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

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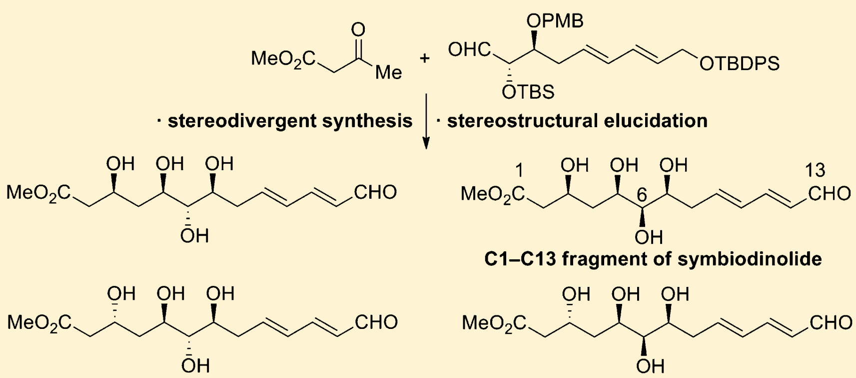
S Supporting Information



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 ($^{3}J_{5,6}$ and $^{3}J_{6,7}$ = 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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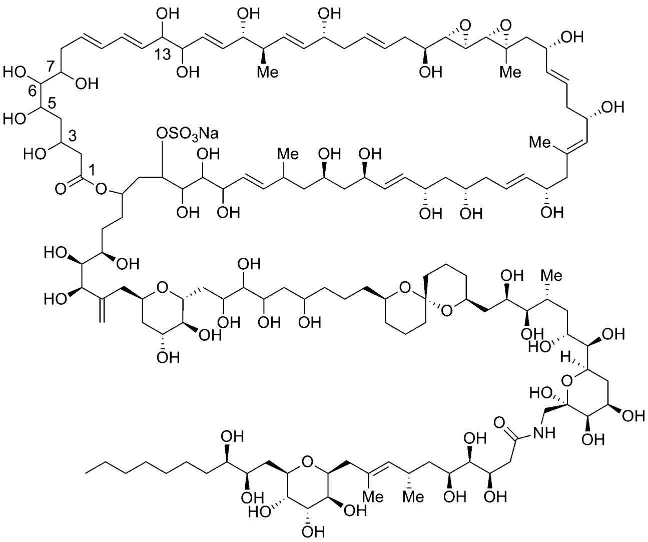
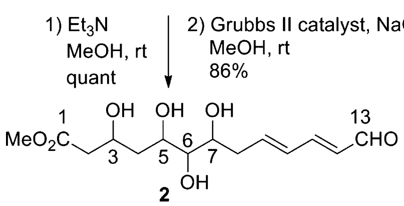


symbiodinolide (1)

Figure 1. Structure of symbiodinolide (1).

Scheme 1. Degradation of Symbiodinolide (1)



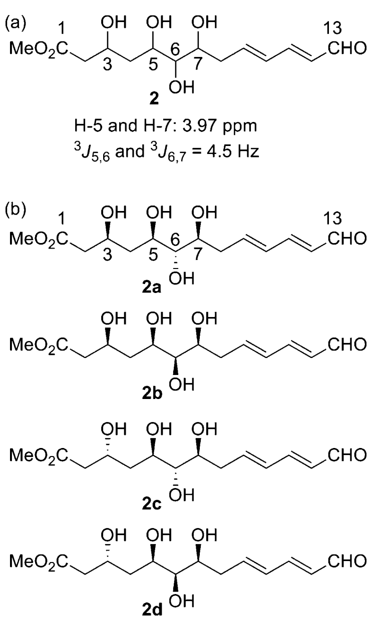


Figure 2. (a) ^{1}H NMR analysis of the degraded product **2**. (b) Four possible diastereomers of the C1−C13 fragment.

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*-bis-alkoxy 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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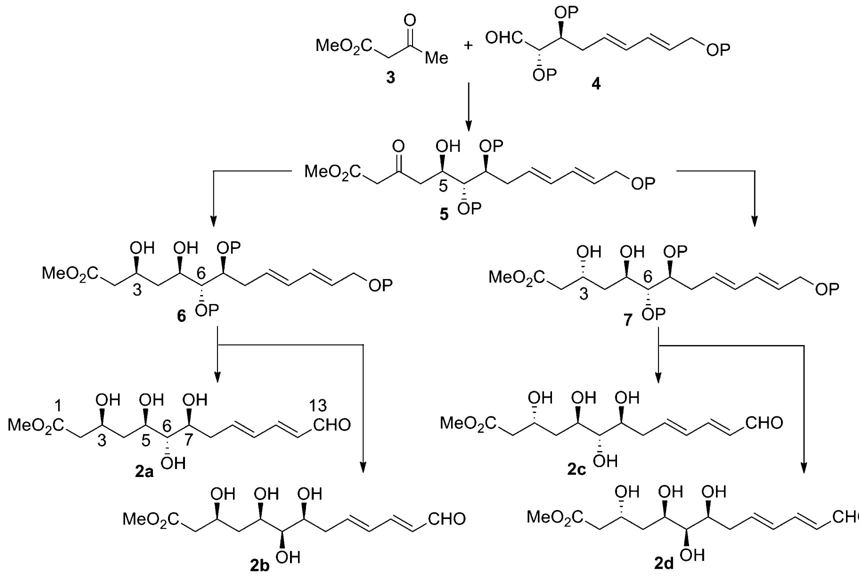
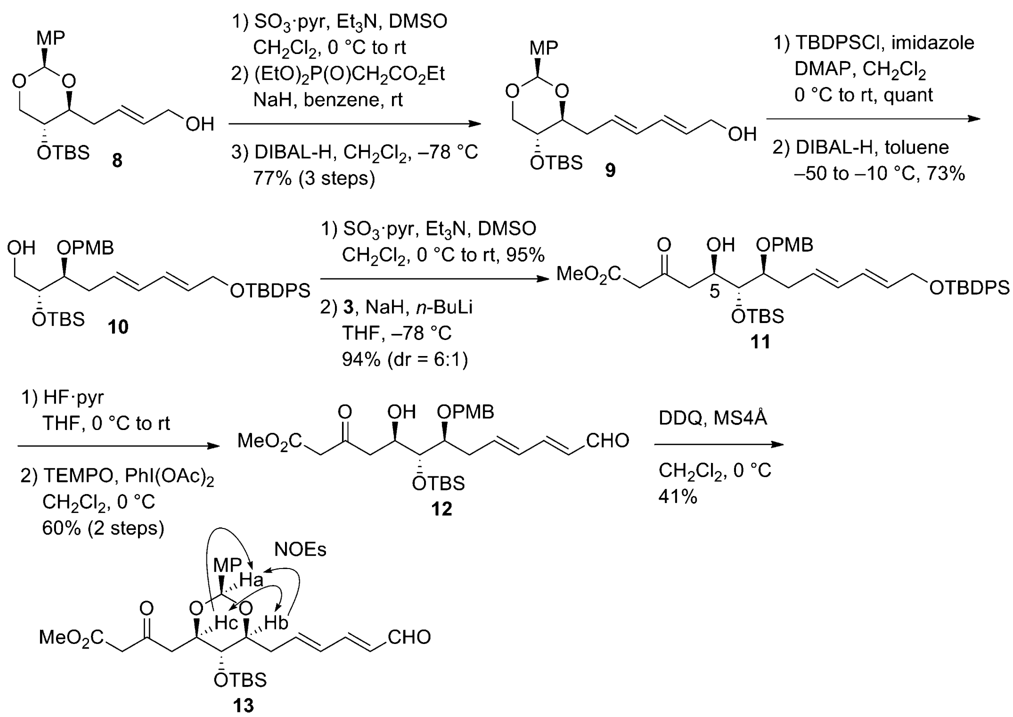
Scheme 2. Stereodivergent Synthetic Plan of 2a−2d



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 stereo-inversion 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 ^{1}H NMR spectrum of **24** was clearly different from that of the secondary alcohol obtained in the first step

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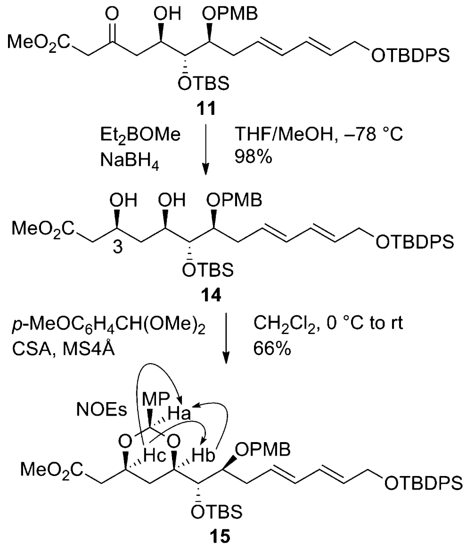
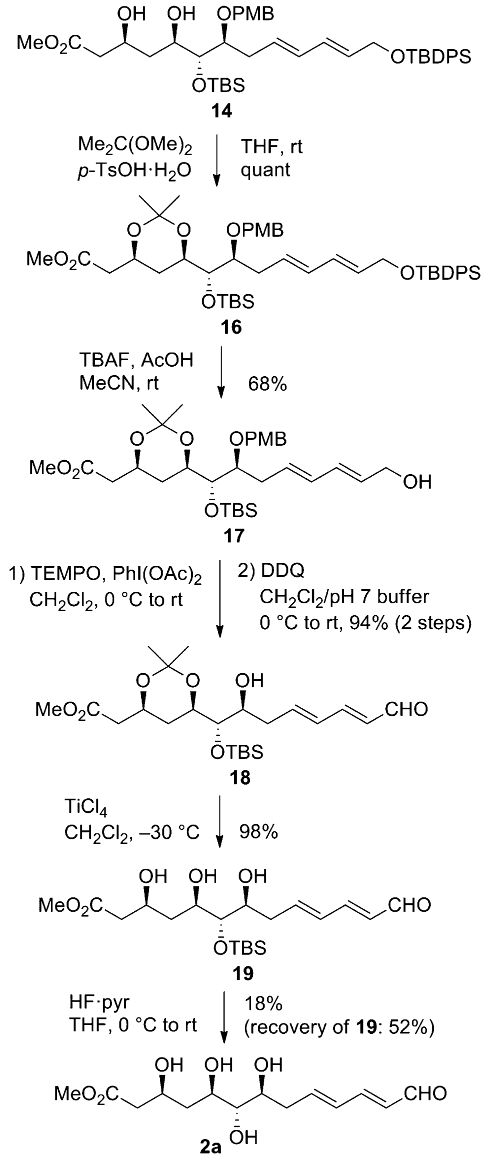
Scheme 4. Synthesis of 14 and Its Stereochemical Confirmation at the C3 Position



Scheme 5. Synthesis of 2a



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 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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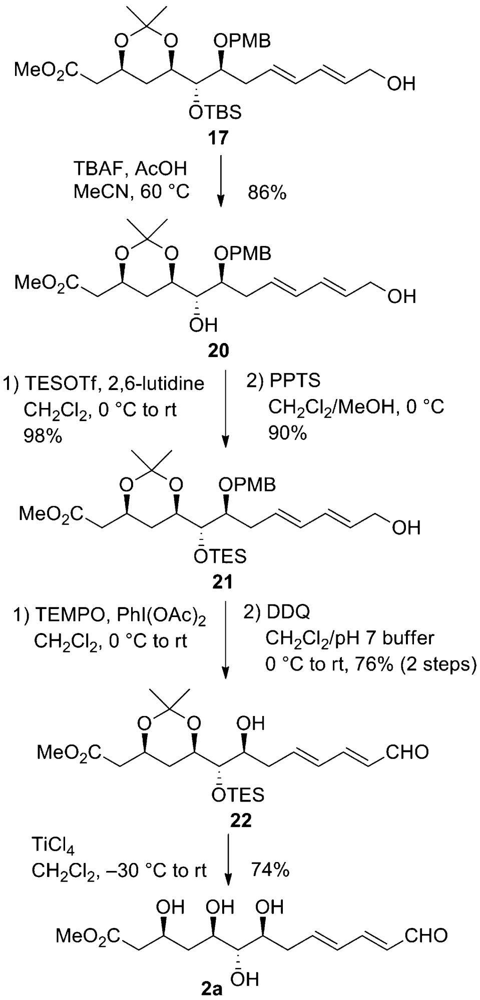
Scheme 6. Improved Synthesis of 2a

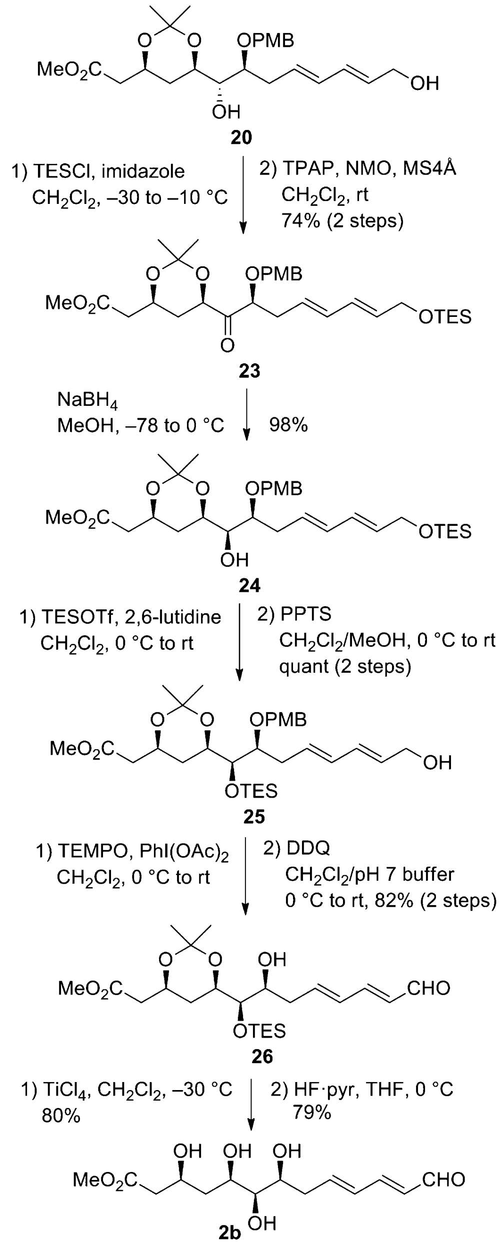


diastereomers **2a**−**2d** by comparing with the universal NMR databases reported by Kishi's research group. Next, we have examined the stereodivergent synthesis of **2a**−**2d** in the unified manner. Thus, the β-hydroxy ketone **11**, which would be the key common synthetic intermediate of **2a**−**2d**, 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 ^{1}H 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

Scheme 7. Synthesis of 2b



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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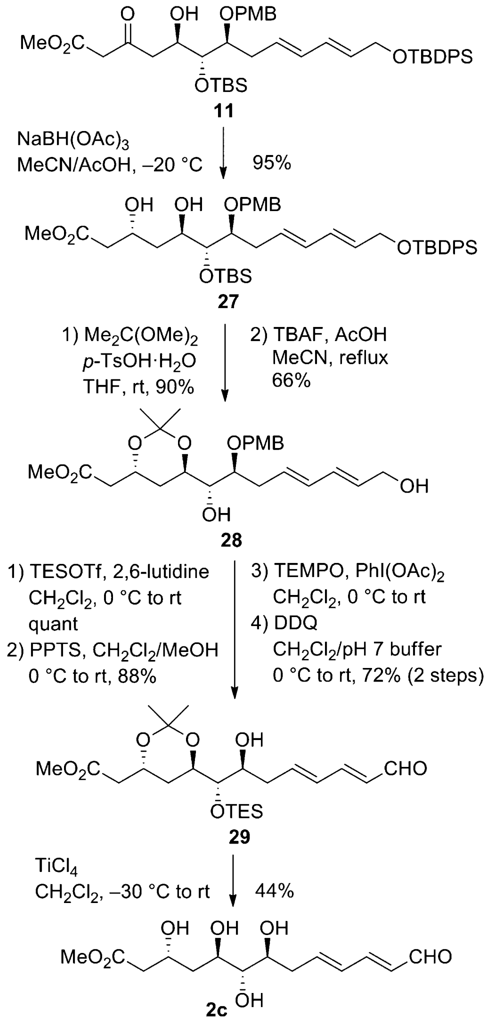
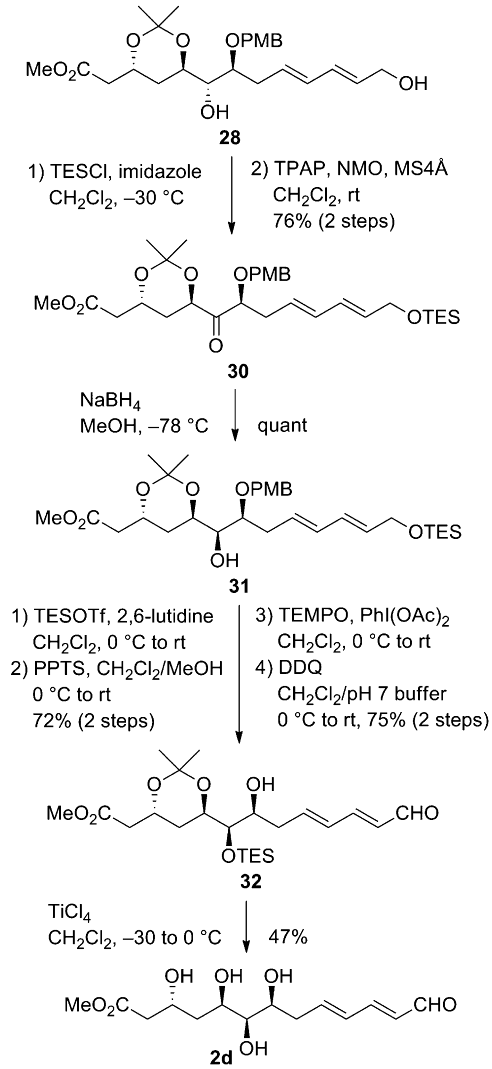
Scheme 8. Synthesis of 2c



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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J. Org. Chem. 2015, 80, 3111−3123

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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J. Org. Chem. 2015, 80, 3111−3123

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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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)

2929, 2856, 1742 cm^{-1}; ^{1}H 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); $[\alpha]^{20}_{D}$ +43.1 (c 0.68, $CHCl_3$); IR (neat) 3459, 2925, 1739, 1612 cm^{-1}; ^{1}H 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); $[\alpha]^{25}_{D}$ +16.4 (c 0.23, $CHCl_3$); IR (neat) 2953, 2871, 1743, 1612 cm^{-1}; ^{1}H 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); $[\alpha]^{23}_{D}$ +12.8 (c 0.74, $CHCl_3$); IR (neat) 3462, 2952, 2875, 1742, 1612 cm^{-1}; ^{1}H 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); $[\alpha]^{23}_{D}$ +5.8 (c 0.88, $CHCl_3$); IR (neat) 3472, 2953, 2876, 1741, 1682, 1639 cm^{-1}; ^{1}H 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); $[\alpha]^{24}_{D}$ −8.9 (c 0.10, $CHCl_3$); IR (neat) 3388, 2925, 2853, 1730, 1674, 1636 cm^{-1}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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}; ^{1}H 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 ^{1}H 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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