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An easy access to halide ion-catalytic α-glycosylation using carbon tetrabromide and triphenylphosphine as multifunctional reagents

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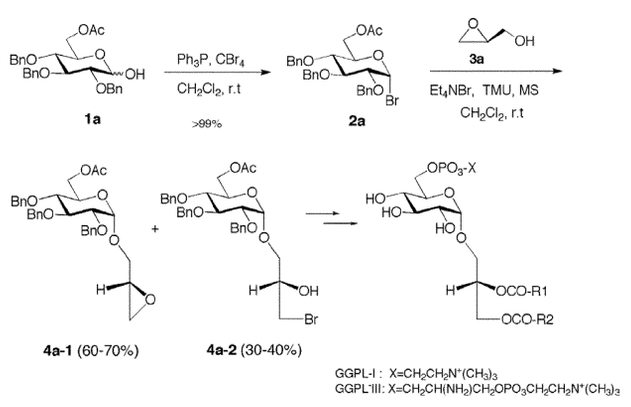
The reaction of a 2-*O*-benzyl-1-hydroxy sugar with CBr_4 and Ph_3P generates a glycosyl bromide *in situ*, which is coupled with an acceptor alcohol in the presence of *N*,*N*-tetramethylurea to afford an α-glycosyl product virtually quantitatively. In a proposed pathway, the reagent combination plays multiple roles such as the generation of a glycosyl donor, the activation of glycosylation, and the dehydration of the reaction system. These roles allow a simple α-glycosylation to be performed without special attention to dehydration. Various α-glycosyl (D-*gluco*-, D-*galacto*- and L-*fuco*-) products including glycosyl glycerols and cholesterols have been prepared with this method.

Introduction

The development of practical 1,2-*cis*-glycosylation methods is a challenging and meaningful objective in bio-organic chemistry.[1] This is because many human oligosaccharide antigens carry the corresponding α-glycosyl linkage which constructs a key determinant structure like α-L-fucopyranoside of sialyl Lewis^X (sLe^X)[2] and α-D-galactopyranoside of globotriaosyl P^k antigens.[3] These glycosyl linkages are expected to possess a high potential applicable to carbohydrate-based medicinal agents. Among representative α-glycosylation methods now available,[4] the halide ion-catalytic method developed by Lemieux *et al.*[5] in the 1970s provides one of the most definitive pathways; the obtained α-selectivity depends scarcely on the reactivity of acceptors, donors, and other reaction conditions. Moreover, the Lemieux method possesses an advantage from an environmental point of view since the glycosylation is performed under mild conditions without heavy metal promoters and strong Lewis acid catalysts.

Also in our stereospecific syntheses of 3-*O*-[6-*O*-phosphorylcholine-α-D-glucopyranosyl]-1,2-diacyl-*sn*-glycerides (GGPL-I and GGPL-III, Scheme 1) as major cell surface glycolipids of *Mycoplasma fermentans*,[6] the halide ion-catalytic method was applied effectively.[7] In practice, however, a synthetic problem, associated with the high instability of 2-*O*-benzylated glycosyl bromides used as α-glycosyl donors, has suspended their large-scale syntheses for biochemical studies. Therefore, we have investigated alternative access to the α-glycosylation pathway.[8] In this article, we propose an advanced halide ion-catalytic α-glycosylation, in which the reagent combination of CBr_4 and Ph_3P, called Appel agents[9] in this paper, is applied effectively.



Scheme 1

Results and discussion

In carbohydrate chemistry, the Appel and analogous phosphine reagents have been applied to the halogeno-dehydroxylation of anomeric[10,11] and primary[12] OH groups. The glycosyl halides prepared in the former have been incorporated within various glycosylation methods. Recently, Khatuntseva *et al.*[11] reported that the reaction of the Appel agents and 2-*O*-benzyl-1-hydroxy-L-fucose derivatives gave the corresponding 1-bromides (α- or β) quantitatively, which were applied without isolation to α-glycosylation in the presence of $Hg(CN)_2$ and $HgBr_2$. Previously,[13] we reported that a 2-*O*-benzyl-1-hydroxy-D-glucose derivative **1a**, treated with the Appel agents, gave an α-glycosyl bromide **2a** exclusively (Scheme 1). The glycosyl donor **2a** was used directly in a halide ion-catalytic α-glycosylation with an acceptor alcohol **3a** in the presence of tetraethylammonium bromide, *N*,*N*-tetramethylurea (TMU),[7] and molecular sieves. The one-pot glycosylation quantitatively gave a mixture of two α-glycosylated products **4a-1** and **4a-2** (*ca.* 7 : 3, the ratio was dependent on the reaction time) both of which are useful for the synthesis of GGPLs and other α-glycosyl-*sn*-glycerolipids. The one-pot reactions reported by Khatuntseva *et al.* and us have proved that the presence of Appel agents and possible side products does not affect the α-glycosylation reaction substantially (Scheme 2 and Table 1, entries 1 and 2).

During additional attempts to optimise the one-pot reaction, we have found two notable facts. The α-glycosylation of **3a** proceeds without $Et_4N^+Br^-$, though the quaternary ammonium salt is essential when using the original method. Furthermore, the reaction, causing little decomposition of the donor **2a**, is very clean even in the absence of molecular sieves (MS) and drying gas. Thus, the observed one-pot α-glycosylation using the Appel agents is apparently different from the authentic one and is expected to provide a simpler α-glycosylation method.

To examine the generality of the observed phenomenon, other primary and secondary acceptor alcohols **3b**–**3e** were subjected to the same reaction in the absence of $Et_4N^+Br^-$ and MS (Scheme 2 and Table 1, Entry 3–7). In every case, the corresponding 1,2-*cis*-glycosides **4b**–**4e** were derived in high yields and with α-selectivity, although the reactions of secondary hydroxyl groups in **3d** and **3e** required prolonged time for completion. Neither a decomposed product **1a** nor a self-condensed product could be observed in the reaction mixture even after the

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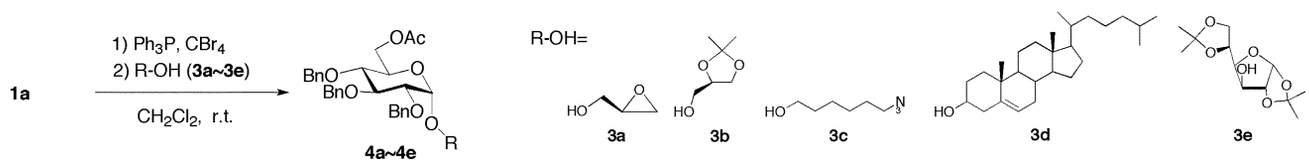
Table 1 One-pot glycosylation[a] of various acceptor alcohols **3a**–**3e** with a donor precursor **1a**

Entry	Acceptors	Conditions	Time/h[c]	Products	Yield (%)[d]	Configuration α : β
1	**3a**	Et_4NBr + TMU[b]	15	**4a-1** + **4a-2**	98[e]	>99 : 1[g]
2	**3d**	Et_4NBr + TMU[b]	53	**4d**	92	98 : 2
3	**3a**	TMU	15	**4a-1** + **4a-2**	98[f]	>99 : 1[g]
4	**3b**	TMU	28	**4b**[h]	96	>99 : 1[g]
5	**3c**	TMU	30	**4c**	92	95 : 5
6	**3d**	TMU	84	**4d**	95	>99 : 1[g]
7	**3e**	TMU	96	**4e**	92	>99 : 1[g]

[a] All reactions were carried out at room temperature with **1a** (200 mg, 0.41 mmol) in CH_2Cl_2 (3 mL), 3 mol equiv. of CBr_4, Ph_3P, and acceptor alcohol, and *N*,*N*-tetramethylurea (TMU, 300 μL). [b] Et_4NBr (1 mol equiv.) was added with TMU. [c] Reaction time/h until the glycosyl bromide donor was completely consumed (TLC analysis) after the addition of acceptor alcohol and TMU. [d] Isolated yields (%) based on the amount of **1a** used for the reaction. [e] Total yields of **4a-1** (63%) and **4a-2** (35%). [f] **4a-1** (65%) and **4a-2** (33%). [g] No β-isomer was detected in ^{1}H-NMR spectra of isolated products (500 MHz, $CDCl_3$). [h] The reaction gave a mixture of 1-*O*- and 3-*O*-α-D-glucosyl-*sn*-glycerols (6 : 5) due to epimerization (ref. 13).

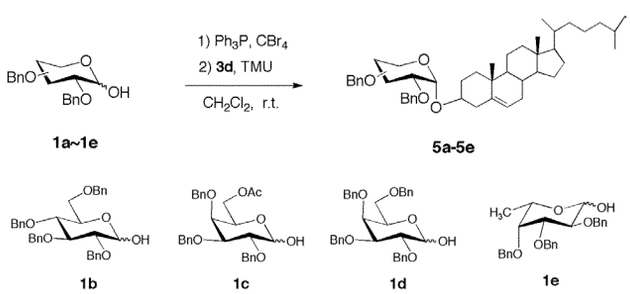


Scheme 2

Table 2 One-pot glycosylation[a] of cholesterol **3d** with various donor precursor **1a**–**1e**

Donors	Time/h	Yield (%)[b]	Configuration (α : β)
1a	84	95	>99 : 1
1b	58	95	90 : 10
1c	72	82	>99 : 1
1d	72	86	88 : 12
1e	24	95	86 : 14

[a] All reactions were carried out at room temperature with **1a**–**1b** (200 mg, 0.41 mmol) in CH_2Cl_2 (3 mL) and 3 mol equiv. of CBr_4, Ph_3P, and cholesterol **3d**, and *N*,*N*-tetramethylurea (TMU, 300 μL). [b] Isolated yields (%) based on the amount of each donor precursor used for the reaction.

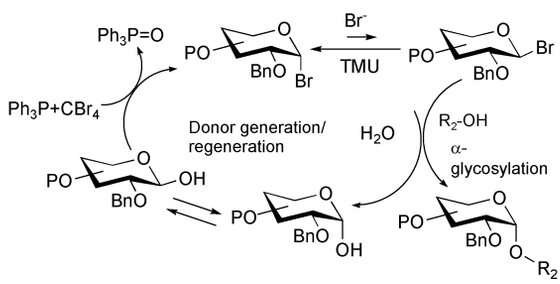


Scheme 3

prolonged reactions of **3d** and **3e**. Though 1,2-*O*-isopropylidene-*sn*-glycerol **3b** underwent a partial epimerization, the α-glycosylation *per se* was nearly perfect. An azido compound **3c** was also useful in spite of the use of a reductive Ph_3P in excess amounts for the donor.

Reactions of other donors **1b**–**1e** with D-*gluco*-, D-*galacto*- and L-*fucose* configurations were also examined with cholesterol **3d** (Scheme 3 and Table 2). All of them showed α-glycosylation in reasonable yields (>80%). There, the donors **1a** and **1c** with 6-*O*-Ac showed higher α-selectivity than **1b** and **1d** with 6-*O*-Bn and **1e** with 6-Me. A similar phenomenon has been observed for 4-*O*-,[11,14] and 6-*O*-acyl[15] donors in variable α-glycosylation reactions and may be explained in terms of a long-range participation effect. On the other hand, the reactivity increased in the reverse order of 6-*O*-Ac < 6-*O*-Bn < 6-Me. Thus, an L-*fucosyl* donor **1e** with 6-Me showed the highest activity with a slight decrease in the α-selectivity.

These experimental data indicated that the present one-pot α-glycosyation is applicable to a wide-range of glycosyl donors and acceptors. Judging from the high α-selectivity, it is obvious that the α-glycosylation conforms to the pathway of a halide ion-catalytic reaction (Scheme 4). That is, α-glycosyl bromide **R_1–Br(α)**, initially produced (as determined by ^{1}H-NMR spectrum, cited in the Experimental section), is located in the equilibrium with β-glycosyl bromide **R_1–Br(β)** in the presence of nucleophilic bromide anions. Then, the highly reactive β-glycosyl bromide permits α-glycosylation in an S_N2 fashion. Our reaction, however, employs the Appel agents with multiple functionalities. First, the reagent converts a 2-*O*-benzyl-1-hydroxy sugar **R_1–OH** to an α-glycosyl bromide **R_1–Br(α)**. The reaction proceeds in the same manner as the dehydroxybromination of primary alcohols. Second, a nucleophilic bromide (Br^-) in the form of triphenylphosphonium salt ($Ph_3P^+CBr_3Br^-$) and HBr–TMU may attain the equilibration of the α- and β-bromides required for the halide ion-catalytic reaction. The existence of such species is suggested from the reaction of **2a** which permitted opening at the epoxide group by a bromide anion. Then, the unstable β-isomer reacts with an acceptor **R_2–OH** to construct an α-glycoside linkage **R_1–O–R_2** more readily than for the α-isomer. Third, the Appel agents work also as dehydrating agents to ensure an anhydrous system.



Scheme 4 Overview of one-pot α-glycosylation with Appel agents.

When water molecules contaminate the reaction, the labile donor **R_1–Br(β)** may be decomposed to **R_1–OH** in competition with the α-glycosylation. In this case, the efficiency of the glycosylation is lowered depending on the extent of water contamination and donor decomposition. In our pathway, the decomposed **R_1–OH** seems reusable as the donor since the Appel agents are added in excess amounts. In a preceding study,[13] we found that 3 mol equiv. of CBr_4 and Ph_3P for a

donor precursor are required to complete the 1-bromination reaction at room temperature, though smaller amounts were reported[11] for similar reactions at elevated temperature. The amount of 3 molar equivalents was also sufficient for the completion of α-glycosylation without MS and special attention to the contamination of water molecules. It is highly probable that the Appel agents can capture water molecules more effectively than what we expect for the conversion of Ph_3P to $Ph_3P{=}O$. CBr_4 may also be associated with the dehydration to finally afford carbon dioxide. Although a precise mechanism for the dehydration as well as the glycosylation pathways is still being investigated, the present reaction using the Appel agents provides a very clean and simple α-glycosylation protocol.

Conclusion

We have demonstrated one-pot halide ion-catalytic α-glycosylation by using the reagent combination of CBr_4 and Ph_3P. The reagent is responsible for the generation, equilibration, and regeneration of glycosyl donors as well as the dehydration of the reaction system. The multiple roles enable us to conduct a simple α-glycosylation conductible at room temperature without paying special attention to the decomposition of the donors by water molecules. Moreover, the glycosylation, conforming to the halide ion-catalytic pathway, shows a near perfect α-selectivity. Mechanistic studies and further applications of the methodology are in progress and will appear elsewhere.

Experimental

General methods

Infrared (IR) spectra were recorded on a JASCO FT/IR-230 Fourier transform infrared spectrometer in the form of KBr disks. All ^{1}H NMR (500 MHz) spectra were recorded using Varian INOVA-500 or Varian Gemini 200 instruments at ambient temperature. ^{1}H chemical shifts are expressed in parts per million (ppm) downfield of tetramethylsilane (TMS). Mass spectra were recorded by a JEOL JMS 700 spectrometer for fast atom bombardment (FAB) spectra. For thin layer chromatography (TLC) analysis, Merck pre-coated TLC plates (silica gel 60 F254, layer thickness 0.25 mm) and Merck TLC aluminium roles (silica gel 60 F254, layer thickness 0.2 mm) were used. Silica gel column chromatography was performed on silica gel 60 (Merck 0.063–0.200 mm and 0.040–0.063 mm). All other chemicals for the synthesis of target compounds were purchased from Tokyo Kasei Kogyo Co., Ltd., Kishida Chemical Co., Ltd., and Sigma-Aldrich Chemical Company, and were used without further purification. 2-*O*-benzyl-1-hydoxy sugars **1a**–**1b** were prepared from the corresponding reducing sugars according to methods in the literature.[11,13,16]

A general protocol for one-pot α-glycosylation. Reactions were carried out in a glass vessel closed with a septum cap. Neither molecular sieves nor drying gas were used. A 2-*O*-benzyl-1-hydroxy sugar (**1a**–**1b**, 200 mg, 0.41 mmol) in 3 mL of CH_2Cl_2 was treated with Ph_3P (3 mol equiv.) and CBr_4 (3 mol equiv.) and stirred for 3 h at room temperature. Then, *N*,*N*-tetramethylurea (TMU, 300 μL) and acceptor alcohol **3a**–**3e** (3 mole equiv.) were added and stirred at room temperature. In all cases, the reaction was continued until the bromide donor was consumed completely as evidenced by TLC analysis. The reaction mixture diluted with $CHCl_3$ was washed with saturated aq. $NaHCO_3$ and aq. NaCl solution and dried (Na_2SO_4) and concentrated. The product was purified by silica gel column chromatography.

6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl bromide (2a). ^{1}H-NMR (500 MHz. $CDCl_3$) δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 6.37 (d, 1H, J = 4.0 Hz, H-1) 5.01, 4.89, 4.83, 4.72, 4.69 and 4.57 (dd, 2H × 3, $-CH_2C_6H_5$), 4.29 (dd, 1H, J = 3.5 and 12.0 Hz, H-6$_S$), 4.28 (dd, 1H, J = 2.5 and 12.0 Hz, H-6$_R$), 4.12 (m, 1H, H-5), 4.06 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.58 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 3.52 (dd, 1H, J = 4.0 and 9.5 Hz, H-2), 2.01 (s, 3H, –Ac); FAB-MS: m/z 577 [M + Na$^+$].

(*S*)-3-*O*-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)glycidol (4a-1). IR (KBr film) ν/cm^{-1}; 3029, 2873, 1741, 1454, 1363, 1238, 1072, 1031, 750, 700. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 4.55–5.02 (dd, 2H × 3, $CH_2C_6H_5$), 4.87 (d, 1H, J = 4.0 Hz, H-1), 4.26 (dd, 1H, J = 4.0 and 12.0 Hz, H-6$_{proR}$), 4.22 (dd, 1H, J = 2.5 and 12.0 Hz, H-6$_{proS}$), 4.02 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.88 (m, 1H, H-5), 3.76 (dd, 1H, J = 3.5 and 12.0 Hz, glycidol H-3$_{proR}$), 3.48 (dd, 1H, J = 6.0 and 12.0 Hz, glycidol H-3$_{proS}$), 3.53 (dd, 1H J = 3.5 and 9.5 Hz, H-2), 3.48 (dd, 1H, J = 9.0 and 9.5 Hz, H-4), 3.20 (m, 1H, glycidol H-2), 2.57 and 2.78 (dd, 1H × 2, J = 4.0 and J = 5.0, J = 3.0 and 5.0 Hz, glycidol H-1$_{proR}$ or H-1$_{proS}$), 1.99 (s, 3H, –Ac). HRMS (FAB); m/z calcd for $C_{32}H_{37}O_8BrNa$ [M + Na$^+$] 571.2308; found 571.2285.

3-*O*-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-1-bromo-1-deoxy-*sn*-glycerol (4a-2). IR (KBr film) ν/cm^{-1}; 3488, 3062, 3029, 2915, 1741, 1496, 1454, 1363, 1330, 1238, 1159, 1072, 1031, 912, 852, 740, 700. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 4.55–5.00 (dd, 2H × 3, $-CH_2C_6H_5$), 4.75 (d, 1H, J = 3.5 Hz, H-1), 4.25 (m, 2H, H-6), 4.02 (m, 1H, glycerol H-2), 3.97 (t, 1H, J = 9.5 and 9.5 Hz, H-3), 3.86 (m, 1H, H-5), 3.80 (dd, 1H, J = 4.0 and 10.5 Hz, glycerol H-3$_{proR}$), 3.55 (dd, 1H J = 3.5 and 9.5 Hz, H-2), 3.52 (dd, 1H, J = 5.5 and 10.5 Hz, glycerol H-3$_{proS}$), 3.52 and 2.91 (m and d, 1H × 2, J = 5.5 Hz (d), glycerol H-1$_{proR}$ or H-1$_{proS}$), 3.47 (dd, 1H, J = 9.5 and 10.0 Hz, H-4), 2.17 (s, 3H, –Ac). ^{13}C-NMR (500MHz, $CDCl_3$); δ_C 170.4, 165.4, 138.3. HRMS (FAB): m/z calcd for $C_{32}H_{37}O_8BrNa$ [M + Na$^+$] 653.1555; found 653.1545.

3-*O*-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-1,2-*O*-isopropylidene-*sn*-glycerol (4b) and *sn*-2,3 isomer. IR (KBr film) ν/cm^{-1} 3031, 2985, 2929, 2877, 1741, 1496, 1454, 1369, 1330, 1238, 1157, 1072, 1031, 921, 840, 738, 700; ^{1}H-NMR (500 MHz, $CDCl_3$): δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 4.56–4.99 (dd, 2H × 3, $-CH_2C_6H_5$), 4.83 (d, 1H, J = 3.5 Hz, H-1), 4.35 (t, 1H, J = 5.5 and 6.5 Hz, glycerol H-2), 4.20–4.28 (dd, 1H × 2 H-6), 3.98 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.85 (m, 1H, H-5), 4.07 and 3.74 (dd, 1H × 2, J = 8.5 and 6.5, J = 6.0 and 8.0 Hz, glycerol H-3$_{proR}$ or H-3$_{proS}$), 3.60 and 3.55 (dd, 2H, J = 6.0 and 10.5, J = 6.5 and 10.5 Hz, glycerol H-1$_{proR}$ or H-1$_{proS}$), 3.54 (dd, 1H, J = 3.5 and 9.5 Hz, H-2), 3.47 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 2.02 (s, 3H, –Ac), 1.42 and 1.36 (s, 3H × 2, isopropyl). An *sn*-2,3-glycerol isomer: δ_H 7.40–7.23 (m, 15H, $-CH_2C_6H_5$), 4.56–4.99 (dd, 2H × 3, $-CH_2C_6H_5$), 4.74 (d, 1H, J = 3.5 Hz, H-1), 4.32 (t, 1H, J = 5.5 and 6.5 Hz, glycerol H-2), 4.20–4.28 (dd, 1H × 2, H-6), 4.00 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.88 (m, 1H, H-5), 4.07 and 3.78 (dd, 1H × 2, J = 6.5 and 8.5, J = 5.5 and J = 8.0 Hz, glycerol H-3$_{proR}$ or H-3$_{proS}$), 3.69 and 3.42 (dd, 1H × 2, J = 6.0 and 10.5, J = 6.5 and 10.5 Hz, glycerol H-1$_{proR}$ or H-1$_{proS}$), 3.54 (dd, 1H, J = 3.5 and 9.5 Hz, H-2), 3.48 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 2.02 (s, 3H, –Ac), 1.41 and 1.35 (s, 3H × 2, isopropyl); HRMS (FAB): m/z calcd for $C_{35}H_{42}O_9Na$ [M + Na$^+$] 629.2727; found 629.2704.

6-Azidohexyl 6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (4c). IR (KBr film) ν/cm^{-1} 3031, 2935, 2865, 2094, 1743, 1496, 1454, 1363, 1236, 1157, 1074, 1031, 910, 734, 698; ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 4.55–5.02 (dd, 2H × 3, $-CH_2C_6H_5$), 4.72 (d, 1H, J = 3.5 Hz, H-1), 4.27 (dd, 1H, J = 4.0 and 12.0 Hz, H-6$_S$), 4.23 (dd, 1H, J = 2.5 and 12.0 Hz, H-6$_R$), 4.01 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.83 (m, 1H, H-5), 3.61 and 3.40 (dt, 1H × 2, $-OCH_2CH_2(CH_2)_2CH_2CH_2N_3$), 3.53 (dd, 1H, J = 3.5 and 9.5

Hz, H-2), 3.48 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 3.24 (t, 2H, J = 7.0 and 7.0 Hz, $-OCH_2CH_2(CH_2)_2CH_2CH_2N_3$), 2.02 (s, 3H, –Ac), 1.59 and 1.66 (br, 2H × 2, $-OCH_2CH_2(CH_2)_2CH_2CH_2N_3$), 1.39 (br, 2H × 2, $-OCH_2CH_2(CH_2)_2CH_2CH_2N_3$), 4.40 (d, 1H, J = 8.0 Hz, H-1β); HRMS (FAB): m/z calcd for $C_{35}H_{43}O_7N_3Na$ [M + Na^+] 640.2999; found 640.2988.

***O*-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-cholesterol (4d).** IR (KBr film) ν/cm^{-1}; 3031, 2938, 2867, 1741, 1457, 1369, 1238, 1155, 1072, 1031, 742, 700. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 5.32 (m, 1H, cholesterol H-6), 4.54–5.03 (dd, 2H × 3, $-CH_2C_6H_5$), 4.89 (d, 1H, J = 4.0 Hz, H-1), 4.25 (dd × 2, 2H, H-$6_{S\ and\ R}$), 4.03 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.96 (m, 1H, H-5), 3.53 (dd, 1H, J = 4.0 and 9.5 Hz, H-2), 3.47 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 3.43 (m, 1H, cholesterol H-3). HRMS (FAB): m/z calcd for $C_{56}H_{76}O_7Na$ [M+Na^+] 883.5489; found 883.5425.

3-*O*-(6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-glucopyranosyl)-1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose (4e). IR (KBr film) ν/cm^{-1}; 3031, 2987, 2933, 1741, 1496, 1454, 1373, 1309, 1236, 1162, 1074, 1029, 912, 848, 781, 736, 698. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 5.83 (d, 1H, J = 3.5 Hz, H-1′), 5.21 (d, 1H, J = 3.5 Hz, H-1), 4.58–5.00 (dd, 2H × 3, $-CH_2C_6H_5$), 4.75 (t, 1H, J = 4.0 and 4.5 Hz, H-2′), 4.23–4.26 (m, 2H × 2, H-$6_{S\ and\ R}$ and H-$6'_{S\ and\ R}$), 4.14 (m, 1H, H-5), 4.08 (dd, 1H, J = 8.5 and 9.0 Hz, H-3′), 4.08 (m, 1H, H-5′), 4.00 (dd, 1H, J = 6.0 and 8.5 Hz, H-4′), 3.98 (t, 1H, J = 9.0 and 9.0 Hz, H-3), 3.58 (dd, 1H J = 4.0 and 9.5 Hz, H-2), 3.50 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 2.00 (s, 3H, –Ac), 1.32, 1.36, 1.45 and 1.56 (s, 3H × 4, isopropyl). HRMS (FAB); m/z calcd for $C_{41}H_{50}O_{12}Na$ [M + Na^+] 757.3200; found 757.3192.

***O*-[2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl]cholesterol (5b).** IR (KBr film) ν/cm^{-1} 3029, 2935, 2933, 1718, 1454, 1361, 1101, 1060, 740, 696; ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 7.40–7.23 (m, 5H × 4, $-CH_2C_6H_5$), 5.28 (m, 1H, cholesterol H-6), 4.44–5.01 (dd, 2H × 4, $-CH_2C_6H_5$), 4.93 (d, 1H, J = 3.5 Hz, H-1), 4.00 (dd, 1H, J = 9.0 and 9.5 Hz, H-3), 3.87 (m, 1H, H-5), 3.74 and 3.64 (dd × 2, 2H, H-$6_{S\ and\ R}$), 3.64 (dd, 1H, J = 9.0 and 10.0 Hz, H-4), 3.35 (dd, 1H, J = 3.5 and 9.5 Hz, H-2), 3.46 (m, 1H, cholesterol H-3); HRMS (FAB): m/z calcd for $C_{61}H_{80}O_6Na$ [M + Na^+] 931.5853; found 931.5820.

***O*-[6-*O*-Acetyl-2,3,4-tri-*O*-benzyl-α-D-galactopyranosyl]-cholesterol (5c).** IR (KBr film) ν/cm^{-1}; 3029, 2938, 1743, 1457, 1369, 1236, 1132, 1099, 1035, 736, 698. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 5.32 (m, 1H, cholesterol H-6), 4.60–4.98 (dd, 2H × 3, $-CH_2C_6H_5$), 4.98 (d, 1H, J = 4.0 Hz, H-1), 4.10 and 4.04 (dd × 2, 2H, H-$6_{S\ and\ R}$), 4.03 (dd, 1H, J = 3.5 and 10.0 Hz, H-2), 4.02 (m, 1H, H-5), 3.95 (dd, 1H, J = 2.5 and 10.0 Hz, H-3), 3.88 (br d, 1H, J = 2.5, H-4), 3.43 (m, 1H, cholesterol H-3). HRMS (FAB); m/z calcd for $C_{56}H_{76}O_7Na$ [M + Na^+] 883.5489; found 883.5427.

***O*-[2,3,4,6-Tetra-*O*-benzyl-α-D-galactopyranosyl]cholesterol (5d).** IR (KBr film) ν/cm^{-1}; 3029, 2937, 2933, 1720, 1457, 1454, 1367, 1101, 1033, 736, 698. ^{1}H-NMR (500 MHz, $CDCl_3$); δ_H 7.40–7.23 (m, 5H × 4, $-CH_2C_6H_5$), 5.25 (m, 1H, cholesterol H-6), 4.39–4.96 (dd, 2H × 4, $-CH_2C_6H_5$), 4.98 (d, 1H, J = 3.5 Hz, H-1), 4.05 (br t, 1H, J = 6.5 and 6.5 Hz, H-5), 4.01 (dd, 1H, J = 4.0 and 10.0 Hz, H-2), 3.98 (m, 1H, H-4), 3.95 (dd, 1H, J = 3.0 and 10.0 Hz, H-3), 3.53 (dd × 2, 2H, H-$6_{S\ and\ R}$), 3.46 (m, 1H, cholesterol H-3). HRMS (FAB); m/z calcd for $C_{61}H_{80}O_6Na$ [M + Na^+] 931.5853; found 931.5798.

***O*-[2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl]cholesterol (5e).** IR (KBr film) ν/cm^{-1} 3062, 3031, 2937, 2933, 1724, 1457, 1454, 1369, 1101, 1037, 738, 700; ^{1}H-NMR (500 MHz, $CDCl_3$) δ_H 7.40–7.23 (m, 5H × 3, $-CH_2C_6H_5$), 5.34 (m, 1H, cholesterol H-6), 4.64–4.99 (dd, 2H × 3, $-CH_2C_6H_5$), 4.95 (d, 1H, J = 4.0 Hz, H-1), 4.02 (dd, 1H, J = 3.5 and 10.0 Hz, H-2), 3.95 (m, 1H, H-5), 3.96 (m, 1H, H-5), 3.94 (dd, 1H, J = 3.0 and 10.0 Hz, H-3), 3.66 (br d, 1H, J = 2.0 Hz, H-4), 3.44 (m, 1H, cholesterol H-3), 1.08 (d, 2H, J = 6.5 Hz, H-6). HRMS (FAB); m/z calcd for $C_{54}H_{74}O_5Na$ [M + Na^+] 825.5434; found 825.5402.

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