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Efficient Synthesis of the Deoxysugar Part of Versipelostatin by Direct and Stereoselective Glycosylation and Revision of the Structure of the Trisaccharide Unit

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Abstract: Efficient synthesis of the deoxysugar part of versipelostatin (VST) was achieved by direct and stereoselective glycosylation of the reduced VST aglycon. Activation of 2-deoxyglycosyl imidate with IBr under basic conditions enables α-selective glycosylation of β-2-deoxylglycosides without anomerization. Comparison of the synthetic and natural VST products using NMR indicates that versipelostatin has a β-D-digitoxose-(1,4)-α-L-oleandrose-(1,4)-β-D-digitoxose trisaccharide. In addition, results of a biological assay indicate that the deoxyoligosaccharide unit of the synthetic glycoside was important for biological activity of the compound.

Keywords: glycosides · glycosylation · iodine · oxidative activation · synthetic methods

Introduction

Deoxysugars are frequently found in naturally occurring, biologically active compounds that contain macrocyclic and aromatic aglycons.[1] Glycosylation of aglycons with 2-deoxysugars is an important strategy for tuning the physical properties of naturally occurring compounds.[2] In addition, deoxysugars also act as effective pharmacophores for binding receptor proteins or DNA. Therefore, modification of the deoxysugars of these natural products is an effective and attractive strategy for the development of new drug candidates and biochemical probes. However, the synthesis of oligodeoxysaccharides using a simple protocol remains difficult owing to the lack of hydroxyl groups.[3] For instance, as a result of the anomeric effect, 2-deoxy-β-glycosides are not thermodynamically or kinetically favored reaction products. To overcome these problems, several methods for the direct β-selective glycosylation are available, in which α-glycosyl halides and glycosyl phosphates are used as glycosyl donors.[4] Recently, we reported an effective method for direct β-selective glycosylation with 2-deoxyglycosides based on activation of 2-deoxyglycosyl imidates with I_2.[5] In contrast to the β-glycosides, 2-deoxy-α-glycosides are more readily synthesized.[6] The α-glycosides are thermodynamically favored products and can be prepared by glycosidation under relatively strong acidic conditions. However, these thermodynamically controlled α-glycosylation methods cannot be adapted to the glycosylation of 2-deoxy-β-glycosides as a result of anomerization and/or cleavage of the pre-installed β-glycosides. Therefore, an effective method for the synthesis of complex 2-deoxyoligosaccharides with both α- and β-glycosidic linkages is still needed.

Versipelostatin (VST **1**) was the first compound discovered to specifically inhibit expression of GRP78 elicited by glucose starved conditions such as the treatment of 2-deoxyglucose. VST **1** causes robust cell death during cellular stress, but exhibits only weak cytotoxicity under normal conditions.[7,8] VST **1** consists of a macrocyclic aglycon that bears a deoxytrisaccharide unit (β-D-digitoxose-(1,4)-α-D-

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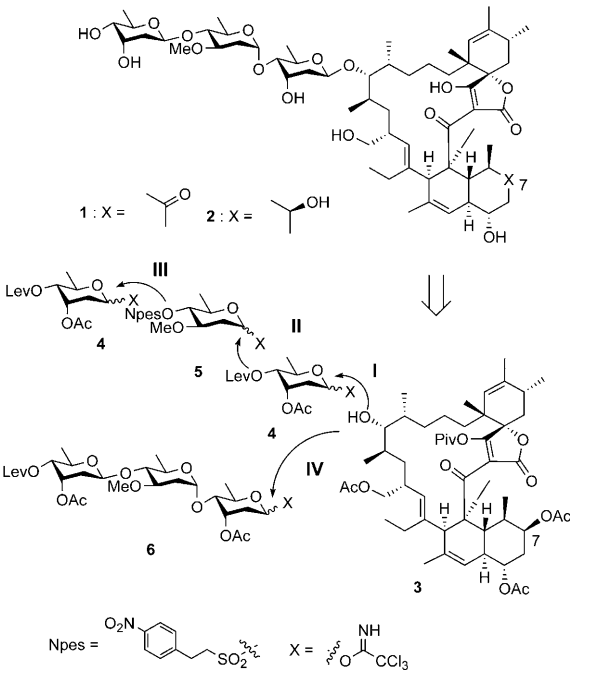
oleandrose-(1,4)-β-D-digitoxose). Our interest in both the biology and structure of the deoxytrisaccharide unit motivated us to develop an effective method for the synthesis of the deoxysugar of VST[9] and to evaluate its biological activity. Herein, we describe an efficient synthesis of the VST trisaccharides attached to the reduced VST aglycon by a direct and stereoselective glycosidation of 2-deoxyglycosides. We also report the effects of the deoxysugar of VST on the biological activity and the structure of the sugar portion of VST.

Results and Discussion

Scheme 1 shows our strategy for the synthesis of the VST trisaccharide **2** attached to a reduced VST aglycon by direct and stereoselective glycosidation of the D-digitoxoside **4** and the D-oleandroside **5**. Reduction of the β-hydroxyl ketone at the 7 position to a hydroxyl group might improve the chemical stability of the aglycon under both acidic and basic conditions. Two approaches for the synthesis of the deoxytrisaccharide **2** were examined. One is based on a stepwise synthetic strategy (I→II→III) and the other, on a convergent synthetic strategy involving coupling of deoxytrisaccharide unit **6** and aglycon **3** (IV). The D-digitoxosyl imidate **4** underwent direct β-selective glycosidation by activation of the glycosyl imidates using our previously reported method. Incorporation of the α-oleandroside requires efficient α-selective glycosylation to produce the 2-deoxy-β-glycoside bearing α-glycoside without anomerization.



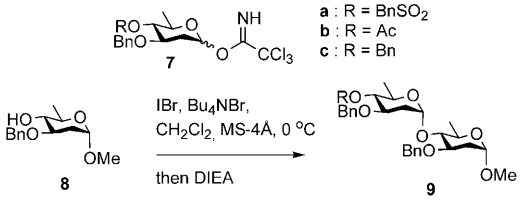
Scheme 1. Strategy for the synthesis of the VST trisaccharide **2** attached on a reduced VST aglycon.

Abstract in Japanese:

直接的かつ立体選択的なグリコシル化反応を利用するバーシペロスタチン(VST)３糖体の合成を行った。イミダート糖をヨウ化臭素を用いて活性化した後、塩基性条件にすることにより、2-デオキシβグリコシドの異性化なく、2-デオキシαグリコシドが得られることを見いだした。得られた配糖体の各種スペクトルデータや、生物活性を比較することにより、天然物VSTの糖鎖部は、L-オレアンドロースを含むデオキシ３糖であることを明らかにした。さらに、デオキシオリゴ糖部が活性発現に重要な役割を果たしていることを明らかにした。

Table 1 shows α-selective glycosidation of a 2-deoxysugar under basic conditions initiated by activation of glycosyl imidates **7a–c** with IBr.[10] Treatment of glycosyl imidate **7a** and acceptor **8** with IBr in the presence of Bu_4NBr at 0°C, followed by addition of *N,N*-diisopropylethylamine (DIEA) provided α-glycoside **9a** as a major product in 87% yield with α/β=97:3. Bu_4NBr played an important role in the α-selective glycosidation.[11] Addition of DIEA shortened the reaction time without adverse effects on yield or α-selectivity. The effects of various protecting groups were examined (Table 1, entries 4 and 5). Glycosidation of the 4-*O*-acetyl and benzyl derivatives **7b** and **7c** provided α-glycoside **9b** and **9c** in good yields but with reduced α-selectivity. These results indicate that a strong electron-withdrawing protecting group at the C4 position results in excellent α-selective glycosidation.

Table 1. α-Selective glycosidation of the 2,6-dideoxyglycosyl imidates **7** initiated by activation with IBr.

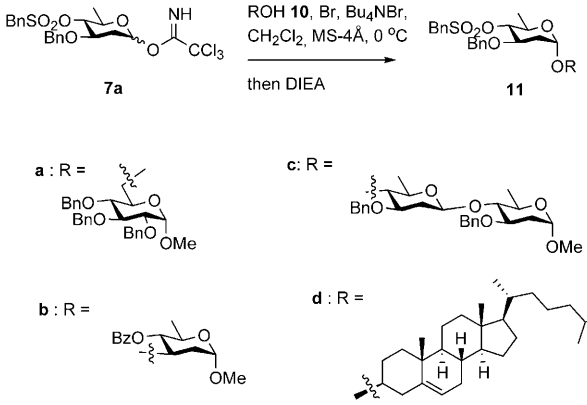


entry	Donor	R^2	Time [h]	Product	Yield [%]	α/β[a]
1	**7a**	$BnSO_2$	20	**9a**	87	93:7
2[b]	**7a**	$BnSO_2$	80	**9a**	87	92:8
3[c]	**7a**	$BnSO_2$	0.1	**9a**	91	33:67
4	**7b**	Ac	15	**9b**	82	89:11
5	**7c**	Bn	10	**9c**	77	77:23

[a] Ratio estimated from ^{1}H NMR spectral data. [b] The reaction was conducted without addition of DIEA. [c] Treatment with only IBr.

To demonstrate the feasibility of the α-selective glycosidation, we next applied the method to glycosylation of glycosyl acceptors **10a–d** (Table 2). Treatment of the 2-deoxysugar **10b** possessing a hydroxyl group at the C3 position with glycosyl imidate **7a** under the above described conditions provided the corresponding α-glycoside **11b** in good yield and selectivity. Glycosylation of the 2-deoxy-β-glycoside **10c** with the imidate **7a** provided trisaccharide **11c** without anomerization of the preinstalled β-glycoside. The steroid derivative **10d** also acted as an effective glycosyl acceptor for the α-selective glycosidation. However, glycosylation of

Table 2. α-Selective glycosidation of the 2,6-dideoxyglycosyl imidate **7a** initiated by activation with IBr.

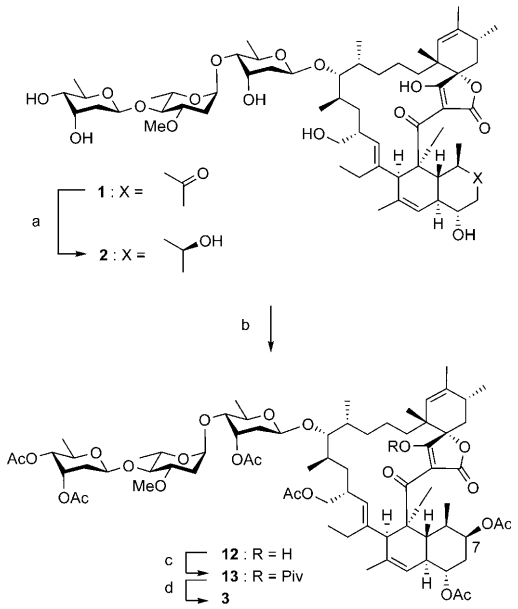


entry	Acceptor	Product	Yield [%]	α/β[a]
1	**10a**	**11a**	91	80:20
2	**10b**	**11b**	87	91:9
3	**10c**	**11c**	86	92:8
4	**10d**	**11d**	83	90:10

[a] Ratio estimated from ^{1}H NMR spectral data.

the primary alcohol **10a** resulted in good coupling yield, but moderate α-selectivity.

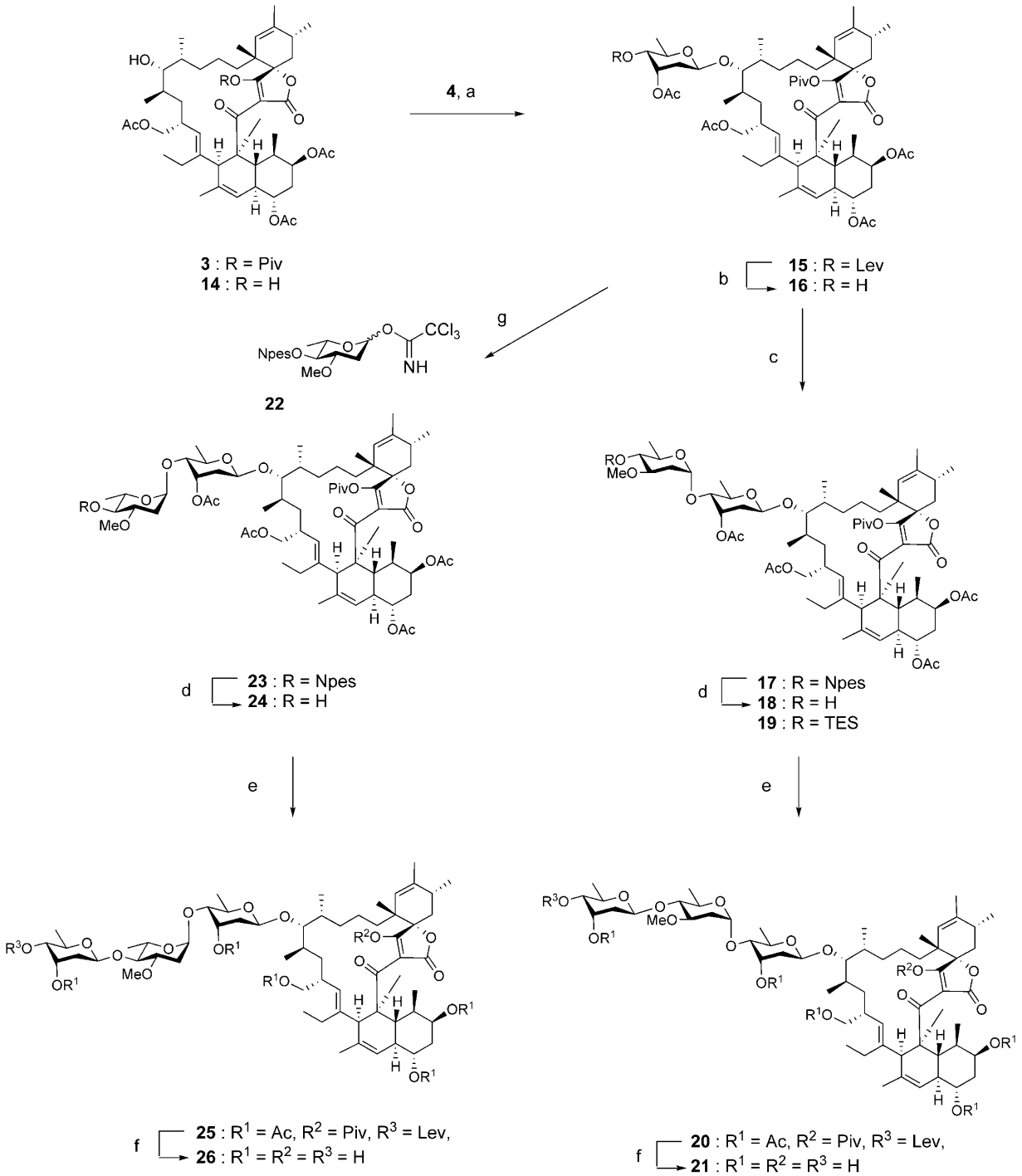
Synthesis of the reduced VST derivative **2** was then examined. Scheme 2 shows the preparation of the partially-protected reduced VST aglycon **3** from VST **1**. Chemo- and stereo-selective reduction of a ketone in VST **1** with L-selectride afforded the reduced VST **2** in 89%. Treatment of the reduced VST **2** with Ac_2O and *N,N,N′,N′*-tetramethylethylenediamine (TMEDA) in the presence of 4-dimethylaminopyridine (DMAP) resulted in acetylation of all hydroxyl groups, except for tetronic acid, to provide the hexaacetylated VST derivative **12** in 90% yield. Treatment of the remaining tetronic acid unit with pivaloyl chloride and TMEDA at reflux in CH_2Cl_2, followed by hydrolysis of the deoxytrisaccharide unit under mildly acidic conditions provided the reduced aglycon **3** in 85% yield in 2 steps. The stereochemistry at the C7 position was determined to be *S* based on ^{1}H NMR analysis, which showed a broad singlet for the C7 position.



Scheme 2. Reagents and conditions: a) L-selectride, THF, 78 °C to RT, 89%. b) Ac_2O, TMEDA, DMAP, CH_2Cl_2, RT, 90%. c) PivCl, TMEDA, DMAP, CH_2Cl_2, reflux. d) 20% TFA in CH_2Cl_2:MeOH (9:1), 85% from **12**.

The glycosylation of the reduced VST aglycon **3** with deoxysugars is shown in Scheme 2. Treatment of the reduced VST aglycon **3** and 2.5 equivalents of the D-digitoxosyl imidate **4** with I_2[5,12] in the presence of a catalytic amount of triethyl silane[13] provided the β-digitoxoside **15** in 82% yield with excellent β-selectivity (α/β = 5:95). Protection of the tetronic acid was required during glycosylation because use of the free tetronic acid **14** as a glycosyl acceptor results in glycosylation of the tetronic acid. Selective deprotection of the Lev group of **15** with $NH_2NH_2{\cdot}H_2O$ afforded acceptor **16** in 90%. The α-selective glycosylation of acceptor **16** with the D-oleandrosyl imidate **5** was conducted. *p*-Nitrophenylethylsulfonyl (Npes) ester[14] was used as a strong electron-withdrawing protecting group at the C4 position instead of benzylsulfonyl ester[15] because it can be selectively removed under mildly basic conditions in the presence of ester protecting groups. Treatment of both acceptor **16** and 2.5 equivalents of D-oleandrosyl imidate **5** with IBr in the presence of Bu_4NBr at 0 °C, followed by addition of DIEA to the reaction mixture at the same temperature, provided the α-D-oleandroside **17** in 75% yield with excellent α-selectivity (α/β = 95:5). Selective removal of the Npes protecting group was achieved by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) treatment to afford acceptor **18** in 77% yield. Pivaloate was an effective protecting group for tetronic acid because it survived under the conditions used for removal of the Npes group. Finally, β-selective glycosylation of acceptor **18** with D-digitoxosyl imidate **4** was achieved by using I_2 and triisopropylsilane to provide the protected, reduced VST derivative **20** in 80% yield with good β-selectivity (α/β = 4:96). Use of triethylsilane instead of triisopropylsilane resulted in formation of a significant amount of the triethylsilyl ether **19**. Treatment of the protected VST derivative **20** with NaOMe at reflux for 24 h provided the reduced VST derivative **21** in good yield. Hydrolysis of the tetronic acid moiety was not observed under these reaction conditions. However, ^{1}H NMR data of the synthetic reduced VST derivative **21** was identical with that of the reduced natural product **2**.

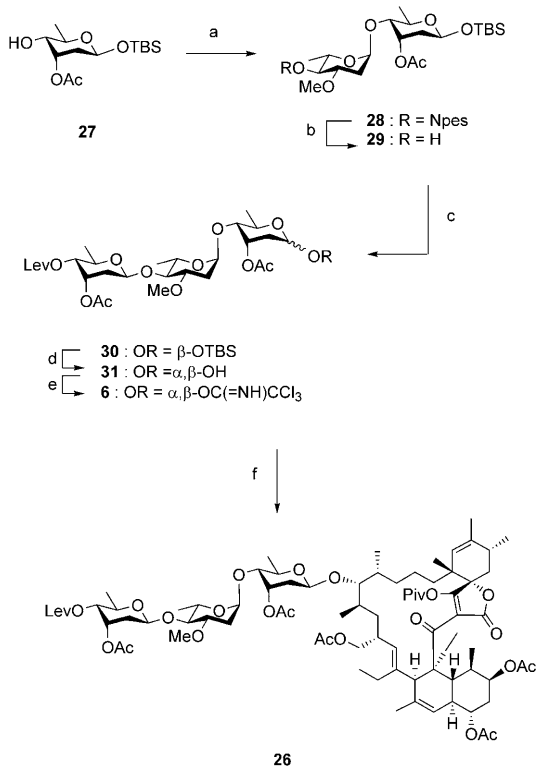
We next examined the synthesis of the trisaccharide derivative **26**, which has an α-L-oleandroside instead of an α-D-oleandroside (Scheme 3). The α-selective glycosidation of the L-oleandrosyl imidate **22** was achieved, using the procedure described for glycosidation of the D-oleandrosyl imidate **5**, to afford the α-L-oleandroside **23** in comparable yield and α-selectivity (80%, α/β = 95:5). Selective removal of the Npes protecting group (75%), followed by β-selective glycosidation of the D-digitoxosyl imidate **4** provided the



Scheme 3. Reagents and conditions: a) **4**, I_2, Et_3SiH, MS-4 Å, toluene, −94 °C, 82 %, α/β = 95:5; b) $H_2NNH_2{\cdot}H_2O$, Py, AcOH, 90 %; c) **5**, IBr, TBAB, MS-4 Å, CH_2Cl_2, 0 °C then DIEA, 75 %, α/β = 95:5; d) DBU, CH_3CN, 77 % for **18**, 75 % for **24**; e) **5**, I_2, iPr_3SiH, MS-4 Å, toluene, −94 °C, 80 %, α/β = 4:96 for **20**, 81 %, α/β = 4:96 for **25**; f) NaOMe, MeOH, reflux, 24 h, 75 % for **21**, 75 % for **26**; g) **22**, IBr, TBAB, MS-4 Å, CH_2Cl_2, 0 °C then DIEA, 80 %, α/β = 95:5.

protected trisaccharide **25** in 81 % yield with good β-selectivity (α/β = 6:94). Removal of the all acyl protecting groups under basic conditions afforded the trisaccharide derivative **26** in 75 % yield. ^1H and ^{13}C NMR data of the synthetic reduced VST derivative **26** were consistent with those of the reduced natural product **2**. These results indicate that the naturally occurring VST trisaccharide has an L-oleandroside instead of a D-oleandroside.[16]

Convergent synthesis of the reduced VST derivative **25** from trisaccharide donor **6** and aglycon **3** was conducted (Scheme 4). The trisaccharide glycosyl donor **6** was prepared from the silyl β-glycoside **27**. Treatment of the D-β-digitoxo-

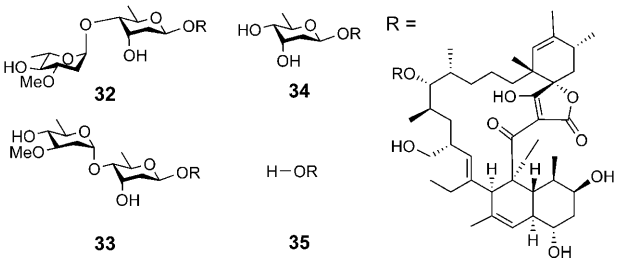


Scheme 4. Reagents and conditions; a) **5**, IBr, TBAB, MS-4 Å, CH_2Cl_2, 0 °C then DIEA, 96 %, α/β = 94:6; b) DBU, CH_3CN, 77 %; c) **4**, I_2, Et_3SiH, MS-4 Å, toluene, −94 °C, 85 %, α/β = 5:95; d) HF·pyridine, pyridine, RT, 80 %; e) CCl_3CN, $CsCO_3$, CH_2Cl_2, RT, 89 %; f) **3**, I_2, Et_3SiH, MS-4 Å, toluene, −94 °C, 40 %, α/β = 5:95.

side **27** and 1.5 equivalents of the the L-oleandrosyl imidate **4** with IBr in the presence of tetrabutylammoniumbromide (TBAB), followed by addition of DIEA afforded the α-L-oleandroside **28** in 96 % yield with excellent α-selectivity (α/β = 96:4). Selective removal of the Npes protecting group was achieved by DBU treatment to afford acceptor **29** in 77 % yield. The β-selective glycosylation of acceptor **29** with D-digitoxosyl imidate **4** was achieved by using I_2 and triisopropylsilane to provide the VST trisacchride **30** in 86 % yield with good β-selectivity (α/β = 5:95). Cleavage of the silyl ether by HF·pyridine in pyridine, followed by reaction of the resulting hemiacetal with CCl_3CN provided the glycosyl imidate **6** in 89 % yield as an anomeric mixture. Coupling of the trisaccharide donor **6** and the reduced VST aglycon **3** was examined. Treatment of the reduced VST aglycon **3** and 2.0 equivalents of the trisaccharide donor **6** with I_2 in the presence of a catalytic amount of triethylsilane[13] provided the reduced VST derivative **26** in 40 % yield with excellent β-selectivity (α/β = 5:95). Although the coupling yield of the method is moderate, this approach would be effective for the synthesis of sugar derivatives from aglycon whose availability is limited.

We next examined the cytotoxicity of the VST derivatives **1**, **2**, **21**, **26**, and **32**–**35** in HeLa cells under glucose-deprivation (Table 3).[8] The VST derivatives **32**–**35** were prepared

Table 3. Cytotoxicity of the VST derivatives **1**, **2**, **21**, **26**, and **32**–**35** against HeLa cells under glucose-deprived conditions.



Entry	compound	IC_{50} [μM]
1	VST (**1**)	1.27
2	**2**[a]	2.72
3	**21**	10.8
4	**26**	2.69
5	**32**	6.74
6	**33**	12.8
7	**34**	>20
8	**35**	>20

[a] Prepared from natural product.

by hydrolysis of **24**, **18**, **15**, and **3**, respectively.[17] Reduction of the ketone at the C7 position did not affect the cytotoxicity (Table 3, entry 2). The activity of the reduced synthetic VST **21**, which reportedly has a trisaccharide derivative, was significantly less than that of the reduced natural product VST **2**. On the other hand, the trisaccharide derivative **26**, which has an L-oleandoroside, exhibited cytotoxicity comparable to that of **2**. These results also support the conclusion that the natural VST trisaccharide was β-D-digitoxose-(1,4)-α-L-oleandrose-(1,4)-β-D-digitoxose. In addition, the difference of biological activities between disaccharides **32** and **33** clearly indicates that L-oleandoroside is important for exhibiting the biological activity. On the other hand, cytotoxicity induced by monosaccharide **34** and aglycon **35** was not observed. These results clearly indicate that the naturally occurring VST has a trisaccharide with L-oleandoroside. In addition, the disaccharide unit ((1,4)-α-L-oleandrose-(1,4)-β-D-digitoxose)) was important for the biological activity of VST.

Conclusions

In conclusion, we report an efficient synthesis of reduced VST derivatives from the reduced VST aglycon **3** by direct and stereoselective glycosidation. Activation of the 2-deoxyglycosyl imidates with IBr in the presence of a halide ion, followed by exposure to basic conditions enabled α-selective glycosidation of 2-deoxysugars without anomerization of the pre-installed 2-deoxy-β-glycosides. ^{1}H NMR analysis and biological assay of the synthetic derivatives confirmed that the VST trisaccharide contained L-oleandrose. In addition, the deoxytrisaccharide unit strongly influenced the biological activity of VST. The synthesis of various sugar-modified VST derivatives using this method is currently in progress.

Experimental Section

General Techniques

NMR spectra were recorded on a JEOL Model EX-270 (270 MHz for ^{1}H, 67.8 MHz for ^{13}C) or a JEOL Model ECP-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C) in the indicated solvent. Chemical shifts were reported in part per million (ppm) relative to the signal (0.00 ppm) for internal tetramethylsilane solutions in $CDCl_3$. ^{1}H NMR spectral data are reported as follows: $CDCl_3$ (7.26 ppm) or CD_2Cl_2 (5.30 ppm). ^{13}C NMR spectral data are reported as follows: $CDCl_3$ (77.1 ppm). NMR multiplicities are reported using the following abbreviations. (s: singlet, d: doublet, t: triplet, q: quartet m: multiplet, br: broad, *J*: coupling constants in Hertz.). Infrared spectra (IR) were recorded on a Perkin–Elmer Spectrum 1. Only the strongest and/or structurally important absorbances are reported as the IR data given in cm^{-1}. Optical rotations were measured on a JASCO model P-1020 polarimeter. The reactions were monitored by thin layer chromatography carried out on Merck precoated TLC plates (60F-254) using UV light and *p*-anisaldehyde H_2SO_4 ethanol solution. Flash column chromatography separations were performed using silica gel (KANTO, silica gel 60 N, spherical, neutral, 40–100 μm). NH column chromatography separations were performed using silica gel (FUJI SILYSIA, NH-functionalized silica gel, 100–200 mesh). Gel permeation chromatography (GPC) for qualitative analysis was performed on Japan Analytical Industry Model LC908 (recycling preparative HPLC) using a polystylene gel column (JAIGEL-1H, 20 mm × 600 mm). Detection of products was made using a UV detector (Japan Analytical Industry Model 310) and a refractive index detector (Japan Analytical Industry Model RI-5). ESI-TOF mass spectra were measured with P. E. Biosystems TK-3500 Biospectrometry Workstation. Dry THF, dry toluene, and dry ether were distilled from sodium wire containing a catalytic amount of benzophenone. Dry CH_2Cl_2 was distilled from P_2O_5. Dry DMF and dry triethylamine were distilled from CaH_2. Dry methanol and dry ethanol were distilled from magnesium contained with a catalytic amount of iodine.

9a: A mixture of **8** (19.0 mg, 75.3 μmol), **7a** (60.6 mg, 113 μmol) and pulverized activated MS-4 Å (113 mg) in dry CH_2Cl_2 (1.13 mL) was stirred at RT for 30 min under argon to remove a trace amount of water. A mixture of 1.00 M IBr in CH_2Cl_2 (151 μL, 151 μmol) and tetrabutylammonium bromide (60.7 mg, 188 μmol) was then added to the reaction mixture at 0 °C. After being stirred for 2 h, *N,N*-diisopropylethylamine (6.58 μL, 37.7 μmol) was added to the reaction mixture at the same temperature. After being stirred for 18 h, the reaction mixture was filtered through Celite. The filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$ with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 70:30 and further purified by gel permeation chromatography (GPC) to give **9a** (41.1 mg, 65.6 μmol, 87 %, α/β = 93:7). The α,β isomers were separated by chromatographed on silica gel with toluene/ethyl acetate 85:15. The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). **α-9a**: $[\alpha]_D^{24} = +45.3°$ (c = 1.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–7.35 (m, 15 H), 5.42 (d, 1 H, J = 3.4 Hz), 4.75 (d, 1 H, J = 3.4 Hz), 4.62 (d, 1 H, J = 11.6 Hz), 4.58 (d, 1 H, J = 11.6 Hz), 4.42 (d, 1 H, J = 11.6 Hz), 4.40 (d, 1 H, J = 11.6 Hz), 4.36 (d, 1 H, J = 14.0 Hz), 4.35 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 4.22 (d, 1 H, J = 14.0 Hz), 3.91–3.99 (m, 2 H), 3.85 (ddd, 1 H, J = 4.8 Hz, J = 9.2 Hz, J = 11.1 Hz), 3.67 (dq, 1 H, J = 6.3 Hz, J = 9.2 Hz), 3.33 (s, 3 H), 3.31 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 2.29 (dd, 1 H, J = 4.8 Hz, J = 12.6 Hz), 2.24 (dd, 1 H, J = 4.8 Hz, J = 12.1 Hz), 1.63 (ddd, 1 H, J = 3.4 Hz, J = 11.1 Hz, J = 12.6 Hz), 1.60 (ddd, 1 H, J = 3.4 Hz, J = 11.6 Hz, J = 12.1 Hz), 1.28 (d, 3 H, J = 6.3 Hz), 1.27 ppm (d, 3 H, J = 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 137.7, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.9, 127.8, 127.7, 98.3, 98.2, 84.8, 81.6, 77.8, 74.4, 71.0, 70.8, 66.6, 66.4, 57.4, 54.7, 35.6, 35.2, 18.6, 17. ppm; IR (solid): $\tilde{\nu}$ = 2935, 2905, 1455, 1360, 1173, 1098, 1050, 995 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{42}O_9S$ $[M+Na]^+$ m/z = 649.2447, found: 649.2452; **β-9a**: $[\alpha]_D^{22} = +38.0°$ (c = 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21–7.36 (m, 15 H), 4.65–4.73 (m, 4 H), 4.61 (d, 1 H, J = 11.6 Hz), 4.46 (d, 1 H, J = 11.1 Hz), 4.37 (d, 1 H, J = 14.0 Hz), 4.35 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 4.23 (d, 1 H, J = 14.0 Hz), 3.87 (ddd, 1 H, J = 5.3 Hz, J = 8.7 Hz, J = 11.1 Hz), 3.64–3.74 (m, 2 H), 3.36 (dq, 1 H, J = 6.3 Hz, J = 9.2 Hz), 3.27–3.32 (m, 4 H), 2.44 (ddd, 1 H, J = 1.9 Hz, J = 4.8 Hz, J = 12.6 Hz), 2.25 (dd, 1 H, J = 4.8 Hz, J = 13.0 Hz), 1.62–1.72 (m, 2 H), 1.29 (d, 3 H, J = 6.3 Hz), 1.27 ppm (d, 3 H, J = 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 137.2, 130.6, 128.8, 128.7, 128.6, 128.3, 127.6, 127.5, 99.7, 98.2, 84.1, 83.3, 76.1, 75.5, 72.0, 70.6, 70.3, 66.6, 57.5, 54.6, 36.9, 35.7, 18.3, 17.9 ppm; IR (solid): $\tilde{\nu}$ = 3032, 2935, 1496, 1455, 1355, 1051, 986, 834, 737, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{42}O_9S$ $[M+Na]^+$ m/z = 649.2447, found: 649.2420.

11a: According to the method for the synthesis of **9a**, a mixture of **10a** (22.1 mg, 47.7 μmol), **7a** (38.3 mg, 71.5 μmol), and MS-4 Å (71.5 mg) in CH_2Cl_2 (0.953 mL) was treated with a mixture of 1.00 M IBr in CH_2Cl_2 (95.3 μL, 95.3 μmol) and TBAB (38.4 mg, 119 μmol) at 0 °C for 2 h. *N,N*-Diisopropylethylamine (4.18 μL, 24.0 μmol) was then added to the reaction mixture. After being stirred for 10 h at the same temperature, to give **11a** (36.1 mg, 43.0 μmol, 91 %, β/α = 20:80) after purification. The α,β isomers were separated by chromatography on silica gel with hexane/ethyl acetate 85:15. **α-11a**: $[\alpha]_D^{20} = +47.7°$ (c = 0.685, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.40 (m, 25 H), 5.02 (d, 1 H, J = 10.6 Hz), 4.96 (d, 1 H, J = 11.1 Hz), 4.92 (d, 1 H, J = 3.4 Hz), 4.82 (d, 1 H, J = 10.6 Hz), 4.81 (d, 1 H, J = 12.6 Hz), 4.70 (d, 1 H, J = 12.6 Hz), 4.66 (d, 1 H, J = 11.1 Hz), 4.62 (d, 1 H, J = 3.4 Hz), 4.54 (d, 1 H, J = 11.1 Hz), 4.47 (d, 1 H, J = 11.1 Hz), 4.36 (d, 1 H, J = 13.5 Hz), 4.35 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 4.21 (d, 1 H, J = 13.5 Hz), 4.02 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 3.98 (ddd, 1 H, J = 4.8 Hz, J = 9.2 Hz, J = 11.1 Hz), 3.71–3.80 (m, 3 H), 3.47–3.59 (m, 3 H), 3.37 (s, 3 H), 2.42 (dd, 1 H, J = 4.8 Hz, J = 12.6 Hz), 1.68 (ddd, 1 H, J = 3.4 Hz, J = 11.1 Hz, J = 12.6 Hz), 1.18 ppm (d, 3 H, J = 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7, 138.2, 137.5, 130.7, 128.8, 128.8, 128.6, 128.6, 128.2, 128.1, 128.1, 128.0, 127.8, 127.6, 98.0, 97.1, 84.6, 82.3, 80.1, 77.9, 75.9, 75.0, 74.0, 73.4, 70.7, 69.8, 66.1, 66.0, 57.4, 55.2, 35.3, 17.7 ppm; IR (neat): $\tilde{\nu}$ = 2924, 1455, 1357, 1160, 1093, 1073, 993 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{48}H_{54}O_{11}S$ $[M+Na]^+$ m/z = 861.3285, found: 861.3286; **β-11a**: $[\alpha]_D^{25} = +12.7°$ (c = 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.52 (m, 25 H), 5.00 (d, 1 H, J = 11.1 Hz), 4.90 (d, 1 H, J = 11.6 Hz), 4.81 (d, 1 H, J = 11.1 Hz), 4.79 (d, 1 H, J = 12.1 Hz), 4.66 (d, 1 H, J = 11.1 Hz), 4.65 (d, 1 H, J = 12.1 Hz), 4.60 (d, 1 H, J = 3.4 Hz), 4.56 (d, 1 H, J = 11.6 Hz), 4.46 (d, 1 H, J = 11.1 Hz), 4.38 (d, 1 H, J = 14.0 Hz), 4.32 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 4.23 (d, 1 H, J = 14.0 Hz), 4.18 (dd, 1 H, J = 1.9 Hz, J = 9.7 Hz), 4.03 (dd, 1 H, J = 1.9 Hz, J = 11.1 Hz), 3.99 (dd, 1 H, J = 9.2 Hz, J = 9.2 Hz), 3.75 (ddd, 1 H, J = 1.9 Hz, J = 4.3 Hz, J = 9.2 Hz), 3.65 (ddd, 1 H, J = 4.8 Hz, J = 9.2 Hz, J = 11.6 Hz), 3.48–3.59 (m, 3 H), 3.34–3.40 (m, 4 H), 2.27 (ddd, 1 H, J = 1.9 Hz, J = 4.8 Hz, J = 12.6 Hz), 1.67 (ddd, 1 H, J = 9.7 Hz, J = 11.6 Hz, J = 12.6 Hz,), 1.31 ppm (d, 3 H, J = 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.6, 138.2, 137.2, 128.9, 128.8, 128.7, 128.6, 128.5, 128.5, 128.2, 128.2, 128.1, 128.1, 128.0, 127.9, 127.8, 127.7, 99.5, 98.1, 84.1, 82.2, 76.0, 75.8, 74.8, 73.4, 70.6, 70.2, 69.6, 67.8 57.5, 55.3, 36.3, 17.8 ppm; IR (solid) $\tilde{\nu}$ = 3029, 2932, 1496, 1454, 1356, 1073, 994, 941, 697 cm^{-1}.

11b: According to the method for the synthesis of **9a**, a mixture of **10b** (22.5 mg, 84.0 μmol), **7a** (68.2 mg, 127 μmol), and MS-4 Å (127 mg) in CH_2Cl_2 (1.68 mL) was treated with a mixture of 1.00 M IBr in CH_2Cl_2 (168 μL, 168 μmol) and TBAB (67.6 mg, 210 μmol) at 0 °C for 2 h. *N,N*-Diisopropylethylamine (7.31 μL, 42.0 μmol) was then added to the reaction mixture. After being stirred for 16 h at the same temperature, to give **11b** (46.3 mg, 72.2 μmol, 86 %, β/α = 8:92) after purification. The α,β isomers were separated by chromatography on silica gel with toluene/ethyl acetate 92:8. **α-11b**: $[\alpha]_D^{24} = +26.3°$ (c = 1.04, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, 2 H, J = 7.2 Hz), 7.19–7.60 (m, 13 H), 4.97 (dd, 1 H, J = 9.7 Hz, J = 9.7 Hz), 4.95 (d, 1 H, J = 3.9 Hz), 4.79 (d, 1 H, J = 3.4 Hz), 4.48 (d, 1 H, J = 11.1 Hz), 4.35 (d, 1 H, J = 11.1 Hz), 4.30 (d, 1 H, J = 14.0 Hz), 4.29 (dd, 1 H, J = 9.7 Hz, J = 9.7 Hz), 4.19 (d, 1 H, J = 14.0 Hz), 4.14 (ddd, 1 H, J = 5.3 Hz, J = 9.7 Hz, J = 11.6 Hz), 3.84–4.00 (m, 3 H), 3.36 (s, 3 H), 2.21 (dd, 1 H, J = 12.6 Hz, J = 5.3 Hz), 2.07 (dd, 1 H, J = 4.8 Hz, J = 12.6 Hz), 1.87 (ddd, 1 H, J = 3.4 Hz, J = 11.6 Hz, J = 12.6 Hz), 1.45 (ddd, 1 H, J = 3.9 Hz, J = 11.1 Hz, J = 12.6 Hz), 1.28 (d, 3 H, J = 6.3 Hz), 1.23 ppm (d, 3 H, J = 6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.8, 137.5, 133.5, 130.6, 129.8, 129.6, 128.8, 128.7, 128.6, 128.1, 127.9, 98.7, 98.2, 84.7, 74.8, 73.9, 70.6, 66.3, 65.9, 57.3, 54.9, 37.2, 35.6, 17.8,

17.7 ppm; IR (solid): $\tilde{\nu}$=3065, 3035, 2936, 1717, 1495, 1453, 1357, 1271, 996, 892, 832, 790, 755, 708, 620 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{40}O_{10}S$ $[M+Na]^+$ m/z=663.2234, found: 663.2239. **β-11b**: $[\alpha]_D^{25}$=+4.2° (c=1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.06 (d, 2H, J=7.2 Hz), 7.16–7.54 (m, 13H), 4.91 (dd, 1H, J=9.7 Hz, J=9.7 Hz), 4.82 (d, 1H, J=2.9 Hz), 4.61 (d, 1H, J=11.1 Hz), 4.52 (dd, 1H, J=1.4 Hz, J=9.7 Hz), 4.38 (d, 1H, J=11.1 Hz), 4.31 (d, 1H, J=13.5 Hz), 4.27 (ddd, 1H, J=4.8 Hz, J=9.7 Hz, J=11.6 Hz), 4.16 (d, 1H, J=13.5 Hz), 4.15 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 3.91 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.66 (ddd, 1H, J=5.3 Hz, J=9.2 Hz, J=12.1 Hz), 3.38 (s, 3H), 3.32 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 2.33 (ddd, 1H, J=1.4 Hz, J=5.3 Hz, J=12.6 Hz), 2.22 (dd, 1H, J=4.8 Hz, J=12.6 Hz), 1.82 (ddd, 1H, J=2.9 Hz, J=11.6 Hz, J=12.6 Hz), 1.57 (ddd, 1H, J=9.7 Hz, J=12.1 Hz, J=12.6 Hz), 1.24 (d, 3H, J=6.3 Hz), 1.07 ppm (d, 3H, J=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ=166.1, 137.2, 133.1, 130.6, 130.4, 129.9, 128.8, 128.7, 128.6, 128.3, 128.1, 128.0, 98.2, 96.8, 84.1, 76.0, 75.6, 72.8, 70.3, 70.0, 66.1, 57.4, 54.8, 38.7, 35.9, 17.8, 17.6 ppm; IR (solid): $\tilde{\nu}$=3033, 2981, 2916, 1722, 1496, 1454, 1353, 1271, 1049, 977, 863, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{40}O_{10}S$ $[M+Na]^+$ m/z=663.2234, found: 663.2231.

11c: According to the method for the synthesis of **9a**, a mixture of **11c** (27.6 mg, 58.9 μmol), **7a** (47.0 mg, 87.6 μmol), and MS-4 Å (87.6 mg) in CH_2Cl_2 (1.17 mL) was treated with a mixture of 1.00 M IBr in CH_2Cl_2 (117 μL, 117 μmol) and TBAB (47.0 mg, 146 μmol) at 0 °C for 2 h. *N,N*-Diisopropylethylamine (5.08 μL, 29.2 μmol) was then added to the reaction mixture. After being stirred for 20 h at the same temperature, to **11c** (46.3 mg, 72.2 μmol, 86 %, β/α=8:92) after purification. The α,β isomers were separated by chromatography on silica gel with toluene/ethyl acetate 92:8. **α-11c**: $[\alpha]_D^{26}$=+38.5° (c=0.400, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ=7.47 (d, 2H, J=7.2 Hz), 6.99–7.30 (m, 18H), 5.48 (d, 1H, J=2.9 Hz), 4.83 (d, 1H, J=11.6 Hz), 4.65 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 4.64 (dd, 1H, J=1.9 Hz, J=9.7 Hz), 4.60 (d, 1H, J=11.6 Hz), 4.59 (d, 1H, J=2.9 Hz), 4.41 (d, 1H, J=11.6 Hz), 4.35 (d, 1H, J=11.6 Hz), 4.28 (d, 1H, J=14.0 Hz), 4.05–4.19 (m, 5H), 4.02 (ddd, 1H, J=5.3 Hz, J=9.2 Hz, J=11.6 Hz), 3.94 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.55 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 3.36–3.42 (m, 2H), 3.22 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.14 (s, 3H), 2.22–2.33 (m, 3H), 1.68–1.76 (m, 2H), 1.49 (d, 3H, J=5.8 Hz), 1.40–1.46 (m, 4H), 1.35 ppm (d, 3H, J=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ=139.1, 138.1, 137.7, 130.6, 128.8, 128.7, 128.6, 128.6, 128.3, 128.1, 128.0, 127.9, 127.7, 127.6, 127.5, 100.1, 98.2, 98.1, 84.7, 83.2, 80.9, 79.7, 75.8, 74.3, 72.1, 71.0, 70.8, 70.7, 66.8, 66.6, 57.4, 54.6, 36.7, 35.8, 35.6, 18.7, 18.4, 17.6 ppm; IR (solid): $\tilde{\nu}$=3026, 2932, 2879, 1451, 1352, 1161, 1088, 1042, 932, 751, 695 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{47}H_{58}O_{12}S$ $[M+Na]^+$ m/z=869.3541, found: 869.3562. **β-11c**: $[\alpha]_D^{24}$=+32.0° (c=1.23, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6): δ=7.50 (d, 2H, J=7.2 Hz), 7.44 (d, 2H, J=7.2 Hz), 7.04–7.30 (m, 16H), 4.93 (d, 1H, J=11.6 Hz), 4.53–4.69 (m, 6H), 4.46 (dd, 1H, J=1.4 Hz, J=9.7 Hz), 4.28 (d, 1H, J=11.1 Hz), 4.23 (d, 1H, J=13.5 Hz), 4.16 (d, 1H, J=13.5 Hz), 4.09 (ddd, 1H, J=4.8 Hz, J=9.2 Hz, J=11.1 Hz), 4.07 (d, 1H, J=11.1 Hz), 3.92 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.55 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 3.47 (ddd, 1H, J=5.3 Hz, J=9.2 Hz, J=11.6 Hz), 3.38 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 3.26–3.35 (m, 2H), 3.14 (dq, 1H J=5.8 Hz, J=9.7 Hz), 3.13 (s, 3H), 2.37 (ddd, 1H, J=1.4 Hz, J=5.3 Hz, J=12.6 Hz), 2.26 (dd, 1H, J=4.8 Hz, J=13.0 Hz), 2.18 (ddd, 1H, J=1.4 Hz, J=5.3 Hz, J=12.6 Hz), 1.87 (ddd, 1H, J=9.7 Hz, J=11.6 Hz, J=12.6 Hz), 1.73 (ddd, 1H, J=3.9 Hz, J=11.1 Hz, J=13.0 Hz), 1.63 (ddd, 1H, J=9.7 Hz, J=11.6 Hz, J=12.6 Hz), 1.44 (d, 3H, J=5.8 Hz), 1.40 (d, 3H, J=6.3 Hz), 1.34 ppm (d, 3H, J=6.3 Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ=139.1, 138.6, 137.3, 130.6, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2, 128.0, 127.7, 127.5, 127.4, 100.2, 99.9, 98.2, 84.0, 83.2, 82.9, 77.6, 76.1, 75.9, 72.1, 71.9, 71.2, 70.7, 70.3, 66.7, 57.5, 54.6, 37.5, 36.9, 35.8, 18.4, 18.2, 17.9 ppm; IR (neat): $\tilde{\nu}$=2934, 1497, 1455, 1357, 1158, 1103, 1053, 989, 738, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{47}H_{58}O_{12}S$ $[M+Na]^+$ m/z=869.3541, found: 869.3531.

11d: According to the method for the synthesis of **9a**, **11d** (18.2 mg, 47.0 μmol), **7a** (37.8 mg, 70.5 μmol), and MS-4 Å (70.5 mg) in CH_2Cl_2 (0.940 mL) were treated with a mixture of 1.00 M IBr in CH_2Cl_2 (94.0 μL, 94.0 μmol) and TBAB (37.9 mg, 118 μmol) at 0 °C for 2 h. *N,N*-Diisopropylethylamine (4.09 μL, 23.5 μmol) was then added to the reaction mixture. After being stirred for 15 h at the same temperature, to **11d** (29.9 mg, 39.0 μmol, 83 %, β/α=10:90) after purification. The α,β isomers were separated by chromatography on silica gel with toluene. **α-11d**: $[\alpha]_D^{24}$=+46.0° (c=0.740, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.20–7.40 (m, 10H), 5.35 (m, 1H), 5.07 (d, 1H, J=3.4 Hz), 4.70 (d, 1H, J=11.1 Hz), 4.50 (d, 1H, J=11.1 Hz), 4.39 (dd, 1H, J=9.7 Hz, J=9.7 Hz), 4.36 (d, 1H, J=13.5 Hz), 4.23 (d, 1H, J=13.5 Hz), 4.09 (ddd, 1H, J=5.3 Hz, J=9.7 Hz, J=11.6 Hz), 3.94 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.43 (m, 1H), 2.39 (dd, 1H, J=5.3 Hz, J=12.6 Hz), 2.21–2.36 (m, 2H), 0.84–2.03 (m, 42H), 0.68 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=140.7, 137.8, 130.6, 128.7, 128.6, 128.2, 128.0, 127.9, 122.0, 94.6, 85.1, 76.6, 76.5, 74.5, 70.8, 66.0, 57.4, 56.9, 56.3, 50.2, 42.4, 40.1, 39.9, 39.6, 37.1, 36.8, 36.3, 36.0, 35.9, 32.0, 29.8, 28.3, 28.1, 27.8, 24.4, 23.9, 22.9, 22.6, 21.2, 19.5, 18.8, 17.8, 12.0 ppm; IR (solid): $\tilde{\nu}$=2933, 1455, 1374, 1352, 1168, 1124, 1097, 997 cm^{-1}. **β-11d**: $[\alpha]_D^{21}$=−30.0° (c=0.150, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=7.23–7.44 (m, 10H), 5.35 (m, 1H), 4.71 (d, 1H, J=11.6 Hz), 4.61 (dd, 1H, J=1.4 Hz, J=9.7 Hz), 4.48 (d, 1H, J=11.6 Hz), 4.38 (d, 1H, J=14.0 Hz), 4.36 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 4.24 (d, 1H, J=14.0 Hz), 3.75 (ddd, 1H, J=5.3 Hz, J=9.2 Hz, J=11.6 Hz), 3.55 (m, 1H), 3.45 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 2.44 (ddd, 1H, J=1.4 Hz, J=5.3 Hz, J=12.6 Hz), 2.19–2.34 (m, 2H), 0.84–2.03 (m, 42H), 0.68 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=140.7, 137.3, 130.7, 128.8, 128.8, 128.7, 128.2, 128.1, 122.1, 97.3, 76.3, 70.6, 70.2, 57.6, 56.9, 56.3, 50.3, 42.4, 39.9, 39.6, 38.9, 37.4, 37.2, 36.9, 36.3, 35.9, 32.1, 32.0, 29.8, 29.7, 28.3, 28.1, 24.4, 23.9, 22.9, 22.6, 21.1, 19.4, 18.8, 18.0, 12.0 ppm; IR (solid): $\tilde{\nu}$=2925, 2852, 1734, 1455, 1375, 1351, 1175, 1098, 996 cm^{-1}.

2: 1.00 M L-Selectride in THF (363 μL, 363 μmol) was added to a stirred solution of **1** (100 mg, 91.0 μmol) in THF (1.00 mL) at −78 °C. After being stirred at the same temperature for 30 min, the reaction mixture was warmed to room temperature. One drop of acetic acid was then added to the reaction mixture. The reaction mixture was poured into a mixture of 5 % aq. $NaHCO_3$ and 5 % aq. $NaBO_3{\cdot}4H_2O$. After being stirred at RT for 2 h, the aqueous layer was neutralized with 1 M HCl at 0 °C and extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with $CHCl_3$/methanol 94:6 to give **2** (89.1 mg, 80.9 μmol, 89 %). $[\alpha]_D^{24}$=−37.7° (c=0.435, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.82 (brs, 1H), 5.27 (s, 1H), 5.08 (d, 1H, J=10.1 Hz), 5.06 (dd, 1H, J=1.9 Hz, J=9.2 Hz), 4.96 (d, 1H, J=3.4 Hz), 4.81 (dd, 1H, J=1.4 Hz, J=9.2 Hz), 4.11 (m, 1H), 4.08 (m, 1H), 3.92 (brs, 1H), 3.76–3.88 (m, 2H), 3.69 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.55–3.66 (m, 2H), 3.49 (ddd, 1H, J=4.8 Hz, J=9.2 Hz, J=11.6 Hz), 3.42 (m, 1H), 3.40 (s, 3H), 3.31 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 3.28 (dd, 1H, J=2.9 Hz, J=9.2 Hz), 3.22–3.27 (m, 2H), 2.87 (dd, 1H, J=10.1 Hz, J=10.1 Hz), 2.84 (s, 1H), 2.54 (q, 1H, J=7.2 Hz), 2.39 (m, 1H), 2.25–2.35 (m, 2H), 2.23 (dd, 1H, J=4.8 Hz, J=13.0 Hz), 2.00–2.17 (m, 7H), 1.95 (m, 1H), 1.86 (dd, 1H, J=8.2 Hz, J=14.0 Hz), 1.79 (m, 1H), 1.53–1.72 (m, 15H), 1.23–1.31 (m, 8H), 1.21 (d, 3H, J=6.3 Hz), 1.11 (m, 1H), 1.05 (d, 3H, J=7.2 Hz), 1.02 (s, 3H), 0.88–0.97 (m, 12H), 0.84 (d, 3H, J=7.2 Hz), 0.66 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=205.4, 203.4, 166.5, 140.1, 135.3, 135.2, 133.1, 127.5, 121.4, 103.1, 100.5, 99.2, 98.5, 91.4, 87.3, 81.3, 80.7, 78.3, 73.2, 70.7, 70.6, 69.3, 68.4, 68.3, 67.8, 65.0, 61.1, 57.5, 57.4, 48.8, 43.6, 42.0, 41.8, 38.2, 38.0, 37.4, 36.7, 35.7, 35.2, 35.1, 34.9, 33.1, 32.2, 32.0, 31.1, 29.8, 29.0, 23.7, 23.2, 23.1, 22.0, 21.5, 20.5, 20.4, 19.3, 18.1, 17.8, 17.3, 14.8, 12.7 ppm; IR (solid): $\tilde{\nu}$=3445, 2962, 2928, 1744, 1626, 1455, 1380, 1124, 1058, 1014, 988 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{61}H_{96}O_{17}$ $[M+Na]^+$ m/z=1123.6545, found: 1123.6541.

12: *N,N,N′,N′*-Tetramethylenediamine (300 μL), acetic anhydride (150 μL), and a catalytic amount of DMAP (2.00 mg, 16.2 μmol) were added to a stirred solution of **2** (89.1 mg, 80.9 μmol) in CH_2Cl_2 (1.00 mL) at 0 °C. After being stirred at RT for 3 h, the reaction mixture was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with saturated aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl aetate 60:40 to give **12** (121 mg, 72.7 μmol, 90 %). $[\alpha]_D^{25}$=+1.62° (c=1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.44 (brs, 1H), 5.42 (m, 1H), 5.32 (s, 1H), 5.24 (m, 1H), 5.10 (brs, 1H), 5.05 (dd, 1H, J=1.9 Hz, J=9.7 Hz), 4.98 (d, 1H, J=9.7 Hz), 4.90 (d, 1H, J=3.4 Hz), 4.90 (ddd, 1H, J=4.8 Hz, J=10.6 Hz, J=10.6 Hz), 4.65 (brd, 1H, J=

8.7 Hz), 4.54 (dd, 1H, J=2.9 Hz, J=9.7 Hz), 4.16 (dd, 1H, J=2.9 Hz, J=11.1 Hz), 3.88 (dq, 1H, J=9.7 Hz, J=6.3 Hz), 3.82 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.63 (dd, 1H, J=8.7 Hz, J=11.1 Hz), 3.56 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.44 (ddd, 1H, J=4.8 Hz, J=9.2 Hz, J=11.6 Hz), 3.37 (s, 3H, Me), 3.21–3.28 (m, 3H), 3.03 (s, 1H), 2.83 (dd, 1H, J=10.6 Hz, J=10.6 Hz), 2.65 (q, 1H, J=7.7 Hz), 2.59 (m, 1H), 2.41 (m, 1H), 2.28–2.37 (m, 2H), 2.23 (dd, 1H, J=4.8 Hz, J=12.6 Hz), 2.12–2.21 (m, 2H), 2.12 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.05 (m, 1H), 2.00 (s, 3H), 1.87–1.99 (m, 7H), 1.78–1.84 (m, 2H), 1.75 (m, 1H), 1.64–1.72 (m, 6H), 1.15–1.62 (m, 20H), 1.03–1.09 (m, 12H), 0.99 (t, 3H, J=7.7 Hz), 0.90 (d, 3H, J=6.8 Hz), 0.74 (d, 3H, J=6.8 Hz), 0.70 ppm (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=205.1, 202.1, 170.9, 170.7, 170.4, 170.3, 170.1, 166.6, 140.0, 135.9, 135.5, 133.8, 126.6, 120.4, 103.3, 99.8, 99.8, 98.7, 90.3, 87.3, 81.8, 79.9, 78.6, 74.8, 73.1, 72.8, 70.7, 69.1, 68.0, 67.8, 66.7, 60.9, 57.3, 45.3, 41.4, 41.1, 37.3, 36.1, 35.4, 35.0, 34.7, 33.4, 32.8, 31.5, 30.4, 30.0, 23.8, 22.6, 21.6, 21.3, 21.1, 21.0, 20.9, 20.8, 19.5, 19.3, 18.2, 17.9, 16.9, 14.0, 12.5 ppm; IR (neat): $\tilde{\nu}$=2971, 2936, 1743, 1450, 1372, 1244, 1059, 1018, 988 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{73}H_{108}O_{23}$ $[M+Na]^+$ m/z=1375.7179, found: 1375.7190.

3: *N,N,N′,N′*-Tetramethylenediamine (200 μL), pivaloyl chloride (100 μL), and DMAP (8.88 mg, 72.7 μmol) were added to a stirred solution of **9** (121 mg, 72.7 μmol) in CH_2Cl_2 (1.00 mL) at RT. After being stirred under reflux for 12 h, the reaction mixture was poured into a saturated aq. $NaHCO_3$. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with saturated brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was used for the next reaction without further purification. To a stirred solution of the residue in CH_2Cl_2 (0.900 mL) and methanol (0.100 mL) was added trifluoroacetic acid (0.250 mL) at RT. After being stirred at room temperature for 1 h, the reaction mixture was concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 60:40 and further purified by gel permeation chromatography (GPC) to give **3** (56.0 mg, 61.7 μmol, 2 steps, 85%). $[\alpha]_D^{27}=-25.1°$ (c=0.960, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.46 (br s, 1H), 5.42 (s, 1H), 5.28 (m, 1H), 5.18 (d, 1H, J=9.2 Hz), 4.74 (ddd, 1H, J=7.7 Hz, J=10.6 Hz, J=10.6 Hz), 4.08 (dd, 1H, J=2.9 Hz, J=10.6 Hz), 3.81 (s, 1H), 3.77 (dd, 1H, J=6.8 Hz, J=10.6 Hz), 3.11 (br d, 1H, J=8.2 Hz), 2.63 (dd, 1H, J=8.7 Hz, J=14.5 Hz), 2.61 (m, 1H), 2.31–2.47 (m, 4H), 2.17 (m, 1H), 2.10 (s, 3H), 2.02 (s, 3H), 2.00 (s, 3H), 1.96 (q, 1H, J=7.7 Hz), 1.92 (m, 1H), 1.89 (q, 1H, J=7.7 Hz), 1.82 (q, 1H, J=7.7 Hz), 1.73–1.82 (m, 2H), 1.69 (s, 3H), 1.58 (s, 3H), 1.17–1.55 (m, 18H), 1.12 (s, 3H), 1.08 (t, 3H, J=6.3 Hz), 1.07 (d, 3H, J=6.3 Hz), 0.99 (t, 3H, J=7.7 Hz), 0.97 (d, 3H, J=7.2 Hz), 0.97 (d, 3H, J=7.2 Hz), 0.94 (d, 3H, J=6.8 Hz), 0.88 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=198.9, 180.7, 171.7, 171.2, 170.6, 170.4, 167.7, 140.5, 135.7, 135.3, 135.2, 126.3, 120.9, 115.8, 88.0, 82.0, 72.9, 71.8, 65.6, 61.9, 57.3, 41.5, 39.8, 37.1, 35.5, 34.5, 34.0, 33.6, 32.3, 31.1, 30.3, 29.7, 26.6, 26.5, 23.5, 22.9, 22.2, 21.7, 21.3, 21.2, 21.1, 20.9, 20.2, 19.1, 18.3, 16.5, 14.0, 11.2 ppm; IR (solid): $\tilde{\nu}$=3529, 2935, 2875, 1789, 1739, 1681, 1588, 1458, 1374, 1239, 1100, 1063, 969 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{53}H_{78}O_{12}$ $[M+H]^+$ m/z=907.5572, found: 907.5596.

15: A mixture of **3** (34.0 mg, 37.4 μmol), **4** (40.5 mg, 93.7 μmol), and pulverized activated MS-4 Å (56.0 mg) in dry toluene (0.560 mL) was stirred at RT for 30 min under argon to remove a trace amount of water. The reaction mixture was then cooled to −94 °C (hexane–liquid N_2 bath). After 5 min, a solution of iodine (28.4 mg, 112.2 μmol) in toluene (0.200 mL) and triethylsilane (0.600 μL, 3.74 μmol) were added to the reaction mixture. After being stirred for 1.5 h, the reaction mixture was neutralized with triethylamine at −94 °C and filtered through Celite. Immediately the filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$ with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 50:50 and further purified by gel permeation chromatography (GPC) to give **15** (36.7 mg, 30.7 μmol, 82%, β/α=95:5). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). $[\alpha]_D^{22}=-4.92°$ (c=1.25, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.42 (br s, 1H), 5.41 (m, 1H), 5.40 (s, 1H), 5.24 (m, 1H), 5.15 (d, 1H, J=9.7 Hz), 4.77 (dd, 1H, J=1.0 Hz, J=9.7 Hz), 4.76 (m, 1H), 4.55 (dd, 1H, J=2.9 Hz, J=10.1 Hz), 4.11 (dd, 1H, J=2.9 Hz, J=11.1 Hz), 3.87 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.69–3.75 (m, 2H), 3.23 (br d, 1H, J=6.8 Hz), 2.26–2.85 (m, 11H), 2.18 (s, 3H), 2.10 (s, 3H), 2.10 (s, 3H), 2.07 (m, 1H), 2.03 (s, 3H), 1.97 (s, 3H), 1.71–1.96 (m, 7H), 1.68 (s, 3H), 1.67 (m, 1H), 1.20–1.63 (m, 20H), 1.19 (d, 3H, J=6.3 Hz), 1.10 (s, 3H), 1.09 (d, 3H, J=6.3 Hz), 1.07 (t, 3H, J=7.7 Hz), 1.00 (t, 3H, J=7.2 Hz), 0.98 (d, 3H, J=7.2 Hz), 0.92 (d, 3H, J=6.3 Hz), 0.90 (d, 3H, J=6.3 Hz), 0.85 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=206.4, 181.2, 171.9, 171.7, 171.0, 170.4, 170.1, 167.9, 140.4, 135.7, 135.5, 135.2, 126.6, 120.7, 116.2, 99.6, 90.7, 87.9, 76.6, 73.0, 72.9, 72.5, 68.1, 68.0, 65.9, 61.3, 61.2, 57.5, 41.9, 39.6, 39.2, 38.0, 37.0, 36.0, 34.6, 34.1, 33.7, 33.1, 32.9, 30.9, 30.7, 29.8, 29.7, 28.8, 27.9, 26.8, 23.4, 22.8, 22.0, 21.6, 21.3, 21.2, 21.1, 21.0, 20.9, 20.0, 19.3, 18.9, 18.5, 17.9, 16.3, 13.9, 11.5 ppm; IR (neat): $\tilde{\nu}$=2927, 1787, 1741, 1370, 1244, 1157, 1065, 1036 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{66}H_{96}O_{18}$ $[M+Na]^+$ m/z=1199.6494, found: 1199.6498.

16: Acetic acid (361 μL) and hydrazine monohydrate (11.6 μL, 241 μmol) were added to a stirred solution of **15** (28.8 mg, 24.1 μmol) in pyridine (180 μL) at 0 °C. After being stirred at RT for 3 h, the reaction mixture was poured into a saturated aq. $NaHCO_3$. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with 1 M HCl, saturated aq. $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl aetate 50:50 to give **16** (23.2 mg, 21.5 μmol, 90%). $[\alpha]_D^{22}=-8.24°$ (c=1.17, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.42 (br s, 1H), 5.40 (s, 1H), 5.25–5.27 (m, 2H), 5.14 (d, 1H, J=9.7 Hz), 4.77 (m, 1H), 4.70 (dd, 1H, J=1.0 Hz, J=9.7 Hz), 4.10 (dd, 1H, J=2.4 Hz, J=10.6 Hz), 3.72 (dd, 1H, J=7.2 Hz, J=10.6 Hz), 3.71 (br s, 1H), 3.64 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.41 (m, 1H), 3.22 (dd, 1H, J=1.9 Hz, J=7.2 Hz), 2.59 (m, 1H), 2.26–2.56 (m, 6H), 2.15 (ddd, 1H, J=1.0 Hz, J=2.9 Hz, J=14.4 Hz), 2.13 (s, 3H), 2.11 (s, 3H), 2.03 (s, 3H), 1.97 (s, 3H), 1.71–1.97 (m, 8H), 1.69 (s, 3H), 1.66 (m, 1H), 1.58 (s, 3H), 1.22–1.58 (m, 20H), 1.10 (s, 3H), 1.08 (d, 3H, J=6.3 Hz), 1.06 (t, 3H, J=7.7 Hz), 1.00 (t, 3H, J=7.7 Hz), 0.98 (d, 3H, J=6.8 Hz), 0.91 (d, 3H, J=6.3 Hz), 0.90 (d, 3H, J=6.3 Hz), 0.85 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=198.1, 181.2, 171.7, 171.2, 171.0, 170.6, 170.4, 167.6, 140.4, 135.6, 135.5, 135.1, 126.6, 120.7, 116.1, 99.5, 90.5, 87.9, 72.9, 72.6, 72.2, 71.7, 70.2, 66.0, 60.4, 57.4, 53.4, 41.9, 39.5, 39.0, 36.9, 36.0, 34.6, 34.1, 33.8, 33.1, 32.9, 30.8, 30.6, 29.7, 28.9, 26.7, 23.3, 22.8, 21.9, 21.6, 21.2, 21.1, 21.0, 20.9, 19.9, 19.2, 18.9, 18.6, 18.1, 16.3, 14.2, 13.8, 11.4 ppm; IR (neat): $\tilde{\nu}$=3458, 2962, 2933, 1788, 1681, 1372, 1241, 1216, 1066, 1023 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{61}H_{90}O_{16}$ $[M+Na]^+$ m/z=1101.6127, found: 1101.6177.

17: A mixture of **16** (26.3 mg, 24.3 μmol), **5** (31.7 mg, 60.9 μmol) and pulverized activated MS-4 Å (48.7 mg) in dry CH_2Cl_2 (490 μL) was stirred at RT for 30 min under argon to remove a trace amount of water. A mixture of 1.00 M IBr in CH_2Cl_2 (73.1 μL, 73.1 μmol) and tetrabutylammonium bromide (31.4 mg, 97.5 μmol) was then added to the reaction mixture at 0 °C. After being stirred for 2 h, *N,N*-diisopropylethylamine (2.10 μL, 12.2 μmol) was added to the reaction mixture at the same temperature. After being stirred for 24 h, the reaction mixture was filtered through Celite. The filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$ with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 50:50 and further purified by gel permeation chromatography (GPC) to give **17** (26.2 mg, 18.3 μmol, 75%, α/β=95:5). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). $[\alpha]_D^{22}=+9.45°$ (c=0.600, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.20 (d, 2H, J=8.7 Hz), 7.40 (d, 2H, J=8.7 Hz), 5.50 (m, 1H), 5.43 (br s, 1H), 5.39 (s, 1H), 5.25 (m, 1H), 5.15 (d, 1H, J=9.7 Hz), 5.09 (d, 1H, J=3.4 Hz), 4.78 (m, 1H), 4.78 (d, 1H, J=9.7 Hz), 4.20 (dd, 1H, J=9.7 Hz, J=9.7 Hz), 4.11 (dd, 1H, J=2.9 Hz, J=11.1 Hz), 3.81 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.77 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.70–3.75 (m, 2H), 3.48–3.63 (m, 3H), 3.38 (dd, 1H, J=2.9 Hz, J=9.7 Hz), 3.23–3.32 (m, 6H), 2.59 (m, 1H), 2.54 (m, 1H), 2.49 (m, 1H), 2.44 (q, 1H, J=7.7 Hz), 2.31–2.40 (m, 3H), 2.15 (dd, 1H, J=5.3 Hz, J=12.5 Hz), 2.11 (s, 3H), 2.10 (s, 3H), 2.06 (m, 1H), 2.03 (s, 3H), 1.97 (s, 3H), 1.97 (q, 1H, J=7.7 Hz), 1.90 (m, 1H), 1.86 (q, 1H, J=7.7 Hz), 1.80 (q, 1H, J=7.7 Hz), 1.69–1.80 (m, 3H), 1.69 (s, 3H), 1.68 (m, 1H), 1.20–1.61 (m, 27H), 1.10 (s, 3H), 1.09 (d, 3H, J=6.3 Hz), 1.07 (t,

3H, J=7.7 Hz), 1.01 (t, 3H, J=7.7 Hz), 0.99 (d, 3H, J=6.8 Hz), 0.91 (d, 3H, J=6.3 Hz), 0.91 (d, 3H, J=6.3 Hz), 0.86 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=198.2, 181.3, 171.7, 171.0, 170.6, 170.4, 170.2, 167.6, 147.2, 145.4, 140.4, 135.7, 135.5, 135.1, 129.3, 126.6, 124.1, 120.7, 116.2, 99.6, 93.3, 90.7, 87.9, 84.9, 75.4, 74.4, 73.0, 72.6, 68.7, 66.6, 66.0, 65.9, 61.2, 57.5, 51.6, 42.0, 41.2, 39.6, 39.1, 37.0, 36.1, 34.7, 34.2, 34.1, 33.9, 33.2, 32.9, 30.9, 30.6, 29.8, 29.0, 26.8, 23.4, 22.8, 22.0, 21.6, 21.3, 21.2, 21.1, 20.9, 20.0, 19.3, 19.0, 18.8, 18.7, 17.6, 16.4, 13.9, 11.5 ppm; IR (neat): $\tilde{\nu}$= 2962, 2933, 1789, 1740, 1681, 1589, 1524, 1369, 1347, 1243, 1097, 1063, 994 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{76}H_{109}NO_{23}S$ $[M+Na]^+$ m/z= 1458.7009, found: 1458.6998.

18: DBU (18.0 μL, 121 mmol) was added to a stirred solution of **17** (17.5 mg, 12.1 μmol) in CH_3CN (360 μL) at 0 °C. After being stirred at RT for 3 h, the reaction mixture was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with 1 M HCl, saturated aq. $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl aetate 40:60 to give **18** (11.4 mg, 9.31 μmol, 77 %). $[\alpha]_D^{26}$=+3.53° (c=0.390, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.51 (m, 1H), 5.42 (brs, 1H), 5.40 (s, 1H), 5.25 (m, 1H), 5.15 (d, 1H, J=9.2 Hz), 5.06 (d, 1H, J=3.4 Hz), 4.77 (m, 1H), 4.77 (dd, 1H, J=1.9 Hz, J=10.1 Hz), 4.11 (dd, 1H, J=2.9 Hz, J= 11.1 Hz), 3.77 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.70–3.75 (m, 2H), 3.67 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.42 (dd, 1H, J=2.9 Hz, J=9.7 Hz), 3.38 (m, 1H), 3.36 (s, 3H), 3.16 (dd, 1H, J=1.4 Hz, J=7.2 Hz), 3.15 (dd, 1H, J=9.7 Hz, J=9.7 Hz), 2.59 (m, 1H), 2.55 (m, 1H), 2.49 (m, 1H), 2.44 (q, 1H, J=7.7 Hz), 2.26–2.38 (m, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.03–2.10 (m, 2H), 2.03 (s, 3H), 1.97 (s, 3H), 1.97 (q, 1H, J=7.7 Hz), 1.90 (m, 1H), 1.88 (q, 1H, J=7.7 Hz), 1.80 (q, 1H, J=7.7 Hz), 1.69–1.78 (m, 3H), 1.68 (s, 3H), 1.67 (m, 1H), 1.18–1.65 (m, 27H), 1.10 (s, 3H), 1.09 (d, 3H, J=6.3 Hz), 1.07 (t, 3H, J=7.7 Hz), 1.00 (t, 3H, J=7.7 Hz), 0.98 (d, 3H, J=7.2 Hz), 0.81–0.93 ppm (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 198.3, 181.2, 171.8, 171.1, 171.0, 170.6, 170.4, 170.2, 167.6, 140.4, 135.7, 135.6, 135.2, 126.6, 120.8, 116.2, 99.7, 93.8, 90.7, 87.9, 78.2, 76.0, 73.9, 73.0, 72.6, 69.0, 68.3, 66.0, 65.9, 61.3, 57.5, 56.4, 41.9, 39.6, 39.2, 37.0, 36.1, 34.6, 34.2, 33.8, 33.5, 33.1, 33.0, 32.0, 30.9, 30.7, 29.8, 28.8, 26.8, 23.5, 22.8, 22.0, 21.6, 21.3, 21.2, 21.1, 21.1, 20.9, 20.0, 19.3, 18.9, 18.5, 17.8, 16.4, 13.9, 11.4 ppm; IR (neat): $\tilde{\nu}$=3483, 2964, 2934, 1789, 1742, 1681, 1589, 1456, 1371, 1241, 1068, 1023, 986 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{68}H_{102}O_{19}$ $[M+Na]^+$ m/z=1245.6913, found: 1245.6876.

20: A mixture of **18** (9.20 mg, 7.52 μmol), **4** (9.80 mg, 22.6 μmol) and pulverized activated MS-4 Å (23.0 mg) in dry toluene (0.225 mL) was stirred at RT for 30 min under argon to remove a trace amount of water. The reaction mixture was then cooled to −94 °C (hexane–liquid N_2 bath). After 5 min, a solution of iodine (6.70 mg, 26.3 μmol) in toluene (50.0 μL) and triisopropylsilane (0.310 μL, 1.51 μmol) were added to the reaction mixture. After being stirred for 1.5 h, the reaction mixture was neutralized with triethylamine at −94 °C and filtered through Celite. Immediately the filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$ with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 50:50 and further purified by gel permeation chromatography (GPC) to give **20** (8.90 mg, 5.96 μmol, 80 %, β/α=94:6). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). $[\alpha]_D^{26}$=+13.4° (c=0.290, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.49 (m, 1H), 5.40–5.43 (m, 3H), 5.25 (m, 1H), 5.15 (d, 1H, J=9.7 Hz), 5.00 (brd, 1H, J=1.9 Hz), 4.97 (dd, 1H, J=1.9 Hz, J=9.7 Hz), 4.73–4.80 (m, 2H), 4.57 (dd, 1H, J= 2.9 Hz, J=9.7 Hz), 4.10 (dd, 1H, J=2.9 Hz, J=10.6 Hz), 3.93 (dq, 1H, J=6.3 Hz, J=9.7 Hz), 3.70–3.79 (m, 3H), 3.66 (dq, 1H, J=6.3 Hz, J= 9.2 Hz), 3.54 (ddd, 1H, J=4.8 Hz, J=8.2 Hz, J=10.6 Hz), 3.41 (s, 3H), 3.39 (dd, 1H, J=2.4 Hz, J=9.7 Hz), 3.23 (dd, 1H, J=1.4 Hz, J=7.2 Hz), 3.18 (dd, 1H, J=8.2 Hz, J=9.2 Hz), 2.25–2.86 (m, 11H), 2.18 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.10 (s, 3H), 2.08 (m, 1H), 2.03 (s, 3H), 2.00–2.03 (m, 2H), 1.97 (s, 3H), 1.96 (q, 1H, J=7.7 Hz), 1.93 (m, 1H), 1.70–1.90 (m, 6H), 1.69 (s, 3H), 1.65 (m, 1H), 1.15–1.60 (m, 30H), 1.10 (s, 3H), 1.09 (d, 3H, J=6.8 Hz), 1.07 (t, 3H, J=7.7 Hz), 1.00 (t, 3H, J= 7.7 Hz), 0.98 (d, 3H, J=6.8 Hz), 0.81–0.94 ppm (m, 7H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=206.5, 198.3, 181.2, 171.9, 171.8, 171.0, 170.6, 170.4, 170.2, 170.1, 167.6, 140.4, 135.7, 135.6, 135.2, 126.6, 120.8, 116.2, 99.7, 99.0, 93.6, 90.7, 87.9, 83.6, 74.1, 73.0, 72.7, 72.5, 70.6, 68.9, 68.3, 67.7, 67.3, 66.1, 66.0, 65.9, 61.3, 57.5, 57.2, 41.9, 39.6, 39.2, 37.9, 36.9, 36.2, 36.1, 34.6, 34.2, 33.7, 33.1, 32.0, 30.9, 30.7, 30.4, 29.9, 29.7, 27.9, 26.8, 23.5, 22.8, 22.7, 22.0, 21.6, 21.3, 21.2, 21.1, 20.9, 20.0, 19.3, 18.8, 18.5, 18.1, 18.0, 16.4, 14.2, 13.4, 11.5 ppm; IR (neat): $\tilde{\nu}$=2961, 2930, 1788, 1742, 1681, 1456, 1371, 1242, 1151, 1095, 1067, 1023 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{81}H_{120}O_{25}$ $[M+Na]^+$ m/z=1515.8016, found: 1515.8000.

21: NaOMe (20.0 mg) was added to a stirred solution of **20** (5.50 mg, 3.68 μmol) in methanol (500 μL) at RT. After being stirred under reflux for 24 h, the reaction mixture was neutralized with Dowex 50WX4 and filtered. The filtrate was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with $CHCl_3$/methanol 94:6 to give **21** (3.00 mg, 2.72 μmol, 75 %). $[\alpha]_D^{24}$=+10.7° (c= 0.150, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=5.82 (brs, 1H), 5.27 (s, 1H), 5.09 (d, 1H, J=10.6 Hz), 4.98–5.01 (m, 2H), 4.82 (dd, 1H, J= 1.4 Hz, J=9.2 Hz), 4.20 (m, 1H), 4.12 (m, 1H), 3.92 (brs, 1H), 3.85 (ddd, 1H, J=4.3 Hz, J=10.6 Hz, J=10.6 Hz), 3.80 (dq, 1H, J=6.3 Hz, J= 9.2 Hz), 3.73 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.73 (dq, 1H, J=6.3 Hz, J= 9.2 Hz), 3.58–3.64 (m, 2H), 3.43 (s, 3H), 3.43 (m, 1H), 3.38 (dd, 1H, J= 2.9 Hz, J=9.2 Hz), 3.31 (dd, 1H, J=2.9 Hz, J=9.2 Hz), 3.23 (m, 1H), 3.22 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 2.86 (dd, 1H, J=10.6 Hz, J= 10.6 Hz), 2.85 (s, 1H), 2.53 (q, 1H, J=7.2 Hz), 2.40 (m, 1H), 2.24–2.35 (m, 2H), 2.19 (m, 1H), 1.98–2.18 (m, 7H), 1.96 (brdd, 1H, J=10.6 Hz, J=10.6 Hz), 1.86 (dd, 1H, J=14.5 Hz, J=8.2 Hz), 1.80 (m, 1H), 1.78 (m, 1H), 1.53–1.73 (m, 14H), 1.22–1.31 (m, 11H), 1.13 (m, 1H), 1.05 (d, 3H, J=7.2 Hz), 1.03 (s, 3H), 0.99 (t, 3H, J=7.2 Hz), 0.98 (t, 3H, J=7.2 Hz), 0.96 (d, 3H, J=7.2 Hz), 0.91 (d, 3H, J=6.8 Hz), 0.84 (d, 3H, J=6.8 Hz), 0.66 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=205.5, 203.0, 166.4, 140.2, 135.4, 135.2, 133.1, 127.4, 103.1, 100.7, 98.9, 93.2, 91.6, 87.3, 83.2, 75.7, 73.3, 73.0, 70.7, 70.5, 69.7, 68.4, 68.0, 67.8, 64.9, 64.1, 61.0, 57.5, 57.4, 48.8, 43.6, 42.0, 41.8, 38.2, 38.0, 37.1, 36.8, 35.7, 35.2, 35.1, 34.5, 33.1, 32.2, 31.1, 29.5, 29.1, 23.7, 23.2, 23.0, 22.0, 21.5, 20.6, 20.4, 19.3, 18.4, 18.2, 17.3, 14.8, 12.7 ppm; IR (solid): $\tilde{\nu}$=3450, 2930, 2962, 1739, 1625, 1456, 1380, 1261, 1068 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{61}H_{96}O_{17}$ $[M+Na]^+$ m/z= 1123.6545, found: 1123.6556.

23: A mixture of **16** (24.7 mg, 22.9 μmol), **22** (29.8 mg, 57.2 μmol) and pulverized activated MS-4 Å (40.0 mg) in dry CH_2Cl_2 (450 mL) was stirred at RT for 30 min under argon to remove a trace amount of water. A mixture of 1.00 M IBr in CH_2Cl_2 (68.4 mL, 68.4 μmol) and tetrabutylammonium bromide (29.5 mg, 91.5 mmol) was then added to the reaction mixture at 0 °C. After being stirred for 2 h, *N,N*-diisopropylethylamine (2.00 mL, 11.4 μmol) was added to the reaction mixture at the same temperature. After being stirred for 24 h, the reaction mixture was filtered through Celite. The filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$, with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 50:50 and further purified by gel permeation chromatography (GPC) to give **23** (26.3 mg, 18.3 μmol, 80 %, α/β=95:5). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). $[\alpha]_D^{22}$=−10.7° (c=1.15, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): d 8.20 (d, 2H, J=8.2 Hz), 7.39 (d, 2H, J=8.2 Hz), 5.42 (brs, 1H,), 5.39 (s, 1H), 5.22–5.27 (m, 2H), 5.14 (d, 1H, J=9.7 Hz), 4.97 (brd, 1H, J=2.9 Hz), 4.77 (m, 1H), 4.68 (brd, 1H, J=8.7 Hz), 4.18 (dd, 1H, J=9.2 Hz, J=9.2 Hz), 4.11 (dd, 1H, J=2.9 Hz, J=11.1 Hz), 3.83 (dq, 1H, J=6.3 Hz, J=9.2 Hz), 3.81 (dq, 1H, J= 6.3 Hz, J=9.2 Hz), 3.68–3.73 (m, 2H), 3.47–3.65 (m, 3H), 3.26–3.34 (m, 6H), 3.20 (dd, 1H, J=1.9 Hz, J=7.2 Hz), 2.59 (m, 1H), 2.53 (m, 1H), 2.47 (m, 1H), 2.42 (q, 1H, J=7.7 Hz), 2.28–2.40 (m, 4H), 2.16 (m, 1H), 2.12 (s, 3H), 2.10 (s, 3H), 2.03 (s, 3H), 1.97 (s, 3H), 1.96 (q, 1H, J= 7.7 Hz), 1.91 (m, 1H), 1.87 (q, 1H, J=7.7 Hz), 1.82 (q, 1H, J=7.7 Hz), 1.71–1.80 (m, 3H), 1.69 (s, 3H), 1.65 (m, 1H), 1.21–1.62 (m, 27H), 1.10 (s, 3H), 1.07 (d, 3H, J=7.2 Hz), 1.06 (t, 3H, J=7.7 Hz), 1.00 (t, 3H, J= 7.7 Hz), 0.98 (d, 3H, J=7.2 Hz), 0.91 (d, 3H, J=6.3 Hz), 0.88 (d, 3H, J= 6.3 Hz), 0.85 ppm (m, 1H); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ=198.2,

181.3, 171.8, 171.1, 170.7, 170.4, 170.1, 167.6, 147.2, 145.4, 140.4, 135.7, 135.5, 135.1, 129.3, 126.6, 124.1, 120.8, 116.2, 99.6, 99.3, 90.9, 88.0, 84.8, 80.0, 76.4, 75.3, 73.0, 72.6, 70.5, 69.0, 66.7, 66.0, 61.2, 57.5, 55.9, 51.6, 42.0, 39.6, 39.1, 36.9, 36.7, 36.2, 35.0, 34.7, 34.2, 33.9, 33.3, 32.9, 30.9, 30.6, 29.8, 29.7, 29.1, 26.8, 23.4, 22.8, 22.0, 21.6, 21.3, 21.2, 21.0, 20.0, 19.3, 19.0, 18.8, 18.3, 17.6, 16.4, 13.9, 11.5 ppm; IR (neat): $\tilde{\nu}$ = 2933, 1789, 1740, 1681, 1591, 1524, 1457, 1368, 1347, 1243, 1100, 1065 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{76}H_{109}NO_{23}S$ $[M+Na]^+$ m/z = 1458.7009, found: 1458.6974.

24: DBU (20.8 mL, 139 mmol) was added to a stirred solution of **23** (20.0 mg, 13.9 mmol) in CH_3CN (500 mL) at 0 °C. After being stirred at RT for 3 h, the reaction mixture was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with 1 M HCl, saturated aq. $NaHCO_3$, and brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 40:60 to give **24** (12.8 mg, 10.5 mmol, 75 %). $[\alpha]_D^{21} = -15.8°$ (c = 0.625, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.42 (brs, 1H), 5.40 (s, 1H), 5.28 (m, 1H), 5.25 (m, 1H), 5.15 (d, 1H, $J_{15,16}$ = 9.7 Hz), 4.96 (brd, 1H, J = 2.4 Hz), 4.77 (m, 1H), 4.68 (d, 1H, $J_{1,2ax}$ = 9.2 Hz), 4.11 (dd, 1H, $J_{16,37a}$ = 2.4 Hz, J_{gem} = 11.1 Hz), 3.81 (dq, 1H, $J_{4,5}$ = 9.2 Hz, $J_{5,6}$ = 6.3 Hz), 3.67–3.74 (m, 2H), 3.63 (dq, 1H, $J_{4,5}$ = 9.2 Hz, $J_{5,6}$ = 6.3 Hz), 3.39 (s, 3H, Me), 3.39 (m, 1H), 3.29 (dd, 1H, $J_{3,4}$ = 2.4 Hz, $J_{4,5}$ = 9.2 Hz), 3.20 (brd, 1H, J = 6.8 Hz), 3.12 (dd, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz), 2.59 (m, 1H), 2.54 (m, 1H), 2.47 (m, 1H), 2.28–2.42 (m, 5H), 2.25 (dd, 1H, $J_{2eq,2ax}$ = 13.0 Hz, $J_{2eq,3}$ = 4.8 Hz), 2.17 (m, 1H), 2.11 (s, 3H, Ac), 2.11 (s, 3H, Ac), 2.03 (s, 3H, Ac), 1.97 (s, 3H, Ac), 1.97 (q, 1H, $J_{35,36}$ = 7.2 Hz), 1.91 (m, 1H), 1.86 (q, 1H, $J_{35,36}$ = 7.2 Hz), 1.82 (q, 1H, $J_{31,32}$ = 7.2 Hz), 1.74–1.81 (m, 3H), 1.72 (m, 1H), 1.69 (s, 3H), 1.59 (s, 3H), 1.22–1.59 (m, 24H), 1.10 (s, 3H), 1.09 (d, 3H, $J_{18,38}$ = 6.8 Hz), 1.07 (t, 3H, $J_{31,32}$ = 7.2 Hz), 1.01 (t, 3H, $J_{35,36}$ = 7.2 Hz), 0.98 (d, 3H, $J_{27,42}$ = 6.8 Hz), 0.91 (d, 3H, $J_{6,33}$ = 6.3 Hz), 0.88 (d, 3H, $J_{20,39}$ = 6.8 Hz), 0.85 ppm (m, H-17$_b$); ^{13}C NMR (67.8 MHz, $CDCl_3$): δ = 198.2, 181.2, 171.8, 171.1, 170.6, 170.4, 170.3, 167.6, 140.3, 135.6, 135.5, 135.1, 126.6, 120.7, 116.1, 100.1, 99.6, 90.7, 87.9, 79.7, 78.0, 76.0, 73.0, 72.5, 70.8, 69.2, 68.5, 68.2, 65.9, 61.3, 57.5, 56.5, 41.9, 39.5, 39.1, 36.8, 36.1, 34.3, 34.1, 33.7, 33.1, 32.9, 31.6, 30.9, 30.6, 29.7, 28.8, 26.7, 23.4, 22.8, 22.7, 22.0, 21.6, 21.3, 21.2, 21.1, 21.0, 20.0, 19.3, 18.8, 18.5, 18.2, 17.7, 16.3, 13.8, 11.5 ppm; IR (neat): $\tilde{\nu}$ = 3464, 2936, 1788, 1741, 1680, 1590, 1455, 1373, 1239, 1065, 1021 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{68}H_{102}O_{19}$ $[M+Na]^+$ m/z = 1245.6913, found: 1245.6958.

25: A mixture of **24** (12.8 mg, 10.5 mmol, 1.00 equiv), **4** (13.6 mg, 31.4 μmol) and pulverized activated MS-4 Å (30.0 mg) in dry toluene (0.300 mL) was stirred at RT for 30 min under argon to remove a trace amount of water. The reaction mixture was then cooled to −94 °C (hexane–liquid N_2 bath). After 5 min, a solution of iodine (9.29 mg, 36.6 μmol) in toluene (50.0 mL) and triisopropylsilane (0.430 mL, 2.09 μmol) was added to the reaction mixture. After being stirred for 1.5 h, the reaction mixture was neutralized with triethylamine at −94 °C and filtered through Celite. Immediately the filtrate was poured into a mixture of saturated aq. $NaHCO_3$ and saturated aq. $Na_2S_2O_3$, with cooling. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 50:50 and further purified by gel permeation chromatography (GPC) to give **25** (12.7 mg, 8.50 mmol, 81 %, β/α = 94:6). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). $[\alpha]_D^{25} = -4.21°$ (c = 0.700, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.42 (brs, 1H), 5.39 (s, 1H), 5.39 (m, 1H), 5.22–5.26 (m, 2H), 5.15 (d, 1H, J = 9.7 Hz), 5.05 (dd, 1H, J = 1.4 Hz, J = 9.7 Hz), 4.92 (brd, 1H, J = 2.9 Hz), 4.76 (m, 1H), 4.66 (brd, 1H, J = 8.7 Hz), 4.54 (dd, 1H, J = 2.9 Hz, J = 9.7 Hz), 4.10 (dd, 1H, J = 2.9 Hz, J = 11.1 Hz), 3.89 (dq, 1H, J = 6.3 Hz, J = 9.7 Hz), 3.80 (dq, 1H, J = 6.3 Hz, J = 9.7 Hz), 3.71 (m, 1H), 3.71 (m, 1H), 3.56 (dq, 1H, J = 6.3 Hz, J = 9.7 Hz), 3.44 (ddd, 1H, J = 4.8 Hz, J = 9.7 Hz, J = 11.6 Hz), 3.36 (s, 3H), 3.26 (dd, 1H, J = 2.9 Hz, J = 9.7 Hz), 3.23 (dd, 1H, J = 9.7 Hz, J = 9.7 Hz), 3.20 (m, 1H), 2.40–2.84 (m, 8H), 2.28–2.39 (m, 3H), 2.22 (dd, 1H, J = 4.8 Hz, J = 13.0 Hz), 2.19 (m, 1H), 2.18 (s, 3H), 2.10 (s, 3H), 2.09 (s, 3H), 2.05 (m, 1H), 2.03 (s, 3H), 1.97 (s, 3H), 1.95 (q, 1H, J = 7.7 Hz), 1.90 (m, 1H), 1.88 (q, 1H, J = 7.7 Hz), 1.83 (q, 1H, J = 7.7 Hz), 1.70–1.82 (m, 4H), 1.69 (s, 3H), 1.65 (s, 1H), 1.58 (s, 3H), 1.20–1.58 (m, 24H), 1.17 (d, 3H, J = 6.3 Hz), 1.10 (s, 3H), 1.07 (d, 3H, J = 7.7 Hz), 1.07 (t, 3H, J = 7.7 Hz), 1.00 (t, 3H, J = 7.7 Hz), 0.98 (d, 3H, J = 6.8 Hz), 0.91 (d, 3H, J = 6.8 Hz), 0.87 (d, 3H, J = 6.8 Hz), 0.86 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 206.4, 198.3, 181.2, 171.9, 170.6, 170.4, 170.2, 167.6, 140.4, 135.6, 135.5, 135.2, 126.6, 120.7, 116.1, 99.9, 99.6, 98.7, 90.8, 87.9, 81.8, 80.0, 78.5, 73.0, 72.5, 70.8, 69.2, 68.0, 67.9, 67.8, 66.0, 57.5, 57.3, 42.0, 39.6, 39.1, 37.9, 36.9, 36.1, 36.0, 35.3, 34.6, 34.1, 33.7, 33.1, 32.9, 30.9, 30.6, 29.8, 29.7, 28.9, 27.9, 26.7, 23.4, 22.8, 22.7, 22.0, 21.6, 21.3, 21.2, 21.0, 20.9, 20.0, 19.3, 18.9, 18.6, 18.3, 17.9, 17.8, 16.4, 13.9, 11.5 ppm; IR (neat): $\tilde{\nu}$ = 2970, 2936, 1788, 1743, 1680, 1588, 1455, 1371, 1241, 1154, 1092, 1065, 1011 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{81}H_{120}O_{25}$ $[M+Na]^+$ m/z = 1515.8016, found: 1515.8007.

26: NaOMe (20.0 mg) was added to a stirred solution of **25** (5.50 mg, 3.68 μmol) in methanol (500 mL) at RT. After being stirred under reflux for 24 h, the reaction mixture was neutralized with Dowex 50WX4 and filtered. The filtrate was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with $CHCl_3$/methanol 94:6 to give **26** (3.00 mg, 2.72 μmol, 75 %). $[\alpha]_D^{24} = -38.9°$ (c = 0.305, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.82 (brs, 1H), 5.27 (s, 1H), 5.08 (d, 1H, J = 10.1 Hz), 5.06 (dd, 1H, J = 1.9 Hz, J = 9.2 Hz), 4.96 (d, 1H, J = 3.4 Hz), 4.81 (dd, 1H, J = 1.4 Hz, J = 9.2 Hz), 4.11 (m, 1H), 4.08 (m, 1H), 3.92 (brs, 1H), 3.76–3.88 (m, 2H), 3.69 (dq, 1H, J = 6.3 Hz, J = 9.2 Hz), 3.55–3.66 (m, 2H), 3.49 (ddd, 1H, J = 4.8 Hz, J = 11.6 Hz, J = 9.2 Hz), 3.42 (m, 1H), 3.40 (s, 3H), 3.31 (dd, 1H, J = 9.2 Hz, J = 9.2 Hz), 3.28 (dd, 1H, J = 2.9 Hz, J = 9.2 Hz), 3.22–3.27 (m, 2H), 2.87 (dd, 1H, J = 10.1 Hz, J = 10.1 Hz), 2.84 (s, 1H), 2.54 (q, 1H, J = 7.2 Hz), 2.39 (m, 1H), 2.25–2.35 (m, 2H), 2.23 (dd, 1H, J = 4.8 Hz, J = 13.0 Hz), 2.00–2.17 (m, 7H), 1.95 (m, 1H), 1.86 (dd, 1H, J = 8.2 Hz, J = 14.0 Hz), 1.79 (m, 1H), 1.53–1.72 (m, 15H), 1.23–1.31 (m, 8H), 1.21 (d, 3H, J = 6.3 Hz), 1.11 (m, 1H), 1.05 (d, 3H, J = 7.2 Hz), 1.02 (s, 3H), 0.88–0.97 (m, 12H), 0.84 (d, 3H, J = 7.2 Hz), 0.66 ppm (m, 1H,); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 205.4, 203.0, 166.5, 140.1, 135.3, 135.2, 133.1, 127.5, 121.4, 103.1, 100.6, 99.2, 98.5, 91.4, 87.3, 81.3, 80.7, 78.3, 73.2, 70.7, 70.5, 69.3, 68.4, 68.3, 67.8, 65.0, 61.1, 57.5, 57.4, 48.8, 43.6, 42.0, 41.8, 38.2, 38.0, 37.4, 36.7, 35.7, 35.2, 35.1, 34.9, 33.2, 32.3, 32.0, 31.1, 29.8, 29.0, 23.7, 23.2, 23.1, 22.0, 21.5, 20.5, 20.4, 19.3, 18.1, 17.8, 17.3, 14.8, 12.7 ppm; IR (solid): $\tilde{\nu}$ = 3439, 2961, 2926, 1742, 1624, 1462, 1380, 1059, 1015, 989 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{61}H_{96}O_{17}$ $[M+Na]^+$ m/z = 1123.6545, found: 1123.6553.

28: According to the method for the synthesis of **17**, **27** (0.548 g, 1.80 mmol), **22** (1.41 g, 2.71 mmol) and MS-4 Å (2.71 g) in CH_2Cl_2 (18.0 mL) were treated with a mixture of 1.00 M IBr in CH_2Cl_2 (3.60 mL, 3.60 mmol) and TBAB (1.45 g, 4.50 mmol) at 0 °C for 2 h. *N,N*-Diisopropylethylamine (0.156 mL, 0.900 mmol) was then added to the reaction mixture. Stirring for 20 h at the same temperature gave **28** (1.15 g, 1.74 mmol, 94 %, β/α = 94:6) after purification. The α,β isomers were separated by chromatography on silica gel with toluene/ethyl acetate 92:8. $[\alpha]_D^{28} = -13.8°$ (c = 0.910, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (d, 2H, J = 8.7 Hz), 7.39 (d, 2H, J = 8.7 Hz), 5.28 (ddd, 1H, J = 3.4 Hz, J = 3.4 Hz, J = 3.4 Hz), 5.01 (dd, 1H, J = 1.9 Hz, J = 9.2 Hz), 4.96 (d, 1H, J = 3.9 Hz), 4.18 (dd, 1H, J = 9.2 Hz, J = 9.2 Hz), 3.87 (dq, 1H, J = 6.3 Hz, J = 9.2 Hz), 3.85 (dq, 1H, J = 6.3 Hz, J = 9.2 Hz), 3.62 (ddd, 1H, J = 5.3 Hz, J = 9.2 Hz, J = 11.1 Hz), 3.47–3.43 (m, 2H), 3.35 (dd, 1H, J = 3.4 Hz, J = 9.2 Hz), 3.22–3.32 (m, 5H), 2.36 (dd, 1H, J = 5.3 Hz, J = 13.0 Hz), 2.12 (s, 3H), 2.09 (ddd, 1H, J = 1.9 Hz, J = 3.4 Hz, J = 14.5 Hz), 1.75 (ddd, 1H, J = 3.4 Hz, J = 9.2 Hz, J = 14.5 Hz), 1.56 (ddd, 1H, J = 3.4 Hz, J = 11.1 Hz, J = 13.0 Hz), 1.31 (d, 3H, J = 6.3 Hz), 1.25 (d, 3H, J = 6.3 Hz), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.1, 147.2, 145.4, 129.3, 124.1, 99.0, 92.8, 84.8, 79.5, 75.3, 70.2, 69.3, 66.7, 55.9, 51.6, 38.4, 35.0, 29.6, 25.8, 21.2, 18.4, 18.1, 17.6, −4.1, −5.1 ppm; IR (solid): $\tilde{\nu}$ = 2933, 2859, 1736, 1607, 1523, 1451, 1316, 1243, 1173, 1065, 1002 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{29}H_{47}NO_{12}SSi$ $[M+Na]^+$ m/z = 684.2486, found: 684.2490.

29: DBU was added to a stirred solution of **28** (1.12 g, 1.69 mmol) in CH_3CN (8.45 mL) (252 μL, 1.69 mmol) at 0 °C. After being stirred at RT for 6 h, the reaction mixture was poured into saturated aq. NH_4Cl. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with 1 M HCl, saturated aq. $NaHCO_3$, and

brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl aetate 60:40 to give **29** (0.580 mg, 1.29 mmol, 77%). $[\alpha]_D^{29} = -14.8°$ ($c = 0.930$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.28$ (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 3.4$ Hz), 5.01 (dd, 1H, $J = 1.9$ Hz, $J = 9.2$ Hz), 4.95 (d, 1H, $J = 3.9$ Hz), 3.88 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.65 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.31–3.42 (m, 5H), 3.33 (ddd, 1H, $J = 2.4$ Hz, $J = 9.2$ Hz, $J = 9.2$ Hz), 2.37 (d, 1H, $J = 2.4$ Hz), 2.25 (dd, 1H, $J = 5.3$ Hz, $J = 13.0$ Hz), 2.12 (s, 3H), 2.10 (ddd, 1H, $J = 1.9$ Hz, $J = 3.4$ Hz, $J = 14.5$ Hz), 1.75 (ddd, 1H, $J = 3.4$ Hz, $J = 9.2$ Hz, $J = 14.5$ Hz), 1.50 (ddd, 1H, $J = 3.9$ Hz, $J = 11.1$ Hz, $J = 13.0$ Hz), 1.26 (d, 3H, $J = 6.3$ Hz), 1.24 (d, 3H, $J = 6.3$ Hz), 0.89 (s, 9H), 0.11 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 170.2$, 99.9, 92.9, 79.3, 78.1, 76.1, 70.5, 69.5, 68.6, 56.5, 38.5, 34.3, 25.8, 21.2, 18.4, 18.2, 17.7, −4.1, −5.0 ppm; IR (neat): $\tilde{\nu} = 3469$, 2933, 2859, 1744, 1370, 1242, 1089, 987 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{21}H_{40}O_8Si$ $[M+Na]^+$ $m/z = 471.2390$, found: 471.2396.

30: According to the method for the synthesis of **15**, **29** (0.515 mg, 1.15 mmol), **4** (496 mg, 1.72 mmol), and pulverized activated MS-4 Å (1.72 g) in toluene (23.0 mL) were treated with a solution of iodine (582 mg, 2.30 mmol) in toluene (0.230 mL) and triisopropylsilane (23.5 μL, 0.115 mmol) at −94 °C for 1.5 h to provide **30** (705 mg, 0.981 mmol, 85%, β/α = 95:5) after purification. $[\alpha]_D^{21} = -14.7°$ ($c = 1.02$, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.39$ (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 3.4$ Hz), 5.25 (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 3.4$ Hz), 5.04 (dd, 1H, $J = 1.4$ Hz, $J = 9.2$ Hz), 4.99 (dd, 1H, $J = 1.9$ Hz, $J = 9.2$ Hz), 4.91 (d, 1H, $J = 3.4$ Hz), 4.54 (dd, 1H, $J = 3.4$ Hz, $J = 9.2$ Hz), 3.83–3.92 (m, 2H), 3.57 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.43 (ddd, 1H, $J = 4.8$ Hz, $J = 9.2$ Hz, $J = 11.6$ Hz), 3.36 (s, 3H), 3.30 (dd, 1H, $J = 3.4$ Hz, $J = 9.2$ Hz), 3.23 (dd, 1H, $J = 9.2$ Hz, $J = 9.2$ Hz), 2.38–2.84 (m, 4H), 2.22 (dd, 1H, $J = 4.8$ Hz, $J = 13.0$ Hz), 2.17 (s, 3H), 2.10 (s, 3H), 2.10 (m, 1H), 2.09 (s, 3H), 2.08 (m, 1H), 1.68–1.82 (m, 2H), 1.50 (ddd, 1H, $J = 3.4$ Hz, $J = 11.6$ Hz, $J = 13.0$ Hz), 1.25 (d, 3H, $J = 6.3$ Hz), 1.21 (d, 3H, $J = 6.3$ Hz), 1.16 (d, 3H, $J = 6.3$ Hz), 0.88 (s, 9H), 0.10 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 206.4$, 171.9, 170.2, 99.7, 98.7, 92.9, 81.8, 79.5, 78.6, 70.5, 69.5, 68.0, 67.9, 67.8, 57.3, 38.3, 38.0, 36.2, 35.4, 29.9, 27.9, 25.9, 21.2, 21.1, 18.4, 18.2, 17.9, 17.8, −4.1, −5.0 ppm; IR (neat): $\tilde{\nu} = 2934$, 2858, 1745, 1723, 1370, 1243, 1154, 1067, 1012 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{58}O_{14}Si$ $[M+Na]^+$ $m/z = 741.3494$, found: 741.3491.

31: Hydrogen fluoride pyridine (1.41 mL) was added to a stirred solution of **30** (0.510 g, 0.709 mmol) in pyridine (5.65 mL) at 0 °C. After being stirred at RT for 5 h, the reaction mixture was poured into saturated aq. $NaHCO_3$. The aqueous layer was extracted with two portions of ethyl acetate. The combined extract was washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel with hexane/ethyl acetate 35:65 to give **31** (343 mg, 0.567 mmol, 80%, α/β = 29:71). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 5.38$–5.40 (m, 2H), 5.29 (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 3.4$ Hz), 5.27 (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 3.4$ Hz), 5.15 (m, 1H), 5.03–5.08 (m, 3H), 4.96 (d, 1H, $J = 3.4$ Hz), 4.93 (d, 1H, $J = 3.4$ Hz), 4.54 (dd, 1H, $J = 3.4$ Hz, $J = 9.2$ Hz), 4.54 (dd, 1H, $J = 3.4$ Hz, $J = 9.2$ Hz), 4.26 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.95 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.91 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.91 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.64 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.57 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.44 (ddd, 1H, $J = 4.8$ Hz, $J = 9.2$ Hz, $J = 11.6$ Hz), 3.44 (ddd, 1H, $J = 4.8$ Hz, $J = 9.2$ Hz, $J = 11.6$ Hz), 3.38 (s, 3H), 3.37 (s, 3H), 3.28–3.35 (m, 3H), 3.25 (dd, 1H, $J = 9.2$ Hz, $J = 9.2$ Hz), 3.24 (dd, 1H, $J = 9.2$ Hz, $J = 9.2$ Hz), 3.01 (d, 1H, $J = 5.8$ Hz), 2.40–2.85 (m, 8H), 2.04–2.27 (m, 24H), 1.96 (ddd, 1H, $J = 3.4$ Hz, $J = 3.4$ Hz, $J = 15.0$ Hz), 1.76–1.83 (m, 2H), 1.69 (ddd, 1H, $J = 3.4$ Hz, $J = 9.7$ Hz, $J = 14.0$ Hz), 1.49–1.58 (m, 2H), 1.21–1.31 (m, 12H), 1.17 (d, 3H, $J = 6.3$ Hz), 1.17 ppm (d, 3H, $J = 6.3$ Hz); IR (neat): $\tilde{\nu} = 3450$, 2979, 2938, 1743, 1722, 1348, 1245, 1170, 1067, 1037 cm^{-1}.

6: Trichloroacetonitrile (35.2 μL, 350 μmol) and a catalytic amount of Cs_2CO_3 (5.71 mg, 17.5 μmol) were added to a solution of **31** (53.0 mg, 87.7 μmol) in dry CH_2Cl_2 (0.877 mL) at RT. After being stirred at the same temperature for 4 h, the reaction mixture was filtered through Celite, and concentrated in vacuo. The residue was chromatographed on NH-functionalized silica gel with CH_2Cl_2 to give **6** (59.7 mg, 78.0 mmol, 89%, β/α = 95:5). The β/α ratio was determined by ^{1}H NMR analysis (400 MHz). ^{1}H NMR (400 MHz, CD_2Cl_2): $\delta = 8.54$ (s, 1H), 6.10 (dd, 1H, $J = 2.9$ Hz, $J = 7.7$ Hz), 5.30–5.35 (m, 2H), 5.05 (dd, 1H, $J = 1.9$ Hz, $J = 9.7$ Hz), 4.91 (d, 1H, $J = 3.9$ Hz), 4.47 (dd, 1H, $J = 3.4$ Hz, $J = 9.7$ Hz), 4.06 (dq, 1H, $J = 6.8$ Hz, $J = 6.8$ Hz), 3.87 (dq, 1H, $J = 6.3$ Hz, $J = 9.7$ Hz), 3.60 (dq, 1H, $J = 6.3$ Hz, $J = 9.2$ Hz), 3.51 (dd, 1H, $J = 2.9$ Hz, $J = 6.8$ Hz), 3.43 (ddd, 1H, $J = 5.3$ Hz, $J = 9.2$ Hz, $J = 11.6$ Hz), 3.32 (s, 3H), 3.21 (dd, 1H, $J = 9.2$ Hz, $J = 9.2$ Hz), 2.27–2.76 (m, 5H), 2.21 (dd, $J = 5.3$ Hz, $J = 13.0$ Hz), 2.10 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 1.92–2.05 (m, 2H), 1.73 (ddd, 1H, $J = 2.9$ Hz, $J = 9.7$ Hz, $J = 14.0$ Hz), 1.48 (ddd, 1H, $J = 3.9$ Hz, $J = 11.6$ Hz, $J = 13.0$ Hz,), 1.30 (d, 3H, $J = 6.3$ Hz), 1.17 (d, 3H, $J = 6.3$ Hz), 1.13 ppm (d, 3H, $J = 6.3$ Hz); IR (solid): $\tilde{\nu} = 3315$, 2979, 2940, 1743, 1721, 1674, 1370, 1245, 1157 cm^{-1}.

26: According to the method for the synthesis of **15**, **3** (12.0 mg, 13.2 μmol), **6** (20.2 mg, 26.4 μmol), and pulverized activated MS-4 Å (26.0 mg) in toluene (390 μL) were treated with a solution of iodine (8.32 mg, 33.0 μmol) in toluene (30.0 μL) and triethylsilane (0.421 μL, 2.64 μmol) at −94 °C for 1.5 h, to provide **26** (7.90 mg, 5.23 μmol, 40%, β/α = 95:5).

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[16] Re-examination involving degradation of natural product **1** also indicated that natural product **1** contained an L-oleandroside.
[17] Detail was described in Supporting Information.

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