Zinc Acetate Catalyzed Stereoselective 1,2-*trans*-Glycosylation Using Glycosyl Chlorides

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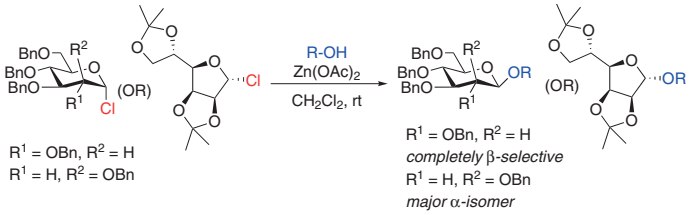

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Abstract We report a strategy for the stereoselective synthesis of 1,2-*trans*-glycosides in the absence of neighboring group participation. The present protocol for the selective glycosylation mainly relies on catalyst control rather than protecting group selection. By using this protocol, several glycosides were prepared. Zinc acetate was found to be the optimal catalyst, providing the desired 1,2-*trans*-glycosides from glucose- and mannose-derived glycosyl halides at room temperature instead of low-temperature conditions.

Key words glycosyl chloride, no neighboring group participation, 1,2-*trans*-glycosylation, zinc acetate

Biological functionality of the carbohydrate molecules is highly dependent on the nature of the glycosidic bonds. Therefore, the stereoselective synthesis of 1,2-*trans*-glycosidic bonds in the absence of anchimeric assistance is one of the most important and challenging reactions in carbohydrate chemistry.[1] Several elegant methodologies have been developed for the synthesis of oligo- and polysaccharides with stereocontrol of the glycosidic linkages;[2] however, most of the developed methodologies rely on neighboring group participation for stereoselective control of the glycosidic linkages,[3] despite having certain limitations. Specifically, such protocols require the introduction of groups such as OAc, OBz, OPiv, OLev, OPicolyl, N-TCA, or N-Troc into the glycoside moiety to direct nucleophilic attack of the coupling partner.[3c] However, the incorporation of such groups is often troublesome, requiring additional steps for the regioselective introduction and removal of the participating group. In addition, this approach can limit substrate scope and often decreases overall efficiency.

Other methods that provide *trans*-glycosylated products in the absence of anchimeric assistance are fluorine-directed,[4] and alkoxymethyl-directed[5] glycosylation. However, most of these methods require several steps to synthesize orthogonally protected monomer building blocks as starting materials. Furthermore, they require excess of metal triflates to convert stable orthoester intermediates into the desired glycosides.[6] Therefore, the development of catalytic stereoselective methods for 1,2-*trans* glycosylation is highly desirable.

Recently, reagent-controlled glycosylation has become an effective strategy for activation of sugar donors using S_N2 displacement reactions with different nucleophiles.[7] Most often, the activation of glycosyl chlorides requires stoichiometric amount of reagents, such as silver(I) or mercury(II) salts.[8] There have been a few reports in which activation of glycosyl chlorides takes place in the absence of anchimeric assistance using $FeCl_3$[9a] and bis-thioureas.[9b] However, the outcome of the stereochemistry was unpredictable and provided mixtures of α- and β-anomers. Separation of these diastereomers is extremely challenging. Another important strategy for 1,2-*trans*-glycosylation is S_N2 type displacement of highly unstable *in situ* generated per-*O*-TMS glycosyl iodides with suitable nucleophile in the presence of a suitable activator.[10] Other than glycosyl halides, recently Bennet et al.[11] reported activation of thioglycosides using aryl(trifluoroethyl)iodonium triflimide as an activator. However, this procedure requires the use of the bulky base 2,4,6-tri-*tert*-butylpyrimidine (TTBP) and a multiple solvent system. Thus, development of general and catalytic methodologies to stereocontrol glycosylations without

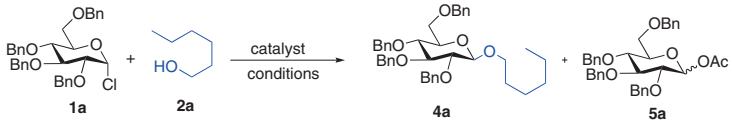
neighboring group participation is highly desirable. The processes outlined herein rely on catalyst control rather than on neighboring group participation. As a prelude to this, we observed that the readily available and stable $Zn(OAc)_2$ catalyst in the absence of base, ligand, and promotors is a useful alternative metal catalyst for the Koenigs–Knorr type glycosylation at room temperature.

Optimization of the reaction parameters was explored using 2,3,4,6-tetra-*O*-benzyl-α-D-glucosyl halide (**1a**)[12] as the glycosyl donor and *n*-hexanol (**2a**) as the acceptor (Table 1). Most of the classical Lewis acids [$ZnCl_2$, $InCl_3$, $Cu(OTf)_2$, $Zn(OTf)_2$] failed to promote the glycosylation reaction at room temperature, while, at higher temperatures, decomposition of the glucosyl halides was observed (entries 1–4). Interestingly, diethylzinc provided the desired 1,2-*trans*-glycoside product in moderate yield (entry 5).

To improve the yield of the desired product **4a**, we further continued our screening with $Zn(OAc)_2$ in toluene, and found that **4a** was obtained in moderate yield along with unwanted glucosyl acetate **5a** (Table 1, entry 6). We then explored the reaction by replacing toluene with DCM. Zinc acetate successfully catalyzed Koenigs–Knorr glycosylation at room temperature in DCM, and provided the desired compound **4a** in 75% yield with complete 1,2-*trans*-selectivity (entry 7). However, with increasing catalyst load, the amount of unwanted byproduct **5a** also increased (entry 8). Anomeric α-participating solvents such as acetonitrile[13] (entry 9) did not change the selectivity, and β-participating solvents such as Et_2O[14] (entry 10) did not alter the selectivity either. Further attempts to improve yield of the desired product with $Pd(OAc)_2$-catalyzed activation of the glycosyl halide was also not successful (entry 11). These observations led us to choose $Zn(OAc)_2$ (50 mol%), in CH_2Cl_2 at room temperature as the optimal conditions (entry 7).

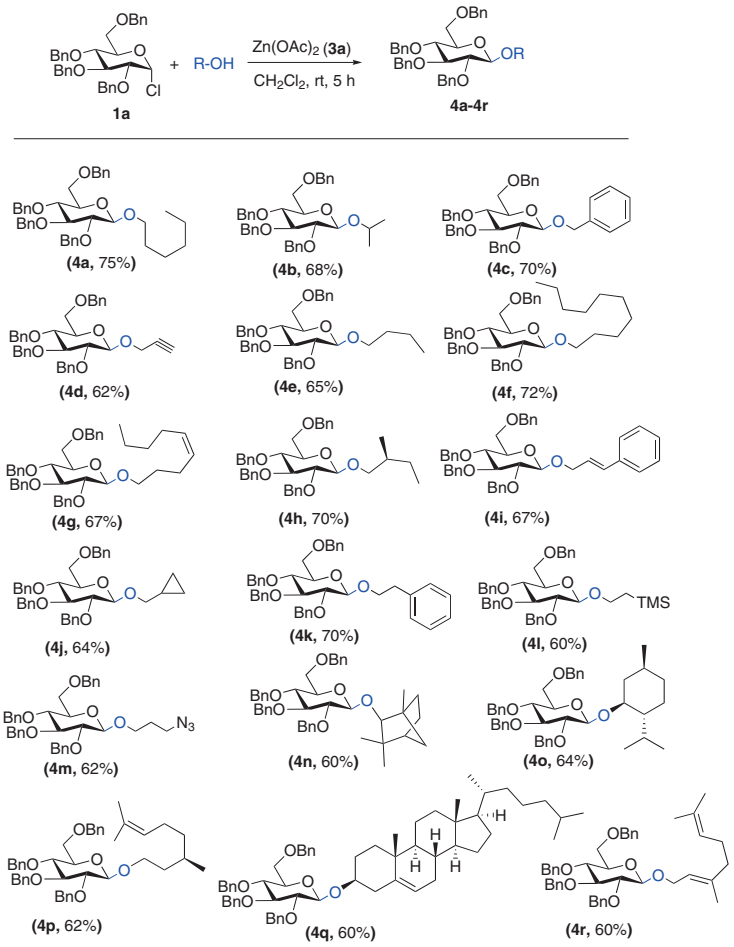
The structure and anomeric selectivity for the formation of the desired glucoside **4a** were confirmed from ^{1}H NMR spectroscopy, where the anomeric proton (H1) appeared at δ = 4.39 ppm (d, *J* = 7.8 Hz, 1H). The corresponding ^{13}C NMR signal for the β-isomer carbon (C1) appeared at δ = 103.7 ppm.[15a] A very diagnostic ^{13}C signal for the α-isomer would appear at δ = 96.8 (C1) ppm.[15b] We next examined the scope and generality of the optimized reagent system with a wide range of nucleophiles. Initially, we explored the utility of the protocol for the synthesis of β-glucosides. Scheme 1 lists the $Zn(OAc)_2$-catalyzed glycosylation reaction between glucosyl donor **1a** and various aglycone *O*-nucleophiles, including primary and secondary alcohols. Various alcohols including *n*-hexanol, geraniol, citronellol, phenyl ethanol, cholesterol, fenchol, and menthol reacted with glucosyl chloride to give the corresponding 1,2-*trans*-glycosides **4a**–**r** in 60–75% yields with complete 1,2-*trans*-selectivity. It is pertinent to mention that the current glycosylation strategy was extended to acid-sensitive

Table 1 Screening of Reaction Condition for Synthesis of *trans*-Glycosides using Glucosyl Chloride **1a** and *n*-Hexanol **2a**[a]



Entry	Reagent (mol%)	Solvent	Temp. (°)	Time (h)	Yield (%) (**4a**/**5a**)[b]
1	$ZnCl_2$(20)	CH_2Cl_2	40	24	NR
2	$InCl_3$(20)	CH_2Cl_2	40	24	NR
3	$Cu(OTf)_2$(20)	CH_2Cl_2	40	24	NR
4	$Zn(OTf)_2$(20)	CH_2Cl_2	40	24	NR
5	Et_2Zn (150)	toluene	60	12	58 (4a)
6	$Zn(OAc)_2$ (20)	toluene	60	12	50:10
7	$Zn(OAc)_2$ (50)	CH_2Cl_2	rt	5	75:10
8	$Zn(OAc)_2$ (100)	CH_2Cl_2	rt	5	78:20
9	$Zn(OAc)_2$ (100)	CH_3CN	rt	12	45:24
10	$Zn(OAc)_2$ (100)	Et_2O/CH_2Cl_2 (1:1)	rt	12	40:20
11	$Pd(OAc)_2$ (10)	CH_2Cl_2	40	24	NR

[a] Reaction conditions: 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride **1a** (1 equiv), *n*-hexanol **2a** (1.2 equiv).
[b] Isolated yields α/β ratio calculated from ^{1}H NMR analysis after column chromatography purification. NR: No Reaction.



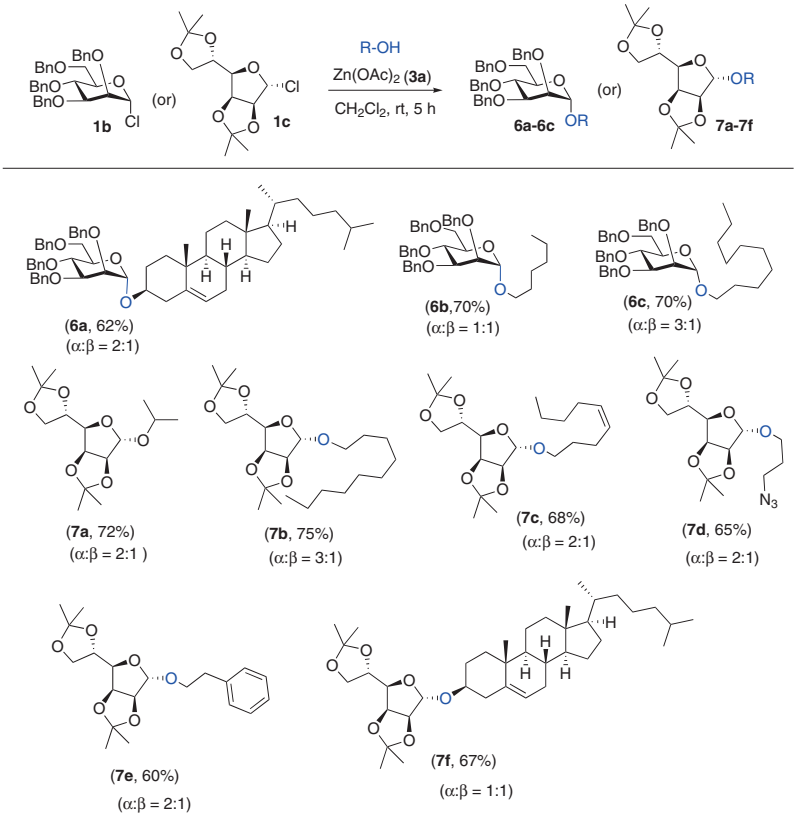
Scheme 1 $Zn(OAc)_2$-catalyzed reaction between glucosyl chlorides and *O*-nucleophiles. *Reagents and conditions*: Glycosyl halide (1 equiv) reacted with corresponding alcohol (1.2 equiv) in the presence of $Zn(OAc)_2$ (50 mol%) at room temperature.

TMS-protected alcohols such as TMS-ethanol (compound **4l**), and the nitrogen containing 3-azido-1-propanol also reacted smoothly to yield desired compound **4m** (62%).

Having obtained excellent results with glucosyl chlorides, we turned our attention to mannopyranoside chloride and mannofuranoside chloride donors (Scheme 2).[11] In this case, the reaction using donors **1b** and **1c** gave the desired mannopyranoside glycosides **6a–c** and mannofuranoside glycosides **7a–f** with good yields, but the stereoselectivity was compromised. We presume that, due to the strong *endo*-anomeric effect in mannose derivatives, competition between S_N2 and S_N1 pathways leads to diastereomeric mixtures with the *trans*-glycosylated product as the major stereoisomer.

The scope of the reaction was further tested with various nucleophiles to yield the desired glycosides in good yields (Scheme 2). Furthermore, a gram-scale synthesis of β-allyl glucopyranoside **4s** was achieved using allyl alcohol and glucosyl chloride in 60% yield (Scheme 3)[20].

The mechanistic pathway for this 1,2-*trans*-glycosylation is not currently conclusive, although a proposed mechanism is depicted in Figure 1. The initial activation of the alcohol acceptor with $Zn(OAc)_2$ produces reaction intermediate **I**, which coordinates with the glucosyl chloride and delivers the nucleophile from the β-face via an S_N2 mechanism, resulting in the 1,2-*trans*-glycosylated product as the sole diastereomer. The catalytic cycle continues by the activation of the glycosyl chloride with intermediate **II**, which leaves $ZnCl_2$ in the reaction medium that reacts further with acetic acid to reform $Zn(OAc)_2$.[16a] In the case of mannopyranosides and furanosides, a mixture of diastereomers with the 1,2-*trans*-glycosylated product as major isomers was observed. This is probably due to the strong *endo*-anomeric effect operating via an S_N1 mechanism.[16b–d]



Scheme 2 $Zn(OAc)_2$-catalyzed reaction between glycosyl chlorides**1b**, **1c** with different alcohols. *Reagents and conditions*: Sugar donor (1 equiv) reacted with the corresponding O-nucleophile (1.2 equiv) in the presence of $Zn(OAc)_2$ (50 mol%) at room temperature.

Scheme 3 Gram-scale synthesis of β-allyl-glucopyranoside (**4s**)

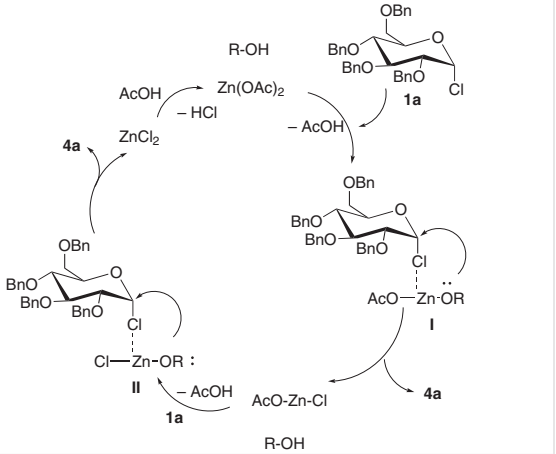


Figure 1 Plausible Zn-catalyzed activation of glucosyl chloride **1a**

In summary, we have developed a 1,2-*trans*-glycosylation protocol of glycosyl chlorides with various O-nucleophiles in the presence of $Zn(OAc)_2$. The protocol described herein is efficient and furnishes the desired 1,2-*trans*-glycosylated products from glucopyranoside, mannopyranoside, and mannofuranoside chlorides. Mechanistic investigations as well as applications of this protocol in the synthesis of glycoconjugates are in progress.

Synthesis of 4a–r, 6a–c, and 7a–f; General Procedure

To a stirred solution of glycosyl chloride **1a–c** (83 mg, 0.15 mmol) in anhydrous CH_2Cl_2 (3 mL) was added the requisite alcohol (0.18 mmol) and $Zn(OAc)_2$ (0.075 mmol) at room temperature, and the resulting solution was stirred at room temperature for 5 h. The reaction mixture was evaporated under reduced pressure, and the residue was purified using silica gel column chromatography (EtOAc/hexane, 2:8).

n-Hexyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4a)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and *n*-hexanol (0.18 mmol, 23 μL).[17] Column chromatography purification using EtOAc/hexane (2:8) gave **4a** as a white solid (β-anomer only, 70 mg, 75%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.24 (m, 18 H), 7.16–7.14 (m, 2 H), 4.97–4.92 (m, 2 H), 4.83–4.80 (m, 2 H), 4.72 (d, *J* = 10.9 Hz, 1 H), 4.63–4.51 (m, 3 H), 4.39 (d, *J* = 7.8 Hz, 1 H), 3.97 (dt, *J* = 9.4, 6.5 Hz, 1 H), 3.74 (d, *J* = 10.7 Hz, 1 H), 3.71–3.61 (m, 2 H), 3.61–3.49 (m, 2 H), 3.47–3.43 (m, 2 H), 1.72–1.60 (m, 2 H), 1.47–1.35 (m, 2 H), 1.33–1.23 (m, 6 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7, 138.5, 138.2, 138.1, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.6, 103.7, 84.7, 82.3, 78.0, 75.7, 75.0, 74.9, 74.8, 73.5, 70.2, 69.0, 31.7, 29.8, 25.9, 22.6, 14.1.

Propargyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4d)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and propargyl alcohol (0.18 mmol, 11 μL).[18] Column chromatography purification using EtOAc/hexane (2:8) gave **4d** as a gum (β-anomer only, 53 mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.18 (m, 18 H), 7.09–7.07 (m, 2 H), 4.91–4.84 (m, 2 H), 4.76–4.69 (m, 2 H), 4.62 (d, *J* = 10.8 Hz, 1 H), 4.55 (dd, *J* = 9.9, 7.5 Hz, 2 H), 4.46 (dd, *J* = 11.5, 3.7 Hz, 2 H), 4.37 (qd, *J* = 15.8, 2.4 Hz, 2 H), 3.70–3.61 (m, 2 H), 3.60–3.51 (m, 2 H), 3.45–3.38 (m, 2 H), 2.39 (t, *J* = 2.4 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.6, 138.4, 138.1, 128.4, 128.3, 127.98, 127.91, 127.8, 127.78, 127.72, 127.67, 127.64, 101.4, 84.6, 82.0, 79.0, 77.6, 75.7, 75.0, 74.9, 74.9, 74.8, 73.5, 68.8, 56.0.

cis-3-Nonene-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4g)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and *cis*-3-nonen-1-ol (0.18 mmol, 31 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4g** as a white solid (β-anomer only, 66 mg, 67%).

Mp 93–95 °C; $[\alpha]_D^{22}$ +2.42 (*c* = 0.019, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.32–7.14 (m, 18 H), 7.13–7.03 (m, 2 H), 5.44–5.29 (m, 2 H), 4.87 (dd, *J* = 16.0, 10.9 Hz, 2 H), 4.72 (dd, *J* = 16.3, 10.9 Hz, 2 H), 4.63 (d, *J* = 11.0 Hz, 1 H), 4.57–4.41 (m, 3 H), 4.32 (t, *J* = 7.6 Hz, 1 H), 3.90 (ddd, *J* = 9.3, 7.4, 6.2 Hz, 1 H), 3.67 (dd, *J* = 10.8, 1.9 Hz, 1 H), 3.63–3.58 (m, 1 H), 3.57–3.48 (m, 2 H), 3.47–3.43 (m, 1 H), 3.39–3.36 (m, 2 H), 2.35 (dt, *J* = 14.8, 7.4 Hz, 1 H), 1.97 (q, *J* = 7.0 Hz, 1 H), 1.29–1.24 (m, 2 H), 1.23–1.19 (m, 4 H), 0.80 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.6, 138.5, 138.2, 138.1, 132.30, 128.39, 128.2, 128.0, 127.9, 127.8, 127.69, 127.63, 125.3, 103.7, 84.7, 82.3, 77.9, 75.7, 75.0, 74.9, 74.8, 73.5, 69.8, 69.0, 31.5, 29.3, 28.0, 27.4, 22.6, 14.1.

HRMS (ESI-TOF): *m*/*z* [M + NH_4]$^+$ calcd. for $C_{43}H_{56}NO_6$: 682.4108; found: 682.4113.

Cyclopropylmethane-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4j)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and cyclopropylmethanol (0.18 mmol, 15 μL).[19] Column chromatography purification using EtOAc/hexane (2:8) gave **4j** as a white solid (β-anomer only, 57 mg, 64%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.16 (m, 18 H), 7.08 (dd, *J* = 7.3, 1.8 Hz, 1 H), 4.93 (d, *J* = 10.9 Hz, 1 H), 4.86 (d, *J* = 10.9 Hz, 1 H), 4.78–4.62 (m, 3 H), 4.53 (d, *J* = 12.2 Hz, 1 H), 4.46 (dd, *J* = 11.5, 7.1 Hz,2 H), 4.37 (d, *J* = 7.8 Hz, 1 H), 3.71 (dd, *J* = 10.4, 6.8 Hz, 1 H), 3.66 (dd, *J* = 10.7, 1.7 Hz, 1 H), 3.59 (dd, *J* = 10.6, 5.2 Hz, 1 H), 3.56 (d, *J* = 9.0 Hz, 1 H), 3.49 (t, *J* = 9.3 Hz, 1 H), 3.42–3.36 (m, 2 H), 3.35–3.31 (m, 2 H), 1.11–1.00 (m, 1 H), 0.52–0.41 (m, 2 H), 0.19 (dd, *J* = 4.8, 0.7 Hz, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.7, 138.6, 138.29, 138.20, 128.4, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6, 103.3, 84.8, 82.3, 78.0, 75.7, 75.0, 74.9, 74.8, 74.6, 73.5, 69.1, 10.6, 3.4, 3.0.

3-Methylbutane-2,3,4,6-tetra-*O*-benzyl-β-D- glucopyranoside (4h)

Prepared by the general procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and 3-methylbutanol (0.18 mmol, 20 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4h** as a yellow viscous liquid (β-anomer only, 64 mg, 70%).

$[\alpha]_D^{22}$ +4.65 (*c* = 0.016, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.23 (m, 18 H), 7.16 (dd, *J* = 7.1, 2.2 Hz, 2 H), 4.98–4.91 (m, 2 H), 4.80 (dd, *J* = 12.8, 11.0 Hz, 2 H), 4.71 (d, *J* = 10.9 Hz, 1 H), 4.67–4.50 (m, 3 H), 4.38 (d, *J* = 7.8 Hz, 1 H), 3.88 (dd, *J* = 9.3, 5.6 Hz, 1 H), 3.75 (dd, *J* = 10.8, 1.8 Hz, 1 H), 3.70–3.61 (m, 2 H), 3.57 (t, *J* = 9.2 Hz, 1 H), 3.50–3.41 (m, 2 H), 3.29 (dd, *J* = 9.3, 7.2 Hz, 1 H), 1.73 (dd, *J* = 13.0, 6.4 Hz, 1 H), 1.48 (ddd, *J* = 13.3, 7.4, 5.7 Hz, 1 H), 1.24–1.16 (m, 1 H), 0.98 (d, *J* = 6.7 Hz, 3 H), 0.91 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.7, 138.5, 138.2, 138.1, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.6, 103.8, 84.8, 82.3, 78.0, 75.7, 75.1, 75.0, 74.9, 73.4, 69.0, 35.1, 29.7, 26.2, 16.9, 11.0.

HRMS (ESI-TOF): *m*/*z* [M + NH_4]$^+$ calcd. for $C_{39}H_{50}NO_6$: 628.3638; found: 628.3642.

Cinnamyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4i)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and cinnamyl alcohol (0.18 mmol, 24 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4i** as a white solid (β-anomer only, 66 mg, 67%).

Mp 92–94 °C; $[\alpha]_D^{22}$ +0.869 (*c* = 0.023, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.12 (m, 23 H), 7.11–7.03 (m, 2 H), 6.57 (d, *J* = 15.9 Hz, 1 H), 6.23 (dt, *J* = 15.9, 6.0 Hz, 1 H), 4.93–4.84 (m, 2 H), 4.78–4.64 (m, 3 H), 4.56–4.48 (m, 3 H), 4.47–4.42 (m, 2 H), 4.25 (ddd, *J* = 12.9, 6.4, 1.2 Hz, 1 H), 3.68 (dd, *J* = 10.7, 1.8 Hz, 1 H), 3.64–3.60 (m, 1 H), 3.60–3.56 (m, 1 H), 3.53–3.50 (m, 1 H), 3.46–3.38 (m, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.6, 138.5, 138.2, 138.1, 136.6, 132.7, 128.6, 128.4, 128.1, 128.0, 127.9, 127.8, 127.6, 126.6, 125.4, 102.7, 84.8, 82.4, 77.9, 75.7, 75.0, 74.9, 73.5, 70.0, 69.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{43}H_{44}NaO_6$: 679.3036; found: 679.3037.

2-(Trimethylsilyl)ethane-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4l)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and 2-(trimethylsilyl)ethanol (0.18 mmol, 26 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4l** as a white solid (β only, 57 mg, 60%).

Mp 102–104 °C; $[\alpha]_D^{22}$ +9.198 (*c* = 0.014, $CHCl_3$).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 18 H), 7.13 (d, *J* = 7.0 Hz, 2 H), 4.94–4.88 (m, 2 H), 4.80–4.74 (m, 2 H), 4.70 (d, *J* = 11.0 Hz, 1 H), 4.59–4.49 (m, 3 H), 4.37 (dd, *J* = 7.8, 1.0 Hz, 1 H), 4.04–3.98 (m, 1 H), 3.72 (d, *J* = 10.7 Hz, 1 H), 3.68–3.50 (m, 4 H), 3.45–3.39 (m, 2 H), 1.10–0.95 (m, 2 H), 0.00 (s, 9 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.06, 140.03, 139.6, 139.5, 129.7, 129.5, 129.3, 129.2, 129.1, 128.9, 104.5, 86.1, 83.8, 79.4, 77.0, 76.4, 76.2, 76.2, 74.8, 70.4, 68.8, 19.9, 0.02.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{39}H_{48}NaSiO_6$: 663.3118; found: 663.3186.

1,3,3-Trimethyl-2-norbornane-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4n)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and fenchol (0.18 mmol, 30 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4n** as a yellow viscous liquid (β-anomer only, 61 mg, 60%).

$[\alpha]_D^{22}$ +92.685 (*c* = 0.0175, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.16 (m, 18 H), 7.16–7.02 (m, 2 H), 4.97 (d, *J* = 10.8 Hz, 1 H), 4.87 (d, *J* = 11.0 Hz, 1 H), 4.73 (dd, *J* = 10.9, 8.3 Hz, 2 H), 4.66 (d, *J* = 10.8 Hz, 1 H), 4.52 (dd, *J* = 12.2, 6.1 Hz, 3 H), 4.22 (d, *J* = 7.7 Hz, 1 H), 3.62 (d, *J* = 2.6 Hz, 2 H), 3.58–3.50 (m, 2 H), 3.43–3.29 (m, 2 H), 3.08 (d, *J* = 1.5 Hz, 1 H), 1.80–1.58 (m, 4 H), 1.36 (dd, *J* = 12.9, 8.7 Hz, 2 H), 1.04 (s, 3 H), 1.02–0.98 (m, 1 H), 0.96 (s, 3 H), 0.85 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.8, 138.5, 138.3, 138.2, 128.4, 128.3, 128.1, 127.7, 127.69, 127.64, 127.5, 127.4, 105.0, 93.7, 84.8, 82.5, 78.0, 75.6, 75.0, 74.5, 73.6, 69.3, 49.2, 48.0, 41.1, 39.1, 29.7, 29.6, 26.3, 26.2, 21.7, 19.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{44}H_{52}NaO_6$: 699.3662; found: 699.3666.

Citronellyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4p)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride (0.15 mmol, 84 mg) and citronellol (0.18 mmol, 34 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **4p** as a white solid (β-anomer only, 63 mg, 62%).

Mp 110–112 °C; $[\alpha]_D^{22}$ +1.25 (*c* = 0.008, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.15 (m, 18 H), 7.08 (dd, *J* = 7.1, 2.2 Hz, 2 H), 5.01 (t, *J* = 7.1 Hz, 1 H), 4.86 (dd, *J* = 10.9, 7.4 Hz, 2 H), 4.72 (dd, *J* = 13.1, 11.0 Hz, 2 H), 4.64 (d, *J* = 11.0 Hz, 1 H), 4.59–4.41 (m, 3 H), 4.31 (d, *J* = 7.8 Hz, 1 H), 3.95 (ddd, *J* = 9.2, 7.7, 5.4 Hz, 1 H), 3.67 (dd, *J* = 10.7, 1.7 Hz, 1 H), 3.63–3.54 (m, 2 H), 3.50–3.45 (m, 2 H), 3.40–3.35 (m, 2 H), 1.91 (m, 2 H), 1.75–1.61 (m, 2 H), 1.58 (s, 3 H), 1.51 (s, 3 H), 1.37–1.35 (m, 3 H), 1.18 (s, 3 H), 1.16–1.05 (m, 1 H), 0.83 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.6, 138.5, 138.2, 138.1, 131.2, 128.3, 128.1, 128.0, 127.9, 127.8, 127.6, 127.6, 124.8, 103.7, 84.7, 82.3, 78.0, 75.7, 75.0, 74.9, 74.8, 73.5, 69.0, 68.3, 37.3, 36.7, 29.7, 29.4, 25.7, 25.5, 19.3, 17.7.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{44}H_{54}NaO_6$: 701.3818; found: 701.3827.

Allyl-2,3,4,6-tetra-*O*-benzyl-β-D-glucopyranoside (4s)

To a stirred solution of glycosyl chloride **1a** (1.68 g, 3 mmol) in anhydrous CH_2Cl_2 (15 mL) was added allyl alcohol (244 μL, 3.6 mmol) and $Zn(OAc)_2$ (328 mg, 1.5 mmol) at room temperature, and the resulting solution was stirred at room temperature for 7 h. The reaction mixture was evaporated under reduced pressure, and the residue was purified using silica gel column chromatography (EtOAc/hexane, 2:8) to obtained the desired product **4s** as a white solid (β-anomer only, 1.04 g, 60%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.29–7.17 (m, 18 H), 7.11–7.04 (m, 2 H), 5.89 (ddd, *J* = 15.8, 10.8, 5.5 Hz, 1 H), 5.27 (dd, *J* = 17.2, 1.5 Hz, 1 H), 5.12 (d, *J* = 10.4 Hz, 1 H), 4.87 (dd, *J* = 17.4, 10.9 Hz, 2 H), 4.72 (dd, *J* = 15.3, 10.9 Hz, 2 H), 4.65 (d, *J* = 10.9 Hz, 1 H), 4.54 (d, *J* = 12.2 Hz, 1 H), 4.51–4.42 (m, 2 H), 4.41–4.32 (m, 2 H), 4.07 (ddd, *J* = 13.0, 5.9, 1.2 Hz, 1 H), 3.67 (dd, *J* = 10.8, 1.6 Hz, 1 H), 3.64–3.47 (m, 3 H), 3.39 (ddd, *J* = 10.8, 6.5, 5.2 Hz, 2 H).

Cholesterol-2,3,4,6-tetra-*O*-Benzyl-α/β-D-mannopyranoside (6a)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl chloride (0.15 mmol, 84 mg) and cholesterol (0.18 mmol, 70 mg). Column chromatography purification using EtOAc/hexane (2:8) gave **6a** as a yellow viscous liquid (α-/β-anomers = 2:1, 84 mg, 62%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 18 H), 7.22–7.12 (m, 2 H), 5.34–5.26 (m, 1 H), 5.01–4.98 (m, 1 H), 4.94–4.85 (m, 1 H), 4.78–4.72 (m, 1 H), 4.69–4.62 (m, 2 H), 4.60–4.56 (m, 1 H), 4.57–4.47 (m, 2 H), 4.04–3.90 (m, 1 H), 3.90–3.77 (m, 2 H), 3.77–3.67 (m, 1 H), 3.55–3.42 (m, 1 H), 2.32–2.25 (m, 2 H), 2.13–1.88 (m,2 H), 1.85–1.78 (m, 2 H), 1.65–1.44 (m, 6 H), 1.42–1.23 (m, 6 H), 1.21–1.05 (m, 6 H), 1.05–0.96 (m, 6 H), 0.92 (dd, *J* = 6.5, 2.7 Hz, 1 H), 0.87 (d, *J* = 1.7 Hz, 3 H), 0.86 (d, *J* = 1.7 Hz, 3 H), 0.68 (d, *J* = 5.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.7, 140.6, 138.9, 130.7, 138.5, 138.2, 128.5, 128.3, 128.2, 128.1, 128.0, 127.86, 127.82, 127.6, 127.5, 127.4, 127.3, 121.8, 99.7, 95.8, 82.5, 80.4, 78.7, 77.2, 76.5, 75.9, 75.2, 75.0, 74.1, 73.8, 73.4, 73.3, 72.6, 72.1, 71.7, 71.4, 69.9, 69.4, 56.8, 56.2, 50.2, 50.1, 42.3, 39.9, 39.8, 39.5, 39.0, 37.3, 37.0, 36.8, 36.7, 36.2, 35.8, 31.9, 29.8, 29.7, 28.3, 28.0, 27.6, 24.3, 23.8, 22.8, 22.6, 21.1, 19.5, 19.4, 18.7, 11.9.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{61}H_{80}NaO_6$: 931.5853; found: 931.6009.

n-Hexyl-2,3,4,6-tetra-*O*-benzyl-α/β-D-mannopyranoside (6b)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl chloride (0.15 mmol, 84 mg) and *n*-hexanol (0.18 mmol, 23 μL). Column chromatography purification using EtOAc/hexane (2:8) gave **6b** as a yellow viscous liquid (α-,β-anomers = 1:1, 65 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 7.7, 1.6 Hz, 2 H), 7.39–7.23 (m, 34 H), 7.19–7.15 (m, 4 H), 4.99 (d, *J* = 12.5 Hz, 1 H), 4.92–4.85 (m, 4 H), 4.73 (d, *J* = 5.2 Hz, 2 H), 4.66 (d, *J* = 12.2 Hz, 1 H), 4.64–4.59 (m, 3 H), 4.58–4.48 (m, 4 H), 4.43 (d, *J* = 11.8 Hz, 1 H), 4.37 (s, 1 H), 4.02–3.94 (m, 2 H), 3.90 (dt, *J* = 4.8, 2.4 Hz, 2 H), 3.86–3.83 (m, 1 H), 3.82–3.69 (m, 6 H), 3.68–3.62 (m, 1 H), 3.50 (dd, *J* = 9.4, 3.0 Hz, 1 H), 3.46–3.42 (m, 2 H), 3.38–3.32 (m, 2 H), 1.68–1.57 (m, 4 H), 1.53–1.44 (m, 3 H), 1.36–1.22 (m, 16 H), 0.89 (m, 8 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.6, 138.5, 138.49, 138.40, 138.2, 128.4, 128.3, 128.1, 127.89, 127.85, 127.80, 127.68, 127.61, 127.5, 127.49, 127.41, 101.7, 97.87, 82.4, 80.3, 75.9, 75.2, 75.09, 75.05, 74.9, 73.7, 73.6, 73.5, 73.3, 72.6, 72.2, 71.8, 71.4, 70.1, 69.8, 69.3, 67.7, 31.7, 31.6, 29.7, 29.4, 25.9, 25.8, 2 2.69, 22.62, 14.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{40}H_{48}NaO_6$: 647.3349; found: 647.3396.

n-Decyl-2,3,4,6-tetra-*O*-benzyl-α/β-D-mannopyranoside (6c)

Prepared by the General Procedure using 2,3,4,6-tetra-*O*-benzyl-α-D-mannopyranosyl chloride (0.15 mmol, 84 mg) and *n*-decanol (0.18 mmol, 36 μL). Column chromatography purification using EtOAc/Hexane (2:8) gave **6c** as a yellow viscous liquid (α-/β-anomers 3:1, 71 mg, 70%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46 (t, *J* = 9.2 Hz, 1 H), 7.39–7.21 (m, 22 H), 7.17–7.15 (m, 2 H), 4.95–4.84 (m, 2 H), 4.73 (q, *J* = 12.5 Hz, 2 H), 4.68–4.59 (m, 3 H), 4.57–4.48 (m, 2 H), 4.47–4.34 (m, 1 H), 4.01–3.88

(m, 2 H), 3.83–3.70 (m, 4 H), 3.67–3.62 (m, 1 H), 3.51–3.48 (m, 1 H), 3.37–3.33 (m, 1 H), 1.64–1.50 (m, 3 H), 1.25 (bs, 19 H), 0.88 (t, *J* = 6.7 Hz, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.6, 138.5, 138.4, 128.4, 128.3, 128.0, 127.9, 127.85, 127.81, 127.68, 127.61, 127.4, 10, 101.7, 97.8, 82.4, 80.4, 76.0, 75.2, 75.0, 74.9, 73.7, 73.6, 73.5, 73.3, 72.6, 72.2, 71.8, 71.4, 70.1, 69.8, 69.3, 67.7, 31.9, 29.6, 29.49, 29.41, 26.2, 22.7, 14.2.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{44}H_{60}NO_6$: 698.4421; found: 698.4411.

n-Decyl-2,3:5,6-di-*O*-isopropylidene-α/β-D-mannofuranoside (7b)

Prepared by the General Procedure using 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (0.15 mmol, 42 mg) and *n*-decanol (0.18 mmol, 36 µL). Column chromatography purification using EtOAc/hexane (2:8) gave **7b** as a yellow viscous liquid (α/β = 3:1, 45 mg, 75%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.90 (s, 1 H), 4.71 (dd, *J* = 5.9, 3.6 Hz, 1 H), 4.51 (d, *J* = 5.9 Hz, 1 H), 4.33 (ddd, *J* = 7.8, 6.3, 4.4 Hz, 1 H), 4.04 (dd, *J* = 8.7, 6.3 Hz, 1 H), 3.96 (dd, *J* = 8.7, 4.4 Hz, 1 H), 3.85 (dd, *J* = 7.8, 3.6 Hz, 1 H), 3.54 (dt, *J* = 9.7, 6.7 Hz, 1 H), 3.30 (dt, *J* = 9.7, 6.6 Hz, 1 H), 1.49–1.45 (m, 2 H), 1.40 (s, 3 H), 1.38 (s, 3 H), 1.31 (s, 3 H), 1.25 (s, 3 H), 1.19 (s, 14 H), 0.81 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 112.6, 112.5, 109.2, 106.2, 106.0, 85.1, 84.8, 80.2, 79.5, 79.2, 73.2, 70.5, 67.5, 67.0, 64.6, 31.9, 30.9, 29.6, 29.5, 29.4, 29.3, 26.9, 26.1, 25.9, 25.2, 24.5, 22.7, 14.1.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{22}H_{40}NaO_6$: 423.2723; found: 423.2681.

cis-3-Nonene-2,3:5,6-di-*O*-isopropylidene-α/β-D-mannofuranoside (7c)

Prepared by the General Procedure using 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (0.15 mmol, 42 mg) and *cis*-3-nonen-1-ol (0.18 mmol, 31 µL). Column chromatography purification using EtOAc/hexane (2:8) gave **7c** as a yellow viscous liquid (α/β = 2:1, 39 mg, 68%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.47–5.32 (m, 1 H), 5.31–5.21 (m, 1 H), 4.92 (s, 1 H), 4.70 (dd, *J* = 5.9, 3.6 Hz, 1 H), 4.51 (d, *J* = 5.9 Hz, 1 H), 4.33 (ddd, *J* = 7.7, 6.3, 4.4 Hz, 1 H), 4.04 (dd, *J* = 8.7, 6.3 Hz, 1 H), 3.96 (dd, *J* = 8.7, 4.4 Hz, 1 H), 3.86 (dd, *J* = 7.8, 3.6 Hz, 1 H), 3.54 (dt, *J* = 9.6, 7.0 Hz, 1 H), 3.33 (dt, *J* = 9.6, 6.9 Hz, 1 H), 2.23 (q, *J* = 7.0 Hz, 2 H), 2.00–1.90 (m, 2 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.31 (s, 3 H), 1.26 (s, 3 H), 1.24–1.15 (m, 3 H), 0.82 (t, *J* = 6.9 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 132.4, 125.1, 112.7, 112.5, 109.2, 106.2, 105.9, 85.1, 84.8, 80.2, 80.1, 79.5, 79.2, 73.1, 70.6, 67.0, 64.6, 31.5, 30.9, 29.7, 29.3, 27.6, 27.3, 26.9, 25.95, 25.92, 25.2, 24.6, 24.5, 22.5, 14.0.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{21}H_{36}NaO_6$: 407.2410; found: 407.2363.

3-Azido-1-propane-2,3:5,6-di-*O*-isopropylidene-α/β-D-mannofuranoside (7d)

Prepared by the General Procedure using 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (0.15 mmol, 42 mg) and 3-azido-1-propanol (0.18 mmol, 17 µL). Column chromatography purification using EtOAc/hexane (2:8) gave **7d** as a yellow viscous liquid (α/β = 2:1, 33 mg, 65%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.91 (s, 1 H), 4.71 (dd, *J* = 5.9, 3.6 Hz, 1 H), 4.52 (d, *J* = 5.9 Hz, 1 H), 4.33 (ddd, *J* = 7.6, 6.3, 4.5 Hz, 1 H), 4.05 (dd, *J* = 8.7, 6.3 Hz, 1 H), 3.97 (dd, *J* = 8.7, 4.5 Hz, 1 H), 3.85 (dd, *J* = 7.6, 3.6 Hz, 1 H), 3.65 (dt, *J* = 10.1, 5.9 Hz, 1 H), 3.40 (dt, *J* = 10.0, 6.1 Hz, 1 H), 3.30 (t, *J* = 6.7 Hz, 2 H), 1.76 (p, *J* = 6.5 Hz, 2 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.31 (s, 3 H), 1.26 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.7, 112.6, 109.2, 106.4, 106.1, 85.0, 84.8, 80.4, 80.1, 79.5, 79.2, 73.1, 70.3, 66.9, 64.3, 64.0, 63.9, 48.4, 48.3, 30.9, 29.7, 28.8, 26.9, 25.97, 25.92, 25.2, 24.6, 24.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{15}H_{25}N_3NaO_6$: 366.1641; found: 366.1590.

Phenylethane-2,3:5,6-di-*O*-isopropylidene-α/β-D-mannofuranoside (7e)

Prepared by the General Procedure using 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (0.15 mmol, 42 mg) and phenylethanol (0.18 mmol, 22 µL). Column chromatography purification using EtOAc/hexane (2:8) gave **7e** as a yellow viscous liquid (α/β = 2:1, 32 mg, 60%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25–7.20 (m, 2 H), 7.14 (dd, *J* = 9.9, 4.5 Hz, 3 H), 4.92 (d, *J* = 7.0 Hz, 1 H), 4.67 (dd, *J* = 5.9, 3.6 Hz, 1 H), 4.50 (d, *J* = 5.9 Hz, 1 H), 4.30 (ddd, *J* = 7.8, 6.3, 4.5 Hz, 1 H), 4.02 (dd, *J* = 8.6, 6.3 Hz, 1 H), 3.89 (dd, *J* = 8.7, 4.5 Hz, 1 H), 3.82–3.67 (m, 2 H), 3.56 (dt, *J* = 9.8, 6.9 Hz, 1 H), 2.79 (t, *J* = 6.9 Hz, 2 H), 1.39 (s, 3 H), 1.37 (s, 3 H), 1.31 (s, 3 H), 1.24 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 138.7, 138.6, 128.8, 128.8, 128.4, 126.3, 112.6, 112.5, 109.2, 106.2, 105.8, 85.0, 84.8, 80.3, 80.1, 79.5, 79.1, 73.1, 70.5, 68.0, 67.9, 67.0, 64.5, 35.9, 30.9, 26.9, 25.9, 25.2, 24.6, 24.5.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{20}H_{28}NaO_6$: 387.1784; found: 387.1725.

Cholesterol-2,3:5,6-di-*O*-isopropylidene-α/β-D-mannofuranoside (7f)

Prepared by the General Procedure using 2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl chloride (0.15 mmol, 42 mg) and cholesterol (0.18 mmol, 70 mg). Column chromatography purification using EtOAc/hexane (2:8) gave **7f** as a yellow viscous liquid (α/β = 1:1, 63 mg, 67%).

^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.27 (d, *J* = 5.1 Hz, 1 H), 5.07 (s, 1 H), 4.72 (dd, *J* = 5.8, 3.6 Hz, 1 H), 4.50 (d, *J* = 5.9 Hz, 1 H), 4.36–4.29 (m, 1 H), 4.04 (dd, *J* = 8.6, 6.4 Hz, 1 H), 3.96 (dd, *J* = 8.7, 4.5 Hz, 1 H), 3.91 (dd, *J* = 7.7, 3.5 Hz, 1 H), 3.41–3.30 (m, 1 H), 2.30–2.13 (m, 2 H), 1.97–1.85 (m, 2 H), 1.85–1.68 (m, 3 H), 1.52–1.35 (m, 12 H), 1.33–1.28 (m, 3 H), 1.30–1.20 (m, 6 H), 1.21–1.13 (m, 2 H), 1.11–0.96 (m,7 H), 0.92 (s, 6 H), 0.84 (t, *J* = 7.5 Hz, 3 H), 0.80 (d, *J* = 2.2 Hz, 3 H), 0.79 (d, *J* = 2.2 Hz, 3 H), 0.60 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.5, 121.9, 112.6, 112.4, 109.2, 104.9, 104.3, 85.4, 85.1, 80.2, 79.6, 79.2, 73.2, 70.5, 67.0, 64.6, 56.7, 56.1, 50.1, 42.3, 40.1, 39.7, 39.5, 37.0, 36.7, 36.2, 35.8, 31.9, 30.9, 28.2, 28.0, 27.9, 27.8, 26.9, 25.96, 25.91, 25.2, 24.6, 24.5, 24.3, 23.8, 22.8, 22.5, 21.0, 19.3, 18.7, 11.8.

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd. for $C_{39}H_{64}NaO_6$: 651.4601; found: 651.4593.

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1941-3801.

References and Notes

(1) (a) Crich, D. *Acc. Chem. Res.* **2010**, *43*, 1144. (b) Seeberger, P. H. *Acc. Chem. Res.* **2015**, *48*, 1450. (c) Galonic, D. P.; Gin, D. Y. *Nature* **2007**, *446*, 1000. (d) Zhu, X.; Schmidt, R. R. *Angew. Chem. Int. Ed.* **2009**, *48*, 1900.

(2) (a) Pornsuriyasak, P.; Demchenko, A. V. *Angew. Chem. Int. Ed.* **2005**, *44*, 7123. (b) Nukada, T.; Berces, A.; Zgierski, M. Z.; Whitfield, D. M. *J. Am. Chem. Soc.* **1998**, *120*, 13291. (c) Singh, G. P.; Watson, A. J. A.; Fairbanks, A. J. *Org. Lett.* **2015**, *17*, 4376. (d) Speciale, G.; Farren-Dai, M.; Shidmoossavee, F. S.; Williams, S. J.; Bennet, A. J. *J. Am. Chem. Soc.* **2016**, *138*, 14012. (e) Elferink, H.; Mensink, R. A.; White, P. B.; Boltje, T. J. *Angew. Chem. Int. Ed.* **2016**, *55*, 11217.

(3) (a) Nukada, T.; Berces, A.; Zgierski, M. Z.; Whitfield, D. M. *J. Am. Chem. Soc.* **1998**, *120*, 13291. (b) Jensen, K. J. *J. Chem. Soc., Perkin Trans. 1* **2002**, 2219. (c) Boltje, T. J.; Buskas, T.; Boons, G.-J. *Nat. Chem.* **2009**, *1*, 611.

(4) Aiguabella, N.; Holland, M. C.; Gilmour, R. *Org. Biomol. Chem.* **2016**, *14*, 5534.

(5) Karak, M.; Joh, Y.; Suenaga, M.; Oishi, T.; Torikai, K. *Org. Lett.* **2019**, *21*, 1221.

(6) (a) Helferich, B.; Zirner, J. *Chem. Ber.* **1962**, *95*, 2604. (b) Bock, K.; Meldal, M. *Acta Chem. Scand., Ser. B* **1983**, *37*, 775. (c) Conrow, R. B.; Bernstein, S. *J. Org. Chem.* **1971**, *36*, 863. (d) Ogawa, T.; Matsui, M. *Carbohydr. Res.* **1976**, *51*, C13. (e) Mukherjee, D.; Ray, P. K.; Chowdhury, U. S. *Tetrahedron* **2001**, *57*, 7701. (f) Li, C.; Liang, H.; Zhang, Z. X.; Wang, Z.; Yu, L.; Liu, H.; An, F.; Wang, S.; Ma, L.; Xue, W. *Tetrahedron* **2018**, *74*, 3963. (g) Igarashi, K.; Honma, T.; Irisawa, J. *Carbohydr. Res.* **1970**, *15*, 329. (h) Hanessian, S.; Banoub, J. *Carbohydr. Res.* **1977**, *53*, C13. (i) Verlhac, P.; Leteux, C.; Toupet, L.; Veyrieres, A. *Carbohydr. Res.* **1996**, *291*, 11. (j) Kaeothip, S.; Pornsuriyasak, P.; Demchenko, A. V. *Tetrahedron Lett.* **2008**, *49*, 1542.

(7) Yao, H.; DuyVu, M.; Liu, X.-W. *Carbohydr. Res.* **2019**, *473*, 72.

(8) (a) Igarashi, K.; Honma, T.; Irisawa, J. *Carbohydr. Res.* **1970**, *15*, 329. (b) Matsuoka, K.; Terabatake, M.; Umino, A.; Esumi, Y.; Hatano, K.; Terunuma, D.; Kuzuhara, H. *Biomacromolecules* **2006**, *7*, 2274.

(9) (a) Geringer, S. A.; Demchenko, A. V. *Org. Biomol. Chem.* **2018**, *16*, 9133. (b) Park, Y.; Harper, K. C.; Kuhl, N.; Kwan, E. E.; Liu, R. Y.; Jacobsen, E. N. *Science* **2017**, *355*, 162.

(10) Kulkarni, S. S.; Gervay-Hague, J. *Org. Lett.* **2008**, *10*, 4739.

(11) Adam Chu, A.-H.; Minciunescu, A.; Bennett, C. S. *Org. Lett.* **2015**, *17*, 6262.

(12) (a) Tatina, M. B.; Khong, D. T.; Judeh, Z. M. A. *Eur. J. Org. Chem.* **2018**, 2208. (b) Boettcher, S.; Matwiejuk, M.; Thiem, J. *Beilstein J. Org. Chem.* **2012**, *8*, 413.

(13) Bracinni, I.; Derouet, C.; Esnault, J.; Penhoat, C. H.; Mallet, J. M.; Michon, V.; Sinay, P. *Carbohydr. Res.* **1993**, *246*, 23.

(14) Wulff, G.; Rohle, G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 157.

(15) (a) Suna, G.; Wua, Y.; Liua, A.; Qiua, S.; Zhanga, W.; Wangb, Z.; Zhang, J. *Synlett* **2018**, *29*, 668. (b) Dong, X.; Chen, L.; Zheng, Z.; Ma, X.; Luo, Z.; Zhang, L. *Chem. Commun.* **2018**, *54*, 8626.

(16) (a) Thorat, B. R.; Gurav, A.; Dalvi, B.; Sawant, A.; Lokhande, V.; Mali, S. N. *Curr. Chin. Chem.* **2021**, *1*, 30. (b) Cai, F.; Wu, B.; Crich, D. *Adv. Carbohydr. Chem. Biochem.* **2009**, *62*, 251. (c) Crich, D.; Sun, S. X. *Tetrahedron* **1998**, *54*, 8321. (d) Crich, D.; Sun, S. X. *J. Am. Chem. Soc.* **1997**, *119*, 11217.

(17) Guo, H.; Si, W.; Li, J.; Yang, G.; Tang, T.; Wang, Z.; Tang, J.; Zhang, J. *Synthesis* **2019**, *51*, 2984.

(18) Geng, Y.; Kumar, A.; Faidallah, H. M.; Albar, H. A.; Mhkalid, I. A.; Schmidt, R. R. *Angew. Chem. Int. Ed.* **2013**, *52*, 10089.

(19) Dubey, A.; Sangwan, R.; Mandal, P. K. *Catal. Commun.* **2019**, *125*, 123.

(20) Guo, H.; Sia, W.; Li, J.; Yang, G.; Tang, T.; Wang, Z.; Tang, J.; Zhang, J. *Synthesis* **2019**, *51*, 2984.