (1). Having succeeded in the total synthesis of 1a and 1b, we analyzed their 2D NMR spectra and assigned the signals in their 1H and 13C NMR spectra. Tables 1 and 2 depict the chemical shifts and their differences of natural sarcophytonolide C (1) and the synthetic products 1a and 1b in the 1H and 13C NMR spectra, respectively. The 1H and 13C NMR data of 1a were in excellent agreement with those of natural sarcophytonolide C (1), meanwhile the 1H and 13C NMR data of 1b were clearly different from those of natural product 1. It was found that there were critical differences of the chemical shifts between the natural product and the synthetic 1b at the C7, C8, and C9 positions in the 1H NMR data and at the C9, C10, and C11 positions in the 13C NMR data. The sign of specific rotation of the synthesized 1a, [α]D29 = +92.2 (c = 0.19, CHCl3), was same as that of the data reported for the natural product, [α]D20 = +31.0 (c = 0.20, CHCl3). Therefore, the absolute configuration of sarcophytonolide C (1) isolated from nature was clarified to be 1S, 2S, and 8S as shown in 1a.

### Table 1. 1H NMR Chemical Shifts and Their Deviations of Natural Sarcophytonolide C (1) and the Synthetic Products 1a and 1b

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$^a$NMR spectra of the natural product and the synthetic products were recorded at 400 MHz. Chemical shifts are reported in ppm with reference to the internal residual solvent (CDCl$_3$, 7.26 ppm). $^b$Data from reference 10a.
C8 carbon is located more inside the macrocycle structure in comparison with the case of the most stable conformer of 1b, which seems to make the distances between C1/C2 and C8 in 1a shorter than those in 1b. This conformational difference of 1a and 1b may have resulted in the deviation in their NMR data in spite of the C8 stereocenter remote from the C1 and C2 positions.

Figure 2. Calculated lowest-energy conformers of 1a (above) and 1b (below).

**Total Synthesis of Sarcophytonolide E (2).** Next, we examined the stereoselective synthesis of sarcophytonolide E (2) possessing the chiral alcohol moiety at the C6 position. First, we surveyed the reaction conditions in asymmetric alkoxy carbonylallylation of the aldehyde prepared from the alcohol 25a and it was proven that treatment of the aldehyde with chiral allylic boronate 35 in toluene at room temperature provided the desired alcohol 36 in a 4.4:1 diastereomeric ratio (Scheme 6). Further transformation from 36 to sarcophytonolide E (2) was identical to that used for the total synthesis of 1a and 1b. Thus, MOM protection of the resulting hydroxy group of 36 and removal of the TBS moiety afforded alcohol 37. Alkaline hydrolysis of the ethyl ester 37 followed by Shiina macrolactonization yielded 15-membered macrolactone 38. Deprotection of the MOM ether 38 with BF₃·OEt₂/Me₂S and subsequent transannular RCM produced sarcophytonolide E (2). The ¹H and ¹³C NMR data and the specific rotation of the synthesized 2 were in good accordance with those of the natural product, which elucidated the absolute stereochemistry of natural sarcophytonolide E to be that described in 2.
Scheme 6. Total Synthesis of Sarcophytonolide E (2)

Total Synthesis of Sarcophytonolides F (3) and G (4). Having completed the total synthesis of 1a, 1b, and 2 bearing the chiral centers at the C8 positions, we next investigated the stereoselective synthesis of sarcophytonolides F (3) and G (4) with the C7/C8 (E)-trisubstituted alkene portions. First, as shown in Scheme 7, the synthesis of allylic bromide 41, which is a coupling partner of the sulfone 20, was carried out. Protection of geraniol with PivCl gave pivalate 39. Treatment of 39 with SeO2/TBHP/salicylic acid provided the mixture of allylic alcohol 40 and the corresponding α,β-unsaturated aldehyde. The mixture was treated with NaBH4 to afford the allylic alcohol 40 in 57% yield in two steps. The structure of 40 was confirmed by NOE observations of H2-1/H-3. The allylic alcohol 40 was converted to the allylic bromide 41 with CBr4/PPh3.

Scheme 7. Synthesis of Allylic Bromide 41
We next tried the connection of the sulfone 20 and the allylic bromide 41, and transformation to sarcophytonolides F (3) and G (4). Thus, the sulfone 20 was coupled with the allylic bromide 41 in the presence of NaHMDS to afford the desired product 42 (Scheme 8). After deprotection of the pivalate 42 with DIBAL-H, reductive desulfonylation was conducted under Birch conditions\textsuperscript{26} to give alcohol 43 in 79% yield in two steps.\textsuperscript{42} The alcohol 43 was converted to alkene 45 by the following sequence: 1) protection as the pivalate, 2) selective removal of the primary TBS moiety, 3) TEMPO oxidation\textsuperscript{28} of alcohol 44, 4) Wittig methylation, and 5) deprotection of the pivalate. The aldehyde, synthesized from the alcohol 45, was treated with the chiral allylic boronate 35\textsuperscript{38} to result in the diastereoselective formation of alcohol 46 in a 17:1 ratio.\textsuperscript{22} After protection of the alcohol 46 and subsequent desilylation, hydrolysis of 47 and Shiina lactonization\textsuperscript{17,30} were carried out to afford macrolactone 48. Transannular RCM\textsuperscript{18} of the tetraene 48 proceeded smoothly in the presence of the second-generation Hoveyda–Grubbs catalyst (33),\textsuperscript{32} wherein two trisubstituted alkene portions of 48 were inert to the reaction conditions, to produce the corresponding butenolide in 76% yield. Finally, the MOM protecting group was cleaved with trimethylsilyl iodide (TMSI)/HMDS\textsuperscript{43,44} to furnish sarcophytonolide F (3). We next tried to transform sarcophytonolide F (3) to sarcophytonolide G (4) by stereoinversion at the C6 position. Mitsunobu reaction\textsuperscript{45} of 3 with p-nitrobenzoic acid/diethyl azodicarboxylate (DEAD)/Ph\textsubscript{3}P\textsuperscript{46} followed by alkaline hydrolysis with Na\textsubscript{2}CO\textsubscript{3} in MeOH provided sarcophytonolides G (4) and F (3) in 31% and 13% yields in two steps, respectively. The formation of 3 was caused by the esterification with stereoretention in the first step.\textsuperscript{47} Changing reaction temperature and carboxylic acid in Mitsunobu reaction\textsuperscript{45} could not improve the chemical yield of 4. Therefore, we next examined the stereoselective reduction of the ketone. Treatment of the allylic alcohol 3 with Dess–Martin periodinane\textsuperscript{48} gave α,β-unsaturated ketone 49. Corey–Bakshi–Shibata (CBS) reduction\textsuperscript{49} using (R)-Me-CBS/BH\textsubscript{3}∙SM\textsubscript{2} was applied to 49 to result in the formation of 4 and 3 in a 1:1 diastereomeric ratio. After investigation of the reaction conditions, fortunately, Luche reduction conditions\textsuperscript{50} in MeOH/CH\textsubscript{2}Cl\textsubscript{2} was found to be effective and sarcophytonolide G (4) was produced in 72% yield as a sole product. Although the detailed conformational analysis of 49 was not conducted, the stereochemical outcome in this Luche reduction is understandable by the formation of chelation structure as described in Figure 3. In this structure, the proton of methanol could coordinate to two carbonyl oxygens at the C6 and C18 positions and hydride could approach from the outside of the macrocyclic structure. Detailed comparison of the NMR data and specific rotations between the natural products\textsuperscript{10b} and the synthetic products in 3 and 4 revealed the absolute configurations of natural sarcophytonolides F and G to be those shown in 3 and 4, respectively.\textsuperscript{40}
Scheme 8. Total Synthesis of Sarcophytonolides F (3) and G (4)

1) DIBAL-H, CH₂Cl₂, -78 °C
2) Li, liq. NH₃, THF/i-BuOH, -78 °C

79% (2 steps)

1) TEMPO, Ph(OAc)₂, CH₂Cl₂, rt
2) Ph₃P⁺CH₂Br⁻, NaHMDS, THF, 0 °C to rt
3) DIBAL-H, CH₂Cl₂, -78 °C
74% (3 steps)

1) TEMPO, Ph(OAc)₂, CH₂Cl₂, rt
2) 35, toluene, rt

dr = 17:1

1) LiOH·H₂O, THF/MeOH/H₂O, rt
2) MNBA, DMAP, CH₂Cl₂, 40 °C
66% (2 steps)

1) 33, toluene, 100 °C
76%
2) TMSI, HMDS, CH₂Cl₂, 0 °C
75%

1) p-nitrobenzoic acid, DEAD, Ph₃P, THF, 0 °C
2) Na₂CO₃, MeOH, 0 °C to rt
31% (2 steps)

Dess–Martin periodinane

1) NaBH₄, CeCl₃, CH₂Cl₂, 40 °C
96%
2) MeOH/CH₂Cl₂, -78 °C
72%

sarcophytonolide G (4)
Total Synthesis of Sarcophytonolide H (6). We next focused on the total synthesis of sarcophytonolides possessing the acetoxy groups at their C14 positions. First, we tried to synthesize sarcophytonolide H (6). We initially envisioned that the oxygen-functional group at the C14 position could be introduced by oxidative desulfurization of the sulfone 42, which is the synthetic intermediate of the total synthesis of sarcophytonolides F (3) and G (4). Actually, deprotonation of 42 with n-BuLi or lithium diisopropylamide (LDA) and subsequent treatment with Davis oxaziridine (50) or bis(trimethylsilyl)peroxide did not produce the desired ketone 51 (Scheme 9). Therefore, we planned to introduce the C14 oxymethylene moiety by other fragment couplings. Our synthesis of the C14 stereoisomers 53a and 53b, wherein the SmI$_2$-mediated reaction was used as the fragment coupling, is described in Scheme 10. Selective acetylation of the diol 16 followed by TBS protection of the resulting secondary alcohol gave the corresponding silyl ether. Reductive deprotection of the acetate with DIBAL-H afforded the alcohol, which was oxidized to aldehyde 52 with TEMPO/PhI(OAc)$_2$. The aldehyde 52 was connected with the allylic bromide 41 by using SmI$_2$ to furnish the desired α-adducts 53a and 53b in 53% and 40% yields, respectively. It is noteworthy that the coupling was successful by using 1.2 equiv of the allylic bromide 41 to the aldehyde 52 and the corresponding γ-allylated product was not formed at all. The observed NOEs of H-11/H$_2$-13 of 53a and 53b confirmed the geometries at their C11/C12 alkene portions, respectively. The stereochemistry at the C14 position of 53a was determined by the modified Mosher method.

Scheme 9. Unsuccessful Attempt for Oxidative Desulfurization of Sulfone 42
Scheme 10. Synthesis of Alcohols 53a and 53b

1) AcCl, pyr, CH$_2$Cl$_2$, −20 °C
2) TBSOTf, 2,6-lutidine, CH$_2$Cl$_2$, 0 °C
3) DIBAL-H, CH$_2$Cl$_2$, −78 °C
   85% (3 steps)
4) TEMPO, Ph($\text{OAc}_2$), CH$_2$Cl$_2$, rt
   97%

53a: 53%, 53b: 40%

Scheme 11. Total Synthesis of Sarcophytonolide H (6)

1) MOMCl, i-Pr$_2$NEt, TBAI, CH$_2$Cl$_2$, reflux
   97%
2) CSA, MeOH/CH$_2$Cl$_2$, 0 °C
   77%
3) TEMPO, Ph($\text{OAc}_2$), CH$_2$Cl$_2$, rt
4) Ph$_2$PCH$_2$Br, NaHMDS, THF, 0 °C to rt
   86% (2 steps)

1) TEMPO, Ph($\text{OAc}_2$)
   CH$_2$Cl$_2$, rt
   88% (2 steps, dr = 13:1)
2) 35, toluene, rt
3) 35, PPTS
   reflux
4) PMBO
   TBAF, THF, reflux
   61% (2 steps)
5) LiOH, H$_2$O
   THF/MeOH/H$_2$O, 40 °C
   96%

1) 33, toluene, 100 °C
2) HCl, i-PrOH, 50 °C
   52% (2 steps)

sarcophytonolide H (6)
Further transformation toward the total synthesis of sarcophytonolide H (6) is depicted in Scheme 11. Thus, protection of the hydroxy group of 53a with MOMCl and subsequent selective removal of the primary TBS moiety gave the corresponding alcohol. Introduction of the terminal alkene portion followed by deprotection of the obtained pivalate 54 afforded alcohol 55. TEMPO oxidation of 55 and reaction of the aldehyde with the chiral boronate 35 provided the desired allylated product 56 in 88% yield in two steps in a diastereomeric ratio of 13:1. After the C6 hydroxy group of 56 was protected as the p-methoxybenzyl (PMB) ether, the TBS ether underwent deprotection and hydrolysis of the ester to yield hydroxycarboxylic acid 58. Shiina macrolactonization and subsequent transannular RCM were successfully performed to produce the corresponding butenolide. The obtained MOM ether was selectively deprotected with HCl in i-PrOH to provide alcohol 60. Finally, acetylation of the alcohol 60 and removal of the PMB moiety with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) took place to furnish sarcophytonolide H (6). The synthetic sarcophytonolide H (6) was in full agreement with the natural product in the 1H and 13C NMR data and the specific rotation. Therefore, the absolute configuration of natural sarcophytonolide H was confirmed as shown in 6.

**Total Synthesis and Structural Revision of Isosarcophytonolide D.** We next investigated synthesis of the proposed structure 10 of isosarcophytonolide D with the 14R stereochemistry. Thus, as shown in Scheme 12, the alcohol 53b was converted to 10 in 15 steps by a synthetic route similar to that used toward the total synthesis of sarcophytonolide H (6). Having synthesized the proposed structure 10 of isosarcophytonolide D, we analyzed the 2D NMR data of the synthetic product 10. As a result, the significant differences in the 1H and 13C NMR data between natural isosarcophytonolide D 10d and the synthesized 10 were observed. The detailed comparison revealed that the chemical shift deviations were especially critical around the C14 position (Figure 4). We also considered that the stereochemistries at the C1 and C2 positions of isosarcophytonolide D would be same as those of other sarcophytonolides. Therefore, we predicted the correct structure of isosarcophytonolide D isolated from nature to be that drawn in 68, which is the C14 stereoisomer of 10 (Scheme 13). The predicted structure 68 was synthesized by oxidation of the synthetic sarcophytonolide H (6) with Dess–Martin periodinane. As anticipated, the 1H and 13C NMR data and the specific rotation of the synthetic 68 matched those of the natural product. Therefore, the absolute configuration of natural isosarcophytonolide D was reassigned to be that shown in 68.
Scheme 12. Total Synthesis of the Proposed Structure 10 of Isosarcophytonolide D

Figure 4. Deviations of the $^{13}$C NMR chemical shifts between natural isosarcophytonolide D and the synthetic product 10 ($\Delta \delta = \delta_N - \delta_{10}$ in ppm). N = natural product. The x and y axes represent the carbon number and $\Delta \delta$, respectively.
Structural Prediction, Total Synthesis, and Structural Determination of Sarcophytonolide J. As noted in Introduction, the relative configurations at the C1, C2, and C14 positions of natural sarcophytonolides I (8), J (9), and isosarcophytonolide D (10) were determined by the similarity of their NMR data to those of sarcophytonolide D (7). This way of structural assignment and the stereochemical revision at the C14 position of isosarcophytonolide D indicate that the C14 stereochemistries of sarcophytonolides D (7), I (8), and J (9), which were originally assigned as 14R, should be also reexamined. Therefore, we next decided to verify the stereostructure of sarcophytonolide J (9, Figure 5a), of which the C8 configuration was not identified. First, in order to predict the C14 stereochemistry of sarcophytonolide J, we compared the 1H and 13C NMR data of natural sarcophytonolide J (9) with those of the synthetic products 68 (revised structure of isosarcophytonolide D) and 10 (C14 epimer of 68). Deviations of the 13C NMR chemical shifts at the C1, C2, C13, and C14 positions between natural sarcophytonolide J and the synthetic products 68 and 10 are graphically depicted in Figure 5b. From these comparisons, it was found that the chemical shift differences between natural sarcophytonolide J and 68 were smaller than those between natural sarcophytonolide J and 10. In addition, for the prediction of the C8 stereochemistry of sarcophytonolide J, the 1H and 13C NMR data between natural sarcophytonolide J (10c) and the synthetic products 1a (sarcophytonolide C) and 1b (C8 epimer of 1a) were compared. As a result, it was elucidated that the chemical shift characteristics at the C7 to C10 positions of 1a were more similar to those of 1b. Taken together, we could propose the predicted structure 69 of sarcophytonolide J (Figure 6), which bears the 8S and 14S absolute configurations same as those of 1a and 68.
Figure 5. (a) Structures of 9, 68, 10, 1a, and 1b. (b) Deviations of the $^{13}$C NMR chemical shifts between natural sarcophytonolide J and the synthetic products ($\Delta \delta = \delta_N - \delta_S$ in ppm). $N =$ natural product. $S =$ synthetic product. The x and y axes represent the carbon number and $\Delta \delta$, respectively.

Figure 6. Predicted structure 69 of sarcophytonolide J.
Scheme 14. Total Synthesis of the Predicted Structure 69 of Sarcophytonolide J

1) TEMPO, Phi(OAc)$_2$, CH$_2$Cl$_2$, rt
2) Ph$_3$P*CH$_2$Br$^-$
   NaHMDS
   THF, 0 °C
   81% (2 steps)

1) Dibal-H
   CH$_2$Cl$_2$, -78 °C
2) TEMPO, Phi(OAc)$_2$
   CH$_2$Cl$_2$, rt
3) 26, Zn dust
   THF/NH$_3$Cl aq, 0 °C
   92% (3 steps)

1) LiOH-H$_2$O
   THF/MeOH/H$_2$O, rt
2) MNBA, DMAP
   CH$_2$Cl$_2$, 40 °C
   81% (2 steps)

1) LiOH-H$_2$O
   THF/MeOH/H$_2$O, rt
2) MNBA, DMAP
   CH$_2$Cl$_2$, 40 °C
   81% (2 steps)

3) toluene, 100 °C
   recovery of 76: 31%
In order to confirm our stereostructural prediction of sarcophytonolide J as discussed above, we commenced the total synthesis of the predicted structure 69. Sequence of the transformation toward 69 was similar to that used toward the total synthesis of sarcophytonolide H (6). Thus, SmI₂-mediated reaction of the aldehyde 52 and the allylic bromide 21a gave the desired product 70a and its C14 epimer 70b in 29% and 40% yields, respectively (Scheme 14). The absolute stereochemistry at the C14 position of 70a was verified by its derivatization and NOE experiments. Subsequently, the alcohol 70a was transformed to our predicted structure 69 of sarcophytonolide J in overall 16 steps. As expected, the synthetic 69 provided the 1H and 13C NMR data and the specific rotation which were identical to those reported for natural sarcophytonolide J. These findings clearly revealed that our stereochemical prediction of sarcophytonolide J is correct and this natural product possesses the 8S and 14S absolute configurations as shown in 69.

Cytotoxicity of the Synthetic Products. Having successfully completed the total synthesis and established the stereostructures of sarcophytonolides, we next turned our attention to assessment of the biological activity of the synthetic products. First, we evaluated the growth-inhibitory activity by using the MTT assay with HL60 human leukemia cells. The cells were treated in 96-well plates with various concentrations of the synthetic compounds for 72 h. As described in Table 3, interestingly, the synthetic sarcophytonolide C (1a) was inactive, whereas 8-epi-sarcophytonolide C (1b) inhibited the growth of the cells with an IC₅₀ value of 18.9 μM, which indicates that the activity is affected by the C8 stereochemistries. Compared to 1a, 1b was observed to be more soluble in water, which may also contribute to the growth-inhibitory activity. Sarcophytonolide E (2), which possesses the C6 alcohol moiety, exhibited the activity with an IC₅₀ value of 33.0 μM. Sarcophytonolide F (3) bearing the C7/C8 trisubstituted alkene group showed the activity similar to that of 2 (IC₅₀ = 35.9 μM). Introduction of the C14 acetoxy moiety was found to lower the inhibitory activity by comparing IC₅₀ values of sarcophytonolides F (3, 35.9 μM) and H (6, 53.5 μM). Since 8-epi-sarcophytonolide C (1b) was the most active among five sarcophytonolides, the key synthetic intermediates of 1b were next biologically evaluated. The cytotoxic activity of the butenolide construction precursor 32b (IC₅₀ = 13.7 μM) was slightly improved in comparison with that of 1b. The macrolactonization precursor 30b and the alcohol 25b retained the activity, while their activities were decreased to IC₅₀ values of 55.8 and 24.0 μM, respectively.
Table 3. Growth-Inhibitory Activity against HL60 Human Leukemia Cells$^a$

<table>
<thead>
<tr>
<th>compound</th>
<th>IC$_{50}$</th>
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<tr>
<td>1a</td>
<td>$&gt;100$</td>
</tr>
<tr>
<td>1b</td>
<td>18.9</td>
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<td>2</td>
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</tr>
<tr>
<td>32b</td>
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</tr>
<tr>
<td>30b</td>
<td>55.8</td>
</tr>
<tr>
<td>25b</td>
<td>24.0</td>
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</tbody>
</table>

$^a$IC$_{50}$ values are given in μM

**Antifouling Activity and Toxicity of the Synthetic Products.** Since sarcophytonolides H (6) and J (69) which were isolated from nature are reported to be antifouling active against the cypris larvae of barnacle Balanus (Amphibalanus) amphitrite,$^{13,14}$ we next evaluated the antifouling activity$^5$ and toxicity of the synthetic sarcophytonolides H (6) and J (69) and their analogues against the cypris larvae of the same barnacle. The larvae were treated in 24-well polystyrene plates with various concentrations of the synthetic compounds in the dark for 96 h and the results are summarized in Table 4. The synthetic sarcophytonolide H (6) displayed the antifouling activity with an EC$_{50}$ value of 3.36 μg/mL, which was in good agreement with that of the natural product (5.98 μg/mL).$^{13}$ Diol 79$^{60}$ retained the antifoulant activity (EC$_{50}$ = 3.08 μg/mL), which indicates the acetyl group of 6 has little influence on this activity. The antifouling activity of the butenolide construction precursor 80$^{60}$ was marginally increased in comparison with those of 6 and 79 (EC$_{50}$ = 1.61 μg/mL). The hydroxycarboxylic acid 58 turned out to be antifouling active (EC$_{50}$ = 3.27 μg/mL), while the alkoxycarbonylation precursor 55 exhibited no antifouling activity. Furthermore, the toxicity was also evaluated.
and it was found that 58 was weak toxic (LC$_{50}$ = 19.4 µg/mL) and other compounds 6, 79, 80, and 55 had no toxicity. In addition to the sarcophytonolide H series, we next evaluated the biological activity of the synthetic sarcophytonolide J (69) and its synthetic intermediates. The synthetic sarcophytonolide J (69), the triene 76, and the hydroxyester 74 were antifouling active with EC$_{50}$ values of 0.95–2.36 µg/mL without regard to difference of the molecular framework. Interestingly, alcohol 81 also showed the antifoulant activity (EC$_{50}$ = 1.74 µg/mL) in contrast to the allylic alcohol 55 in the sarcophytonolide H series. In the sarcophytonolide J series, only compound 69 displayed the weak toxicity with a LC$_{50}$ value of 34.5 µg/mL and other compounds 76, 74, and 81 were non-toxic. These obtained results of the biological activity assessment shown in Table 4 denote that the triene 76, which exhibited the strongest antifouling activity and no toxicity, is a promising candidate for the creation of environmentally friendly antifouling agents.

**Table 4. Antifouling Activity (EC$_{50}$) and Toxicity (LC$_{50}$) of the Synthetic Sarcophytonolides H (6) and J (69) and Their Analogues**

<table>
<thead>
<tr>
<th>compound</th>
<th>EC$_{50}$</th>
<th>LC$_{50}$</th>
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<tbody>
<tr>
<td>6</td>
<td>3.36</td>
<td>&gt;50</td>
</tr>
<tr>
<td>79</td>
<td>3.08</td>
<td>&gt;50</td>
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<tr>
<td>80</td>
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<tr>
<td>55</td>
<td>&gt;50</td>
<td>&gt;50</td>
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<tr>
<td></td>
<td>EC50 (μg/mL)</td>
<td>LC50 (μg/mL)</td>
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<tr>
<td>---</td>
<td>-------------</td>
<td>--------------</td>
</tr>
<tr>
<td>69</td>
<td>1.50</td>
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</tr>
<tr>
<td>76</td>
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<td>&gt;50</td>
</tr>
<tr>
<td>81</td>
<td>1.74</td>
<td>&gt;50</td>
</tr>
</tbody>
</table>

*Against the cypris larvae of barnacle *Balanus* (*Amphibalanus*) *amphitrite*. EC50 and LC50 values are given in μg/mL.

**Conclusion**

Unified total synthesis of sarcophytonolides, cembranolide diterpenes isolated from the soft corals of genus *Sarcophyton*, was accomplished. In their synthetic routes, NaHMDS-mediated reaction of allylic bromide/sulfone in methylene series at the C14 position and SmI2-mediated reaction of allylic bromide/aldehyde in acetoxyethylene series at the C14 position were utilized as the fragment couplings, respectively. In addition, the total synthesis features alkoxy carbonylation, macrolactonization, and transannular RCM. Because the chirality at the C8 position of sarcophytonolide C (1) was not determined, the C8 stereoisomers 1a and 1b were stereoselectively synthesized, which elucidated the absolute configuration of natural 1 to be that as drawn in 1a. Stereoselective total synthesis of sarcophytonolides E (2), F (3), G (4), and H (6) culminated in the absolute stereochemical determination of 2, 3, and 4 and confirmation of 6. Furthermore, total synthesis of the proposed structure 10 and the predicted structure 68 of isosarcophytonolide D revealed the correct structure of this natural product to be that in 68. This stereochemical revision at the C14 position of isosarcophytonolide D and the stereostructural elucidation of sarcophytonolide C led us to the stereochemical prediction of sarcophytonolide J. Total synthesis of the predicted structure 69 of this natural product verified the correct structure of natural sarcophytonolide J. After completing the total synthesis of sarcophytonolides, we assayed the cytotoxicity of selected synthetic products against HL60 cells and found that 1b, 2, 3, 6, 32b, 30b, and 25b showed the cytotoxicity, while 1a was inactive. Moreover, we conducted evaluation of the antifouling activity and toxicity of the synthetic sarcophytonolides H (6) and J (69) and their synthetic analogues against the cypris larvae of barnacle *Balanus* (*Amphibalanus*) *amphitrite*. The obtained findings suggest that 76, a synthetic intermediate of 69, is a good candidate for further developing environmentally benign antifouling compounds. Further synthetic study of other classes of cembranolide is currently underway.

**Experimental Section**

**General Methods.** Reagents were used as received from commercial suppliers unless otherwise indicated. All reactions were carried out under an atmosphere of argon. Reaction solvents were purchased as dehydrated solvents and stored with active molecular sieves 4Å under argon prior to use for reactions. All solvents for work-up procedure were used as received. Analytical thin-layer chromatography (TLC) was performed with aluminium TLC plates (Merck TLC silica gel 60F254). Column chromatography was performed with Fuji
Silysia silica gel BW-300 or Kanto Chemical silica gel 60N. Optical rotations were recorded on a JASCO DIP-1000. IR spectra were recorded on a JASCO FT/IR-460 plus. ¹H and ¹³C NMR spectra were recorded on JEOL JNM-AL400 or Varian 400-MR. Chemical shifts in the NMR spectra are reported in ppm with reference to the internal residual solvent (¹H NMR, CDCl₃ 7.26 ppm, C₆D₆ 7.15 ppm; ¹³C NMR, CDCl₃ 77.0 ppm, C₆D₆ 128.0 ppm). The following abbreviations are used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Coupling constants (J) are in hertz. High resolution mass spectra were recorded on a Micromass LCT (ESI–TOF–MS) spectrometer.

**TBS Ether S₁.** To a solution of cis-2-butene-1,4-diol (5.5 mL, 66.9 mmol) in DMF (67 mL) were added imidazole (4.55 g, 66.9 mmol) and TBSCl (10.1 g, 66.9 mmol) at –30 °C. The mixture was stirred at the same temperature for 2 h. The mixture was diluted at the same temperature for 2 h. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane, hexane/EtOAc = 6:1) gave mono-TBS ether S₁ (6.31 g, 47%): colorless oil; R_f = 0.36 (hexane/ EtOAc = 4:1); IR (neat) 3367, 2953, 2929, 2858 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.74–5.64 (m, 2 H), 4.26 (d, J = 5.1 Hz, 2 H), 4.20 (d, J = 5.9 Hz, 2 H), 2.01 (brs, 1 H), 0.91 (s, 9 H), 0.09 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 131.3, 130.0, 59.6, 58.9, 26.0, 18.4, –5.2; HRMS (ESI–TOF) calcd for C₁₀H₂₄O₂SiNa [M + Na]⁺ 225.1287, found 225.1284.

**Epoxy Alcohol 15.** To a suspension of powdered MS4Å (3.20 g) in CH₂Cl₂ (130 mL) were added (+)-DET (3.3 mL, 19.1 mmol), Ti(Oi-Pr)₄ (5.7 mL, 19.1 mmol), and allylic alcohol S₁ (3.21 g, 15.9 mmol) in CH₂Cl₂ (17 mL + 6.0 mL) at –25 °C. After the resulting mixture was stirred at the same temperature for 20 min, TBHP (ca. 5.0 M solution in 2,2,4-trimethylpentane, 6.4 mL, 32.0 mmol) was added to the mixture at the same temperature. After the resulting mixture was stirred at the same temperature for 63 h, the reaction was quenched with 3 M aqueous NaOH and the mixture was stirred at room temperature for 30 min. The mixture was filtered through a Celite pad and washed with EtOAc. The mixture was washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 6:1) gave epoxy alcohol 15 (2.98 g, 86%, enantiomeric ratio = 17:1): colorless oil; R_f = 0.36 (hexane/EtOAc = 4:1); [α]D₂⁵ –12.6 (c 1.00, CHCl₃); IR (neat) 3399, 2953, 2930, 2858 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.92 (dd, J = 11.7, 5.6 Hz, 1 H), 3.79–3.71 (m, 3 H), 3.25–3.17 (m, 2 H), 2.24 (brs, 1 H), 0.09 (s, 3 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 61.6, 60.9, 56.4, 56.0, 25.9, 18.3, –5.2, –5.3; HRMS (ESI–TOF) calcd for C₁₀H₂₂O₃SiNa [M + Na]⁺ 241.1236, found 241.1231.

**Diol 16.** To a suspension of CuBr·SMe₂ (294 mg, 1.43 mmol) in Et₂O (38 mL) was added isopropenylmagnesium bromide (0.5 M in THF, 31.4 mL, 15.7 mmol) at –50 °C. The mixture was gradually warmed up to –20 °C and stirred at the same temperature for 10 min. To the resulting mixture was added epoxy alcohol 15 (1.04 g, 4.76 mmol) in Et₂O (5.2 mL + 2.0 mL) at –20 °C. The mixture was stirred at the same temperature for 21 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with Et₂O, washed with
saturated aqueous NH₄Cl, H₂O, and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 3:1) gave diol 16 (1.09 g, 84%): colorless oil; Rf = 0.43 (hexane/EtOAc = 2:1); [α]D²⁵ = 4.9 (c 1.00, CHCl₃); IR (neat) 3399, 2929, 2857 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.00 (t, J = 1.6 Hz, 1 H), 4.86 (s, 1 H), 3.81–3.60 (m, 5 H), 2.46–2.37 (m, 3 H), 1.80 (s, 3 H), 0.91 (s, 9 H), 0.09 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 143.4, 114.5, 71.3, 65.5, 62.2, 52.6, 25.9, 21.3, 18.3, –5.3, –5.3; HRMS (ESI–TOF) calcd for C₁₃H₂₈O₃SiNa [M + Na]+ 283.1705, found 283.1711.

**Alkane 17.** A mixture of alkene 16 (2.65 g, 10.2 mmol) and (Ph₃P)₃RhCl (236 mg, 0.255 mmol) in benzene (48 mL) and EtOH (16 mL) was stirred for 5 h under H₂ atmosphere at room temperature. Short column chromatography (hexane/EtOAc = 1:1), concentration, and column chromatography (hexane/EtOAc = 7:1) gave alkane 17 (2.48 g, 93%): colorless oil; Rf = 0.50 (hexane/EtOAc = 2:1); [α]D²⁶ = 9.9 (c 1.00, CHCl₃); IR (neat) 3389, 2956, 2930, 2886, 2855 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 3.92–3.87 (m, 1 H), 3.80–3.63 (m, 4 H), 2.70 (brs, 1 H), 1.86–1.78 (m, 1 H), 1.64–1.58 (m, 1 H), 0.99 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 0.92 (s, 9 H), 0.11 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 72.8, 64.6, 60.9, 49.6, 26.2, 25.9, 21.7, 20.0, 18.3, –5.2, –5.3; HRMS (ESI–TOF) calcd for C₁₃H₃₀O₃SiNa [M + Na]+ 285.1862, found 285.1862.

**Sulfide 18.** To a solution of diol 17 (1.74 g, 6.63 mmol) and (PhS)₂ (4.34 g, 19.9 mmol) in pyridine (33 mL) was added n-Bu₃P (5.0 mL, 19.9 mmol) at room temperature. The mixture was stirred at the same temperature for 1 h. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 60:1) gave sulfide 18 (1.92 g, 82%): colorless oil; Rf = 0.50 (hexane/EtOAc = 2:1); [α]D²⁷ = 16.0 (c 1.00, CHCl₃); IR (neat) 3490, 2955, 2928, 2855 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.33 (m, 2 H), 7.29–7.26 (m, 2 H), 7.17 (tt, J = 7.3, 1.5 Hz, 1 H), 3.89–3.84 (m, 1 H), 3.75 (dd, J = 10.0, 3.4 Hz, 1 H), 3.60 (dd, J = 10.0, 8.3 Hz, 1 H), 2.99 (dd, J = 12.8, 4.5 Hz, 1 H), 2.90 (dd, J = 12.8, 7.6 Hz, 1 H), 2.56 (brd, J = 2.9 Hz, 1 H), 2.17–2.08 (m, 1 H), 1.67–1.61 (m, 1 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.8 Hz, 3 H), 0.91 (s, 9 H), 0.08 (s, 6 H); ¹³C NMR (100 MHz, CDCl₃) δ 137.2, 129.2, 128.8, 125.9, 72.5, 65.9, 45.9, 31.7, 27.5, 26.0, 21.3, 18.7, 18.3, –5.2, –5.2; HRMS (ESI–TOF) calcd for C₁₉H₃₄O₂SSiNa [M + Na]+ 377.1946, found 377.1950.

**TBS Ether 19.** To a solution of alcohol 18 (1.29 g, 3.64 mmol) in CH₂Cl₂ (36 mL) were added 2,6-lutidine (0.64 mL, 5.46 mmol) and TBSOTf (1.0 mL, 4.37 mmol) at 0 °C. The mixture was diluted at the same temperature for 30 min. The mixture was washed with Et₂O and H₂O and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 1:0, 70:1) gave TBS ether 19 (1.68 g, 98%): colorless oil; Rf = 0.66 (hexane/EtOAc = 20:1); [α]D²⁸ = 34.8 (c 1.00, CHCl₃); IR (neat) 2955, 2929, 2862 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.34–7.32 (m, 2 H), 7.27–7.24 (m, 2 H), 7.16–7.12 (m, 1 H), 4.14 (td, J = 6.6, 2.9 Hz, 1 H), 3.58 (dd, J = 6.6, 2.7 Hz, 2 H), 3.05 (dd, J = 12.7, 3.9 Hz, 1 H), 2.95 (dd, J = 12.7, 9.6 Hz, 1 H), 2.08–2.00 (m, 1 H), 1.75–1.70 (m, 1 H), 0.96 (d, J = 6.8 Hz, 3 H)
Hz, 3 H), 0.93 (d, J = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.85 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 137.2, 129.2, 128.6, 125.5, 73.3, 65.0, 44.8, 31.0, 26.4, 26.0, 26.0, 22.6, 19.1, 18.3, 18.2, −4.1, −4.7, −5.2, −5.4; HRMS (ESI–TOF) calcd for C₂₅H₄₈O₂SSi₂Na [M + Na]⁺ 491.2811, found 491.2809.

**Sulfone 20.** To a solution of sulfide 19 (1.68 g, 3.58 mmol) in EtOH (36 mL) were added 30% aqueous H₂O₂ (3.6 mL, 35.8 mmol) and (NH₄)₆Mo₇O₂₄·4H₂O (442 mg, 0.358 mmol) at 0 °C. The mixture was stirred at the same temperature for 2 h and at room temperature for 4 h. The reaction was quenched with saturated aqueous Na₂S₂O₃ at 0 °C. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 40:1) gave sulfone 20 (1.72 g, 96%): colorless oil; Rₛ = 0.34 (hexane/EtOAc = 10:1); [α]₀²⁹ –17.8 (c 1.00, CHCl₃); IR (neat) 2955, 2929, 2855 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.92–7.90 (m, 2 H), 7.65–7.61 (m, 1 H), 7.56–7.52 (m, 2 H), 4.16–4.12 (m, 1 H), 3.57 (dd, J = 10.0, 5.7 Hz, 1 H), 3.50 (dd, J = 10.0, 8.1 Hz, 1 H), 3.36 (dd, J = 14.8, 8.6 Hz, 1 H), 2.97 (dd, J = 14.8, 2.3 Hz, 1 H), 2.17–2.14 (m, 1 H), 0.88 (s, 9 H), 0.87 (s, 9 H), 0.83 (d, J = 6.8 Hz, 3 H), 0.62 (d, J = 7.1 Hz, 3 H), 0.14 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.04 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 139.6, 133.3, 129.0, 128.1, 73.4, 64.3, 52.5, 40.1, 25.9, 25.6, 21.8, 18.4, 18.2, 18.1, −4.2, −4.7, −5.3, −5.5; HRMS (ESI–TOF) calcd for C₂₅H₄₈O₄SSi₂Na [M + Na]⁺ 523.2709, found 523.2709.

**Sulfone 22a.** To a solution of sulfone 20 (1.83 g, 3.65 mmol) in THF (28 mL) was added NaHMDS (1.0 M in THF, 4.4 mL, 4.40 mmol) at −78 °C. The mixture was stirred at the same temperature for 30 min. To the mixture was added allylic bromide 21a (1.40 g, 4.38 mmol) in THF (4.0 mL + 2.0 mL + 2.0 mL) at −78 °C. The mixture was gradually warmed up to room temperature for 2 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 20:1) gave sulfone 22a (2.38 g, 88%): colorless oil; Rₛ = 0.34 (hexane/EtOAc = 10:1); [α]₀²⁹ +15.1 (c 1.00, CHCl₃); IR (neat) 2957, 2929, 2862, 1727 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.82–7.79 (m, 2 H), 7.58–7.54 (m, 1 H), 7.49–7.45 (m, 2 H), 5.11 (t, J = 6.7 Hz, 1 H), 4.33–4.30 (m, 1 H), 4.10–4.06 (m, 2 H), 3.73 (dd, J = 10.5, 4.4 Hz, 1 H), 3.67 (dd, J = 10.5, 6.8 Hz, 1 H), 3.48 (brd, J = 7.8 Hz, 1 H), 2.70–2.58 (m, 2 H), 2.36 (brd, J = 7.8 Hz, 1 H), 2.17–2.09 (m, 1 H), 1.82–1.60 (m, 3 H), 1.53–1.35 (m, 2 H), 1.33–1.06 (m, 2 H), 1.20 (s, 9 H), 1.20 (s, 3 H), 0.97–0.89 (m, 9 H), 0.94 (s, 9 H), 0.87 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.5, 140.9, 132.8, 130.3, 128.8, 128.5, 127.9, 73.8, 68.4, 62.9, 61.9, 44.3, 38.8, 36.6, 35.7, 35.6, 35.5, 29.9, 27.3, 26.3, 26.2, 25.5, 23.2, 20.6, 19.6, 18.7, 18.5, 15.3, −3.2, −4.7, −5.1, −5.2; HRMS (ESI–TOF) calcd for C₄₀H₇₄O₆SSi₂Na [M + Na]⁺ 761.4642, found 761.4632.

**Sulfone 22b.** To a solution of sulfone 20 (1.52 g, 3.03 mmol) in THF (24 mL) was added NaHMDS (1.0 M in THF, 3.6 mL, 3.60 mmol) at −78 °C. The mixture was stirred at the same temperature for 30 min. To the mixture was added allylic bromide 21b (1.22 g, 3.82 mmol) in THF (4.0 mL + 1.0 mL + 1.0 mL) at −78 °C. The mixture was gradually warmed up to room
temperature for 2 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 20:1) gave sulfone 22b (2.03 g, 91%): colorless oil; Rₓ = 0.14 (hexane/EtOAc = 20:1); [∅]D³⁰ +17.7 (c 1.00, CHCl₃); IR (neat) 2956, 2929, 2858, 1728 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.82–7.79 (m, 2 H), 7.58–7.54 (m, 1 H), 7.49–7.45 (m, 2 H), 5.10 (t, J = 6.7 Hz, 1 H), 4.31–4.30 (m, 1 H), 4.11–4.05 (m, 2 H), 3.73 (dd, J = 10.5, 4.6 Hz, 1 H), 3.67 (dd, J = 10.5, 6.8 Hz, 1 H), 3.48 (brd, J = 8.3 Hz, 1 H), 2.71–2.58 (m, 2 H), 2.36 (brd, J = 6.8 Hz, 1 H), 2.17–2.09 (m, 1 H), 1.78–1.60 (m, 3 H), 1.53–1.38 (m, 2 H), 1.31–1.08 (m, 2 H), 1.20 (s, 9 H), 1.20 (s, 3 H), 0.96 (d, J = 6.6 Hz, 3 H), 0.94 (s, 9 H), 0.90 (d, J = 6.6 Hz, 3 H), 0.89 (d, J = 6.6 Hz, 3 H), 0.87 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 141.0, 132.8, 130.3, 128.8, 128.5, 127.9, 73.8, 68.4, 62.9, 61.9, 44.3, 38.7, 36.6, 35.7, 35.6, 29.9, 27.3, 26.3, 26.2, 26.2, 25.5, 23.2, 20.6, 19.5, 18.7, 18.5, 15.3, –3.2, –4.7, –5.1, –5.2; HRMS (ESI–TOF) calcd for C₄₀H₇₄O₆SSi₂Na [M + Na]⁺ 761.4642, found 761.4641.

Alcohol 23a. To a solution of lithium wire (2.23 g, 0.322 mol) in liquid NH₃ (90 mL) was added sulfone 22a (2.38 g, 3.22 mmol) in THF/t-BuOH (44 mL/22 mL) and THF (6.0 mL for rinse) at –78 °C. The mixture was stirred at the same temperature for 5 min. The reaction was quenched with a 1:1 solution of saturated aqueous NH₄Cl and MeOH. The mixture was diluted with EtOAc, warmed up to room temperature, and stirred at the same temperature. The mixture was washed with H₂O and brine, and then dried over Na₂SO₄. Concentration gave the mixture of the corresponding pivalate and alcohol, which was used for the next step without further purification.

To a solution of the mixture obtained above in CH₂Cl₂ (30 mL) were added pyridine (0.39 mL, 4.83 mmol) and PivCl (0.47 mL, 3.86 mmol) at room temperature. The mixture was stirred at the same temperature for 11 h. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 100:1) gave the corresponding pivalate (1.23 g), which was used for the next step without further purification.

To a solution of the bis-TBS ether obtained above (1.23 g) in MeOH (10 mL) and CH₂Cl₂ (10 mL) was added CSA (142 mg, 0.615 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et₃N. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 25:1) gave alcohol 23a (430 mg) and the bis-TBS ether (617 mg).

To a solution of the bis-TBS ether recovered above (617 mg) in MeOH (5.0 mL) and CH₂Cl₂ (5.0 mL) was added CSA (71.8 mg, 0.309 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et₃N. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 25:1) gave alcohol 23a (310 mg, totally 741 mg,
Alcohol 23b. To a solution of lithium wire (1.91 g, 0.275 mol) in liquid NH₃ (80 mL) was added sulfone 22b (2.03 g, 2.75 mmol) in THF/t-BuOH (39 mL/19 mL) and THF (4.0 mL for rinse) at −78 °C. The mixture was stirred at the same temperature for 10 min. The reaction was quenched with a 1:1 solution of saturated aqueous NH₄Cl and MeOH. The mixture was diluted with EtOAc, warmed up to room temperature, and stirred at the same temperature. The mixture was washed with H₂O and brine, and then dried over Na₂SO₄. Concentration gave the mixture of the corresponding pivalate and alcohol, which was used for the next step without further purification.

To a solution of the mixture obtained above in CH₂Cl₂ (28 mL) were added pyridine (0.33 mL, 4.13 mmol) and PivCl (0.40 mL, 3.30 mmol) at room temperature. The mixture was stirred at the same temperature for 11 h. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 100:1) gave the corresponding pivalate (1.37 g), which was used for the next step without further purification.

To a solution of the bis-TBS ether obtained above (1.37 g) in MeOH (12 mL) and CH₂Cl₂ (12 mL) was added CSA (160 mg, 0.687 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et₃N. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 25:1) gave alcohol 23b (562 mg) and the bis-TBS ether (366 mg).

To a solution of the bis-TBS ether recovered above (366 mg) in MeOH (3.0 mL) and CH₂Cl₂ (3.0 mL) was added CSA (42.6 mg, 0.183 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et₃N. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 25:1) gave alcohol 23b (169 mg, totally 731 mg, 55% in three steps): colorless oil; \( R_f = 0.29 \) (hexane/EtOAc = 10:1); \([\alpha]_D^{25} +3.8 \) (c 1.00, CHCl₃); IR (neat) 3520, 2956, 2930, 2862, 1731 cm⁻¹; \(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) 5.09 (t, \( J = 6.6 \) Hz, 1 H), 4.14–4.04 (m, 2 H), 3.81–3.77 (m, 1 H), 3.61–3.53 (m, 2 H), 2.06–1.91 (m, 4 H), 1.86–1.78 (m, 1 H), 1.71–1.53 (m, 3 H), 1.60 (s, 3 H), 1.48–1.15 (m, 6 H), 1.19 (s, 9 H), 0.93–0.88 (m, 9 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H); \(^1\)C NMR (100 MHz, CDCl₃) \( \delta \) 178.5, 135.4, 124.3, 74.6, 64.4, 62.9, 47.2, 39.7, 38.8, 37.1, 35.6, 29.7, 27.9, 27.3, 26.0, 25.4, 24.7, 21.7, 19.5, 19.4, 18.2, 16.1, −4.2, −4.3; HRMS (ESI–TOF) calcd for C₂₆H₅₆O₄SiNa [M + Na]+ 507.3846, found 507.3836.
To a solution of alcohol 23a (715 mg, 1.47 mmol) in CH₂Cl₂ (15 mL) were added PhI(OAc)₂ (712 mg, 2.21 mmol) and TEMPO (45.9 mg, 0.294 mmol) at room temperature. The mixture was stirred at the same temperature for 3 h. The reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with Et₂O, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 70:1) gave the corresponding aldehyde (629 mg), which was used for the next step without further purification.

To a suspension of Ph₃P⁺CH₃Br⁻ (1.31 g, 3.68 mmol) in THF (9.0 mL) was added NaHMDS (1.0 M in THF, 3.5 mL, 3.50 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. To the mixture was added the aldehyde obtained above (629 mg) in THF (4.0 mL + 1.0 mL + 1.0 mL) at 0 °C. The mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 70:1) gave alkene 24a (580 mg, 82% in two steps): colorless oil; Rf = 0.50 (hexane/EtOAc = 20:1); [α]D²⁶ +3.2 (c 1.00, CHCl₃); IR (neat) 2957, 2930, 2855, 1731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.81 (ddd, J = 16.6, 10.4, 5.9 Hz, 1 H), 5.15 (d, J = 16.6 Hz, 1 H), 5.09–5.06 (m, 2 H), 4.14 (t, J = 5.9 Hz, 1 H), 4.11–4.07 (m, 1 H), 2.08–1.85 (m, 5 H), 1.72–1.63 (m, 1 H), 1.58 (s, 3 H), 1.57–1.52 (m, 1 H), 1.48–1.26 (m, 6 H), 1.20 (s, 9 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.90 (d, J = 6.0 Hz, 3 H), 0.88 (d, J = 6.4 Hz, 3 H), 0.04 (s, 3 H), 0.02 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.5, 140.7, 135.6, 124.2, 114.5, 75.5, 62.9, 50.0, 39.7, 38.8, 37.1, 35.6, 29.7, 27.7, 27.3, 26.0, 25.4, 24.5, 21.9, 19.5, 19.0, 18.3, 16.0, –4.0, –4.8; HRMS (ESI–TOF) calcd for C₂₉H₅₆O₃SiNa [M + Na]⁺ 503.3896, found 503.3895.

To a suspension of Ph₃P⁺CH₃Br⁻ (1.29 g, 3.60 mmol) in THF (9.0 mL) was added NaHMDS (1.0 M in THF, 3.5 mL, 3.50 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. To the mixture was added the aldehyde obtained above (626 mg) in THF (4.0 mL + 1.0 mL + 1.0 mL) at 0 °C. The mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with Et₂O, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 70:1) gave alkene 24b (605 mg, 87% in two steps): colorless oil; Rf = 0.50
(hexane/EtOAc = 20:1); \([\alpha]_D^{28} +6.1\) (c 1.00, CHCl3); IR (neat) 2957, 2930, 2858, 1731 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \(\delta\) 5.81 (ddd, \(J = 17.0, 10.4, 5.7\) Hz, 1 H), 5.15 (dt, \(J = 17.0, 1.5\) Hz, 1 H), 5.09–5.06 (m, 2 H), 4.14 (t, \(J = 5.7\) Hz, 1 H), 4.11–4.07 (m, 2 H), 2.07–1.85 (m, 5 H), 1.72–1.63 (m, 1 H), 1.58 (s, 3 H), 1.57–1.52 (m, 1 H), 1.48–1.14 (m, 6 H), 1.20 (s, 9 H), 0.92 (d, \(J = 6.4\) Hz, 3 H), 0.90 (d, \(J = 6.4\) Hz, 3 H), 0.90 (s, 9 H), 0.88 (d, \(J = 6.8\) Hz, 3 H), 0.04 (s, 3 H), 0.02 (s, 3 H); \(^13\)C NMR (100 MHz, CDCl3) \(\delta\) 178.5, 140.7, 135.6, 124.2, 114.5, 75.5, 62.9, 50.0, 39.7, 38.8, 37.1, 35.6, 29.7, 27.7, 27.3, 26.0, 25.4, 24.5, 21.9, 19.6, 19.0, 18.3, 16.0, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{29}\)H\(_{56}\)O\(_3\)SiNa [M + Na\(^+\)] 503.3896, found 503.3903.

**Alcohol 25a.** To a solution of pivalate 24a (554 mg, 1.15 mmol) in CH\(_2\)Cl\(_2\) (12 mL) was added DIBAL-H (1.02 M in hexane, 3.4 mL, 3.45 mmol) at –78 °C. The mixture was stirred at the same temperature for 20 min. The reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 10:1) gave alcohol 25a (443 mg, 97%): colorless oil; \(R_f = 0.11\) (hexane/EtOAc = 10:1); \([\alpha]_D^{25} +3.0\) (c 1.00, CHCl3); IR (neat) 3336, 2955, 2928, 2858 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \(\delta\) 5.81 (ddd, \(J = 17.2, 10.4, 6.8\) Hz, 1 H), 5.09–5.05 (m, 2 H), 4.14–4.07 (m, 2 H), 2.07–1.85 (m, 5 H), 1.66–1.54 (m, 2 H), 1.58 (s, 3 H), 1.45–1.15 (m, 7 H), 0.92–0.87 (m, 9 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); \(^13\)C NMR (100 MHz, CDCl3) \(\delta\) 140.7, 135.5, 124.4, 114.5, 75.5, 61.3, 49.9, 40.0, 39.7, 37.3, 29.3, 27.7, 26.0, 25.4, 24.4, 21.9, 19.6, 19.0, 18.3, 16.0, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{24}\)H\(_{48}\)O\(_2\)SiNa [M + Na\(^+\)] 419.3321, found 419.3329.

**Alcohol 25b.** To a solution of pivalate 24b (585 mg, 1.22 mmol) in CH\(_2\)Cl\(_2\) (12 mL) was added DIBAL-H (1.02 M in hexane, 3.4 mL, 3.45 mmol) at –78 °C. The mixture was stirred at the same temperature for 15 min. The reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 10:1) gave alcohol 25b (473 mg, 98%): colorless oil; \(R_f = 0.11\) (hexane/EtOAc = 10:1); \([\alpha]_D^{30} +8.2\) (c 1.00, CHCl3); IR (neat) 3347, 2955, 2929, 2858 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \(\delta\) 5.81 (ddd, \(J = 17.2, 10.4, 6.3\) Hz, 1 H), 5.09–5.05 (m, 2 H), 4.14–4.07 (m, 2 H), 2.07–1.85 (m, 5 H), 1.66–1.54 (m, 2 H), 1.58 (s, 3 H), 1.45–1.15 (m, 7 H), 0.92–0.87 (m, 9 H), 0.90 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); \(^13\)C NMR (100 MHz, CDCl3) \(\delta\) 140.7, 135.5, 124.4, 114.5, 75.5, 61.3, 49.9, 40.0, 39.7, 37.3, 29.3, 27.7, 26.0, 25.4, 24.4, 21.9, 19.6, 19.0, 18.3, 16.0, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{24}\)H\(_{48}\)O\(_2\)SiNa [M + Na\(^+\)] 419.3321, found 419.3329.

**Alcohol 27a.** To a solution of alcohol 25a (420 mg, 1.05 mmol) in CH\(_2\)Cl\(_2\) (10 mL) were added PhI(OAc)\(_2\) (509 mg, 1.58 mmol) and TEMPO (32.8 mg, 0.210 mmol) at room temperature. The mixture was stirred at the same temperature for 2 h. The reaction was quenched with saturated aqueous Na\(_2\)S\(_2\)O\(_3\). The mixture was diluted with Et\(_2\)O, washed with saturated aqueous NaHCO\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and
short column chromatography (hexane/EtOAc = 70:1) gave the corresponding aldehyde (386 mg), which was used for the next step without further purification.

To a solution of the aldehyde obtained above (386 mg) in THF (8.0 mL) and saturated aqueous NH₄Cl (1.6 mL) were added ethyl (2-bromomethyl)acrylate (26) (0.20 mL, 1.47 mmol) and zinc dust (192 mg, 2.93 mmol) at 0 °C. The mixture was stirred at the same temperature for 15 min. The mixture was filtered through a Celite pad and washed with EtOAc. The mixture was concentrated, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 10:1) gave alcohol 27a (420 mg, 79% in two steps) as a 1:1 diastereomeric mixture: colorless oil; Rᶠ = 0.20 (hexane/EtOAc = 10:1); IR (neat) 3464, 2956, 2929, 2857, 1716, 1631 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.25 (t, J = 1.8 Hz, 1 H), 5.81 (ddd, J = 17.2, 10.5, 5.7 Hz, 1 H), 5.65 (s, 1 H), 5.14 (d, J = 17.2 Hz, 1 H), 5.10–5.05 (m, 2 H), 4.26–4.18 (m, 2 H), 4.14 (t, J = 5.7 Hz, 1 H), 3.85 (brs, 1 H), 2.61 (dd, J = 14.0, 3.2 Hz, 0.5 H), 2.56 (dd, J = 14.0, 3.6 Hz, 0.5 H), 2.34 (dd, J = 14.0, 8.4 Hz, 0.5 H), 2.26 (dd, J = 14.0, 8.4 Hz, 0.5 H), 2.07–1.85 (m, 6 H), 1.74–1.48 (m, 2 H), 1.58 (s, 3 H), 1.44–1.35 (m, 3 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.27–1.10 (m, 3 H), 0.95–0.87 (m, 9 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.01 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 167.5, 140.7, 137.8, 135.5, 135.4, 127.4, 127.3, 124.4, 124.4, 114.5, 75.5, 68.7, 68.4, 61.0, 49.9, 44.8, 44.7, 41.2, 40.6, 39.7, 37.9, 36.9, 29.5, 29.2, 27.7, 26.0, 25.5, 25.4, 24.5, 21.9, 20.2, 19.3, 19.0, 18.3, 16.0, 14.2, –4.0, –4.8; HRMS (ESI–TOF) calcd for C₃₀H₅₆O₄SiNa [M + Na]⁺ 531.3846, found 531.3845.

Alcohol 27b. To a solution of alcohol 25b (453 mg, 1.14 mmol) in CH₂Cl₂ (11 mL) were added PhI(OAc)₂ (550 mg, 1.71 mmol) and TEMPO (35.6 mg, 0.228 mmol) at room temperature. The mixture was stirred at the same temperature for 2 h. The reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with Et₂O, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 70:1) gave the corresponding aldehyde (429 mg), which was used for the next step without further purification.

To a solution of the aldehyde obtained above (429 mg) in THF (10 mL) and saturated aqueous NH₄Cl (2.0 mL) were added ethyl (2-bromomethyl)acrylate (26) (0.23 mL, 1.71 mmol) and zinc dust (224 mg, 3.42 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. The mixture was filtered through a Celite pad and washed with EtOAc. The mixture was concentrated, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 10:1) gave alcohol 27b (538 mg, 93% in two steps) as a 1:1 diastereomeric mixture: colorless oil; Rᶠ = 0.20 (hexane/EtOAc = 10:1); IR (neat) 3463, 2955, 2929, 2857, 1717, 1635 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 6.25 (t, J = 1.8 Hz, 1 H), 5.81 (ddd, J = 17.2, 10.4, 5.7 Hz, 1 H), 5.64 (s, 1 H), 5.14 (dt, J = 17.2, 1.5 Hz, 1 H), 5.10–5.05 (m, 2 H), 4.26–4.18 (m, 2 H), 4.14 (t, J = 5.7 Hz, 1 H), 3.88–3.82 (m, 1 H), 2.61 (dd, J = 14.0, 3.2 Hz, 0.5 H), 2.56 (dd, J = 14.0, 3.2 Hz, 0.5 H), 2.34 (dd, J = 14.0, 8.4 Hz, 0.5 H), 2.26 (dd, J = 14.0, 8.4 Hz, 0.5 H), 2.07–1.85 (m, 6 H),
1.73–1.61 (m, 2 H), 1.58 (s, 3 H), 1.54–1.35 (m, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 1.27–1.10 (m, 3 H), 0.95–0.87 (m, 9 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.5, 140.7, 140.7, 137.8, 135.5, 135.4, 127.4, 127.3, 124.4, 124.4, 114.5, 75.5, 68.8, 68.4, 61.0, 50.0, 50.0, 44.8, 44.7, 41.2, 40.7, 39.7, 37.9, 37.0, 29.5, 29.2, 27.7, 26.0, 25.4, 24.5, 24.5, 21.9, 20.2, 19.3, 19.0, 18.3, 16.0, 14.2, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{30}\)H\(_{56}\)O\(_4\)SiNa \([\text{M} + \text{Na}]^+\) 531.3846, found 531.3842.

**MOM Ether 28a.** To a solution of alcohol 27a (395 mg, 0.777 mmol) in CH\(_2\)Cl\(_2\) (8.0 mL) were added \(i\)-Pr\(_2\)NEt (0.80 mL, 4.66 mmol), MOMCl (0.30 mL, 3.89 mmol), and TBAI (144 mg, 0.389 mmol) at room temperature. The mixture was stirred at the same temperature for 6 h. The reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with Et\(_2\)O, washed with saturated aqueous NH\(_4\)Cl, saturated aqueous NaHCO\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and column chromatography (hexane/EtOAc = 40:1) gave MOM ether 28a (406 mg, 94%): colorless oil; \(R_f\) = 0.50 (hexane/EtOAc = 10:1); IR (neat) 2955, 2929, 2862, 1719, 1632 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.21 (s, 1 H), 5.81 (ddd, J = 17.3, 10.5, 5.7 Hz, 1 H), 5.61 (s, 0.5 H), 5.60 (s, 0.5 H), 5.14 (d, J = 17.3 Hz, 1 H), 5.10–5.06 (m, 2 H), 4.68–4.57 (m, 2 H), 4.21 (q, J = 7.2 Hz, 2 H), 4.13 (t, J = 5.7 Hz, 1 H), 3.88–3.80 (m, 1 H), 3.34 (s, 1.5 H), 3.33 (s, 1.5 H), 2.58–2.38 (m, 2 H), 2.07–1.84 (m, 5 H), 1.66–1.51 (m, 2 H), 1.58 (s, 3 H), 1.42–1.35 (m, 3 H), 1.31 (t, J = 7.2 Hz, 3 H), 1.22–1.12 (m, 3 H), 0.93–0.88 (m, 9 H), 0.89 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.0, 166.9, 140.7, 137.7, 137.7, 135.5, 135.4, 127.1, 124.4, 124.3, 114.5, 95.6, 95.5, 75.5, 74.4, 74.2, 60.7, 60.7, 55.7, 55.6, 50.0, 42.5, 39.7, 38.4, 38.0, 37.8, 37.1, 29.3, 29.0, 27.7, 26.0, 25.5, 25.3, 24.5, 21.9, 20.0, 19.4, 19.0, 18.3, 16.0, 14.3, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{32}\)H\(_{60}\)O\(_5\)SiNa \([\text{M} + \text{Na}]^+\) 575.4108, found 575.4110.

**MOM Ether 28b.** To a solution of alcohol 27b (518 mg, 1.02 mmol) in CH\(_2\)Cl\(_2\) (10 mL) were added \(i\)-Pr\(_2\)NEt (1.1 mL, 6.12 mmol), MOMCl (0.39 mL, 5.10 mmol), and TBAI (188 mg, 0.510 mmol) at room temperature. The mixture was stirred at the same temperature for 11 h. The reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with Et\(_2\)O, washed with saturated aqueous NH\(_4\)Cl, saturated aqueous NaHCO\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and column chromatography (hexane/EtOAc = 40:1) gave MOM ether 28b (544 mg, 96%): colorless oil; \(R_f\) = 0.50 (hexane/EtOAc = 10:1); IR (neat) 2955, 2929, 2862, 1719, 1632 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 6.21 (s, 1 H), 5.81 (ddd, J = 17.1, 10.4, 5.6 Hz, 1 H), 5.61 (s, 0.5 H), 5.60 (s, 0.5 H), 5.14 (d, J = 17.1 Hz, 1 H), 5.10–5.05 (m, 2 H), 4.67–4.57 (m, 2 H), 4.21 (q, J = 7.1 Hz, 2 H), 4.13 (t, J = 5.6 Hz, 1 H), 3.88–3.80 (m, 1 H), 3.34 (s, 1.5 H), 3.33 (s, 1.5 H), 2.59–2.38 (m, 2 H), 2.07–1.84 (m, 5 H), 1.65–1.51 (m, 2 H), 1.58 (s, 3 H), 1.44–1.34 (m, 3 H), 1.30 (t, J = 7.1 Hz, 3 H), 1.27–1.09 (m, 3 H), 0.94–0.87 (m, 9 H), 0.90 (s, 9 H), 0.04 (s, 3 H), 0.02 (s, 3 H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.0, 166.9, 140.7, 137.7, 137.7, 135.5, 135.4, 127.1, 124.4, 124.3, 114.5, 95.6, 95.5, 75.5, 74.4, 74.2, 60.7, 60.7, 55.7, 55.6, 50.0, 42.5, 39.7, 38.4, 38.0, 37.8, 37.1, 29.3, 29.0, 27.7, 26.0, 25.5, 25.3, 24.5, 21.9, 20.0, 19.4, 19.0, 18.3, 16.0, 14.3, –4.0, –4.8; HRMS (ESI–TOF) calcd for C\(_{32}\)H\(_{60}\)O\(_5\)SiNa \([\text{M} + \text{Na}]^+\) 575.4108, found 575.4110.
calcd for C\textsubscript{32}H\textsubscript{60}O\textsubscript{5}SiNa [M + Na]\textsuperscript{+} 575.4108, found 575.4108.

**Alcohol 29a.** To a solution of TBS ether 28a (380 mg, 0.687 mmol) in THF (4.8 mL) was added TBAF (1.0 M in THF, 2.1 mL, 2.10 mmol) at room temperature. The mixture was stirred at 60 °C for 5 h. The mixture was diluted with EtOAc, washed with H\textsubscript{2}O and brine, and then dried over Na\textsubscript{2}SO\textsubscript{4}. Concentration and column chromatography (hexane/EtOAc = 7:1) gave alcohol 29a (245 mg, 81%): colorless oil; \(R_f = 0.43\) (hexane/EtOAc = 4:1); IR (neat) 3483, 2954, 2929, 1715, 1625 cm\textsuperscript{-1}; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3) \delta 6.21 \text{ (s, 1 H), 5.90 \text{ (ddd, } J = 17.3, 10.5, 6.1 \text{ Hz, 1 H), 5.61 \text{ (s, 0.5 H), 5.60 \text{ (s, 0.5 H), 5.24 \text{ (d, } J = 17.3 \text{ Hz, 1 H), 5.15 \text{ (d, } J = 10.5 \text{ Hz, 1 H), 5.10 \text{ (t, } J = 6.8 \text{ Hz, 1 H), 4.67-4.57 \text{ (m, 2 H), 4.21 \text{ (q, } J = 7.1 \text{ Hz, 2 H), 4.14-4.10 \text{ (m, 1 H), 3.87-3.79 \text{ (m, 1 H), 3.33 (s, 1.5 H), 2.58-2.38 (m, 2 H), 2.06-1.89 (m, 5 H), 1.67-1.50 (m, 2 H), 1.58 (s, 3 H), 1.45 (brs, 1 H), 1.42-1.24 (m, 5 H), 1.30 (t, } J = 7.1 \text{ Hz, 3 H), 1.22-1.13 (m, 1 H), 0.94-0.88 \text{ (m, 9 H); } ^{13}\text{C NMR (100 MHz, CDCl}_3) \delta 167.0, 166.9, 140.4, 137.7, 137.6, 135.1, 135.1, 127.1, 124.8, 124.7, 115.3, 95.6, 95.5, 74.9, 74.4, 74.2, 60.7, 55.7, 55.6, 48.7, 42.4, 39.4, 38.4, 38.0, 37.7, 37.0, 29.2, 28.9, 27.8, 25.4, 25.3, 24.6, 21.2, 20.0, 19.4, 18.9, 16.0, 14.3; HRMS (ESI–TOF) calcd for C\textsubscript{26}H\textsubscript{46}O\textsubscript{5}Na [M + Na]\textsuperscript{+} 461.3243, found 461.3236.

**Alcohol 29b.** To a solution of TBS ether 28b (524 mg, 0.948 mmol) in THF (7.0 mL) was added TBAF (1.0 M in THF, 2.8 mL, 2.80 mmol) at room temperature. The mixture was stirred at 60 °C for 6 h. The mixture was diluted with EtOAc, washed with H\textsubscript{2}O and brine, and then dried over Na\textsubscript{2}SO\textsubscript{4}. Concentration and column chromatography (hexane/EtOAc = 7:1) gave alcohol 29b (347 mg, 83%): colorless oil; \(R_f = 0.43\) (hexane/EtOAc = 4:1); IR (neat) 3475, 2954, 2930, 1698, 1629 cm\textsuperscript{-1}; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3) \delta 6.21 \text{ (s, 1 H), 5.90 \text{ (ddd, } J = 17.1, 10.5, 6.1 \text{ Hz, 1 H), 5.61 \text{ (s, 0.5 H), 5.60 \text{ (s, 0.5 H), 5.24 \text{ (d, } J = 17.1 \text{ Hz, 1 H), 5.15 \text{ (d, } J = 10.5 \text{ Hz, 1 H), 5.10 \text{ (t, } J = 6.8 \text{ Hz, 1 H), 4.67-4.57 \text{ (m, 2 H), 4.21 \text{ (q, } J = 7.1 \text{ Hz, 2 H), 4.12 \text{ (t, } J = 6.1 \text{ Hz, 1 H), 3.87-3.79 \text{ (m, 1 H), 3.34 (s, 1.5 H), 3.33 (s, 1.5 H), 2.58-2.38 (m, 2 H), 2.06-1.89 (m, 5 H), 1.66-1.50 (m, 2 H), 1.58 (s, 3 H), 1.42-1.25 (m, 6 H), 1.30 (t, } J = 7.1 \text{ Hz, 3 H), 1.22-1.13 (m, 1 H), 0.94-0.88 \text{ (m, 9 H); } ^{13}\text{C NMR (100 MHz, CDCl}_3) \delta 167.0, 167.0, 140.4, 137.7, 137.6, 135.1, 135.1, 127.1, 124.8, 124.7, 115.2, 95.6, 95.5, 74.9, 74.4, 74.3, 60.7, 55.6, 48.8, 42.5, 39.4, 38.4, 38.0, 37.7, 37.1, 29.2, 29.0, 27.8, 25.4, 25.3, 24.7, 21.2, 20.0, 19.4, 18.9, 16.0, 14.3; HRMS (ESI–TOF) calcd for C\textsubscript{26}H\textsubscript{46}O\textsubscript{5}Na [M + Na]\textsuperscript{+} 461.3243, found 461.3247.

**Carboxylic Acid 30a.** To a solution of ester 29a (210 mg, 0.479 mmol) in THF (3.0 mL), MeOH (1.0 mL), and H\textsubscript{2}O (1.0 mL) was added LiOH·H\textsubscript{2}O (30.1 mg, 0.718 mmol) at room temperature. The mixture was stirred at the same temperature for 12 h. The mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc, washed with H\textsubscript{2}O and brine, and then dried over Na\textsubscript{2}SO\textsubscript{4}. Concentration and column chromatography (hexane/EtOAc = 6:1, 3:1) gave carboxylic acid 30a (174 mg, 88%): colorless oil; \(R_f = 0.17\) (hexane/EtOAc = 2:1); IR (neat) 3466, 2955, 2930, 1698, 1629 cm\textsuperscript{-1}; \(^1\text{H} \text{NMR (400 MHz, CDCl}_3) \delta 6.34 \text{ (t, } J = 2.1 \text{ Hz, 1 H), 5.90 \text{ (ddd, } J = 17.3, 10.5, 5.8 \text{ Hz, 1 H), 5.74 (s, 0.5 H),
5.72 (s, 0.5 H), 5.25 (d, J = 17.3 Hz, 1 H), 5.16 (dd, J = 10.5, 1.3 Hz, 1 H), 5.12–5.08 (m, 1 H), 4.67–4.60 (m, 2 H), 4.15 (q, J = 5.8 Hz, 1 H), 3.89–3.82 (m, 1 H), 3.34 (s, 1.5 H), 3.30 (s, 1.5 H), 2.58–2.40 (m, 2 H), 2.06–1.89 (m, 5 H), 1.67–1.53 (m, 2 H), 1.58 (s, 3 H), 1.43–1.12 (m, 8 H), 0.93–0.90 (m, 9 H); 13C NMR (100 MHz, CDCl 3) δ 170.9, 170.9, 140.2, 140.1, 137.0, 136.9, 135.0, 129.4, 124.9, 115.4, 95.6, 95.5, 75.0, 74.6, 74.4, 55.7, 48.5, 42.4, 42.3, 39.3, 39.3, 38.0, 37.6, 37.3, 37.0, 29.1, 28.8, 27.8, 27.8, 25.1, 24.5, 21.1, 20.0, 19.6, 19.0, 18.9, 16.0; HRMS (ESI–TOF) calcd for C 24H42O 5Na [M + Na] + 433.2930, found 433.2934.

Carboxylic Acid 30b. To a solution of ester 29b (326 mg, 0.743 mmol) in THF (4.5 mL), MeOH (1.5 mL), and H 2O (1.5 mL) was added LiOH·H 2O (46.6 mg, 1.11 mmol) at room temperature. The mixture was stirred at the same temperature for 10 h. The mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc, washed with H 2O and brine, and then dried over Na 2SO 4. Concentration and column chromatography (hexane/EtOAc = 6:1, 3:1) gave carboxylic acid 30b (222 mg, 73%): colorless oil; R f  = 0.17 (hexane/EtOAc = 2:1); IR (neat) 3433, 2955, 2930, 1697, 1631 cm –1; 1H NMR (400 MHz, CDCl 3) δ 6.33 (d, J = 1.5 Hz, 1 H), 5.90 (ddd, J = 17.1, 10.5, 6.6 Hz, 1 H), 5.73 (s, 0.5 H), 5.71 (s, 0.5 H), 5.25 (dt, J = 17.1, 1.4 Hz, 1 H), 5.16 (dd, J = 10.5, 1.4 Hz, 1 H), 5.14–5.10 (m, 1 H), 4.66–4.60 (m, 2 H), 4.19–4.13 (m, 1 H), 3.88–3.82 (m, 1 H), 3.35 (s, 3 H), 2.57–2.42 (m, 2 H), 2.06–1.89 (m, 5 H), 1.67–1.52 (m, 2 H), 1.58 (s, 3 H), 1.43–1.10 (m, 8 H), 0.93–0.90 (m, 9 H); 13C NMR (100 MHz, CDCl 3) δ 170.4, 140.1, 140.1, 136.9, 135.0, 134.9, 129.3, 129.2, 125.0, 124.9, 115.5, 95.6, 95.5, 75.1, 75.0, 74.7, 74.5, 55.7, 48.4, 48.4, 42.6, 42.4, 39.3, 39.2, 38.0, 37.7, 37.3, 37.1, 29.2, 29.0, 27.8, 25.4, 25.3, 24.5, 24.4, 21.1, 20.0, 19.7, 19.1, 19.0, 16.0; HRMS (ESI–TOF) calcd for C 24H42O 5Na [M + Na] + 433.2930, found 433.2927.

Lactone 31a. To a solution of MNBA (76.1 mg, 0.221 mmol) and DMAP (53.9 mg, 0.441 mmol) in CH 2Cl 2 (64 mL) was slowly added hydroxycarboxylic acid 30a (60.4 mg, 0.147 mmol) in CH 2Cl 2 (6.0 mL at 0.4 mL/h + 2.0 mL at 4.0 mL/h + 2.0 mL at 4.0 mL/h) at room temperature with a syringe pump for 16 h. The mixture was stirred at the same temperature for further 4 h. The reaction was quenched with saturated aqueous NH 4Cl. The mixture was concentrated, washed with saturated aqueous NaHCO 3, H 2O, and brine, and then dried over Na 2SO 4. Concentration and column chromatography (hexane/EtOAc = 20:1) gave lactone 31a (42.6 mg, 85%): colorless oil; R f  = 0.47 (hexane/EtOAc = 20:1); IR (neat) 2954, 2930, 1714, 1631 cm –1; 1H NMR (400 MHz, CDCl 3) δ 6.23 (s, 0.5 H), 6.21 (s, 0.5 H), 5.91–5.80 (m, 1 H), 5.74 (s, 0.5 H), 5.66 (s, 0.5 H), 5.62–5.61 (m, 1 H), 5.26–5.18 (m, 2.5 H), 4.98 (t, J = 6.8 Hz, 0.5 H), 4.73–4.52 (m, 2 H), 3.87–3.81 (m, 0.5 H), 3.53–3.47 (m, 0.5 H), 3.38 (s, 1.5 H), 3.30 (s, 1.5 H), 2.89 (dd, J = 13.7, 4.8 Hz, 0.5 H), 2.77 (dd, J = 13.7, 3.7 Hz, 0.5 H), 2.31–2.24 (m, 1 H), 2.11–1.91 (m, 4.5 H), 1.84–1.77 (m, 0.5 H), 1.58 (s, 1.5 H), 1.57 (s, 1.5 H), 1.53–1.43 (m, 4.5 H), 1.37–1.21 (m, 3 H), 1.15–1.05 (m, 0.5 H), 0.97–0.86 (m, 9 H); 13C NMR (100 MHz, CDCl 3) δ 166.0, 165.6, 138.0, 137.4, 135.8, 134.7, 134.1, 127.0, 125.9, 125.7, 116.4, 115.9, 95.3, 94.8, 75.9, 75.3, 74.6, 55.6, 55.4, 45.9, 45.7, 43.4, 40.7, 38.3, 37.9,
Lactone 31b. To a solution of MNBA (54.3 mg, 0.158 mmol) and DMAP (38.6 mg, 0.316 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (36 mL) was slowly added hydroxycarboxylic acid 30b (36.0 mg, 87.7 μmol) in CH\textsubscript{2}Cl\textsubscript{2} (4.0 mL at 0.4 mL/h + 2.0 mL at 4.0 mL/h + 2.0 mL at 4.0 mL/h) at 40 °C with a syringe pump for 11 h. The mixture was stirred at the same temperature for further 7 h. The reaction was quenched with saturated aqueous NH\textsubscript{4}Cl. The mixture was concentrated, washed with saturated aqueous NaHCO\textsubscript{3}, H\textsubscript{2}O, and brine, and then dried over Na\textsubscript{2}SO\textsubscript{4}. Concentration and column chromatography (hexane/EtOAc = 20:1) gave lactone 31b (26.7 mg, 78%): colorless oil; \( R_f = 0.47 \) (hexane/EtOAc = 7:1); IR (neat) 2954, 2929, 1716, 1631 cm\textsuperscript{-1}; \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 6.30 (s, 0.5 H), 6.25 (s, 0.5 H), 5.91–5.76 (m, 1 H), 5.68–5.58 (m, 2 H), 5.26–5.16 (m, 1 H), 5.06 (t, \( J = 7.2 \) Hz, 1 H), 4.65–4.62 (m, 2 H), 3.85–3.78 (m, 0.5 H), 3.72–3.66 (m, 0.5 H), 3.35 (s, 1.5 H), 3.34 (s, 1.5 H), 2.68–2.63 (m, 1 H), 2.50–2.43 (m, 1 H), 2.13–1.86 (m, 4.5 H), 1.85–1.77 (m, 0.5 H), 1.60 (s, 1.5 H), 1.58 (s, 1.5 H), 1.54–1.20 (m, 8 H), 0.97–0.92 (m, 6 H), 0.88 (d, \( J = 6.1 \) Hz, 3 H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) 166.1, 166.0, 137.8, 137.1, 135.5, 135.4, 134.6, 127.7, 127.6, 126.0, 125.5, 116.9, 115.7, 95.1, 94.9, 76.3, 76.2, 75.3, 73.7, 55.5, 55.5, 47.1, 45.9, 42.9, 38.5, 38.4, 37.4, 37.3, 36.6, 36.5, 28.8, 28.5, 28.0, 25.3, 24.6, 24.1, 23.8, 21.3, 21.1, 20.1, 20.0, 19.9, 18.8, 16.3, 15.9; HRMS (ESI–TOF) calcd for C\textsubscript{24}H\textsubscript{40}O\textsubscript{4}Na \([\text{M + Na}]^+\) 415.2824, found 415.2818.

Alcohol 32a. To a solution of MOM ether 31a (29.5 mg, 75.1 μmol) in Me\textsubscript{2}S (1.5 mL) was added BF\textsubscript{3}·OEt\textsubscript{2} (46 μL, 0.376 mmol) at 0 °C. The mixture was stirred at the same temperature for 10 min. The mixture was quenched with saturated aqueous NaHCO\textsubscript{3}. The mixture was diluted with EtOAc, washed with H\textsubscript{2}O and brine, and then dried over Na\textsubscript{2}SO\textsubscript{4}. Concentration and column chromatography (hexane/EtOAc = 8:1) gave alcohol 32a (24.8 mg, 95%): colorless oil; \( R_f = 0.29 \) (hexane/EtOAc = 4:1); IR (neat) 3417, 2955, 2928, 2873, 1714, 1625 cm\textsuperscript{-1}; \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}) \( \delta \) 6.28 (brs, 0.5 H), 6.20 (brs, 0.5 H), 5.91–5.80 (m, 1 H), 5.67 (s, 0.5 H), 5.65 (s, 0.5 H), 5.62–5.59 (m, 1 H), 5.26–5.18 (m, 2.5 H), 5.02 (t, \( J = 6.3 \) Hz, 0.5 H), 3.92–3.86 (m, 0.5 H), 3.80 (d, \( J = 13.8 \) Hz, 1.1 Hz, 0.5 H), 2.69 (dd, \( J = 13.4 \), 5.9, 1.0 Hz, 0.5 H), 2.36 (dd, \( J = 13.4 \), 6.6, 0.7 Hz, 0.5 H), 2.26 (dd, \( J = 13.8 \), 7.1 Hz, 0.5 H), 2.12–1.95 (m, 4 H), 1.86–1.78 (m, 1 H), 1.61–1.37 (m, 8 H), 1.59 (s, 1.5 H), 1.58 (s, 1.5 H), 1.25–1.10 (m, 1 H), 0.98–0.90 (m, 9 H); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}) \( \delta \) 166.6, 165.8, 137.8, 137.7, 135.5, 134.6, 134.4, 134.0, 127.7, 127.0, 125.8, 125.7, 116.4, 115.9, 76.0, 75.8, 69.5, 69.0, 46.3, 45.9, 45.3, 42.6, 41.7, 40.7, 37.5, 37.2, 37.1, 35.0, 29.3, 28.8, 28.3, 28.1, 25.4, 23.8, 23.4, 23.1, 21.8, 20.8, 20.7, 20.3, 20.0, 18.5, 16.1, 15.9; HRMS (ESI–TOF) calcd for C\textsubscript{22}H\textsubscript{36}O\textsubscript{3}Na \([\text{M + Na}]^+\) 371.2562, found 371.2559.

Alcohol 32b. To a solution of MOM ether 31b (42.7 mg, 0.109 mmol) in Me\textsubscript{2}S (2.2 mL) was added BF\textsubscript{3}·OEt\textsubscript{2} (67 μL, 0.545 mmol) at 0 °C. The mixture was stirred at the same temperature for 10 min. The mixture was quenched with saturated aqueous NaHCO\textsubscript{3}. The
mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 8:1) gave alcohol 32b (34.6 mg, 91%): colorless oil; \( R_f = 0.29 \) (hexane/EtOAc = 4:1); IR (neat) 3417, 2955, 2927, 2868, 1714, 1627 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \( \delta \) 6.29 (t, \( J = 1.3 \) Hz, 1 H), 5.91–5.78 (m, 1 H), 5.69–5.62 (m, 2 H), 5.26–5.18 (m, 1 H), 5.14–5.06 (m, 1 H), 5.03–4.98 (m, 1 H), 4.94–4.88 (m, 1 H), 4.82–4.77 (m, 1 H), 4.67–4.62 (m, 1 H), 4.56–4.50 (m, 1 H), 4.48–4.43 (m, 1 H), 4.37–4.32 (m, 1 H), 4.26–4.21 (m, 1 H), 4.13–4.08 (m, 1 H), 2.74 (dd, \( J = 14.3, 3.8 \) Hz, 0.5 H), 2.55 (d, \( J = 5.6 \) Hz, 1 H), 2.30 (dd, \( J = 14.3, 7.7 \) Hz, 0.5 H), 2.11–1.95 (m, 1 H), 1.89–1.76 (m, 1 H), 1.65–1.29 (m, 8 H), 1.60 (s, 1 H), 1.58 (s, 1 H), 1.18–1.07 (m, 1 H), 0.96–0.91 (m, 9 H); \(^1\)C NMR (100 MHz, CDCl3) \( \delta \) 166.3, 165.9, 138.1, 137.2, 135.5, 135.0, 134.4, 134.4, 127.9, 127.6, 126.2, 125.6, 117.0, 116.2, 76.3, 75.6, 69.9, 68.2, 47.6, 46.0, 44.6, 44.6, 40.7, 40.6, 38.6, 37.4, 36.7, 36.1, 29.1, 28.9, 28.4, 25.4, 25.0, 24.4, 24.2, 21.3, 21.0, 21.0, 20.6, 20.0, 19.4, 16.3, 16.1; HRMS (ESI–TOF) calcd for C\(_{22}\)H\(_{36}\)O\(_3\)Na [M + Na\(^+\)] 371.2562, found 371.2567.

**Butenolide 1a.** To a solution of triene 32a (10.3 mg, 29.6 \( \mu \)mol) in toluene (6.0 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (1.9 mg, 2.96 \( \mu \)mol) at room temperature. The mixture was stirred at 100 °C for 30 h. The mixture was filtered through short column chromatography (hexane/EtOAc = 1:1). Concentration and column chromatography (hexane/EtOAc = 3:1) gave butenolide 34a (3.3 mg) and triene 32a (3.9 mg, 38% recovery). Butenolide 34a was used for the next step without further purification.

To a solution of alcohol 34a obtained above (3.3 mg) in CH\(_2\)Cl\(_2\) (1.0 mL) were added MS4Å (3.0 mg), NMO (6.0 mg, 51.5 \( \mu \)mol), and a catalytic amount of TPAP at room temperature. The mixture was stirred at the same temperature for 10 min. The mixture was filtered through short column chromatography (hexane/EtOAc = 3:1). Concentration and column chromatography (hexane/EtOAc = 8:1) gave butenolide 1a (2.5 mg, 27% in two steps, 43% based on recovered 32a in two steps): colorless amorphous solid; \( R_f = 0.46 \) (hexane/EtOAc = 2:1); \([\alpha]_D^{29} +92.2\) (c 0.19, CHCl3); IR (neat) 2955, 2914, 2886, 1746, 1710 cm\(^{-1}\); \(^1\)H and \(^1\)C NMR Table S1; HRMS (ESI–TOF) calcd for C\(_{20}\)H\(_{30}\)O\(_3\)Na [M + Na\(^+\)] 341.2093, found 341.2092.

**Butenolide 1b.** To a solution of triene 32b (13.0 mg, 37.3 \( \mu \)mol) in toluene (7.5 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (1.2 mg, 1.87 \( \mu \)mol) at room temperature. The mixture was stirred at 100 °C for 30 h. The mixture was filtered through short column chromatography (hexane/EtOAc = 1:1). Concentration and column chromatography (hexane/EtOAc = 3:1) gave butenolide 34b (4.2 mg) and triene 32b (4.8 mg, 37% recovery). Butenolide 34b was used for the next step without further purification.

To a solution of alcohol 34b obtained above (4.2 mg) in CH\(_2\)Cl\(_2\) (1.0 mL) were added MS4Å (5.0 mg), NMO (7.7 mg, 65.5 \( \mu \)mol), and a catalytic amount of TPAP at room temperature. The mixture was stirred at the same temperature for 10 min. The mixture was filtered through short column chromatography (hexane/EtOAc = 3:1). Concentration and column chromatography (hexane/EtOAc = 8:1) gave butenolide 1b (3.6 mg, 30% in two steps, 48% based on recovered 32b in two steps): colorless amorphous solid; \( R_f = 0.46 \)
Alcohol 37. To a solution of alcohol 25a (77.3 mg, 0.195 mmol) in CH₂Cl₂ (2.0 mL) were added PhI(OAc)₂ (94.2 mg, 0.293 mmol) and TEMPO (6.01 mg, 39.0 μmol) at room temperature. The mixture was stirred at the same temperature for 2 h. The reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with Et₂O, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 80:1) gave the corresponding aldehyde (62.5 mg), which was used for the next step without further purification.

A mixture of the aldehyde obtained above (62.5 mg) and chiral allylic boronate 35 (68.7 mg, 0.187 mmol) in toluene (0.1 mL) was stirred at room temperature for 38 h. After the reaction was quenched with H₂O, the mixture was diluted with EtOAc and dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1) gave a diastereomeric mixture of alcohol 36 and its C₆ stereoisomer (100 mg, dr = 4.4:1), which was used for the next step without further purification.

To a solution of a diastereomeric mixture of alcohol 36 and its C₆ stereoisomer (100 mg, dr = 4.4:1) in CH₂Cl₂ (1.5 mL) were added i-Pr₂NEt (0.48 mL, 2.78 mmol), MOMCl (0.18 mL, 2.34 mmol), and TBAI (28.8 mg, 78.0 μmol) at room temperature. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NH₄Cl, saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 30:1) gave a diastereomeric mixture of the corresponding MOM ethers (96.7 mg, dr = 4.4:1), which was used for the next step without further purification.

To a solution of a diastereomeric mixture of the TBS ethers obtained above (96.7 mg, dr = 4.4:1) in THF (1.6 mL) was added TBAF (1.0 M in THF, 0.8 mL, 0.800 mmol) at room temperature. The mixture was stirred at 60 °C for 5 h. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 7:1) gave a diastereomeric mixture of alcohol 37 and its C₆ stereoisomer (52.2 mg, 61% in four steps, dr = 4.4:1): colorless oil; Rₐ = 0.42 (hexane/EtOAc = 4:1); [α]D₂⁶ +97.4 (c 0.21, CHCl₃); IR (neat) 2956, 2925, 2876, 1751, 1710 cm⁻¹; ¹H and ¹³C NMR Table S2; HRMS (ESI–TOF) calced for C₂₀H₃₀O₃Na [M + Na]+ 341.2093, found 341.2098.
Lactone 38. To a solution of a diastereomeric mixture of ester 37 and its C6 stereoisomer (148 mg, 0.339 mmol, dr = 4.4:1) in THF (4.1 mL), MeOH (1.4 mL), and H2O (1.4 mL) was added LiOH·H2O (42.6 mg, 1.01 mmol) at room temperature. The mixture was stirred at the same temperature for 17 h. The mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc and washed with H2O and brine. The aqueous phase was extracted with EtOAc three times and the combined organic phase was dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 3:1) gave a diastereomeric mixture of the corresponding carboxylic acids (130 mg, dr = 4.4:1), which was used for the next step without further purification.

To a solution of MNBA (158 mg, 0.458 mmol) and DMAP (112 mg, 0.918 mmol) in CH2Cl2 (138 mL) was slowly added a diastereomeric mixture of the hydroxycarboxylic acids obtained above (130 mg, dr = 4.4:1) in CH2Cl2 (9.0 mL at 0.4 mL/h + 3.0 mL at 6.0 mL/h) at room temperature with a syringe pump for 24 h. The mixture was stirred at the same temperature for further 11 h. The reaction was quenched with saturated aqueous NH4Cl. The mixture was concentrated, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 30:1) gave a diastereomeric mixture of lactone 38 and its C6 stereoisomer (102 mg, 77% in two steps, dr = 4.4:1): colorless oil; Rf = 0.58 (hexane/EtOAc = 7:1); [α]D27 –2.8 (c 0.99, CHCl3); IR (neat) 2954, 2927, 1714 cm –1; 1H NMR (400 MHz, CDCl3) δ 6.25–6.20 (m, 1 H), 5.92–5.80 (m, 1 H), 5.74 (s, 1 H), 5.69–5.62 (m, 1 H), 5.27–5.18 (m, 2 H), 4.98 (t, J = 6.8 Hz, 1 H), 4.73–4.52 (m, 2 H), 3.87–3.81 (m, 1 H), 3.39–3.29 (m, 3 H), 2.91–2.74 (m, 1 H), 2.31–2.24 (m, 1 H), 2.11–1.93 (m, 5 H), 1.85–1.77 (m, 1 H), 1.59–1.21 (m, 10 H), 0.98–0.86 (m, 9 H); 13C NMR (100 MHz, CDCl3) δ 165.6, 137.4, 135.8, 134.7, 134.1, 127.0, 125.7, 116.4, 115.9, 95.3, 94.8, 75.9, 75.3, 74.6, 55.5, 55.4, 45.9, 45.7, 43.4, 40.8, 38.4, 37.9, 37.6, 37.1, 37.0, 35.5, 29.7, 28.3, 27.9, 27.1, 24.4, 23.7, 23.5, 23.3, 21.7, 21.0, 20.5, 20.0, 19.6, 18.5, 16.2, 15.7; HRMS (ESI–TOF) calcd for C24H40O4Na [M + Na]+ 415.2824, found 415.2825.

Alcohol S8. To a solution of a diastereomeric mixture of MOM ether 38 and its C6 stereoisomer (6.9 mg, 17.6 μmol, dr = 4.4:1) in Me2S (0.4 mL) was added BF3·OEt2 (11 μL, 88.0 μmol) at 0 °C. The mixture was stirred at the same temperature for 30 min. The mixture was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 7:1) gave a diastereomeric mixture of alcohol S8 and its C6 stereoisomer (5.3 mg, 86%, dr = 4.4:1): colorless oil; Rf = 0.38 (hexane/EtOAc = 4:1); [α]D26 –1.5 (c 1.02, CHCl3); IR (neat) 3415, 2955, 2927, 2870, 1713 cm–1; 1H NMR (400 MHz, CDCl3) δ 6.28 (s, 0.19 H), 6.20 (s, 0.81 H), 6.28–6.20 (m, 1 H), 5.86 (ddd, J = 16.8, 10.8, 5.6 Hz, 1 H), 5.67–5.60 (m, 2 H), 5.23 (d, J = 16.8 Hz, 1 H), 5.20 (d, J = 10.8 Hz, 1 H), 5.03–5.00 (m, 1 H), 3.92–3.86 (m, 1 H), 2.87 (dd, J = 13.6, 3.6 Hz, 0.19 H), 2.69 (dd, J = 13.6,
6.0 Hz, 0.81 H), 2.38–2.23 (m, 1 H), 2.05–1.96 (m, 4 H), 1.86–1.78 (m, 1 H), 1.68–1.36 (m, 7 H), 1.57 (s, 3 H), 1.17–1.10 (m, 1 H), 0.99–0.89 (m, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 166.6, 165.8, 137.8, 137.7, 135.5, 135.0, 134.6, 134.4, 134.0, 127.6, 127.0, 125.8, 116.4, 116.0, 76.0, 75.8, 69.5, 69.0, 46.3, 45.9, 45.3, 42.6, 41.7, 40.7, 37.4, 37.2, 37.1, 35.0, 29.3, 28.8, 28.3, 25.4, 23.8, 23.4, 23.1, 21.8, 20.8, 20.7, 20.3, 20.0, 18.5, 16.1, 16.0; HRMS (ESI–TOF) calcd for C$_{22}$H$_{36}$O$_3$Na [M + Na]$^+$ 371.2562, found 371.2562.

**Sarcophytonolide E (2).** To a solution of a diastereomeric mixture of triene S8 and its C6 stereoisomer (4.0 mg, 11.5 μmol, dr = 4.4:1) in toluene (2.3 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (0.7 mg, 1.15 μmol) at room temperature. The mixture was stirred at 100 °C for 32 h. The mixture was filtered through short column chromatography (hexane/EtOAc = 1:1). Concentration and column chromatography (hexane/EtOAc = 7:1, 2:1) gave sarcophytonolide E (2) (1.3 mg, 35%, 51% based on recovered S8) and triene S8 (1.2 mg, 30% recovery): colorless oil; $R_f$ = 0.39 (hexane/EtOAc = 1:1); $[\alpha]_D^{27} +48.7$ (c 0.17, CHCl$_3$); literature$^{10b}$ $[\alpha]_D^{20} +30$ (c 0.29, CHCl$_3$); IR (neat) 3424, 2950, 2925, 2870, 1754 cm$^{-1}$; $^1$H and $^{13}$C NMR Table S3; HRMS (ESI–TOF) calcd for C$_{20}$H$_{32}$O$_3$Na [M + Na]$^+$ 343.2249, found 343.2250.

**Pivalate 39.** To a solution of geraniol (1.0 mL, 5.71 mmol) in CH$_2$Cl$_2$ (19 mL) were added pyridine (0.69 mL, 8.57 mmol) and PivCl (0.83 mL, 6.85 mmol) at room temperature. After the mixture was stirred at the same temperature for 2 h, the reaction was quenched with saturated aqueous NH$_4$Cl. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 30:1) gave pivalate 39 (1.31 g, 96%): colorless oil; $R_f$ = 0.50 (hexane/EtOAc = 10:1); IR (neat) 2970, 2924, 2870, 1730 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.32 (td, $J$ = 6.8, 1.2 Hz, 1 H), 5.10–5.06 (m, 1 H), 4.57 (d, $J$ = 6.8 Hz, 2 H), 2.13–2.02 (m, 4 H), 1.70 (s, 3 H), 1.68 (s, 3 H), 1.61 (s, 3 H), 1.20 (s, 9 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 178.4, 141.5, 131.6, 123.7, 118.7, 61.3, 39.5, 38.8, 27.3, 26.4, 25.7, 17.7, 16.5; HRMS (ESI–TOF) calcd for C$_{15}$H$_{26}$O$_2$Na [M + Na]$^+$ 261.1830, found 261.1832.

**Allylic Alcohol 40.** To a mixture of SeO$_2$ (8.2 mg, 73.5 μmol) and salicylic acid (20.3 mg, 0.147 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added TBHP (ca. 5.0 M solution in 2,2,4-trimethylpentane, 0.59 mL, 2.94 mmol) at room temperature. After the mixture was stirred at the same temperature for 10 min, the mixture was stirred at room temperature for 7 h, the reaction was quenched with saturated aqueous Na$_2$S$_2$O$_3$ at 0 °C. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration gave the mixture of allylic alcohol 40 and the corresponding α,β-unsaturated aldehyde (414 mg), which was used for the next step without further purification.

To a solution of the mixture obtained above (414 mg) in EtOH (7.4 mL) was added NaBH$_4$ (27.8 mg, 0.735 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h,
the reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 5:1) gave allylic alcohol 40 (214 mg, 57% in two steps): colorless oil; Rf = 0.22 (hexane/EtOAc = 4:1); IR (neat) 3437, 2973, 2927, 2868, 1727 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.36 (td, J = 6.8, 1.3 Hz, 1 H), 5.31 (td, J = 6.8, 1.2 Hz, 1 H), 4.56 (d, J = 6.8 Hz, 2 H), 3.99 (s, 2 H), 2.20–2.14 (m, 2 H), 2.10–2.07 (m, 2 H), 1.70 (s, 3 H), 1.67 (s, 3 H), 1.19 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.5, 140.9, 135.1, 125.3, 119.1, 68.9, 61.4, 39.1, 38.8, 27.3, 25.8, 16.5, 13.8; HRMS (ESI–TOF) calcd for C₁₅H₂₆O₃Na [M + Na]⁺ 277.1780, found 277.1783.

Allylic Bromide 41. To a solution of allylic alcohol 40 (524 mg, 2.06 mmol) in CH₃CN (10 mL) were added PPh₃ (808 mg, 3.08 mmol) and CB₄r₄ (1.01 g, 3.05 mmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, the mixture was filtered through short column chromatography (hexane/EtOAc = 10:1). Concentration and column chromatography (hexane/EtOAc = 50:1) gave allylic bromide 41 (615 mg, 94%): colorless oil; Rf = 0.36 (hexane/EtOAc = 20:1); IR (neat) 2972, 2932, 2870, 1726 cm –¹; ¹H NMR (400 MHz, CDCl₃) δ 5.57 (t, J = 6.8 Hz, 1 H), 5.34–5.30 (m, 1 H), 4.57 (d, J = 6.8 Hz, 2 H), 3.96 (s, 2 H), 2.19–2.07 (m, 4 H), 1.76 (s, 3 H), 1.70 (s, 3 H), 1.20 (s, 9 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 140.6, 132.3, 130.4, 119.3, 61.2, 41.5, 38.8, 38.6, 27.3, 26.5, 16.5, 14.7; HRMS (ESI–TOF) calcd for C₁₅H₂₅BrO₂Na [M + Na]⁺ 339.0936, found 339.0946.

Sulfone 42. To a solution of sulfone 20 (142 mg, 0.284 mmol) in THF (2.0 mL) was added NaHMDS (1.0 M in THF, 0.34 mL, 0.340 mmol) at –78 °C. The mixture was stirred at the same temperature for 30 min. To the mixture was added allylic bromide 41 (117 mg, 0.369 mmol) in THF (0.5 mL + 0.3 mL + 0.2 mL) at –78 °C. The mixture was gradually warmed up to room temperature for 3 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 20:1) gave sulfone 42 (186 mg, 89%): colorless oil; Rf = 0.36 (hexane/EtOAc = 10:1); [α]D²⁵ +18.0 (c 1.05, CHCl₃); IR (neat) 2956, 2924, 2852, 1728 cm–¹; ¹H NMR (400 MHz, CDCl₃) δ 7.82–7.80 (m, 2 H), 7.58–7.55 (m, 1 H), 7.49–7.45 (m, 2 H), 5.29 (t, J = 6.8 Hz, 1 H), 5.11 (t, J = 6.3 Hz, 1 H), 4.55 (d, J = 6.8 Hz, 2 H), 4.33–4.30 (m, 1 H), 3.74–3.64 (m, 2 H), 3.47 (d, J = 8.5 Hz, 1 H), 2.72–2.58 (m, 2 H), 2.36 (d, J = 6.7 Hz, 1 H), 2.17–2.09 (m, 1 H), 1.98–1.96 (m, 2 H), 1.91–1.84 (m, 2 H), 1.67 (s, 3 H), 1.22 (s, 3 H), 1.20 (s, 9 H), 0.95 (d, J = 8.4 Hz, 3 H), 0.94 (s, 9 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.87 (s, 9 H), 0.14 (s, 3 H), 0.13 (s, 3 H), 0.13 (s, 3 H), 0.13 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 141.3, 140.9, 132.9, 130.8, 128.8, 128.5, 127.0, 118.8, 73.8, 68.3, 61.8, 61.3, 44.2, 39.0, 38.8, 35.6, 27.3, 26.4, 26.3, 26.2, 23.2, 20.6, 18.7, 18.4, 16.5, 15.4, –3.2, –4.7, –5.1, –5.2; HRMS (ESI–TOF) calcd for C₄₀H₇₀O₆S₂Si₂Na [M + Na]⁺ 759.4486, found 759.4490.

Alcohol 43. To a solution of pivalate 42 (1.14 g, 1.55 mmol) in CH₂Cl₂ (16 mL) was added DIBAL-H (1.02 M in hexane, 4.6 mL, 4.69 mmol) at –78 °C. The mixture was stirred at the
same temperature for 20 min. The reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and short column chromatography (hexane/EtOAc = 3:1) gave the corresponding alcohol (949 mg), which was used for the next step without further purification.

To a solution of lithium wire (1.01 g, 145 mmol) in liquid NH₃ (60 mL) was added sulfone 42 (949 mg, 1.45 mmol) in THF/t-BuOH (20 mL/10 mL) and THF (3.0 mL + 2.0 mL for rinse) at −78 °C. The mixture was stirred at the same temperature for 20 min. The reaction was quenched with a 1:1 solution of saturated aqueous NH₄Cl and MeOH. The mixture was diluted with EtOAc, warmed up to room temperature, and stirred at the same temperature. The mixture was washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 7:1, 3:1) gave alcohol 43 (508 mg) and sulfone 42 (201 mg).

To a solution of lithium wire (214 mg, 30.8 mmol) in liquid NH₃ (30 mL) was added sulfone 42 recovered above (201 mg) in THF/t-BuOH (4.2 mL/2.1 mL) and THF (1.0 mL + 1.0 mL for rinse) at −78 °C. The mixture was stirred at the same temperature for 20 min. The reaction was quenched with a 1:1 solution of saturated aqueous NH₄Cl and MeOH. The mixture was diluted with EtOAc, warmed up to room temperature, and stirred at the same temperature. The mixture was washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 7:1) gave alcohol 43 (117 mg, totally 625 mg, 79% in two steps): colorless oil; Rf = 0.41 (hexane/EtOAc = 4:1); [α]D²⁴ = −3.9 (c 1.07, CHCl₃); IR (neat) 3324, 2955, 2727, 2856 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.42 (td, J = 6.8, 1.2 Hz, 1 H), 5.11 (t, J = 6.2 Hz, 1 H), 4.16 (d, J = 6.8 Hz, 2 H), 3.79–3.76 (m, 1 H), 3.60–3.50 (m, 2 H), 2.14–2.02 (m, 5 H), 1.92–1.85 (m, 2 H), 1.69 (s, 3 H), 1.61 (s, 3 H), 1.48–1.29 (m, 4 H), 0.90–0.88 (m, 6 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 139.8, 135.9, 123.6, 123.3, 74.8, 65.8, 59.4, 46.1, 39.7, 39.1, 27.1, 26.4, 26.1, 26.1, 24.3, 22.6, 19.4, 18.4, 18.3, 16.4, 16.1, −3.9, −4.7, −5.2, −5.3; HRMS (ESI–TOF) calcd for C₂₉H₆₀O₃Si₂Na [M + Na]⁺ 535.3979, found 535.3976.

**Alcohol 44.** To a solution of alcohol 43 (701 mg, 1.37 mmol) in CH₂Cl₂ (14 mL) were added pyridine (0.17 mL, 2.06 mmol) and PivCl (0.20 mL, 1.64 mmol) at room temperature. The mixture was stirred at the same temperature for 5 h. The reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 60:1) gave the corresponding pivalate (770 mg), which was used for the next step without further purification.

To a solution of the bis-TBS ether obtained above (770 mg) in MeOH (6.5 mL) and CH₂Cl₂ (6.5 mL) was added CSA (89.9 mg, 0.387 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 15:1) gave alcohol 44 (317 mg) and the bis-TBS ether...
To a solution of the bis-TBS ether recovered above (309 mg) in MeOH (2.6 mL) and CH$_2$Cl$_2$ (2.6 mL) was added CSA (36.0 mg, 0.155 mmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et$_3$N. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 15:1) gave alcohol 44 (135 mg) and the bis-TBS ether (112 mg).

To a solution of the bis-TBS ether recovered above (112 mg) in MeOH (1.0 mL) and CH$_2$Cl$_2$ (1.0 mL) was added CSA (13.1 mg, 56.4 μmol) at 0 °C. The mixture was stirred at the same temperature for 1 h. The reaction was quenched with Et$_3$N. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 15:1) gave alcohol 44 (50.8 mg, totally 503 mg, 76% in two steps): colorless oil; $R_f$ = 0.39 (hexane/EtOAc = 7:1); [α]$_D^{24}$ +5.9 (c 1.05, CHCl$_3$); IR (neat) 3501, 2956, 2927, 2852, 1730 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) δ 5.32 (td, $J$ = 6.8, 1.2 Hz, 1 H), 5.11–5.08 (m, 1 H), 4.57 (d, $J$ = 6.8 Hz, 2 H), 3.81–3.77 (m, 1 H), 3.58–3.56 (m, 2 H), 2.11–1.94 (m, 6 H), 1.86–1.78 (m, 1 H), 1.70 (s, 3 H), 1.63 (brs, 1 H), 1.60 (s, 3 H), 1.43–1.25 (m, 3 H), 1.20 (s, 9 H), 0.92 (s, 9 H), 0.91 (d, $J$ = 6.0 Hz, 3 H), 0.89 (d, $J$ = 6.8 Hz, 3 H), 0.11 (s, 3 H), 0.10 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ 178.4, 141.6, 135.8, 123.6, 118.7, 74.6, 64.3, 61.4, 47.2, 39.7, 39.6, 38.8, 27.9, 27.3, 26.4, 26.0, 24.7, 21.7, 19.4, 18.2, 16.6, 16.1, –4.2, –4.3; HRMS (ESI–TOF) calcd for C$_{28}$H$_{54}$O$_4$SiNa [M + Na]$^+$ 505.3689, found 505.3694.

**Alcohol 45.** To a solution of alcohol 44 (250 mg, 0.518 mmol) in CH$_2$Cl$_2$ (5.2 mL) were added PhI(OAc)$_2$ (250 mg, 0.777 mmol) and TEMPO (16.3 mg, 0.104 mmol) at room temperature. The mixture was stirred at the same temperature for 22 h. The reaction was quenched with saturated aqueous Na$_2$S$_2$O$_3$. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO$_3$, H$_2$O, and brine, and then dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 30:1) gave the corresponding aldehyde (212 mg), which was used for the next step without further purification.

To a suspension of Ph$_3$P$^+CH_3Br^-$ (393 mg, 1.10 mmol) in THF (3.0 mL) was added NaHMDS (1.0 M in THF, 1.06 mL, 1.06 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. To the mixture was added the aldehyde obtained above (212 mg) in THF (1.0 mL + 0.2 mL + 0.2 mL) at 0 °C. The mixture was stirred at room temperature for 1 h. The reaction was quenched with saturated aqueous NH$_4$Cl. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 60:1) gave the corresponding alkene (199 mg), which was used for the next step without further purification.

To a solution of the pivalate obtained above (199 mg) in CH$_2$Cl$_2$ (4.1 mL) was added DIBAL-H (1.02 M in hexane, 1.2 mL, 1.24 mmol) at –78 °C. The mixture was stirred at the same temperature for 20 min. The reaction was quenched with MeOH. The mixture was
filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 7:1) gave alcohol 45 (152 mg, 74% in three steps): colorless oil; $R_f = 0.36$ (hexane/EtOAc = 4:1); $[\alpha]_D^{24} +7.0$ (c 1.08, CHCl$_3$); IR (neat) 3324, 2955, 2927, 2856 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.81 (ddd, $J = 17.2$, 10.4, 6.4 Hz, 1 H), 5.42 (td, $J = 6.9$, 1.1 Hz, 1 H), 5.15 (dt, $J = 17.2$, 1.4 Hz, 1 H), 5.09–5.06 (m, 2 H), 4.16–4.12 (m, 3 H), 2.14–2.01 (m, 5 H), 1.95–1.85 (m, 2 H), 1.69 (s, 3 H), 1.59 (s, 3 H), 1.43–1.35 (m, 2 H), 1.30–1.17 (m, 2 H), 0.90 (d, $J = 6.0$ Hz, 3 H), 0.90 (s, 9 H), 0.88 (d, $J = 6.8$ Hz, 3 H), 0.05 (s, 3 H), 0.02 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 140.7, 139.8, 136.0, 136.0, 123.6, 123.3, 114.5, 75.5, 59.4, 49.9, 39.6, 27.7, 26.4, 26.0, 24.5, 21.9, 19.0, 18.3, 16.4, 16.0, –4.0, –4.8; HRMS (ESI–TOF) calcd for C$_{24}$H$_{46}$O$_2$SiNa [M + Na]$^+$ 417.3165, found 417.3166.

**Alcohol 47.** To a solution of alcohol 45 (127 mg, 0.322 mmol) in CH$_2$Cl$_2$ (3.2 mL) were added PhI(OAc)$_2$ (156 mg, 0.483 mmol) and TEMPO (10.1 mg, 64.4 μmol) at room temperature. The mixture was stirred at the same temperature for 5 h. The reaction was quenched with saturated aqueous Na$_2$S$_2$O$_3$. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO$_3$, H$_2$O, and brine, and then dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 20:1) gave the corresponding aldehyde (121 mg), which was used for the next step without further purification.

A mixture of the aldehyde obtained above (121 mg) and chiral allylic boronate 35 (136 mg, 0.370 mmol) in toluene (0.2 mL) was stirred at room temperature for 2 days. After the reaction was quenched with H$_2$O, the mixture was diluted with EtOAc and dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 8:1) gave alcohol 46 (231 mg, dr = 17:1), which was used for the next step without further purification.

To a solution of alcohol 46 obtained above (231 mg) in CH$_2$Cl$_2$ (3.1 mL) were added i-Pr$_2$NEt (0.95 mL, 5.54 mmol), MOMCl (0.35 mL, 4.62 mmol), and TBAI (56.9 mg, 0.154 mmol) at room temperature. The mixture was stirred at the same temperature for 2 h. The reaction was quenched with saturated aqueous NH$_4$Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NH$_4$Cl, saturated aqueous NaHCO$_3$, H$_2$O, and brine, and then dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 15:1) gave the corresponding MOM ether (210 mg), which was used for the next step without further purification.

To a solution of the TBS ether obtained above (210 mg) in THF (3.1 mL) was added TBAF (1.0 M in THF, 1.5 mL, 1.50 mmol) at room temperature. The mixture was stirred at 60 °C for 5 h. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 5:1) gave alcohol 47 (107 mg, 76% in four steps): colorless oil; $R_f = 0.31$ (hexane/EtOAc = 4:1); $[\alpha]_D^{21} +53.2$ (c 1.06, CHCl$_3$); IR (neat) 3481, 2954, 2932, 1716 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 6.20 (d, $J = 1.6$ Hz, 1 H), 5.90 (ddd, $J = 17.1$, 10.5, 6.4 Hz, 1 H), 5.60 (s, 1 H), 5.25 (d, $J = 17.1$ Hz, 1 H), 5.16 (d, $J = 10.5$ Hz, 1 H), 5.07 (t, $J = 6.5$ Hz, 1 H), 5.01 (d, $J = 9.0$ Hz, 1 H), 4.64 (d, $J = 6.4$ Hz, 1 H), 4.58–4.53 (m, 1 H), 4.45 (d, $J = 6.4$ Hz, 1 H), 4.22 (q, $J = 7.1$ Hz, 2 H), 4.12 (t,
J = 6.4 Hz, 1 H), 3.31 (s, 3 H), 2.60 (dd, J = 13.8, 7.9 Hz, 1 H), 2.47 (dd, J = 13.8, 5.7 Hz, 1 H), 2.10–1.91 (m, 7 H), 1.66 (d, J = 1.0 Hz, 3 H), 1.59 (s, 3 H), 1.54 (brs, 1 H), 1.37–1.26 (m, 3 H), 1.31 (t, J = 7.1 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.91 (d, J = 6.8 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 167.0, 140.4, 137.2, 135.6, 127.1, 124.5, 123.9, 115.3, 93.2, 74.9, 70.4, 60.6, 55.2, 48.8, 39.6, 39.4, 38.6, 27.8, 26.4, 24.6, 21.2, 18.9, 16.7, 16.1, 14.3; HRMS (ESI–TOF) calcd for C26H44O5Na [M + Na]+ 459.3087, found 459.3083.

Lactone 48. To a solution of ester 47 (38.8 mg, 88.9 μmol) in THF (0.6 mL), MeOH (0.2 mL), and H2O (0.2 mL) was added LiOH·H2O (7.5 mg, 0.178 mmol) at room temperature. The mixture was stirred at the same temperature for 41 h. The mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc and washed with H2O and brine. The aqueous phase was extracted with EtOAc three times and the combined organic phase was dried over Na2SO4. Concentration and short column chromatography (CH2Cl2/MeOH = 20:1) gave the corresponding carboxylic acid (39.9 mg), which was used for the next step without further purification.

To a solution of MNBA (73.3 mg, 0.213 mmol) and DMAP (52.2 mg, 0.427 mmol) in CH2Cl2 (34 mL) was slowly added the hydroxycarboxylic acid obtained above (39.9 mg) in CH2Cl2 (6.4 mL at 0.4 mL/h + 2.0 mL at 2.0 mL/h + 2.0 mL at 2.0 mL/h) at 40 °C with a syringe pump for 18 h. The mixture was stirred at the same temperature for further 33 h. The reaction was quenched with saturated aqueous NH4Cl. The mixture was concentrated, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 30:1) gave lactone 48 (22.8 mg, 66% in two steps): colorless oil; Rf = 0.44 (hexane/EtOAc = 7:1); [α]D21 +134 (c 1.03, CHCl3); IR (neat) 2954, 2929, 1714 cm–1; 1H NMR (400 MHz, CDCl3) δ 6.22 (d, J = 1.2 Hz, 1 H), 5.93–5.85 (m, 1 H), 5.73 (s, 1 H), 5.71–5.69 (m, 1 H), 5.27–5.18 (m, 2 H), 4.96–4.91 (m, 2 H), 4.87–4.81 (m, 1 H), 4.68 (d, J = 6.4 Hz, 1 H), 4.54 (d, J = 6.4 Hz, 1 H), 3.39 (s, 3 H), 3.04 (dd, J = 13.2, 5.2 Hz, 1 H), 2.35 (dd, J = 13.2, 8.9 Hz, 1 H), 1.76–1.68 (m, 1 H), 1.58 (s, 1 H), 1.54 (s, 3 H), 1.51–1.38 (m, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.92 (d, J = 7.1 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 165.2, 140.7, 137.4, 134.6, 127.3, 125.1, 124.2, 116.3, 93.3, 76.0, 69.3, 55.3, 45.1, 38.5, 38.4, 36.9, 29.9, 24.3, 23.8, 21.6, 20.0, 15.9, 15.8; HRMS (ESI–TOF) calcd for C24H38O4Na [M + Na]+ 413.2668, found 413.2673.

Butenolide S11. To a solution of tetraene 48 (4.0 mg, 10.2 μmol) in toluene (2.0 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (0.6 mg, 1.02 μmol) at room temperature. The mixture was stirred at 100 °C for 2 days. The mixture was filtered through short column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 6:1) gave butenolide S11 (2.8 mg, 76%): colorless solid; Rf = 0.22 (hexane/EtOAc = 4:1); [α]D22 +212 (c 0.49, CHCl3); IR (neat) 2959, 2928, 2845, 1747 cm–1; 1H NMR (400 MHz, CDCl3) δ 7.21 (s, 1 H), 4.98–4.91 (m, 2 H), 4.69 (d, J = 6.4 Hz, 1 H), 4.69–4.64 (m, 2 H), 4.56 (d, J = 6.4 Hz, 1 H), 3.40 (s, 3 H), 2.83 (d, J = 12.8 Hz, 1 H), 2.40 (dd, J = 12.8, 11.1 Hz, 1 H), 2.18–2.10 (m, 6 H), 1.71–1.50 (m, 2 H), 1.54 (s, 3 H), 1.50
(s, 3 H), 1.31–1.21 (m, 2 H), 0.94 (d, J = 5.9 Hz, 3 H), 0.92 (d, J = 6.3 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 173.0, 151.6, 141.1, 133.0, 129.0, 125.6, 124.9, 93.4, 83.6, 69.4, 55.4, 44.9, 38.7, 37.0, 32.5, 28.8, 23.8, 22.8, 20.1, 17.7, 16.1, 16.0; HRMS (ESI–TOF) calcd for C22H34O4Na [M + Na]+ 385.2355, found 385.2353.

**Sarcophytonolide F (3).** To a solution of MOM ether S11 (5.0 mg, 13.8 μmol) in CH2Cl2 (1.0 mL) were added HMDS (58 μL, 0.276 mmol) and TMSI (20 μL, 0.138 mmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. The reaction was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 2:1) gave sarcophytonolide F (3) (3.3 mg, 75%): colorless solid; Rf = 0.28 (hexane/EtOAc = 1:1); [α]D23 +145 (c 0.54, CHCl3); literature 10b [α]D20 +115 (c 0.54, CHCl3); IR (neat) 3438, 2936, 2883, 1727 cm–1; 1H and 13C NMR Table S4; HRMS (ESI–TOF) calcd for C20H30O3Na [M + Na]+ 341.2093, found 341.2092.

**Synthesis of Sarcophytonolide G (4) by Mitsunobu Reaction.** To a mixture of sarcophytonolide F (3) (1.6 mg, 5.02 μmol), Ph3P (5.2 mg, 20.1 μmol), and p-nitrobenzoic acid (3.4 mg, 20.1 μmol) in THF (1.0 mL) was added DEAD (40% solution in toluene, 9.1 μL, 20.1 μmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 6:1, 2:1) gave the diastereomeric mixture of the corresponding benzoates (2.0 mg), which was used for the next step without further purification.

To a solution of the mixture of benzoates obtained above (2.0 mg) in MeOH (0.5 mL) was added Na2CO3 (0.6 mg, 6.02 μmol) at 0 °C. The mixture was stirred at the same temperature for 20 min. To the mixture was added Na2CO3 (0.6 mg, 6.02 μmol) at 0 °C. The mixture was stirred at the same temperature for 10 min. After the mixture was stirred at room temperature for 1 h, the mixture was filtered through short column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 3:2) gave sarcophytonolide G (4) (0.5 mg, 31% in two steps) and sarcophytonolide F (3) (0.2 mg, 13% in two steps). Sarcophytonolide G (4): colorless solid; Rf = 0.41 (hexane/EtOAc = 1:1); [α]D21 +18.1 (c 0.12, CHCl3); literature10b,61 [α]D20 −1.6 (c 0.17, CHCl3); IR (neat) 3420, 2958, 2923, 2851, 1736 cm–1; 1H and 13C NMR Table S5; HRMS (ESI–TOF) calcd for C20H30O3Na [M + Na]+ 341.2093, found 341.2096.

**Ketone 49.** To a solution sarcophytonolide F (3) (4.3 mg, 13.5 μmol) in CH2Cl2 (1.0 mL) was added Dess–Martin periodinane (17.2 mg, 40.5 μmol) at room temperature. After the mixture was stirred at 40 °C for 10 h, to the mixture were added CH2Cl2 (0.5 mL) and Dess–Martin periodinane (5.7 mg, 13.5 μmol) at the same temperature. After the mixture was stirred at the same temperature for 13 h, the mixture was filtered through short column chromatography (hexane/EtOAc = 1:1). Concentration and column chromatography
(hexane/EtOAc = 7:2) gave ketone 49 (4.1 mg, 96%): colorless oil; $R_f = 0.49$ (hexane/EtOAc = 2:1); $[\alpha]_D^{23} = -8.1$ (c 0.21, CHCl$_3$); IR (neat) 2958, 2922, 1758, 1686, 1617 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.17 (s, 1 H), 6.05 (s, 1 H), 5.04 (dd, $J = 6.1, 1.2$ Hz, 1 H), 4.91–4.88 (m, 1 H), 3.58 (d, $J = 14.1$ Hz, 1 H), 3.13 (d, $J = 14.1$ Hz, 1 H), 2.33–2.26 (m, 2 H), 2.19–2.12 (m, 2 H), 2.09 (s, 3 H), 2.03–1.96 (m, 2 H), 1.84–1.76 (m, 1 H), 1.66–1.61 (m, 2 H), 1.54 (s, 3 H), 1.44–1.35 (m, 1 H), 1.02 (d, $J = 6.8$ Hz, 3 H), 1.01 (d, $J = 6.8$ Hz, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 194.8, 160.8, 150.3, 135.9, 129.3, 124.9, 123.9, 123.2, 83.8, 47.0, 41.7, 41.1, 39.3, 30.0, 26.9, 24.3, 20.4, 20.2, 18.7, 16.2; HRMS (ESI–TOF) calcd for C$_{20}$H$_{28}$O$_3$Na [M + Na]$^+$ 339.1936, found 339.1935.

**Synthesis of Sarcophytonolide G (4) by Stereoselective Reduction.** To a solution of ketone 49 (2.9 mg, 9.16 $\mu$mol) in MeOH (0.6 mL) and CH$_2$Cl$_2$ (0.4 mL) were added CeCl$_3$ (6.8 mg, 27.5 $\mu$mol) and NaBH$_4$ (0.5 mg, 13.7 $\mu$mol) at –78 °C. After the mixture was stirred at the same temperature for 2 h, the mixture was diluted with Et$_2$O. The reaction was quenched with 1 M aqueous NaHSO$_4$. The mixture was warmed up to room temperature, and stirred at the same temperature for 20 min. The mixture was washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 3:2) gave sarcophytonolide G (4) (2.1 mg, 72%).

**Alcohol S12.** To a solution of diol 16 (3.95 g, 15.0 mmol) in CH$_2$Cl$_2$ (150 mL) were added pyridine (2.4 mL, 29.3 mmol) and AcCl (1.8 mL, 24.8 mmol) at –20 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous NH$_4$Cl. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration gave the corresponding acetate (4.61 g), which was used for the next step without further purification.

To a solution of the alcohol obtained above (4.61 g) in CH$_2$Cl$_2$ (150 mL) were added 2,6-lutidine (2.7 mL, 22.8 mmol) and TBSOTf (4.2 mL, 18.2 mmol) at 0 °C. After the mixture was stirred at the same temperature for 30 min, the mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration gave the corresponding TBS ether (5.44 g), which was used for the next step without further purification.

To a solution of the acetate obtained above (5.44 g) in CH$_2$Cl$_2$ (130 mL) was added DIBAL-H (1.02 M in hexane, 31.0 mL, 31.6 mmol) at –78 °C. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 20:1) gave alcohol S12 (4.79 g, 85% in three steps): colorless oil; $R_f = 0.33$ (hexane/EtOAc = 10:1); $[\alpha]_D^{25} = +2.0$ (c 0.96, CHCl$_3$); IR (neat) 3436, 2955, 2858 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.49–7.45 (m, 1 H), 3.83 (brd, $J = 2.3$ Hz, 1 H), 3.73–3.71 (m, 2 H), 3.64–3.59 (m, 2 H), 1.79–1.70 (m, 1 H), 1.52–1.48 (m, 1 H), 0.97 (d, $J = 6.8$ Hz, 3 H), 0.92 (d, $J = 5.9$ Hz, 3 H), 0.91 (s, 9 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H), 0.09 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 74.0, 64.9, 60.4, 51.6, 26.1,

Aldehyde 52. To a solution of alcohol S12 (643 mg, 1.71 mmol) in CH2Cl2 (17 mL) were added PhI(OAc)2 (1.05 g, 3.26 mmol) and TEMPO (79.7 mg, 0.510 mmol) at room temperature. After the mixture was stirred at the same temperature for 10 h, the reaction was quenched with saturated aqueous Na2S2O3. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 50:1) gave aldehyde 52 (620 mg, 97%): colorless oil; Rf = 0.48 (hexane/EtOAc = 20:1); [α]D26 = +0.4 (c 1.34, CHCl3); IR (neat) 2956, 2927, 2856, 1723 cm–1; 1H NMR (400 MHz, CDCl3) δ 9.77 (d, J = 3.4 Hz, 1 H), 4.17–4.10 (m, 1 H), 3.65 (dd, J = 10.2, 4.9 Hz, 1 H), 3.56 (dd, J = 10.2, 5.6 Hz, 1 H), 2.30–2.17 (m, 2 H), 1.03 (d, J = 6.6 Hz, 3 H), 0.99 (d, J = 6.8 Hz, 3 H), 0.89 (s, 9 H), 0.88 (s, 9 H), 0.09 (s, 3 H), 0.09 (s, 3 H), 0.04 (s, 3 H), 0.04 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 204.3, 71.9, 65.9, 62.2, 26.0, 25.9, 25.7, 21.6, 19.7, 18.4, 18.1, –4.1, –4.9, –5.4; HRMS (ESI–TOF) calcd for C19H42O3Si2Na [M + Na]+ 397.2570, found 397.2574.

Alcohols 53a and 53b. To a solution of aldehyde 52 (176 mg, 0.468 mmol) and allylic bromide 41 (178 mg, 0.562 mmol) in THF (4.7 mL) was slowly added SmI2 (0.1 M in THF, 14.1 mL, 1.41 mmol) at 0 °C for 10 min. After the mixture was stirred at the same temperature for 1 h, to the mixture was added SmI2 (0.1 M in THF, 7.0 mL, 0.700 mmol) at 0 °C for 5 min. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with saturated aqueous Na2S2O3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 30:1) gave alcohols 53a (154 mg, 53%) and 53b (115 mg, 40%). Alcohol 53a: colorless oil; Rf = 0.43 (hexane/EtOAc = 10:1); [α]D21 = +1.5 (c 1.27, CHCl3); IR (neat) 3547, 2956, 2930, 2857, 1731 cm–1; 1H NMR (400 MHz, CDCl3) δ 5.35–5.23 (m, 1 H), 5.22–5.16 (m, 1 H), 4.57 (d, J = 6.8 Hz, 2 H), 4.10–4.03 (m, 1 H), 3.98–3.92 (m, 1 H), 3.68–3.62 (m, 2 H), 2.48 (brs, 1 H), 2.27–2.03 (m, 6 H), 2.03–1.93 (m, 1 H), 1.70 (s, 3 H), 1.65 (s, 3 H), 1.47–1.41 (m, 1 H), 1.20 (s, 9 H), 1.05 (d, J = 6.8 Hz, 3 H), 1.01 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 178.4, 141.4, 133.4, 126.9, 118.8, 73.5, 67.3, 66.3, 61.3, 53.2, 46.6, 39.5, 38.8, 27.3, 26.4, 26.1, 26.0, 25.9, 22.7, 22.5, 18.5, 18.2, 16.5, 16.1, –3.9, –4.7, –5.3; HRMS (ESI–TOF) calcd for C34H68O5Si2Na [M + Na]+ 635.4503, found 635.4504. Alcohol 53b: colorless oil; Rf = 0.44 (hexane/EtOAc = 10:1); [α]D24 = +1.3 (c 0.75, CHCl3); IR (neat) 3448, 2954, 2929, 2856, 1730 cm–1; 1H NMR (400 MHz, CDCl3) δ 5.36–5.29 (m, 1 H), 5.21–5.14 (m, 1 H), 4.57 (d, J = 7.1 Hz, 2 H), 4.16–4.10 (m, 1 H), 3.95–3.88 (m, 1 H), 3.74–3.65 (m, 2 H), 3.07 (d, J = 4.6 Hz, 1 H), 2.36–1.94 (m, 7 H), 1.70 (s, 3 H), 1.67 (s, 3 H), 1.49–1.44 (m, 1 H), 1.20 (s, 9 H), 1.05 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.11 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 178.4, 141.5, 133.2, 126.6, 118.8, 74.3, 68.7, 66.1, 61.3,

**MOM Ether S15.** To a mixture of alcohol 53a (104 mg, 0.167 mmol) and TBAI (19.9 mg, 53.9 μmol) in CH₂Cl₂ (0.5 mL) were added i-Pr₂NEt (0.17 mL, 1.00 mmol) and MOMCl (60 μL, 0.835 mmol) at room temperature. After the mixture was stirred at reflux for 24 h, to the mixture were added i-Pr₂NEt (0.17 mL, 1.00 mmol) and MOMCl (60 μL, 0.835 mmol) at room temperature. After the mixture was stirred at reflux for 4 h, the reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NH₄Cl, saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1) gave MOM ether S15 (107 mg, 97%): colorless oil; Rf = 0.46 (hexane/EtOAc = 10:1); [α]D²² –19.0 (c 1.44, CHCl₃); IR (neat) 2955, 2929, 2857, 1731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.35–5.29 (m, 1 H), 5.22–5.15 (m, 1 H), 4.62 (d, J = 6.8 Hz, 1 H), 4.57 (d, J = 7.1 Hz, 2 H), 4.46 (d, J = 6.8 Hz, 1 H), 4.07–4.01 (m, 1 H), 3.96–3.89 (m, 1 H), 3.63 (dd, J = 10.0, 5.0 Hz, 1 H), 3.55 (dd, J = 10.0, 6.8 Hz, 1 H), 3.31 (s, 3 H), 2.27–2.01 (m, 6 H), 1.99–1.94 (m, 1 H), 1.70 (s, 3 H), 1.66 (s, 3 H), 1.68–1.51 (m, 1 H), 1.20 (s, 9 H), 1.02 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.88 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H), 0.05 (s, 3H), 0.04 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 141.5, 133.1, 126.1, 118.7, 95.1, 74.9, 72.5, 68.0, 61.3, 55.5, 49.3, 42.7, 39.4, 38.8, 27.3, 26.6, 26.2, 26.1, 25.6, 22.9, 22.0, 18.6, 18.3, 16.6, 16.2, –3.4, –4.6, –5.2, –5.2; HRMS (ESI–TOF) calcd for C₃₆H₇₂O₆Si₂Na [M + Na]+ 679.4765, found 679.4769.

**Alcohol S16.** To a solution of bis-TBS ether S15 (326 mg, 0.500 mmol) in MeOH (2.5 mL) and CH₂Cl₂ (2.5 mL) was added CSA (34.0 mg, 0.146 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 7:1) gave alcohol S16 (113 mg) and bis-TBS ether S15 (176 mg).

To a solution of bis-TBS ether S15 recovered above (176 mg) in MeOH (1.4 mL) and CH₂Cl₂ (1.4 mL) was added CSA (18.4 mg, 80.7 μmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 7:1) gave alcohol S16 (63.3 mg) and bis-TBS ether S15 (90.1 mg).

To a solution of bis-TBS ether S15 recovered above (176 mg) in MeOH (0.7 mL) and CH₂Cl₂ (0.7 mL) was added CSA (9.2 mg, 39.6 μmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 7:1) gave alcohol S16 (31.7 mg, totally 208 mg, 77%) and bis-TBS ether S15 (46.5 mg). Alcohol S16: colorless oil; Rf = 0.33 (hexane/EtOAc = 4:1); [α]D²² –14.1 (c 0.53, CHCl₃); IR (neat) 3501, 2956, 2930, 2857, 1729
cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.35–5.28 (m, 1 H), 5.21–5.14 (m, 1 H), 4.62 (d, $J = 6.8$ Hz, 1 H), 4.57 (d, $J = 7.1$ Hz, 2 H), 4.54 (d, $J = 6.8$ Hz, 1 H), 4.00–3.91 (m, 2 H), 3.69 (dd, $J = 11.5$, 5.4 Hz, 1 H), 3.61 (dd, $J = 11.5$, 4.6 Hz, 1 H), 3.33 (s, 3 H), 2.32–2.17 (m, 2 H), 2.17–2.00 (m, 5 H), 1.70 (s, 3 H), 1.66 (s, 3 H), 1.67–1.61 (m, 1 H), 1.20 (s, 9 H), 1.04 (d, $J = 6.8$ Hz, 3 H), 0.96 (d, $J = 6.8$ Hz, 3 H), 0.90 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 178.4, 141.4, 132.7, 126.6, 118.8, 95.9, 75.1, 71.9, 66.4, 61.3, 55.7, 50.4, 43.3, 38.8, 27.3, 26.5, 26.0, 25.6, 22.4, 21.6, 18.3, 16.5, 16.2, –3.9, –4.3; HRMS (ESI–TOF) calcd for C$_{30}$H$_{58}$O$_6$SiNa [M + Na]$^+$ 565.3900, found 565.3901.

**Alkene 54.** To a solution of alcohol S16 (97.5 mg, 0.180 mmol) in CH$_2$Cl$_2$ (1.8 mL) were added PhI(OAc)$_2$ (86.6 mg, 0.269 mmol) and TEMPO (5.6 mg, 35.8 μmol) at room temperature. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous Na$_2$S$_2$O$_3$. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO$_3$, H$_2$O, and brine, and then dried over Na$_2$SO$_4$. Concentration and short column chromatography (hexane/EtOAc = 30:1) gave the corresponding aldehyde (91.0 mg), which was used for the next step without further purification.

To a suspension of Ph$_3$P$^+CH_3Br^-$ (147 mg, 0.412 mmol) in THF (1.1 mL) was added NaHMDS (1.0 M in THF, 0.40 mL, 0.400 mmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, to the mixture was added the aldehyde obtained above (91.0 mg) in THF (0.2 mL + 0.2 mL + 0.2 mL) at 0 °C. After the mixture was stirred at room temperature for 1 h, the reaction was quenched with saturated aqueous NH$_4$Cl. The mixture was diluted with EtOAc, washed with H$_2$O and brine, and then dried over Na$_2$SO$_4$. Concentration and column chromatography (hexane/EtOAc = 30:1) gave alkene 54 (83.1 mg, 86% in two steps): colorless oil; $R_f$ = 0.31 (hexane/EtOAc = 30:1); $[\alpha]_{D}^{22}$ –8.0 (c 0.87, CHCl$_3$); IR (neat) 2956, 2930, 2857, 1730 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.93 (ddd, $J = 17.2$, 10.4, 6.8 Hz, 1 H), 5.36–5.29 (m, 1 H), 5.20–5.11 (m, 2 H), 5.04 (d, $J = 10.4$ Hz, 1 H), 4.58–4.56 (m, 3 H), 4.49 (d, $J = 6.6$ Hz, 1 H), 4.45–4.42 (m, 1 H), 3.87 (td, $J = 6.8$, 3.0 Hz, 1 H), 3.32 (s, 3 H), 2.26 (d, $J = 6.8$ Hz, 2 H), 2.15–1.95 (m, 5 H), 1.70 (s, 3 H), 1.63 (s, 3 H), 1.48–1.43 (m, 1 H), 1.20 (d, $J = 6.7$ Hz, 3 H), 1.04 (d, $J = 6.7$ Hz, 3 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.03 (s, 3 H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 178.4, 141.9, 141.5, 133.0, 126.3, 118.7, 114.1, 96.1, 75.6, 73.0, 61.3, 55.6, 53.7, 44.1, 39.4, 38.8, 27.3, 26.5, 26.1, 25.8, 22.9, 21.8, 18.3, 16.6, 16.2, –3.6, –4.6; HRMS (ESI–TOF) calcd for C$_{31}$H$_{58}$O$_5$SiNa [M + Na]$^+$ 561.3951, found 561.3951.

**Alcohol 55.** To a solution of pivalate 54 (145 mg, 0.268 mmol) in CH$_2$Cl$_2$ (2.7 mL) was added DIBAL-H (1.02 M in hexane, 0.79 mL, 0.806 mmol) at –78 °C. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 4:1) gave alcohol 55 (120 mg, 98%): colorless oil; $R_f$ = 0.27 (hexane/EtOAc = 4:1); $[\alpha]_{D}^{21}$ –8.4 (c 0.97, CHCl$_3$); IR (neat) 3349, 2955, 2929, 2857 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 5.93 (ddd, $J = 17.2$, 10.4, 6.8 Hz, 1 H), 5.45–5.38 (m, 1
H), 5.20–5.10 (m, 2 H), 5.04 (d, J = 10.4 Hz, 1 H), 4.57 (d, J = 6.8 Hz, 1 H), 4.50 (d, J = 6.8 Hz, 1 H), 4.46–4.41 (m, 1 H), 4.15 (d, J = 6.8 Hz, 2 H), 3.90–3.83 (m, 1 H), 3.32 (s, 3 H), 2.26 (d, J = 6.8 Hz, 2 H), 2.17–1.95 (m, 5 H), 1.68 (s, 3 H), 1.63 (s, 3 H), 1.48–1.43 (m, 1 H), 1.04 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.04 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 141.9, 139.4, 133.0, 126.4, 123.5, 114.2, 96.0, 75.7, 73.0, 59.4, 55.6, 53.8, 44.0, 39.4, 26.4, 26.1, 25.8, 22.8, 21.8, 18.3, 16.3, –3.6, –4.6; HRMS (ESI–TOF) calcd for C26H50O4SiNa [M + Na]+ 477.3376, found 477.3373.

**Alcohol 56.** To a solution of alcohol 55 (114 mg, 0.252 mmol) in CH2Cl2 (2.5 mL) were added PhI(OAc)2 (121 mg, 0.377 mmol) and TEMPO (11.4 mg, 73.0 μmol) at room temperature. After the mixture was stirred at the same temperature for 4 h, the reaction was quenched with saturated aqueous Na2S2O3. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 10:1) gave the corresponding aldehyde (106 mg), which was used for the next step without further purification.

A mixture of the aldehyde obtained above (106 mg) and chiral allylic boronate 35 (104 mg, 0.281 mmol) in toluene (0.2 mL) was stirred at room temperature for 2 days. After the reaction was quenched with H2O, the mixture was diluted with EtOAc and dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 7:1) gave alcohol 56 (127 mg, 88% in two steps, dr = 13:1): colorless oil; Rf = 0.29 (hexane/EtOAc = 4:1); [α]D21 −10.5 (c 1.01, CHCl3); IR (neat) 3460, 2955, 2929, 2857, 1716 cm−1; 1H NMR (400 MHz, CDCl3) δ 6.24 (d, J = 1.4 Hz, 1 H), 5.94 (ddd, J = 17.2, 10.4, 6.8 Hz, 1 H), 5.64 (brs, 1 H), 5.22–5.10 (m, 3 H), 5.04 (d, J = 10.4 Hz, 1 H), 4.60–4.53 (m, 2 H), 4.50 (d, J = 6.6 Hz, 1 H), 4.46–4.41 (m, 1 H), 4.23 (q, J = 7.1 Hz, 2 H), 3.90–3.83 (m, 1 H), 3.32 (s, 3 H), 2.57–2.44 (m, 2 H), 2.26 (d, J = 5.8 Hz, 2 H), 2.15–1.95 (m, 5 H), 1.68 (d, J = 1.2 Hz, 3 H), 1.63 (s, 3 H), 1.48–1.42 (m, 1 H), 1.31 (t, J = 7.1 Hz, 3 H), 1.04 (d, J = 6.6 Hz, 3 H), 1.03 (d, J = 6.6 Hz, 3 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H); 13C NMR (100 MHz, CDCl3) δ 167.3, 142.0, 138.4, 137.2, 133.0, 127.5, 127.0, 126.4, 114.1, 96.0, 75.7, 72.9, 67.5, 60.9, 55.6, 53.9, 43.9, 40.7, 39.4, 26.5, 26.1, 25.8, 22.8, 21.8, 18.3, 16.7, 16.3, 14.3, –3.6, –4.5; HRMS (ESI–TOF) calcd for C32H58O6SiNa [M + Na]+ 589.3900, found 589.3897.

**Alcohol S19.** To a solution of alcohol 56 (120 mg, 0.211 mmol) in CH2Cl2 (2.1 mL) were added p-methoxybenzyl 2,2,2-trichloroacetimidate (97 μL, 0.528 mmol) and PPTS (26.4 mg, 0.106 mmol) at room temperature. After the mixture was stirred at reflux for 9 h, the reaction was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 10:1) gave the corresponding PMB ether (79.9 mg) and alcohol 56 (97.4 mg including impurity).

To a solution of alcohol 56 recovered above (97.4 mg including impurity) in CH2Cl2 (1.7 mL) were added p-methoxybenzyl 2,2,2-trichloroacetimidate (70 μL, 0.379 mmol) and PPTS (20.8 mg, 82.4 μmol) at room temperature. After the mixture was stirred at reflux for 13 h, the
reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1, 5:1) gave the corresponding PMB ether (42.2 mg) and alcohol 56 (82.7 mg including impurity).

To a solution of alcohol 56 recovered above (82.7 mg including impurity) in CH₂Cl₂ (1.4 mL) were added p-methoxybenzyl 2,2,2-trichloroacetimidate (63 μL, 0.365 mmol) and PPTS (18.0 mg, 71.3 μmol) at room temperature. After the mixture was stirred at reflux for 16 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1, 5:1) gave the corresponding PMB ether (27.6 mg) and alcohol 56 (80.2 mg including impurity). The combined PMB ether (150 mg) was used for the next step without further purification.

To a solution of the TBS ether obtained above (150 mg) in THF (1.5 mL) was added TBAF (1.0 M in THF, 0.45 mL, 0.450 mmol) at room temperature. After the mixture was stirred at reflux for 10 h, the mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 10:1, 5:1) gave alcohol S19 (73.7 mg, 61% in two steps): colorless oil; Rf = 0.22 (hexane/EtOAc = 4:1); [α]D²¹ +24.7 (c 0.87, CHCl₃); IR (neat) 3478, 2932, 1714 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.20 (d, J = 8.6 Hz, 2 H), 6.84 (d, J = 8.6 Hz, 2 H), 6.18 (d, J = 1.7 Hz, 1 H), 6.01 (ddd, J = 17.2, 10.4, 6.8 Hz, 1 H), 5.57 (brs, 1 H), 5.29 (d, J = 17.2 Hz, 1 H), 5.24–5.18 (m, 1 H), 5.15–5.07 (m, 2 H), 4.61 (d, J = 6.8 Hz, 1 H), 4.53 (d, J = 6.8 Hz, 1 H), 4.51–4.43 (m, 2 H), 4.31–4.21 (m, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 3.98–3.92 (m, 1 H), 3.79 (s, 3 H), 3.35 (s, 3 H), 2.63 (dd, J = 13.9, 7.6 Hz, 1 H), 2.48–2.31 (m, 3 H), 2.25–2.00 (m, 5 H), 1.96–1.86 (m, 1 H), 1.68–1.60 (m, 1 H), 1.64 (s, 3 H), 1.59 (s, 3 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 167.1, 158.9, 141.4, 139.5, 137.2, 132.4, 131.0, 129.1, 127.0, 125.6, 114.5, 113.6, 96.0, 77.4, 73.3, 72.9, 69.4, 60.5, 55.7, 55.3, 51.7, 42.8, 39.5, 38.6, 26.6, 26.0, 22.8, 21.6, 16.8, 16.1, 14.3; HRMS (ESI–TOF) calcd for C₃₄H₅₂O₇Na [M + Na]⁺ 595.3611, found 595.3608.

**Carboxylic Acid 58.** To a solution of ester S19 (68.2 mg, 0.119 mmol) in THF (0.7 mL), MeOH (0.2 mL), and H₂O (0.2 mL) was added LiOH·H₂O (7.5 mg, 0.179 mmol) at room temperature. After the mixture was stirred at 40 °C for 5 h, to the mixture was added LiOH·H₂O (7.5 mg, 0.179 mmol) at room temperature. After the mixture was stirred at 40 °C for 5 h, the mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc and washed with H₂O and brine. The aqueous phase was extracted with EtOAc three times and the combined organic phase was dried over Na₂SO₄. Concentration and column chromatography (CH₂Cl₂/MeOH = 30:1) gave carboxylic acid 58 (62.0 mg, 96%): colorless oil; Rf = 0.41 (hexane/EtOAc = 1:1); [α]D²⁵ +18.1 (c 0.27, CHCl₃); IR (neat) 3459, 2925, 1697 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.21 (d, J = 8.6 Hz, 2 H), 6.85 (d, J = 8.6 Hz, 2 H), 6.28 (d, J = 1.5 Hz, 1 H), 6.01 (ddd, J = 17.2, 10.4, 6.8 Hz, 1 H), 5.64 (brs, 1 H), 5.28 (dt, J =
17.2, 1.5 Hz, 1 H), 5.24–5.19 (m, 1 H), 5.14–5.11 (m, 2 H), 4.62 (d, J = 7.2 Hz, 1 H), 4.54–4.50 (m, 3 H), 4.30–4.26 (m, 2 H), 3.99–3.95 (m, 1 H), 3.79 (s, 3 H), 3.34 (s, 3 H), 2.63 (dd, J = 13.9, 7.3 Hz, 1 H), 2.51 (dd, J = 13.9, 5.8 Hz, 1 H), 2.41 (dd, J = 13.9, 9.0 Hz, 1 H), 2.25–2.04 (m, 5 H), 1.98–1.87 (m, 1 H), 1.68–1.63 (m, 1 H), 1.64 (s, 3 H), 1.61 (s, 3 H), 1.06 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.6 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 169.8, 159.1, 141.6, 140.0, 136.9, 132.4, 129.3, 128.9, 126.9, 125.1, 114.4, 113.7, 95.8, 77.2, 74.4, 72.6, 69.5, 55.7, 55.3, 51.9, 42.5, 39.4, 38.0, 26.2, 25.9, 22.7, 21.8, 16.8, 16.1; HRMS (ESI–TOF) calcd for C32H48O7Na [M + Na]+ 567.3298, found 567.3311.

**Lactone 59.** To a solution of MNBA (33.3 mg, 96.7 μmol) and DMAP (23.7 mg, 0.194 mmol) in CH2Cl2 (16 mL) was slowly added hydroxycarboxylic acid 58 (22.2 mg, 40.8 μmol) in CH2Cl2 (3.2 mL at 0.2 mL/h + 1.0 mL at 1.0 mL/h + 1.0 mL at 1.0 mL/h) at 40 °C with a syringe pump for 18 h. After the mixture was stirred at the same temperature for further 2 h, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 10:1) gave lactone 59 (14.7 mg, 68%): colorless oil; Rf = 0.30 (hexane/EtOAc = 7:1); [α]D23 +49.5 (c 1.00, CHCl3); IR (neat) 2928, 1714, 1613 cm–1; 1H NMR (400 MHz, CDCl3) δ 7.25 (d, J = 8.3 Hz, 2 H), 6.86 (d, J = 8.3 Hz, 2 H), 6.09 (s, 1 H), 6.00 (ddd, J = 17.2, 10.4, 6.8 Hz, 1 H), 5.79–5.71 (m, 1 H), 5.58 (s, 1 H), 5.22 (d, J = 17.2 Hz, 1 H), 5.13 (d, J = 10.4 Hz, 1 H), 5.06–4.92 (m, 2 H), 4.65 (s, 2 H), 4.65–4.58 (m, 1 H), 4.46 (d, J = 11.2 Hz, 1 H), 4.31 (d, J = 11.2 Hz, 1 H), 3.90–3.83 (m, 1 H), 3.80 (s, 3 H), 3.38 (s, 3 H), 3.05 (dd, J = 13.1, 5.1 Hz, 1 H), 2.44–1.98 (m, 8 H), 1.96–1.86 (m, 1 H), 1.62 (s, 3 H), 1.62 (s, 3 H), 1.11 (d, J = 6.8 Hz, 3 H), 1.06 (d, J = 6.8 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 165.1, 158.9, 141.3, 137.6, 134.8, 131.8, 131.2, 129.1, 127.0, 126.5, 115.5, 113.7, 96.6, 75.2, 73.4, 69.5, 55.9, 55.3, 51.1, 44.9, 38.9, 37.7, 26.2, 23.8, 21.9, 19.4, 17.0; HRMS (ESI–TOF) calcd for C32H46O6Na [M + Na]+ 549.3192, found 549.3190.

**Alcohol 60.** To a solution of tetraene 59 (34.2 mg, 64.9 μmol) in toluene (13 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (10.0 mg, 16.2 μmol) at room temperature. After the mixture was stirred at 100 °C for 2 days, the mixture was filtered through short column chromatography (hexane/EtOAc = 10:1). Concentration and column chromatography (hexane/EtOAc = 2:1, 7:1, 4:1) gave the corresponding butenolide (25.8 mg) and tetraene 59 (3.8 mg, 11% recovery). The butenolide (25.8 mg) was used for the next step without further purification.

To a solution of the MOM ether obtained above (25.8 mg) in i-PrOH (5.2 mL) was added concentrated aqueous HCl (0.1 mL) at room temperature. After the mixture was stirred at 50 °C for 10 h, the reaction was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 2:1) gave alcohol 60 (15.3 mg, 52% in two steps): colorless solid; Rf = 0.35 (hexane/EtOAc = 1:1); [α]D23 +88.2 (c 0.58, CHCl3); IR
(neat) 3547, 2922, 2842, 1742, 1613 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.29 (s, 1 H), 7.26 (d, \(J = 8.8\) Hz, 2 H), 6.87 (d, \(J = 8.8\) Hz, 2 H), 5.17 (d, \(J = 8.5\) Hz, 1 H), 5.04 (d, \(J = 8.6\) Hz, 1 H), 4.89–4.81 (m, 1 H), 4.50–4.38 (m, 3 H), 3.80 (s, 3 H), 3.81–3.77 (m, 1 H), 2.86 (d, \(J = 13.2\) Hz, 1 H), 2.46 (dd, \(J = 12.9, 9.8\) Hz, 1 H), 2.31–1.98 (m, 7 H), 1.62 (s, 3 H), 1.46 (s, 3 H), 1.46–1.41 (m, 1 H), 1.16 (d, \(J = 6.8\) Hz, 3 H), 1.06 (d, \(J = 6.8\) Hz, 3 H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 173.3, 159.1, 152.0, 141.5, 132.9, 130.4, 129.7, 129.4, 125.3, 124.9, 113.8, 81.5, 72.8, 72.3, 69.9, 55.3, 51.4, 43.7, 39.1, 31.1, 25.3, 24.7, 24.1, 19.7, 19.2, 15.8; HRMS (ESI–TOF) calcd for C\(_{28}\)H\(_{38}\)O\(_5\)Na [M + Na\(^+\)] 477.2617, found 477.2616.

**Sarcophytonolide H (6).** To a solution of alcohol 60 (11.5 mg, 25.3 μmol) in CH\(_2\)Cl\(_2\) (0.5 mL) were added pyridine (10 μL, 0.131 mmol) and AcCl (7.9 μL, 0.111 mmol) at 0 °C. After the mixture was stirred at the same temperature for 30 min, the reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with EtOAc, washed with H\(_2\)O and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and short column chromatography (hexane/EtOAc = 4:1) gave the corresponding acetate (11.0 mg), which was used for the next step without further purification.

To a solution of the PMB ether obtained above (11.0 mg) in CH\(_2\)Cl\(_2\) (0.5 mL) and phosphate pH standard solution (0.1 mL) was added DDQ (10.8 mg, 44.4 μmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous NaHCO\(_3\). The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and column chromatography (hexane/EtOAc = 2:1) gave sarcophytonolide H (6) (7.3 mg, 77% in two steps): colorless solid; \(R_f = 0.27\) (hexane/EtOAc = 1:1); [\(\alpha\)]\(_D\)\(^{23}\) +115 (c 0.10, CHCl\(_3\)); literature\(^{10b}\) [\(\alpha\)]\(_D\)\(^{20}\) +74.7 (c 0.20, CHCl\(_3\)); IR (neat) 3275, 2968, 2948, 2924, 1759, 1732 cm\(^{-1}\); \(^1\)H and \(^1\)C NMR Table S6; HRMS (ESI–TOF) calcd for C\(_{22}\)H\(_{32}\)O\(_5\)Na [M + Na\(^+\)] 399.2148, found 399.2153.

**Acetate S22.** To a solution of alcohol 53b (415 mg, 0.677 mmol) in toluene (6.8 mL) were added pyridine (0.32 mL, 4.06 mmol), Ac\(_2\)O (0.32 mL, 3.39 mmol), and DMAP (8.6 mg, 70.4 μmol) at room temperature. After the mixture was stirred at 100 °C for 10 h, the reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and column chromatography (hexane/EtOAc = 30:1) gave acetate S22 (444 mg, quant): colorless oil; \(R_f = 0.45\) (hexane/EtOAc = 10:1); [\(\alpha\)]\(_D\)\(^{25}\) +5.4 (c 0.48, CHCl\(_3\)); IR (neat) 2954, 2929, 2856, 1737 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 5.36–5.27 (m, 2 H), 5.14–5.06 (m, 1 H), 4.57 (d, \(J = 7.1\) Hz, 2 H), 4.03–3.97 (m, 1 H), 3.67–3.55 (m, 2 H), 2.33 (dd, \(J = 13.7, 9.5\) Hz, 1 H), 2.17–1.97 (m, 5 H), 1.97–1.87 (m, 1 H), 1.96 (s, 3 H), 1.69 (s, 3 H), 1.65 (s, 3 H), 1.53–1.46 (m, 1 H), 1.19 (s, 9 H), 0.97 (d, \(J = 5.6\) Hz, 3 H), 0.96 (d, \(J = 5.6\) Hz, 3 H), 0.91 (s, 9 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H); \(^1\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 178.4, 169.8, 141.5, 132.3, 126.7, 118.7, 73.4, 71.1, 66.8, 61.3, 50.4, 45.1, 39.3, 38.8, 27.3, 26.6, 26.3, 26.1, 22.7, 21.4, 20.7, 18.5, 18.3, 16.6, 16.1, –3.9, –4.6, –5.1, –5.2; HRMS
Alcohol 61. To a solution of bis-TBS ether S22 (444 mg, 0.677 mmol) in MeOH (3.4 mL) and CH₂Cl₂ (3.4 mL) was added CSA (47.5 mg, 0.204 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 8:1) gave alcohol 61 (200 mg) and bis-TBS ether S22 (179 mg).

To a solution of bis-TBS ether S22 recovered above (179 mg) in MeOH (1.4 mL) and CH₂Cl₂ (1.4 mL) was added CSA (47.5 mg, 0.204 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 8:1) gave alcohol 61 (72.5 mg) and bis-TBS ether S22 (82.2 mg).

To a solution of bis-TBS ether S22 recovered above (82.2 mg) in MeOH (0.6 mL) and CH₂Cl₂ (0.6 mL) was added CSA (8.7 mg, 37.5 μmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 8:1) gave alcohol 61 (21.8 mg, totally 294 mg, 80%) and bis-TBS ether S22 (51.2 mg). Alcohol 61: colorless oil; Rf = 0.39 (hexane/EtOAc = 4:1); [α]D24 +6.5 (c 0.77, CHCl₃); IR (neat) 3437, 2958, 2929, 2856, 1732 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.32 (t, J = 6.8 Hz, 1 H), 5.26–5.20 (m, 1 H), 5.17 (t, J = 6.5 Hz, 1 H), 4.57 (d, J = 5.8 Hz, 2 H), 3.99–3.92 (m, 1 H), 3.76 (dd, J = 11.5, 4.9 Hz, 1 H), 3.67 (dd, J = 11.5, 3.4 Hz, 1 H), 2.34 (dd, J = 13.2, 8.2 Hz, 1 H), 2.22 (dd, J = 13.2, 5.6 Hz, 1 H), 2.13–1.99 (m, 4 H), 1.97 (s, 3 H), 1.94–1.86 (m, 1 H), 1.69 (s, 3 H), 1.66 (s, 3 H), 1.61 (td, J = 5.7, 2.0 Hz, 1 H), 1.20 (s, 9 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.92 (s, 9 H), 0.87 (d, J = 6.8 Hz, 3 H), 0.13 (s, 3 H), 0.11 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 169.7, 141.4, 131.7, 127.4, 118.7, 72.7, 70.2, 65.3, 61.3, 49.2, 45.0, 39.3, 38.8, 27.3, 26.5, 26.4, 26.0, 22.1, 21.4, 19.2, 18.2, 16.5, 16.1, −4.2, −4.4; HRMS (ESI–TOF) calcd for C₃₀H₆₆O₆SiNa [M + Na]⁺ 563.3744, found 563.3738.

Alkene 62. To a solution of alcohol 61 (294 mg, 0.544 mmol) in CH₂Cl₂ (5.4 mL) were added PhI(OAc)₂ (264 mg, 0.819 mmol) and TEMPO (25.4 mg, 0.163 mmol) at room temperature. After the mixture was stirred at the same temperature for 10 h, the reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 20:1) gave the corresponding aldehyde (288 mg), which was used for the next step without further purification.

To a suspension of Ph₃P⁺CH₃Br⁻ (478 mg, 1.34 mmol) in THF (3.4 mL) was added NaHMDS (1.0 M in THF, 1.3 mL, 1.30 mmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, to the mixture was added the aldehyde obtained above (288 mg).
in THF (1.0 mL + 0.5 mL + 0.5 mL) at 0 °C. After the mixture was stirred at room temperature for 1 h, the reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1) gave alkene 62 (259 mg, 89% in two steps): colorless oil; $R_f = 0.53$ (hexane/EtOAc = 7:1); $[\alpha]_{D}^{24} +9.2$ (c 0.47, CHCl₃); IR (neat) 2958, 2927, 2856, 1737 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.94 (ddd, $J = 17.2, 10.4, 6.4$ Hz, 1 H), 5.35–5.25 (m, 2 H), 5.22 (d, $J = 17.2$ Hz, 1 H), 5.14–5.04 (m, 2 H), 4.57 (d, $J = 7.1$ Hz, 2 H), 4.34 (t, $J = 6.4$ Hz, 1 H), 2.30–2.17 (m, 2 H), 2.11–1.98 (m, 5 H), 1.96 (s, 3 H), 1.69 (s, 3 H), 1.61 (s, 3 H), 1.53 (td, $J = 5.9, 2.4$ Hz, 1 H), 1.20 (s, 9 H), 0.96 (d, $J = 7.1$ Hz, 3 H), 0.94 (d, $J = 7.1$ Hz, 3 H), 0.91 (s, 9 H), 0.06 (s, 3 H), 0.03 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.4, 169.7, 141.5, 141.0, 132.2, 126.9, 118.7, 114.7, 73.0, 70.6, 61.3, 53.1, 43.7, 39.3, 38.8, 27.3, 26.4, 26.0, 21.8, 21.4, 20.3, 18.3, 16.5, 16.0, −3.8, −4.7; HRMS (ESI–TOF) calcd for C₃₁H₅₆O₅SiNa [M + Na]+ 559.3795, found 559.3796.

Aldehyde 63. To a solution of pivalate 62 (259 mg, 0.482 mmol) in CH₂Cl₂ (4.8 mL) was added DIBAL-H (1.02 M in hexane, 1.1 mL, 1.12 mmol) at −78 °C. After the mixture was stirred at the same temperature for 30 min, to the mixture was added DIBAL-H (1.02 M in hexane, 0.55 mL, 0.561 mmol) at −78 °C. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and short column chromatography (hexane/EtOAc = 6:1) gave the corresponding alcohol (185 mg), which was used for the next step without further purification.

To a solution of the alcohol obtained above (185 mg) in CH₂Cl₂ (4.5 mL) were added PhI(OAc)₂ (215 mg, 0.667 mmol) and TEMPO (21.1 mg, 0.135 mmol) at room temperature. After the mixture was stirred at the same temperature for 3 h, the reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 7:1) gave aldehyde 63 (167 mg, 85% in two steps): colorless oil; $R_f = 0.37$ (hexane/EtOAc = 4:1); $[\alpha]_{D}^{24} +19.2$ (c 0.30, CHCl₃); IR (neat) 3462, 2954, 2928, 2856, 1676 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 9.99 (d, $J = 8.0$ Hz, 1 H), 6.05 (ddd, $J = 17.2, 10.8, 6.8$ Hz, 1 H), 5.88 (d, $J = 8.0$ Hz, 1 H), 5.26–5.12 (m, 3 H), 4.62–4.54 (m, 1 H), 4.03–3.93 (m, 1 H), 3.39–3.28 (m, 1 H), 2.30–2.21 (m, 5 H), 2.17 (s, 3 H), 2.17–2.10 (m, 1 H), 2.05–1.95 (m, 1 H), 1.67 (s, 3 H), 1.49–1.43 (m, 1 H), 1.07 (d, $J = 6.8$ Hz, 3 H), 0.91 (d, $J = 8.8$ Hz, 3 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.06 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 191.0, 163.4, 140.0, 134.4, 127.4, 125.2, 115.4, 74.7, 69.1, 54.1, 46.7, 40.6, 26.6, 25.9, 25.8, 21.2, 21.0, 18.1, 17.7, 16.3, −4.0, −4.8; HRMS (ESI–TOF) calcd for C₂₄H₄₄O₃SiNa [M + Na]+ 431.2957, found 431.2961.

Diol 64. To a solution of aldehyde 63 (160 mg, 0.392 mmol) in THF (3.2 mL) and saturated aqueous NH₄Cl (0.6 mL) were added ethyl (2-bromomethyl)acrylate (26) (0.14 mL, 1.18 mmol) and zinc dust (154 mg, 2.35 mmol) at 0 °C. After the mixture was stirred at the same
temperature for 10 min, the mixture was filtered through a Celite pad and washed with EtOAc. The mixture was washed with H2O and brine and dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 5:1) gave diol 64 (205 mg, quant) as a 1:1 diastereomeric mixture: colorless oil; Rf = 0.56 (hexane/EtOAc = 2:1); IR (neat) 3428, 2956, 2927, 2856, 1716 cm⁻¹; ¹H NMR (400 MHz, CDCl3) δ 6.23 (d, J = 1.6 Hz, 0.5 H), 6.22 (d, J = 1.6 Hz, 0.5 H), 6.08–5.96 (m, 1 H), 5.65–5.59 (m, 1 H), 5.23–5.11 (m, 4 H), 4.61–4.48 (m, 2 H), 4.26–4.16 (m, 2 H), 4.00–3.88 (m, 1 H), 2.53–2.44 (m, 2 H), 2.29–1.95 (m, 7 H), 1.69–1.59 (m, 6 H), 1.47–1.39 (m, 1 H), 1.31 (t, J = 7.2 Hz, 1.5 H), 1.31 (t, J = 7.2 Hz, 1.5 H), 1.06 (d, J = 7.1 Hz, 1.5 H), 1.06 (d, J = 7.1 Hz, 1.5 H), 0.93 (d, J = 7.1 Hz, 3 H), 0.91 (s, 9 H), 0.10 (s, 1.5 H), 0.09 (s, 1.5 H), 0.05 (s, 3 H); ¹³C NMR (100 MHz, CDCl3) δ 167.3, 140.4, 138.2, 137.8, 137.3, 133.1, 128.2, 127.4, 127.3, 127.3, 127.1, 126.7, 115.2, 115.0, 74.5, 74.4, 68.9, 68.2, 67.5, 67.3, 60.8, 60.8, 54.2, 54.1, 46.8, 46.7, 40.6, 40.5, 39.3, 39.3, 26.5, 26.4, 26.3, 26.1, 26.0, 21.5, 21.3, 21.1, 21.0, 18.2, 18.1, 16.7, 16.4, 16.3, 16.0, 14.3, –4.0, –4.1, –4.8, –4.8; HRMS (ESI–TOF) calcd for C30H54O5SiNa [M + Na]^+ 545.3638, found 545.3641.

Diol S23. To a solution of diol 64 (199 mg, 0.381 mmol) in CH₂Cl₂ (3.8 mL) were added p-methoxybenzyl 2,2,2-trichloroacetimidate (0.17 mL, 0.964 mmol) and PPTS (44.0 mg, 0.174 mmol) at room temperature. After the mixture was stirred at reflux for 12 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1, 6:1) gave the corresponding PMB ether (143 mg) and diol 64 (122 mg including impurity). The PMB ether (143 mg) was used for the next step without further purification.

To a solution of the TBS ether obtained above (143 mg) in THF (2.2 mL) was added TBAF (1.0 M in THF, 0.67 mL, 0.670 mmol) at room temperature. After the mixture was stirred at reflux for 2 h, the mixture was diluted with EtOAc and washed with H₂O and brine. The aqueous phase was extracted with EtOAc and the combined organic phase was dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 10:1, 6:1) gave the corresponding PMB ether (143 mg) and diol S23 (122 mg including impurity). The PMB ether (143 mg) was used for the next step without further purification.

To a solution of the TBS ether obtained above (143 mg) in THF (2.2 mL) was added TBAF (1.0 M in THF, 0.67 mL, 0.670 mmol) at room temperature. After the mixture was stirred at reflux for 2 h, the mixture was diluted with EtOAc and washed with H₂O and brine. The aqueous phase was extracted with EtOAc and the combined organic phase was dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 4:1) gave diol S23 (82.4 mg, 33% in two steps): yellow oil; Rf = 0.42 (hexane/EtOAc = 2:1); IR (neat) 7.23–7.15 (m, 2 H), 6.84 (d, J = 8.6 Hz, 2 H), 6.18 (d, J = 1.5 Hz, 1 H), 5.99 (ddd, J = 16.4, 10.4, 5.2 Hz, 1 H), 5.57 (s, 1 H), 5.33–5.24 (m, 2 H), 5.16 (dt, J = 10.5, 1.5 Hz, 1 H), 5.11 (d, J = 9.0 Hz, 1 H), 4.56 (brs, 1 H), 4.51–4.42 (m, 1 H), 4.32–4.21 (m, 2 H), 4.15 (q, J = 7.1 Hz, 2 H), 4.04–3.96 (m, 1 H), 3.79 (s, 3 H), 3.67 (brs, 1 H), 2.68–2.56 (m, 1 H), 2.47–2.37 (m, 1 H), 2.31 (d, J = 16.6 Hz, 1 H), 2.25–2.12 (m, 3 H), 2.12–1.97 (m, 3 H), 1.67 (s, 3 H), 1.60 (s, 3 H), 1.44–1.38 (m, 1 H), 1.25 (t, J = 7.1 Hz, 3 H), 1.09 (d, J = 7.1 Hz, 3 H), 0.91 (d, J = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 167.0, 158.9, 140.3, 139.1, 137.2, 131.9, 130.9, 129.1, 128.8, 128.7, 127.0, 125.9, 114.5, 113.6, 73.3, 72.6, 69.5, 69.4, 68.4, 60.6, 55.3, 52.7, 47.2, 39.4, 38.5, 26.5, 26.4, 21.9, 21.1, 16.8, 16.8, 16.1, 14.3; HRMS (ESI–TOF) calcd for C₃₂H₄₈O₆Na [M + Na]^+ 551.3348, found 551.3353.
**Carboxylic Acid 65.** To a solution of ester S23 (65.4 mg, 0.124 mmol) in THF (0.7 mL), MeOH (0.3 mL), and H2O (0.3 mL) was added LiOH·H2O (7.9 mg, 0.188 mmol) at room temperature. After the mixture was stirred at the same temperature for 2 days, to the mixture was added LiOH·H2O (7.9 mg, 0.188 mmol) at room temperature. After the mixture was stirred at the same temperature for 10 h, the mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc and washed with H2O and brine. The aqueous phase was extracted with EtOAc four times and the combined organic phase was dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 1:1) gave carboxylic acid 65 (54.9 mg, 89%): colorless oil; Rf = 0.56 (EtOAc); IR (neat) 3372, 2954, 2919, 2874, 1696, 1629, 1613 cm–1; 1H NMR (400 MHz, CDCl3) δ 7.21 (d, J = 8.0 Hz, 2 H), 6.85 (d, J = 8.0 Hz, 2 H), 6.32–6.26 (m, 1 H), 5.98 (ddd, J = 16.0, 10.8, 5.6 Hz, 1 H), 5.66 (s, 1 H), 5.34–5.24 (m, 2 H), 5.20–5.08 (m, 2 H), 4.63–4.60 (m, 1 H), 4.50 (d, J = 11.6 Hz, 1 H), 4.34–4.22 (m, 2 H), 4.07–3.98 (m, 1 H), 3.79 (s, 3 H), 2.63 (dd, J = 13.9, 7.1 Hz, 1 H), 2.49 (dd, J = 13.9, 5.6 Hz, 1 H), 2.30–1.97 (m, 7 H), 1.67 (s, 3 H), 1.62 (s, 1.5 H), 1.62 (s, 1.5 H), 1.44–1.38 (m, 1 H), 1.09 (d, J = 7.1 Hz, 3 H), 0.92 (d, J = 7.1 Hz, 3 H); 13C NMR (100 MHz, CDCl3) δ 170.4, 159.0, 140.1, 139.5, 136.8, 136.7, 131.9, 130.4, 129.2, 129.2, 129.1, 129.0, 128.7, 128.6, 125.4, 125.4, 114.6, 113.7, 74.1, 74.0, 72.7, 69.6, 68.4, 55.3, 52.6, 52.5, 47.0, 39.4, 39.3, 38.0, 37.9, 26.4, 26.2, 26.2, 21.9, 21.1, 16.8, 16.8, 16.1; HRMS (ESI–TOF) calcd for C30H44O6Na [M + Na]⁺ 523.3036, found 523.3036.

**Butenolide 67.** To a solution of MNBA (45.1 mg, 0.131 mmol) and DMAP (32.8 mg, 0.268 mmol) in CH2Cl2 (32 mL) was slowly added dihydroxycarboxylic acid 65 (36.6 mg, 73.1 μmol) in CH2Cl2 (3.2 mL at 0.2 mL/h + 1.0 mL at 1.0 mL/h at 1.0 mL/h) at −5 °C with a syringe pump for 18 h. After the mixture was stirred at the same temperature for further 5 h, to the mixture was added a solution of MNBA (15.0 mg, 43.6 μmol) and DMAP (11.0 mg, 90.0 μmol) in CH2Cl2 (1.0 mL) at −5 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and short chromatography (hexane/EtOAc = 6:1) gave lactone 66 (16.8 mg), which was used for the next step without further purification.

To a solution of alcohol 66 obtained above (16.8 mg) in CH2Cl2 (0.4 mL) were added pyridine (7.3 μL, 90.5 μmol) and AcCl (4.9 μL, 69.8 μmol) at 0 °C. After the mixture was stirred at the same temperature for 4 h, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and short chromatography (hexane/EtOAc = 7:1) gave the corresponding acetate (15.9 mg), which was used for the next step without further purification.

To a solution of the tetraene obtained above (15.9 mg) in toluene (6.0 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (4.6 mg, 7.34 μmol) at room temperature. After the mixture was stirred at 100 °C for 2 days, the mixture was filtered through short
column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 7:1, 4:1) gave butenolide 67 (7.1 mg, 20% in three steps): colorless oil; Rf = 0.36 (hexane/EtOAc = 2:1); IR (neat) 2958, 2918, 2878, 2852, 1757, 1739, 1613 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (s, 1 H), 7.28 (d, J = 8.5 Hz, 2 H), 6.87 (d, J = 8.5 Hz, 2 H), 5.28 (dd, J = 11.2, 6.4 Hz, 1 H), 5.11–5.01 (m, 3 H), 4.45 (d, J = 10.8 Hz, 1 H), 4.38 (d, J = 10.8 Hz, 1 H), 3.80 (s, 3 H), 2.95–2.85 (m, 1 H), 2.69–2.58 (m, 1 H), 2.48 (dd, J = 12.8, 11.1 Hz, 1 H), 2.39–2.28 (m, 1 H), 2.28–2.06 (m, 5 H), 2.04 (s, 3 H), 1.54 (s, 3 H), 1.46 (dd, J = 10.5, 2.4 Hz, 1 H), 1.41 (s, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.85 (d, J = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 172.7, 169.5, 159.0, 151.2, 139.5, 130.7, 130.3, 129.3, 129.2, 127.6, 113.8, 79.9, 72.5, 69.9, 68.8, 55.3, 46.7, 44.0, 38.9, 33.4, 28.3, 22.8, 21.7, 21.4, 16.4, 15.9, 15.5; HRMS (ESI–TOF) calcd for C₃₀H₄₀O₆Na [M + Na]⁺ 519.2723, found 519.2728.

Alcohol S24. To a solution of PMB ether 67 (7.1 mg, 14.3 μmol) in CH₂Cl₂ (0.2 mL) and phosphate pH standard solution (50 μL) was added DDQ (6.4 mg, 28.2 μmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc and washed with saturated aqueous NaHCO₃, H₂O, and brine. The aqueous phase was extracted with EtOAc twice and the combined organic phase was dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 1:1) gave alcohol S24 (4.9 mg, 91%): colorless oil; Rf = 0.17 (hexane/EtOAc = 1:1); IR (neat) 3413, 2958, 2919, 2870, 2852, 1731, 1668, 1651 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (s, 1 H), 5.29 (dd, J = 11.2, 6.4 Hz, 1 H), 5.13 (d, J = 9.5 Hz, 1 H), 5.09–4.95 (m, 3 H), 2.85–2.76 (m, 1 H), 2.64 (dd, J = 12.7, 5.9 Hz, 1 H), 2.47 (dd, J = 12.7, 11.2 Hz, 1 H), 2.38–2.26 (m, 1 H), 2.24–2.17 (m, 1 H), 2.16–1.99 (m, 4 H), 2.04 (s, 3 H), 1.54 (s, 3 H), 1.46 (dd, J = 10.7, 2.4 Hz, 1 H), 1.44 (s, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 172.8, 169.5, 151.2, 138.2, 130.3, 129.3, 129.1, 128.8, 79.9, 68.8, 66.1, 46.7, 44.0, 38.9, 33.4, 28.3, 22.8, 21.7, 21.4, 16.4, 15.9, 15.4; HRMS (ESI–TOF) calcd for C₂₂H₃₂O₅Na [M + Na]⁺ 399.2148, found 399.2151.

Proposed Structure 10 of Isosarcophytonolide D. To a solution of alcohol S24 (1.2 mg, 3.18 μmol) in CH₂Cl₂ (1.0 mL) were added MS4Å (2.0 mg), NMO (2.0 mg, 17.1 μmol), and a catalytic amount of TPAP at room temperature. After the mixture was stirred at the same temperature for 16 h, to the mixture were added NMO (2.0 mg, 17.1 μmol) and a catalytic amount of TPAP at room temperature. After the mixture was stirred at the same temperature for 1 h, the mixture was filtered through short column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 1:1) gave alcohol S24 (4.9 mg, 91%): colorless oil; Rf = 0.17 (hexane/EtOAc = 1:1); IR (neat) 3413, 2958, 2919, 2870, 2852, 1731, 1668, 1651 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.36 (s, 1 H), 5.29 (dd, J = 11.2, 6.4 Hz, 1 H), 5.13 (d, J = 9.5 Hz, 1 H), 5.09–4.95 (m, 3 H), 2.85–2.76 (m, 1 H), 2.64 (dd, J = 12.7, 5.9 Hz, 1 H), 2.47 (dd, J = 12.7, 11.2 Hz, 1 H), 2.38–2.26 (m, 1 H), 2.24–2.17 (m, 1 H), 2.16–1.99 (m, 4 H), 2.04 (s, 3 H), 1.54 (s, 3 H), 1.46 (dd, J = 10.7, 2.4 Hz, 1 H), 1.44 (s, 3 H), 0.94 (d, J = 7.1 Hz, 3 H), 0.86 (d, J = 7.1 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 172.8, 169.5, 151.2, 138.2, 130.3, 129.3, 129.1, 128.8, 79.9, 68.8, 66.1, 46.7, 44.0, 38.9, 33.4, 28.3, 22.7, 21.7, 21.4, 16.4, 15.9, 15.4; HRMS (ESI–TOF) calcd for C₂₂H₃₂O₅Na [M + Na]⁺ 399.2148, found 399.2151.

Ketone 68. To a solution of sarcophytonolide H (6) (1.0 mg, 2.66 μmol) in CH₂Cl₂ (0.3 mL)
was added Dess–Martin periodinane (3.4 mg, 8.02 μmol) at room temperature. After the mixture was stirred at the same temperature for 16 h, to the mixture was added Dess–Martin periodinane (6.2 mg, 14.6 μmol) at room temperature. After the mixture was stirred at the same temperature for 6 h, the mixture was filtered through short column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 2:1) gave ketone 68 (0.4 mg, 40%): colorless oil; \( R_f = 0.55 \) (hexane/EtOAc = 1:1); \([\alpha]_D^{24} = -50.9 \) (c 0.07, CHCl3); literature10d \([\alpha]_D^{20} = -66 \) (c 0.67, CHCl3); IR (neat) 2954, 2924, 2874, 2852, 2172, 1734, 1687, 1618 cm\(^{-1}\); \(^1^H\) and \(^{13}^C\) NMR Table S9; HRMS (ESI–TOF) calcd for C\(_{22}\)H\(_{30}\)O\(_5\)Na [M + Na\(^+\)] = 397.1991, found 397.1988.

**Alcohols 70a and 70b.** To a solution of aldehyde 52 (69.8 mg, 0.186 mmol) and allylic bromide 21a (79.2 mg, 0.248 mmol) in THF (1.9 mL) was added SmI\(_2\) (0.1 M in THF, 5.6 mL, 0.560 mmol) at 0 °C. After the mixture was stirred at the same temperature for 30 min, the reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with EtOAc, washed with saturated aqueous Na\(_2\)S\(_2\)O\(_3\), H\(_2\)O, and brine, and then dried over Na\(_2\)SO\(_4\). Concentration and column chromatography (hexane/EtOAc = 20:1) gave alcohols 70a (33.2 mg, 29%) and 70b (45.4 mg, 40%). Alcohol 70a: colorless oil; \( R_f = 0.48 \) (hexane/EtOAc = 10:1); \([\alpha]_D^{23} = -1.0 \) (c 1.28, CHCl3); IR (neat) 3501, 2956, 2929, 2857, 1731 cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta 5.21 \) (t, \( J = 6.8 \) Hz, 1 H), 4.11–4.07 (m, 3 H), 3.98–3.94 (m, 1 H), 3.66 (d, \( J = 5.6 \) Hz, 2 H), 2.46 (brs, 1 H), 2.25–2.12 (m, 2 H), 2.07–1.93 (m, 3 H), 1.74–1.68 (m, 1 H), 1.65 (s, 3 H), 1.61–1.54 (m, 1 H), 1.47–1.33 (m, 3 H), 1.26–1.21 (m, 1 H), 1.19 (s, 9 H), 1.05 (d, \( J = 6.8 \) Hz, 3 H), 1.01 (d, \( J = 6.8 \) Hz, 3 H), 0.92 (d, \( J = 6.4 \) Hz, 3 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.07 (s, 3 H), 0.07 (s, 3 H); \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta 178.5, 127.4, 127.7, 73.6, 67.4, 66.3, 62.8, 53.2, 46.7, 38.7, 37.0, 35.5, 29.8, 27.3, 26.1, 26.0, 25.5, 22.8, 22.5, 19.5, 18.5, 18.2, 16.1, –3.9, –4.7, –5.3; HRMS (ESI–TOF) calcd for C\(_{34}\)H\(_{70}\)O\(_5\)Si\(_2\)Na [M + Na\(^+\)] = 637.4659, found 637.4658. Alcohol 70b: colorless oil; \( R_f = 0.34 \) (hexane/EtOAc = 20:1); \([\alpha]_D^{27} = +0.15 \) (c 2.28, CHCl3); IR (neat) 3547, 2957, 2928, 2857, 1731 cm\(^{-1}\); \(^1^H\) NMR (400 MHz, CDCl\(_3\)) \( \delta 5.18 \) (t, \( J = 8.0 \) Hz, 1 H), 4.15–4.07 (m, 3 H), 3.95–3.89 (m, 1 H), 3.72–3.67 (m, 2 H), 3.09 (d, \( J = 4.8 \) Hz, 1 H), 2.23–2.18 (m, 2 H), 2.07–1.97 (m, 3 H), 1.70–1.66 (m, 1 H), 1.58–1.54 (m, 1 H), 1.48–1.33 (m, 3 H), 1.26–1.22 (m, 1 H), 1.19 (s, 9 H), 1.05 (d, \( J = 7.2 \) Hz, 3 H), 0.94 (d, \( J = 6.4 \) Hz, 3 H), 0.92 (d, \( J = 6.4 \) Hz, 3 H), 0.90 (s, 9 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.11 (s, 3 H), 0.07 (s, 3 H), 0.06 (s, 3 H); \(^{13}^C\) NMR (100 MHz, CDCl\(_3\)) \( \delta 178.4, 132.7, 127.4, 74.4, 68.8, 66.1, 62.9, 51.2, 47.5, 38.7, 37.0, 35.6, 29.8, 27.3, 26.5, 26.1, 26.0, 25.6, 22.0, 20.8, 19.5, 18.4, 18.1, 16.3, –3.9, –4.7, –5.2, –5.3; HRMS (ESI–TOF) calcd for C\(_{34}\)H\(_{70}\)O\(_5\)Si\(_2\)Na [M + Na\(^+\)] = 637.4659, found 637.4659.

**Alcohol 71.** To a mixture of alcohol 70a (1.10 g, 1.79 mmol) and TBAI (212 mg, 0.573 mmol) in CH\(_2\)Cl\(_2\) (3.6 mL) were added i-Pr\(_2\)NEt (1.84 mL, 10.7 mmol) and MOMCl (0.68 mL, 8.95 mmol) at room temperature. After the mixture was stirred at 40 °C for 3 h, the reaction was quenched with saturated aqueous NH\(_4\)Cl. The mixture was diluted with EtOAc,
washed with saturated aqueous NH₄Cl, saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 50:1, 30:1) gave the corresponding MOM ether (1.14 g), which was used for the next step without further purification.

To a solution of the bis-TBS ether obtained above (1.14 g) in MeOH (8.7 mL) and CH₂Cl₂ (8.7 mL) was added CSA (121 mg, 0.519 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 40:1, 15:1, 5:1) gave alcohol 71 (408 mg) and the bis-TBS ether (577 mg).

To a solution of the bis-TBS ether recovered above (577 mg) in MeOH (4.4 mL) and CH₂Cl₂ (4.4 mL) was added CSA (61.1 mg, 0.263 mmol) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 15:1, 5:1) gave alcohol 71 (224 mg) and the bis-TBS ether (274 mg).

To a solution of the bis-TBS ether recovered above (274 mg) in MeOH (2.2 mL) and CH₂Cl₂ (2.2 mL) was added CSA (29.0 mg, 0.125 mmol) at 0 °C. After the mixture was stirred at the same temperature for 2 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 10:1, 5:1) gave alcohol 71 (97.3 mg) and the bis-TBS ether (151 mg).

To a solution of the bis-TBS ether recovered above (151 mg) in MeOH (1.0 mL) and CH₂Cl₂ (1.0 mL) was added CSA (14.5 mg, 57.9 μmol) at 0 °C. After the mixture was stirred at the same temperature for 2 h, the reaction was quenched with Et₃N. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 30:1, 10:1, 5:1) gave alcohol 71 (53.9 mg, totally 783 mg, 83% in two steps) and the bis-TBS ether (46.3 mg). Alcohol 71: colorless oil; Rf = 0.35 (hexane/EtOAc = 4:1); [α]D²⁶ –13.5 (c 1.00, CHCl₃); IR (neat) 3501, 2957, 2928, 2852, 1730 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.18 (t, J = 6.8 Hz, 1 H), 4.62 (d, J = 6.4 Hz, 1 H), 4.54 (d, J = 6.4 Hz, 1 H), 4.11–4.06 (m, 2 H), 3.98–3.94 (m, 2 H), 3.69 (dd, J = 11.6, 5.6 Hz, 1 H), 3.61 (dd, J = 11.0, 4.4 Hz, 1 H), 3.33 (s, 3 H), 2.31–2.20 (m, 2 H), 2.09–1.96 (m, 2 H), 1.69–1.63 (m, 2 H), 1.65 (s, 3 H), 1.58–1.53 (m, 1 H), 1.47–1.32 (m, 2 H), 1.26–1.17 (m, 2 H), 1.19 (s, 3 H), 1.04 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 0.92 (d, J = 6.8 Hz, 3 H), 0.90 (s, 9 H), 0.12 (s, 3 H), 0.08 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.5, 132.2, 127.4, 95.4, 75.2, 72.0, 66.5, 62.8, 55.7, 50.4, 43.3, 38.7, 36.9, 35.5, 29.8, 27.3, 26.0, 25.6, 25.6, 22.4, 21.6, 19.5, 18.3, 16.2, –3.9, –4.3; HRMS (ESI–TOF) calcd for C₃₀H₆₀O₆SiNa [M + Na]⁺ 567.4057, found 567.4054.

Alkene 72. To a solution of alcohol 71 (1.01 g, 1.85 mmol) in CH₂Cl₂ (19 mL) were added
PhI(OAc)₂ (912 mg, 2.83 mmol) and TEMPO (89.2 mg, 0.570 mmol) at room temperature. After the mixture was stirred at the same temperature for 7 h, the reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 40:1, 15:1) gave the corresponding aldehyde (1.01 g), which was used for the next step without further purification.

To a suspension of Ph₃P⁺CH₃Br⁻ (1.68 g, 4.70 mmol) in THF (9.0 mL) was added NaHMDS (1.0 M in THF, 4.5 mL, 4.50 mmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, to the mixture was added the aldehyde obtained above (1.01 g) in THF (4.0 mL + 3.0 mL + 3.0 mL) at 0 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with saturated aqueous NH₄Cl. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 70:1, 30:1) gave alkene 72 (816 mg, 81% in two steps): colorless oil; Rᵢ = 0.57 (hexane/ EtOAc = 10:1); [α]D₂₅ −10.6 (c 0.98, CHCl₃); IR (neat) 2957, 2927, 1731 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 5.94 (ddd, J = 17.2, 10.4, 6.8 Hz, 1 H), 5.18–5.12 (m, 2 H), 5.04 (ddd, J = 10.4, 2.0, 1.2 Hz, 1 H), 4.57 (d, J = 8.0 Hz, 1 H), 4.46 (d, J = 8.0 Hz, 1 H), 4.45–4.43 (m, 1 H), 4.12–4.06 (m, 2 H), 3.87 (td, J = 6.8, 2.8 Hz, 1 H), 3.32 (s, 3 H), 2.26 (d, J = 4.0 Hz, 2 H), 2.05–1.96 (m, 3 H), 1.71–1.65 (m, 1 H), 1.62 (s, 3 H), 1.48–1.32 (m, 3 H), 1.26–1.15 (m, 2 H), 1.20 (s, 9 H), 1.04 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H), 0.92 (d, J = 6.4 Hz, 3 H), 0.89 (s, 9 H), 0.07 (s, 3 H), 0.03 (s, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 178.5, 141.9, 132.6, 127.1, 114.1, 96.1, 75.7, 73.0, 62.9, 55.6, 53.8, 44.1, 38.8, 36.9, 35.6, 29.8, 27.3, 26.1, 25.8, 25.6, 22.9, 21.8, 19.5, 18.3, 16.2, −3.6, −4.5; HRMS (ESI–TOF) calcd for C₃₁H₆₀O₅SiNa [M + Na⁺] 563.4108, found 563.4105.

Alcohol 73. To a solution of pivalate 72 (483 mg, 0.893 mmol) in CH₂Cl₂ (8.9 mL) was added DIBAL-H (1.02 M in THF, 2.63 mL, 2.68 mmol) at –78 °C. After the mixture was stirred at the same temperature for 1 h, the reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and short column chromatography (hexane/EtOAc = 5:1) gave the corresponding alcohol (395 mg), which was used for the next step without further purification.

To a solution of the alcohol obtained above (395 mg) in CH₂Cl₂ (8.7 mL) were added PhI(OAc)₂ (416 mg, 1.30 mmol) and TEMPO (42.9 mg, 0.260 mmol) at room temperature. After the mixture was stirred at the same temperature for 2 h, the reaction was quenched with saturated aqueous Na₂S₂O₃. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO₃, H₂O, and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1) gave the corresponding aldehyde (386 mg), which was used for the next step without further purification.

To a solution of the aldehyde obtained above (386 mg) in THF (7.1 mL) and saturated aqueous NH₄Cl (1.4 mL) were added ethyl (2-bromomethyl)acrylate (26) (0.27 mL, 2.55 mmol) and zinc dust (294 mg, 4.49 mmol) at 0 °C. The mixture was stirred at the same
temperature for 30 min. The mixture was filtered through a Celite pad and washed with EtOAc. The mixture was concentrated, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and column chromatography (hexane/EtOAc = 7:1, 4:1) gave alcohol 73 (468 mg, 92% in three steps) as a 1:1 diastereomeric mixture: colorless oil; \( R_f = 0.37 \) (hexane/EtOAc = 4:1); IR (neat) 3465, 2955, 2928, 2857, 1716, 1630 cm⁻¹; \(^1\)H NMR (400 MHz, CDCl₃) \( \delta \) 6.26–6.25 (m, 1 H), 5.93 (ddd, \( J = 17.2, 10.4, 6.8 \) Hz, 1 H), 5.65 (s, 1 H), 5.19–5.12 (m, 2 H), 5.03 (d, \( J = 10.4 \) Hz, 1 H), 4.57 (d, \( J = 6.8 \) Hz, 1 H), 4.49 (d, \( J = 6.8 \) Hz, 1 H), 4.45–4.42 (m, 1 H), 4.26–4.18 (m, 2 H), 3.86–3.84 (m, 2 H), 3.32 (s, 3 H), 2.63–2.53 (m, 1 H), 2.37–2.24 (m, 3 H), 2.12–1.96 (m, 4 H), 1.71–1.65 (m, 1 H) 1.62 (s, 3 H), 1.47–1.37 (m, 3 H), 1.31 (t, \( J = 7.2 \) Hz, 3 H), 1.26–1.15 (m, 2 H), 1.04 (d, \( J = 6.4 \) Hz, 3 H), 1.02 (d, \( J = 6.4 \) Hz, 3 H), 0.94 (d, \( J = 6.8 \) Hz, 1.5 H), 0.90 (d, \( J = 6.8 \) Hz, 1.5 H), 0.88 (s, 9 H), 0.66 (s, 9 H), 0.03 (s, 3 H); \(^{13}\)C NMR (100 MHz, CDCl₃) \( \delta \) 167.5, 142.0, 137.8, 132.5, 132.4, 127.3, 127.3, 114.1, 96.1, 75.7, 73.0, 68.7, 68.3, 61.0, 55.6, 53.8, 44.8, 44.8, 44.0, 41.3, 40.7, 37.8, 36.8, 29.5, 29.2, 26.1, 25.8, 25.6, 25.5, 22.8, 21.8, 20.2, 19.2, 18.3, 16.2, 14.3, −3.6, −4.5; HRMS (ESI–TOF) calcd for C₃₂H₆₀O₆SiNa [M + Na]⁺ 591.4057, found 591.4059.

**Alcohol 74.** To a solution of alcohol 73 (468 mg, 0.823 mmol) in CH₂Cl₂ (1.6 mL) were added \( p \)-methoxybenzyl 2,2,2-trichloroacetimidate (0.36 mL, 2.06 mmol) and PPTS (104 mg, 0.412 mmol) at room temperature. After the mixture was stirred at 40 °C for 16 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1, 4:1) gave the corresponding PMB ether (217 mg) and alcohol 73 (318 mg including impurity).

To a solution of alcohol 73 recovered above (318 mg including impurity) in CH₂Cl₂ (0.9 mL) were added \( p \)-methoxybenzyl 2,2,2-trichloroacetimidate (0.36 mL, 2.06 mmol) and PPTS (104 mg, 0.412 mmol) at room temperature. After the mixture was stirred at 40 °C for 16 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 10:1, 4:1) gave the corresponding PMB ether (217 mg) and alcohol 73 (318 mg including impurity).

To a solution of alcohol 73 recovered above (224 mg including impurity) in CH₂Cl₂ (0.8 mL) were added \( p \)-methoxybenzyl 2,2,2-trichloroacetimidate (0.17 mL, 0.985 mmol) and PPTS (49.7 mg, 0.197 mmol) at room temperature. After the mixture was stirred at 40 °C for 14 h, the reaction was quenched with saturated aqueous NaHCO₃. The mixture was diluted with EtOAc, washed with H₂O and brine, and then dried over Na₂SO₄. Concentration and short column chromatography (hexane/EtOAc = 7:1, 4:1) gave the corresponding PMB ether (83.1 mg) and alcohol 73 (159 mg including impurity). The combined PMB ether (436 mg) was used for the next step without further purification.

To a solution of the TBS ether obtained above (436 mg) in THF (6.3 mL) was added TBAF (1.0 M in THF, 1.9 mL, 1.90 mmol) at room temperature. After the mixture was stirred at
60 °C for 12 h, the mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 5:1) gave alcohol 74 (266 mg, 56% in two steps): colorless oil; \( R_f = 0.58 \) (hexane/EtOAc = 2:1); IR (neat) 3483, 2955, 2929, 2870, 1714, 1613 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \( \delta \) 7.26–7.21 (m, 2 H), 6.85 (dd, \( J = 8.0, 2.8 \) Hz, 2 H), 6.21 (s, 0.5 H), 6.21 (s, 0.5 H), 6.01 (ddd, \( J = 17.2, 10.8, 6.0 \) Hz, 1 H), 5.62 (s, 0.5 H), 5.61 (s, 0.5 H), 5.30 (dd, \( J = 17.2, 1.6 \) Hz, 1 H), 5.20–5.12 (m, 2 H), 4.60 (d, \( J = 6.8 \) Hz, 1 H), 4.53 (d, \( J = 6.8 \) Hz, 1 H), 4.50–4.38 (m, 3 H), 4.23–4.16 (m, 2 H), 3.96–3.92 (m, 1 H), 3.79 (s, 1.5 H), 3.79 (s, 1.5 H), 3.67–3.59 (m, 1 H), 3.43 (s, 3 H), 2.69 (dd, \( J = 13.6, 6.0 \) Hz, 0.5 H), 2.56–2.32 (m, 2.5 H), 2.20 (dd, \( J = 13.6, 4.4 \) Hz, 0.5 H), 2.05–1.89 (m, 2.5 H), 1.67–1.52 (m, 5 H), 1.61 (s, 3 H), 1.48–1.34 (m, 1 H), 1.32–1.27 (m, 3 H), 1.21–1.10 (m, 1 H), 1.07–1.02 (m, 6 H), 0.90 (d, \( J = 6.4 \) Hz, 1.5 H), 0.80 (d, \( J = 6.4 \) Hz, 1.5 H); \(^{13}\)C NMR (100 MHz, CDCl3) \( \delta \) 167.1, 159.0, 141.4, 141.3, 137.7, 131.9, 131.8, 130.9, 129.3, 128.0, 128.0, 127.1, 114.5, 113.7, 96.0, 77.6, 75.6, 75.3, 73.0, 70.9, 70.8, 60.7, 55.7, 55.3, 51.7, 42.8, 42.0, 41.9, 37.8, 37.6, 36.8, 29.4, 29.0, 29.0, 26.5, 25.6, 25.5, 22.9, 21.6, 20.1, 29.4, 16.1, 14.3; HRMS (ESI–TOF) calcd for C34H54O7Na [M + Na]+ 597.3767, found 597.3766.

**Lactone 75.** To a solution of ester 74 (12.5 mg, 21.7 \( \mu \)mol) in THF (0.6 mL), MeOH (0.2 mL), and H2O (0.2 mL) was added LiOH·H2O (1.4 mg, 32.6 \( \mu \)mol) at room temperature. After the mixture was stirred at the same temperature for 16 h, to the mixture was added LiOH·H2O (2.8 mg, 65.2 \( \mu \)mol) at room temperature. After the mixture was stirred at the same temperature for 7 h, the mixture was neutralized with aqueous HCl at 0 °C. The mixture was diluted with EtOAc and washed with H2O and brine. The aqueous phase was extracted with EtOAc three times and the combined organic phase was dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 2:1) gave the corresponding carboxylic acid (13.7 mg), which was used for the next step without further purification.

To a solution of MNBA (21.5 mg, 60.2 \( \mu \)mol) and DMAP (14.3 mg, 0.120 mmol) in CH2Cl2 (7.4 mL) was slowly added the hydroxycarboxylic acid obtained above (13.7 mg) in CH2Cl2 (1.6 mL at 0.1 mL/h + 1.0 mL at 1.0 mL/h + 1.0 mL at 1.0 mL/h) at 40 °C with a syringe pump for 18 h. After the mixture was stirred at the same temperature for further 2 h, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with H2O and brine. The aqueous phase was extracted with EtOAc three times and the combined organic phase was dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 2:1) gave the corresponding carboxylic acid (13.7 mg), which was used for the next step without further purification.

To a solution of MNBA (21.5 mg, 60.2 \( \mu \)mol) and DMAP (14.3 mg, 0.120 mmol) in CH2Cl2 (7.4 mL) was slowly added the hydroxycarboxylic acid obtained above (13.7 mg) in CH2Cl2 (1.6 mL at 0.1 mL/h + 1.0 mL at 1.0 mL/h + 1.0 mL at 1.0 mL/h) at 40 °C with a syringe pump for 18 h. After the mixture was stirred at the same temperature for further 2 h, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 12:1) gave lactone 75 (9.3 mg, 81% in two steps): colorless oil; \( R_f = 0.50, 0.44 \) (hexane/EtOAc = 4:1); IR (neat) 2952, 2927, 2872, 1714, 1613 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl3) \( \delta \) 7.31–7.18 (m, 2 H), 6.87–6.82 (m, 2 H), 6.24 (d, \( J = 2.0 \) Hz, 0.3 H), 6.15 (d, \( J = 1.2 \) Hz, 0.7 H), 6.06 (ddd, \( J = 15.6, 10.8, 4.9 \) Hz, 0.7 H), 5.71–5.53 (m, 2.3 H), 5.44 (t, \( J = 6.6 \) Hz, 0.3 H), 5.29–5.15 (m, 2 H), 4.93–4.91 (m, 0.7 H), 4.67–4.54 (m, 2.7 H), 4.48–4.32 (m, 1.3 H), 3.83–3.77 (m, 2 H), 3.80 (s, 2.1 H), 3.79 (s, 0.9 H), 3.56–3.42 (m, 1 H), 3.38 (s, 2.1 H), 3.36 (s, 0.9 H), 3.02 (dd, \( J = 13.4, 3.7 \) Hz, 0.7 H), 2.76 (dd, \( J = 14.1, 3.2 \) Hz, 0.3 H), 2.39–1.91 (m, 5 H), 1.81–1.68 (m, 1 H), 1.65–1.56 (m,
2 H), 1.62 (s, 0.9 H), 1.60 (s, 2.1 H), 1.54–1.26 (m, 4 H), 1.15 (d, J = 6.8 Hz, 2.1 H), 1.11 (d, J = 6.8 Hz, 2.1 H), 1.06 (d, J = 7.2 Hz, 0.9 H), 1.00 (d, J = 6.8 Hz, 0.9 H), 0.92 (d, J = 6.4 Hz, 0.9 H), 0.85 (d, J = 6.4 Hz, 2.1 H); 13C NMR (100 MHz, CDCl3) δ 165.9, 165.3, 159.0, 137.9, 137.7, 135.0, 134.5, 132.5, 131.4, 131.0, 130.7, 129.5, 129.2, 128.4, 127.8, 127.6, 126.6, 117.6, 115.4, 113.7, 113.6, 96.9, 95.9, 76.1, 75.8, 75.8, 75.4, 74.0, 70.3, 55.9, 55.7, 55.3, 50.4, 48.1, 45.2, 44.3, 42.5, 38.7, 37.8, 37.6, 36.6, 34.7, 28.4, 26.7, 25.9, 25.6, 24.7, 24.5, 24.0, 22.7, 21.4, 20.5, 20.4, 20.0, 16.7, 16.6; HRMS (ESI–TOF) calcd for C32H48O6Na [M + Na]⁺ 551.3348, found 551.3347.

**Alcohol 76.** To a solution of PMB ether 75 (11.1 mg, 21.0 μmol) in CH2Cl2 (0.4 mL) and phosphate pH standard solution (0.1 mL) was added DDQ (9.2 mg, 40.5 μmol) at 0 °C. After the mixture was stirred at the same temperature for 2 h, the reaction was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with saturated aqueous NaHCO3, H2O, and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 3:1) gave alcohol 76 (7.5 mg, 87%): colorless oil; Rf = 0.42, 0.30 (hexane/EtOAc = 2:1); IR (neat) 3460, 2954, 2927, 1714, 1628 cm–1; 1H NMR (400 MHz, CDCl3) δ 6.29 (d, J = 1.5 Hz, 0.5 H), 6.16 (d, J = 1.4 Hz, 0.5 H), 6.04 (ddd, J = 17.2, 10.8, 4.9 Hz, 0.5 H), 5.73 (ddd, J = 17.2, 10.8, 6.8 Hz, 0.5 H), 5.67–5.64 (m, 1 H), 5.61 (s, 0.5 H), 5.53 (t, J = 6.8 Hz, 0.5 H), 5.31–5.15 (m, 2.5 H), 5.00–4.97 (m, 0.5 H), 4.64 (s, 1 H), 4.63 (d, J = 6.6 Hz, 0.5 H), 4.56 (d, J = 6.6 Hz, 0.5 H), 3.86–3.75 (m, 2 H), 3.36 (s, 1.5 H), 3.36 (s, 1.5 H), 3.28 (dd, J = 13.4, 3.2 Hz, 0.5 H), 2.72 (dd, J = 13.4, 5.4 Hz, 0.5 H), 2.41–2.14 (m, 3 H), 2.09–1.96 (m, 2 H), 1.90–1.84 (m, 1 H), 1.64 (s, 1.5 H), 1.63 (s, 1.5 H), 1.61–1.26 (m, 6 H), 1.13–1.05 (m, 6 H), 1.04–0.98 (m, 1 H), 0.95 (d, J = 6.4 Hz, 1.5 H), 0.92 (d, J = 6.8 Hz, 1.5 H); 13C NMR (100 MHz, CDCl3) δ 165.8, 165.4, 137.9, 137.7, 135.0, 134.5, 132.4, 131.5, 128.3, 128.0, 126.7, 117.8, 115.3, 97.0, 95.9, 76.3, 76.0, 75.4, 74.3, 69.2, 68.8, 55.9, 55.7, 50.2, 48.4, 45.1, 45.1, 44.3, 42.2, 40.9, 40.5, 36.7, 34.9, 29.1, 27.0, 25.9, 25.6, 24.7, 24.4, 24.0, 23.0, 21.3, 20.6, 20.4, 20.3, 16.6; HRMS (ESI–TOF) calcd for C24H40O5Na [M + Na]⁺ 431.2778, found 431.2778.

**Ketone 78.** To a solution of triene 76 (31.7 mg, 77.6 μmol) in toluene (5.1 mL) was added the second-generation Hoveyda–Grubbs catalyst (33) (11.7 mg, 18.7 μmol) at room temperature. After the mixture was stirred at 100 °C for 22 h, the mixture was filtered through short column chromatography (EtOAc). Concentration and column chromatography (hexane/EtOAc = 7:1, 4:1, 1:1) gave butenolide 77 (11.0 mg) and triene 76 (9.9 mg, 31% recovery). Butenolide 77 (11.0 mg) was used for the next step without further purification.

To a solution of alcohol 77 obtained above (11.0 mg) in CH2Cl2 (0.5 mL) were added PhI(OAc)2 (14.0 mg, 43.4 μmol) and TEMPO (1.3 mg, 8.67 μmol) at room temperature. The mixture was stirred at the same temperature for 2 h. Column chromatography (hexane/EtOAc = 5:1) gave ketone 78 (6.2 mg, 21% in two steps, 31% based on recovered 76 in two steps): colorless oil; Rf = 0.61 (hexane/EtOAc = 1:1); [α]D27 +97.0 (c 0.29, CHCl3); IR (neat) 2955, 2920, 2849, 1759, 1705 cm–1; 1H NMR (400 MHz, CDCl3) δ 7.50 (s, 1 H), 5.18 (d, J = 11.2
Hz, 1 H), 4.94 (d, J = 7.2 Hz, 1 H), 4.71 (d, J = 7.2 Hz, 1 H), 4.54 (d, J = 7.2 Hz, 1 H), 3.73 (dd, J = 11.2, 3.2 Hz, 1 H), 3.54 (d, J = 14.8 Hz, 1 H), 3.40 (s, 3 H), 3.22 (d, J = 14.8 Hz, 1 H), 2.51 (dd, J = 12.0, 5.6 Hz, 1 H), 2.31–2.20 (m, 2 H), 2.17–2.05 (m, 4 H), 1.65 (s, 3 H), 1.62–1.44 (m, 4 H), 1.23 (t, J = 6.8 Hz, 3 H), 1.13 (d, J = 7.2 Hz, 3 H), 0.87 (d, J = 6.8 Hz, 3 H); 13C NMR (100 MHz, CDCl 3) δ 205.1, 172.1, 151.8, 131.9, 127.8, 127.7, 94.9, 81.9, 76.9, 55.9, 50.4, 50.1, 41.4, 40.5, 35.4, 29.7, 29.7, 25.8, 25.3, 24.2, 19.9, 18.8, 18.3; HRMS (ESI–TOF) calcd for C22H34O5Na [M + Na]+ 401.2304, found 401.2299.

**Acetate 69.** To a solution of MOM ether 78 (6.2 mg, 16.4 μmol) in i-PrOH (0.5 mL) was added concentrated aqueous HCl (10 μL) at room temperature. After the mixture was stirred at 50 °C for 5 h, the reaction was quenched with saturated aqueous NaHCO3. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and short column chromatography (hexane/EtOAc = 1:1) gave the corresponding alcohol (5.0 mg), which was used for the next step without further purification.

To a solution of the alcohol obtained above (5.0 mg) in CH2Cl2 (0.5 mL) were added pyridine (6.3 μL, 77.5 μmol) and AcCl (4.6 μL, 65.6 μmol) at 0 °C. After the mixture was stirred at the same temperature for 20 min, the reaction was quenched with saturated aqueous NH4Cl. The mixture was diluted with EtOAc, washed with H2O and brine, and then dried over Na2SO4. Concentration and column chromatography (hexane/EtOAc = 4:1) gave acetate 69 (3.7 mg, 60% in two steps): colorless oil; RF = 0.58 (hexane/EtOAc = 1:1); [α]D26 +31.7 (c 0.08, CHCl3); literature10c [α]D20 +32 (c 1.08, CHCl3); IR (neat) 3435, 2922, 2851, 1761, 1733, 1646 cm−1; 1H and 13C NMR Table S14, HRMS (ESI –TOF) calcd for C22H32O5Na [M + Na]+ 399.2148, found 399.2148.

**Cell Growth-Inhibitory Activity.** HL60 cells were cultured at 37 °C with 5% CO2 in RPMI (Nissui, Tokyo, Japan) supplemented with 10% heat-inactivated fetal bovine serum (FBS; Sigma-Aldrich Co., St. Louis, MO), 100 units/mL penicillin, 100 μg/mL streptomycin, 0.25 μg/mL amphotericin, 300 μg/mL L-glutamine, and 2.25 mg/mL NaHCO3. HL60 cells were seeded at 1 × 104 cells/well in 96-well plates (Iwaki, Tokyo, Japan). Various concentrations of the synthetic compounds were then added, and cells were incubated for 72 h. Cell proliferation was measured by the MTT assay.

**Antifouling Activity and Toxicity.** Adult barnacles of Balanus (Amphibalanus) amphitrite were collected at Mega fishing port (Himeji, Hyogo, Japan) and maintained in aquaria at 20 ± 1 °C by feeding with brine shrimp (Artemia salina) nauplii for one week. Cypris larvae of barnacle Balanus (Amphibalanus) amphitrite were obtained by larval culture in the laboratory according to the method reported by Nogata and co-workers.62 Obtained cypris larvae were aged for 2–3 days prior to use at 5 °C. The effects of the synthetic compounds on the barnacle cyprids settlement were tested using 24-well polystyrene plates (Corning, NY, USA) according to our previous report.63 Each compound was dissolved in MeOH. If the compound did not dissolve in MeOH, it was dissolved in a small amount of DMSO. Aliquots of the solution were applied to wells of 24-well polystyrene plates (0.1, 0.3, 1.0, 3.0, 10, and
50 μg) and air-dried. DMSO alone showed no effects on larval settlement at the concentration used in this assay (0.2%). Approximately 10 cypris larvae were added to each well filled with filtered natural seawater (28 psu) at final volume of 1.0 mL. After the incubation at 25 °C in the dark for 96 h, the number of larvae, which settled (including metamorphosed larvae), died, or did not settle, was counted under a microscope. Each level of the experiments was carried out with three wells and the assay was repeated three times. The assay was performed with CuSO₄ (0.01, 0.03, 0.1, 0.3, 1.0, 3.0, and 10 μg) as a positive control. The assay without compound was performed as a control. The antifouling activity and toxicity were expressed as EC₅₀ and LC₅₀ values, respectively. The EC₅₀ and LC₅₀ values were calculated by probit analysis according to Nogata’s report. When probit analysis could not be applied to calculate the values, these were estimated by straight-line graphical interpolation.

Supporting Information
The Supporting Information is available free of charge on the ACS Publications website.
Stereochemical determination of the synthetic products, NMR data comparison of the natural products and the synthetic products, computed geometries and energies of 1a and 1b, and NMR spectra of all compounds (PDF)

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References and Endnotes

Chem. Biodiversity 2013, 10, 2161–2196.


(12) The detailed information on the result of NOE experiments of 7 is not described in reference 10a.


(19) In place of the macrolactonization/transannular RCM sequence, the RCM/lactonization sequence could be applied to construction of the cembranolide framework. However, in the macrolactonization/transannular RCM sequence, there is an advantage that we could control the geometry of the RCM product. Therefore, we selected this strategy.


(22) For the stereochemical determination, see the Supporting Information.


(33) For selected reports of the construction of butenolide units by RCM, see: (a) Tan, M. A.; Kitajima, M.; Kogure, N.; Nonato, M. G.; Takayama, H. Isolation and Total Syntheses of Two New Alkaloids, Dubiusamines-A, and -B, from *Pandanus dubius*. *Tetrahedron* 2010, 66, 3353–3359. (b) Fernandes, R. A.; Chavan, V. P. A 12-Membered to a Strained
11-Membered Ring: First Stereoselective Total Synthesis of (−)-Asteriscunolide C. 

(34) For the total synthesis of (−)-(Z)-deoxypukalide, which is a non-natural furanocembranolide, by utilizing transannular RCM, see: Donohoe, T. J.; Ironmonger, A.; Kershaw, N. M. Synthesis of (−)-(Z)-Deoxypukalide. *Angew. Chem. Int., Ed.* **2008**, *47*, 7314–7316.


(36) The stereoisomers at the C1 and C2 positions of 1a and 1b, which were derived from the minor enantiomer of 15, were separated by silica gel column chromatography at this stage, respectively.

(37) The purity of the synthetic product 1a was confirmed by its NMR spectra. Since we do not have the natural specimen of sarcophytonolide C at present, it is unclear why there is a discrepancy in the absolute values of specific rotations between the synthetic 1a and the natural product.


(39) The minor C6 diastereomer of 2, which was obtained in the reaction of the aldehyde prepared from 25a with 35, was separated in this final stage.

(40) See the Supporting Information for details.


(42) When the sulfone 42 was subjected to Birch conditions, reductive removal of the pivalate moiety was observed as a side reaction. Therefore, the pivaloyl group of 42 was removed prior to desulfonylation by Birch reduction and the side reaction shown above did not occur in this case.


(44) Deprotection of the MOM ether with BF₃∙OEt₂/Me₂S, the deprotection conditions used in the synthesis of 1a, 1b, and 2, gave unknown products and the desired sarcophytonolide F (3) was not obtained.


(54) Souppé, J.; Namy, J. L.; Kagan, H. B. Samarium Diiodide as Coupling Agent between Aldehydes and Organic Halides for the Synthesis of Homoallylic and Homobenzylc


(57) A variety of reaction conditions in macrolactonization of the C14 MOM-protected compound of **65** could not give the desired 15-membered macrolactone. Lactone **66** was selectively obtained by carrying out Shiina lactonization of the dihydroxycarboxylic acid **65** at −5 °C.


(60) For the synthesis, see the Supporting Information.

(61) The observed specific rotation of the synthetic product **4** was different from that of natural sarcophytonolide G. However, the absolute value of the specific rotation reported for the natural product is quite small. Therefore, we have concluded that natural sarcophytonolide G possesses the absolute stereochemistries at the C1 and C2
positions same as those of other sarcophytonolides and the absolute configuration of the natural product is that depicted in 4.

