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Assembly of Digitoxin by Gold(I)-Catalyzed Glycosidation of Glycosyl *o*-Alkynylbenzoates

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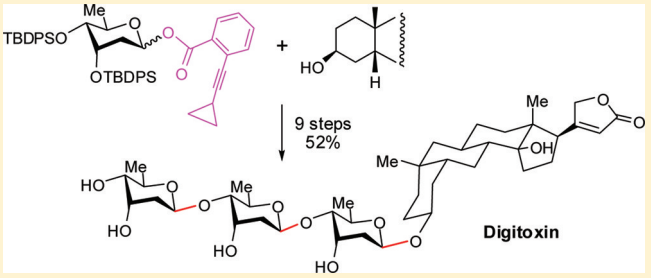
Supporting Information

ABSTRACT: Digitoxin, a clinically important cardiac trisaccharide, was assembled efficiently from digitoxigenin and 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-digitoxosyl *o*-cyclopropylethynylbenzoate in 9 steps and 52% overall yield via alternate glycosylation and protecting group manipulation. The present synthesis showcases the advantage of the gold(I)-catalyzed glycosylation protocol in the synthesis of glycoconjugates containing acid-labile 2-deoxysugar linkages.



INTRODUCTION

Cardiac glycosides constitute a family of the steroid glycosides bearing characteristically a lactone, either a butenolide or a α-pyrone, at C-17 and a mono- or oligosaccharide residue, which consists mostly of deoxysugars, at C-3 of the steroid nucleus.[1] It has been recognized since ancient times that they can enhance the force and velocity of the contraction of the heart, slow the rate of atrioventricular conduction, and cause toxic and lethal effects at high doses. Among cardiac glycosides, digitoxin (**1**, Figure 1) is structurally the prototype, which in homogeneous

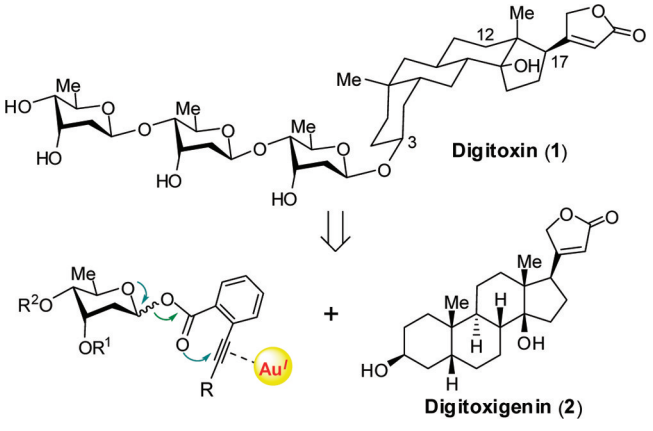


Figure 1. Digitoxin (**1**) and its retrosynthesis with digitoxosyl *o*-alkynylbenzoates as glycosylation donors.

form is a widely prescribed drug for treating congestive heart failure and cardiac arrhythmia.[2] Digitoxin and congeners exert their predominant action through inhibition of the ion transport activity of the enzyme Na/K-ATPase in myocardiac cells.[3] Over the years, the anticancer effect of digitoxin on patients has also attracted attention,[4] and that has trigged current research efforts in this direction.[5] On the structure–activity relationship (SAR) of cardiac glycosides, the steroidal aglycone is the pharmacophore but itself is largely inactive, while the sugar moiety determines the potency of the cardiac glycosides and their pharmacokinetics as well.[1]

Although glycosylation of the digitoxigenin (**2**) to access to the digitoxin analogues with varied sugar moieties have been intensively studied,[6] assembly of the native trisaccharide digoxose onto digitoxigenin has been realized in only three reports.[7−9] Wiesner and co-workers achieved the first synthesis of digitoxin (**1**), employing sequential glycosylation of a furyl precursor of digitoxigenin with 4-*O*-benzyl-3- *O*-(*N*-methylcarbamoyl)-D-digitoxose (*p*-TsOH, benzene, CH_2Cl_2, rt; 47.6%, β/α = 3/1), ethyl 3-*O*-(*p*-methoxybenzoyl)-4-*O*-(*p*-nitrobenzoyl)-1-thio-digitoxoside ($HgCl_2$, $CdCO_3$, CH_2Cl_2, DMF, rt; 60.9%, β/α >25/1), and ethyl 3,4-di-*O*-(*p*-methoxybenzoyl)-1-thio-digitoxoside ($HgCl_2$, $CdCO_3$, CH_2Cl_2, DMF, rt; 57.8%, β only).[7] Of these donors the protecting groups on the 3-OH facilitated formation of the β-glycosidic linkages via 1,3-participation, while those on the 4-OH (of the first two donors) were selectively removable to ensure the next glycosylation. The butenolide residue in digitoxin was finally elaborated from the furyl moiety via oxidation, which was found vulnerable under the alkaline conditions for removal of the *N*-methylcarbamoyl group. McDonald et al. accomplished the synthesis of digitoxin (**1**) via acid-catalyzed coupling of

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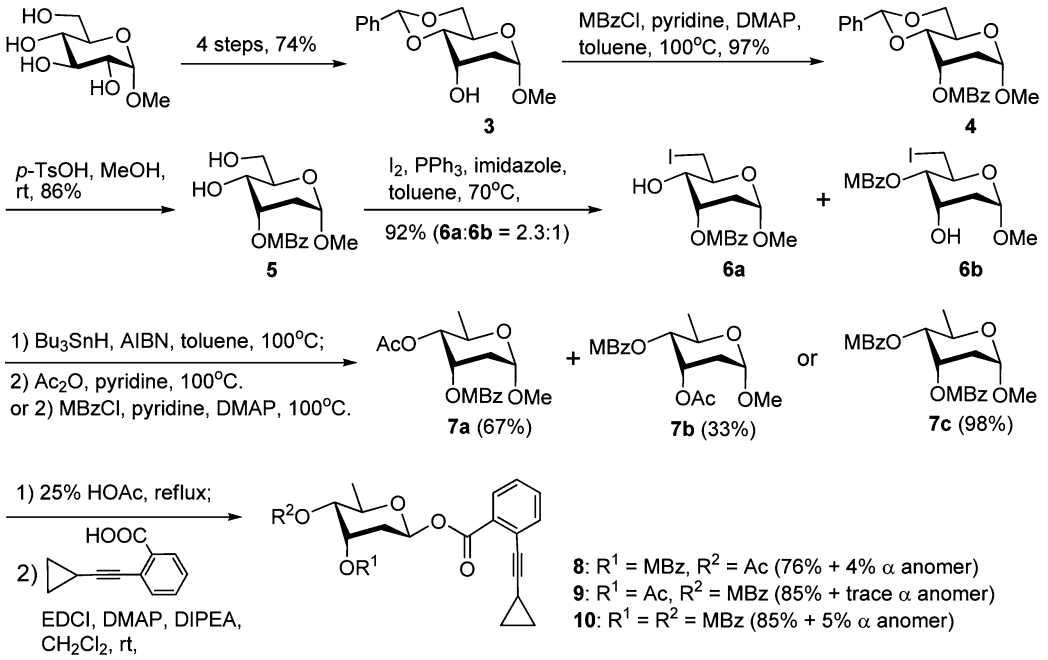
Scheme 1. Preparation of the Digitoxosyl *o*-Cyclopropylethynylbenzoates 8−10



digitoxigenin with a trisaccharide glycal (1 mol % Ph_3PHBr, $CHCl_3$; 82%, β/α = 3/2), which was fabricated by an iterative tungsten-catalyzed endoselective alkynol cyclomerization methodology.[8] More recently, O'Doherty and Zhou developed another de novo approach to the synthesis of digitoxin (**1**), featuring iterative application of palladium-catalyzed glycosylation (with pyranose derivatives), reductive 1,3-transposition, diastereoselective dihydroxylation, and regioselective protection.[9] This recent synthesis requires 15 steps from digitoxigenin (**2**) and a chiral pyranone, which is not only the shortest but also the most stereocontrolled synthesis among the three approaches to the synthesis of digitoxin (**1**).

After the Wiesner synthesis of digitoxin (**1**) in 1985, the scenario of the glycoconjugate synthesis has changed dramatically.[10] Numerous new and powerful glycosylation protocols have been developed.[11] A recent addition is with glycosyl *o*-alkynylbenzoates as donors and Au(I) as catalyst.[12] We envisioned the efficient assembly of digitoxin (**1**) with this new glycosylation method, because the digitoxosyl (2,6-dideoxy-D-*ribo*-hexosyl) *o*-alkynylbenzoates would be stable for convenient handling (in comparison to other types of the favorable donors, such as the corresponding 2,6-dideoxyhexosyl halides, imidates, and phosphites), and their mild and neutral activation conditions would secure the acid-labile β-digitoxosyl linkages staying intact. In fact, glycosylation of the extremely acid-labile substrates, such as the *N*-Boc-protected purine, the dammarane, and the lupane derivatives, has been achieved effectively with this method.[13]

RESULTS AND DISCUSSION

Stereoselective glycosylation with D-digitoxosyl donors (2-deoxy-D-pyranosyl donors in general) to assemble the β-D-digitoxoside linkage could resort to 1,3-participation.[14] Thus, D-digitoxosyl *o*-cyclopropylethynylbenzoates (**8−10**) equipped with a *p*-methoxybenzoyl (MBz) or acetyl group at the 3-OH were desired as the donors and were prepared as shown in Scheme 1.

Through modification of literature approaches, methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (**3**) was readily prepared from methyl α-D-glucopyranoside in four steps with 74% overall yield, i.e., 4,6-*O*-benzylidene protection ($PhCH(OMe)_2$, TsOH, DMF, 40 °C), 2,3-di-*O*-tosyl ester formation (TsCl, CH_2Cl_2, KOH, rt), conversion into 2,3-anhydroallopyranoside (NaOMe, CH_2Cl_2, MeOH, rt),[15] and reduction ($LiAlH_4$, THF, 50 °C).[16,17] The resulting 3-OH in **3** was then protected with MBz group to provide **4** (97%); this axial 3-OH was rather hindered so that forced conditions (MBzCl, pyridine, DMAP, toluene, 100 °C) were required to ensure the completion of the transformation. Compound **4** was subjected to cleavage of the 4,6-*O*-benzylidene group (TsOH, MeOH, rt) to give diol **5** (86%). Treatment of **5** with iodine in the presence of PPh_3 and imidazole (toluene, 70 °C) afforded the desired 6-iodide **6a** in only 64% yield; the major byproduct (in 28% yield) was determined to be the 6-iodo-4-*O*-*p*-methoxybenzoyl derivative **6b**, in that the MBz group migrated from the 3-OH to the 4-OH. Isomers **6a** and **6b** were difficult to separate on silica gel in large scale; in addition, migration of the MBz group also proceeded during the subsequent removal of the 6-iodide under radical conditions. Therefore, the mixture of **6a** and **6b**, without separation, was treated with Bu_3SnH and AIBN (toluene, 100 °C) followed by acetylation to provide **7a** and **7b** in 67% and 33% yield, respectively, which were easily separable on silica gel. Alternatively, after removal of the 6-iodide, MBz protection of the 3- or 4-OH group gave **7c** in 98% yield. Methyl digitoxosides **7a−7c** were subjected to hydrolysis with 25% HOAc to give the corresponding digitoxoses, which were then condensed with *o*-cyclopropylethynylbenzoic acid[18] (EDCI, DMAP, DIPEA, CH_2Cl_2, rt) to afford the desired digitoxosyl *o*-cyclopropylethynylbenzoates **8−10** in good yields, in that the β-anomers were dominant with the α-anomers being isolated in less than 5% yields.

The glycosidic couplings of digitoxigenin **2**[19] with digitoxosyl *o*-cyclopropylethynylbenzoates **8−10** were examined under the action of $Ph_3PAuOTf$ (0.1 equiv) in a mixed solvent of CH_2Cl_2 and toluene at rt, the typical glycosylation conditions for

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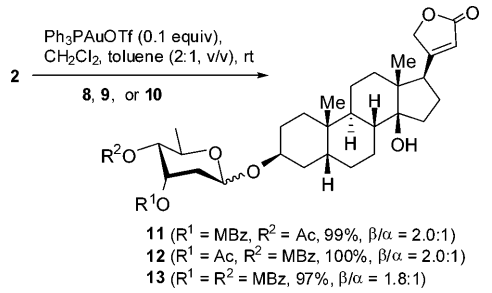
glycosyl *o*-alkynylbenzoates (Scheme 2). The coupled glycosides **11**−**13** were furnished in excellent yields (>97%).

Scheme 2. Glycosylation of Digitoxigenin (2) with Digitoxosyl *o*-Cyclopropylethynylbenzoates 8−10

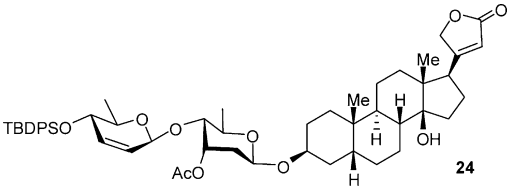


However, the β/α selectivities were only moderate (~2.0:1). Variation of the reaction conditions, e.g., the solvent (dichloromethane, toluene, diethyl ether, 1,2-dichloroethane), temperature (−40 °C to rt), and replacement of $Ph_3PAuOTf$ with $Ph_3PAuNTf_2$, did not improve the β selectivity.

A worthwhile attempt to achieve the β-selective digitoxoside formation was to increase the steric hindrance of the 3-*O*-protecting group in the digitoxosyl donor. Therefore, 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-digitoxosyl *o*-cyclopropylethynylbenzoate **17** was prepared (Scheme 3). Thus, 4,6-*O*-benzylidene **4** was treated with NBS in the presence of AIBN ($BaCO_3$, CCl_4, reflux) to provide the 6-bromo-4-*O*-benzoate **14** in excellent yield (97%).[17c] Treatment of **14** with $LiAlH_4$ in THF at 50 °C afforded digitoxoside **15**,[17c] in that the 6-bromide, 4-*O*-Bz, and 3-*O*-MBz groups were cleaved cleanly. Blocking the 3,4-OHs with a TBDPS group gave **16** quantitatively under forced conditions.[20] Methyl digitoxoside **16** was then converted conveniently into the desired digitoxosyl *o*-cyclopropylethynylbenzoate **17** (74%, β/α = 8.6:1) via hydrolysis and ester formation.

Gratifyingly, glycosylation of digitoxigenin (**2**) with 3,4-di-*O*-TBDPS-D-digitoxosyl *o*-cyclopropylethynylbenzoate **17** under normal conditions (0.1 equiv $Ph_3PAuOTf$, CH_2Cl_2, rt) led to the coupled glycoside nearly quantitatively in high β/α selectivity (ca. β/α = 6.6:1 as measured by ^1H NMR) (Scheme 4). The β and α anomers were inseparable on silica gel and therefore were subjected directly to the next step for removal of the 3,4-di-*O*-TBDPS group. These two TBDPS groups were quite resistant to cleavage (e.g., HF·pyridine, THF, 50 °C), and under some conditions (e.g., TBAF, THF, rt) the butenolide moiety in the aglycone did not survive. Fortunately, under the action of NH_4F·HF in the presence of NMP in DMF at 70 °C,[8b,21] the TBDPS groups were cleaved slowly to give diol **18**[9a] nearly quantitatively in 5 days. Reactions at >80 °C led to decomposition of the substrate. At this stage, the corresponding α anomer could be easily removed by chromatography on silica gel. Diol **18** was then subjected to selective protection of the axial 3′-OH with an acetyl group via 3′,4′-orthoester formation and subsequent cleavage ($CH_3C(OMe)_3$, TsOH, rt),[9,22] leading to monosaccharide **19**[9a] in 98% yield.

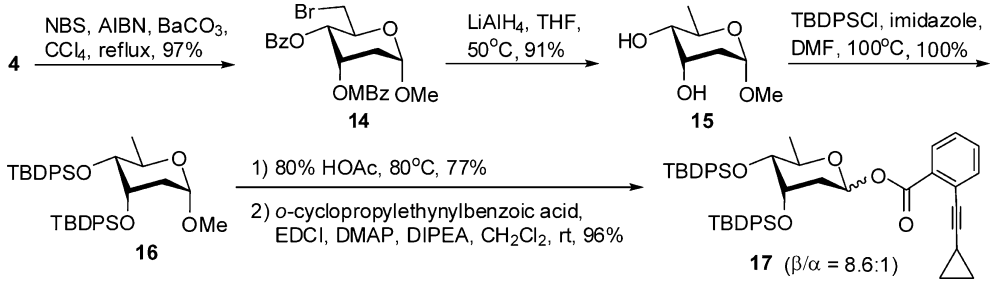
Glycosylation of digitoxigenin 3′-*O*-acetyl-β-D-digitoxoside **19** with 3,4-di-*O*-TBDPS-D-digitoxosyl *o*-cyclopropylethynylbenzoate **17** under normal conditions (0.1 equiv $Ph_3PAuOTf$, CH_2Cl_2, −40 °C) afforded the desired β-disaccharide **20** in high yields (~80%) without detection of the corresponding α-isomer. However, this reaction was poorly reproducible; disaccharide **24** was isolated as the major byproduct (up to 64%), which was derived plausibly via glycal formation (from **17**) followed by a Ferrier-type glycosylation.[23] To our delight, replacement of CH_2Cl_2 with toluene as the solvent completely avoided this side reaction, leading to β-disaccharide **20** nearly quantitatively.



Digitoxigenin disaccharide **20** was then subjected to removal of the 3″,4″-*O*-TBDPS groups with NH_4F·HF in the presence of NMP in DMF. The disaccharide was considerably more robust than the monosaccharide (cf., →**18**), and thus the reaction was performed at 80 °C to provide the corresponding 3″,4″-diol nearly quantitative in 3 days. Selective protection of the axial 3″-OH with an acetyl group under similar conditions as for **18**→**19** gave 3′,3″-di-*O*-acetyl-disaccharide **21**[9a] (98%).

Applying the above glycosylation conditions (0.1 equiv $Ph_3PAuOTf$, toluene, −40 °C) to the coupling of digitoxigenin disaccharide **21** with 3,4-di-*O*-TBDPS-D-digitoxosyl *o*-cyclopropylethynylbenzoate **17** provided the desired trisaccharide **22** in 97% yield with completely β selectivity. Removal of the 3‴,4‴-*O*-TBDPS groups on **22** under similar conditions as on the disaccharide substrate **20** required longer time (5 days), leading to diol **23**[9a] in 91% yield. Finally, the remaining 3′,3″-di-*O*-acetyl groups were removed with LiOH in MeOH and H_2O at rt to furnish the target digitoxin (**1**) in 74% yield. The analytical data (optical rotation, ^1H, and ^{13}C NMR) of the synthetic compound **1** were in good agreement with those reported for the natural product.

Scheme 3. Preparation of the Digitoxosyl *o*-Cyclopropylethynylbenzoate 17



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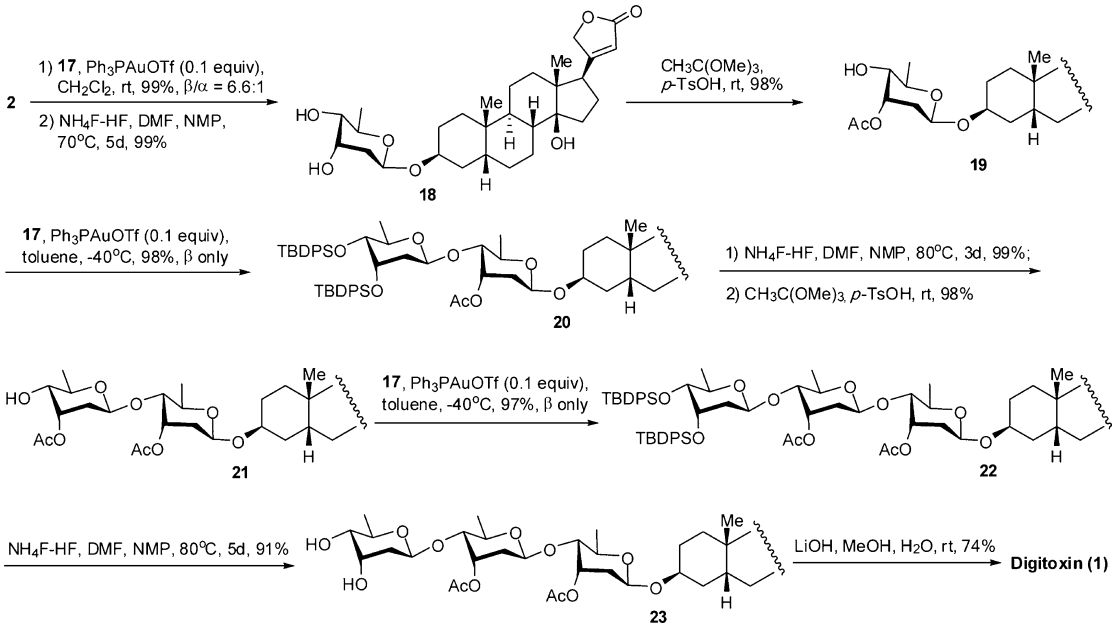
Scheme 4. Efficient Assembly of Digitoxin (1)



In conclusion, digitoxin (**1**), a clinically important cardiac trisaccharide, has been assembled efficiently in 9 steps and 52% overall yield from digitoxigenin and 3,4-di-*O*-*tert*-butyldiphenylsilyl-D-digitoxosyl *o*-cyclopropylethynylbenzoate (**17**) via alternate glycosylation and protecting group manipulation. The digitoxosyl *o*-cyclopropylethynylbenzoate **17**, readily prepared from methyl α-D-glucopyranoside in 10 steps and 50% overall yield, was stable and could be activated by a catalytic amount of $Ph_3PAuOTf$ to afford the β-digitoxosides in excellent yields and β/α selectivity. These results demonstrate that the present gold(I)-catalyzed glycosylation protocol is a favorable method for the synthesis of glycoconjugates containing 2-deoxy-sugars, in that the deoxysugar *o*-alkynylbenzoates donors are stable and the acid-labile deoxysugar linkages remain intact during the glycosylation.

EXPERIMENTAL SECTION

Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (4). To a solution of compound **3** (10.64 g, 40 mmol) in toluene (60 mL) and pyridine (20 mL) at 100 °C were added *p*-methoxybenzoyl chloride (9.12 g, 80 mmol) and DMAP (0.49 g, 4 mmol). After stirring at this temperature for 6 h, the reaction mixture was diluted with MeOH (15 mL) and concentrated under reduced pressure. The residue was diluted with EtOAc, and the organic phase, after being washed with water and brine, respectively, was dried over Na_2SO_4 and then concentrated in vacuo. The residue was purified by silica gel column chromatograph (petroleum ether/EtOAc, 5:1) to give **4** (15.69 g, 97%) as a white solid: $[\alpha]^{25}_D$ = 176.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.8 Hz, 2 H), 7.38−7.40 (m, 2 H), 7.28−7.30 (m, 3 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 5.61 (s, 1 H), 5.52 (d, *J* = 2.4 Hz, 1 H), 4.76 (d, *J* = 4.0 Hz, 1 H), 4.32−4.53 (m, 2 H), 3.84 (s, 3 H), 3.78 (m, 2 H), 3.37 (s, 3 H), 2.36 (dd, *J* = 15.5, 3.1 Hz, 1 H), 2.01 (dt, *J* = 15.6, 3.4 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 165.9, 163.3, 137.3, 131.8, 129.0, 128.2, 126.2, 123.2, 113.5, 101.9, 97.6, 69.5, 66.1, 58.9, 55.4, 55.3, 33.7; HRMS (MALDI) calcd for $C_{22}H_{24}O_7Na$ [M + Na]$^+$ 423.1420, found 423.1420.

Methyl 2-Deoxy-3-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (5). To a solution of **4** (12.0 g, 30 mmol) in methanol (50 mL) was added *p*-toluenesulfonic acid at rt until pH = 3. After stirring at rt for 2 h, the mixture was neutralized with Et_3N and then concentrated. The residue was purified by silica gel column chromatograph (petroleum ether/acetone, 2:1) to provide **5** (8.1 g, 86%) as a colorless syrup: $[\alpha]^{25}_D$ = 115.4 (*c* 3.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 2 H), 6.90 (d, *J* = 8.8 Hz, 2 H), 5.39 (q, *J* = 3.2 Hz, 1 H, H-3), 4.72 (d, *J* = 4.0 Hz, 1 H, H-1), 4.05 (m, 1 H, H-5), 3.88−3.80 (m, 6 H, H-4, H-6, H-6′, 3-OMBz-Me), 3.35 (s, 3 H, 1-OMe), 3.22 (brs, 1 H, -OH), 2.77 (brs, 1 H, -OH), 2.24 (dd, *J* = 15.4, 2.6 Hz, 1 H, H-2), 1.98 (dt, *J* = 15.4, 3.6 Hz, 1 H, H-2′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 163.4, 131.8, 122.6, 113.5, 97.0 (C-1), 69.4 (C-3), 67.8 (C-5), 67.1 (C-6), 62.5 (C-4), 55.3 (4-OMBz-Me), 55.1(1-OMe), 33.2 (C-2); HRMS (ESI) calcd for $C_{15}H_{20}O_7Na$ [M + Na]$^+$ 335.1107, found 335.1103.

Methyl 2,6-Dideoxy-6-iodo-3-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (6a) and Methyl 2,6-Dideoxy-6-iodo-4-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (6b). Diol **5** (8.99 g, 28.7 mmol), PPh_3 (11.39 g, 43.4 mmol), and imidazole (5.91 g, 88.2 mmol) were dissolved in dry toluene (150 mL). After 30 min of stirring at 70 °C, I_2 (9.57 g, 37.6 mmol) was added under an Ar atmosphere. The mixture was stirred at 70 °C for an additional 1 h and then concentrated and diluted with EtOAc. The organic phase, after being washed with aqueous 1 N HCl, saturated $NaHCO_3$, and brine, respectively, was dried over anhydrous Na_2SO_4 and then concentrated in vacuo. The resulting yellow oil was purified carefully by silica gel column chromatograph (petroleum ether/EtOAc, 4:1) to provide **6a** (7.77 g, 64%) and **6b** (3.40 g, 28%) as white solids. **6a**: $[\alpha]^{25}_D$ = 76.3 (*c* 3.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 2 H), 6.92 (d, *J* = 8.8 Hz, 2 H), 5.37 (m, 1 H, H-3), 4.79 (d, *J* = 4.4 Hz, 1 H, H-1), 3.88−3.83 (m, 4 H, H-5, 3-OMBz-Me), 3.64 (m, 2 H, H-4, H-6), 3.45 (s, 3 H, 1-OMe), 3.36 (dd, *J* = 10.4, 7.6 Hz, 1 H, H-6′), 2.72 (brs, 1 H, 4-OH), 2.24 (dd, *J* = 15.4, 2.6 Hz, 1 H, H-2), 2.03 (dt, *J* = 15.4, 4.4 Hz, 1 H, H-2′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 163.5, 131.8, 122.2, 113.6, 97.2 (C-1), 70.9 (C-4), 69.3 (C-3), 67.2 (C-5), 55.4 (1-OMe), 55.3 (3-OMBz-Me), 33.4 (C-2), 8.2 (C-6); HRMS (MALDI) calcd for $C_{15}H_{19}IO_6Na$ [M + Na]$^+$ 445.0117, found 445.0119. **6b**: $[\alpha]^{25}_D$ = 113.0 (*c* 1.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.2 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 4.92 (d, *J* = 3.2 Hz, 1 H, H-1), 4.81 (dd, *J* = 9.8, 3.2 Hz, 1 H, H-4), 4.26 (m, 1 H, H-3), 4.16 (m, 1 H, H-5), 3.86 (s, 3 H, 4-OMBz-Me), 3.51 (s, 3 H, 1-OMe), 3.48 (dd, *J* = 10.6, 2.2 Hz, 1 H, H-6), 3.26 (dd, *J* = 10.8, 8.4 Hz, 1 H, H-6′), 2.18 (ddd, *J* = 14.8, 3.2, 1.2 Hz, 1 H, H-2), 2.06 (dt, *J* = 14.8, 3.2 Hz, 1 H, H-2′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 163.7, 131.9, 121.8, 113.7, 98.9 (C-1), 74.0 (C-4), 65.7 (C-3), 65.4 (C-5), 55.7 (1-OMe), 55.4 (4-OMBz-Me), 35.3 (C-2), 6.2 (C-6); HRMS

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(MALDI) calcd for $C_{15}H_{19}IO_6Na$ $[M + Na]^+$ 445.0117, found 445.0119.

Methyl 4-*O*-Acetyl-2,6-dideoxy-3-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (7a) and Methyl 3-*O*-Acetyl-2,6-dideoxy-4-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (7b). To a solution of the mixture of iodide **6a** and **6b** (0.46 g, 1.1 mmol), which was obtained from the above transformation, and AIBN (0.016 g, 0.1 mmol) in dry toluene (90 mL) at 100 °C was added Bu_3SnH (0.8 mL, 3.0 mmol) under an Ar atmosphere. After 1 h of stirring at this temperature, pyridine (10.0 mL) and Ac_2O (0.8 mL, 8.8 mmol) were added into the mixture, and the stirring was continued for another 5 h. The resulting mixture was concentrated in vacuo and diluted with EtOAc. The organic phase, after being washed with 1 N HCl, saturated aqueous $NaHCO_3$, and brine, respectively, was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting yellow oil was purified by silica gel column chromatography (petroleum ether/EtOAc, 5:1) to provide **7a** (0.25 g, 67%) and **7b** (0.12 g, 33%) as white solids. **7a**: $[\alpha]^{25}_D$ = 176.9 (*c* 2.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.8 Hz, 2 H), 6.95 (d, *J* = 8.8 Hz, 2 H), 5.56 (m, 1 H, H-3), 4.77 (d, *J* = 2.8 Hz, 1 H, H-1), 4.72 (dd, *J* = 9.8, 3.0 Hz, 1 H, H-4), 4.33 (m, 1 H, H-5), 3.87 (s, 3 H, 3-OMBz-Me), 3.42 (s, 3 H, 1-OMe), 2.20 (dd, *J* = 15.0, 2.2 Hz, 1 H, H-2), 2.12 (dt, *J* = 15.0, 4.0 Hz, 1 H, H-2′), 1.99 (s, 3 H, 4-OAc), 1.22 (d, *J* = 6.4 Hz, 3 H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1 (4-OAc), 165.7, 163.4, 131.8, 122.8, 113.6, 97.1 (C-1), 72.6 (C-4), 66.1 (C-3), 61.7 (C-6), 55.4 (3-OMBz-Me), 55.2 (1-OMe), 33.6 (C-2), 20.8 (4-OAc), 17.4 (C-6); HRMS (MALDI) calcd for $C_{17}H_{22}O_7Na$ $[M + Na]^+$ 361.1258, found 361.1258. **7b**: $[\alpha]^{25}_D$ = 98.7 (*c* 1.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.8 Hz, 2 H), 6.92 (d, *J* = 8.8 Hz, 2 H), 5.36 (m, 1 H, H-3), 4.89 (dd, *J* = 9.4, 3.2 Hz, 1 H, H-4), 4.74 (d, *J* = 3.6 Hz, 1 H, H-1), 4.37 (m, 1 H, H-5), 3.86 (s, 3 H, 4-OMBz-Me), 3.39 (s, 3 H, 1-OMe), 2.21 (dd, *J* = 14.8, 2.0 Hz, 1 H, H-2), 2.10−2.05 (m, 4 H, H-2, 3-OAc), 1.26 (d, *J* = 6.0 Hz, 3 H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6 (3-OAc), 165.1, 163.6, 131.6, 122.1, 113.7, 97.1 (C-1), 72.3 (C-4), 61.7 (C-3), 62.2 (C-5), 55.4 (4-OMBz-Me), 55.2 (1-OMe), 33.2 (C-2), 21.2 (3-OAc), 17.5 (C-6); HRMS (MALDI) calcd for $C_{17}H_{22}O_7Na$ $[M + Na]^+$ 361.1258, found 361.1264.

Methyl 2,6-Dideoxy-3,4-di-*O*-(*p*-methoxybenzoyl)-α-D-*ribo*-hexopyranoside (7c). To a solution of the mixture of **6a** and **6b** (10.56 g, 25.0 mmol) and AIBN (0.27 g, 1.7 mmol) in dry toluene (150 mL) at 100 °C was added Bu_3SnH (8.1 mL, 30.0 mmol) under an Ar atmosphere. After 1 h of stirring at this temperature, pyridine (100 mL) and *p*-methoxybenzoyl chloride (11.30 g, 74.2 mmol) were added into the mixture, and the stirring was continued for another 5 h. The resulting mixture was concentrated in vacuo and diluted with EtOAc. The organic phase, after being washed with 1 N HCl, saturated aqueous $NaHCO_3$, and brine, respectively, was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The resulting yellow oil was purified by silica gel column chromatography (toluene/EtOAc, 15:1) to provide **7c** (10.76 g, 98%) as a white solid: $[\alpha]^{25}_D$ = 226.6 (*c* 4.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 2 H), 7.85 (d, *J* = 8.8 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 6.81 (d, *J* = 8.8 Hz, 2 H), 5.64 (m, 1 H), 5.01 (dd, *J* = 9.8, 3.0 Hz, 1 H), 4.81 (d, *J* = 3.6 Hz, 1 H), 4.50 (m, 1 H), 3.85 (s, 3 H), 3.79 (s, 3 H), 3.43 (s, 3 H), 2.29 (dd, *J* = 14.8, 2.8 Hz, 1 H), 2.18 (dt, *J* = 14.8, 4.0 Hz, 1 H), 1.28 (d, *J* = 6.0 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 165.1, 163.4, 163.3, 131.7, 131.6, 122.9, 122.0, 113.50, 113.48, 97.1, 72.5, 66.6, 62.1, 55.29, 55.26, 55.15, 33.6, 17.5; HRMS (MALDI) calcd for $C_{23}H_{26}O_8Na$ $[M + Na]^+$ 453.1520, found 453.1512.

4-*O*-Acetyl-2,6-dideoxy-3-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranosyl *o*-Cyclopropylethynylbenzoate (8). A solution of methyl glycoside **7a** (135 mg, 0.40 mmol) in 25% HOAc (8.0 mL) was stirred at 100 °C for 4 h and was then concentrated in vacuo. The residue was diluted with EtOAc, washed with saturated $NaHCO_3$ solution and brine, respectively, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatograph (petroleum ether/EtOAc, 2:1) to provide 4-*O*-acetyl-2,6-dideoxy-3-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranose as a colorless syrup. The syrup was dissolved in anhydrous CH_2Cl_2 (2.0 mL) at rt, to which 2-(cyclopropylethynyl)benzoic acid (97 mg, 0.48 mmol), DMAP (10 mg, 0.08 mmol), EDCI (154 mg, 0.8 mmol), and DIPEA (0.26 mL) were added. After being stirred overnight at rt, the mixture was diluted with CH_2Cl_2 and washed with 1 N HCl, saturated aqueous $NaHCO_3$, and brine, respectively. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (toluene/EtOAc, 7:1) to provide **8** (159 mg, 80%, β/α = 19/1) as a white solid. **8α**: ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.8 Hz, 2 H), 7.80 (d, *J* = 7.2 Hz, 1 H), 7.47 (d, *J* = 7.2 Hz, 1 H), 7.40 (t, *J* = 7.2 Hz, 1 H), 7.09 (t, *J* = 7.2 Hz, 1 H), 6.70 (d, *J* = 8.8 Hz, 2 H), 6.42 (d, *J* = 3.6 Hz, 1 H), 5.68 (q, *J* = 3.2 Hz, 1 H), 4.80 (dd, *J* = 10.0, 2.8 Hz, 1 H), 4.59 (m, 1 H), 3.83 (s, 3 H), 2.48 (dd, *J* = 15.6, 2.4 Hz, 1 H), 2.36 (dt, *J* = 15.6, 4.0 Hz, 1 H), 2.00 (s, 3 H), 1.46 (m, 1 H), 1.27 (d, *J* = 6.0 Hz, 3 H), 0.83 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.0, 165.6, 164.9, 163.4, 134.2, 131.91, 131.86, 131.5, 130.2, 126.8, 124.8, 122.3, 113.5, 99.7, 91.1, 74.2, 72.3, 65.8, 64.3, 55.4, 32.8, 20.8, 17.6, 8.86, 8.82, 0.92; HRMS (ESI) calcd for $C_{28}H_{28}O_8Na$ $[M + Na]^+$ 515.1676, found 515.1666. **8β**: $[\alpha]^{25}_D$ = 47.2 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.8 Hz, 2 H), 7.96 (d, *J* = 7.2 Hz, 1 H), 7.49 (d, *J* = 7.2 Hz, 1 H), 7.43 (td, *J* = 7.2, 1.2 Hz, 1 H), 7.31 (td, *J* = 7.2, 1.2 Hz, 1 H), 6.97 (d, *J* = 8.8 Hz, 2 H), 6.42 (dd, *J* = 9.2, 2.4 Hz, 1 H), 5.80 (q, *J* = 3.2 Hz, 1 H), 4.79 (dd, *J* = 9.2, 3.2 Hz, 1 H), 4.30 (m, 1 H), 3.89 (s, 3 H), 2.38 (m, 1 H), 2.26 (m, 1 H), 2.01 (s, 3 H), 1.52 (m, 1 H), 1.31 (d, *J* = 6.4 Hz, 3 H), 0.89 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 165.2, 164.4, 163.7, 134.4, 132.0, 131.8, 130.7, 130.6, 127.0, 125.1, 122.0, 113.8, 98.7, 91.3, 74.4, 72.3, 69.6, 67.0, 55.5, 34.4, 20.8, 18.0, 8.8, 0.62; HRMS (ESI) calcd for $C_{28}H_{28}O_8Na$ $[M + Na]^+$ 515.1676, found 515.1666.

3-*O*-Acetyl-2,6-dideoxy-4-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranosyl *o*-Cyclopropylethynylbenzoate (9). Compound **9** (86 mg, 85%, trace α) was prepared from **7b** following a procedure similar to that for **7a**→**8**. **9β**: $[\alpha]^{25}_D$ = 38.8 (*c* 1.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.97−7.94 (m, 3 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.31 (td, *J* = 7.6, 1.2 Hz, 1 H), 6.93 (d, *J* = 7.2 Hz, 2 H), 6.38 (dd, *J* = 8.8, 2.0 Hz, 1 H), 5.67 (m, 1 H), 4.97 (dd, *J* = 8.8, 3.2 Hz, 1 H), 4.34 (m, 1 H), 3.87 (s, 3 H), 2.33 (m, 1 H), 2.21 (m, 1 H), 2.11 (s, 3 H), 1.52 (m, 1 H), 1.34 (d, *J* = 6.0 Hz, 3 H), 0.89 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 165.1, 164.4, 163.7, 134.3, 132.0, 131.6, 130.6, 127.0, 125.0, 121.9, 113.7, 99.7, 91.4, 74.3, 72.0, 70.0, 67.0, 55.4, 34.0, 20.9, 18.1, 8.8, 0.6; HRMS (ESI) calcd for $C_{28}H_{28}O_8Na$ $[M + Na]^+$ 515.1676, found 515.1689.

2,6-Dideoxy-3,4-di-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranosyl *o*-Cyclopropylethynylbenzoate (10). Compound **10** (4.72 g, 90%, β/α = 17/1) was prepared from **7c** following a procedure similar to that for **7a**→**8**. **10α**: $[\alpha]^{25}_D$ = 151.4 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.4 Hz, 2 H), 7.87 (d, *J* = 8.4 Hz, 2 H), 7.80 (d, *J* = 7.6 Hz, 1 H), 7.46 (d, *J* = 7.6 Hz, 1 H), 7.37 (t, *J* = 7.2 Hz, 1 H), 7.04 (t, *J* = 7.2 Hz, 1 H), 6.81 (d, *J* = 8.4 Hz, 2 H), 6.73 (d, *J* = 8.4 Hz, 2 H), 6.48 (d, *J* = 3.2 Hz, 1 H), 5.78 (m, 1 H), 5.10 (dd, *J* = 9.8, 2.2 Hz, 1 H), 4.77 (m, 1 H), 3.80 (s, 3 H), 3.76 (s, 3 H), 2.57 (d, *J* = 14.4 Hz, 1 H), 2.42 (m, 1 H), 1.47 (m, 1 H), 1.34 (d, *J* = 6.0 Hz, 3 H), 0.84 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 164.8, 164.5, 163.3, 163.1, 133.9, 131.59, 131.53, 131.46, 131.2, 129.9, 126.5, 124.5, 122.1, 121.6, 113.4, 113.2, 99.5, 90.9, 74.0, 72.0, 66.0, 64.4, 55.1, 32.6, 17.6, 8.65, 8.59, 0.4; HRMS (ESI) calcd for $C_{34}H_{32}O_9Na$ $[M + Na]^+$ 607.1963, found 607.1939. **10β**: $[\alpha]^{25}_D$ = 87.0 (*c* 3.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 9.2 Hz, 2 H), 7.98 (d, *J* = 7.6 Hz, 1 H), 7.87 (d, *J* = 8.8 Hz, 2 H), 7.49 (d, *J* = 7.6 Hz, 1 H), 7.43 (t, *J* = 7.6 Hz, 1 H), 7.31 (t, *J* = 7.6 Hz, 1 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 6.48 (dd, *J* = 8.8, 2.0 Hz, 1 H), 5.89 (m, 1 H), 5.09 (dd, *J* = 9.0, 2.6 Hz, 1 H), 4.47 (m, 1 H), 3.88 (s, 3 H), 3.82 (s, 3 H), 2.48 (m, 1 H), 2.35 (m, 1 H), 1.53 (m, 1 H), 1.37 (d, *J* = 6.0 Hz, 3 H), 0.90 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 165.0, 164.3, 163.6, 163.5, 134.3, 132.0, 131.73, 131.69, 130.63, 130.59, 127.0, 125.0, 122.1, 121.8, 113.7, 113.6, 99.7, 91.4, 74.4, 72.2, 70.1, 67.3, 55.4, 55.3, 34.3, 18.1, 8.8, 0.6; HRMS (ESI) calcd for $C_{34}H_{32}O_9Na$ $[M + Na]^+$ 607.1963, found 607.1960.

Digitoxigenin 4-*O*-Acetyl-2,6-dideoxy-3-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranoside (11). To a mixture of **2** (12 mg, 0.032 mmol), **8** (19 mg, 0.038 mmol), and 4 Å MS (100 mg) in dry

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CH_2Cl_2/toluene (2 mL/1 mL) was added a solution of PPh_3AuOTf in CH_2Cl_2 (0.05 N, 0.08 mL). After stirring at rt for 3 h, the mixture was filtered through Celite. After being concentrated, the residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 200:1 to 150:1) to provide **11*β*** (14.3 mg, 66%) and **11*α*** (7.2 mg, 33%) as white solids. **11*α***: $[\alpha]^{25}_D$ = 102.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.8 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 5.88 (s, 1 H), 5.50 (m, 1 H), 4.98 (dd, *J* = 18.0, 1.6 Hz, 1 H), 4.94 (d, *J* = 4.0 Hz, 1 H), 4.81 (dd, *J* = 18.0, 1.6 Hz, 1 H), 4.71 (dd, *J* = 9.6, 2.8 Hz, 1 H), 4.41 (m, 1 H), 3.96 (brs, 1H), 3.87 (s, 3 H), 2.78 (m, 1 H), 2.26 (dd, *J* = 15.0, 2.6 Hz, 1 H), 2.20−2.08 (m, 3 H), 2.00 (s, 3 H), 1.91−1.22 (m, 20 H), 1.19 (d, *J* = 6.0 Hz, 3 H), 0.86 (s, 3H), 0.76 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 170.2, 165.8, 163.4, 131.8, 122.9, 117.7, 113.5, 94.0, 85.6, 73.4, 72.9, 71.7, 66.7, 61.7, 55.4, 50.9, 49.6, 41.8, 40.0, 36.6, 35.6, 35.1, 34.0, 33.1, 32.3, 30.0, 26.9, 26.8, 24.0, 23.5, 21.3, 21.1, 20.8, 17.5, 15.7; HRMS (ESI) calcd for $C_{39}H_{52}O_{10}Na$ $[M + Na]^+$ 703.3453, found 703.3461. **11*β***: $[\alpha]^{25}_D$ = 20.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.8 Hz, 2 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 5.88 (s, 1 H), 5.68 (m, 1 H), 4.98 (d, *J* = 17.6 Hz, 1 H), 4.97 (d, *J* = 7.6 Hz, 1 H), 4.80 (d, *J* = 18.0, 1.6 Hz, 1 H), 4.69 (dd, *J* = 9.6, 2.8 Hz, 1 H), 4.04 (m, 2 H), 3.88 (s, 3 H), 2.78 (m, 1 H), 2.19−1.99 (m, 4 H), 1.97 (s, 3 H), 1.90−1.35 (m, 20 H), 1.24 (d, *J* = 6.4 Hz, 3 H), 0.93 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 170.1, 165.2, 163.6, 131.7, 122.5, 117.7, 113.8, 96.2, 85.6, 73.4, 73.3, 72.9, 68.2, 68.0, 55.5, 50.9, 49.6, 41.9, 40.0, 36.4, 36.3, 35.6, 35.2, 33.1, 30.2, 30.1, 26.9, 26.7, 26.6, 23.6, 21.4, 21.1, 20.8, 18.0, 15.7; HRMS (ESI) calcd for $C_{39}H_{52}O_{10}Na$ $[M + Na]^+$ 703.3453, found 703.3481.

Digitoxigenin 3-*O*-Acetyl-2,6-dideoxy-4-*O*-(*p*-methoxybenzoyl)-D-*ribo*-hexopyranoside (12). Compound **12** (21.8 mg, 100%, β/α = 2.0/1) was prepared from **2** (12 mg, 0.032 mmol) and **9** (19 mg, 0.038 mmol) following a procedure similar to that for **8**→**11**. **12*α***: $[\alpha]^{25}_D$ = 70.0 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.8 Hz, 2 H), 6.93 (d, *J* = 8.8 Hz, 2 H), 5.89 (s, 1 H), 5.29 (m, 1 H), 4.99 (d, *J* = 18.0 Hz, 1 H), 4.93 (d, *J* = 2.8 Hz, 1 H), 4.87 (dd, *J* = 9.6, 2.8 Hz, 1 H), 4.81 (dd, *J* = 17.8, 1.0 Hz, 1 H), 4.42 (m, 1 H), 3.92 (brs, 1 H), 3.87 (s, 3 H), 2.79 (m, 1 H), 2.25 (dd, *J* = 14.8, 2.8 Hz, 1 H), 2.19−2.00 (m, 6 H), 1.99−1.25 (m, 20 H), 1.21 (d, *J* = 6.4 Hz, 3 H), 0.95 (s, 3H), 0.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 170.5, 165.3, 163.6, 131.8, 122.1, 117.7, 113.7, 94.7, 85.6, 73.4, 72.7, 72.6, 67.5, 62.4, 55.5, 50.9, 49.6, 41.9, 40.0, 37.1, 35.7, 35.2, 33.8, 33.2, 32.4, 30.2, 26.9, 26.7, 24.8, 23.9, 21.3, 21.2, 17.5, 15.8; HRMS (ESI) calcd for $C_{39}H_{52}O_{10}Na$ $[M + Na]^+$ 703.3453, found 703.3482. **12*β***: $[\alpha]^{25}_D$ = 8.9 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 9.2 Hz, 2 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 5.88 (s, 1 H), 5.57 (m, 1 H), 4.99 (dd, *J* = 17.6 Hz, 1 H), 4.90 (dd, *J* = 9.0, 2.2 Hz, 1 H), 4.86 (dd, *J* = 9.4, 3.0 Hz, 1 H), 4.81 (dd, *J* = 18.0, 1.4 Hz, 1 H), 4.07 (m, 2 H), 3.86 (s, 3 H), 2.79 (m, 1 H), 2.21−2.04 (m, 6 H), 1.99 (dd, *J* = 9.2, 3.2 Hz, 1 H), 1.95−1.34 (m, 20 H), 1.26 (d, *J* = 6.0 Hz, 3 H), 0.94 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 169.8, 163.6, 131.6, 122.1, 117.7, 113.7, 96.0, 85.6, 73.4, 73.1, 72.6, 68.4, 68.0, 55.4, 50.9, 49.6, 41.9, 40.6, 36.3, 36.2, 35.8, 35.2, 33.1, 30.1, 26.9, 26.6, 23.6, 21.4, 21.1, 21.0, 18.1, 15.8; HRMS (ESI) calcd for $C_{39}H_{52}O_{10}Na$ $[M + Na]^+$ 703.3453, found 703.3476.

Digitoxigenin 2,6-Dideoxy-3,4-di-*O*-(*p*-methoxybenzoyl)-*β*-D-*ribo*-hexopyranoside (13). Compound **13** (24.0 mg, 97%, β/α = 1.8/1) was prepared from **2** (12 mg, 0.032 mmol) and **10** (22 mg, 0.038 mmol) following a procedure similar to that for **8**→**11**. **13*α***: $[\alpha]^{25}_D$ = 134.4 (*c* 0.6, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.8 Hz, 2 H), 7.89 (d, *J* = 8.8 Hz, 2 H), 6.92 (d, *J* = 8.8 Hz, 2 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 5.87 (s, 1 H), 5.55 (m, 1 H), 5.01−4.96 (m, 3 H), 4.80 (d, *J* = 17.6 Hz, 1 H), 4.56 (m, 1 H), 3.98 (brs, 1H), 3.87 (s, 3 H), 3.83 (s, 3 H), 2.76 (m, 1 H), 2.37 (dd, *J* = 15.0, 2.6 Hz, 1 H), 2.20−2.08 (m, 3 H), 1.91−1.84 (m, 2 H), 1.77−1.16 (m, 21 H), 0.86 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.47, 174.46, 165.6, 165.3, 163.5, 163.3, 131.76, 131.74, 123.1, 122.2, 117.7, 113.6, 113.5, 94.1, 85.6, 73.4, 72.9, 71.8, 67.3, 62.2, 55.5, 55.4, 50.9, 49.6, 41.8, 40.0, 36.5, 35.6, 35.0, 34.0, 33.1, 32.3, 29.9, 26.9, 26.8, 24.1, 23.5, 21.3, 21.1, 17.7, 15.7; HRMS (ESI) calcd for $C_{45}H_{56}O_{11}Na$ $[M + Na]^+$ 795.3715, found 795.3735. **13*β***: $[\alpha]^{25}_D$ = 64.9 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.4 Hz, 2 H), 7.82 (d, *J* = 8.8 Hz, 2 H), 6.96 (d, *J* = 8.8 Hz, 2 H), 6.81 (d, *J* = 8.8 Hz, 2 H), 5.88 (s, 1 H), 5.75 (m, 1 H), 5.02−4.96 (m, 3 H), 4.80 (dd, *J* = 18.0, 1.4 Hz, 1 H), 4.20 (m, 1 H), 4.09 (brs, 1H), 3.89 (s, 3 H), 3.82 (s, 3 H), 2.78 (m, 1 H), 2.24−2.05 (m, 4 H), 1.92−1.36 (m, 20 H), 1.29 (d, *J* = 6.0 Hz, 3 H), 0.94 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 174.4, 165.2, 165.1, 163.6, 163.5, 131.68, 131.65, 122.6, 122.1, 117.7, 113.8, 113.6, 96.3, 85.6, 73.4, 73.3, 72.8, 55.5, 55.4, 50.9, 49.6, 41.9, 40.1, 36.5, 36.3, 35.8, 35.2, 33.1, 30.2, 30.1, 26.9, 26.7, 26.6, 23.6, 21.4, 21.1, 18.2, 15.7; HRMS (ESI) calcd for $C_{45}H_{56}O_{11}Na$ $[M + Na]^+$ 795.3715, found 795.3735.

Methyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-3-*O*-(*p*-methoxybenzoyl)-*α*-D-*ribo*-hexopyranoside (14). A mixture of **4** (1.80 g, 4.5 mmol), NBS (0.80 g, 4.5 mmol), AIBN (0.036 g, 0.23 mmol), and $BaCO_3$ (0.53 g, 2.7 mmol) in dry CCl_4 (45 mL) was refluxed for 1 h under argon. The mixture was then cooled to room temperature and filtered through Celite. The filtrate was diluted with EtOAc and washed with 1 N HCl, saturated aqueous $NaHCO_3$, and brine, respectively. The organic phase was dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by silica gel column chromatography (toluene/EtOAc, 25:1) to provide **14** (2.09 g, 97%) as a white solid: $[\alpha]^{25}_D$ = 186.4 (*c* 0.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.8 Hz, 2 H), 7.88 (d, *J* = 8.0 Hz, 2 H), 7.52 (d, *J* = 7.4 Hz, 1 H), 7.35 (d, *J* = 7.8 Hz, 2 H), 6.94 (d, *J* = 8.8 Hz, 2 H), 5.72 (m, 1 H), 5.20 (dd, *J* = 9.8, 3.0 Hz, 1 H), 4.92 (d, *J* = 4.0 Hz, 1 H), 4.61 (m, 1 H), 3.88 (s, 3 H), 3.64 (dd, *J* = 11.0, 2.2 Hz, 1 H), 3.54 (m, 1 H), 3.51 (s, 3 H), 2.31 (dd, *J* = 14.8, 2.4 Hz, 1 H), 2.23 (dt, *J* = 15.6, 3.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5, 165.2, 163.5, 133.3, 131.8, 129.7, 129.2, 128.4, 122.6, 113.71, 113.66, 97.6, 70.5, 66.3, 65.5, 55.6, 55.4, 33.5, 32.9; HRMS (MALDI) calcd for $C_{22}H_{23}O_7BrNa$ $[M + Na]^+$ 501.0519, found 501.0505.

Methyl 2,6-Dideoxy-*α*-D-*ribo*-hexopyranoside (15). To a solution of **14** (13.38 g, 27.9 mmol) in anhydrous THF (300 mL) was added lithium aluminum hydride (10.60 g, 279 mmol). After stirring at 50 °C for 5.5 h, the mixture was ice-cooled, to which were added dropwise water (10.6 mL), 15% aq NaOH (10.6 mL), and water (31.8 mL) successively. The resulting mixture was stirred at 50 °C for 1 h. The mixture was then filtered through a pad of Celite. The filtrate was concentrated to give a residue, which was purified by silica gel column chromatography (petroleum ether/EtOAc, 2:1) to afford **15** (4.13 g, 91%) as a colorless oil.

Methyl 3,4-Di-*O*-*tert*-butyldiphenylsilyl-2,6-deoxy-*α*-D-*ribo*-hexopyranoside (16). To a solution of diol **15** (2.00 g, 12.3 mmol) and *tert*-butyldiphenylsilyl chloride (12.8 mL, 49.3 mmol) in dry DMF (12.0 mL) was added imidazole (2.48 g, 36.9 mmol). After being stirred at 100 °C for 12 h, the mixture was concentrated in vacuo. The residue was diluted with ethyl actate and washed with saturated H_2O and brine. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by silica gel column chromatography (petroleum ether/toluene, 2:1) to provide **16** (7.88 g, 100%) as a colorless syrup: $[\alpha]^{25}_D$ = 17.6 (*c* 3.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 6.4 Hz, 2 H), 7.71 (d, *J* = 6.8 Hz, 2 H), 7.66 (d, *J* = 6.8 Hz, 2 H), 7.59 (d, *J* = 7.2 Hz, 2 H), 7.41−7.14 (m, 12 H), 4.40 (m, 1 H), 4.15 (m, 1 H), 4.02 (m, 1 H), 3.56 (m, 1 H), 3.30 (s, 3 H), 2.21 (m, 1 H), 1.63 (dt, *J* = 13.0, 3.8 Hz, 1 H), 1.09 (s, 9 H), 1.00 (s, 9 H), 0.66 (d, *J* = 10.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.22, 136.19, 136.1, 136.0, 134.4, 134.1, 134.0, 133.6, 129.55, 129.50, 129.48, 129.38, 127.4, 97.3, 75.0, 68.9, 54.7, 27.0, 26.9, 19.34, 19.32, 17.2; HRMS (MALDI) calcd for $C_{39}H_{50}O_4Si_2Na$ $[M + Na]^+$ 661.3145, found 661.3117.

3,4-Di-*O*-*tert*-butyldiphenylsilyl-2,6-deoxy-*α*-D-*ribo*-hexopyranosyl *o*-Cyclopropylethynylbenzoate (17). Digitoxosyl *o*-alkynylbenzoate **17** (5.38 g, 74%, β/α = 8.6:1) was prepared from **16** (4.42 g) following a procedure similar to that for **7a**→**8**. **17*α***: $[\alpha]^{25}_D$ = 14.1 (*c* 0.4, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 6.8 Hz, 2 H), 7.63−7.57 (m, 6 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 7.42−7.23 (m, 14 H), 6.04 (brs, 1 H), 4.17 (brs, 1 H), 4.12 (brs, 1 H), 3.64 (brs, 1 H), 2.46 (m, 1 H), 1.88 (m, 1 H), 1.26 (m, 1 H), 1.00−0.98 (m, 18 H), 0.86 (m, 4 H), 0.70 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.1, 136.2, 136.1, 136.0, 134.3,

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134.1, 133.7, 133.5, 133.4, 131.8, 131.5, 130.6, 129.8, 129.6, 127.59, 127.56, 127.53, 127.50, 126.8, 124.8, 99.4, 91.0, 77.2, 74.6, 74.4, 68.5, 27.02, 26.99, 19.4, 19.2, 17.2, 8.8, 0.7; HRMS (ESI) calcd for $C_{50}H_{56}O_5Si_2Na$ $[M + Na]^+$ 815.3559, found 815.3577. **17β**: $[\alpha]^{25}_D$ = −61.7 (*c* 0.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72−7.60 (m, 8 H), 7.44−7.20 (m, 15 H), 7.16 (t, *J* = 7.6 Hz, 1 H), 6.44 (m, 1 H), 4.32 (d, *J* = 8.4 Hz, 1 H), 4.12 (br, 1 H), 3.74 (br, 1 H), 2.54 (br, 1 H), 1.69 (m, 1 H), 1.28 (m, 1 H), 1.11−1.07 (m, 18 H), 0.83−0.81 (m, 7 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 136.1, 135.9, 135.7, 134.2, 134.0, 133.6, 133.5, 133.3, 131.4, 131.3, 130.0, 129.7, 129.6, 129.5, 127.6, 127.54, 127.51, 127.3, 126.6, 125.0, 99.6, 74.4, 27.04, 27.00, 19.4, 19.2, 8.8, 0.6; HRMS (ESI) calcd for $C_{50}H_{56}O_5Si_2Na$ $[M + Na]^+$ 815.3559, found 815.3596.

Digitoxigenin 2,6-Dideoxy-α/β-D-*ribo*-hexopyranoside (18). To a mixture of **17** (127 mg, 0.16 mmol), digitoxigenin **2** (50 mg, 0.13 mmol), and 4 Å MS (200 mg) in dry CH_2Cl_2 (10 mL) was added a solution of PPh_3AuOTf in CH_2Cl_2 (0.3 mL, 0.05 M). After stirring at rt for 2 h, the mixture was filtered through Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (petroleum ether/EtOAc, 4:1) to provide the coupled glycoside as a colorless syrup (130 mg, 99%).

A mixture of the above product (130 mg, 0.13 mmol) and $NH_4F{\cdot}HF$ (340 mg, 14.5 mmol) in a mixed solvent of anhydrous DMF (10 mL) and *N*-methylpyrrolidine (NMP, 5 mL) was kept at 70 °C for 5 days under argon. The solvent was removed under reduced pressure, and the residue was diluted with ethyl acetate. The organic layer, after being washed with H_2O and brine, respectively, was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 40:1) to provide **18β**[9a] (57.6 mg, 86%) and **18α** (8.7 mg, 13%) as white solids. **18α**: $[\alpha]^{25}_D$ = 73.0 (*c* 0.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.88 (s, 1 H), 4.994 (d, *J* = 18.0 Hz, 1 H), 4.993 (d, *J* = 2.8 Hz, 1 H), 4.81 (d, *J* = 18.0 Hz, 1 H), 4.01 (s, 1 H), 4.03 (m, 1H), 3.97 (m, 1 H), 3.78−3.71 (m, 2 H), 2.77 (m, 1 H), 2.54 (d, *J* = 8.8 Hz, 1 H), 2.20−2.08 (m, 3 H), 2.00−1.19 (m, 24H), 0.95 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 117.7, 94.8, 85.5, 73.4, 72.7, 71.8, 67.6, 64.8, 50.8, 49.5, 41.7, 39.9, 37.1, 35.6, 35.4, 35.2, 33.1, 32.2, 30.1, 26.8, 26.5, 23.8, 23.6, 21.2, 21.1, 17.8, 15.7; HRMS (ESI) calcd for $C_{29}H_{44}O_7Na$ $[M + Na]^+$ 527.2979, found 527.2987.

Digitoxigenin 3′-*O*-Acetyl-2,6-dideoxy-β-D-*ribo*-hexopyranoside (19). A round-bottom flask containing alcohol **18** (79 mg, 0.157 mmol) in CH_2Cl_2 (2.0 mL) was stirred at room temperature. To this solution were added trimethylorthoacetate (0.06 mL, 0.470 mmol) and a catalytic amount of *p*-toluenesulfonic acid (1.5 mg, 9.3 μmol). The mixture was stirred for 2 h, and TLC indicated that the starting material was consumed. The solvent was removed under reduced pressure, and the residue was dissolved in THF/H_2O (2 mL, 1:1). *p*-Toluenesulfonic acid (15 mg, 0.093 mmol) was added, and the stirring was continued for 1 h. The reaction was quenched by the addition of satd $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2, and the combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 40:1) to afford compound **19**[9a] (84 mg, 98%) as a white solid.

Digitoxigenin 3″,4″-Di-*O*-*tert*-butyldiphenylsilyl-2″,6″-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-3′-*O*-acetyl-2′,6′-dideoxy-β-D-*ribo*-hexopyranoside (20). To a mixture of **17** (109 mg, 0.14 mmol), **19** (50 mg, 0.09 mmol), and 4 Å MS (200 mg) in dry toluene (5.0 mL) was added a solution of PPh_3AuOTf in CH_2Cl_2 (0.3 mL, 0.05 M) at −40 °C. After stirring for 2 h, the mixture was filtered through Celite. After being concentrated, the residue was purified by silica gel column chromatography (toluene/EtOAc, 7:1) to provide **20** as a white solid (103 mg, 98%): $[\alpha]^{25}_D$ = 19.8 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 9.6 Hz, 2 H), 7.65 (m, 4 H), 7.48−7.30 (m, 12 H), 7.18 (t, *J* = 10.0 Hz, 2 H), 5.87 (s, 1 H), 5.15 (brs, 1 H), 4.98 (d, *J* = 24.0 Hz, 1 H), 4.81 (d, *J* = 12.8 Hz, 1 H), 4.79 (d, *J* = 23.6 Hz, 1 H), 4.65 (d, *J* = 12.0 Hz, 1 H), 4.28 (brs, 1 H), 4.10 (m, 1 H), 3.97 (brs, 1 H), 3.70 (m, 1 H), 3.39 (d, *J* = 10.4 Hz, 1 H), 3.02 (d, *J* = 11.6 Hz, 1 H), 2.76 (m, 1 H), 2.18−1.20 (m, 29 H), 1.14 (d, *J* = 8.4 Hz, 3 H), 1.08 (s, 9 H), 0.91 (s, 3 H), 0.87 (s, 9 H), 0.87 (s, 3 H), 0.73 (d, *J* = 8.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 174.5, 170.2, 137.7, 136.1, 136.0, 135.9, 133.9, 133.72, 133.70, 133.4, 129.8, 129.54, 129.50, 128.9, 128.1, 127.6, 127.45, 127.35, 125.2, 117.5, 95.7, 85.4, 79.3, 75.7, 73.4, 72.8, 68.9, 50.8, 49.5, 41.6, 39.9, 36.1, 36.0, 35.6, 35.0, 32.9, 30.1, 30.0, 27.1, 27.0, 26.8, 26.5, 23.5, 21.3, 21.24, 21.21, 21.0, 19.5, 19.2, 18.4, 18.2, 15.7; HRMS (MALDI) calcd for $C_{69}H_{92}O_{11}Si_2Na$ $[M + Na]^+$ 1175.6070, found 1175.6115.

Digitoxigenin 3″-*O*-Acetyl-2″,6″-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)- 3′-*O*-acetyl-2′,6′-dideoxy-β-D-*ribo*-hexopyranoside (21). A mixture of **20** (103 mg, 0.089 mmol) and $NH_4F{\cdot}HF$ (825 mg, 14.5 mmol) in a mixed solvent of anhydrous DMF (10 mL) and *N*-methylpyrrolidine (NMP, 5 mL) was kept at 80 °C for 3 days under argon. The solvent was removed under reduced pressure. The residue was diluted with ethyl acetate, which was washed with H_2O and brine, respectively. The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 40:1) to provide the deprotected product (60 mg, 99%) as a white solid.

The above product (53 mg, 0.074 mmol) was dissolved in CH_2Cl_2 (2.0 mL), and to this solution were added trimethylorthoacetate (0.03 mL, 0.222 mmol) and a catalytic amount of *p*-toluenesulfonic acid (1 mg, 5.8 μmol). The mixture was stirred for 2 h, and TLC indicated that the starting material was consumed. The solvent was removed under reduced pressure, and the residue was dissolved in THF/H_2O (2 mL, 1:1). *p*-Toluenesulfonic acid (7 mg, 0.04 mmol) was added, and the stirring was continued for 1 h. The reaction was quenched with addition of satd $NaHCO_3$ solution. The mixture was extracted with CH_2Cl_2, and the combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 40:1) to afford compound **21** (55 mg, 98%) as a white solid.

Digitoxigenin 3‴,4‴-Di-*O*-*tert*-butyldiphenylsilyl-2‴,6‴-dideoxy-β-D-*ribo*-hexopyranosyl-(1→4)-3″-*O*-acetyl-2″,6″-dideoxy-β-D-*ribo*-hexopyranosyl−(1→4)-3′-*O*-acetyl-2′,6′-dideoxy-β-D-*ribo*-hexopyranoside (22). To a mixture of **17** (63 mg, 0.079 mmol), **21** (38 mg, 0.052 mmol), and 4 Å MS (200 mg) in dry toluene (5.0 mL) was added a solution of PPh_3AuOTf in CH_2Cl_2 (0.16 mL, 0.05 M) at −40 °C. After stirring for 2 h, the mixture was filtered through Celite. The filtate was concentrated. The residue was purified by silica gel column chromatography (toluene/EtOAc, 6:1) to provide **22** (68 mg, 97%) as a white solid: $[\alpha]^{25}_D$ = 27.8 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71−7.65 (m, 5 H), 7.47−7.20 (m, 15 H), 5.87 (s, 1 H), 5.36 (brs, 1 H), 5.10 (brs, 1 H), 4.98 (d, *J* = 17.6 Hz, 1 H), 4.82−4.71 (m, 3 H), 4.60 (d, *J* = 8.8 Hz, 1 H), 4.29 (brs, 1 H), 4.06 (m, 1 H), 3.99 (brs, 1H), 3.81 (m, 1 H), 3.66 (m, 1 H), 3.40 (d, *J* = 5.2 Hz, 1 H), 3.27 (d, *J* = 9.2 Hz, 1 H), 2.90 (m, 1 H), 2.78 (m, 1 H), 2.20−1.20 (m, 40 H), 1.08 (s, 9 H), 0.90 (s, 12 H), 0.87 (s, 3 H), 0.73 (d, *J* = 8.4 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.52, 174.48, 170.28, 170.26, 136.2, 136.1, 136.0, 134.1, 133.8, 133.5, 129.8, 129.63, 129.58, 127.7, 127.53, 127.50, 127.4, 117.7, 98.7, 95.9, 85.6, 79.6, 79.0, 75.8, 73.4, 73.0, 70.0, 69.03, 69.98, 50.9, 49.6, 41.8, 40.0, 36.2, 35.7, 35.6, 35.1, 33.1, 30.1, 29.7, 37.2, 27.1, 26.9, 26.6, 23.6, 21.4, 21.3, 21.1, 19.6, 19.3, 18.4, 18.2, 18.0, 15.7; HRMS (MALDI) calcd for $[C_{77}H_{104}O_{15}Si_2Na]^+$ 1347.6811, found 1347.6806.

Digitoxigenin 4″-Di-*O*-*tert*-butyldiphenylsilyl-2″,3″,6″-trideoxy-β-D-*erythro*-hex-2-enopyranosyl-(1→4)-3′-*O*-acetyl-2′,6′-dideoxy-β-D-*ribo*-hexopyranoside (24). To a mixture of **17** (161 mg, 0.20 mmol), **19** (74 mg, 0.14 mmol), and 4 Å MS (200 mg) in dry CH_2Cl_2 (5.0 mL) was added a solution of PPh_3AuOTf in CH_2Cl_2 (0.4 mL, 0.05 M) at rt. After stirring for 2 h, the mixture was filtered through Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (toluene/EtOAc, 7:1) to provide **24** as a white solid (79 mg, 64%): $[\alpha]^{25}_D$ = 41.7 (*c* 2.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.2 Hz, 4 H), 7.44−7.35 (m, 6 H), 5.87 (s, 1 H), 5.74 (d, *J* = 10.4 Hz, 1 H), 5.48 (d, *J* = 2.4 Hz, 1 H), 5.38 (d, *J* = 10.4 Hz, 1 H), 4.99 (d, *J* = 17.6 Hz, 1 H), 4.93 (brs, 1 H), 4.83−4.78 (m, 2 H), 4.04 (brs, 1H), 3.93 (d, *J* = 8.4 Hz, 1 H), 3.81 (m, 2 H), 3.55 (dd, *J* = 9.2, 2.8 Hz, 1 H), 2.77 (m, 1 H), 2.14 (m, 2 H), 2.08 (s, 3 H), 2.00−1.38 (m, 18 H), 1.32 (d, *J* = 5.6 Hz, 3 H), 1.30−1.19 (m, 4 H), 1.15 (d, *J* = 6.0 Hz, 3 H), 1.05 (s, 9 H), 0.92 (s, 3 H), 0.87 (s, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7,

174.5, 170.2, 135.90, 135.86, 134.4, 133.9, 133.1, 129.8, 129.7, 127.7, 127.5, 124.9, 117.5, 95.8, 91.3, 85.5, 75.2, 73.4, 73.0, 70.9, 68.7, 68.2, 66.2, 50.8, 49.6, 41.7, 40.0, 36.3, 36.2, 35.7, 35.1, 33.0, 30.12, 30.10, 26.9, 26.8, 26.60, 26.56, 23.5, 21.3, 21.1, 19.3, 18.3, 18.0, 15.7; HRMS (MALDI) calcd for $C_{53}H_{72}O_{10}SiNa$ $[M + Na]^+$ 919.4787, found 919.4746.

Digitoxin (1). A mixture of **22** (25 mg, 0.019 mmol) and $NH_4F{\cdot}HF$ (412 mg, 7.23 mmol) in a mixed solvent of anhydrous DMF (6 mL) and *N*-methylpyrrolidine (NMP, 3 mL) was kept at 80 °C for 5 days under argon. The solvent was removed under reduced pressure. The residue was diluted with ethyl acetate, which was washed with H_2O and brine, respectively. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (CH_2Cl_2/MeOH, 40:1) to provide **23** (14.5 mg, 91%) as a white solid.

To a solution of diacetate **23** (9.0 mg, 10.6 μmol) in MeOH/H_2O (2.5 mL, 4:1) at room temperature was added LiOH (3 mg, 0.125 mmol). The mixture was stirred for 3 h and was then quenched with addition of the pH = 7.0 buffering solution (10 mL). The mixture was extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (EtOAc) to provide **1** (6.0 mg, 74%) as a white solid: $[\alpha]^{25}_D$ = 16.0 (*c* 0.5, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (s, 1 H), 4.99 (d, *J* = 17.6, 1.8 Hz, 1 H), 4.92–4.79 (m, 4 H), 4.24 (m, 2 H), 4.13 (m, 1 H), 4.02 (m, 1 H), 3.85–3.75 (m, 3 H), 3.31 (m, 1 H), 3.25–3.20 (m, 2 H), 3.04 (s, 1 H), 2.98 (s, 1 H), 2.77 (m, 1H), 2.43 (s, 1 H), 2.17–2.05 (m, 7 H), 1.90–1.36 (m, 22 H), 1.29 (d, *J* = 6.4 Hz, 3 H), 1.23 (d, *J* = 6.0 Hz, 6 H), 0.92 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 174.64, 174.58, 117.6, 98.25, 98.18, 95.4, 85.6, 82.5, 82.2, 73.5, 72.7, 72.5, 69.5, 68.2, 68.1, 66.4, 66.3, 50.9, 49.6, 41.8, 40.1, 37.8, 37.1, 36.7, 36.2, 35.7, 35.1, 33.2, 30.2, 29.7, 26.9, 26.6, 26.5, 23.4, 21.4, 21.1, 18.1, 15.7; HRMS (MALDI) calcd for $C_{41}H_{64}O_{13}Na$ $[M + Na]^+$ 787.4239, found 787.4275.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

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