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Diboron-Catalyzed Regio- and 1,2-*cis*-α-Stereoselective Glycosylation of *trans*-1,2-Diols

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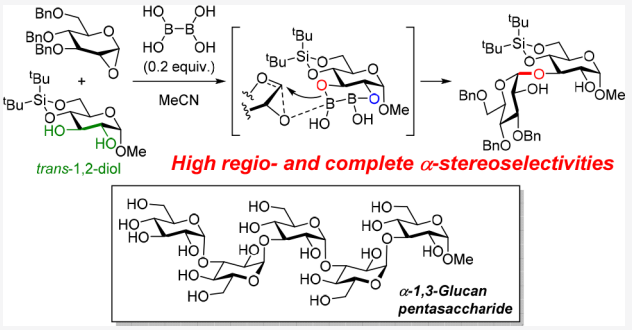
ABSTRACT: Regio- and 1,2-*cis*-α-stereoselective glycosylations were investigated using 1,2-anhydroglucose donors and *trans*-1,2-diol sugar acceptors in the presence of a diboron catalyst. The reactions proceeded smoothly to provide the corresponding 1,2-*cis*-α-glycosides with consistently very high stereoselectivity and were regioselectivity controlled by the protecting groups of the acceptor. The present glycosylation method was applied successfully to the efficient synthesis of α-1,3-glucan pentasaccharide.



Carbohydrates play important roles in many biological processes, including cell proliferation, tumor metastasis, and immune recognition.[1] Methodologies for the efficient synthesis of homogeneous and structurally well-defined carbohydrates have thus attracted attention in various research fields to aid in understanding the precise biological roles and structure−activity relationships of these carbohydrates. Although there are many methods for the chemical synthesis of complex natural glycosides,[2] protecting groups must be carefully selected to control the glycosylation positions and anomeric configuration. The development of an efficient glycosylation method requiring minimal or no use of protecting groups is thus highly desirable. This has led to the development of regio- and stereoselective glycosylation methods using organoboron reagents, which can reversibly bind to *cis*-1,2- and 1,3-diols under mild conditions.[3]

In 1999, Aoyama et al.[4] reported the regio- and Koenigs−Knorr-type glycosylation of a tetra-coordinate boronate ester, formed using a stoichiometric amount of an arylboronic acid and L-fucoside. Recently, Taylor et al. reported an efficient borinic-acid-catalyzed regio- and 1,2-*trans*-stereoselective glycosylation reaction.[5] In a different approach, Kaji et al. reported a regio- and 1,2-*trans*-stereoselective glycosylation using an arylboronic acid as a transient masking reagent, which decreased the nucleophilicity of undesired hydroxyl groups by the formation of the corresponding boronic ester.[6] These glycosylation methods require neighboring group participation from the 2-*O*-acyl functionality of the glycosyl donor to produce the corresponding 1,2-*trans*-glycoside with high stereoselectivity. On the other hand, the efficient synthesis of 1,2-*cis*-glycosides is difficult due to the unavailability of neighboring group participation. To address this, our group has recently developed a boronic-acid-catalyzed regio- and 1,2-*cis*-stereoselective glycosylation approach (Scheme 1A),[7a−f] namely boron-mediated aglycon delivery (BMAD).[7] Cyclic boronic ester **4** or **5**, derived from arylboronic acid **3** and *cis*-1,2-diol **1** or 1,3-diol **2**, respectively, activated 1,2-anhydro donor **6** and induced glycosylation to provide the corresponding 1,2-*cis* glycoside **7** or **8** with high regio- and stereoselectivities. However, the binding affinity between an arylboronic acid and a *trans*-1,2-diol on a pyranose ring is quite low, preventing the effective application of BMAD to *trans*-1,2-diols on pyranosides. In this context, Morken et al. reported that tetrahydroxydiboron (**10**) could reversibly bind to *trans*-1,2-diols on a pyran ring to form 1,2-bonded diboron species.[8] We, therefore, hypothesized that 1,2-bonded diboron species **11**, derived from *trans*-1,2-diol **9** and diboron **10**, can activate **6** and induce glycosylation to form 1,2-*cis* glycoside **12** with high stereoselectivity (Scheme 1B). Herein, we report the diboron-catalyzed regio- and 1,2-*cis*-α-stereoselective glycosylation of *trans*-1,2-diol sugar acceptors and its application to the synthesis of α-1,3-glucan pentasaccharide.

We selected 3,4,6-tri-*O*-benzyl-1,2-anhydroglucose (**14**)[9] and diboron **10** as the glycosyl donor and organoboron catalyst, respectively, and phenylboronic acid (**15**) as a negative control catalyst. First, the glycosylation of methyl

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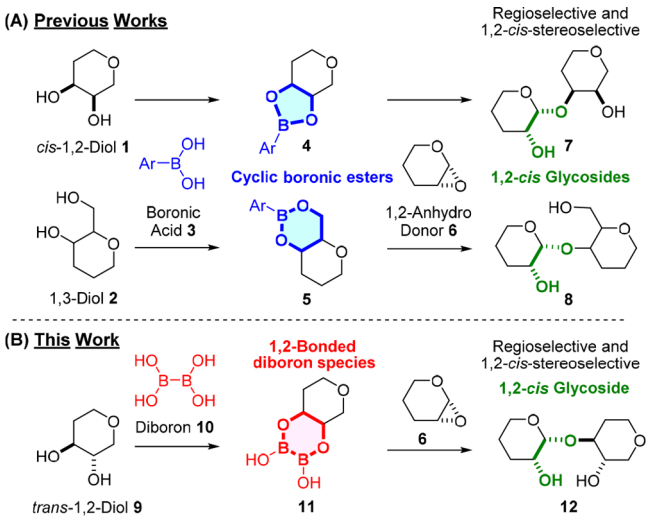
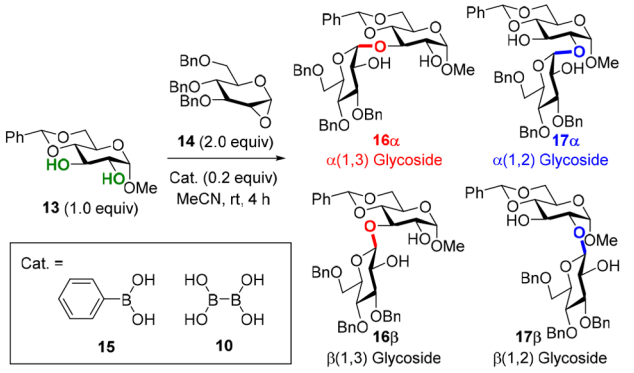
Scheme 1. (A) Boronic-Acid-Catalyzed Regio- and 1,2-*cis*-Stereoselective Glycosylations of *cis*-1,2- and 1,3-Diol Sugar Acceptors; (B) Diboron-Catalyzed Regio- and 1,2-*cis*-Stereoselective Glycosylations of *trans*-1,2-Diol Sugar Acceptors



4,6-*O*-benzilidene-α-D-glucoside (**13**) with **14** was attempted using catalytic amounts of **15** in MeCN at room temperature for 4 h. The reaction proceeded poorly, providing α-glycosides **16α** and **17α** in 9% total yield with low regioselectivity but complete α-stereoselectivity, along with recovered **13** in 75% yield (Table 1, entry 1). Although we have not obtained clear

Table 1. Glycosylation of 1,2-Anhydro Donor 14 and *trans*-1,2-Diol 13



entry	cat.	yield of 16α+17α	yield of 16β+17β	α(1,3)/α(1,2) (16α/17α)	recovery of 13
1	**15**	9%	0%	40:60	75%
2	**10**	93%	0%	71:29	-

evidence at this stage, this result may suggest the formation of the relatively unstable seven-membered ring diarylpyroboronic ester **18**[10] (Figure 1A) and glycosylation catalysis with **14**. In sharp contrast, the use of diboron **10** under the same reaction conditions uniquely resulted in smooth glycosylation to provide **16α** and **17α** in 93% total yield with modest regioselectivity (**16α**/**17α** = 71:29) and complete α-stereoselectivity, suggesting that relatively stable 1,2-bonded diboron

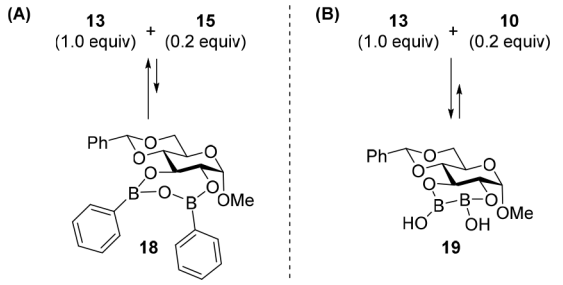


Figure 1. Proposed chemical equilibrium for the formation of (A) diarylpyroboronic ester **18** and (B) 1,2-bonded diboron species **19**.

species **19** was formed as an active species (Figure 1B). Next, to confirm the generation of **19** under these reaction conditions, we conducted ^{1}H NMR studies using **13** (1.0 equiv) and **10** (0.2 equiv) in CD_3CN at room temperature. The results showed a 1:1 complex formation consistent with the proposed **19**, as shown in Figure 2. We thus propose that

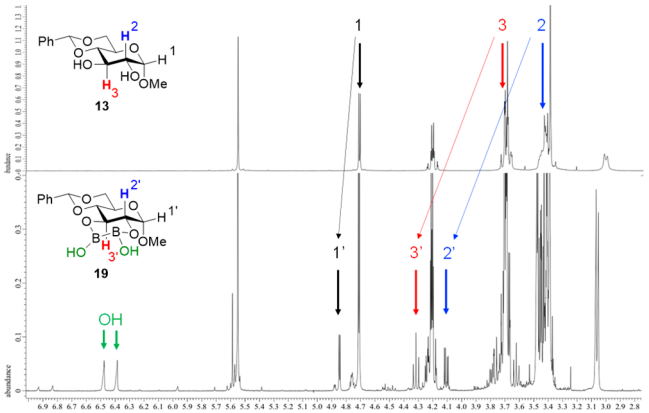


Figure 2. (A) ^{1}H NMR spectrum of **13** (100 mM) in CD_3CN; (B) ^{1}H NMR spectrum of **13** (100 mM) and **10** (20 mM) in CD_3CN.

the reaction mechanism comprises the formation of **19**, which activates glycosyl donor **14** without the need for additives. Sequential rearrangement of the B−O moiety in **20** affords **21**. Finally, a diol exchange reaction between **21** and **13** regenerates **19** and provides 1,2-*cis*-α-glycosides effectively (Scheme 2).

Next, we investigated regioselectivity using the present glycosylation method and several *trans*-1,2-diol sugar acceptors (**22**−**27**) under the same reaction conditions, as shown in Table 2. Using **22**[11] with the cyclic protecting group DTBS (di-*tert*-butylsilylene) as an acceptor resulted in smooth glycosylation with **14** to provide the corresponding α-glycosides **22A** and **22B** in high yields with complete α-stereoselectivity and high α(1,3)-regioselectivity (**22A**/**22B** = 92:8). In sharp contrast, when **23**,[12] possessing TBS groups at the 4 and 6 positions, was used, the reaction provided α(1,2)-glycoside **23B** in moderate yield as a single isomer (entry 2, Table 2), suggesting that steric hindrance by the protecting groups at the 4 and 6 positions significantly affects regioselectivity in this glycosylation reaction. We thus focused on the size of the protecting groups and investigated the glycosylation of acceptors **24**−**27** possessing Ac,[13] Bn,[14] Bz, and Piv groups, respectively. In all cases, glycosylation proceeded smoothly to provide the corresponding 1,2-*cis*-α-glycoside in a moderate to high yield, and α(1,2)-

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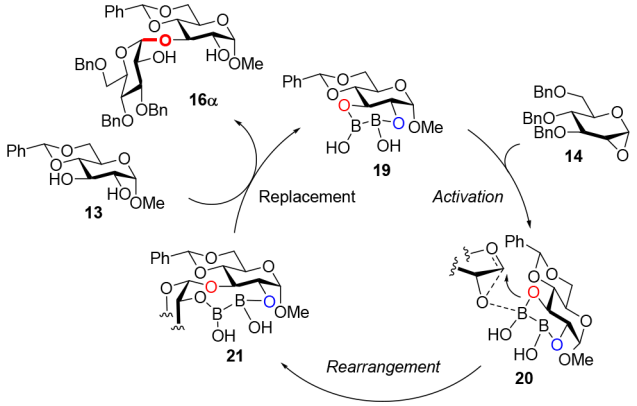
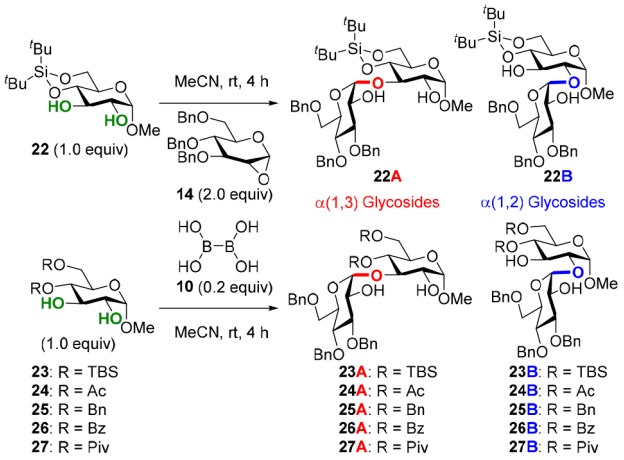
Scheme 2. Proposed Catalytic Cycle for Glycosylation of 13 with 14 Using 10[a]



[a]Only the pathway for the generation of disaccharide **16α** is shown.

Table 2. Glycosylations Using Several *trans*-1,2-Diols

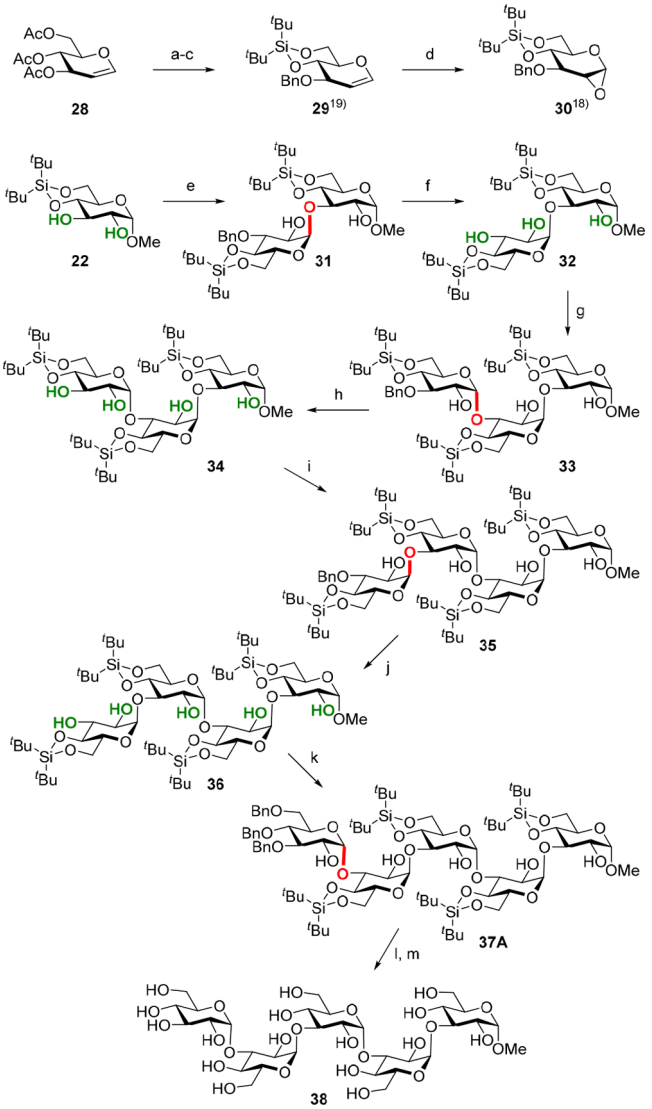


entry	acceptor	yield of α-glycosides (A+B)	α/β ratio	α(1,3)/α(1,2) (A/B)
1	**22**	84%	α only	92 : 8
2	**23**	45%	α only	0 : 100
3	**24**	72%	α only	50 : 50
4	**25**	56%	α only	37 : 63
5	**26**	96%	α only	33 : 67
6	**27**	60%	α only	25 : 75

regioselectivity increased as the size of the protecting group increased (entries 3−6, Table 2). These results indicate that the 1,2-*cis*-*α*-stereoselectivity was consistently very high, and the regioselectivity could be controlled by the size of the protecting group of the acceptor.

Next, we applied the present method to the synthesis of *α*-1,3-glucan (Scheme 3), a major cell wall component of various fungal pathogens, including *Aspergillus fumigatus*.[15] *α*-1,3-Glucans were recently synthesized by Nifantiev et al.[16] and Codée et al.[17] In our synthetic strategy, we selected 3-*O*-Bn-4,6-*O*-DTBS-1,2-anhydroglucose **30**[18] and *trans*-1,2-diol **22** as the glycosyl donor and initial glycosyl acceptor, respectively, to achieve high *α*(1,3)-selectivity. The Bn group at the 3 position of **30** would be selectively removed under mild conditions after the glycosylation of **22** with **30** to generate the *trans*-1,2-diol

Scheme 3. Efficient Synthesis of *α*-1,3-Glucan Pentasaccharide Using Diboron-Catalyzed Regio- and 1,2-*cis*-*α*-Stereoselective Glycosylation Reactions[a]



[a]Reagents and conditions: (a) NaOMe, MeOH, rt, 40 min, 98%; (b) $^{t}Bu_2Si(OTf)_2$, 2,6-lutidine, DMF, 0 °C, 30 min, 78%; (c) NaH, BnBr, TBAI, 0 °C to rt, 16 h, 82%; (d) dimethyldioxirane, CH_2Cl_2, 0 °C, 30 min, 98%.; (e) **30**, **10**, MeCN, 40 °C, 6 h, 84% (*α*(1,3) only) (92% BRSM); (f) $Pd(OH)_2/C$, H_2, EtOAc, rt, 30 min, 95%; (g) **30**, **10**, MeCN, 60 °C, 24 h, 73% (*α*(1,3) only) (90% BRSM); (h) $Pd(OH)_2/C$, H_2, EtOAc, rt, 30 min, 81%; (i) **30**, **10**, MeCN, 50 °C, 24 h, 63% (*α*(1,3) only) (98% BRSM); (j) $Pd(OH)_2/C$, H_2, EtOAc, rt, 30 min, 83%; (k) **14**, **10**, MeCN, rt, 24 h, 81% (*α*(1,3) glycoside **37A**/*α*(1,2) glycoside **37B** = 83:17); (l) $Pd(OH)_2/C$, H_2, EtOAc, rt, 30 min; (m) TBAF, THF, 0 °C to rt, 19 h, 53% in 2 steps.

sugar acceptor used in the next glycosylation. First, **29** was prepared from 3,4,6-tri-*O*-Ac-glycal (**28**) in three steps.[19] Treatment of **29** with DMDO provided **30** in 98% yield with high diastereoselectivity (*α*/*β* = 92:8). Next, we investigated the diboron-catalyzed glycosylation of **22** with **30** in the presence of **10**. After several attempts to optimize the reaction conditions, we found that the glycosylation of **22** (1.0 equiv) and **30** (3.0 equiv) using **10** (0.2 equiv) in MeCN at 40 °C for 6 h provided the best result, producing *α*(1,3)-glycoside **31** in 84% yield (92% BRSM) with excellent regio- and stereo-

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selectivities. The deprotection of the Bn group of **31** under hydrogenolysis conditions gave **32**. Next, glycosylation of triol sugar acceptor **32** with **30** provided the desired $\alpha(1,3)$-glycoside **33** as a single isomer. Deprotection of the Bn group of **33** gave trisaccharide **34**, which possesses four free hydroxyl groups. Repetition of the glycosylation of **34** with **30** and the deprotection cycle generated tetrasaccharide **36**, which possesses five free hydroxyl groups. The next glycosylation of **36** with **14** at room temperature proceeded smoothly to provide $\alpha(1,3)$-glycoside **37A** in 67% yield with good regio- and excellent stereoselectivities. The anomeric configurations and glycosylated positions were confirmed by the coupling constants of the anomeric (H1) protons and the correlations between OH and H2 protons in the ^{1}H−^{1}H COSY NMR spectrum (see Supporting Information). Finally, deprotection of all protecting groups afforded α-1,3-glucan **38**.

In conclusion, we developed the regio- and highly 1,2-*cis*-α-stereoselective glycosylation of *trans*-1,2-diol sugar acceptors to extend the utility of our boron-mediated aglycon delivery (BMAD) method. NMR studies suggested the formation of the proposed 1,2-bonded diboron species **19** intermediate, and reactions proceeded smoothly to provide the corresponding 1,2-*cis*-α-glycosides. The stereoselectivity of the reaction products was consistently very high, and their regioselectivity was controlled by the protecting groups of the acceptor. Furthermore, this glycosylation method was applied successfully to the efficient synthesis of α-1,3-glucan pentasaccharide **38**. Detailed mechanistic studies of this method, its application to other types of *trans*-1,2-diol acceptors, and synthetic studies of other biologically active compounds using BMAD are now in progress.

EXPERIMENTAL SECTION

General Experimental Methods. NMR spectra were recorded on a JEOL ECA-500 (500 MHz for ^{1}H, 125 MHz for ^{13}C) or JEOL ECZ-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C) spectrometer. ^{1}H NMR data are reported as follows: chemical shift in parts per million (ppm) downfield or upfield form $CDCl_3$ (δ 7.26), D_2O (δ 4.79), CD_3CN (δ 1.94), or tetramethylsilane (δ 0.00) integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), and coupling constants (Hz). ^{13}C chemical shifts are reported in ppm downfield or upfield from $CDCl_3$ (δ 77.0). Using D_2O as an NMR solvent, ^{13}C chemical shifts are reported in ppm downfield or upfield from acetone (δ 29.8) as an external reference. ESI-TOF mass spectra were measured on a Waters LCT Premier XE. Melting points were determined on a micro hot-stage (Yanako MP-S3). Optical rotations were measured on a JASCO P-2200 polarimeter. Silica gel TLC and column chromatography were performed using Merck TLC 60F-254 (0.25 mm) and Silica Gel 60N (spherical, neutral, 63−210 μm or 40−50 μm) (Kanto Chemical Co., Inc.), respectively. Reverse-phase column chromatography separation was performed using a Sep-Pak C18 reversed-phase cartridge (Waters). Air- and/or moisture-sensitive reactions were carried out under an argon atmosphere using oven-dried glassware.

Procedures for the Synthesis of Compound 26. To a solution of methyl 2,3-di-*O*-Bn-α-D-glucoside[20] (727 mg, 1.94 mmol) in pyridine (0.3 M, 6.47 mL) was added benzoyl chloride (541 μL, 4.66 mmol) at 0 °C under an Ar atmosphere. After the reaction mixture was stirred for 17 h at room temperature, the reaction was quenched by the addition of H_2O (10 mL). The aqueous layer was extracted with EtOAc (20 mL × 3), and then the combined extracts were washed with brine (20 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 *n*-hexane/EtOAc) gave methyl 2,3-di-*O*-Bn-4,6-di-*O*-Bz-α-D-glucoside (**39**) (1.09 g, 1.88 mmol, 97% yield).

Compound 39: white solid; mp 96−97 °C; R_f 0.43 (2:1 *n*-hexane/EtOAc); $[\alpha]_D^{26}$ +14.8° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01−7.97 (4H, m), 7.64−7.30 (12H, m), 7.14−7.06 (4H, m), 5.39 (1H, dd, *J* = 9.6 Hz, *J* = 10.0 Hz), 4.85 and 4.65 (2H, ABq, *J* = 11.2 Hz), 4.83 and 4.68 (2H, ABq, *J* = 12.0 Hz), 4.65 (1H, d, *J* = 3.6 Hz), 4.50 (1H, dd, *J* = 2.8, 12.0 Hz), 4.33 (1H, dd, *J* = 5.6, 12.0 Hz), 4.16 (1H, m), 4.11 (1H, dd, *J* = 9.2, 9.6 Hz), 3.68 (1H, dd, *J* = 3.6, 9.2 Hz), 3.43 (3H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.1, 165.2, 137.9, 137.8, 133.5, 133.2, 132.9, 130.0, 129.7, 129.6 × 2, 129.4, 129.3, 128.4, 128.3 × 2, 128.2, 128.1, 128.0 × 2, 127.9, 127.4, 98.1, 79.6, 78.9, 75.5, 73.5, 70.8, 67.5, 63.2, 55.4; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{35}H_{34}O_8Na$ 605.2151, found 605.2180.

A solution of methyl 2,3-di-*O*-Bn-4,6-di-*O*-Bz-α-D-glucoside (**39**) (304 mg, 0.522 mmol) in dry THF (0.3 M, 1.74 mL) was stirred under H_2 atmosphere in the presence of 20% $Pd(OH)_2/C$ (30.4 mg) for 2 h at room temperature. After changing the atmosphere to Ar, the mixture was filtered through a Celite pad (washed with EtOAc), and then the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 toluene/acetone) gave **26** (199 mg, 0.496 mmol, 95% yield).

Compound 26: colorless foam; R_f 0.23 (2:1 toluene/acetone); $[\alpha]_D^{27}$ +166.3° (*c* 0.33, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07−8.01 (4H, m), 7.60−7.53 (2H, m), 7.46−7.38 (4H, m), 5.25 (1H, dd, *J* = 9.6, 10.0 Hz), 4.88 (1H, d, *J* = 4.0 Hz), 4.58 (1H, dd, *J* = 2.8, 12.4 Hz), 4.40 (1H, dd, *J* = 5.6, 12.4 Hz), 4.22 (1H, m), 4.04 (1H, dd, *J* = 9.2, 9.6 Hz), 3.72 (1H, dd, *J* = 4.0, 9.2 Hz), 3.49 (3H, s), 2.76 (1H, br-s), 2.34 (1H, br-s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.1, 165.9, 133.3, 133.0, 129.8 × 2, 129.6 × 3, 129.2, 128.3 × 2, 128.2 × 2, 99.1, 72.4 × 2, 71.6, 67.6, 63.4, 55.4; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{22}O_8Na$ 425.1192, found 425.1192.

Procedures for the Synthesis of Compound 27. To a solution of methyl 2,3-di-*O*-Bn-α-D-glucoside[20] (183 mg, 0.489 mmol) in pyridine (0.3 M, 1.63 mL) was added pivaloyl chloride (147 μL, 1.17 mmol) at 0 °C under an Ar atmosphere. After the reaction mixture was stirred for 22.5 h at 80 °C, the reaction was quenched by the addition of H_2O (5 mL). The aqueous layer was extracted with EtOAc (10 mL × 3), and then the combined extracts were washed with brine (10 mL), dried over anhydrous sodium sulfate, filtered, and concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (4:1 *n*-hexane/EtOAc) gave 2,3-di-*O*-Bn-4,6-di-*O*-Piv-α-D-glucoside (**40**) (249 mg, 0.460 mmol, 94% yield). Compound **40**: white solid; mp 117−118 °C; R_f 0.57 (2:1 *n*-hexane/EtOAc); $[\alpha]_D^{26}$ +25.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.24 (10H, m), 5.01 (1H, dd, *J* = 9.6, 10.0 Hz), 4.90 and 4.63 (2H, ABq, *J* = 11.2 Hz), 4.77 and 4.61 (2H, ABq, *J* = 12.0 Hz), 4.60 (1H, d, *J* = 3.6 Hz), 4.13 (1H, dd, *J* = 2.0, 12.0 Hz), 4.02 (1H, dd, *J* = 6.0, 12.0 Hz), 3.93 (1H, dd, *J* = 9.6, 10.0 Hz), 3.90 (1H, m), 3.59 (1H, dd, *J* = 3.6, 9.6 Hz), 3.40 (3H, s), 1.21 (9H, s), 1.17 (9H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 178.1, 176.8, 138.3, 137.9, 128.5 × 2, 128.2 × 2, 128.1 × 2, 128.0, 127.4, 127.2 × 2, 98.1, 79.6, 79.4, 75.4, 73.5, 69.6, 67.9, 62.4, 55.3, 38.8, 38.7, 27.1 × 3, 27.0 × 3; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{42}O_8Na$ 565.2777, found 565.2786.

A solution of methyl 2,3-di-*O*-Bn-4,6-di-*O*-Piv-α-D-glucoside (**40**) (174 mg, 0.321 mmol) in dry THF (0.3 M, 1.07 mL) was stirred under H_2 atmosphere in the presence of 20% $Pd(OH)_2/C$ (17.4 mg) for 3 h at room temperature. After changing the atmosphere to Ar, the mixture was filtered through a Celite pad (washed with EtOAc), and then the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 *n*-hexane/acetone) gave **27** (110 mg, 0.305 mmol, 95% yield).

Compound 27: colorless syrup; R_f 0.37 (1:5 *n*-hexane/EtOAc); $[\alpha]_D^{27}$ +105.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.83 (1H, dd, *J* = 9.2, 10.0 Hz), 4.81 (1H, d, *J* = 4.0 Hz), 4.20 (1H, dd, *J* = 2.4, 12.0 Hz), 4.12 (1H, dd, *J* = 5.6, 12.0 Hz), 3.94 (1H, m), 3.83 (1H, ddd, *J* = 4.0, 9.2, 9.6 Hz), 3.59 (1H, ddd, *J* = 4.0, 8.4, 9.6 Hz), 3.45 (3H, s), 2.55 (1H, d, *J* = 4.0 Hz), 2.21 (1H, d, *J* = 8.4 Hz), 1.23 (9H, s), 1.22 (9H, s); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 178.1 × 2, 99.1, 72.8, 72.7, 70.3, 67.9, 62.4, 55.4, 38.9, 38.8, 27.1 × 3, 27.0 ×

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3; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{17}H_{31}O_8$ 363.2019, found 363.2015.

Compound 16α and 17α. To a solution of tetrahydroxydiboron (**10**) (0.80 mg, 8.92 μmol) and **13**[21] (12.6 mg, 44.6 μmol) in dry MeCN (0.2 M, 446 μL) was added a solution of **14**[9] (38.6 mg, 89.2 μmol) in dry MeCN (0.2 M, 446 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 9.81 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (1:1 *n*-hexane/EtOAc) gave a mixture of **16α** and **17α** (29.7 mg, 41.5 μmol, 93% yield, $\alpha(1,3)/\alpha(1,2)$ = 2.5:1) as an inseparable mixture.[22] Compound **16α**: white solid; mp 164−165 °C; R_f 0.35 (1:1 *n*-hexane/EtOAc); $[\alpha]_D^{27}$ +76.4° (*c* 0.76, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.47−7.45 (2H, m), 7.39−7.24 (16H, m), 7.16−7.13 (2H, m), 5.56 (1H, s), 5.12 (1H, s, *J* = 2.8 Hz), 4.93 and 4.78 (2H, ABq, *J* = 11.6 Hz), 4.80 (1H, d, *J* = 4.0 Hz), 4.82 and 4.47 (2H, ABq, *J* = 10.8 Hz), 4.57 and 4.51 (2H, ABq, *J* = 12.0 Hz), 4.31 (1H, dd, *J* = 4.8, 10.0 Hz), 4.19 (1H, m), 3.99 (1H, dd, *J* = 9.2, 9.6 Hz), 3.83 (1H, m), 3.77−3.72 (3H, m), 3.68−3.55 (4H, m), 3.46 (1H, dd, *J* = 8.8, 10.0 Hz), 3.42 (3H, s), 3.14 (1H, d, *J* = 7.6 Hz), 2.41 (1H, d, *J* = 9.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.7, 138.0, 137.7, 136.8, 129.0, 128.3, 128.2, 127.8, 127.6, 127.5, 125.8, 101.4, 100.2, 100.1, 83.4, 80.4, 80.1, 77.3, 75.1, 74.9, 73.4, 71.7, 70.9, 68.9, 68.7, 62.2, 55.4; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{41}H_{46}O_{11}Na$ 737.2938, found 737.2928.

Compound 17α: white solid; mp 166−167 °C; R_f 0.35 (1:1 *n*-hexane/EtOAc); $[\alpha]_D^{27}$ +109.6° (*c* 0.98, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.48 (2H, m), 7.40−7.24 (16H, m), 7.15−7.12 (2H, m), 5.53 (1H, s), 4.98 (1H, d, *J* = 3.6 Hz), 4.97 and 4.84 (2H, ABq, *J* = 11.6 Hz), 4.85 (1H, d, *J* = 5.6 Hz), 4.81 and 4.49 (2H, ABq, *J* = 10.8 Hz), 4.63 and 4.48 (2H, ABq, *J* = 12.0 Hz), 4.29 (1H, m), 4.12 (1H, m), 4.05 (1H, dd, *J* = 8.0, 8.8 Hz), 3.85−3.61 (8H, m), 3.48 (1H, dd, *J* = 8.8, 9.6 Hz), 3.43 (3H, s), 2.89 (1H, d, *J* = 2.4 Hz), 2.41 (1H, d, *J* = 9.6 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.7, 138.0, 137.8, 137.0, 129.2, 128.3 × 2, 127.9 × 3, 127.7 × 2, 127.6, 126.3, 102.0, 97.8, 97.7, 83.2, 81.2, 78.3, 77.2, 75.3, 75.1, 73.4, 72.8, 70.9, 69.3, 68.9, 68.3, 62.0, 55.3; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{41}H_{47}O_{11}$ 715.3118, found 715.3107.

Compound 22A and 22B. To a solution of **10** (0.56 mg, 6.25 μmol) and **22**[11] (10.4 mg, 31.2 μmol) in dry MeCN (0.2 M, 313 μL) was added a solution of **14** (27.0 mg, 62.5 μmol) in dry MeCN (0.2 M, 313 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 6.86 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (4:1 toluene/EtOAc) to afford **22A** (18.4 mg, 24.0 μmol, 77% yield) and **22B** (1.6 mg, 2.18 μmol, 7% yield).

Compound 22A: colorless syrup; R_f 0.57 (2:1 *n*-hexane/EtOAc); $[\alpha]_D^{25}$ +61.6° (*c* 1.20, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.38 (2H, m), 7.34−7.25 (11H, m), 7.14−7.12 (2H, m), 5.04 (1H, d, *J* = 3.5 Hz), 5.03 and 4.76 (2H, ABq, *J* = 11.0 Hz), 4.83 and 4.45 (2H, ABq, *J* = 11.0 Hz), 4.75 (1H, d, *J* = 5.5 Hz), 4.56 and 4.52 (2H, ABq, *J* = 12.5 Hz), 4.15−4.12 (2H, m), 3.88 (1H, dd, *J* = 10.0, 10.0 Hz), 3.81−3.69 (5H, m), 3.66 (1H, dd, *J* = 2.0, 10.0 Hz), 3.58−3.53 (2H, m), 3.45−3.41 (4H, m), 3.30 (1H, d, *J* = 5.5 Hz), 3.03 (1H, d, *J* = 10.0 Hz), 1.07 (9H, s), 1.01 (9H, s); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 138.8, 138.0, 137.7, 128.4, 128.3 × 2, 128.0, 127.9, 127.8, 127.7 × 2, 127.5, 101.5, 99.8, 85.1, 83.9, 76.2, 75.3, 75.1, 74.2, 73.4, 71.5, 71.2, 68.7, 66.6, 66.0, 55.6, 27.5, 26.9, 22.7, 19.9; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{42}H_{58}O_{11}SiNa$ 789.3646, found 789.3622.

Compound 22B: colorless syrup; R_f 0.49 (2:1 *n*-hexane/acetone); $[\alpha]_D^{25}$ +37.2° (*c* 0.46, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.38 (2H, m), 7.35−7.24 (11H, m), 7.16−7.14 (2H, m), 4.98 and 4.82 (2H, ABq, *J* = 11.5 Hz), 4.96 (1H, d, *J* = 4.0 Hz), 4.83 and 4.50 (2H, ABq, *J* = 11.0 Hz), 4.78 (1H, d, *J* = 4.0 Hz), 4.65 and 4.47 (2H, ABq, *J* = 12.0 Hz), 4.19 (1H, m), 4.11 (1H, dd, *J* = 5.0, 10.0 Hz), 3.86 (1H, dd, *J* = 10.0, 10.0 Hz), 3.82−3.77 (3H, m), 3.74−3.63 (6H, m), 3.42 (3H, s), 2.64 (1H, br-s), 2.46 (1H, d, *J* = 10.0 Hz), 1.05 (9H, s), 0.99 (9H, s); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 138.8, 138.3, 137.9, 128.3 × 2, 127.9 × 2, 127.8, 127.6 × 2, 127.5, 97.3, 83.6, 77.4, 76.4, 75.3, 74.9, 73.4, 73.0, 72.1, 70.6, 68.3, 66.4, 65.6, 55.4, 27.4, 26.9, 22.7, 19.9; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{42}H_{59}O_{11}Si$ 767.3827, found 767.3803.

Compound 23B. To a solution of **10** (0.57 mg, 6.36 μmol) and **23**[12] (13.4 mg, 31.8 μmol) in dry MeCN (0.2 M, 318 μL) was added a solution of **14** (27.5 mg, 63.6 μmol) in dry MeCN (0.2 M, 318 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 7.00 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (5:1 *n*-hexane/acetone) to afford **23B** (12.3 mg, 14.3 μmol, 45% yield): colorless syrup; R_f 0.31 (5:1 *n*-hexane/acetone); $[\alpha]_D^{28}$ +102.9° (*c* 0.73, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 7.40−7.39 (2H, m), 7.34−7.26 (11H, m), 7.13−7.11 (2H, m), 4.99 and 4.82 (2H, ABq, *J* = 11.0 Hz), 4.96 (1H, d, *J* = 4.0 Hz), 4.82 and 4.47 (2H, ABq, *J* = 11.0 Hz), 4.78 (1H, d, *J* = 3.5 Hz), 4.61 and 4.51 (2H, ABq, *J* = 12.0 Hz), 4.04 (1H, m), 3.85 (1H, br-d, *J* = 11.0 Hz), 3.77−3.67 (6H, m), 3.60−3.55 (2H, m), 3.51−3.49 (2H, m), 3.38 (3H, s), 2,57 (1H, d, *J* = 3.5 Hz), 2.50 (1H, d, *J* = 10.0 Hz), 0.89 (9H, s), 0.88 (9H, s), 0.12 (3H, s), 0.09 (3H, s), 0.06 (6H, s); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 138.7, 138.0, 137.8, 128.4 × 2, 128.0, 127.9, 127.7 × 2, 127.6, 97.8, 96.7, 83.5, 78.7, 75.3, 75.1, 73.4, 73.1, 72.9, 72.3, 71.1, 71.0, 68.3, 62.4, 54.7, 25.9 × 2, 18.4, 18.3, −3.9, −4.9, −5.1, −5.4; HRMS (ESI-TOF) m/z $[M + K]^+$ calcd for $C_{46}H_{70}O_{11}Si_2K$ 893.4094, found 893.4112.

Compound 24A and 24B. To a solution of **10** (0.64 mg, 7.14 μmol) and **24**[13] (10.2 mg, 35.7 μmol) in dry MeCN (0.2 M, 357 μL) was added a solution of **14** (30.9 mg, 71.4 μmol) in dry MeCN (0.2 M, 357 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 7.85 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (4:1 toluene/EtOAc) to afford **24A** (9.3 mg, 13.0 μmol, 36% yield) and **24B** (8.9 mg, 12.9 μmol, 36% yield).

Compound 24A: colorless syrup; R_f 0.42 (4:1 toluene/acetone); $[\alpha]_D^{25}$ +89.3° (*c* 0.72, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.37−7.27 (13H, m), 7.15−7.13 (2H, m), 5.05 (1H, dd, *J* = 9.6, 10.0 Hz), 4.91 (1H, d, *J* = 4.0 Hz), 4.90 and 4.80 (2H, ABq, *J* = 11.2 Hz), 4.80 (1H, d, *J* = 5.2 Hz), 4.80 and 4.46 (2H, ABq, *J* = 11.2 Hz), 4.56 and 4.49 (2H, ABq, *J* = 13.2 Hz), 4.28−4.21 (2H, m), 4.07 (1H, br-d, *J* = 12.4 Hz), 3.90−3.84 (2H, m), 3.72−3.55 (5H, m), 3.45 (1H, dd, *J* = 9.2, 9.6 Hz), 3.40 (3H, s), 3.24 (1H, d, *J* = 8.0 Hz), 2.10 (3H, s), 2.07 (3H, s), 1.93 (1H, d, *J* = 9.2 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.7 × 2, 138.5, 138.0, 137.6, 128.4 × 2, 127.9 × 2, 127.8, 127.7, 127.6, 100.4, 99.6, 83.1, 81.8, 77.5, 75.4, 74.9, 73.5, 72.9, 71.1, 70.9, 69.3, 68.8, 67.3, 62.1, 55.5, 20.9, 20.7; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{38}H_{46}O_{13}Na$ 733.2836, found 733.2801.

Compound 24B: white solid; mp 125−126 °C; R_f 0.36 (4:1 toluene/acetone); $[\alpha]_D^{25}$ +103.8° (*c* 0.95, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.27 (13H, m), 7.15−7.13 (2H, m), 4.96−4.88 (3H, m), 4.84−4.79 (3H, m), 4.59 and 4.48 (2H, ABq, *J* = 12.4 Hz), 4.48 (1H, ABq, *J* = 12.8 Hz), 4.25 (1H, dd, *J* = 4.8, 12.4 Hz), 4.10−4.06 (2H, m), 3.94 (1H, dd, *J* = 9.2, 9.2 Hz), 3.90 (1H, m), 3.78−3.66 (5H, m), 3.58 (1H, dd, *J* = 9.2, 9.2 Hz), 3.41 (3H, s), 3.03 (1H, br-s), 2.35 (1H, br-s), 2.08 (3H, s), 2.07 (3H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 170.7, 170.3, 138.6, 138.0, 137.7, 128.4, 127.9 × 2, 127.7, 127.6, 97.9, 97.3, 83.2, 78.6, 77.2, 75.3, 75.0, 73.5, 72.7, 71.0,

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70.5, 70.3, 68.5, 67.2, 62.2, 55.3, 20.8, 20.7; HRMS (ESI-TOF) m/z $[M + K]^+$ calcd for $C_{38}H_{46}O_{13}K$ 749.2576, found 749.2556.

Compound 25A and 25B. To a solution of **10** (0.51 mg, 5.69 μmol) and **25**[14] (10.6 mg, 28.4 μmol) in dry MeCN (0.2 M, 285 μL) was added a solution of **14** (24.6 mg, 56.9 μmol) in dry MeCN (0.2 M, 285 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 6.25 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (4:1 $CHCl_3$/EtOAc) to afford **25A** (4.7 mg, 5.82 μmol, 21% yield) and **25B** (8.1 mg, 10.0 μmol, 35% yield).

Compound 25A: colorless syrup; R_f 0.47 (4:1 $CHCl_3$/EtOAc); $[\alpha]_D^{27}$ +131.7° (*c* 0.19, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.16 (25H, m), 5.19 (1H, d, J = 3.5 Hz), 4.86−4.77 (5H, m), 4.67 (1H, ABq, J = 12.0 Hz), 4.59−4.45 (5H, m), 4.27 (1H, m), 3.92 (1H, dd, J = 9.0, 9.0 Hz), 3.79−3.56 (9H, m), 3.48 (1H, dd, J = 8.5 Hz, J = 8.0 Hz), 3.42 (1H, d, J = 10.0 Hz), 3.37 (3H, s), 2.22 (1H, d, J = 8.0 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.6, 138.0, 137.8 × 2, 128.4, 128.0, 127.9 × 2, 127.8 × 2, 127.7, 99.6, 83.1 × 2, 77.7, 77.2, 75.3, 74.9, 74.6, 73.6, 73.5, 72.9, 71.5, 71.0, 69.9, 68.8, 68.4, 55.2; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{48}H_{54}O_{11}Na$ 829.3564, found 829.3571.

Compound 25B: colorless syrup; R_f 0.33 (4:1 $CHCl_3$/EtOAc); $[\alpha]_D^{25}$ +94.7° (*c* 0.69, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.14 (25H, m), 4.98−4.96 (2H, m), 4.84−4.79 (4H, m), 4.64−4.60 (2H, m), 4.52−4.48 (4H, m), 4.07 (1H, m), 3.99 (1H, dd, J = 9.0, 9.0 Hz), 3.77−3.52 (10H, m), 3.38 (3H, s), 2.76 (1H, d, J = 3.0 Hz), 2.37 (1H, d, J = 9.5 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 138.7, 138.4, 138.1, 128.0, 137.8, 128.4, 127.9, 127.7, 127.6, 97.9, 97.2, 83.4, 78.7, 77.6, 77.2, 77.1, 75.3, 75.0, 74.8, 73.5 × 2, 73.0, 72.9, 71.0, 69.8, 68.5, 55.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{48}H_{54}O_{11}Na$ 829.3564, found 829.3527.

Compound 26A and 26B. To a solution of **10** (0.68 mg, 7.59 μmol) and **26** (15.3 mg, 37.9 μmol) in dry MeCN (0.2 M, 380 μL) was added a solution of **14** (32.8 mg, 75.9 μmol) in dry MeCN (0.2 M, 380 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 8.34 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (5:1 toluene/acetone) to afford **26A** (10.3 mg, 12.3 μmol, 32% yield) and **26B** (20.2 mg, 24.1 μmol, 64% yield).

Compound 26A: colorless syrup; R_f 0.52 (5:1 toluene/acetone); $[\alpha]_D^{25}$ +84.2° (*c* 0.61, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02−8.01 (4H, m), 7.58−7.53 (2H, m), 7.44−7.39 (4H, m), 7.34−7.24 (13H, m), 7.13−7.12 (2H, m), 5.42 (1H, dd, J = 9.5, 9.5 Hz), 4.94 (1H, d, J = 4.0 Hz), 4.83 (1H, d, J = 4.0 Hz), 4.83 and 4.73 (2H, ABq, J = 11.5 Hz), 4.78 and 4.43 (2H, ABq, J = 10.5 Hz), 4.58−4.48 (3H, m), 4.38 (1H, dd, J = 5.5, 12.0 Hz), 4.26−4.19 (2H, m), 4.08 (1H, dd, J = 9.0, 9.5 Hz), 3.75−3.64 (3H, m), 3.56−3.49 (2H, m), 3.45 (3H, s), 3.43 (1H, d, J = 8.0 Hz), 3.39 (1H, dd, J = 9.5, 10.0 Hz), 1.82 (1H, d, J = 9.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2, 166.0, 138.6, 138.0, 137.6, 133.6, 133.1, 129.8, 129.7, 129.1, 128.6, 128.4, 127.9, 127.8, 127.7, 127.6, 100.2, 99.5, 83.0, 81.8, 77.2, 75.4, 74.9, 73.5, 72.9, 71.3, 70.9, 70.5, 68.8, 67.4, 63.1, 55.5; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{48}H_{50}O_{13}Na$ 857.3149, found 857.3174.

Compound 26B: colorless syrup; R_f 0.45 (5:1 toluene/acetone); $[\alpha]_D^{25}$ +51.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06−8.01 (4H, m), 7.59−7.52 (2H, m), 7.44−7.37 (6H, m), 7.34−7.20 (11H, m), 7.14−7.11 (2H, m), 5.28 (1H, dd, J = 9.0, 9.0 Hz), 5.01 (1H, d, J = 4.0 Hz), 4.95 and 4.83 (2H, ABq, J = 11.0 Hz), 4.90 (1H, d, J = 3.5 Hz), 4.80 and 4.45 (2H, ABq, J = 11.5 Hz), 4.59−4.55 (2H, m), 4.48 (1H, ABq, J = 12.5 Hz), 4.38 (1H, dd, J = 5.5, 12.5 Hz), 4.21 (1H, m), 4.18−4.07 (2H, m), 3.82−3.70 (3H, m), 3.66 (2H, d), 3.59 (1H, dd, J = 9.0, 10.0 Hz), 3.46 (3H, s), 3.01 (1H, d, J = 4.5 Hz), 2,30 (1H, d, J = 9.5 Hz); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.2, 165.9, 138.6, 138.0, 137.6, 133.4, 133.1, 129.9, 129.7, 129.4, 128.4 × 2, 127.9 × 2, 127.8, 127.7 × 2, 98.0, 97.3, 83.2, 78.6, 77.2, 75.3, 75.0, 73.5, 72.8, 71.5, 71.0, 70.7, 68.4, 67.4, 63.2, 55.4; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{48}H_{50}O_{13}Na$ 857.3149, found 857.3113.

Compound 27A and 27B. To a solution of **10** (0.45 mg, 5.02 μmol) and **27** (9.10 mg, 25.1 μmol) in dry MeCN (0.2 M, 251 μL) was added a solution of **14** (21.7 mg, 50.2 μmol) in dry MeCN (0.2 M, 251 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 4 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 5.52 μmol). The aqueous layer was extracted with EtOAc (3 mL × 5), and then the combined extracts were washed with sat. NH_4Cl (aq, 2 mL), sat. $NaHCO_3$ (aq, 2 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (3:1 toluene/EtOAc) to afford **27A** (3.0 mg, 3.77 μmol, 15% yield) and **27B** (8.9 mg, 11.3 μmol, 45% yield).

Compound 27A: colorless syrup; R_f 0.48 (3:1 toluene/EtOAc); $[\alpha]_D^{25}$ + 93.8° (*c* 0.31, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38−7.37 (2H, m), 7.32−7.25 (11H, m), 7.13−7.11 (2H, m), 5.05 (1H, dd, J = 9.0, 9.5 Hz), 4.97 and 4.78 (2H, ABq, J = 11.5 Hz), 4.90 (1H, d, J = 4.0 Hz), 4.81 and 4.44 (2H, ABq, J = 10.5 Hz), 4.76 (1H, d, J = 4.0 Hz), 4.56 and 4.49 (2H, ABq, J = 12.5 Hz), 4.27 (1H, m), 4.17 (1H, br-d, 12.0 Hz), 4.04 (1H, dd, J = 5.5, 12.0 Hz), 3.92 (1H, m), 3.86 (1H, dd, J = 9.0, 9.5 Hz), 3.77−3.74 (1H, dd, J = 6.5, 6.5 Hz), 3.70−3.56 (5H, m), 3.44 (1H, dd, J = 8.5, 8.5 Hz), 3.39 (3H, s), 3.08 (1H, d, J = 9.0 Hz), 1.90 (1H, d, J = 10.5 Hz), 1.22 (18H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.1, 138.7, 138.1, 137.7, 128.4, 128.3, 128.0, 127.9 × 2, 127.7 × 2, 127.5, 100.4, 99.5, 83.3, 81.5, 77.2, 75.4, 74.9, 73.6, 73.1, 71.2, 70.7, 69.3, 68.9, 67.6, 62.1, 55.5, 39.1, 38.9, 27.1, 27.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{44}H_{58}O_{13}Na$ 817.3775, found 817.3813.

Compound 27B: colorless syrup; R_f 0.34 (3:1 toluene/EtOAc); $[\alpha]_D^{25}$ +89.0° (*c* 0.86, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.37 (2H, m), 7.34−7.26 (11H, m), 7.13−7.11 (2H, m), 4.98−4.94 (2H, m), 4.89−4.81 (3H, m), 4.80 and 4.47 (2H, ABq, J = 10.5 Hz), 4.60 and 4.48 (2H, ABq, J = 12.0 Hz), 4.18 (1H, dd, J = 1.5, 12.0 Hz), 4.13−4.06 (2H, m), 3.98−3.92 (2H, m), 3.76−3.62 (5H, m), 3.59 (1H, dd, J = 8.5, 9.5 Hz), 3.42 (3H, s), 2.78 (1H, d, J = 5.0 Hz), 2.34 (1H, d, J = 9.5 Hz), 1.22 (9H, s), 1.21 (9H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 178.1, 177.8, 138.7, 138.1, 137.7, 128.4 × 2, 128.3, 128.0, 127.9, 127.8 × 2, 127.7, 127.6, 97.7, 97.1, 83.3, 78.3, 77.2, 75.3, 75.0, 73.4, 72.8, 70.9, 70.8, 70.2, 68.3, 67.5, 62.3, 55.3, 38.9, 27.1, 27.0; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{44}H_{58}O_{13}Na$ 817.3775, found 817.3813.

Compound 31. To a solution of **10** (34.2 mg, 0.381 mmol) and **22** (637.7 mg, 1.90 mmol) in dry MeCN (28.6 mL) was added a solution of **30**[18] (2.24 g, 5.72 mmol) in dry MeCN (28.6 mL) at 40 °C under an Ar atmosphere. After the reaction mixture was stirred for 6 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 0.419 mmol, 7.6 mL). The aqueous layer was extracted with EtOAc (50 mL × 3), and then the combined extracts were washed with sat. NH_4Cl (aq, 50 mL), sat. $NaHCO_3$ (aq, 50 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash silica gel column chromatography (5:1 toluene/EtOAc) gave **31** (1.16 g, 1.596 mmol, 84% yield) and unreacted substrate **22** (58.2 mg, 174 μmol): colorless foam; R_f 0.74 (2:1 toluene/EtOAc); $[\alpha]_D^{26}$ +69.1° (*c* 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.44 (2H, m), 7.34−7.24 (3H, m), 5.11 (1H, d, J = 4.4 Hz), 5.01 and 4.80 (2H, ABq, J = 11.6 Hz), 4.77 (1H, d, J = 4.0 Hz), 4.18−4.08 (3H, m), 3.90−3.83 (4H, m), 3.74−3.57 (5H, m), 3.45 (3H, s), 2.75 (1H, d, J = 8.8 Hz), 2.43 (1H, d, J = 8.4 Hz), 1.08 (9H, s), 1.07 (9H, s), 1.01 (9H, s), 1.00 (9H, s); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 139.1, 128.1, 127.7, 127.3, 101.1, 96.6, 83.0, 82.1, 77.7, 76.7, 74.8, 72.5, 71.2, 67.0, 66.6, 66.5, 66.1, 55.6, 27.4, 27.3, 22.6 × 2, 19.9, 19.8; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{36}H_{62}O_{11}NaSi_2$ 749.3728, found 749.3735.

Compound 32. To a solution of **31** (704.9 mg, 0.970 mmol) in dry EtOAc (19.4 mL) was added 20% $Pd(OH)_2/C$ (704.9 mg) at room temperature, and the mixture was stirred under a H_2

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atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, the reaction was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 toluene/EtOAc) gave **32** (586.6 mg, 0.921 mmol, 95% yield): colorless foam; R_f 0.30 (2:1 toluene/EtOAc); $[\alpha]_D^{22}$ +72.4° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.08 (1H, d, *J* = 4.0 Hz), 4.77 (1H, d, *J* = 4.0 Hz), 4.15−4.08 (3H, m), 3.91−3.81 (3H, m), 3.77−3.56 (6H, m), 3.45 (3H, s), 2.75 (1H, d, *J* = 10.0 Hz), 2.69 (1H, br-s), 2.47 (1H, d, *J* = 8.4 Hz), 1.07 (9H, s), 1.05 (9H, s), 1.00 (9H, s), 0.99 (9H, s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 100.9, 99.7, 83.4, 77.2, 76.8, 74.7, 72.6, 71.3, 66.8, 66.4 × 2, 66.2, 55.6, 27.4 × 2, 27.0, 26.9, 22.6 × 2, 19.9, 19.8; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{29}H_{57}O_{11}Si_2$ 637.3439, found 637.3427.

Compound 33. To a solution of **10** (3.68 mg, 0.041 mmol) and **32** (130.8 mg, 0.205 mmol) in dry MeCN (616 μL) was added a solution of **30** (241.9 mg, 0.616 mmol) in dry MeCN (616 μL) at 60 °C under an Ar atmosphere. After the reaction mixture was stirred for 24 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 0.045 mmol, 820 μL). The aqueous layer was extracted with EtOAc (50 mL × 3), and then the combined extracts were washed with sat. NH_4Cl (aq, 50 mL) and sat. $NaHCO_3$ (aq, 50 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash silica gel column chromatography (4:1 toluene/EtOAc) gave **33** (153.4 mg, 0.149 mmol, 73% yield) and unreacted substrate **32** (24.8 mg, 38.9 μmol): colorless foam; R_f 0.71 (2:1 toluene/EtOAc); $[\alpha]_D^{24}$ +85.5° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.46−7.26 (5H, m), 5.18 (1H, d, *J* = 2.4 Hz), 5.10 (1H, d, *J* = 4.0 Hz), 5.03 and 4.87 (2H, ABq, *J* = 12.0 Hz), 4.76 (1H, d, *J* = 3.6 Hz), 4.31−4.07 (5H, m), 3.91−3.56 (13H, m), 3,45 (3H, s), 2.60 (1H, d, *J* = 8.4 Hz), 2.54 (1H, d, *J* = 9.6 Hz), 2.34 (1H, d, *J* = 8.8 Hz), 1.07−0.99 (54H, 6s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.3, 128.1, 127.7, 127.3, 101.2, 100.6, 99.7, 83.2, 82.3, 82.0, 77.9, 77.3, 74.8, 72.5, 71.3, 71.1, 66.7, 66.5, 66.4, 66.2, 55.7, 27.4 × 2, 27.0, 26.9, 22.6, 19.9, 19.8; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{43}H_{83}O_{16}Si_3$ 939.4989, found 939.4984.

Compound 34. To a solution of **33** (533.5 mg, 0.518 mmol) in dry EtOAc (5.18 mL) was added 20% $Pd(OH)_2/C$ (533.5 mg) at room temperature, and the mixture was stirred under a H_2 atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, the reaction was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 toluene/EtOAc) gave **34** (394.1 mg, 0.420 mmol, 81% yield): colorless foam; R_f 0.31 (2:1 toluene/EtOAc); $[\alpha]_D^{26}$ +101.6° (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.09 (1H, d, *J* = 3.6 Hz), 5.03 (1H, d, *J* = 4.4 Hz), 4.69 (1H, d, *J* = 4.0 Hz), 4.21−4.00 (5H, m), 3.83−3.48 (13H, m), 3.37 (3H, s), 2.74 (1H, br-s), 2.59 (1H, d, *J* = 9.6 Hz), 2.50 (1H, d, *J* = 9.6 Hz), 2.35 (1H, d, *J* = 8.8 Hz), 1.00−0.91 (54H, 6s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 101.2, 100.4, 99.7, 83.2, 82.2, 77.2, 76.8, 74.7, 72.6, 71.3, 71.0, 66.5, 66.4, 66.3, 66.2 × 2, 55.6, 27.4 × 2, 27.3, 26.9 × 3, 22.6, 22.5, 19.9, 19.8; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{36}H_{62}O_{11}NaSi_2$ 749.3728, found 749.3735.

Compound 35. To a solution of **10** (0.38 mg, 4.28 μmol) and **34** (20.1 mg, 21.4 μmol) in dry MeCN (64 μL) was added a solution of **30** (25.2 mg, 64.2 μmol) in dry MeCN (64 μL) at 50 °C under an Ar atmosphere. After the reaction mixture was stirred for 24 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 4.71 μmol, 85.6 μL). The aqueous layer was extracted with EtOAc (50 mL × 3), and then the combined extracts were washed with sat. NH_4Cl (aq, 50 mL) and sat. $NaHCO_3$ (aq, 50 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. Purification of the residue by flash silica gel column chromatography (4:1 *n*-hexane/EtOAc) gave **35** (17.9 mg, 13.4 μmol, 63% yield) and unreacted substrate **34** (7.3 mg, 7.77 μmol): colorless foam; R_f 0.74 (2:1 toluene/EtOAc); $[\alpha]_D^{22}$ +102.8° (*c* 0.86, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.46−7.24 (5H, m), 5.19 (1H, d, *J* = 2.8 Hz), 5.17 (1H, d, *J* = 4.0 Hz), 5.09 (1H, d, *J* = 4.0 Hz), 5.03 and 4.87 (2H, ABq, *J* = 11.2 Hz), 4.76 (1H, d, *J* = 3.6 Hz), 4.33−4.27 (2H, m), 4.20−4.06 (5H, m), 3.90−3.56 (17H, m), 3.45 (3H, s), 2.64 (1H, d, *J* = 8.0 Hz), 2.53 (1H, d, *J* = 9.6 Hz), 2.43 (1H, d, *J* = 9.6 Hz), 2.33 (1H, d, *J* = 8.8 Hz), 1.07−0.96 (72H, 8s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.4, 128.1, 127.7, 127.3, 101.3, 100.7, 100.6, 99.8, 83.4, 82.4, 82.3, 82.0, 77.9, 77.2, 77.1, 76.8, 74.9, 72.6, 71.4, 71.2, 71.1, 66.8, 66.5, 66.4, 66.3, 66.2, 66.1, 55.7, 27.4 × 2, 27.1, 27.0, 26.9, 22.6 × 3, 20.0 × 2, 19.9, 19.8; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{64}H_{115}O_{21}Si_4$ 1331.7008, found 1331.7008.

Compound 36. To a solution of **35** (46.0 mg, 34.5 μmol) in dry EtOAc (1.73 mL) was added 20% $Pd(OH)_2/C$ (23.0 mg) at room temperature, and the mixture was stirred under a H_2 atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, the reaction was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. Purification of the residue by silica gel column chromatography (2:1 toluene/EtOAc) gave **36** (35.6 mg, 28.7 μmol, 83% yield): colorless foam; R_f 0.48 (2:1 toluene/EtOAc); $[\alpha]_D^{22}$ +113.0° (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.16 (2H, dd, *J* = 3.6 Hz, *J* = 4.0 Hz), 5.09 (1H, d, *J* = 3.6 Hz), 4.76 (1H, d, *J* = 3.6 Hz), 4.33−4.23 (2H, m), 4.20−4.06 (5H, m), 3.90−3.54 (17H, m), 3,45 (3H, s), 2.72 (1H, br-s), 2.66 (1H, d, *J* = 10.4 Hz), 2.53 (1H, d, *J* = 10.0 Hz), 2.46 (1H, d, *J* = 9.2 Hz), 2.35 (1H, d, *J* = 8.8 Hz), 1.05−0.98 (72H, 8s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 101.3, 100.8, 100.4, 99.7, 83.4, 82.4, 77.2, 76.8, 74.8, 72.7, 71.5, 71.2, 71.1, 66.5, 66.4, 66.3, 66.2, 66.1, 55.7, 27.4 × 2, 27.3, 27.0, 26.9 × 2, 22.6 × 2, 22.5, 20.0, 19.9, 19.8; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{57}H_{109}O_{21}Si_4$ 1241.6539, found 1241.6504.

Compound 37A and 37B. To a solution of **10** (0.25 mg, 2.74 μmol) and **36** (17.0 mg, 13.7 μmol) in dry MeCN (51 μL) was added a solution of **14** (17.8 mg, 41.1 μmol) in dry MeCN (51 μL) at room temperature under an Ar atmosphere. After the reaction mixture was stirred for 24 h, the reaction was quenched by the addition of 50 mM $NaBO_3$ (aq, 3.01 μmol, 54.8 μL). The aqueous layer was extracted with EtOAc (50 mL × 3), and then the combined extracts were washed with sat. NH_4Cl (aq, 50 mL) and sat. $NaHCO_3$ (aq, 50 mL), and brine, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by preparative TLC (2:1 *n*-hexane/EtOAc) to afford **37A** (15.3 mg, 9.14 μmol, 67% yield) and **37B** (3.1 mg, 1.85 μmol, 14% yield).

Compound 37A: colorless foam; R_f 0.70 (2:1 toluene/EtOAc); $[\alpha]_D^{22}$ +105.4° (*c* 0.99, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.11 (15H, m), 5.26 (1H, d, *J* = 4.0 Hz), 5.14 (1H, d, *J* = 2.8 Hz), 5.14 (1H, d, *J* = 4.0 Hz), 5.10 (1H, d, *J* = 4.0 Hz), 5.04 and 4.79 (2H, ABq, *J* = 11.2 Hz), 4.83 and 4.45 (2H, ABq, *J* = 10.8 Hz), 4.76 (1H, d, *J* = 4.0 Hz), 4.62 and 4.48 (2H, ABq, *J* = 12.4 Hz), 4.40 (1H, m), 4.31−4.05 (7H, m), 3.90−3.51 (22H, m), 3.45 (3H, s), 2.95 (1H, d, *J* = 9.6 Hz), 2.82 (1H, d, *J* = 8.4 Hz), 2.53 (1H, d, *J* = 9.6 Hz), 2.37 (1H, d, *J* = 9.6 Hz), 2.32 (1H, d, *J* = 8.4 Hz), 1.06−0.94 (72H, 8s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.1, 138.4, 138.0, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.6, 127.5, 127.4, 101.3 × 2, 100.9, 100.2, 99.8, 84.0, 83.9, 83.4, 82.5, 81.2, 77.2, 76.9, 76.8, 75.2, 74.9, 74.2, 73.3, 71.7, 71.2, 71.1, 70.7, 68.5, 66.5 × 2, 66.4, 66.3 × 2, 66.0, 65.9, 55.7, 27.4 × 2, 27.3, 27.0, 26.9, 22.6 × 3, 22.5, 20.0 × 2, 19.9; HRMS (ESI-TOF) *m*/*z* $[M + H]^+$ calcd for $C_{84}H_{137}O_{26}Si_4$ 1673.8475, found 1673.8419.

Compound 37B: colorless foam; R_f 0.80 (2:1 toluene/EtOAc); $[\alpha]_D^{22}$ +102.5° (*c* 0.7, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.16 (15H, m), 5.76 (1H, d, *J* = 3.6 Hz), 5.24 (1H, d, *J* = 3.6 Hz), 5.11 (1H, d, *J* = 3.6 Hz), 5.08 (1H, d, *J* = 3.6 Hz), 5.04 and 4.53 (2H, ABq, *J* = 10.8 Hz), 4.83 and 4.79 (2H, ABq, *J* = 11.6 Hz), 4.76 (1H, d, *J* = 3.6 Hz), 4.65 and 4.53 (2H, ABq, *J* = 12.0 Hz), 4.37−4.28 (2H, m), 4.23−3.54 (28H, m), 3.45 (3H, s), 2.67 (1H, d, *J* = 10.0 Hz), 2.57 (1H, br-s), 2.51 (1H, d, *J* = 9.6 Hz), 2.30 (1H, d, *J* = 9.2 Hz), 2.14 (1H, d, *J* = 9.6 Hz), 1.07−0.95 (72H, 8s); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 139.0, 138.5 138.2, 128.3, 127.9 × 2, 127.8, 127.5 × 2, 127.4, 101.3, 99.8, 99.7, 95.7, 94.5, 84.0, 83.6, 80.9, 78.5, 77.5, 77.2, 76.8, 76.0, 75.4, 74.9, 74.6, 73.2, 73.0, 72.4, 71.0, 70.9, 70.5, 68.6, 66.3, 65.9, 65.8, 64.9, 55.7, 27.5, 27.4 × 2, 27.2, 27.1, 27.0, 26.9, 23.0, 22.6, 22.4, 20.0 × 2, 19.9; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{84}H_{136}O_{26}NaSi_4$ 1695.8295, found 1695.8324.

Compound 38. To a solution of **37** (41.8 mg, 25.0 μmol) in dry EtOAc (2.5 mL) was added 20% $Pd(OH)_2/C$ (41.8 mg) at room

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temperature, and the mixture was stirred under H_2 atmosphere. After the reaction mixture was stirred for 30 min at the same temperature, the reaction was filtered through a Celite pad, and the filtrate was concentrated *in vacuo*. To a solution of the residue in THF (1.25 mL) was added tetrabutyl-ammonium fluoride (43.4 μL, 0.150 mmol) at 0 °C under an Ar atmosphere. After the reaction mixture was stirred for 22 h at room temperature, the reaction was quenched by H_2O (1 mL) and EtOAc (1 mL). The aqueous layer was concentrated *in vacuo*. Purification of the residue by reverse phase column chromatography (H_2O) gave **38** (11.1 mg, 13.2 μmol, 53% yield): colorless foam; R_f 0.23 (10:10:3 $CHCl_3$/MeOH/H_2O); $[\alpha]_D^{25}$ + 55.1° (*c* 1.11, H_2O); ^1H NMR (400 MHz, D_2O) δ 5.38−5.34 (4H, m), 4.83 (1H, br-s), 4.05−3.99 (4H, m), 3.92−3.63 (25H, m), 3.55 (1H, dd, *J* = 4.0, 10.0 Hz), 3.41 (3H, s); $^{13}C\{^1H\}$ NMR(100 MHz, D_2O) δ 99.7, 99.6, 99.5, 99.4, 80.2, 80.1, 79.9, 73.2, 72.1, 72.0, 71.9, 71.8, 71.6, 70.7, 70.6, 70.3, 70.2, 70.1 × 2, 69.8, 60.8, 60.6 × 2, 60.4, 55.3; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{31}H_{54}O_{26}Na$ 865.2801, found 865.2817.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.0c02093.

^1H, ^{13}C, and $^1H-^1H$ COSY NMR spectrum charts for all new compounds (PDF)

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Notes

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