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Stereodivergent Synthesis and Relative Stereostructure of the C1−C13 Fragment of Symbiodinolide

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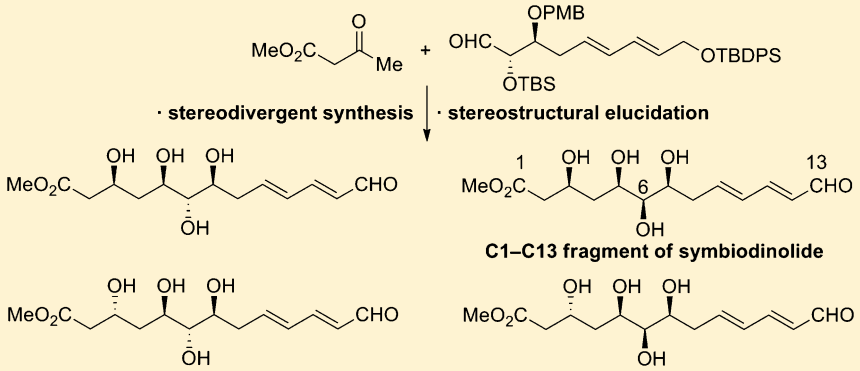
Supporting Information



ABSTRACT: Four possible diastereomers of the C1−C13 fragment of symbiodinolide, which were proposed by the stereostructural analysis of the degraded product, were synthesized in a stereodivergent and stereoselective manner. The key transformations were aldol reaction of methyl acetoacetate with the aldehyde, diastereoselective reduction of the resulting β-hydroxy ketone, and the stereoinversion at the C6 position. Comparison of the ^{1}H NMR data between the four synthetic products and the degraded product revealed the relative stereostructure of the C1−C13 fragment of symbiodinolide.

INTRODUCTION

Integrated use of a spectroscopic method and chemical synthesis is well recognized as a reliable approach to the structural elucidation of natural products.[1] In particular, if the target molecule has a huge molecular size or a number of functional groups, the chemical synthesis is often required for the unambiguous configurational assignment.[2]

Symbiodinolide (**1**, Figure 1), a 62-membered polyol macrolide marine natural product, was isolated from the 80% aqueous ethanol extract of the cultured dinoflagellate *Symbiodinium* sp. by one of the authors (D.U.).[3] This natural product exhibits voltage-dependent N-type Ca^{2+} channel-opening activity at 7 nM and COX-1 inhibition effect at 2 μM (65% inhibition). The planar structure of symbiodinolide (**1**) was assigned by the detailed 2D NMR spectroscopic techniques. However, the stereostructure of **1** has not been elucidated yet because of its complicated molecular structure characterized by 61 stereocenters and molecular weight of 2860. Therefore, we are now examining the degradation of natural symbiodinolide (**1**)[3,4] and chemical synthesis of each fragment including the stereoisomers[5] toward the complete stereochemical establishment of **1**. Previously, as a degradation of symbiodinolide (**1**), we carried out the methanolysis and subsequent oxidative cleavage with Grubbs II catalyst/NaClO to yield the C1−C13 fragment **2** (Scheme 1).[4a,c] Herein, as a part of our efforts toward the complete configurational determination of symbiodinolide (**1**), we describe the stereostructural analysis of the degraded product **2**, and stereodivergent and stereoselective synthesis of all four possible diastereomers of the C1−C13 fragment **2**,[6] which has established the relative stereostructure of this fragment.

RESULTS AND DISCUSSION

Stereochemical Analysis of the Degraded Product 2.

Prior to starting the synthesis of the C1−C13 fragment, we first analyzed the stereostructure of the degraded product **2** to reduce the number of the possible diastereomers of this fragment. As shown in Figure 2a, the chemical shifts of the H-5 and H-7 in the ^{1}H NMR spectrum were the same value (3.97 ppm in D_2O); in addition, the two coupling constants were also the same ($^3J_{5,6}$ and $^3J_{6,7}$ = 4.5 Hz). Comparison of these results with universal NMR databases for 1,2,3-triols reported by Kishi and co-workers[7] indicates that the relative stereochemical relationships at the C5 and C7 positions to the C6 position are the same, that is, *syn*/*syn* or *anti*/*anti*. Thus, the possible

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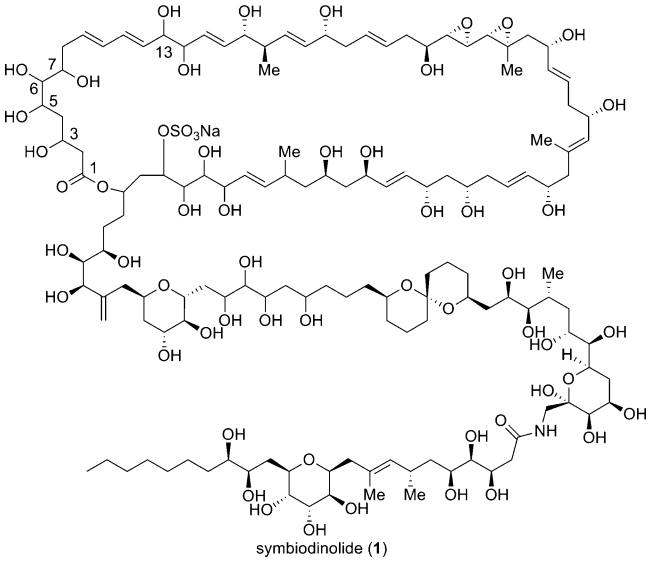
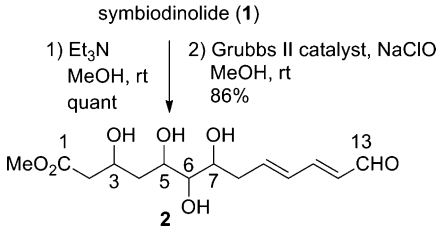


Figure 1. Structure of symbiodinolide (**1**).

Scheme 1. Degradation of Symbiodinolide (1)



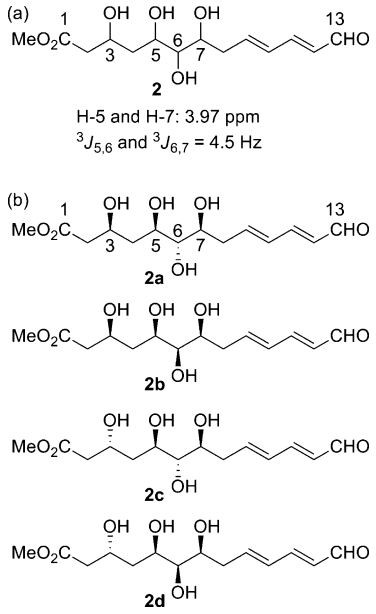


Figure 2. (a) ^{1}H NMR analysis of the degraded product **2**. (b) Four possible diastereomers of the C1−C13 fragment.

diastereomers of the C1−C13 fragment were narrowed down from the eight potential diastereomers and found to be four, which are described as **2a**−**2d** in Figure 2b. We next examined the synthesis of all four of these possible diastereomers **2a**−**2d** in the unified strategy.[8]

Stereodivergent Synthetic Plan of 2a−2b. The unified and stereodivergent synthetic plan of **2a**−**2d** is depicted in Scheme 2. Aldol reaction of methyl acetoacetate (**3**) with aldehyde **4** would provide the coupling product **5** with the desired oxymethine stereochemistry at the C5 position. The substrate-controlled diastereoselective reduction of β-hydroxy ketone **5** by utilizing the resulting C5 stereochemistry with the appropriate reducing reagent could afford *syn*-diol **6** and *anti*-diol **7**, respectively. The *syn*-diol **6** could be transformed to the tetraol **2a** through the deprotection and oxidation of the allylic alcohol. The tetraol **2b** would be also synthesized via the stereoinversion at the C6 position from **6**. In the similar way, the tetraols **2c** and **2d** could be stereoselectively supplied, respectively, by using the *anti*-diol **7** as the common synthetic intermediate.

Stereoselective Synthesis of 2a. We investigated the stereoselective synthesis of the first target molecule **2a**. Parikh−Doering oxidation[9] of the known alcohol **8**, which was prepared from 2-deoxy-D-ribose in four steps,[10] followed by two-carbon elongation with $(EtO)_2P(O)CH_2CO_2Et$ and DIBAL-H reduction, provided allylic alcohol **9** in 77% yield in three steps (Scheme 3). The alcohol **9** was protected as the TBDPS ether, and the regioselective reductive cleavage of the *p*-methoxybenzylidene acetal moiety with DIBAL-H afforded primary alcohol **10**. The alcohol **10** was oxidized to the corresponding aldehyde with SO_3·pry/Et_3N/DMSO.[9] Stereoselective aldol addition of methyl acetoacetate (**3**) to the resulting α,β-bisalkoxy aldehyde by using NaH and *n*-BuLi as bases produced β-hydroxy ketone **11** possessing the desired C5 configuration in 94% yield as the inseparable 6:1 diastereomeric mixture.[11,12] We next tried the derivatization of **11** for the stereochemical confirmation at the C5 position. Thus, removal of the TBDPS protective group with HF·pyr and subsequent oxidation of the allylic alcohol with TEMPO/PhI(OAc)$_2$[13] gave unsaturated aldehyde **12**. Treatment of the alcohol **12** with DDQ provided *p*-methoxybenzylidene acetal **13**.[14] The observed NOEs of Ha/Hb, Ha/Hc, and Hb/Hc in **13**, as shown by arrows, indicated that they were in *syn* relationships. Thereby, the absolute stereochemistry at the C5 position of **11** was unambiguously confirmed. Next, we introduced the C3 oxymethine stereochemistry. Thus, diastereoselective reduction of **11** was carried out with $Et_2BOMe/NaBH_4$[15] to afford *syn*-diol **14** in 98% yield as a single product (Scheme 4). For the stereochemical confirmation at the C3 position, the diol **14** was protected with *p*-$MeOC_6H_4CH(OMe)_2$/CSA to give *p*-methoxybenzylidene acetal **15**. The NOE correlations of Ha/Hb, Ha/Hc, and Hb/Hc in **15** suggested that all of them were oriented in axial positions, respectively. Thus, the absolute configuration at the C3 position of **14** was elucidated.

Next, we examined the transformation of the diol **14** to the tetraol **2a**. Protection of **14** with $Me_2C(OMe)_2$/*p*-TsOH·H_2O gave acetonide **16** (Scheme 5). The TBDPS moiety of **16** was selectively removed with TBAF/AcOH[16] to provide allylic alcohol **17** in 68% yield. TEMPO oxidation[13] of **17** and removal of the PMB group with DDQ afforded unsaturated aldehyde **18** in 94% yield in two steps. The acetonide moiety of **18** was removed with $TiCl_4$[17] in CH_2Cl_2 at −30 °C to afford triol **19** in 98% yield. Finally, treatment of the TBS ether **19** with HF·pyr at 0 °C to room temperature produced the tetraol **2a**. Although we could obtain the first target molecule **2a**, the conversion of **19** to **2a** was quite slow and the starting material **19** was recovered in 52% yield. When the reaction time was prolonged, we observed the formation of several byproducts; furthermore, this transformation was irreproducible. Since this deprotection would be problematic in the subsequent synthesis

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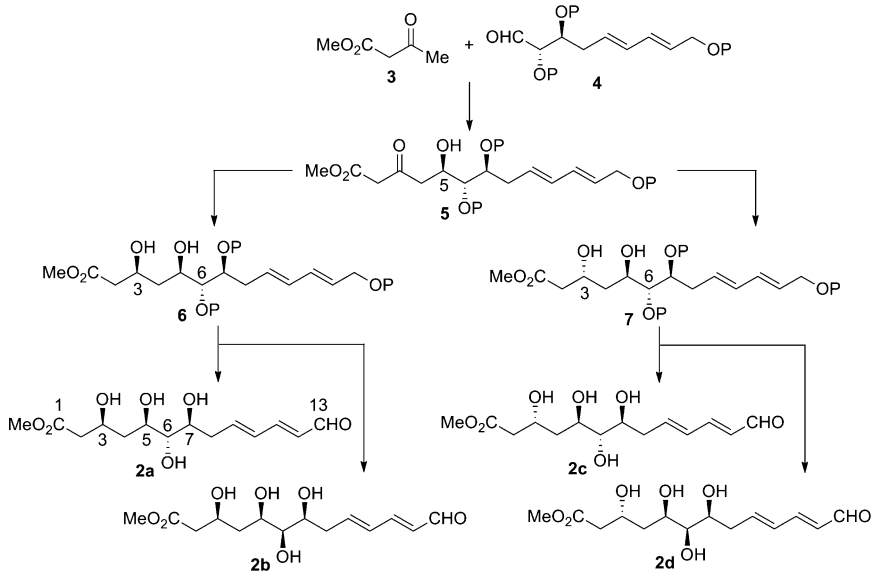
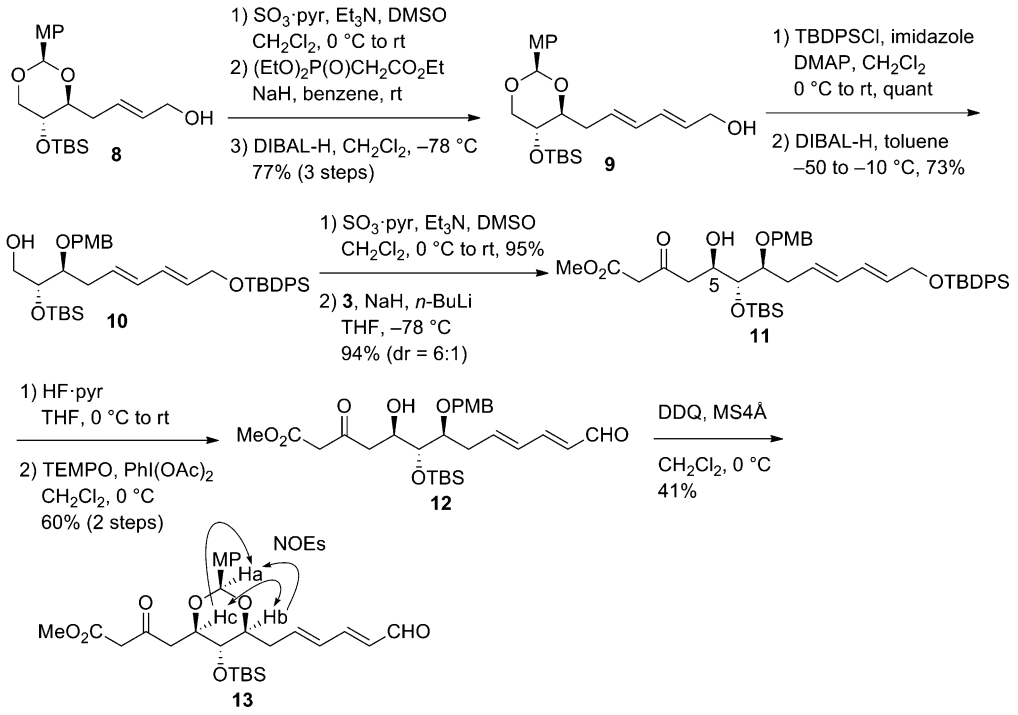
Scheme 2. Stereodivergent Synthetic Plan of 2a−2d



Scheme 3. Synthesis of 11 and Its Stereochemical Confirmation at the C5 Position



of **2b−2d**, a change from the TBS protective group to a less-hindered and more easily removed group in the final step was needed.

Removal of the TBS moiety of **17** was carried out with TBAF/AcOH in MeCN at 60 °C to give diol **20** in 86% yield (Scheme 6).[18] Treatment of **20** with TESOTf/2,6-lutidine, followed by selective removal of the primary TES moiety, provided secondary TES ether **21**. TEMPO oxidation[13] of the allylic alcohol **21** and subsequent removal of the PMB group afforded unsaturated aldehyde **22** in 76% yield in two steps. Finally, when **22** was treated with $TiCl_4$[17] at −30 °C to room temperature, the acetonide deprotection and subsequent removal of the TES moiety proceeded in one-pot to produce the tetraol **2a** in 74% yield.

Stereoselective Synthesis of 2b. We next examined the stereoselective synthesis of the second target molecule **2b**, which is the C6-epimer of **2a**. We envisioned the stereoinversion at the C6 position by the oxidation−reduction process. Thus, selective protection of the primary hydroxy group of the diol **20** with TESCl/imidazole yielded the secondary alcohol, which was subjected to the TPAP oxidation[19] to afford ketone **23** (Scheme 7). Diastereoselective reduction of **23** with $NaBH_4$ proceeded successfully to provide the desired alcohol **24** in 98% yield as the sole diastereomer. This stereochemical outcome is in line with a Felkin−Anh model, which is doubly effected by the C5 and C7 stereogenic centers. The ^1H NMR spectrum of **24** was clearly different from that of the secondary alcohol obtained in the first step

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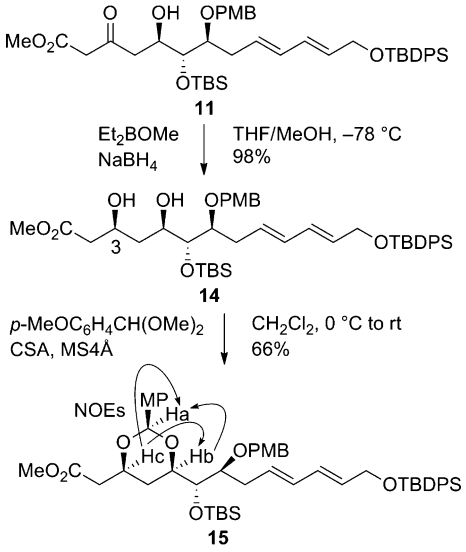
Scheme 4. Synthesis of 14 and Its Stereochemical Confirmation at the C3 Position

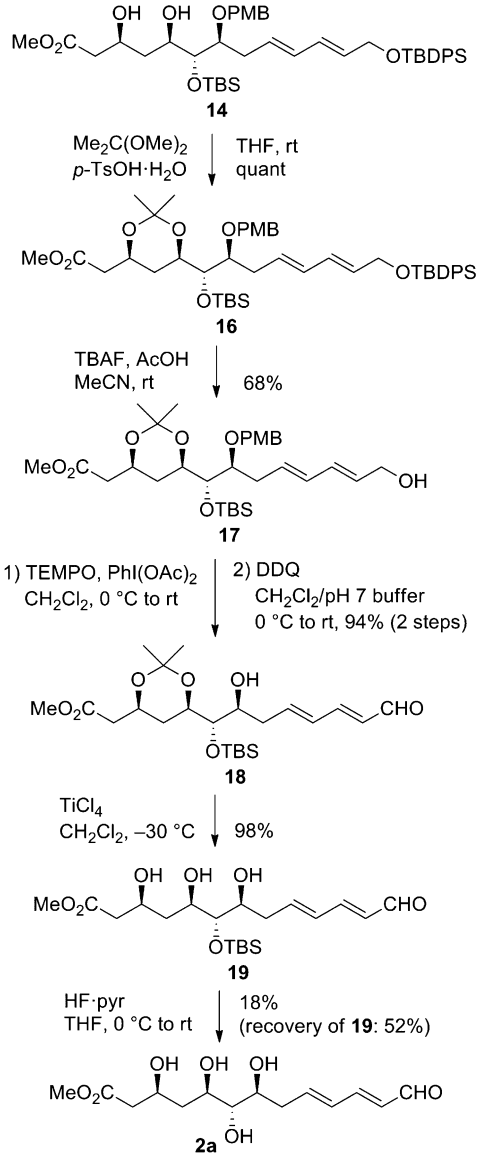


from **20**, which resulted in the configurational confirmation at the C6 stereogenic center of **24**. TES protection of the resulting secondary hydroxy moiety of **24**, followed by selective removal of the primary TES group, yielded alcohol **25**. Oxidation of **25** with TEMPO/PhI(OAc)$_2$[13] and subsequent removal of the PMB group gave unsaturated aldehyde **26** in 82% yield in two steps. Stepwise deprotection of **26**, that is, removal of the acetonide moiety by $TiCl_4$[17] and the TES group by HF·pyr, furnished the second target molecule **2b**.

Stereoselective Synthesis of 2c and 2d. Having completed the stereoselective and stereodivergent synthesis of the first and second target molecules **2a** and **2b** bearing the *syn* relationships at the C3 and C5 positions, we next commenced the synthesis of the third and fourth target molecules **2c** and **2d** with the C3/C5 *anti* correlations. The stereoselective synthesis of **2c** is illustrated in Scheme 8. Treatment of the *β*-hydroxy ketone **11** with NaBH(OAc)$_3$[20] furnished the desired *anti*-diol **27** in 95% yield as a single diastereomer, as judged by its ^{1}H NMR spectrum, which was clearly different from that of the *syn*-diol **14**. Further transformation of **27** toward **2c** was similar to that used in the synthesis of **2a**. Protection of the resulting diol moiety of **27** and desilylation afforded diol **28**. The diol **28** was transformed to unsaturated aldehyde **29** by the following four-step sequence: (1) bis-silylation, (2) selective desilylation of the primary TES moiety, (3) TEMPO oxidation[13] of the allylic alcohol, and (4) removal of the PMB group. Simultaneous removal of the acetonide and TES moieties was performed with $TiCl_4$[17] to provide the third target molecule **2c** in 44% yield.

The stereocontrolled synthesis of **2d**, whose synthetic route was analogous to that of **2b**, is shown in Scheme 9. The alcohol **28**, which was the key synthetic intermediate toward **2c**, was converted to ketone **30** through the selective silylation of the primary alcohol and TPAP oxidation[19] of the secondary alcohol. The ketone **30** was reduced with $NaBH_4$ to give alcohol **31** as the sole diastereomer. The resulting stereochemistry at the C6 position of **31** was confirmed by comparing the ^{1}H NMR spectra between **31** and the secondary alcohol synthesized in the first transformation from **28**. Acetonide **32**, which was synthesized from the alcohol **31** in 54% overall yield

Scheme 5. Synthesis of 2a



in four steps, was deprotected with $TiCl_4$[17] to provide the fourth target molecule **2d** in 47% yield.

Relative Stereostructure of the C1−C13 Fragment. With all four possible diastereomers **2a**−**2d** in hand, we next compared these ^{1}H NMR data with those of the degraded product **2**. As described in Table 1, the ^{1}H NMR chemical shifts of the synthetic **2b** were found to be in full agreement with those of the degraded product **2**.[21] On the other hand, the ^{1}H NMR chemical shifts of the synthetic **2a**, **2c**, and **2d** were clearly different from those of the degraded product **2**, respectively. Especially, the chemical shifts of two geminal protons at the C4 position of **2a**, **2c**, and **2d** were different to each other, respectively, whereas the chemical shifts of these protons of **2** and **2b** were found to be the same. Therefore, the relative stereostructure of the C1−C13 fragment of symbiodinolide (**1**) was elucidated to be that described in **2b**.

■ CONCLUSION

First, we have analyzed the ^{1}H NMR chemical shifts and coupling constants of the degraded product **2** obtained from natural symbiodinolide (**1**) and proposed its four possible

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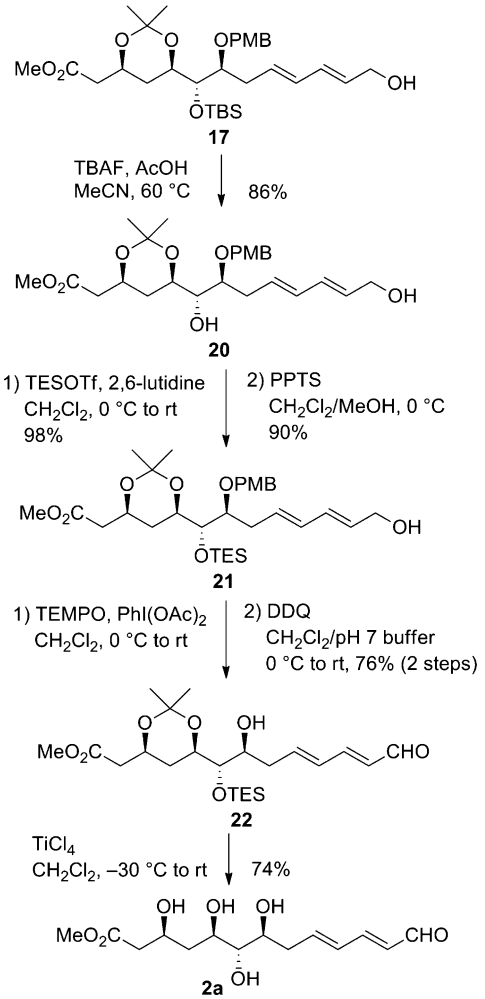
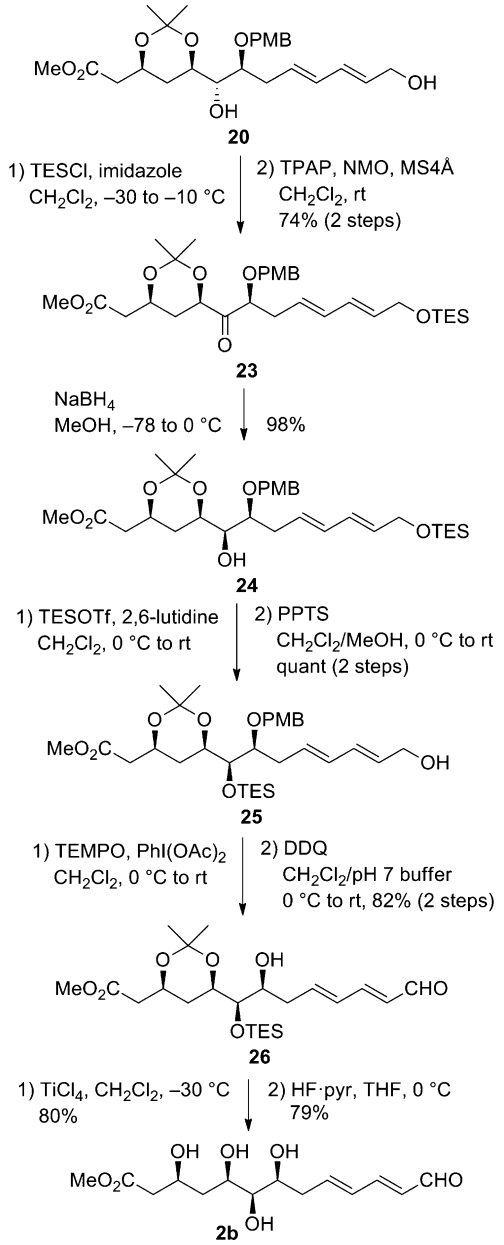
Scheme 6. Improved Synthesis of 2a



Scheme 7. Synthesis of 2b



diastereomers **2a**–**2d** by comparing with the universal NMR databases reported by Kishi's research group. Next, we have examined the stereodivergent synthesis of **2a**–**2d** in the unified manner. Thus, the *β*-hydroxy ketone **11**, which would be the key common synthetic intermediate of **2a**–**2d**, was synthesized by aldol reaction between methyl acetoacetate (**3**) and the aldehyde derived from **10**. Diastereoselective reduction of **11** provided the *syn*-diol **14** (by $Et_2BOMe/NaBH_4$) and the *anti*-diol **27** (by $NaBH(OAc)_3$), respectively. Deprotection and oxidation of the allylic alcohol moiety of **14** produced the first target molecule **2a**. The second target molecule **2b** was synthesized via the stereoinversion at the C6 position by diastereoselective reduction of the ketone **23**. In the similar synthetic route, the third and fourth target molecules **2c** and **2d** were yielded from the *anti*-diol **27**, respectively and stereoselectively. Comparison of the ^1H NMR data of the synthetic **2a**–**2d** with those of the degraded product **2** determined the relative stereochemistry of the C1–C13 fragment of symbiodinolide (**1**) to be depicted in **2b**.

EXPERIMENTAL SECTION

Allylic Alcohol 9. To a solution of allylic alcohol **8** (5.04 g, 12.8 mmol) in CH_2Cl_2 (51 mL) and DMSO (13 mL) were added Et_3N (7.8 mL, 56.3 mmol) and SO_3·pyr (4.07 g, 25.6 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h. The mixture was diluted with EtOAc, washed with saturated aqueous NH_4Cl, H_2O, and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 10:1) gave the corresponding *α*,*β*-unsaturated aldehyde (4.53 g), which was used for the next reaction without further purification.

To a suspension of NaH (60% dispersion in oil, 1.11 g, 27.8 mmol, washed with hexane in advance) in benzene (15 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (6.0 mL, 30.2 mmol) at 0 °C. After the mixture was stirred at room temperature for 15 min, the aldehyde obtained above (4.53 g) in benzene (10 mL + 6.0 mL + 4.0 mL) was added at room temperature. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with H_2O 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 = 20:1) gave the corresponding *α*,*β*-unsaturated ester (4.85 g), which was used for the next reaction without further purification.

To a solution of the ester obtained above (4.85 g) in CH_2Cl_2 (50 mL) was added DIBAL-H (1.04 M solution in hexane, 20 mL, 20.8 mmol) at −78 °C. After the mixture was stirred at −78 °C for 30 min, the reaction was quenched with MeOH. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and

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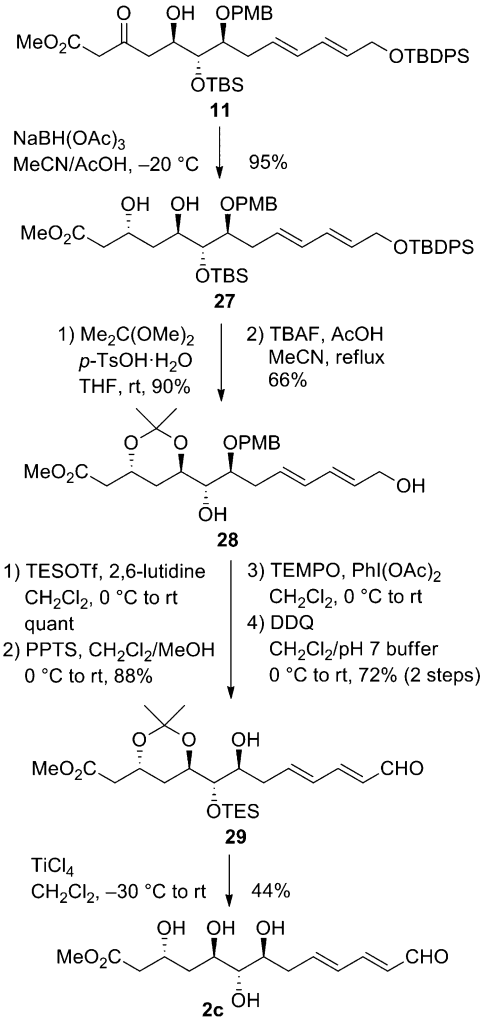
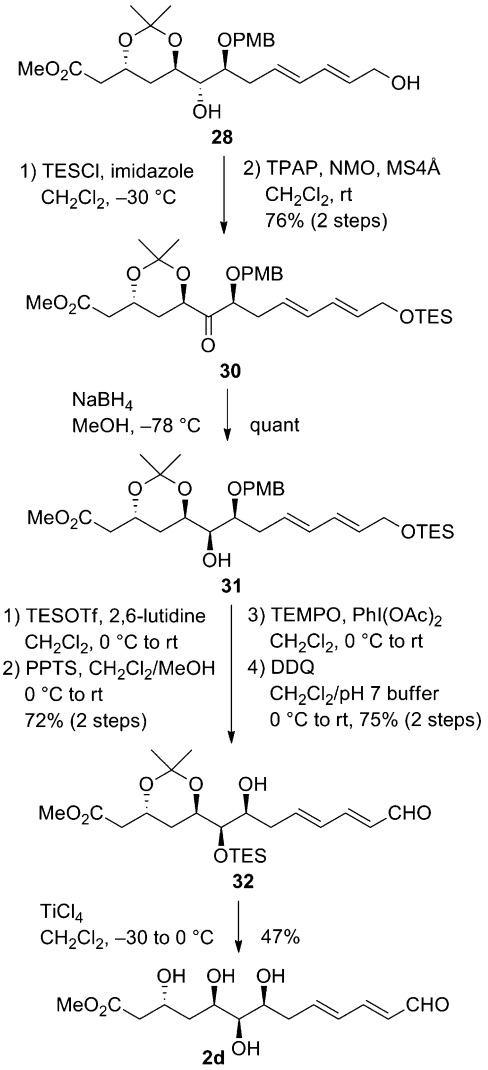
Scheme 8. Synthesis of 2c



Scheme 9. Synthesis of 2d



column chromatography (hexane/EtOAc = 4:1) gave allylic alcohol **9** (4.11 g, 77% in three steps) as a colorless oil: R_f = 0.19 (hexane/EtOAc = 4:1); $[\alpha]_D^{25}$ −60.6 (*c* 0.92, $CHCl_3$); IR (neat) 3427, 2929, 2856, 1615 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 2 H), 6.88 (d, *J* = 8.5 Hz, 2 H), 6.28−6.11 (m, 2 H), 5.85 (dt, *J* = 15.0, 6.6 Hz, 1 H), 5.75 (dt, *J* = 15.0, 6.6 Hz, 1 H), 5.43 (s, 1 H), 4.19−4.16 (m, 3 H), 3.80 (s, 3 H), 3.60−3.57 (m, 3 H), 2.64 (dd, *J* = 14.4, 6.6 Hz, 1 H), 2.36 (dd, *J* = 14.4, 6.6 Hz, 1 H), 1.30−1.25 (m, 1 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 131.7, 130.5, 130.4, 130.0, 127.6, 127.3, 113.5, 100.7, 81.9, 71.7, 66.2, 63.5, 55.3, 34.8, 25.8, 18.0, −4.0, −4.6; HRMS (ESI−TOF) calcd for $C_{23}H_{36}O_5SiNa$ $[M + Na]^+$ 443.2230, found 443.2236.

Alcohol 10. To a solution of alcohol **9** (234 mg, 0.558 mmol) in CH_2Cl_2 (5.0 mL) were added DMAP (107 mg, 0.873 mmol), imidazole (59.6 mg, 0.873 mmol), and TBDPSCl (0.17 mL, 0.670 mmol) at 0 °C. After the mixture was stirred at room temperature for 20 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 50:1, 10:1) gave the corresponding TBDPS ether (400 mg, quant) as a colorless oil: R_f = 0.76 (hexane/EtOAc = 2:1); $[\alpha]_D^{24}$ −33.7 (*c* 0.95, $CHCl_3$); IR (neat) 2930, 2844, 1615 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.69 (m, 4 H), 7.45−7.37 (m, 8 H), 6.91 (dd, *J* = 8.6, 1.8 Hz, 2 H), 6.32−6.14 (m, 2 H), 5.87 (dt, *J* = 14.9, 7.8 Hz, 1 H), 5.71 (dt, *J* = 14.9, 4.9 Hz, 1 H), 5.47 (s, 1 H), 4.26 (d, *J* = 4.9 Hz, 2 H), 4.19 (dt, *J* = 8.6, 2.0 Hz, 1 H), 3.82 (s, 3 H), 3.64−3.56 (m, 3 H), 2.67 (dd, *J* = 14.9, 6.9 Hz, 1 H), 2.42−2.39 (m, 1 H), 1.10 (s, 9 H), 0.94 (s, 9 H), 0.14 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (100

Table 1. ^1H NMR Chemical Shifts of the Degraded Product 2 and the Synthetic Products 2a−2d[a]

position	2[b]	2a[c]	2b[c]	2c[c]	2d[c]
1-CO_2Me	3.67	3.67	3.67	3.67	3.67
2	2.56	2.56	2.56	2.49	2.48
	2.44	2.44	2.44	2.49	2.48
3	4.21	4.31	4.22	4.31	4.27
4	1.75	1.85	1.75	1.78	1.70
	1.75	1.70	1.75	1.60	1.59
5	3.88	3.84	3.89	3.91	3.93
6	3.33	3.39	3.32	3.39	3.23
7	3.81	3.72	3.80	3.73	3.82
8	2.52	2.61	2.52	2.62	2.52
	2.48	2.40	2.47	2.42	2.48
9	6.47	6.48	6.47	6.50	6.49
10	6.47	6.48	6.47	6.50	6.49
11	7.29	7.29	7.29	7.30	7.29
12	6.09	6.08	6.09	6.08	6.09
13-CHO	9.49	9.49	9.49	9.49	9.49

[a]Chemical shifts are reported in ppm with reference to the solvent signal (CD_3OD, 3.30 ppm). [b]Recorded at 800 MHz. [c]Recorded at 600 MHz.

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MHz, $CDCl_3$) δ 159.8, 135.5, 135.5, 135.4, 133.7, 132.1, 130.4, 129.9, 129.5, 129.3, 127.6, 127.6, 127.3, 113.5, 100.7, 82.0, 71.7, 66.2, 64.2, 55.3, 34.9, 26.9, 25.8, 19.3, 18.0, −4.0, −4.6; HRMS (ESI−TOF) calcd for $C_{39}H_{54}O_5Si_2Na$ $[M + Na]^+$ 681.3408, found 681.3398.

To a solution of the corresponding *p*-methoxybenzylidene acetal (610 mg, 0.926 mmol) in toluene (19 mL) was added DIBAL-H (1.04 M solution in hexane, 5.4 mL, 5.55 mmol) at −50 °C. After the mixture was gradually warmed up to −10 °C for 2 h, 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, 7:1, 4:1) gave alcohol **10** (447 mg, 73%) as a colorless oil and the acetal (70.0 mg, 12% recovery). Alcohol **10**: R_f = 0.73 (hexane/EtOAc = 2:1); $[\alpha]_D^{23}$ −14.1 (*c* 1.00, $CHCl_3$); IR (neat) 3476, 2930, 2864 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71−7.68 (m, 4 H), 7.45−7.26 (m, 8 H), 6.89 (d, *J* = 8.6 Hz, 2 H), 6.27 (dd, *J* = 15.0, 10.6 Hz, 1 H), 6.14 (dd, *J* = 15.0, 10.6 Hz, 1 H), 5.73−5.68 (m, 2 H), 4.55 (s, 2 H), 4.26 (d, *J* = 4.2 Hz, 2 H), 3.79 (s, 3 H), 3.79−3.55 (m, 4 H), 2.52−2.46 (m, 1 H), 2.39−2.33 (m, 1 H), 2.21 (brs, 1 H), 1.08 (s, 9 H), 0.93 (s, 9 H), 0.12 (s, 3 H), 0.11 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 135.4, 133.7, 132.3, 130.4, 130.3, 129.9, 129.7, 129.5, 127.6, 113.8, 80.4, 74.0, 72.5, 64.2, 55.3, 34.5, 26.9, 25.9, 19.3, 18.1, −4.3, −4.5; HRMS (ESI−TOF) calcd for $C_{39}H_{56}O_5Si_2Na$ $[M + Na]^+$ 683.3564, found 683.3555.

β-Hydroxy Ketone 11. To a solution of alcohol **10** (79.3 mg, 0.148 mmol) in CH_2Cl_2 (1.0 mL) and DMSO (0.3 mL) were added Et_3N (0.10 mL, 0.740 mmol) and SO_3·pyr (94.2 mg, 0.592 mmol) at 0 °C. The mixture was stirred at room temperature for 2 h. 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 = 20:1) gave the corresponding aldehyde (75.4 mg, 95%) as a colorless oil: R_f = 0.70 (hexane/EtOAc = 2:1) $[\alpha]_D^{21}$ −14.1 (*c* 1.06, $CHCl_3$); IR (neat) 2931, 2858, 1739 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.60 (s, 1 H), 7.73−7.68 (m, 4 H), 7.44−7.36 (m, 6 H), 7.25 (d, *J* = 8.3 Hz, 2 H), 6.87 (d, *J* = 8.3 Hz, 2 H), 6.27−6.10 (m, 2 H), 5.70 (dt, *J* = 14.4, 4.6 Hz, 1 H), 5.55 (dt, *J* = 14.4, 6.8 Hz, 1 H), 4.58−4.49 (m, 2 H), 4.25 (d, *J* = 4.6 Hz, 2 H), 4.14−4.12 (m, 1 H), 3.80 (s, 3 H), 3.73−3.69 (m, 1 H), 2.43 (t, *J* = 6.8 Hz, 2 H), 1.08 (s, 9 H), 1.00 (s, 9 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 159.1, 135.4, 133.6, 133.2, 131.0, 130.0, 129.5, 129.4, 128.6, 127.6, 113.7, 80.8, 79.0, 71.9, 64.2, 55.3, 33.9, 26.9, 25.8, 19.3, 18.3, −4.6, −4.7; HRMS (ESI−TOF) calcd for $C_{39}H_{54}O_5Si_2Na$ $[M + Na]^+$ 681.3408, found 681.3410.

To a suspension of NaH (60% dispersion in oil, 19.7 mg, 0.493 μmol, washed with hexane in advance) in THF (1.0 mL) was added methyl acetoacetate (**3**) (29.5 μL, 0.247 mmol) at 0 °C. After the mixture was stirred at 0 °C for 20 min, *n*-BuLi (1.57 M solution in hexane, 0.19 mL, 0.301 mmol) was added at 0 °C. After the mixture was stirred at 0 °C for 10 min, the corresponding aldehyde (90.3 mg, 0.137 mmol) in THF (0.3 mL + 0.2 mL) was added at −78 °C. After the mixture was stirred at −78 °C for 15 min, the reaction was quenched with saturated aqueous NH_4Cl. 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) gave β-hydroxy ketone **11** (100 mg, 94%, dr = 6:1) as a colorless oil: R_f = 0.21 (hexane/EtOAc = 4:1); $[\alpha]_D^{22}$ +2.2 (*c* 1.00, $CHCl_3$); IR (neat) 3517, 2930, 2856, 1748, 1715 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.80−7.78 (m, 4 H), 7.23−7.22 (m, 8 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 6.42 (dd, *J* = 15.0, 10.6 Hz, 1 H), 6.22 (dd, *J* = 15.0, 10.6 Hz, 1 H), 5.84 (dt, *J* = 15.0, 7.4 Hz, 1 H), 5.69 (dt, *J* = 15.0, 5.1 Hz, 1 H), 4.41 (d, *J* = 4.6 Hz, 2 H), 4.32−4.28 (m, 1 H), 4.24 (d, *J* = 4.6 Hz, 2 H), 3.87 (t, *J* = 4.6 Hz, 1 H), 3.62−3.58 (m, 1 H), 3.32 (s, 3 H), 3.26 (s, 3 H), 3.03 (s, 2 H), 2.80−2.78 (m, 1 H), 2.74 (d, *J* = 2.8 Hz, 1 H), 2.69−2.61 (m, 1 H), 2.50−2.45 (m, 2 H), 1.19 (s, 9 H), 1.01 (s, 9 H), 0.19 (s, 3 H), 0.18 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 203.3, 159.8, 135.9, 134.2, 132.6, 130.9, 130.8, 130.5, 129.9, 114.1, 79.9, 77.1, 72.1, 69.0, 64.7, 54.9, 51.8, 49.8, 45.6, 34.0, 27.2, 26.5, 19.6, 18.7, −3.9, −4.0; HRMS (ESI−TOF) calcd for $C_{44}H_{62}O_8Si_2Na$ $[M + Na]^+$ 797.3881, found 797.3875.

Unsaturated Aldehyde 12. To a solution of TBDPS ether **11** (27.9 mg, 36.0 μmol) in THF (3.6 mL) was added HF·pyr (100 μL) at 0 °C. The mixture was stirred at 0 °C for 1 h. After the mixture was stirred at room temperature for 6 h, HF·pyr (100 μL) was added at 0 °C. The mixture was stirred at 0 °C for 1 h. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, H_2O, and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 10:1, 2:1) gave the corresponding alcohol (15.4 mg), which was used for the next reaction without further purification.

To a solution of the alcohol obtained above (15.4 mg) in CH_2Cl_2 (3.0 mL) were added $PhI(OAc)_2$ (25.0 mg, 77.8 μmol) and TEMPO (0.48 mg, 3.10 μmol) at 0 °C. After the mixture was stirred at 0 °C for 6 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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 = 4:1) gave unsaturated aldehyde **12** (11.6 mg, 60% in two steps) as a colorless oil: R_f = 0.43 (hexane/EtOAc = 1:1); $[\alpha]_D^{25}$ −1.8 (*c* 0.10, $CHCl_3$); IR (neat) 3483, 2927, 2855, 1747, 1682, 1638 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.8 Hz, 1 H), 7.21 (d, *J* = 8.3 Hz, 2 H), 7.03 (dd, *J* = 15.2, 10.2 Hz, 1 H), 6.86 (d, *J* = 8.3 Hz, 2 H), 6.38−6.32 (m, 1 H), 6.28−6.20 (m, 1 H), 6.12−6.04 (m, 1 H), 4.52 (d, *J* = 11.5 Hz, 1 H), 4.42 (d, *J* = 11.5 Hz, 1 H), 4.17−4.11 (m, 1 H), 3.80 (s, 3 H), 3.74 (s, 3 H), 3.44 (s, 2 H), 2.91−2.85 (m, 1 H), 2.74−2.67 (m, 1 H), 2.50 (t, *J* = 6.2 Hz, 2 H), 0.91 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 193.6, 167.1, 159.3, 152.1, 143.3, 130.5, 130.3, 129.6, 113.8, 78.9, 76.0, 71.9, 68.6, 55.3, 52.4, 49.7, 45.8, 34.0, 26.1, 18.3, −4.0, −4.4; HRMS (ESI−TOF) calcd for $C_{28}H_{42}O_8SiNa$ $[M + Na]^+$ 557.2546, found 557.2552.

***p*-Methoxybenzylidene Acetal 13.** To a suspension of alcohol **12** (5.9 mg, 11.0 μmol) and MS4 Å (10.0 mg) in CH_2Cl_2 (0.5 mL) was added DDQ (3.7 mg, 16.5 μmol) at 0 °C. After the mixture was stirred at 0 °C for 1 h, the mixture was filtered through a Celite pad and washed with EtOAc. The mixture was washed with saturated aqueous $NaHCO_3$ and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 5:1) gave *p*-methoxybenzylidene acetal **13** (2.4 mg, 41%) as a colorless oil: R_f = 0.47 (hexane/EtOAc = 2:1); $[\alpha]_D^{25}$ −27.6 (*c* 0.09, $CHCl_3$); IR (neat) 2925, 2854, 1732, 1682, 1642 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 9.38 (d, *J* = 7.8 Hz, 1 H), 7.41 (d, *J* = 8.8 Hz, 2 H), 6.78 (d, *J* = 8.8 Hz, 2 H), 6.44−6.37 (m, 1 H), 6.05−6.01 (m, 2 H), 5.92 (dd, *J* = 15.4, 7.8 Hz, 1 H), 5.28 (s, 1 H), 3.86−3.80 (m, 1 H), 3.50−3.45 (m, 2 H), 3.34−3.20 (m, 4 H), 3.31 (s, 3 H), 3.18 (s, 3 H), 2.61−2.58 (m, 1 H), 2.29−2.22 (m, 1 H), 1.00 (s, 9 H), 0.09 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 192.2, 164.4, 160.8, 159.9, 150.3, 140.1, 131.4, 130.3, 130.0, 114.0, 109.0, 100.9, 81.0, 79.1, 71.6, 54.9, 52.1, 35.8, 31.7, 26.1, 26.0, 18.4, −3.2, −3.4; HRMS (ESI−TOF) calcd for $C_{28}H_{40}O_8SiNa$ $[M + Na]^+$ 555.2390, found 555.2383.

Diol 14. To a solution of β-hydroxy ketone **11** (311 mg, 0.401 mmol) in THF (8.6 mL) and MeOH (2.1 mL) was added Et_2BOMe (0.48 mL, 0.481 mmol) at −78 °C. After the mixture was stirred at −78 °C for 15 min, $NaBH_4$ (18.2 mg, 0.481 mmol) was added. After the mixture was stirred at −78 °C for 1 h, the reaction was quenched with AcOH. The mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ and brine, and then dried over Na_2SO_4. Addition of MeOH (10 mL) to the mixture and concentration (five times repetition), and column chromatography (hexane/EtOAc = 5:1) gave diol **14** (304 mg, 98%) as a colorless oil: R_f = 0.45 (hexane/EtOAc = 2:1); $[\alpha]_D^{25}$ −2.5 (*c* 1.00, $CHCl_3$); IR (neat) 3464, 2930, 2857, 1739, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.80−7.79 (m, 4 H), 7.25−7.22 (m, 8 H), 6.81 (d, *J* = 8.5 Hz, 2 H), 6.43 (dd, *J* = 15.1, 10.5 Hz, 1 H), 6.28 (dd, *J* = 15.1, 10.5 Hz, 1 H), 5.94 (dt, *J* = 15.1, 7.1 Hz, 1 H), 5.74 (dt, *J* = 15.1, 5.1 Hz, 1 H), 4.45 (d, *J* = 4.2 Hz, 2 H), 4.24 (d, *J* = 4.2 Hz, 2 H), 4.07−3.98 (m, 1 H), 3.88−3.75 (m, 2 H), 3.65−3.54 (m, 1 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 2.63−2.60 (m, 2 H), 2.44 (t, *J* = 5.1 Hz, 1 H), 2.25 (dd, *J* = 16.3, 8.5 Hz, 1 H), 2.12 (dd, *J* = 16.3, 3.6 Hz, 1 H), 1.78−1.59 (m, 2 H), 1.20 (s, 9 H), 1.03 (s, 9 H), 0.26 (s, 3 H), 0.20 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 172.6, 159.7, 135.9, 134.2, 132.9, 132.4, 131.4, 131.1, 130.7, 130.5, 130.2, 129.9, 114.0, 79.9, 77.7, 73.6, 72.1, 69.6, 64.7, 54.8, 51.2, 41.8, 38.6,

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33.9, 27.2, 26.6, 19.6, 18.8, −3.7, −3.9; HRMS (ESI−TOF) calcd for $C_{44}H_{64}O_8Si_2Na$ $[M + Na]^+$ 799.4037, found 799.4037.

***p*-Methoxybenzylidene Acetal 15.** To a suspension of diol **14** (5.3 mg, 6.82 μmol) and MS4 Å (5.0 mg) in CH_2Cl_2 (0.5 mL) were added *p*-$MeOC_6H_4CH(OMe)_2$ (1.7 μL, 10.2 μmol) and CSA (1.0 mg, 4.30 μmol) at 0 °C. The mixture was stirred at room temperature for 4 h. To the mixture were added *p*-$MeOC_6H_4CH(OMe)_2$ (1.7 μL, 10.2 μmol) and CSA (1.0 mg, 4.30 μmol) at 0 °C. After the mixture was stirred at room temperature for a further 12 h, the reaction was quenched with Et_3N. The mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 10:1) gave *p*-methoxybenzylidene acetal **15** (4.0 mg, 66%) as a colorless oil: R_f = 0.44 (hexane/EtOAc = 4:1); $[\alpha]_D^{25}$ −16.3 (*c* 0.09, $CHCl_3$); IR (neat) 2928, 2855, 1741, 1614 cm^{-1}; ^1H NMR (400 MHz, C_5D_5N) δ 7.85−7.83 (m, 5 H), 7.65 (d, *J* = 8.5 Hz, 2 H), 7.47−7.44 (m, 6 H), 7.04−7.01 (m, 5 H), 6.55 (dd, *J* = 15.1, 10.4 Hz, 1 H), 6.38 (dd, *J* = 15.1, 10.4 Hz, 1 H), 6.00 (dt, *J* = 15.1, 7.3 Hz, 1 H), 5.86 (dt, *J* = 15.1, 4.8 Hz, 1 H), 5.73 (s, 1 H), 4.62 (s, 2 H), 4.54−4.47 (m, 1 H), 4.36 (d, *J* = 4.8 Hz, 2 H), 4.29−4.24 (m, 1 H), 4.17 (t, *J* = 4.8 Hz, 1 H), 3.88−3.84 (m, 1 H), 3.68 (s, 3 H), 3.64 (s, 3 H), 3.63 (s, 3 H), 2.89 (dd, *J* = 15.1, 7.3 Hz, 1 H), 2.76−2.64 (m, 2 H), 1.93−1.80 (m, 2 H), 1.25−1.23 (m, 1 H), 1.13 (s, 9 H), 1.01 (s, 9 H), 0.24 (s, 6 H); ^{13}C NMR (100 MHz, C_5D_5N) δ 171.1, 160.3, 159.7, 135.9, 135.0, 134.2, 132.4, 131.9, 131.5, 131.2, 130.8, 130.7, 130.2, 128.3, 128.2, 123.0, 114.2, 113.9, 101.2, 79.1, 77.5, 76.5, 73.8, 71.7, 64.8, 55.3, 51.6, 41.5, 33.5, 32.5, 27.1, 26.5, 19.6, 18.8, −3.7, −3.9; HRMS (ESI−TOF) calcd for $C_{52}H_{70}O_9Si_2Na$ $[M + Na]^+$ 917.4456, found 917.4457.

Acetonide 16. To a solution of diol **14** (202 mg, 0.260 mmol) in THF (2.6 mL) were added $Me_2C(OMe)_2$ (0.32 mL, 2.26 mmol) and *p*-TsOH·H_2O (4.9 mg, 26.0 μmol) at room temperature. After the mixture was stirred at room temperature for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 7:1) gave acetonide **16** (212 mg, quant) as a colorless oil: R_f = 0.62 (hexane/EtOAc = 2:1); $[\alpha]_D^{22}$ −8.2 (*c* 1.25, $CHCl_3$); IR (neat) 2929, 2858, 1741 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, *J* = 7.6, 1.4 Hz, 4 H), 7.44−7.36 (m, 6 H), 7.25 (d, *J* = 8.6 Hz, 2 H), 6.86 (d, *J* = 8.6 Hz, 2 H), 6.25 (dd, *J* = 15.1, 10.5 Hz, 1 H), 6.11 (dd, *J* = 15.1, 10.5 Hz, 1 H), 5.76−5.65 (m, 2 H), 4.47 (s, 2 H), 4.25−4.24 (m, 3 H), 3.97 (ddd, *J* = 7.3, 4.9, 2.4 Hz, 1 H), 3.79 (s, 3 H), 3.70−3.68 (m, 1 H), 3.68 (s, 3 H), 3.52−3.48 (m, 1 H), 2.54 (dd, *J* = 15.1, 7.3 Hz, 1 H), 2.42−2.33 (m, 3 H), 1.48−1.35 (m, 2 H), 1.41 (s, 3 H), 1.37 (s, 3 H), 1.08 (s, 9 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 159.1, 135.5, 133.7, 131.7, 130.7, 130.1, 130.0, 129.6, 129.5, 129.3, 127.6, 113.6, 98.7, 78.8, 76.4, 71.6, 69.3, 66.0, 64.3, 55.3, 51.6, 41.6, 33.5, 31.7, 29.9, 26.9, 26.2, 19.8, 19.3, 18.5, −4.0, −4.3; HRMS (ESI−TOF) calcd for $C_{47}H_{68}O_8Si_2Na$ $[M + Na]^+$ 839.4351, found 839.4358.

Allylic Alcohol 17. To a solution of TBDPS ether **16** (174 mg, 0.213 mmol) in MeCN (2.2 mL) was added a mixed solution of TBAF (1.0 M solution in THF, 0.26 mL, 0.260 mmol) and AcOH (15 μL, 0.256 mmol) at room temperature. After the mixture was stirred at room temperature for 5 h, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 10:1, 2:1) gave allylic alcohol **17** (84.8 mg, 68%) as a colorless oil: R_f = 0.33 (hexane/EtOAc = 2:1); $[\alpha]_D^{23}$ −5.5 (*c* 0.98, $CHCl_3$); IR (neat) 3459, 2952, 2858, 1740, 1612 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8.8 Hz, 2 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 6.20 (dd, *J* = 15.3, 10.6 Hz, 1 H), 6.08 (dd, *J* = 15.3, 10.6 Hz, 1 H), 5.76−5.70 (m, 2 H), 4.45 (s, 2 H), 4.24−4.16 (m, 4 H), 3.94 (ddd, *J* = 12.6, 4.9, 2.4 Hz, 1 H), 3.80 (s, 3 H), 3.68 (s, 3 H), 3.48 (dt, *J* = 7.1, 4.4 Hz, 1 H), 2.53 (dd, *J* = 15.3, 7.1 Hz, 1 H), 2.38−2.33 (m, 3 H), 1.47 (dt, *J* = 12.6, 2.4 Hz, 1 H), 1.40 (s, 3 H), 1.36 (s, 3 H), 1.28−1.24 (m, 1 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 159.0, 131.9, 131.7, 131.3, 130.6, 129.8, 129.6, 113.6, 98.7, 78.7, 76.3, 71.6, 69.3, 65.9, 63.5, 55.3, 51.6, 41.6, 33.4, 31.7, 29.9, 26.2, 19.8, 18.5, −4.0, −4.3; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3169.

Alcohol 18. To a solution of alcohol **17** (102 mg, 0.176 mmol) in CH_2Cl_2 (2.0 mL) were added $PhI(OAc)_2$ (146 mg, 0.440 mmol) and TEMPO (5.5 mg, 35.2 μmol) at 0 °C. After the mixture was stirred at room temperature for 1 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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) gave the corresponding unsaturated aldehyde (102 mg), which was used for the next reaction without further purification.

To a solution of the PMB ether obtained above (102 mg) in CH_2Cl_2 (4.0 mL) and phosphate pH standard solution (0.2 mL) was added DDQ (47.9 mg, 0.211 mmol) at 0 °C. After the mixture was stirred at room temperature for 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 3:1) gave alcohol **18** (76.0 mg, 94% in two steps) as a colorless oil: R_f = 0.52 (hexane/EtOAc = 1:1); $[\alpha]_D^{23}$ −14.4 (*c* 0.97, $CHCl_3$); IR (neat) 3490, 2953, 2858, 1739, 1681, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.8 Hz, 1 H), 7.09 (dd, *J* = 15.3, 9.9 Hz, 1 H), 6.43−6.31 (m, 2 H), 6.10 (dd, *J* = 15.3, 7.8 Hz, 1 H), 4.34−4.27 (m, 1 H), 4.03 (ddd, *J* = 8.0, 5.4, 2.4 Hz, 1 H), 3.81−3.76 (m, 1 H), 3.68 (s, 3 H), 3.53 (t, *J* = 5.4 Hz, 1 H), 2.56 (dd, *J* = 15.3, 7.0 Hz, 1 H), 2.55−2.49 (m, 1 H), 2.42−2.31 (m, 3 H), 1.70 (dt, *J* = 12.7, 2.4 Hz, 1 H), 1.45 (s, 3 H), 1.36 (s, 3 H), 0.90 (s, 9 H), 0.12 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 171.1, 151.9, 143.0, 130.8, 130.6, 98.8, 77.2, 72.7, 69.7, 65.9, 51.7, 41.5, 36.5, 32.7, 29.9, 26.0, 19.8, 18.3, −3.8, −4.2; HRMS (ESI−TOF) calcd for $C_{23}H_{40}O_7SiNa$ $[M + Na]^+$ 479.2441, found 479.2440.

Triol 19. To a solution of acetonide **18** (4.8 mg, 10.5 μmol) in CH_2Cl_2 (0.8 mL) was added $TiCl_4$ (1.7 μL, 15.7 μmol) at −30 °C. After the mixture was stirred at −30 °C for 5 min, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc three times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 4:1, 1:1) gave triol **19** (4.3 mg, 98%) as a colorless oil: R_f = 0.09 (hexane/EtOAc = 1:1); $[\alpha]_D^{27}$ −5.1 (*c* 0.73, $CHCl_3$); IR (neat) 3449, 2928, 2856, 1737, 1681, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 8.0 Hz, 1 H), 7.09 (dd, *J* = 15.3, 9.8 Hz, 1 H), 6.41−6.33 (m, 2 H), 6.10 (dd, *J* = 15.3, 8.0 Hz, 1 H), 4.33−4.27 (m, 1 H), 3.97 (ddd, *J* = 10.4, 5.6, 2.0 Hz, 1 H), 3.89−3.85 (m, 1 H), 3.73 (s, 3 H), 3.55 (t, *J* = 5.2 Hz, 1 H), 2.63−2.57 (m, 1 H), 2.53−2.51 (m, 2 H), 2.43−2.35 (m, 2 H), 1.86 (dt, *J* = 14.4, 2.4 Hz, 1 H), 1.67−1.55 (m, 3 H), 0.91 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 172.8, 152.0, 143.2, 130.8, 130.5, 77.9, 73.7, 72.6, 69.2, 51.9, 41.4, 38.4, 36.7, 26.1, 18.3, −4.0; HRMS (ESI−TOF) calcd for $C_{20}H_{36}O_7SiNa$ $[M + Na]^+$ 439.2128, found 439.2126.

Tetraol 2a from 19. To a solution of TBS ether **19** (12.4 mg, 29.8 μmol) in THF (1.5 mL) was added HF·pyr (60 μL) at 0 °C. The mixture was stirred at 0 °C for 2 h. After the mixture was stirred at room temperature for 2 h, HF·pyr (70 μL) was added at 0 °C. The mixture was stirred at 0 °C for 30 min. After the mixture was stirred at room temperature for 6 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$, H_2O, and brine. The aqueous phase was washed with EtOAc three times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (CH_2Cl_2/MeOH = 20:1) gave tetraol **2a** (1.6 mg, 18%) as a colorless oil and TBS ether **19** (6.4 mg, 52% recovery). Tetraol **2a**: R_f = 0.33 (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{22}$ +13.2 (*c* 0.12, $CHCl_3$); IR (neat) 3417, 2925, 1731, 1679, 1636 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 9.49 (d, *J* = 7.8 Hz, 1 H), 7.33−7.27 (m, 1 H), 6.50−6.46 (m, 2 H), 6.08 (dd, *J* = 15.0, 7.8 Hz, 1 H), 4.33−4.27 (m, 1 H), 3.85−3.81 (m, 1 H), 3.73−3.69 (m, 1 H), 3.67 (s, 3 H), 3.39 (t, *J* = 6.3 Hz, 1 H), 2.66−2.54 (m, 2 H), 2.46−2.37 (m, 2 H), 1.85 (ddd, *J* = 14.4, 5.4, 2.4 Hz, 1 H), 1.73−1.67 (m, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 196.0, 173.8, 155.0, 145.7, 131.9, 131.0, 77.8, 73.0, 72.6, 68.3, 52.0, 43.0, 39.9,

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37.9; HRMS (ESI−TOF) calcd for $C_{14}H_{22}O_7Na$ $[M + Na]^+$ 325.1263, found 325.1271.

Diol 20. To a solution of TBS ether **17** (160 mg, 0.277 mmol) in MeCN (2.8 mL) was added a mixed solution of TBAF (1.0 M solution in THF, 2.8 mL, 2.80 mmol) and AcOH (0.16 mL, 2.77 mmol) at room temperature. After the mixture was stirred at 60 °C for 6 days, the reaction was quenched with saturated aqueous NH_4Cl. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc three times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 2:1, EtOAc) gave diol **20** (111 mg, 86%) as a colorless oil: R_f = 0.09 (hexane/EtOAc = 1:1); $[\alpha]_D^{22}$ +10.5 (*c* 0.71, $CHCl_3$); IR (neat) 3420, 2928, 2858, 1738, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.17 (d, *J* = 8.6 Hz, 2 H), 6.80 (d, *J* = 8.6 Hz, 2 H), 6.26−6.16 (m, 2 H), 5.91−5.86 (m, 1 H), 5.62 (dt, *J* = 14.0, 5.6 Hz, 1 H), 4.51−4.47 (m, 1 H), 4.43 (d, *J* = 11.2 Hz, 1 H), 4.33−4.29 (m, 1 H), 4.22 (d, *J* = 11.2 Hz, 1 H), 4.11−4.06 (m, 1 H), 3.92−3.84 (m, 3 H), 3.60−3.56 (m, 1 H), 3.33 (s, 3 H), 3.31 (s, 3 H), 2.62−2.48 (m, 3 H), 2.18 (dd, *J* = 15.6, 5.2 Hz, 1 H), 1.46−1.40 (m, 2 H), 1.39 (s, 3 H), 1.29 (s, 3 H), 0.92 (t, *J* = 7.2 Hz, 1 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.9, 159.9, 132.7, 131.2, 130.9, 130.7, 130.0, 114.2, 99.0, 77.6, 73.8, 71.2, 69.7, 66.3, 63.3, 54.9, 51.2, 41.6, 32.9, 31.4, 30.3, 19.9; HRMS (ESI−TOF) calcd for $C_{25}H_{36}O_8Na$ $[M + Na]^+$ 487.2308, found 487.2306.

Allylic Alcohol 21. To a solution of diol **20** (94.4 mg, 0.163 mmol) in CH_2Cl_2 (1.6 mL) were added 2,6-lutidine (67 μL, 0.456 mmol) and TESOTf (88 μL, 0.391 mmol) at 0 °C. After the mixture was stirred at room temperature for 40 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 20:1, 10:1) gave the corresponding bis-TES ether (111 mg, 98%) as a colorless oil: R_f = 0.71 (hexane/EtOAc = 2:1); $[\alpha]_D^{26}$ +4.2 (*c* 0.49, $CHCl_3$); IR (neat) 2953, 2871, 1742, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.24 (d, *J* = 8.6 Hz, 2 H), 6.84 (d, *J* = 8.6 Hz, 2 H), 6.41 (dd, *J* = 15.0, 10.6 Hz, 1 H), 6.30 (dd, *J* = 15.0, 10.6 Hz, 1 H), 5.95−5.87 (m, 1 H), 5.73 (dt, *J* = 15.0, 5.3 Hz, 1 H), 4.48 (d, *J* = 11.2 Hz, 1 H), 4.35 (d, *J* = 11.2 Hz, 1 H), 4.35−4.27 (m, 1 H), 4.15 (d, *J* = 5.3 Hz, 2 H), 4.12−4.07 (m, 1 H), 3.95 (t, *J* = 5.0 Hz, 1 H), 3.61 (q, *J* = 5.4 Hz, 1 H), 3.35 (s, 3 H), 3.33 (s, 3 H), 2.60−2.53 (m, 3 H), 2.22 (dd, *J* = 15.4, 5.4 Hz, 1 H), 1.50−1.44 (m, 2 H), 1.46 (s, 3 H), 1.33 (s, 3 H), 1.09 (t, *J* = 8.2 Hz, 9 H), 1.02 (t, *J* = 7.4 Hz, 9 H), 0.80 (q, *J* = 8.2 Hz, 6 H), 0.62 (q, *J* = 7.4 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.5, 131.3, 131.1, 131.0, 130.4, 130.0, 114.1, 99.0, 78.8, 76.9, 71.9, 69.8, 66.4, 63.5, 54.9, 51.1, 41.8, 33.7, 31.8, 30.2, 19.9, 7.5, 7.2, 5.9, 5.2; HRMS (ESI−TOF) calcd for $C_{37}H_{64}O_8Si_2Na$ $[M + Na]^+$ 715.4037, found 715.4031.

To a solution of the corresponding TES ether (99.7 mg, 0.144 mmol) in CH_2Cl_2 (7.0 mL) and MeOH (0.7 mL) was added PPTS (11.0 mg, 43.0 μmol) at 0 °C. After the mixture was stirred at room temperature for 1 h, the reaction was quenched with Et_3N. 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 = 10:1, 2:1) gave allylic alcohol **21** (75.1 mg, 90%) as a colorless oil: R_f = 0.53 (hexane/EtOAc = 1:1); $[\alpha]_D^{21}$ +2.5 (*c* 1.53, $CHCl_3$); IR (neat) 3460, 2952, 2875, 1739, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.23 (d, *J* = 8.0 Hz, 2 H), 6.83 (d, *J* = 8.0 Hz, 2 H), 6.26−6.16 (m, 2 H), 5.90−5.83 (m, 1 H), 5.64−5.57 (m, 1 H), 4.48 (d, *J* = 11.5 Hz, 1 H), 4.36 (d, *J* = 11.5 Hz, 1 H), 4.32−4.31 (m, 1 H), 4.11−4.07 (m, 1 H), 3.96−3.93 (m, 1 H), 3.90 (brs, 2 H), 3.62−3.58 (m, 1 H), 3.34 (s, 3 H), 3.33 (s, 3 H), 2.59−2.54 (m, 3 H), 2.24 (dd, *J* = 15.5, 5.1 Hz, 1 H), 1.49−1.46 (m, 2 H), 1.46 (s, 3 H), 1.33 (s, 3 H), 1.08 (t, *J* = 7.9 Hz, 9 H), 0.79 (q, *J* = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.9, 159.8, 132.4, 131.3, 131.2, 131.1, 131.0, 130.0, 114.1, 99.0, 78.7, 76.8, 71.8, 69.8, 66.4, 63.2, 54.9, 51.2, 41.8, 33.7, 31.7, 30.2, 19.9, 7.5, 5.9; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3171.

Alcohol 22. To a solution of alcohol **21** (45.6 mg, 78.8 μmol) in CH_2Cl_2 (1.6 mL) were added $PhI(OAc)_2$ (65.0 mg, 0.197 mmol) and TEMPO (2.5 mg, 15.8 μmol) at 0 °C. After the mixture was stirred at room temperature for 5 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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 = 5:1) gave the corresponding unsaturated aldehyde (44.5 mg), which was used for the next reaction without further purification.

To a solution of the PMB ether obtained above (44.5 mg) in CH_2Cl_2 (1.7 mL) and phosphate pH standard solution (0.1 mL) was added DDQ (26.0 mg, 0.116 mmol) at 0 °C. After the mixture was stirred at room temperature for 3 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 2:1) gave alcohol **22** (27.5 mg, 76% in two steps) as a colorless oil: R_f = 0.23 (hexane/EtOAc = 2:1); $[\alpha]_D^{23}$ −15.2 (*c* 1.00, $CHCl_3$); IR (neat) 3479, 2953, 2876, 1739, 1682, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.8 Hz, 1 H), 7.09 (dd, *J* = 15.4, 10.0 Hz, 1 H), 6.44−6.30 (m, 2 H), 6.10 (dd, *J* = 15.4, 7.8 Hz, 1 H), 4.35−4.28 (m, 1 H), 4.05−4.01 (m, 1 H), 3.78−3.75 (m, 1 H), 3.68 (s, 3 H), 3.54 (d, *J* = 5.5 Hz, 1 H), 2.60−2.51 (m, 2 H), 2.43−2.32 (m, 2 H), 1.72−1.64 (m, 2 H), 1.46 (s, 3 H), 1.36 (s, 3 H), 0.97 (t, *J* = 8.0 Hz, 9 H), 0.65 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 171.1, 151.9, 143.0, 130.8, 130.6, 98.8, 72.8, 70.0, 65.9, 51.7, 41.5, 36.6, 32.5, 29.9, 19.8, 7.0, 5.3; HRMS (ESI−TOF) calcd for $C_{23}H_{40}O_7SiNa$ $[M + Na]^+$ 479.2441, found 479.2446.

Tetraol 2a from 22. To a solution of acetonide **22** (4.1 mg, 8.99 μmol) in CH_2Cl_2 (0.5 mL) was added $TiCl_4$ (2.0 μL, 18.2 μmol) at −30 °C. The mixture was gradually warmed up to room temperature for 1 h. After the mixture was stirred at room temperature for 27 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc four times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (CH_2Cl_2/MeOH = 10:1) gave tetraol **2a** (2.0 mg, 74%).

Ketone 23. To a solution of diol **20** (59.5 mg, 0.128 mmol) in CH_2Cl_2 (1.2 mL) were added imidazole (12.2 mg, 0.179 mmol) and TESCl (26 μL, 0.154 mmol) at −30 °C. After the mixture was gradually warmed up to −10 °C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 5:1) gave the corresponding mono-TES ether (60.8 mg), which was used for the next reaction without further purification.

To a suspension of the alcohol obtained above (60.8 mg) and MS4 Å (50.0 mg) in CH_2Cl_2 (1.3 mL) were added NMO (64.0 mg, 0.546 mmol) and TPAP (1.8 mg, 5.30 μmol) at room temperature. After the mixture was stirred at room temperature for 8 h, the mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 4:1) gave ketone **23** (54.8 mg, 74% in two steps) as a colorless oil: R_f = 0.56 (hexane/EtOAc = 2:1); $[\alpha]_D^{22}$ +15.6 (*c* 0.50, $CHCl_3$); IR (neat) 2953, 2871, 1738, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.31 (d, *J* = 8.5 Hz, 2 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 6.31 (dd, *J* = 14.0, 10.6 Hz, 1 H), 6.17 (dd, *J* = 15.0, 10.6 Hz, 1 H), 5.86 (dt, *J* = 15.0, 7.6 Hz, 1 H), 5.72 (dt, *J* = 14.0, 5.0 Hz, 1 H), 4.59−4.51 (m, 2 H), 4.37−4.16 (m, 3 H), 4.10 (d, *J* = 4.7 Hz, 2 H), 3.30 (s, 3 H), 3.29 (s, 3 H), 2.66−2.55 (m, 2 H), 2.43 (dd, *J* = 15.8, 7.6 Hz, 1 H), 2.09 (dd, *J* = 15.8, 5.0 Hz, 1 H), 1.65 (dt, *J* = 12.9, 2.7 Hz, 1 H), 1.42−1.35 (m, 1 H), 1.40 (s, 3 H), 1.20 (s, 3 H), 1.00 (t, *J* = 7.9 Hz, 9 H), 0.60 (q, *J* = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 206.8, 170.5, 159.8, 132.9, 132.1, 130.6, 130.0, 129.7, 129.1, 114.1, 99.4, 80.4, 73.4, 72.3, 66.1, 63.4, 54.8, 51.2, 41.2, 35.7, 32.2, 30.1, 19.3, 7.2, 5.1; HRMS (ESI−TOF) calcd for $C_{31}H_{48}O_8SiNa$ $[M + Na]^+$ 599.3016, found 599.3012.

Alcohol 24. To a solution of ketone **23** (8.5 mg, 14.7 μmol) in MeOH (0.5 mL) was added $NaBH_4$ (1.0 mg, 26.4 μmol) at −78 °C. After the mixture was gradually warmed up to 0 °C for 20 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 3:1) gave alcohol **24** (8.3 mg, 98%) as a colorless oil: R_f =

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0.30 (hexane/EtOAc = 2:1); $[\alpha]_D^{22}$ +20.8 (*c* 0.44, $CHCl_3$); IR (neat) 3518, 2953, 2885, 1740, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.20 (d, *J* = 8.5 Hz, 2 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 6.40 (dd, *J* = 15.1, 10.5 Hz, 1 H), 6.25 (dd, *J* = 15.1, 10.5 Hz, 1 H), 5.80−5.69 (m, 2 H), 4.49 (d, *J* = 11.2 Hz, 1 H), 4.28−4.24 (m, 2 H), 4.15 (d, *J* = 4.9 Hz, 2 H), 4.00−3.97 (m, 1 H), 3.52 (t, *J* = 4.7 Hz, 2 H), 3.33 (s, 3 H), 3.32 (s, 3 H), 2.68−2.63 (m, 2 H), 2.50−2.44 (m, 2 H), 2.12 (dd, *J* = 15.6, 4.9 Hz, 1 H), 1.41 (s, 3 H), 1.41−1.34 (m, 1 H), 1.30 (s, 3 H), 1.02 (t, *J* = 7.9 Hz, 9 H), 0.62 (q, *J* = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.8, 131.6, 131.1, 130.2, 130.2, 129.9, 114.1, 99.1, 78.4, 74.7, 71.7, 70.0, 66.2, 63.4, 54.9, 51.1, 41.4, 34.2, 32.4, 30.3, 19.8, 7.2, 5.1; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3183.

Allylic Alcohol 25. To a solution of alcohol **24** (8.3 mg, 14.4 μmol) in CH_2Cl_2 (0.5 mL) were added 2,6-lutidine (17 μL, 0.113 mmol) and TESOTf (24 μL, 0.107 mmol) at 0 °C. After the mixture was stirred at room temperature for 4 h, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 10:1) gave the corresponding bis-TES ether (10.1 mg), which was used for the next reaction without further purification.

To a solution of the TES ether obtained above (10.1 mg) in CH_2Cl_2 (0.5 mL) and MeOH (0.1 mL) was added PPTS (1.8 mg, 7.30 μmol) at 0 °C. After the mixture was stirred at 0 °C for 2 h, the reaction was quenched with Et_3N. Concentration and column chromatography (hexane/EtOAc = 3:1) gave allylic alcohol **25** (8.5 mg, quant in two steps) as a colorless oil: R_f = 0.22 (hexane/EtOAc = 2:1); $[\alpha]_D^{21}$ +11.2 (*c* 1.15, $CHCl_3$); IR (neat) 3463, 2952, 2871, 1739, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.22 (d, *J* = 8.6 Hz, 2 H), 6.80 (d, *J* = 8.6 Hz, 2 H), 6.25−6.21 (m, 2 H), 5.81−5.74 (m, 1 H), 5.64−5.57 (m, 1 H), 4.53 (d, *J* = 11.5 Hz, 1 H), 4.35 (d, *J* = 11.5 Hz, 1 H), 4.33−4.30 (m, 1 H), 4.16−4.10 (m, 1 H), 3.89 (d, *J* = 2.9 Hz, 2 H), 3.73 (dd, *J* = 7.1, 3.2 Hz, 1 H), 3.54−3.49 (m, 1 H), 3.32 (s, 3 H), 3.31 (s, 3 H), 2.75−2.68 (m, 1 H), 2.57−2.48 (m, 2 H), 2.16 (dd, *J* = 15.6, 4.9 Hz, 1 H), 1.48 (s, 3 H), 1.48−1.42 (m, 2 H), 1.41 (s, 3 H), 1.10 (t, *J* = 7.8 Hz, 9 H), 0.76 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.9, 159.8, 132.4, 131.5, 131.2, 130.9, 129.8, 129.6, 114.1, 99.1, 79.6, 76.4, 71.4, 66.1, 63.2, 54.9, 51.2, 41.6, 33.5, 32.9, 30.4, 19.8, 7.6, 5.9; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3170.

Alcohol 26. To a solution of alcohol **25** (8.5 mg, 14.6 μmol) in CH_2Cl_2 (0.5 mL) were added $PhI(OAc)_2$ (12.1 mg, 36.5 μmol) and TEMPO (1.0 mg, 6.40 μmol) at 0 °C. After the mixture was stirred at room temperature for 3 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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 = 5:1) gave the corresponding unsaturated aldehyde (7.6 mg), which was used for the next reaction without further purification.

To a solution of the PMB ether obtained above (7.6 mg) in CH_2Cl_2 (0.4 mL) and phosphate pH standard solution (40 μL) was added DDQ (3.6 mg, 16.0 μmol) at 0 °C. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc, washed with saturated aqueous $NaHCO_3$, H_2O, and brine, and then dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 2:1) gave alcohol **26** (5.5 mg, 82% in two steps) as a colorless oil: R_f = 0.16 (hexane/EtOAc = 2:1); $[\alpha]_D^{21}$ −35.7 (*c* 0.47, $CHCl_3$); IR (neat) 3490, 2954, 2871, 1739, 1682, 1641 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.55 (d, *J* = 8.1 Hz, 1 H), 7.08 (dd, *J* = 15.2, 10.4 Hz, 1 H), 6.42−6.26 (m, 2 H), 6.09 (dd, *J* = 15.2, 7.8 Hz, 1 H), 4.32−4.26 (m, 1 H), 3.98−3.94 (m, 1 H), 3.71−3.69 (m, 1 H), 3.69 (s, 3 H), 3.45 (d, *J* = 6.6 Hz, 1 H), 2.57−2.30 (m, 4 H), 1.65−1.60 (m, 1 H), 1.45 (s, 3 H), 1.38 (s, 3 H), 1.26−1.17 (m, 1 H), 0.97 (t, *J* = 7.9 Hz, 9 H), 0.69−0.61 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 171.0, 151.9, 142.6, 130.7, 130.6, 98.9, 77.1, 71.0, 69.3, 65.5, 51.7, 41.4, 39.2, 31.9, 29.9, 19.6, 7.1, 5.3; HRMS (ESI−TOF) calcd for $C_{23}H_{40}O_7SiNa$ $[M + Na]^+$ 479.2441, found 479.2442.

Tetraol 2b. To a solution of acetonide **26** (4.1 mg, 8.98 μmol) in CH_2Cl_2 (0.4 mL) was added $TiCl_4$ (1.2 μL, 10.8 μmol) at −30 °C. After the mixture was stirred at −30 °C for 5 min, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$, H_2O, and brine. The aqueous phase was washed with EtOAc three times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 1:1) gave the corresponding triol (3.0 mg, 80%) as a colorless oil: R_f = 0.09 (hexane/EtOAc = 1:1); $[\alpha]_D^{24}$ −14.1 (*c* 0.42, $CHCl_3$); IR (neat) 3451, 2954, 2871, 1737, 1681, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.8 Hz, 1 H), 7.09 (dd, *J* = 15.2, 10.1 Hz, 1 H), 6.44−6.29 (m, 2 H), 6.09 (dd, *J* = 15.2, 7.8 Hz, 1 H), 4.27−4.21 (m, 1 H), 3.96−3.92 (m, 1 H), 3.87 (brs, 1 H), 3.72 (s, 3 H), 3.59−3.57 (m, 1 H), 2.52 (d, *J* = 5.9 Hz, 2 H), 2.43 (t, *J* = 6.3 Hz, 2 H), 1.71 (d, *J* = 5.9 Hz, 2 H), 0.99 (t, *J* = 7.9 Hz, 9 H), 0.67 (q, *J* = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.7, 172.9, 152.0, 142.8, 130.7, 130.6, 75.9, 73.3, 69.7, 69.1, 51.9, 41.4, 39.0, 37.7, 7.0, 5.3; HRMS (ESI−TOF) calcd for $C_{20}H_{36}O_7SiNa$ $[M + Na]^+$ 439.2128, found 439.2131.

To a solution of the corresponding TES ether (9.6 mg, 23.0 μmol) in THF (1.0 mL) was added HF·pyr (50 μL) at 0 °C. After the mixture was stirred at 0 °C for 3 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with saturated aqueous $NaHCO_3$, H_2O, and brine. The aqueous phase was washed with EtOAc three times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (CH_2Cl_2/MeOH = 30:1) gave tetraol **2b** (5.5 mg, 79%) as a colorless oil: R_f = 0.35 (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{21}$ −6.1 (*c* 0.10, $CHCl_3$); IR (neat) 3367, 2924, 2858, 1727, 1675, 1635 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 9.49 (d, *J* = 7.8 Hz, 1 H), 7.29 (dd, *J* = 15.6, 9.9 Hz, 1 H), 6.51−6.41 (m, 2 H), 6.09 (dd, *J* = 15.6, 7.8 Hz, 1 H), 4.25−4.20 (m, 1 H), 3.90−3.86 (m, 1 H), 3.83−3.79 (m, 1 H), 3.67 (s, 3 H), 3.33−3.31 (m, 1 H), 2.56 (dd, *J* = 15.0, 4.2 Hz, 1 H), 2.53−2.43 (m, 2 H), 2.44 (dd, *J* = 15.0, 8.7 Hz, 1 H), 1.76−1.72 (m, 2 H); ^{13}C NMR (100 MHz, CD_3OD) δ 196.0, 173.7, 154.8, 145.0, 131.9, 131.2, 76.1, 72.9, 71.7, 67.7, 52.0, 43.1, 41.1, 38.7; HRMS (ESI−TOF) calcd for $C_{14}H_{22}O_7Na$ $[M + Na]^+$ 325.1263, found 325.1266.

Diol 27. To a solution of β-hydroxy ketone **11** (595 mg, 0.767 mmol) in MeCN (9.0 mL) and AcOH (9.0 mL) was added $NaBH(OAc)_3$ (244 mg, 1.15 mmol) at −20 °C. After the mixture was stirred at −20 °C for 2 h, $NaBH(OAc)_3$ (81.3 mg, 0.383 mmol) was added. After the mixture was stirred at −20 °C for a further 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 5:1) gave diol **27** (565 mg, 95%) as a colorless oil: R_f = 0.45 (hexane/EtOAc = 2:1); $[\alpha]_D^{24}$ −9.1 (*c* 1.00, $CHCl_3$); IR (neat) 3476, 2930, 2857, 1739, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.73−7.71 (m, 4 H), 7.25−7.09 (m, 8 H), 6.77 (d, *J* = 8.8 Hz, 2 H), 6.35 (dd, *J* = 15.1, 10.5 Hz, 1 H), 6.18 (dd, *J* = 15.1, 10.5 Hz, 1 H), 5.84 (dt, *J* = 15.1, 7.6 Hz, 1 H), 5.61 (dt, *J* = 15.1, 4.9 Hz, 1 H), 4.40 (d, *J* = 1.9 Hz, 2 H), 4.37−4.30 (m, 1 H), 4.16 (d, *J* = 4.6 Hz, 2 H), 4.07 (brs, 1 H), 3.84−3.81 (m, 1 H), 3.70−3.67 (m, 1 H), 3.25 (s, 3 H), 3.21 (s, 3 H), 2.52 (t, *J* = 6.4 Hz, 2 H), 2.34−2.29 (m, 2 H), 2.20−2.15 (m, 1 H), 1.71−1.66 (m, 2 H), 1.12 (s, 9 H), 0.94 (s, 9 H), 0.16 (s, 3 H), 0.12 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 173.1, 159.7, 135.9, 134.2, 132.4, 131.4, 131.1, 130.7, 130.5, 129.9, 114.0, 80.3, 77.7, 72.2, 70.0, 66.3, 64.7, 54.8, 51.3, 41.4, 38.4, 34.2, 27.2, 26.5, 19.6, 18.8, −3.6, −4.1; HRMS (ESI−TOF) calcd for $C_{44}H_{64}O_8Si_2Na$ $[M + Na]^+$ 799.4037, found 799.4036.

Diol 28. To a solution of diol **27** (871 mg, 1.12 mmol) in THF (11 mL) were added $Me_2C(OMe)_2$ (1.4 mL, 11.2 mmol) and *p*-TsOH·H_2O (21.0 mg, 0.112 mmol) at room temperature. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 7:1) gave the corresponding acetonide (822 mg, 90%) as a colorless oil: R_f = 0.62 (hexane/EtOAc = 2:1); $[\alpha]_D^{24}$ −0.4 (*c* 0.99, $CHCl_3$); IR (neat)

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2929, 2856, 1742 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 7.8, 1.5 Hz, 4 H), 7.44−7.36 (m, 6 H), 7.25 (d, J = 8.5 Hz, 2 H), 6.86 (d, J = 8.5 Hz, 2 H), 6.26 (dd, J = 15.0, 10.5 Hz, 1 H), 6.11 (dd, J = 15.0, 10.5 Hz, 1 H), 5.73−5.65 (m, 2 H), 4.47 (s, 2 H), 4.25−4.16 (m, 3 H), 3.99−3.94 (m, 1 H), 3.81−3.78 (m, 1 H), 3.79 (s, 3 H), 3.69 (s, 3 H), 3.42−3.38 (m, 1 H), 2.52 (dd, J = 15.6, 8.3 Hz, 1 H), 2.44−2.33 (m, 3 H), 2.08−2.01 (m, 1 H), 1.59 (brs, 1 H), 1.34 (s, 3 H), 1.31 (s, 3 H), 1.08 (s, 9 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 159.1, 135.5, 133.7, 131.9, 130.5, 130.2, 130.0, 129.5, 129.3, 127.6, 113.7, 100.6, 79.3, 75.9, 71.8, 66.8, 64.3, 63.8, 55.3, 51.6, 40.7, 33.8, 32.8, 26.9, 26.2, 24.6, 24.5, 19.3, 18.4, −4.0, −4.3; HRMS (ESI−TOF) calcd for $C_{47}H_{68}O_8Si_2Na$ $[M + Na]^+$ 839.4351, found 839.4348.

To a solution of the corresponding bis-silyl ether (409 mg, 0.501 mmol) in MeCN (5.0 mL) was added a mixed solution of TBAF (1.0 M solution in THF, 2.0 mL, 2.00 mmol) and AcOH (0.10 mL, 2.00 mmol) at room temperature. After the mixture was stirred at reflux for 3 days, the reaction was quenched with saturated aqueous NH_4Cl. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc twice. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (hexane/EtOAc = 4:1, 1:1) gave diol **28** (154 mg, 66%) as a colorless oil: R_f = 0.19 (hexane/EtOAc = 1:1); $[\alpha]_D^{20}$ +43.1 (c 0.68, $CHCl_3$); IR (neat) 3459, 2925, 1739, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.19−7.16 (m, 2 H), 6.79 (d, J = 8.6 Hz, 2 H), 6.25−6.15 (m, 2 H), 5.92−5.85 (m, 1 H), 5.63−5.57 (m, 1 H), 4.43 (d, J = 11.5 Hz, 1 H), 4.37−4.30 (m, 1 H), 4.23 (d, J = 11.5 Hz, 1 H), 4.18−4.13 (m, 1 H), 3.96 (d, J = 5.7 Hz, 1 H), 3.89 (d, J = 5.4 Hz, 2 H), 3.54−3.50 (m, 1 H), 3.33 (s, 3 H), 3.33 (s, 3 H), 2.61−2.55 (m, 2 H), 2.48 (dd, J = 15.6, 8.8 Hz, 1 H), 2.23−2.18 (m, 2 H), 2.08−2.01 (m, 1 H), 1.37 (s, 3 H), 1.28 (s, 3 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.8, 131.2, 131.2, 130.9, 130.6, 129.8, 114.2, 100.8, 77.8, 73.8, 71.3, 67.1, 64.2, 63.3, 54.9, 51.1, 40.9, 32.9, 32.5, 25.1, 25.0; HRMS (ESI−TOF) calcd for $C_{25}H_{36}O_8Na$ $[M + Na]^+$ 487.2308, found 487.2302.

Alcohol 29. To a solution of diol **28** (22.4 mg, 48.2 μmol) in CH_2Cl_2 (1.0 mL) were added 2,6-lutidine (40 μL, 0.270 mmol) and TESOTf (52 μL, 0.232 mmol) at 0 °C. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 10:1, 4:1) gave the corresponding bis-TES ether (34.1 mg, quant) as a colorless oil: R_f = 0.50 (hexane/EtOAc = 4:1); $[\alpha]_D^{25}$ +16.4 (c 0.23, $CHCl_3$); IR (neat) 2953, 2871, 1743, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.23 (d, J = 8.8 Hz, 2 H), 6.82 (d, J = 8.8 Hz, 2 H), 6.46−6.35 (m, 1 H), 6.34−6.24 (m, 1 H), 5.95−5.86 (m, 1 H), 5.73 (dt, J = 15.1, 5.4 Hz, 1 H), 4.47 (d, J = 11.2 Hz, 1 H), 4.46−4.38 (m, 1 H), 4.34 (d, J = 11.2 Hz, 1 H), 4.22−4.13 (m, 3 H), 4.05 (dd, J = 5.9, 4.1 Hz, 1 H), 3.50 (q, J = 5.3 Hz, 1 H), 3.34 (s, 3 H), 3.33 (s, 3 H), 2.62−2.45 (m, 3 H), 2.25 (dd, J = 15.5, 5.1 Hz, 1 H), 2.21−2.12 (m, 1 H), 1.44 (s, 3 H), 1.43−1.34 (m, 1 H), 1.32 (s, 3 H), 1.10 (t, J = 7.9 Hz, 9 H), 1.02 (t, J = 7.9 Hz, 9 H), 0.84−0.76 (q, J = 7.9 Hz, 6 H), 0.62 (q, J = 7.9 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.6, 131.3, 130.7, 130.4, 129.9, 114.1, 100.9, 79.2, 76.4, 71.9, 67.3, 64.2, 63.5, 54.9, 51.1, 41.0, 33.9, 32.9, 24.9, 24.8, 7.5, 7.2, 5.9, 5.2; HRMS (ESI−TOF) calcd for $C_{37}H_{64}O_8Si_2Na$ $[M + Na]^+$ 715.4037, found 715.4037.

To a solution of the corresponding TES ether (15.0 mg, 21.6 μmol) in CH_2Cl_2 (0.7 mL) and MeOH (70 μL) was added PPTS (1.6 mg, 6.32 μmol) at 0 °C. The mixture was stirred at 0 °C for 2 h. After the mixture was stirred at room temperature for 30 min, the reaction was quenched with Et_3N. 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 = 7:1, 2:1) gave the corresponding allylic alcohol (10.7 mg, 88%) as a colorless oil: R_f = 0.66 (hexane/EtOAc = 1:1); $[\alpha]_D^{23}$ +12.8 (c 0.74, $CHCl_3$); IR (neat) 3462, 2952, 2875, 1742, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.23 (d, J = 8.6 Hz, 2 H), 6.81 (d, J = 8.6 Hz, 2 H), 6.24−6.15 (m, 2 H), 5.88−5.81 (m, 1 H), 5.63−5.57 (m, 1 H), 4.47 (d, J = 11.5 Hz, 1 H), 4.44−4.39 (m, 1 H), 4.35 (d, J = 11.5 Hz, 1 H), 4.20−4.15 (m, 1 H), 4.04 (t, J = 4.9 Hz, 1 H), 3.89 (d, J = 5.4 Hz, 2 H), 3.51−3.47 (m, 1 H), 3.33 (s, 3 H), 3.33 (s, 3 H), 2.59−2.49 (m, 4 H), 2.25 (dd, J = 15.5, 4.9 Hz, 1 H), 2.19−2.12 (m, 1 H), 1.44 (s, 3 H), 1.40−1.30 (m, 1 H), 1.32 (s, 3 H), 1.10 (t, J = 8.0 Hz, 9 H), 0.79 (q, J = 8.0 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.5, 131.2, 131.1, 131.0, 129.9, 114.1, 100.9, 79.1, 76.3, 71.9, 67.3, 64.2, 63.2, 54.9, 51.1, 41.0, 33.8, 32.8, 24.9, 24.8, 7.5, 5.9; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3168.

To a solution of the corresponding allylic alcohol (52.8 mg, 91.3 μmol) in CH_2Cl_2 (1.8 mL) were added $PhI(OAc)_2$ (76.0 mg, 0.228 mmol) and TEMPO (2.9 mg, 18.3 μmol) at 0 °C. After the mixture was stirred at room temperature for 4 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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 = 5:1) gave the corresponding unsaturated aldehyde (48.8 mg), which was used for the next reaction without further purification.

To a solution of the PMB ether obtained above (48.8 mg) in CH_2Cl_2 (1.7 mL) and phosphate pH standard solution (0.1 mL) was added DDQ (26.0 mg, 0.115 mmol) at 0 °C. After the mixture was stirred at room temperature for 2 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 2:1) gave alcohol **29** (29.9 mg, 72% in two steps) as a colorless oil: R_f = 0.61 (hexane/EtOAc = 1:1); $[\alpha]_D^{23}$ +5.8 (c 0.88, $CHCl_3$); IR (neat) 3472, 2953, 2876, 1741, 1682, 1639 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, J = 7.8 Hz, 1 H), 7.09 (dd, J = 15.2, 10.2 Hz, 1 H), 6.44−6.29 (m, 2 H), 6.10 (dd, J = 15.2, 7.8 Hz, 1 H), 4.26−4.19 (m, 1 H), 4.00−3.95 (m, 1 H), 3.68 (s, 3 H), 3.67−3.63 (m, 2 H), 2.59−2.51 (m, 2 H), 2.46 (dd, J = 15.6, 5.2 Hz, 1 H), 2.39−2.31 (m, 2 H), 2.07−2.00 (m, 1 H), 1.63−1.56 (m, 1 H), 1.35 (s, 3 H), 1.34 (s, 3 H), 0.97 (t, J = 7.8 Hz, 9 H), 0.65 (q, J = 7.8 Hz, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 171.2, 151.8, 142.9, 131.0, 130.7, 100.8, 72.8, 67.3, 63.7, 51.7, 40.7, 36.8, 33.5, 24.6, 24.5, 7.0, 5.4; HRMS (ESI−TOF) calcd for $C_{23}H_{40}O_7SiNa$ $[M + Na]^+$ 479.2441, found 479.2446.

Tetraol 2c. To a solution of acetonide **29** (20.7 mg, 45.4 μmol) in CH_2Cl_2 (2.3 mL) was added $TiCl_4$ (10 μL, 90.8 μmol) at −30 °C. The mixture was gradually warmed up to room temperature for 2 h. After the mixture was stirred at room temperature for 3 h, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc four times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (CH_2Cl_2/MeOH = 10:1) gave tetraol **2c** (6.1 mg, 44%) as a colorless oil: R_f = 0.35 (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{24}$ −8.9 (c 0.10, $CHCl_3$); IR (neat) 3388, 2925, 2853, 1730, 1674, 1636 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 9.49 (d, J = 7.8 Hz, 1 H), 7.33−7.28 (m, 1 H), 6.50−6.47 (m, 2 H), 6.08 (dd, J = 15.0, 7.8 Hz, 1 H), 4.32−4.27 (m, 1 H), 3.93−3.89 (m, 1 H), 3.75−3.71 (m, 1 H), 3.67 (s, 3 H), 3.39 (t, J = 6.6 Hz, 1 H), 2.65−2.61 (m, 1 H), 2.54−2.47 (m, 2 H), 2.43−2.37 (m, 1 H), 1.78 (ddd, J = 14.4, 9.6, 2.4 Hz, 1 H), 1.60 (ddd, J = 14.4, 9.6, 2.4 Hz, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 196.0, 173.8, 155.5, 145.8, 131.8, 131.0, 78.1, 73.1, 70.6, 66.4, 52.0, 43.9, 40.3, 37.8; HRMS (ESI−TOF) calcd for $C_{14}H_{22}O_7Na$ $[M + Na]^+$ 325.1263, found 325.1271.

Ketone 30. To a solution of diol **28** (10.8 mg, 23.4 μmol) in CH_2Cl_2 (0.3 mL) were added imidazole (2.2 mg, 32.8 μmol) and TESCl (4.7 μL, 28.1 μmol) at −30 °C. After the mixture was stirred at −30 °C for 30 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 4:1) gave the corresponding mono-TES ether (12.9 mg), which was used for the next reaction without further purification.

To a suspension of the alcohol obtained above (12.9 mg) and MS4 Å (15.0 mg) in CH_2Cl_2 (0.3 mL) were added NMO (13.4 mg, 0.115 mmol) and TPAP (1.0 mg, 2.85 μmol) at room temperature. After the mixture was stirred at room temperature for 8 h, the mixture was filtered through a Celite pad and washed with EtOAc. Concentration and column chromatography (hexane/EtOAc = 4:1) gave ketone **30**

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(10.3 mg, 76% in two steps) as a colorless oil: R_f = 0.56 (hexane/EtOAc = 2:1); $[\alpha]_D^{22}$ +28.7 (*c* 0.53, $CHCl_3$); IR (neat) 2953, 2871, 1739, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.28 (d, *J* = 8.5 Hz, 2 H), 6.80 (d, *J* = 8.5 Hz, 2 H), 6.34 (dd, *J* = 13.7, 10.2 Hz, 1 H), 6.15 (dt, *J* = 15.1, 10.2 Hz, 1 H), 5.83−5.76 (m, 1 H), 5.72−5.64 (m, 1 H), 4.56 (dd, *J* = 10.8, 3.3 Hz, 1 H), 4.47 (t, *J* = 5.9 Hz, 1 H), 4.34−4.27 (m, 3 H), 4.10 (t, *J* = 4.6 Hz, 2 H), 3.31 (s, 6 H), 2.64−2.58 (m, 2 H), 2.38 (dd, *J* = 16.0, 8.4 Hz, 1 H), 2.13−2.04 (m, 2 H), 1.60−1.53 (m, 1 H), 1.36 (s, 3 H), 1.25 (s, 3 H), 1.00 (t, *J* = 8.0 Hz, 9 H), 0.60 (q, *J* = 8.0 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 207.5, 170.4, 159.9, 133.0, 132.1, 130.6, 129.9, 128.8, 114.1, 101.3, 81.2, 72.2, 70.5, 63.8, 63.4, 54.9, 51.2, 40.4, 35.8, 33.1, 25.1, 24.5, 7.2, 5.1; HRMS (ESI−TOF) calcd for $C_{31}H_{48}O_8SiNa$ $[M + Na]^+$ 599.3016, found 599.3013.

Alcohol 31. To a solution of ketone **30** (5.2 mg, 9.02 μmol) in MeOH (0.4 mL) was added $NaBH_4$ (1.0 mg, 26.4 μmol) at −78 °C. After the mixture was stirred at −78 °C for 20 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 3:1) gave alcohol **31** (5.4 mg, quant) as a colorless oil: R_f = 0.33 (hexane/EtOAc = 2:1); $[\alpha]_D^{22}$ +32.0 (*c* 1.11, $CHCl_3$); IR (neat) 3518, 2953, 2871, 1739, 1613 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.19 (d, *J* = 7.6 Hz, 2 H), 6.79 (d, *J* = 7.6 Hz, 2 H), 6.39 (dd, *J* = 15.0, 10.5 Hz, 1 H), 6.24 (dd, *J* = 15.0, 10.5 Hz, 1 H), 5.78−5.67 (m, 2 H), 4.47 (d, *J* = 11.2 Hz, 1 H), 4.34−4.25 (m, 1 H), 4.26 (d, *J* = 11.2 Hz, 1 H), 4.14 (d, *J* = 4.9 Hz, 2 H), 4.04−3.98 (m, 1 H), 3.54−3.48 (m, 2 H), 3.32 (s, 3 H), 3.32 (s, 3 H), 2.69−2.62 (m, 1 H), 2.53−2.38 (m, 2 H), 2.12 (dd, *J* = 11.2, 4.4 Hz, 1 H), 1.80−1.73 (m, 1 H), 1.38 (s, 3 H), 1.27 (s, 3 H), 1.22−1.15 (m, 1 H), 1.01 (t, *J* = 7.8 Hz, 9 H), 0.61 (q, *J* = 7.8 Hz, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.7, 159.8, 132.9, 131.6, 130.1, 130.1, 129.9, 129.8, 114.1, 100.9, 78.3, 74.4, 71.7, 67.7, 63.9, 63.4, 54.9, 51.1, 40.7, 34.1, 33.8, 24.9, 7.2, 5.1; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3165.

Alcohol 32. To a solution of alcohol **31** (23.2 mg, 40.0 μmol) in CH_2Cl_2 (0.4 mL) were added 2,6-lutidine (17 μL, 0.113 mmol) and TESOTf (24 μL, 0.107 mmol) at 0 °C. After the mixture was stirred at room temperature for 30 min, the reaction was quenched with saturated aqueous NH_4Cl. 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 = 10:1) gave the corresponding bis-TES ether (28.1 mg), which was used for the next reaction without further purification.

To a solution of the TES ether obtained above (28.1 mg) in CH_2Cl_2 (1.4 mL) and MeOH (0.2 mL) was added PPTS (3.1 mg, 12.5 μmol) at 0 °C. The mixture was stirred at 0 °C for 2 h. After the mixture was stirred at room temperature for 20 min, the reaction was quenched with Et_3N. 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 = 7:1, 1:1) gave the corresponding allylic alcohol (16.9 mg, 72% in two steps) as a colorless oil: R_f = 0.44 (hexane/EtOAc = 1:1); $[\alpha]_D^{22}$ +27.5 (*c* 0.65, $CHCl_3$); IR (neat) 3465, 2952, 2885, 1739, 1612 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 7.24 (d, *J* = 8.8 Hz, 2 H), 6.80 (d, *J* = 8.8 Hz, 2 H), 6.27−6.11 (m, 2 H), 5.83−5.74 (m, 1 H), 5.65−5.54 (m, 1 H), 4.53 (d, *J* = 11.5 Hz, 1 H), 4.42 (d, *J* = 11.5 Hz, 1 H), 4.40−4.32 (m, 1 H), 4.17−4.08 (m, 1 H), 3.88 (d, *J* = 4.9 Hz, 2 H), 3.78 (dd, *J* = 10.8, 3.7 Hz, 1 H), 3.57−3.48 (m, 1 H), 3.33 (s, 6 H), 2.74−2.65 (m, 1 H), 2.59−2.44 (m, 3 H), 2.20 (dd, *J* = 15.8, 5.0 Hz, 1 H), 1.92−1.83 (m, 1 H), 1.44 (s, 3 H), 1.42 (s, 3 H), 1.09 (t, *J* = 7.9 Hz, 9 H), 0.80−0.69 (m, 6 H); ^{13}C NMR (100 MHz, C_6D_6) δ 170.8, 159.8, 132.3, 131.5, 131.4, 131.2, 131.0, 129.7, 114.1, 100.9, 80.1, 75.6, 71.7, 68.3, 63.9, 63.2, 54.9, 51.1, 40.9, 34.6, 33.8, 25.2, 24.6, 7.5, 5.9; HRMS (ESI−TOF) calcd for $C_{31}H_{50}O_8SiNa$ $[M + Na]^+$ 601.3173, found 601.3170.

To a solution of the corresponding allylic alcohol (16.9 mg, 29.2 μmol) in CH_2Cl_2 (0.7 mL) were added $PhI(OAc)_2$ (24.2 mg, 73.0 μmol) and TEMPO (1.0 mg, 6.40 μmol) at 0 °C. After the mixture was stirred at room temperature for 3 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$. 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 = 5:1) gave the corresponding unsaturated aldehyde (13.5 mg), which was used for the next reaction without further purification.

To a solution of the PMB ether obtained above (13.5 mg) in CH_2Cl_2 (0.5 mL) and phosphate pH standard solution (25 μL) was added DDQ (6.3 mg, 28.0 μmol) at 0 °C. The mixture was stirred at 0 °C for 1 h. After the mixture was stirred at room temperature for 4 h, the reaction was quenched with saturated aqueous $NaHCO_3$. 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 = 4:1, 2:1) gave alcohol **32** (10.0 mg, 75% in two steps) as a colorless oil: R_f = 0.23 (hexane/EtOAc = 2:1); $[\alpha]_D^{24}$ −5.8 (*c* 1.16, $CHCl_3$); IR (neat) 3490, 2952, 2871, 1739, 1681, 1640 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.54 (d, *J* = 7.8 Hz, 1 H), 7.08 (dd, *J* = 15.0, 10.0 Hz, 1 H), 6.42−6.26 (m, 2 H), 6.09 (dd, *J* = 15.0, 7.8 Hz, 1 H), 4.27−4.19 (m, 1 H), 3.93−3.87 (m, 1 H), 3.68 (s, 3 H), 3.68−3.65 (m, 1 H), 3.47 (dd, *J* = 17.1, 7.6 Hz, 1 H), 2.59−2.30 (m, 5 H), 1.76−1.69 (m, 1 H), 1.65−1.57 (m, 1 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 0.97 (t, *J* = 7.8 Hz, 9 H), 0.69−0.61 (m, 6 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 193.6, 171.2, 151.8, 142.5, 130.7, 130.7, 100.9, 69.3, 67.9, 63.3, 51.7, 40.5, 39.4, 34.0, 24.8, 24.3, 7.1, 5.4; HRMS (ESI−TOF) calcd for $C_{23}H_{40}O_7SiNa$ $[M + Na]^+$ 479.2441, found 479.2438.

Tetraol 2d. To a solution of acetonide **32** (18.2 mg, 39.9 μmol) in CH_2Cl_2 (2.0 mL) was added $TiCl_4$ (8.8 μL, 80.3 μmol) at −30 °C. After the mixture was gradually warmed up to 0 °C for 30 min, the reaction was quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with EtOAc and washed with H_2O and brine. The aqueous phase was washed with EtOAc four times. The combined organic layer was dried over Na_2SO_4. Concentration and column chromatography (CH_2Cl_2/MeOH = 10:1) gave tetraol **2d** (5.7 mg, 47%) as a colorless oil: R_f = 0.25 (CH_2Cl_2/MeOH = 10:1); $[\alpha]_D^{26}$ −19.1 (*c* 0.03, $CHCl_3$); IR (neat) 3390, 2921, 2852, 1730, 1677, 1637 cm^{-1}; ^1H NMR (600 MHz, CD_3OD) δ 9.49 (d, *J* = 7.8 Hz, 1 H), 7.29 (dd, *J* = 15.6, 10.4 Hz, 1 H), 6.51−6.41 (m, 2 H), 6.09 (dd, *J* = 15.6, 7.8 Hz, 1 H), 4.29−4.24 (m, 1 H), 3.95−3.91 (m, 1 H), 3.82−3.79 (m, 1 H), 3.67 (s, 3 H), 3.23 (t, *J* = 3.9 Hz, 1 H), 2.56−2.43 (m, 4 H), 1.70 (ddd, *J* = 14.4, 10.2, 3.0 Hz, 1 H), 1.59 (ddd, *J* = 14.4, 10.2, 3.0 Hz, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 196.0, 173.7, 154.8, 145.0, 131.9, 131.2, 77.1, 72.8, 70.1, 66.4, 52.0, 43.8, 41.9, 38.7; HRMS (ESI−TOF) calcd for $C_{14}H_{22}O_7Na$ $[M + Na]^+$ 325.1263, found 325.1270.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

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Notes

The authors declare no competing financial interest.

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