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Aryl-β-C-glucosidation using glucal boronate: application to the synthesis of tri-*O*-methylnorbergenin

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ABSTRACT

Novel aryl-β-C-glucosidation method using glucal boronate was developed. This protocol can offer several advantages including use of non-toxic, easily handling glucal boronate as a crystalline solid and storable at room temperature for several months. Tri-*O*-methylnorbergenin (8,10-di-*O*-methylbergenin), an anti-HIV active bergenin derivative, was concisely synthesized by application of the aryl-β-C-glucosidation method.

1. Introduction

C-Glucoside derivatives such as carthamin,[1] mangiferin,[2] and bergenin[3,4] have attracted much attention in recent years because of their interesting biological activities. In addition, *C*-glucosides are inherently stable toward hydrolysis compared with their *O*-analogues and, thus, they are promising candidates for therapeutic applications.[5] Therefore, new C-glucosidation method provides a powerful tool toward organic and medicinal chemistry.[6–9]

Several approaches to aryl-β-C-glucosidation had been reported. Treatment of tetra-*O*-benzylgluconolactone with phenyllithium followed by reduction with triisopropylsilane and boron trifluoride etherate ($BF_3 \cdot Et_2O$) afforded phenyl-β-*C*-glucoside with about 45:1 stereoselectivity.[10] Reaction of 2,3,4,6-tetra-*O*-methyl-D-glucose with phenol derivative such as 2-naphthol in the presence of $BF_3 \cdot Et_2O$ provided β-*C*-glucoside through Fries-type rearrangement.[11] On the other hand, palladium (Pd)-catalyzed coupling reaction of either 1-stannylglucal with aryl halide,[12–14] or 1-iodoglucal with arylmetals[15] gave the corresponding aryl-β-*C*-glucoside stereoselectively after hydroboration and oxidation.[16]

Among them, we focused on glucal-based coupling approach because it could be widely applied. However, the procedure should be modified not only the toxicity of tin compounds but also low yield of coupling products. Therefore we chose boronate as a glucal synthon due to its stability, non-toxicity, and easy handling.[17] Here we report the novel coupling reactions between the glucal boronate and aryl bromide and its application to the synthesis of tri-*O*-methylnorbergenin (8,10-di-*O*-methylbergenin).[18]

2. Result and discussion

In the preparation of 1-stannylglucal from *tert*-butyldimethylsilyl (TBS)-protected glucal through lithiation with *tert*-butyllithium (*t*-BuLi), Friesen had found inevitable side-stannylation on the TBS group.[16] Therefore, we at first designed triisopropylsilyl (TIPS)-protected glucal boronate (Scheme 1). Commercially available D-glucal **1** was reacted with TIPS chloride and imidazole in DMF[19] to afford tri-TIPS-protected glucal **2**, which was converted to glucal boronate by treatment with trimethylborate after lithiation followed by protection of the boronic acid function with pinacol to give **3**. Pd-catalyzed coupling reaction of **3** with bromobenzene provided a phenyl glucal **4** in 99% yield, however, hydroboration–oxidation with borane–tetrahydrofuran complex followed by alkaline hydrogen peroxide[14] resulted in the low yield formation of unexpected ring-opening **6**, instead of a glucoside **5**, as an isolable product.

It has been known that the $^5H_4$ conformation (see **4B** in Scheme 2) is strongly preferred to $^4H_5$ conformation (see **4A** in Scheme 2) for glucals due to vinylogous anomeric effect.[20] In the tri-TIPS-protected phenyl glucal **4** more shift to the $^5H_4$ conformation **4B** is reasonably expected by steric repulsion between bulky TIPS-protecting groups.[21] Thus, hydroboration occurred from sterically less hindered side to produce an adduct **7**, rearrangement of which through bond formation between the boron and the ring-oxygen atoms afforded a ring-opening product **8**, which leads to a seven-membered boracycle **9** via intramolecular hydroboration. Finally, **9** was oxidized with hydrogen peroxide and sodium hydroxide to afford **6** (Scheme 2).[22]

Next, we designed a bicyclic system **10** as a glucal boronate based on prediction that bicyclic derivative such as 4,6-di-*O*-*tert*-butylsilylene group would not cause axial–equatorial flip on the

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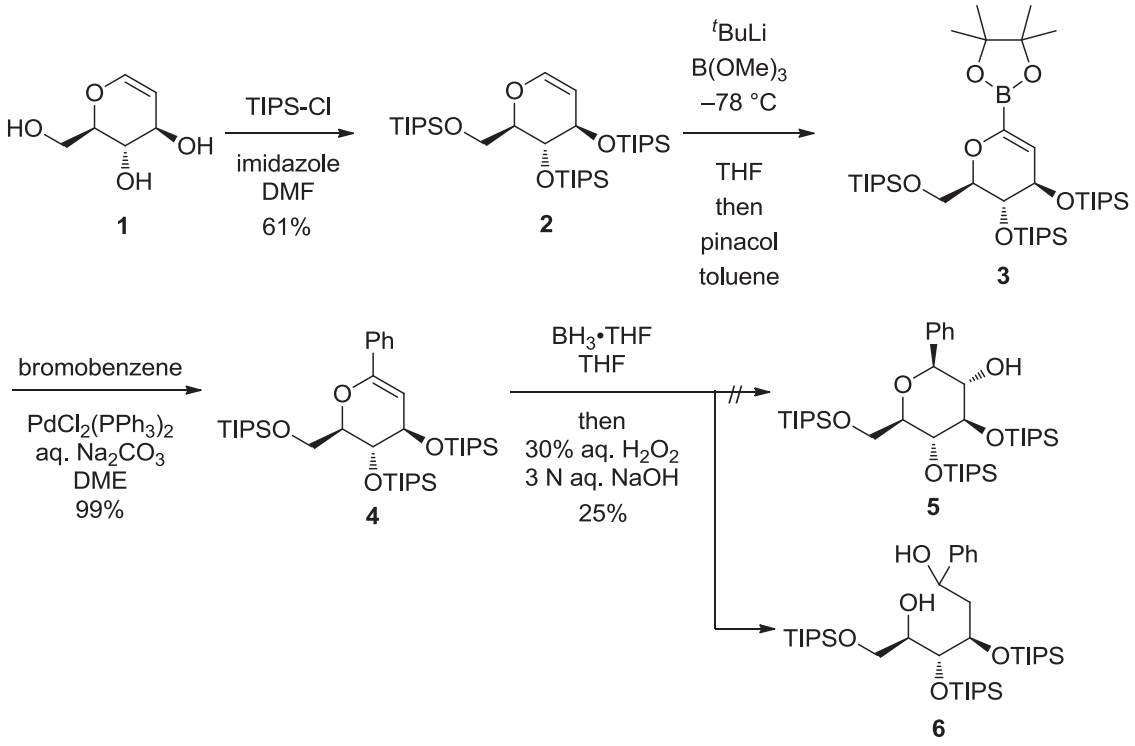
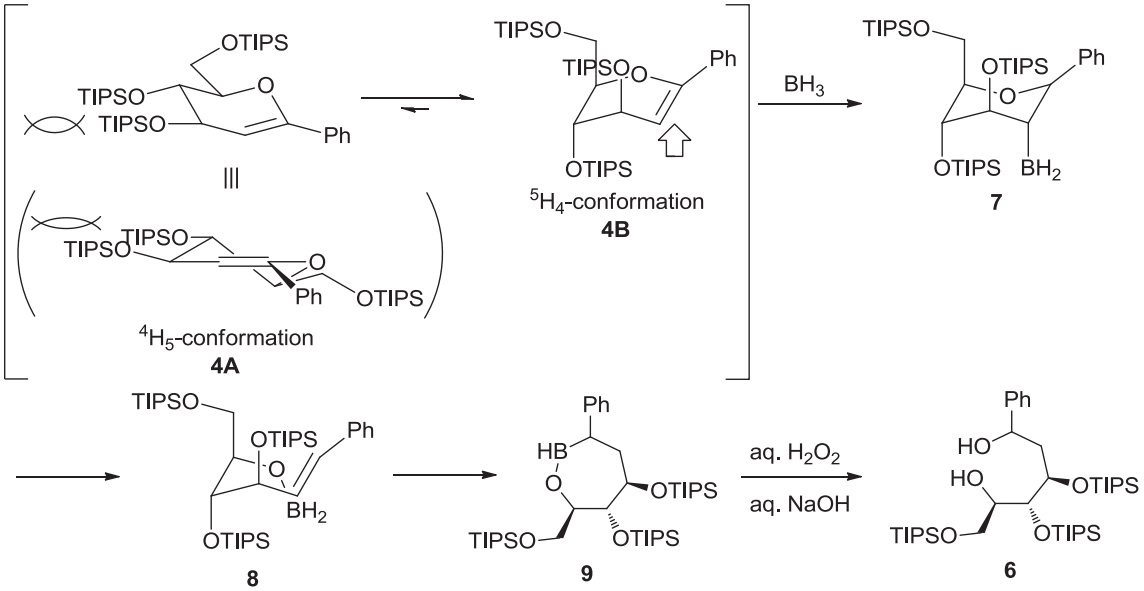


Scheme 1. A trial for the preparation of tri-TIPS-protected β-D-glucoside **5**.

pyranose ring (Fig. 1). Synthesis of the bicyclic boronate **10** was shown in Scheme 3. D-Glucal **1** was converted into a bridged-silyl protected glucal **11** according to the literature.[23] Then **11** was treated with *t*-BuLi and trimethylborate, followed by protection with pinacol to give the bicyclic boronate **10** as a crystalline solid. The structure of **10** was established by single-crystal X-ray analysis (Fig. 2).[24] As well as other boronic acid esters, **1** was found to be stable at room temperature for several months (six months at room temperature).

Cross-couplings of the bicyclic glucal boronate **10** with a kind of aryl bromides including heteroaryl bromide were examined (Table 1). Reactions proceed smoothly with phenyl (**12a**, entry 1), electron-rich phenyl (**12b**, entry 2), electron-deficient phenyl (**12c** and **12d**, entries 3 and 4), and heteroaryl (**12e** and **12f**, entries 5 and 6) bromides to afford glucals in excellent yields. The coupling products **12** were subjected to hydroboration–oxidation reactions (Table 2). Desired aryl-β-*C*-glucosides **13** with correct configuration ($J_{1,2} \approx 9.5$ Hz) were obtained in moderate yields. Deprotection of the silyl functions in **13** with tetra-*n*-butylammonium fluoride (TBAF) provided aryl-β-*C*-glucosides **14a**–**14e** in moderate to good yields (Table 2).

In the case of **12f**, a nitrogen-containing glucal boronate, hydroboration–oxidation was unsuccessful. Therefore, we explored another route (Scheme 4). Compound **12a** was, as a model substrate,



Scheme 2. Plausible mechanism for the formation of **6** from **4**.

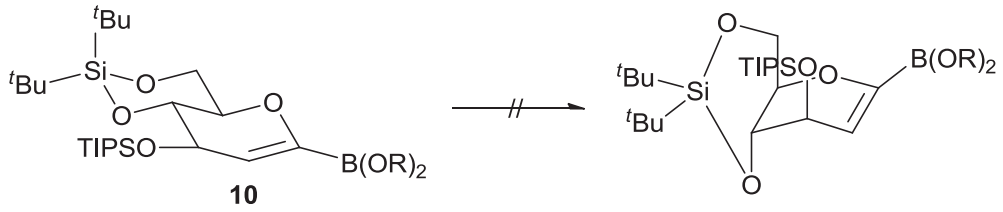


Fig. 1. Design of a bicyclic system **10**.

treated with oxone to give **15a** in 60% yield as an anomeric mixture (ca. 10:1). Hydrogenolysis of **15a** with triethylsilane (TES) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) afforded a TIPS-deprotected *C*-glucoside **16a** in 52% yield with complete stereoselectivity of anomeric carbon. The desired β-stereochemistry of which was confirmed by coupling constant in the ^{1}H NMR spectrum ($J_{1,2}$=9.4 Hz). Compound **16a** was deprotected with TBAF to give phenyl-β-*C*-glucoside **14a** in 71% yield. Thus, phenyl-β-*C*-glucoside **14a** was alternatively prepared from arylglucal **12a** using oxone in the oxidation step, in almost the same overall yield. Next, this route was applied to the preparation of a nitrogen-containing glucoside **14f**. As a result, quinolinyl-β-*C*-glucoside **14f** was given, but ineffective hydrogenolysis and deprotection were observed (overall 2% yield from **12f**).

Tri-*O*-methylnorbergenin **23** was isolated from *Ardisia japonica*[4] and the demethyl derivative, bergenin, shows anti-HIV activity. We attempted to synthesize tri-*O*-methylnorbergenin **23** by application of the novel aryl-β-C-glucosidation method established by us (Scheme 5). Aryl bromide **18** carrying a gallic acid function was prepared from commercially available methyl 3,4,5-trimethoxybenzoate **17** by treatment with bromine in acetic anhydride in 82% yield. Pd-catalyzed coupling reaction of glucal boronate **10** and aryl bromide **18** gave arylglucal **19** in an excellent yield. After hydroboration–oxidation aryl-β-*C*-glucoside **20** was obtained in a moderate yield. Compound **20** was oxidized with manganese dioxide to provide lactone **22** in 86% yield through lactol **21**. Deprotection of the silyl function in **22** afforded lactone-ring opening product, which was cyclized using thionyl chloride in methanol to give the targeted compound tri-*O*-methylnorbergenin **23** in 85% yield, whose analytical data including ^{1}H and ^{13}C NMR, MS, IR, and specific rotation were identical with reported data.[25] Thus, we developed a short synthesis of the bergenin derivative **23** from glucal boronate **10** in 47% overall yield, which was advantageous over reported yield (33%).[25]

3. Conclusion

In summary, we established a novel preparation method of aryl-β-*C*-glucoside using glucal boronate as a key compound and successfully applied the method to the short synthesis of tri-*O*-methylnorbergenin. Our glucosidation method offers an advantage such as the non-toxic, easily handling crystalline boronate, which is stable when stored at room temperature for several months.

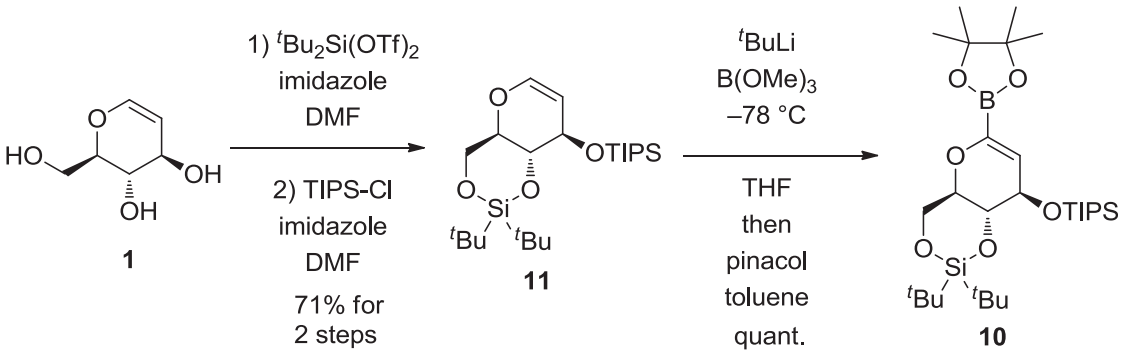
4. Experimental section

4.1. General information

NMR spectra were collected on JEOL JNM-ECX400P and Varian UNITY INOVA500 spectrometers. Chemical shifts were given in parts per million (ppm) downfield from internal reference tetramethylsilane standard; coupling constants (*J* value) were given in hertz (Hz). Elemental analyses and X-ray analyses were conducted by Medicinal Chemistry Laboratory, Mitsubishi Tanabe Pharma. Melting points were measured by BÜCHI Melting Point B-545 and were uncorrected. Infrared spectra were measured on Perkin–Elmer PARAGON1000. APCI- and ESI-MS spectra were obtained on Finnigan MAT SSQ7000C or ThermoQuest LCQ Advantage eluting with 10 mM $AcONH_4$/MeOH. HRMS spectra were measured by Agilent 1100.

4.2. 1,5-Anhydro-2-deoxy-4,6-*O*-di-(*tert*-butyl)silanediyl-3-*O*-triisopropylsilyl-D-*arabino*-hex-1-enitolylboronic acid pinacol ester (10)

To a solution of **11**[23] (6.63 g) in THF (70 mL) was added *tert*-butyllithium (1.42 M, 47.0 mL) at −78 °C dropwise, then stirred at 0 °C for 1 h. To a mixture was added trimethylborate (8.4 mL) at −78 °C, then stirred at 0 °C for 15 min and gradually warmed to room temperature and stirred for 1 h. The mixture was quenched by H_2O, then the mixture was extracted with ether, washed with brine, dried over sodium sulfate, filtered, the filtrate was evaporated to give crude boronic acid as a colorless viscous oil. To a solution of boronic acid in toluene (70 mL) was added pinacol (2.12 g), then the mixture was stirred at room temperature for overnight. The reaction mixture was washed with water and brine, dried over sodium sulfate, and filtered. The filtrate was evaporated to afford quantitative yield of glucal boronic acid ester (11.03 g) as a colorless viscous oil, which was used without further purification.



Scheme 3. Synthesis of the bicyclic glucal boronate **10**.

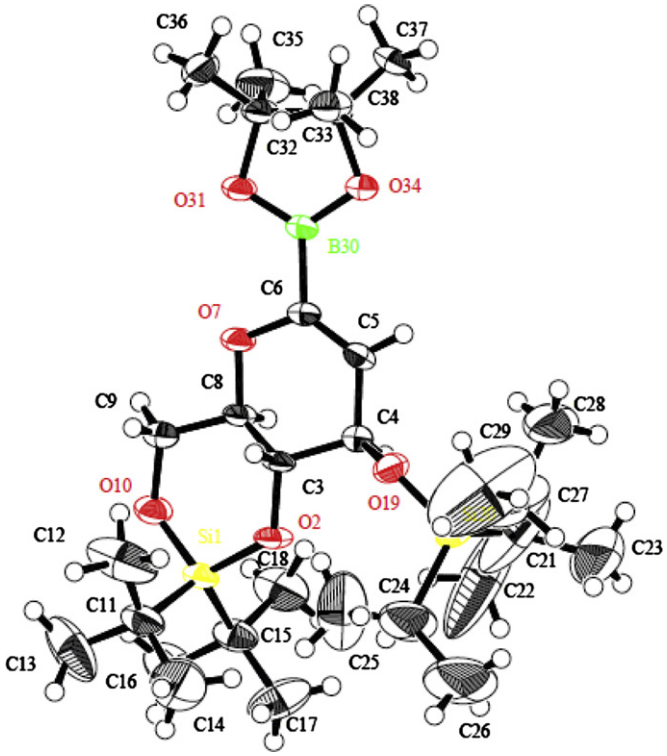


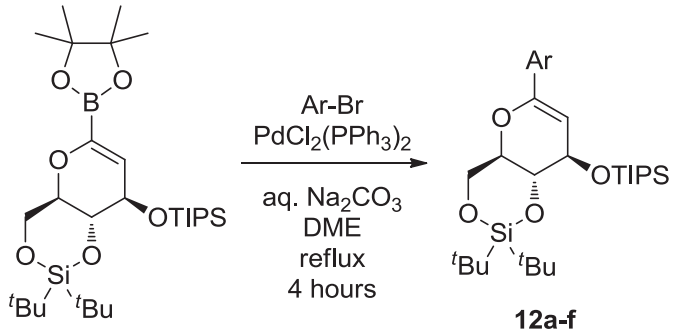
Fig. 2. ORTEP drawing of **10**. The displacement ellipsoids are drawn at the 50% probability level.

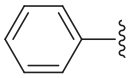
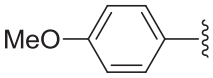
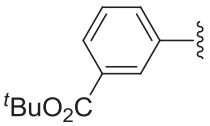
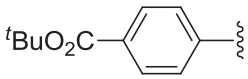
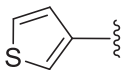
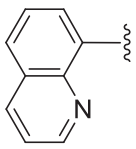
An analytical sample was prepared by purification using preparative HPLC and recrystallization from MeOH to afford pure glucal boronic acid ester **10** as a colorless fine needle. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.45 (d, J=2.2 Hz, 1H), 4.44 (dd, J=2.2, 7.2 Hz, 1H), 4.26 (dd, J=5.0, 10.5 Hz, 1H), 4.02 (m, 1H), 3.99 (dd, J=3.0, 7.4 Hz, 1H), 3.77 (td, J=5.0, 10.5 Hz, 1H), 1.27 (s, 12H), 1.10–1.16 (m, 21H), 1.05 (s, 9H), 0.98 (s, 9H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9 (br), 119.3, 84.3, 77.3, 73.0, 71.4, 66.3, 27.5, 27.0, 24.6, 22.7, 19.8, 18.2, 12.6. MS (CI, m/z) 569 $[M+H]^+$. IR (KBr, cm^{-1}) 2941, 2864, 1643, 1471, 1418, 1373, 1109. Anal. Calcd for $C_{29}H_{57}BO_6Si_2$: C, 61.24; H, 10.10, B, 1.90. Found: C, 61.12; H, 10.02; B, 1.70. Mp 169–171 °C. $[\alpha]_D^{25}$ −32.0 (c 0.2, $CHCl_3$).

4.3. (1,5-Anhydro-2-deoxy-3,4,6-tris-*O*-triisopropylsilyl-D-*arabino*-hex-1-enitolyl)benzene (4)

Compound **2** was synthesized from D-glucal **1** according to literature.[19] To a solution of **2** (21.28 g) in THF (160 mL) was added *tert*-butyllithium (1.50 M, 103 mL) at −78 °C dropwise, then stirred at 0 °C for 1 h. To a mixture was added trimethylborate (19.4 mL) at −78 °C, then stirred at 0 °C for 15 min and gradually warmed to room temperature and stirred for 1 h. The mixture was quenched by H_2O, then the mixture was extracted with ether, washed with brine, dried over sodium sulfate, filtered, the filtrate was evaporated to give crude boronic acid as a colorless viscous oil. To a solution of boronic acid in toluene (250 mL) was added pinacol (4.91 g), then the mixture was stirred at room temperature for overnight. The reaction mixture was washed with water and brine, dried over sodium sulfate, and filtered. The filtrate was evaporated to afford quantitative yield of glucal boronic acid ester **3** (27.4 g) as a colorless viscous oil. To a mixture of boronic acid ester **3** (7.92 g) and bromobenzene (785 mg) in DME (50 mL) were added dichlorobis(triphenylphosphine)palladium (175 mg) and 2 M aqueous Na_2CO_3 (12.5 mL), then the mixture was refluxed for 3 h. The mixture was cooled to ambient temperature and diluted with AcOEt, then washed with water, brine, dried over sodium sulfate, and filtered. After the filtrate was concentrated, the crude material was purified by silica gel column chromatography (hexane) to give **4** (3.62 g, 99%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.64 (m, 2H), 7.28–7.34 (m, 3H), 5.34 (dd, J=1.5, 5.4 Hz, 1H), 4.46 (m, 1H), 4.18 (td, J=1.9, 5.2 Hz, 1H), 4.14 (m, 1H), 4.10 (m, 1H), 3.91 (dd, J=4.4, 11.3 Hz, 1H), 1.00–1.10 (m, 63H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 136.4, 128.2, 127.9, 125.4, 96.7, 81.3, 70.1, 66.8, 62.0, 18.2, 18.2, 18.1, 18.1, 18.0, 18.0, 12.6, 12.5, 12.1. MS (APCI, m/z) 691 $[M+H]^+$. IR (neat, cm^{-1}) 1944, 2867, 1652, 1464, 1060. Anal. Calcd for $C_{39}H_{74}O_4Si_3$: C, 67.76; H, 10.79. Found: C, 67.86; H, 11.03. $[\alpha]_D^{25}$ −10.0 (c 0.2, $CHCl_3$).

Table 1
Suzuki cross-couplings of glucal boronate **10** with aryl bromides



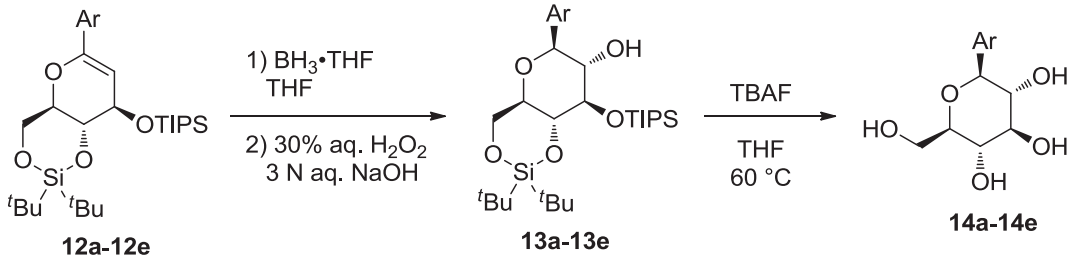
Entry	Ar	Product	Yield[a] (%)
1		**12a**	99
2		**12b**	99
3		**12c**	99
4		**12d**	99
5		**12e**	99
6		**12f**	99

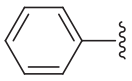
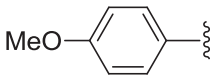
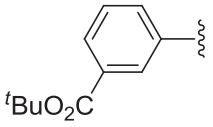
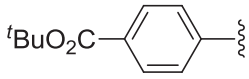
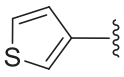
[a] Isolated yield.

4.4. 2-Deoxy-1-*C*-phenyl-3,4,6-tris-*O*-(triisopropylsilyl)-D-*arabino*-hexitol (6)

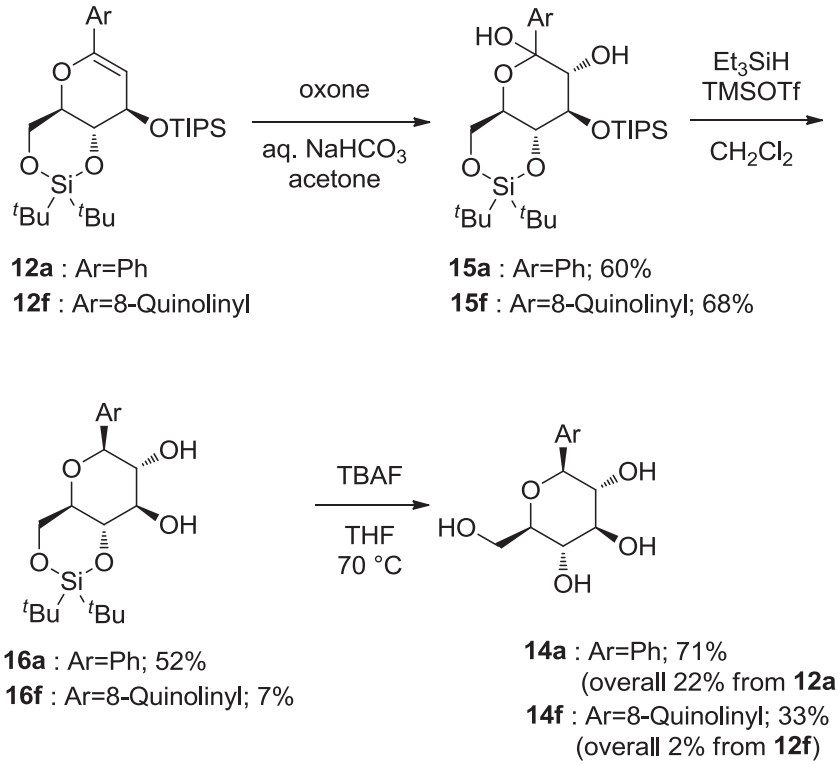
To a solution of compound **4** (640 mg) in THF (10 mL) was added borane–tetrahydrofuran complex (1.0 M in THF, 2.30 mL) dropwise at 0 °C. After being stirred at 0 °C for overnight, to the mixture were added 30% aqueous hydrogen peroxide (5 mL) and 3 N aqueous sodium hydroxide (5 mL), and stirred at 0 °C for 4 h. The reaction mixture was extracted with Et_2O, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography (0–5% AcOEt in hexane) to give compound **6**

Table 2
Stereoselective synthesis of aryl-β-*C*-glucosides **14**

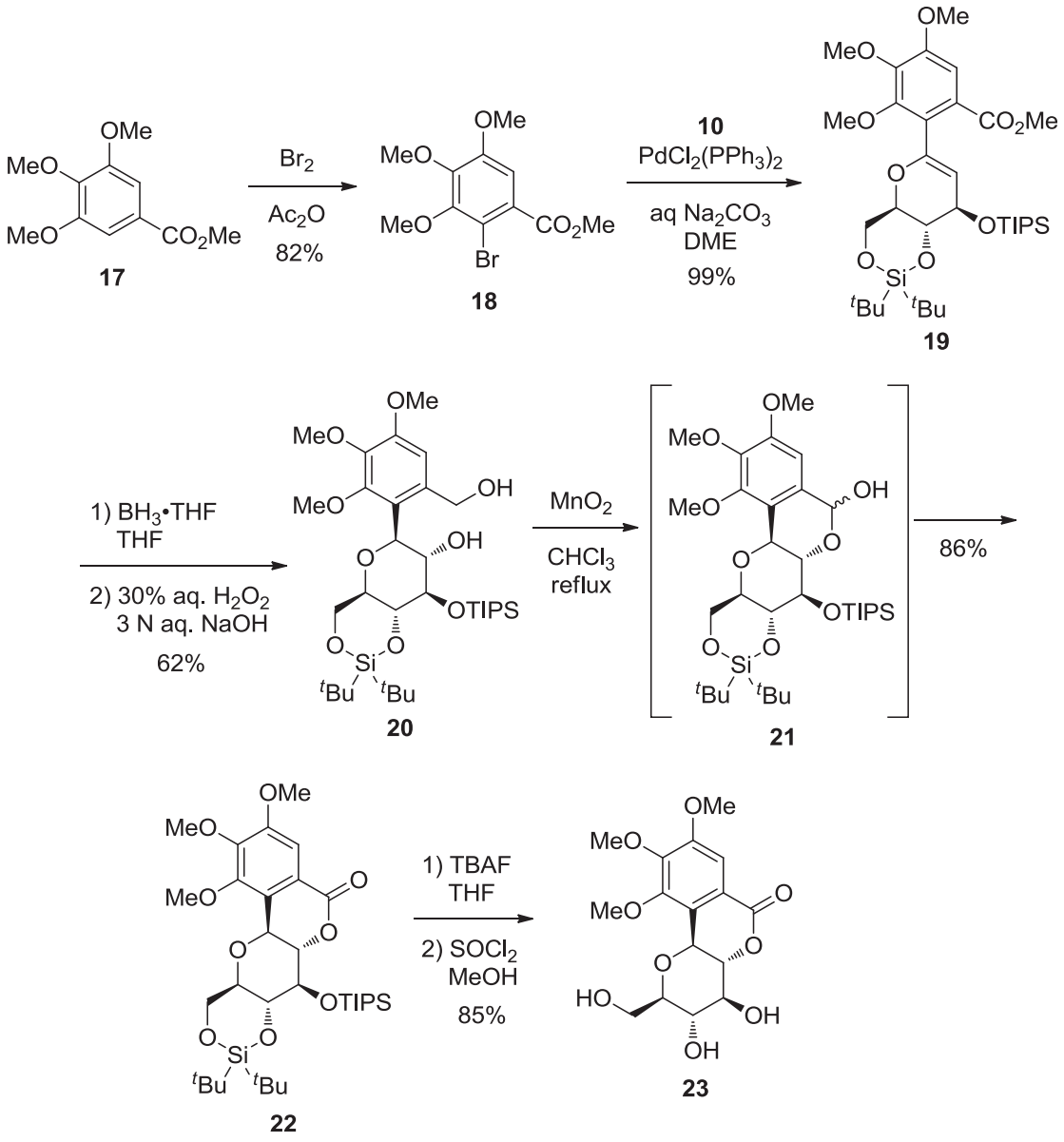


Entry	Material	Ar	Product	Yield[a] (%)	Product	Yield[a] (%)
1	**12a**		**13a**	58	**14a**	43[b]
2	**12b**		**13b**	60	**14b**	52
3	**12c**		**13c**	52	**14c**	83
4	**12d**		**13d**	41	**14d**	90
5	**12e**		**13e**	49	**14e**	37

[a] Isolated yield.
[b] Overall 25% yield from **12a**.



Scheme 4. Alternative synthesis of β-*C*-glucosides **14a** and **14f** from aryl-glucals **12a** and **12f** using oxone.



Scheme 5. Synthesis of tri-*O*-methylnorbergenin.

(167 mg, 25%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.36 (m, 5H), 5.01 (td, J=2.4, 9.8 Hz, 1H), 4.40 (td, J=3.6, 6.6 Hz, 1H), 4.15 (t, J=3.9 Hz, 1H), 4.01 (dtd, J=2.1, 4.5, 6.5 Hz, 1H), 3.84–3.86 (m, 2H), 3.23 (d, J=1.9 Hz, 1H), 2.66 (d, J=2.5 Hz, 1H), 2.29 (ddd, J=3.0, 6.9, 14.3 Hz, 1H), 1.94 (ddd, J=6.3, 10.0, 14.2 Hz, 1H), 1.01–1.18 (m, 63H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 128.4, 127.3, 125.7, 74.8, 74.1, 73.8, 72.4, 65.7, 42.5, 18.2, 18.2, 18.0, 12.9, 12.9, 12.0. MS (APCI, m/z) 711.5 $[M+H]^+$. IR (KBr, cm^{-1}) 3419, 2944, 2892, 1463. HRMS (ESI, m/z) calcd for $C_{10}H_{14}NaO_5S$ $[M+H]^+$ 711.5235, found 711.5259. $[\alpha]_D^{25}$ +13.3 (c 0.15, $CHCl_3$).

4.5. Typical experimental procedure for the synthesis of 1-arylglucal derivative

To a mixture of boronic acid ester **10** (2.5 mmol) and aryl bromide (1 mmol) in DME (20 mL) were added dichlorobis(-triphenylphosphine)palladium (0.05 mmol) and 2 M aqueous Na_2CO_3 (5 mL), then the mixture was refluxed for 4 h. The mixture was cooled to ambient temperature and diluted with AcOEt, then washed with water, brine, dried over sodium sulfate, and filtered. After the filtrate was concentrated, the crude material was purified by silica gel column chromatography to give compounds **12a**–**12f**.

*4.5.1. (1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)benzene (**12a**).* Following the general method described above, the title compound **12a** was isolated in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.52 (m, 2H), 7.28–7.36 (m, 3H), 5.23 (d, J=2.5 Hz, 1H), 4.59 (dd, J=2.5 Hz, 1H), 4.32 (dd, J=5.0, 10.2 Hz, 1H), 4.10 (J=7.5, 10.5 Hz, 1H), 4.00 (dd, J=5.0, 10.2 Hz, 1H), 1.08 (s, 9H), 1.01 (s, 9H), 0.95–1.20 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 134.2, 128.6, 128.2, 125.1, 101.3, 77.5, 73.0, 71.8, 66.2, 27.5, 27.0, 22.8, 19.9, 18.2, 18.2, 12.5. MS (APCI, m/z) 519 $[M+H]^+$. IR (Nujol, cm^{-1}) 2925, 2859, 1652, 1463, 1110. Mp 91–94 °C. HRMS (ESI, m/z) calcd for $C_{29}H_{51}O_4Si_2$ $[M+H]^+$ 519.3326, found 519.3290. $[\alpha]_D^{25}$ −26.0 (c 0.2, $CHCl_3$).

*4.5.2. (1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)-4-methoxybenzene (**12b**).* Following the general method described above, the title

compound **12b** was isolated in 99% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J=9.0 Hz, 2H), 6.84 (d, J=9.0 Hz, 2H), 5.11 (d, J=2.4 Hz, 1H), 4.57 (dd, J=2.4, 6.8 Hz, 1H), 4.30 (dd, J=5.0, 10.5 Hz, 1H), 4.10 (m, 1H), 4.08 (m, 1H), 3.98 (dd, J=5.1, 10.5 Hz, 1H), 3.80 (s, 3H), 1.08 (s, 9H), 1.01 (s, 9H), 0.82–1.30 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0, 150.9, 130.5, 126.5, 113.6, 99.7, 77.7, 72.9, 71.9, 66.2, 55.3, 27.5, 27.0, 22.8, 20.0, 18.2, 18.2, 12.5. MS (APCI, m/z) 549 $[M+H]^+$. IR (KBr, cm^{-1}) 2891, 2862, 1653, 1611, 1513, 1252, 1113. HRMS (ESI, m/z) calcd for $C_{30}H_{53}O_5Si_2$ $[M+H]^+$ 549.3432, found 549.3431. $[\alpha]_D^{25}$ −20.0 (c 0.2, $CHCl_3$).

*4.5.3. 3-(1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)benzoic acid tert-butyl ester (**12c**).* Following the general method described above, the title compound **12c** was isolated in 99% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (t, J=1.4 Hz, 1H), 7.92 (td, J=1.5, 7.8 Hz, 1H), 7.66 (td, J=1.2, 7.8 Hz, 1H), 7.37 (t, J=7.8 Hz, 1H), 5.29 (d, J=2.4 Hz, 1H), 4.60 (dd, J=2.4, 6.6 Hz, 1H), 4.33 (dd, J=4.6, 10.8 Hz, 1H), 4.12 (d, J=10.2 Hz, 1H), 4.09 (dd, J=3.1, 10.2 Hz, 1H), 4.02 (dd, J=4.6, 10.5 Hz, 1H), 1.59 (s, 9H), 1.13–1.18 (m, 21H), 1.09 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 150.3, 134.3, 132.1, 129.5, 128.9, 128.1, 126.2, 101.9, 81.1, 77.5, 73.1, 71.7, 66.1, 28.2, 27.5, 27.0, 22.8, 19.9, 18.3, 18.2, 12.5. MS (APCI, m/z) 619 $[M+H]^+$. HRMS (ESI, m/z) calcd for $C_{34}H_{59}O_6Si_2$ $[M+H]^+$ 619.3850, found 619.3860. $[\alpha]_D^{25}$ −24.0 (c 0.2, $CHCl_3$).

*4.5.4. 4-(1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)benzoic acid tert-butyl ester (**12d**).* Following the general method described above, the title compound **12d** was isolated in 99% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J=8.6 Hz, 2H), 7.54 (d, J=8.8 Hz, 2H), 5.33 (d, J=2.4 Hz, 1H), 4.60 (dd, J=2.5, 6.7 Hz, 1H), 4.32 (dd, J=4.9, 10.2 Hz, 1H), 4.11 (dd, J=6.8, 10.3 Hz, 1H), 4.11 (app t, J=10.3 Hz, 1H), 4.01 (dd, J=4.2, 10.0 Hz, 1H), 1.59 (s, 9H), 1.12–1.15 (m, 21H), 1.09 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 150.3, 137.9, 131.9, 129.4, 124.7, 103.1, 81.1, 77.4, 73.1, 71.7, 66.1, 28.2, 27.5, 27.0, 22.8, 19.9, 18.2, 18.2, 12.5. MS (APCI, m/z) 619 $[M+H]^+$. Anal. Calcd for $C_{34}H_{58}O_6Si_2$: C, 65.97; H, 9.44. Found: C, 65.71; H, 9.62. $[\alpha]_D^{25}$ −11.0 (c 0.2, $CHCl_3$).

*4.5.5. 3-(1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)thiophene (**12e**).* Following the general method described above, the title compound **12e** was isolated in 99% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (dd, J=1.0, 3.1 Hz, 1H), 7.23–7.30 (m, 1H), 7.14 (dd, J=1.2, 5.2 Hz, 1H), 5.12 (d, J=2.2 Hz, 1H), 4.56 (dd, J=2.4, 6.8 Hz, 1H), 4.30 (dd, J=4.9, 10.5 Hz, 1H), 4.05–4.11 (m, 2H), 3.94–4.00 (m, 1H), 1.12–1.16 (m, 21H), 1.08 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.8, 136.3, 125.7, 124.8, 121.8, 101.1, 77.5, 72.9, 71.6, 66.1, 27.5, 27.0, 22.8, 19.9, 18.2, 17.7, 12.5. MS (APCI, m/z) 525 $[M+H]^+$. IR (neat, cm^{-1}) 2941, 2891, 2863, 1657, 1470. Anal. Calcd for $C_{27}H_{48}O_4SSi_2$: C, 61.78; H, 9.22. Found: C, 62.06; H, 9.52.

*4.5.6. 8-(1,5-Anhydro-2-deoxy-4,6-O-di-(tert-butyl)silanediyl-3-O-triisopropylsilyl-D-arabino-hex-1-enitolyl)quinoline (**12f**).* Following the general method described above, the title compound **12f** was isolated in 99% yield as a colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (dd, J=2.0, 4.1 Hz, 1H), 8.14 (dd, J=8.2, 1.8 Hz, 1H), 7.91 (dd, J=7.3, 1.5 Hz, 1H), 7.76 (dd, J=1.5, 8.2 Hz, 1H), 7.51 (dd, J=7.3, 8.2 Hz, 1H), 7.40 (dd, J=4.2, 8.2 Hz, 1H), 6.11 (d, J=2.4 Hz, 1H), 4.76 (dd, J=2.3, 6.8 Hz, 1H), 4.32 (dd, J=4.4, 9.6 Hz, 1H), 4.26 (dd, J=6.9, 10.2 Hz, 1H), 4.20 (td, J=10.0, 4.3 Hz, 1H), 4.11 (app t, J=9.7 Hz, 1H), 1.14–1.26 (m, 21H), 1.10 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 148.9, 145.8, 136.3, 132.9, 128.9, 128.7, 128.5, 125.9, 120.9, 108.8, 77.7, 73.1, 72.1, 66.3, 27.5, 27.0, 22.8, 19.9, 18.2, 12.5. Mp 89–92 °C. MS (APCI, m/z) 570 $[M+H]^+$. IR (neat+$CHCl_3$, cm^{-1}) 1470, 1387, 1163, 1127, 1109, 1065. HRMS (ESI, m/z) calcd for $C_{32}H_{51}NNaO_4Si_2$ $[M+Na]^+$ 592.3254, found 592.3255. $[\alpha]_D^{25}$ 0.0 (c 0.2, $CHCl_3$).

4.6. Typical experimental procedure for the synthesis of β-D-glucopyranosyl derivative

To a solution of compound **12a**–**12e** (1 mmol) in THF (5.8 mL) was added borane–tetrahydrofuran complex (1.0 M in THF (2.5 mmol)) dropwise at 0 °C. After being stirred at 0 °C for overnight, to the mixture were added 30% aqueous hydrogen peroxide (3.3 mL) and 3 N aqueous sodium hydroxide (3.3 mL), and stirred at 0 °C for 4 h. The reaction mixture was extracted with Et_2O, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography to give compounds **13a**–**13e**.

*4.6.1. (4aR,6S,7S,8R,8aR)-2,2-Di-tert-butyl-6-phenyl-8-[(triisopropylsilyl)oxy]hexahydropyrano[3,2-d][1,3,2]dioxasilin-7-ol (**13a**).* Following the general method described above, the title compound **13a** was isolated in 58% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31–7.39 (m, 5H), 4.23 (d, J=9.7 Hz, 1H), 4.19 (dd, J=5.1, 10.2 Hz, 1H), 3.91 (t, J=8.3 Hz, 1H), 3.88 (m, 1H), 3.84 (t, J=8.5 Hz, 1H), 3.53–3.58 (m, 1H), 3.50 (t, J=9.0 Hz, 1H), 1.95 (br s, 1H, OH), 1.17–1.29 (m, 3H), 1.10–1.13 (m, 18H), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 128.5, 128.5, 127.4, 82.2, 79.8, 78.2, 76.6, 75.4, 66.7, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. MS (APCI, m/z) 554 $[M+NH_4]^+$. IR (KBr, cm^{-1}) 3472, 2942, 2863, 1471, 1164, 1109. Anal. Calcd for $C_{29}H_{52}O_5Si_2$: C, 64.88; H, 9.76. Found: C, 64.64; H, 9.99. $[\alpha]_D^{25}$ −10.0 (c 0.2, $CHCl_3$).

*4.6.2. (4aR,6S,7S,8R,8aR)-2,2-Di-tert-butyl-6-(4-methoxyphenyl)-8-[(triisopropylsilyl)oxy]hexahydropyrano[3,2-d][1,3,2]dioxasilin-7-ol (**13b**).* Following the general method described above, the title compound **13b** was isolated in 60% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J=8.6 Hz, 2H), 6.89 (d, J=8.8 Hz, 2H), 4.18 (d, J=9.7 Hz, 1H), 4.17 (m, 1H), 3.89 (t, J=10.0 Hz, 1H), 3.85 (m, 1H), 3.83 (t, J=8.5 Hz, 1H), 3.79 (s, 3H), 3.53–3.57 (m, 1H), 3.46–3.51 (m, 1H), 1.94 (d, J=2.7 Hz, 1H, OH), 1.17–1.29 (m, 3H), 1.10–1.13 (m, 18H), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8, 130.6, 128.6, 114.0, 81.9, 79.8, 78.2, 76.6, 75.3, 66.7, 55.3, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. IR (Nujol, cm^{-1}) 3601, 1613, 1514, 1463. MS (APCI, m/z) 584 $[M+NH_4]^+$. Anal. Calcd for $C_{30}H_{54}O_6Si_2$: C, 63.56; H, 9.60. Found: C, 63.73; H, 9.75. $[\alpha]_D^{25}$ −5.0 (c 0.2, $CHCl_3$).

*4.6.3. tert-Butyl 3-{(4aR,6S,7S,8R,8aR)-2,2-di-tert-butyl-7-hydroxy-8-[(triisopropylsilyl)oxy]-hexahydropyrano[3,2-d][1,3,2]dioxasilin-6-yl}benzoate (**13c**).* Following the general method described above, the title compound **13c** was isolated in 52% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (t, J=1.7 Hz, 1H), 7.94 (td, J=1.5, 7.7 Hz, 1H), 7.54 (td, J=1.5, 7.7 Hz, 1H), 7.41 (t, J=7.7 Hz, 1H), 4.30 (d, J=9.5 Hz, 1H), 4.18 (dd, J=4.9, 10.3 Hz, 1H), 3.92 (t, J=10.2 Hz, 1H), 3.87–3.89 (m, 1H), 3.85 (t, J=8.3 Hz, 1H), 3.48–3.61 (m, 2H), 2.03 (d, J=2.9 Hz, 1H, OH), 1.59 (s, 9H), 1.17–1.31 (m, 3H), 1.13 (d, J=4.8 Hz, 12H), 1.11 (d, J=4.8 Hz, 6H), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 138.9, 132.4, 131.5, 129.5, 128.3, 128.3, 81.7, 81.1, 79.9, 78.1, 76.6, 75.4, 66.6, 28.2, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. IR (KBr, cm^{-1}) 3499, 1718, 1589, 1463. MS (APCI, m/z) 654 $[M+H]^+$. Anal. Calcd for $C_{34}H_{60}O_7Si_2$: C, 64.11; H, 9.49. Found: C, 64.03; H, 9.65. $[\alpha]_D^{25}$ −50.0 (c 0.2, $CHCl_3$).

*4.6.4. tert-Butyl 4-{(4aR,6S,7S,8R,8aR)-2,2-di-tert-butyl-7-hydroxy-8-[(triisopropylsilyl)oxy]-hexahydropyrano[3,2-d][1,3,2]dioxasilin-6-yl}benzoate (**13d**).* Following the general method described above, the title compound **13d** was isolated in 41% yield as

a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (td, J=8.4, 1.8 Hz, 2H), 7.43 (td, J=1.6, 8.3 Hz, 2H), 4.30 (d, J=9.3 Hz, 1H), 4.19 (dd, J=4.9, 10.3 Hz, 1H), 3.81–3.96 (m, 3H), 3.56 (ddd, J=4.9, 9.0, 10.1 Hz, 1H), 3.43 (ddd, J=2.8, 8.2, 9.6 Hz, 1H), 2.02 (d, J=3.1 Hz, 1H, OH), 1.58 (s, 9H), 1.16–1.28 (m, 3H), 1.12 (d, J=4.9 Hz, 12H), 1.10 (d, J=5.1 Hz, 6H), 1.08 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 143.2, 132.1, 129.5, 127.1, 81.6, 81.0, 79.9, 78.1, 76.7, 75.3, 66.6, 28.2, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. MS (APCI, m/z) 654 $[M+H]^+$. IR (KBr, cm^{-1}) 3500, 1716, 1613, 1472. Anal. Calcd for $C_{34}H_{60}O_7Si_2$: C, 64.11; H, 9.49. Found: C, 63.89; H, 9.76. $[\alpha]_D^{25}$ −70.0 (c 0.2, $CHCl_3$).

*4.6.5. (4aR,6S,7S,8R,8aR)-2,2-Di-tert-butyl-6-(3-thienyl)-8-[(triisopropylsilyl)oxy]hexahydropyrano[3,2-d][1,3,2]dioxasilin-7-ol (**13e**).* Following the general method described above, the title compound **13e** was isolated in 49% yield as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32–7.35 (m, 2H), 7.13 (dd, J=2.5, 3.7 Hz, 1H), 4.37 (d, J=9.8 Hz, 1H), 4.19 (dd, J=5.0, 10.0 Hz, 1H), 3.80–3.91 (m, 3H), 3.48–3.56 (m, 2H), 2.04 (d, J=2.9 Hz, 1H, OH), 1.11–1.14 (m, 21H), 1.07 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8, 126.2, 123.2, 79.8, 78.2, 78.1, 76.3, 75.3, 66.6, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. MS (APCI, m/z) 560 $[M+NH_4]^+$. IR (neat+$CHCl_3$, cm^{-1}) 3606, 2943, 2864, 1471, 1163, 1109. HRMS (ESI, m/z) calcd for $C_{27}H_{51}O_5SSi_2$ $[M+H]^+$ 543.2996, found 543.2989.

4.7. Typical experimental procedure for the synthesis of 1-aryl-β-D-glucopyranose

To a solution of compound **13a**–**13e** (1 mmol) in THF (7.5 mL) was added tetra-*n*-butylammonium fluoride (TBAF) (1.0 M in THF, 5 mmol) dropwise, then the mixture was stirred at 60 °C for 4 h. The mixture was concentrated and dried, then the crude material was purified by silica gel column chromatography to give compounds **14a**–**14e**.

*4.7.1. (1S)-1,5-Anhydro-1-phenyl-D-glucitol (**14a**).* Following the general method described above, the title compound **14a** was isolated in 43% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.23–7.38 (m, 5H), 4.95 (d, J=3.2 Hz, 1H), 4.94 (d, J=3.5 Hz, 1H), 4.78 (d, J=5.8 Hz, 1H), 4.45 (t, J=5.9 Hz, 1H), 4.01 (d, J=9.5 Hz, 1H), 3.67–3.73 (m, 1H), 3.42–3.47 (m, 1H), 3.21–3.30 (m, 3H), 3.14–3.19 (m, 2H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 140.3, 127.7, 127.5, 127.2, 81.3, 81.1, 78.4, 74.6, 70.3, 61.4. MS (APCI, m/z) 258 $[M+NH_4]^+$. IR (neat+$CHCl_3$, cm^{-1}) 3361, 2918, 1637, 1455, 1082, 1026. HRMS (ESI, m/z) calcd for $C_{12}H_{16}NaO_5$ $[M+Na]^+$ 263.0895, found 263.0896. $[\alpha]_D^{25}$ +30.0 (c 0.2, MeOH) (lit.[26] $[\alpha]_D$=+30.3 (c 1.9, MeOH)).

*4.7.2. (1S)-1,5-Anhydro-1-(4-methoxyphenyl)-D-glucitol (**14b**).* Following the general method described above, the title compound **14b** was isolated in 52% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.25 (d, J=8.7 Hz, 2H), 6.86 (d, J=8.7 Hz, 2H), 4.92 (d, J=4.5 Hz, 1H), 4.91 (d, J=5.0 Hz, 1H), 4.71 (d, J=5.6 Hz, 1H), 4.43 (t, J=5.8 Hz, 1H), 3.95 (d, J=9.5 Hz, 1H), 3.73 (s, 3H), 3.67–3.72 (m, 1H), 3.40–3.46 (m, 1H), 3.10–3.30 (m, 4H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 158.5, 132.4, 128.8, 112.9, 81.0, 80.9, 78.4, 74.6, 70.4, 61.4, 54.9. MS (APCI, m/z) 288 $[M+NH_4]^+$. IR (KBr, cm^{-1}) 3403, 3238, 2924, 2854, 1509, 1459, 1105. HRMS (ESI, m/z) calcd for $C_{13}H_{18}NaO_6$ $[M+Na]^+$ 293.1001, found 293.1006. $[\alpha]_D^{25}$ +27.0 (c 0.2, MeOH).

*4.7.3. (1S)-1,5-Anhydro-1-(3-tert-butoxycarbonylphenyl)-D-glucitol (**14c**).* Following the general method described above, the title compound **14c** was isolated in 83% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.87 (t, J=1.6 Hz, 1H), 7.81 (td, J=1.5, 7.8 Hz, 1H), 7.59 (td, J=1.3, 7.6 Hz, 1H), 7.44 (t, J=7.7 Hz, 1H), 4.93 (d, J=5.1 Hz, 2H), 4.83 (d, J=5.6 Hz, 1H), 4.44 (t, J=5.7 Hz, 1H), 4.10 (d, J=9.5 Hz, 1H), 3.72 (ddd, J=1.8, 5.5, 13.7 Hz, 1H), 3.47 (quint, J=5.9 Hz, 1H), 3.12–3.33 (m, 4H), 1.55 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 165.0, 140.8, 132.2, 130.7, 128.3, 128.0, 127.8, 81.2, 80.9, 80.5, 78.2, 74.7, 70.3, 61.3, 27.7. MS (APCI, m/z) 358 $[M+NH_4]^+$. IR (Nujol, cm^{-1}) 3352, 2920, 2852, 1711, 1458. HRMS (ESI, m/z) calcd for $C_{17}H_{24}NaO_7$ $[M+Na]^+$ 363.1420, found 363.1413. $[\alpha]_D^{25}$ +227.72 (c 0.2, $CHCl_3$).

*4.7.4. (1S)-1,5-Anhydro-1-(4-tert-butoxycarbonylphenyl)-D-glucitol (**14d**).* Following the general method described above, the title compound **14d** was isolated in 90% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.84 (d, J=8.3 Hz, 2H), 7.46 (d, J=8.3 Hz, 2H), 4.93–4.95 (m, 2H), 4.83 (d, J=5.9 Hz, 1H), 4.44 (t, J=5.7 Hz, 1H), 4.10 (d, J=9.3 Hz, 1H), 3.72 (ddd, J=1.8, 5.4, 11.8 Hz, 1H), 3.48 (quint, J=5.9 Hz, 1H), 3.14–3.33 (m, 3H), 3.10 (td, J=5.9 Hz, 9.0 Hz, 1H), 1.54 (s, 9H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 164.9, 145.3, 130.3, 128.3, 127.6, 81.1, 80.8, 80.4, 78.2, 75.0, 70.2, 61.3, 27.7. MS (APCI, m/z) 358 $[M+NH_4]^+$. IR (Nujol, cm^{-1}) 3453, 2977, 2920, 2874, 1701, 1612. Anal. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11. Found: C, 59.74; H, 7.33. $[\alpha]_D^{25}$ +21.78 (c 0.2, MeOH).

*4.7.5. (1S)-1,5-Anhydro-1-(3-thienyl)-D-glucitol (**14e**).* Following the general method described above, the title compound **14e** was isolated in 37% yield as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.40–7.43 (m, 2H), 7.12 (dd, J=1.5, 4.9 Hz, 1H), 4.91 (d, J=3.9 Hz, 1H), 4.88 (d, J=5.2 Hz, 1H), 4.83 (d, J=5.7 Hz, 1H), 4.41 (t, J=6.0 Hz, 1H), 4.12 (d, J=9.0 Hz, 1H), 3.69 (ddd, J=2.0, 5.6, 11.7 Hz, 1H), 3.43 (quint, J=6.0 Hz, 1H), 3.13–3.26 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 141.5, 127.3, 124.8, 122.6, 81.0, 78.4, 77.3, 74.3, 70.3, 61.3. MS (APCI, m/z) 264 $[M+NH_4]^+$. IR (neat+$CHCl_3$, cm^{-1}) 3374, 2925, 1731, 1635, 1425, 1241, 1083. HRMS (ESI, m/z) calcd for $C_{10}H_{14}NaO_5S$ $[M+Na]^+$ 269.0460, found 269.0461.

4.8. (4a*R*,7*R*,8*R*,8a*R*)-2,2-Di-*tert*-butyl-6-phenyl-8-[(triisopropylsilyl)oxy]hexahydropyrano[3,2-*d*][1,3,2]dioxasiline-6,7-diol (15a)

To a solution of compound **12a** (129 mg) in acetone (10 mL) was added $NaHCO_3$ (210 mg) at 0 °C, then oxone (461 mg) in water (5 mL) was added and stirred at room temperature for 4 h. The mixture was filtered and the filtrate was concentrated, then extracted with AcOEt, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography (2–10% AcOEt in hexane) to give **15a** (75 mg, 60%) as a colorless amorphous gum and anomeric diastereomixture (approximately 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, major diastereomer) δ 7.56–7.58 (m, 2H), 7.34–7.40 (m, 3H), 4.14 (m, 2H), 4.05 (m, 1H), 3.99 (m, 1H), 3.88 (m, 1H), 3.50 (ddd, J=1.2, 5.6, 8.6 Hz, 1H), 3.01 (d, J=1.1 Hz, 1H), 2.13 (d, J=5.5 Hz, 1H), 1.18–1.26 (m, 3H), 1.09–1.13 (m, 18H), 1.09 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, major diastereomer) δ 141.8, 129.1, 128.8, 128.3, 125.8, 98.3, 78.3, 77.9, 76.8, 67.9, 66.9, 27.6, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. MS (ESI, m/z) 575 (M+Na). IR (Nujol, cm^{-1}) 3435, 1463, 1377. HRMS (ESI) calcd for $C_{29}H_{53}O_6Si_2$ $[M+H]^+$ 553.3381, found 553.3367.

4.9. (4a*R*,6*S*,7*R*,8*R*,8a*S*)-2,2-Di-*tert*-butyl-6-phenylhexahydropyrano[3,2-*d*][1,3,2]dioxasiline-7,8-diol (16a)

To a solution of compound **15a** (50 mg) in methylene chloride (5 mL) were added triethylsilane (0.06 mL) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.06 mL) at −78 °C. After being stirred at −78 °C for 1 h and room temperature for 1.5 h, the mixture was quenched by saturated aqueous $NaHCO_3$ and extracted with

$CHCl_3$, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography (10–20% AcOEt in hexane) to give compound **16a** (18 mg, 52%) as a colorless amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33–7.39 (m, 5H), 4.26 (d, J=9.4 Hz, 1H), 4.21 (dd, J=5.2, 10.2 Hz, 1H), 3.91 (t, J=10.2 Hz, 1H), 3.82 (t, J=9.1 Hz, 1H), 3.70 (t, J=8.7 Hz, 1H), 3.62 (t, J=9.1 Hz, 1H), 3.57–3.61 (m, 1H), 2.81 (d, J=1.5 Hz, 1H), 2.10 (d, J=2.7 Hz, 1H), 1.09 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.0, 128.7, 128.6, 127.5, 82.2, 78.2, 77.2, 74.8, 74.8, 66.5, 27.5, 27.0, 22.7, 20.0. MS (APCI, m/z) 398 (M+NH_4). IR (KBr, cm^{-1}) 3460, 1474, 1388. HRMS (ESI) calcd for $C_{20}H_{33}O_5Si$ $[M+H]^+$ 381.2097, found 381.2092.

4.10. (4a*R*,7*R*,8*R*,8a*R*)-2,2-Di-*tert*-butyl-6-quinolin-8-yl-8-[(triisopropylsilyl)oxy]hexahydropyrano[3,2-*d*][1,3,2]dioxasiline-6,7-diol (15f)

To a solution of compound **12f** (300 mg) in acetone (20 mL) was added $NaHCO_3$ (442 mg) at 0 °C, then oxone (970 mg) in water (10 mL) was added and stirred at room temperature for 4 h. The mixture was filtered and the filtrate was concentrated, then extracted with AcOEt, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography (5–20% AcOEt in hexane) to give compound **15f** (215 mg, 68%) as a colorless amorphous powder and anomeric diastereomixture (approximately 10:1). ^{1}H NMR (400 MHz, $CDCl_3$, major diastereomer) δ 11.60 (s, 1H), 8.79 (dd, J=1.8, 4.3 Hz, 1H), 8.24 (dd, J=1.8, 8.4 Hz, 1H), 7.92 (dd, J=1.4, 7.4 Hz, 1H), 7.82 (dd, J=1.1, 8.8 Hz, 1H), 7.61 (t, J=7.7 Hz, 1H), 7.45 (dd, J=4.3, 8.4 Hz, 1H), 4.30 (td, J=5.0, 10.0 Hz, 1H), 4.19 (t, J=8.5 Hz, 1H), 4.13 (dd, J=5.0, 9.9 Hz, 1H), 3.86–3.93 (m, 3H), 2.31 (s, 1H), 1.18–1.31 (m, 3H), 1.04–1.16 (m, 18H), 1.09 (s, 9H), 1.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$, major diastereomer) δ 147.3, 146.7, 137.9, 134.7, 129.1, 128.7, 128.7, 127.0, 120.7, 101.6, 78.7, 78.2, 77.1, 67.4, 67.3, 27.6, 27.1, 22.8, 20.0, 18.5, 18.5, 13.0. MS (ESI, m/z) 604 $[M+H]^+$. IR (KBr, cm^{-1}) 3450, 1471, 1166, 1072. HRMS (ESI) calcd for $C_{32}H_{54}NO_6Si_2$ $[M+H]^+$ 604.3490, found 604.3473.

4.11. (4a*R*,6*S*,7*R*,8*R*,8a*S*)-2,2-Di-*tert*-butyl-6-quinolin-8-yl-hexahydropyrano[3,2-*d*][1,3,2]dioxasiline-7,8-diol (16f)

To a solution of compound **15f** (214 mg) in methylene chloride (10 mL) were added triethylsilane (0.28 mL) and trimethylsilyl trifluoromethanesulfonate (TMSOTf) (0.32 mL) at −78 °C. After being stirred at −78 °C for 1 h and room temperature for 1.5 h, the mixture was quenched by saturated aqueous $NaHCO_3$ and extracted with $CHCl_3$, washed with brine, dried over sodium sulfate, and filtered. The filtrate was concentrated and dried, then the crude material was purified by silica gel column chromatography (5–10% AcOEt in hexane) to give compound **16f** (14 mg, 7%) as a colorless amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (dd, J=1.9, 4.4 Hz, 1H), 8.26 (dd, J=1.8, 8.4 Hz, 1H), 7.93 (dt, J=1.2, 7.3 Hz, 1H), 7.77 (d, J=8.0 Hz, 1H), 7.59 (t, J=7.7 Hz, 1H), 5.55 (d, J=8.5 Hz, 1H), 4.94 (t, J=7.4 Hz, 1H), 4.31 (m, 1H), 4.15 (dd, J=6.7, 8.4 Hz, 1H), 4.02–4.06 (m, 2H), 3.84–3.89 (m, 1H), 2.23 (s, 1H), 1.08 (s, 9H), 1.01 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.8, 145.2, 138.7, 137.7, 128.6, 127.1, 127.1, 125.8, 121.2, 82.5, 81.6, 80.3, 74.8, 73.9, 64.8, 27.2, 27.2, 21.4, 21.3. MS (APCI, m/z) 432 (M+H). IR (KBr, cm^{-1}) 3448, 1470, 1162, 1086. HRMS (ESI) calcd for $C_{23}H_{34}NO_5Si$ $[M+H]^+$ 432.2206, found 432.2215. $[\alpha]_D^{25}$ +132.86 (c 0.7, $CHCl_3$).

4.12. (1*S*)-1,5-Anhydro-1-(quinolin-8-yl)-D-glucitol (14f)

To a solution of compound **16f** (14 mg) in THF (1 mL) was added TBAF (1.0 M in THF, 0.5 mL) dropwise, then the mixture was stirred at 60 °C for 4 h. The mixture was concentrated and dried, then the crude material was purified by silica gel column chromatography (10% MeOH in AcOEt) to give **14f** (3 mg, 33%) as a colorless amorphous powder. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.85 (dd, J=1.8, 4.3 Hz, 1H), 8.38 (dd, J=1.7, 8.3 Hz, 1H), 7.89 (dd, J=1.2, 8.1 Hz, 1H), 7.59 (dd, J=6.6, 7.4 Hz, 1H), 7.55 (t, J=3.7, 7.8 Hz, 1H), 5.31 (d, J=3.8 Hz, 1H), 4.29 (t, J=2.8 Hz, 1H), 4.14 (ddd, J=3.3, 6.0, 9.1 Hz, 1H), 4.07 (dd, J=3.3, 8.3 Hz, 1H), 3.87 (dd, 3.3, 11.6 Hz, 1H), 3.71 (dd, J=5.8, 11.6 Hz, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ 150.1, 146.2, 138.9, 138.3, 130.0, 129.3, 127.7, 122.4, 97.3, 88.7, 85.0, 82.8, 79.7, 71.2, 65.6. MS (APCI, m/z) 292 (M+H). IR (Nujol, cm^{-1}) 3380, 2924, 1455, 1082, 1026. HRMS (ESI) calcd for $C_{15}H_{17}NNaO_5$ $[M+Na]^+$ 314.1004, found 314.1030.

4.13. Methyl 2-bromo-3,4,5-trimethoxybenzoate (18)[27]

To a solution of methyl 3,4,5-trimethoxybenzoate **17** (4.5 g) in acetic anhydride (25 mL) was added bromine (3.2 g) in acetic anhydride (15 mL) dropwise at 0 °C, and the mixture was stirred at 0 °C for 4 h and room temperature for 1 h. After acetic anhydride was concentrated, the crude material was purified by silica gel column chromatography (10–20% AcOEt in hexane) to give compound **18** (4.95 g, 82%) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (s, 1H), 3.93 (s, 3H), 3.92 (s, 3H), 3.89 (s, 3H), 3.89 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 152.4, 151.6, 146.1, 127.6, 110.2, 109.6, 61.2, 61.0, 56.3, 52.5. MS (APCI, m/z) 305/307 $[M+H]^+$. IR (neat, cm^{-1}) 1734, 1484, 1386, 1339. Anal. Calcd for $C_{11}H_{13}BrO_5$: C, 43.30; H, 4.29. Found: C, 43.32; H, 4.40.

4.14. Methyl 2-{(4a*R*,8*R*,8a*R*)-2,2-di-*tert*-butyl-8-[(triisopropylsilyl)oxy]-4,4a,8,8a-tetrahydropyrano[3,2-*d*][1,3,2]dioxasilin-6-yl}-3,4,5-trimethoxybenzoate (19)

To a mixture of boronic acid ester **10** (1.42 g) and bromide **18** (305 mg) in DME (10 mL) were added dichlorobis(-triphenylphosphine)palladium (35 mg) and 2 M aqueous Na_2CO_3 (2.5 mL), then the mixture was refluxed for 3 h. The mixture was cooled to ambient temperature and diluted with AcOEt, then washed with water, brine, dried over sodium sulfate, and filtered. After the filtrate was concentrated, the crude material was purified by silica gel column chromatography (5–10% AcOEt in hexane) to give compound **19** (722 mg, 99%) as a colorless amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (s, 1H), 4.80 (d, J=2.2 Hz, 1H), 4.56 (dd, J=2.3, 6.7 Hz, 1H), 4.17 (m, 1H), 4.09 (m, 1H), 3.99–4.04 (m, 2H), 3.90 (s, 3H), 3.88 (s, 3H), 3.86 (s, 3H), 3.85 (s, 3H), 1.08 (s, 9H), 1.02 (s, 9H), 1.07–1.12 (m, 21H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 153.6, 152.4, 147.3, 145.2, 127.4, 123.2, 108.8, 106.0, 77.9, 73.4, 71.9, 66.1, 61.7, 60.9, 56.2, 52.2, 27.5, 27.0, 22.8, 19.9, 18.2, 12.5. MS (ESI, m/z) 667 $[M+H]^+$. IR (neat, cm^{-1}) 1721, 1463, 1342, 1109, 1059. HRMS (ESI, m/z) calcd for $C_{34}H_{58}NaO_9Si_2$ $[M+Na]^+$ 689.3517, found 689.3541. $[\alpha]_D^{25}$ −54.0 (c 0.2, $CHCl_3$).

4.15. (6a*S*,7*R*,7a*R*,11a*R*,12a*S*)-9,9-Di-*tert*-butyl-1,2,3-trimethoxy-7-[(triisopropylsilyl)oxy]-6a,7,7a,11,11a,12a-hexahydro-5*H*-[1,3,2]dioxasilino[4′,5′:5,6]pyrano[3,2-*c*]isochromen-5-one (22)

To a solution of compound **19** (870 mg) in THF (15 mL) was added borane–tetrahydrofuran complex (1.0 M in THF, 6.5 mL) dropwise at 0 °C. After being stirred at 0 °C for overnight, the mixture were added 30% aqueous hydrogen peroxide (10 mL) and 3 N aqueous sodium hydroxide (10 mL), and stirred at 0 °C for 4 h. The reaction mixture was neutralized with 10% aqueous citric acid and extracted with Et_2O, washed with brine, dried over sodium sulfate, and filtered. After the filtrate was concentrated, the crude material was purified by silica gel column chromatography (5–20% AcOEt in hexane) to give compound **20** (516 mg, 62%) as a colorless

amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.72 (s, 1H), 4.85 (d, J=12.1 Hz, 1H), 4.37 (dd, J=8.7, 11.1 Hz, 1H), 4.19 (dd, J=5.0, 10.2 Hz, 1H), 3.84–3.94 (m, 13H), 3.76–3.82 (m, 1H), 3.54 (td, J=4.8, 9.6 Hz, 1H), 1.54–1.55 (m, 2H), 1.18–1.32 (m, 3H), 0.99–1.13 (m, 18H), 1.08 (s, 9H), 1.03 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$)[28] δ 154.4, 151.9, 151.7, 135.6, 108.1, 97.4, 79.9, 78.1, 77.2, 75.9, 73.9, 66.4, 61.5, 60.9, 55.9, 27.5, 27.0, 22.8, 20.0, 18.5, 18.4, 13.0. MS (APCI, m/z) 674 $[M+NH_4]^+$. IR (Nujol, cm^{-1}) 3421, 1599, 1467, 1329, 1166. HRMS (ESI) calcd for $C_{33}H_{60}NaO_9Si_2$ $[M+Na]^+$ 679.3674, found 679.3692. $[\alpha]_D^{25}$ +6.0 (c 0.2, $CHCl_3$).

To a solution of compound **20** (300 mg) in chloroform (5 mL) was added manganese dioxide (794 mg), then the mixture was refluxed for 2 days. After being cooled to ambient temperature, the insoluble material was filtered off and the filtrate was concentrated. The crude material was purified by silica gel column chromatography (10–20% AcOEt in hexane) to give lactone **22** (255 mg, 86%) as a colorless amorphous powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (s, 1H), 4.75 (d, J=10.2 Hz, 1H), 4.33 (dd, J=5.0, 9.9 Hz, 1H), 4.10 (m, 1H), 4.03 (m, 1H), 3.96 (m, 1H), 3.93 (s, 3H), 3.90 (s, 3H), 3.87 (dd, J=8.0, 9.6 Hz, 1H), 3.78 (s, 3H), 3.64 (td, J=5.0, 9.9 Hz, 1H), 1.22–1.34 (m, 3H), 1.12–1.16 (m, 18H), 1.06 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.6, 153.6, 151.2, 148.7, 125.9, 119.5, 109.9, 81.1, 78.5, 75.7, 73.0, 66.4, 61.6, 61.1, 56.2, 27.5, 27.0, 22.8, 20.0, 18.4, 12.8. MS (APCI, m/z) 653 $[M+H]^+$. IR (Nujol, cm^{-1}) 1737, 1597, 1469, 1332. HRMS (ESI, m/z) calcd for $C_{33}H_{57}O_9Si_2$ $[M+H]^+$ 653.3541, found 653.3535. $[\alpha]_D^{25}$ −47.0 (c 0.2, $CHCl_3$).

4.16. Tri-*O*-methylnorbergenin (23)

To a solution of lactone **22** (125 mg) in THF (4 mL) was added TBAF (1.5 mL), then the mixture was stirred at 70 °C for 4 h. After the mixture was concentrated, the crude material was dissolved in MeOH (10 mL). To a mixture was added thionyl chloride (1.2 mL) at 0 °C, then the mixture was stirred at room temperature for overnight. After the solvent was concentrated, the crude material was purified by silica gel column chromatography (0–10% MeOH in AcOEt) to give tri-*O*-methylnorbergenin **23** (59 mg, 85%) as a colorless amorphous powder. The analytical data were correspondent with reported data.[25] ^{1}H NMR (400 MHz, MeOH) δ 7.43 (s, 1H), 4.80 (d, J=10.3 Hz, 1H), 3.69–4.03 (m, 13H), 3.43–3.55 (m, 2H). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.33 (s, 1H), 5.58 (d, J=5.4 Hz, 1H, D_2O exchangeable), 5.30 (d, J=5.4 Hz, 1H, D_2O exchangeable), 4.80 (d, J=10.3 Hz, 1H), 4.52 (dd, J=4.8 Hz, 6.0 Hz, 1H, D_2O exchangeable), 3.91 (t, J=10.0 Hz, 1H, D_2O exchangeable), 3.85 (s, 3H), 3.82 (s, 3H), 3.79 (s, 3H), 3.64–3.70 (m, 1H), 3.50–3.57 (m, 2H), 3.24–3.46 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 166.0, 155.1, 152.6, 150.0, 127.9, 120.4, 110.9, 82.7, 81.8, 76.0, 73.2, 71.7, 62.7, 62.3, 61.6, 56.8. MS (APCI, m/z) 374 $[M+NH_4]^+$. IR (KBr, cm^{-1}) 3516, 3425, 1708 (C=O), 1620, 1591, 1463. HRMS (ESI, m/z) calcd for $C_{16}H_{21}O_9$ $[M+H]^+$ 357.1186, found 357.1193. $[\alpha]_D^{25}$ −27.3 (c 0.22, MeOH) (lit.[25] $[\alpha]_D^{23}$ −27.1 (c 1, MeOH)).

Supplementary data

^{1}H NMR and ^{13}C NMR spectra of all new compounds, CIF data of compound **10**. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2012.05.035.

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24. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included at their calculated positions. Crystal data for **10**: $C_{29}H_{57}BO_6Si_2$; M 568.74 g mol^{-1}, triclinic, T=193 K, a=11.8809(17) Å, b=12.8533(17) Å, c=13.8274(19) Å, V=1711.8(4) Å^3, Z=2. CCDC-860013.
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28. We attempted several carbon NMR analysis, including solvent ($CDCl_3$, CD_3OD, DMSO-d_6) and elevated temperature measurement, but in all cases, incomplete peak assignment was observed.