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High-Yield Syntheses of Tetra-*O*-benzyl-α-*D*-glucopyranosyl bromide and Tetra-*O*-pivaloyl-α-*D*-glucopyranosyl bromide and their Advantage in the *Koenigs-Knorr* Reaction

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Summary. Several improved approaches for the preparation of tetra-*O*-benzyl-α-*D*-glucopyranosyl bromide and tetra-*O*-pivaloyl-α-*D*-glucopyranosyl bromide are discussed. The importance of these compounds, which are useful glycosyl donors, was demonstrated by successful preparation of cholesteryl glucopyranosides in an almost neutral medium without the formation of orthoesters. In addition, accurate ^{1}H and ^{13}C NMR resonance assignments of the synthesized cholesteryl glycosides were performed by 2D NMR spectroscopy.

Keywords. *Koenigs-Knorr* reaction; Glycosidation; Orthoester; Cholesteryl glycosides.

Introduction

The well-established *Koenigs-Knorr* glycosylation [1–3] (reaction between a glycosyl halide and an alcohol) is still one of the most commonly used methods for the generation of glycosidic bonds [4, 5]. Due to the formation of orthoesters in a side reaction, the yields for this glycosylation are frequently low [6–9], especially when acid-sensitive compounds are coupled in the presence of proton acceptors [10, 11]. Orthoester formation can be avoided by replacing the traditionally used glycosyl donor **1** with the sterically hindered tetrapivaloate **2** [12, 13] or with the tetrabenzyl-derivative **3** [14]. However, the lack of an easy and rapid synthesis of these advanced glycosyl bromides has restricted until now a broader application.

Here we discuss several simplified strategies for the efficient preparation of **2** and **3** in high yields. The improved activity of these glycosyl donors was demonstrated using neutral reaction conditions.

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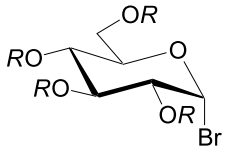

1: R = CO-CH_3
2: R = CO-$C(CH_3)_3$
3: R = CH_2-C_6H_5

Formulae 1

Results and Discussion

Preparation of Tetra-O-pivaloyl-α-D-glucopyranosyl Bromide (***2***)

A number of naturally occurring glycosides have β-glycosidic bonds. The selective formation of these 1,2-*trans* glycosides requires the assistance of a neighbouring participating group, generally an acyl moiety [15]. In contrast to the easily and rapidly available acetobromoglucose (**1**) [16–22] there is only one single method reported for the synthesis of the tetrapivaloate **2**, which provides the desired bromide in a range between 60 and 65% [12, 23].

We describe here an efficient preparation of **2** under very mild conditions in good to excellent yields (76–97%). In our approach, several *Lewis* acids such as $BiBr_3$, $ZnBr_2$, or $CoBr_2$ were employed to convert the readily available pentapivaloate **4** [12] in the presence of Me_3SiBr into the corresponding glycosyl bromide at room temperature. The reaction proceeded most favourable using $BiBr_3$ (97%). The workup is easy and in most cases further purification is not necessary. The NMR-data agree with those partially reported in Ref. [12]. In each case only the α-anomer of the glycosyl bromide is formed.

Preparation of Tetra-O-benzyl-α-D-glucopyranosyl Bromide (***3***)

In natural compounds, 1,2-*cis* glycosyl residues (α-glycosides of *D*-glucose, *D*-galactose, *etc.*) are of almost the same relevance as their 1,2-*trans* counterparts. The stereoselective synthesis of 1,2-*cis* glycosides requires the use of a glycosyl donor bearing a non-participating group at C-2. Such a building block is the commonly used perbenzylated glycosyl bromide **3**, however, this useful reagent is only available *via* multistep reactions [14, 24–26]. Our approach enables its synthesis by a shorter route, starting from the readily available precursors **5** [27], **6** [28–30], or **7** [31]. For the preparation of **6**, we developed a superior route *via Fischer*'s glycosylation and subsequent benzylation.

Generally, methyl and isopropyl glycosides can be converted directly to the corresponding glycosyl bromides [32, 33]. However, the application of these procedures to **5** and **6** afforded only decomposition products. Therefore, we attempted an alternative approach *via* the 2,3,4,6-tetra-*O*-benzyl-*D*-glucopyranoside (**8**) (Fig. 1). This key compound is accessible by acidic hydrolysis of its methyl glycoside **5** [27] or by regioselective debenzylation of **7** using Pd–Al_2O_3 and ammonium formate [34]. Acidic hydrolysis of the benzyl glycoside

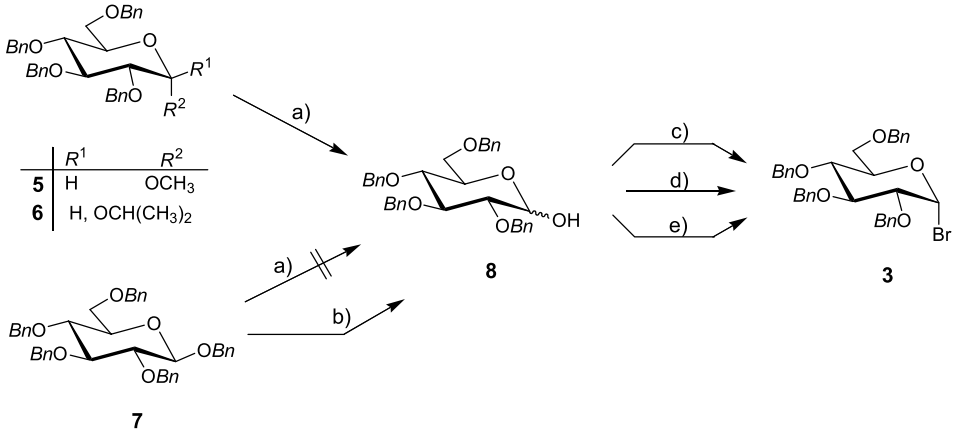

Fig. 1. Preparation of glycosyl bromide **3**; reagents and conditions: (a) HO*Ac*–H_2SO_4, 100°C, 12–24 h, 56% from **5**, 74% from **6**, 17% from **7**; (b) 10% Pd–Al_2O_3, ammonium formate, *Me*OH, rt, 3 h, 46%; (c) Et_3SiH, $PdCl_2$, CBr_4, CH_2Cl_2, rt, 2 h, 44%; (d) $CoBr_2$, Me_3SiBr, CH_2Cl_2, rt, 1 h, 92%; (e) oxalyl bromide, CH_2Cl_2, rt, 2.5 h, 98%

7 gave only poor yields of **8**, but when the same reaction conditions were applied to the isopropyl glycoside **6**, the best yields (74%) of hemiacetal **8** were obtained.

Hemiacetals and 1-*O*-acetates have been converted into the corresponding glycosyl bromides with a $Et_3SiH/PdCl_2/CBr_4$ system [20]. However, treatment of **8** as described provided the desired glycosyl bromide **3** only in moderate yields, probably due to decomposition during the essential purification step. In contrast, the glycosyl bromide was generated in high yields by treatment of **8** with Me_3SiBr and $CoBr_2$ following the instructions of *Koto et al.* [35]. The proposed but tedious conversion of **8** to the pure α-anomer prior to the bromination turned out to be dispensable. It is remarkable that no formation of the bromide was observed when $CoBr_2$ was replaced by $BiBr_3$ (which was used for the preparation of **2**). The superior method for the transformation of the hemiacetal to the glycosyl bromide was a slightly modified procedure of *Spohr et al.* [36]. Compound **8** was smoothly converted to the corresponding bromide in the presence of oxalyl bromide in nearly quantitative yield and high purity, so that filtration and evaporation of the solvent gave the bromide ready for immediate use. The ^1H NMR spectrum of the product was identical with that specified in Ref. [20].

Glycosylation of Cholesterol

In spite of considerable progress in carbohydrate chemistry in the past few years, the efficient partial synthetic formation of *O*-glycosidic bonds between carbohydrates and naturally occurring terpenes and steroids still causes many difficulties [37]. Reasons are the low reactivity of the secondary alcohol functions and excessive orthoester formation during glycosidation of acid-sensitive aglycons.

We demonstrate here the advantage of the glycosyl donors **2** and **3** compared to the frequently used acetobromoglucose (**1**) by coupling with the secondary alcohol

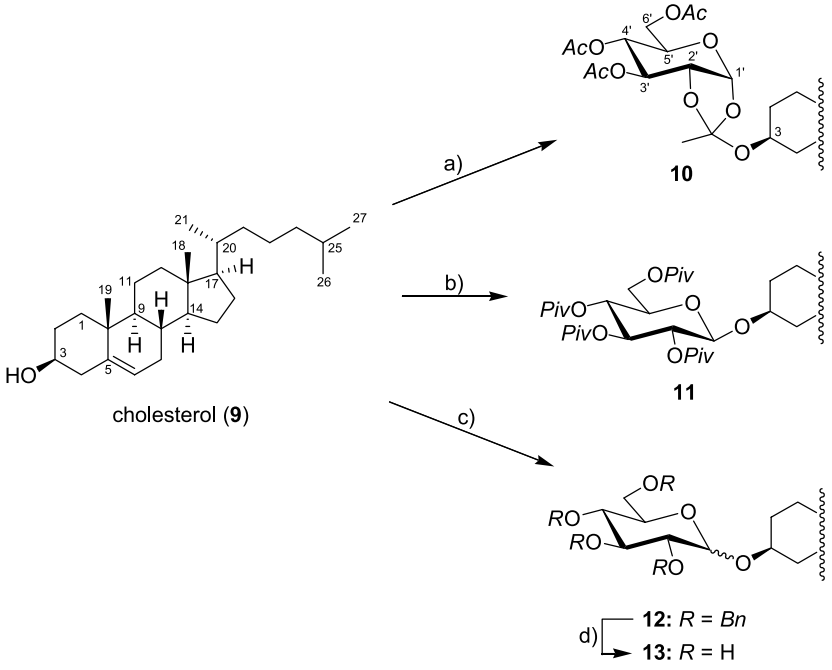

Fig. 2. Preparation of cholesteryl glycosides; reagents and conditions: (a) aceto-bromoglucose, AgO*Tf*, *TMU*, CH_2Cl_2, 4 Å molecular sieve, $-20°C \rightarrow$ rt, 16 h, 29%; (b) pivalobromoglucose, AgO*Tf*, *TMU*, CH_2Cl_2, 4 Å molecular sieve, $-20°C \rightarrow$ rt, 16 h, 58%; (c) benzylbromoglucose, AgO*Tf*, *TMU*, CH_2Cl_2, 4 Å molecular sieve, $-20°C \rightarrow$ rt, 16 h, 67%; (d) 20% $Pd(OH)_2/C$, cyclohexene, *Et*OH, reflux, 5 h, 83%

group of cholesterol (Fig. 2). Based on preliminary results, we chose as a standard glycosylation procedure a very mild coupling method mediated by silver triflate (AgO*Tf*) in the presence of tetramethyl urea (*TMU*) as acid scavenger [38].

In agreement with the findings of *Garegg et al.* [3], the reaction of cholesterol with **1** afforded almost exclusively the orthoester **10**. In contrast, glycosylation of the same aglycone with **2** resulted exclusively in the formation of the β-*D*-glucoside **11** in good yield. When glycosylation was performed with **3**, the cholesteryl 2,3,4,6-tetra-*O*-benzyl-*D*-glucopyranoside (**12**) was obtained in 67% yield as a mixture of α- and β-anomers (α:$\beta = 3$:2). Higher amounts of the α-anomer were obtained using other reaction conditions, solvents, or promoter systems [39]. By utilizing the glycosyl donors **2** and **3** no orthoester was obtained.

In addition, this publication describes for the first time the complete and consistent NMR resonance assignments of the cholesteryl glycosides **10**–**13** using high-field NMR spectroscopy. This will facilitate the structural characterization of other derivatives in future work. The unprotected derivative **13** was synthesized by hydrogenolysis of **12** *via* catalytic transfer hydrogenation, using 20% palladium hydroxide on carbon with cyclohexene as the hydrogen source [40]. The 5,6-double bond of cholesterol was not affected under these conditions.

In conclusion, several simplified and high yield syntheses of the glycosyl bromides **2** and **3** were accomplished. These glycosyl donors generate a glycosidic linkage without orthoester formation as side reaction and are, therefore, widely

applicable for rapid synthesis of new pharmacological active compounds. The different protecting groups make these compounds useful precursors for the systematic formation of α- and β-glucosides under very mild conditions.

Experimental

Melting points were obtained on a digital melting point apparatus Büchi 535. The optical rotations were determined on a polarimeter 241 MC (Perkin Elmer). The IR spectra were recorded on an infrared spectrometer system 2000 FT (Perkin Elmer). The UV/VIS values were recorded on a UV-160A UV-visible recording spectrophotometer (Shimadzu). The NMR spectra were measured on a Varian Unity Inova 400 (^{1}H at 400 MHz, ^{13}C at 100 MHz) and a Varian Unity Inova 600 (^{1}H at 600 MHz, ^{13}C at 150 MHz) instrument at 24°C. The Me_4Si resonance was used as internal standard. ^{1}H- and ^{13}C-resonances were assigned using 1D proton and carbon experiments as well as 2D DQF-COSY, HSQC, HSQC-TOCSY, and HMBC techniques. The latter were optimized for 7 Hz heteronuclear coupling constant. Spin systems were identified in DQF-COSY, HSQC, and HSQC-TOCSY spectra. Subsequently, these spin systems and the quaternary carbons were connected by correlation found in the HMBC experiment. ^{1}H- and ^{13}C-resonances are numbered as given in the formulae. Carbon shift values marked with an asterisk are interchangeable. Mass spectra (ESI-MS) were recorded on a Finnigan LCQ Deca XP Plus ion trap mass spectrometer configured for positive ionisation. TLC was carried out on Merck DC-Alufolien with silica gel F254. TLC plates were visualized in UV light at 254 nm and by spraying with vanillin-sulphuric acid and subsequent heating with a heat gun. Column-chromatography was performed on silica gel 60 (Merck, 70–230 mesh, pore-diameter 60 Å) with cyclohexane/ethyl acetate (= CH/*Et*OA*c*), CH_2Cl_2/*Et*OA*c*, toluene/*Et*OA*c*, and *Et*OA*c*/*Et*OH as eluents. The solvents were concentrated by rotary evaporation below 40°C. CH_2Cl_2 was dried by distilling from CaH_2 at 760 Torr and kept under Ar on 4 Å molecular sieves. AgO*Tf* was prepared according to Ref. [11]. Compound **5** was prepared from the commercially available methyl α-*D*-glucopyranoside according to Ref. [27]. Compound **7** was obtained according to Ref. [31].

2,3,4,6-Tetra-O-pivaloyl-α-D-glucopyranosyl bromide (***2***)

To a stirred solution of 1.0 g pentapivaloate (1 equiv) and 75 mg $BiBr_3$ (0.1 equiv) in 20 cm^3 CH_2Cl_2, 0.88 cm^3 Me_3SiBr (4.0 equiv) were added under Ar. The reaction was stirred at room temperature for 24 h and monitored by TLC. For workup, the solution was diluted with CH_2Cl_2 and filtered. The organic layer was washed successively with cold 1 *N* $NaHCO_3$ and cold H_2O, dried over Na_2SO_4, and concentrated. Because in this case no further purification was necessary, the reagent that resulted was ready for immediate use: 0.93 g (97%). Its data agreed with those of Ref. [12], but we have completed the given assignment of the ^{1}H and ^{13}C NMR resonances. $R_f = 0.63$ (CH_2Cl_2/*Et*OA*c* = 25/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.60$ (*d*, $J = 4.1$ Hz, H-1), 5.60 (t, $J = 9.6$ Hz, H-3), 5.19 (t, $J = 9.9$ Hz, H-4), 4.78 (dd, $J = 9.9$, 4.1 Hz, H-2), 4.29 (m, H-5), 4.15 (m, H-6$_a$, H-6$_b$), 1.20, 1.17, 1.15, 1.11 (4s, (C*H*$_3$)$_3$C) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.8$, 177.2, 176.7, 176.3 (4 × (CH$_3$)$_3$C*C*O), 86.8 (C-1), 72.5 (C-5), 78.8 (C-2), 69.5 (C-3), 66.4 (C-4), 60.8 (C-6), 38.8, 38.7, 38.6 (4 × (CH$_3$)$_3$*C*CO), 27.1, 27.0, 26.9 (4 × (*C*H$_3$)$_3$CCO) ppm.

2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl bromide (***3***)

(a) Halogenation with $CoBr_2$: To a stirred solution of 1.0 g **8** (1.85 mmol) in 20 cm^3 anhydrous CH_2Cl_2, 0.40 g $CoBr_2$ (1.85 mmol) and 0.25 cm^3 Me_3SiBr (1.85 mmol) were added under Ar. After stirring for 1 h at room temperature, the mixture was diluted with CH_2Cl_2, filtered quickly through Celite®, and concentrated to give 1.03 g pure **3** (92%) as a colourless oil.

(b) Halogenation with oxalyl bromide: To a stirred solution of 1.0 g **8** (1.85 mmol) in 15 cm^3 anhydrous CH_2Cl_2, 0.22 cm^3 oxalyl bromide (2.31 mmol) were added under Ar. After stirring for 2.5 h at room temperature the mixture was diluted with CH_2Cl_2, filtered quickly through Celite®,

and concentrated to give 1.1 g **3** (98%) as a colourless oil. With both variations a further purification was not necessary, the reagent that resulted was ready for immediate use. The recorded data agreed with those of Ref. [20], but we have completed the given assignment of the ^{1}H and ^{13}C NMR resonances. $R_f = 0.66$ (toluene/*Et*OA*c* = 7/1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.37–7.11$ (m, aromatic *H*), 6.41 (d, $J = 3.7$ Hz, H-1), 4.98 (d, $J = 10.5$ Hz, PhCH_2-3_a), 4.85 (d, $J = 11.0$ Hz, PhCH_2-4_a), 4.83 (d, $J = 10.5$ Hz, PhCH_2-3_b), 4.71 (m, PhCH_2-2_a, PhCH_2-2_b), 4.58 (d, $J = 12.0$ Hz, PhCH_2-6_a), 4.52 (d, $J = 11.0$ Hz, PhCH_2-4_b), 4.47 (d, $J = 12.0$ Hz, PhCH_2-6_b), 4.06 (m, H-5), 4.04 (m, H-3), 3.79 (m, H-6_a), 3.78 (m, H-4), 3.66 (d, $J = 11.0$ Hz, H-6_b), 3.54 (dd, $J = 9.3$, 3.7 Hz, H-2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 138.4$, 137.9, 137.6, 137.3, 128.6, 128.4, 128.1, 128.0, 127.9, 127.8, 127.7 (aromatic *C*), 91.8 (C-1), 82.1 (C-3), 79.6 (C-2), 76.0 (C-4), 75.8 (Ph*C*H_2-3), 75.2 (Ph*C*H_2-4), 75.1 (C-5), 73.5 (Ph*C*H_2-6), 72.8 (Ph*C*H_2-2), 67.5 (C-6) ppm.

1,2,3,4,6-Penta-O-pivaloyl-β-D-glucopyranose (***4***)

A stirred solution of 5.5 cm^3 pivaloyl chloride (44.4 mmol), 6.2 cm^3 triethylamine (44.4 mmol), and 50 mg *DMAP* in 20 cm^3 anhydrous CH_2Cl_2 was cooled to 0°C and treated with 1.0 g anhydrous *D*-glucose (5.55 mmol) in portions within 30 min. The solution was allowed to warm gradually to room temperature and stirred for 24 h in the dark. The mixture was poured into a separating funnel containing CH_2Cl_2 and 2 *N* H_2SO_4. The aqueous layer was extracted with CH_2Cl_2 and the combined organic layers were washed with 2 *N* H_2SO_4, 1 *N* $NaHCO_3$, and H_2O, dried (Na_2SO_4), and concentrated. Recrystallization from ethanol gave 2.4 g **4** (73%) as fine needles, mp 156–158°C; $R_f = 0.51$ (CH_2Cl_2/*Et*OA*c* = 25/1); the recorded data agree with those of Ref. [12].

Isopropyl 2,3,4,6-tetra-O-benzyl-α,β-D-glucopyranoside (***6***)

To a suspension of 4.0 g anhydrous *D*-glucose (22.2 mmol) in 250 cm^3 isopropyl alcohol, 7.4 cm^3 triisopropyl orthoformate (33.3 mmol) and 4.0 cm^3 HCl (4 *N* in dioxane) were added and the mixture was heated under reflux for 3 h. After cooling, the solution was neutralized with Et_3N and concentrated under reduced pressure. The resulting isopropyl glycoside was dissolved in 250 cm^3 anhydrous *DMF* and treated in portions with 8.0 g NaH (60% in mineral oil, 200 mmol) at 0°C. After stirring for 1 h, 15.8 cm^3 benzyl bromide (133 mmol) and 9.8 g Bu_4NI (26.6 mmol) were added. The reaction mixture was allowed to warm gradually to ambient temperature and stirred for further 24 h. The reaction was quenched with 10 cm^3 *Me*OH and stirred for 10 min. Subsequently the reaction mixture was poured into 350 cm^3 ice-water and extracted with cyclohexane (3 × 100 cm^3). The combined organic phases were dried over Na_2SO_4 and concentrated. Column chromatography of the residue over silica with toluene/*Et*OA*c* (15/1) gave 9.4 g **6** (73%) as a slightly yellowish semi-solid substance as an α,β-mixture (2:1). $R_f = 0.34$ (toluene/*Et*OA*c* = 15/1). The NMR data agree with those of Ref. [29].

2,3,4,6-Tetra-O-benzyl-α,β-D-glucopyranose (***8***)

This procedure is a modification of that of Ref. [27]. The methyl or isopropyl glycoside (3.4 mmol) was mixed with 30 cm^3 glacial acetic acid and 15 cm^3 2 *N* sulphuric acid and the solution was stirred at 100°C for 12–24 h. The product precipitated partly toward the end of this period. The hydrolysate was cooled to room temperature, poured into 300 cm^3 cold H_2O, and stirred slowly for 15 min. The crude product was filtered, washed with cold H_2O (10 cm^3), and purified on a silica gel column with CH_2Cl_2/*Et*OA*c* (6/1) as eluent to give **8** as white solid as an α,β-mixture (2:1); yield 56% from **5**, 74% from **6**; mp 151–152°C; $R_f = 0.48$ (CH_2Cl_2/*Et*OA*c* = 6/1). Its data agree with those reported in Ref. [41].

Glycosylation of Cholesterol

To a stirred solution of the appropriate glycosyl halide (1.0 mmol) in 20 cm^3 anhydrous CH_2Cl_2, 100 mg activated 4 Å molecular sieve was added. The mixture was cooled to −20°C and treated successively with 0.54 g cholesterol (1.4 mmol) and 0.18 cm^3 *TMU* (1.5 mmol). After 30 min, 0.31 g freshly prepared AgO*Tf* (1.2 mmol) were added and stirring at −20°C was continued in the dark for

further 30 min. The mixture was allowed to warm gradually to room temperature and stirred for 20 h protected from light. The suspension was diluted with CH_2Cl_2, filtered, and washed successively with 1 *N* $NaHCO_3$ and H_2O. After drying (Na_2SO_4) and evaporation of the solvent, the residue was purified as described below.

3,4,6-Tri-O-acetyl-α-D-glucopyranose-1,2-(cholesteryl orthoacetate) (***10***)
The compound was purified on a silica gel column using CH_2Cl_2/*Et*OA*c* (5/1). Yield 29%; white solid; $R_f = 0.64$ (CH_2Cl_2/*Et*OA*c* = 5/1). The data agree with those of Ref. [42]. However, the accurate ^{1}H and ^{13}C NMR data could be assigned: ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 5.69$ (d, $J = 5.1$ Hz, H-1′), 5.36 (s, H-6), 5.18 (t, $J = 2.5$ Hz, H-3′), 4.90 (dd, $J = 9.5$, 2.5 Hz, H-4′), 4.35 (m, H-2′), 4.19 (d, $J = 3.8$ Hz, H-6′$_a$, H-6′$_b$), 3.94 (dt, $J = 9.5$, 3.7 Hz , H-5′), 3.49 (m, H-3), 2.28 (m, H-4$_a$), 2.21 (m, H-4$_b$), 2.10 (s, C*H*$_3$COO-3′, C*H*$_3$COO-4′), 2.09 (s, C*H*$_3$COO-6′), 2.00 (m, H-12$_a$), 1.97 (m, H-7$_a$), 1.83 (m, H-1$_a$, H-16$_a$), 1.76 (m, H-2$_a$), 1.72 (s, C*H*$_3$COOO), 1.57 (m, H-15$_a$), 1.56 (m, H-2$_b$), 1.52 (m, H-25), 1.51 (m, H-7$_b$), 1.49 (m, H-11$_a$), 1.44 (m, H-8, H-11$_b$), 1.38 (m, H-20), 1.33 (m, H-22$_a$, H-23$_a$), 1.25 (m, H-16$_b$), 1.16 (m, H-12$_b$), 1.14 (m, H-23$_b$), 1.12 (m, H-24$_a$), 1.09 (m, H-17, H-24$_b$), 1.07 (m, H-15$_b$), 1.05 (m, H-1$_b$), 0.99 (m, H-14, H-22$_b$), 0.98 (s, H-19), 0.91 (m, H-9), 0.91 (d, $J = 6.6$ Hz, H-21), 0.87 (d, $J = 6.6$ Hz, H-26, H-27), 0.67 (s, H-18) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 170.7 (CH$_3$*C*OO-6′), 169.7 (CH$_3$*C*OO-4′), 169.2 (CH$_3$*C*OO-3′), 140.5 (C-5), 122.1 (C-6), 121.4 (CH$_3$*C*OOO), 96.9 (C-1′), 73.8 (C-3), 73.0 (C-2′), 70.2 (C-3′), 68.3 (C-4′), 67.0 (C-5′), 63.1 (C-6′), 56.8 (C-14), 56.2 (C-17), 50.2 (C-9), 42.3 (C-13), 40.4 (C-4), 39.8 (C-12), 39.5 (C-24), 37.3 (C-1), 36.5 (C-10), 36.2 (C-22), 35.8 (C-20), 31.9 (C-7, C-8), 29.8 (C-2), 28.2 (C-16), 28.0 (C-25), 24.3 (C-15), 23.8 (C-23), 22.8* (C-27), 22.6* (C-26), 21.7 (*C*H$_3$COOO), 21.1 (C-11), 20.8 (*C*H$_3$COO-3′, *C*H$_3$COO-4′, *C*H$_3$COO-6′), 19.3 (C-19), 18.7 (C-21), 11.9 (C-18) ppm.

Cholesteryl 2,3,4,6-tetra-O-pivaloyl-β-D-glucopyranoside (***11***)
The compound was purified on a silica gel column using CH/*Et*OA*c* (3/1). Yield 58%; white solid; $R_f = 0.66$ (CH/*Et*OA*c* = 3/1). The data agree with those of Ref. [12]. However, the accurate ^{1}H and ^{13}C NMR data could be assigned: ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 5.31$ (m, H-3′, H-6), 5.06 (t, $J = 9.5$ Hz, H-4′), 4.98 (t, $J = 9.3$ Hz, H-2′), 4.62 (d, $J = 8.2$ Hz, H-1′), 4.21 (d, $J = 12.5$ Hz, H-6′$_a$), 4.03 (dd, $J = 12.5$, 6.1 Hz, H-6′$_b$), 3.73 (t, $J = 7.5$ Hz, H-5′), 3.46 (m, H-3), 2.22 (m, H-4$_a$, H-4$_b$), 2.01 (m, H-12$_a$), 1.96 (m, H-7$_a$), 1.91 (m, H-2$_a$), 1.83 (m, H-16$_a$), 1.82 (m, H-1$_a$), 1.58 (m, H-2$_b$), 1.56 (m, H-15$_a$), 1.52 (m, H-25), 1.50 (m, H-7$_b$), 1.48 (m, H-11$_a$), 1.45 (m, H-11$_b$), 1.44 (m, H-8), 1.37 (m, H-20), 1.34 (m, H-22$_a$), 1.33 (m, H-23$_a$), 1.26 (m, H-16$_b$), 1.20 (s, (C*H*$_3$)$_3$CCOO-6′), 1.17 (s, (C*H*$_3$)$_3$CCOO-2′), 1.16 (m, H-12$_b$), 1.15 (s, (C*H*$_3$)$_3$CCOO-4′), 1.14 (m, H-23$_b$), 1.13 (m, H-24$_a$), 1.10 (s, (C*H*$_3$)$_3$CCOO-3′), 1.09 (m, H-17, H-24$_b$), 1.06 (m, H-15$_b$), 1.00 (m, H-1$_b$, H-22$_b$), 0.98 (m, H-14), 0.97 (s, H-19), 0.92 (d, $J = 6.6$ Hz, H-21), 0.89 (m, H-9), 0.86 (d, $J = 6.6$ Hz, H-26, H-27), 0.67 (s, H-18) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 178.1$ ((CH$_3$)$_3$C*C*OO-6′), 177.2 ((CH$_3$)$_3$C*C*OO-3′), 176.6 ((CH$_3$)$_3$C*C*OO-4′), 176.4 ((CH$_3$)$_3$C*C*OO-2′), 140.4 (C-5), 122.1 (C-6), 99.7 (C-1′), 79.8 (C-3), 72.4 (C-3′), 72.2 (C-5′), 71.4 (C-2′), 68.4 (C-4′), 62.3 (C-6′), 56.8 (C-14), 56.2 (C-17), 50.2 (C-9), 42.3 (C-13), 39.8 (C-12), 39.5 (C-24), 38.9 (C-4, (CH$_3$)$_3$*C*COO-4′, (CH$_3$)$_3$*C*COO-6′), 38.8 ((CH$_3$)$_3$*C*COO-2′), 38.7 ((CH$_3$)$_3$*C*COO-3′), 37.2 (C-1), 36.7 (C-10), 36.2 (C-22), 35.8 (C-20), 32.0 (C-7, C-8), 29.6 (C-2), 28.2 (C-16), 28.0 (C-25), 27.2 ((*C*H$_3$)$_3$CCOO-2′, (*C*H$_3$)$_3$CCOO-3′), 27.1 ((*C*H$_3$)$_3$CCOO-4′, (*C*H$_3$)$_3$CCOO-6′), 24.3 (C-15), 23.8 (C-23), 22.8* (C-27), 22.6* (C-26), 21.1 (C-11), 19.2 (C-19), 18.7 (C-21), 11.9 (C-18) ppm.

Cholesteryl 2,3,4,6-tetra-O-benzyl-α,β-D-glucopyranoside (***12***)
The compound was purified on a silica gel column using toluene/*Et*OA*c* (15/1) yielding the anomers **12*α*** and **12*β*** as white solids (67%, ratio 3:2); $R_f = 0.45$ (toluene/*Et*OA*c* = 15/1). The recorded data agree with those of Ref. [43]. However, the accurate ^{1}H and ^{13}C NMR data could be assigned.

12*α*: ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.36$–7.12 (m, aromatic *H*), 5.28 (s, H-6), 5.01–4.46 (m, 4 × PhC*H*$_2$), 4.94 (d, $J = 4.2$ Hz, H-1′), 4.00 (t, $J = 9.4$ Hz, H-3′), 3.88 (d, $J = 3.8$ Hz, H-5′), 3.73

(m, H-6′$_a$), 3.68 (m, H-6′$_b$), 3.63 (t, $J = \sim 8$ Hz, H-4′), 3.57 (m, H-2′), 3.55 (m, H-3), 2.43 (m, H-4$_a$), 2.29 (m, H-4$_b$), 2.04 (m, H-2$_a$), 2.00 (m, H-12$_a$), 1.97 (m, H-7$_a$), 1.87 (m, H-1$_a$), 1.83 (m, H-16$_a$), 1.57 (m, H-15$_a$), 1.56 (m, H-2$_b$), 1.54 (m, H-7$_b$), 1.52 (m, H-25), 1.49 (m, H-11$_a$), 1.46 (m, H-11$_b$), 1.44 (m, H-8), 1.39 (m, H-20), 1.33 (m, H-22$_a$, H-23$_a$), 1.26 (m, H-16$_b$), 1.17 (m, H-12$_b$), 1.14 (m, H-23$_b$), 1.12 (m, H-24$_a$), 1.10 (m, H-17, H-24$_b$), 1.06 (m, H-15$_b$), 1.05 (m, H-1$_b$), 1.02 (s, H-19), 1.00 (m, H-22$_b$), 0.99 (m, H-14), 0.92 (m, H-9), 0.92 (d, $J = 6.6$ Hz, H-21), 0.87 (d, $J = 6.6$ Hz, H-26, H-27), 0.68 (s, H-18) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 140.9$ (C-5), 138.7–127.5 (aromatic *C*), 121.7 (C-6), 94.6 (C-1′), 82.1 (C-3′), 79.6 (C-2′), 78.0 (C-3), 77.9 (C-4′), 75.8–73.2 (4 × Ph*C*H$_2$), 70.0 (C-5′), 68.6 (C-6′), 56.8 (C-14), 56.2 (C-17), 50.2 (C-9), 42.3 (C-13), 39.9 (C-4), 39.8 (C-12), 39.2 (C-24), 37.3 (C-1), 36.5 (C-10), 36.2 (C-22), 35.8 (C-20), 32.0 (C-7), 31.9 (C-8), 30.0 (C-2), 28.2 (C-16), 28.0 (C-25), 24.3 (C-15), 23.8 (C-23), 22.8* (C-27), 22.6* (C-26), 21.1 (C-11), 19.2 (C-19), 18.7 (C-21), 11.9 (C-18) ppm.

12*β*: ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.36$–7.12 (m, aromatic *H*), 5.34 (s, H-6), 5.01–4.46 (m, 4 × PhC*H*$_2$), 4.50 (d, $J = \sim 8$ Hz, H-1′), 3.73 (m, H-6′$_a$), 3.68 (m, H-6′$_b$), 3.63 (t, $J = \sim 9$ Hz, H-3′), 3.55 (t, $J = 8.8$ Hz, H-4′), 3.48 (m, H-3), 3.46 (m, H-5′), 3.44 (t, $J = 8.7$ Hz, H-2′), 2.40 (m, H-4$_a$), 2.35 (m, H-4$_b$), 2.04 (m, H-2$_a$), 2.00 (m, H-12$_a$), 1.97 (m, H-7$_a$), 1.87 (m, H-1$_a$), 1.83 (m, H-16$_a$), 1.57 (m, H-15$_a$), 1.56 (m, H-2$_b$), 1.54 (m, H-7$_b$), 1.52 (m, H-25), 1.49 (m, H-11$_a$), 1.46 (m, H-11$_b$), 1.44 (m, H-8), 1.39 (m, H-20), 1.33 (m, H-22$_a$, H-23$_a$), 1.26 (m, H-16$_b$), 1.17 (m, H-12$_b$), 1.14 (m, H-23$_b$), 1.12 (m, H-24$_a$), 1.10 (m, H-17, H-24$_b$), 1.06 (m, H-15$_b$), 1.05 (m, H-1$_b$), 1.02 (s, H-19), 1.00 (m, H-22$_b$), 0.99 (m, H-14), 0.92 (m, H-9), 0.92 (d, $J = 6.6$ Hz, H-21), 0.87 (d, $J = 6.6$ Hz, H-26, H-27), 0.68 (s, H-18) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 140.7$ (C-5), 138.7–127.5 (aromatic *C*), 121.9 (C-6), 102.3 (C-1′), 84.8 (C-3′), 82.4 (C-2′), 78.0 (C-4′), 76.7 (C-3), 75.8–73.2 (4 × Ph*C*H$_2$), 74.8 (C-5′), 69.1 (C-6′), 56.8 (C-14), 56.2 (C-17), 50.2 (C-9), 42.3 (C-13), 39.8 (C-12), 39.2 (C-4, C-24), 37.3 (C-1), 36.5 (C-10), 36.2 (C-22), 35.8 (C-20), 32.0 (C-7), 31.9 (C-8), 30.0 (C-2), 28.2 (C-16), 28.0 (C-25), 24.3 (C-15), 23.8 (C-23), 22.8* (C-27), 22.6* (C-26), 21.1 (C-11), 19.4 (C-19), 18.7 (C-21), 11.9 (C-18) ppm.

Cholesteryl α,β-D-glucopyranoside (***13***)

The compound was prepared from **12** by treatment with cyclohexene and 20% palladium hydroxide on carbon as described in Ref. [40]. Purification was performed on a silica gel column using *Et*OA*c*/*Et*OH (2/1) yielding the anomers **13*α*** and **13*β*** as white solids (83%, ratio 3:2). The data agree with those of Ref. [44]. However, the accurate ^{1}H and ^{13}C NMR data could be assigned.

13*α*: Mp 206–208°C, $R_f = 0.30$ (*Et*OA*c*/*Et*OH = 2/1); ^{1}H NMR (600 MHz, *DMSO*-d$_6$): $\delta = 5.29$ (s, H-6), 4.78 (d, $J = 3.5$ Hz, H-1′), 4.43 (m, H-6′$_a$), 3.59 (d, $J = 9.6$ Hz, H-6′$_b$), 3.45 (m, H-5′), 3.39 (m, H-3′), 3.36 (m, H-3), 3.15 (dd, $J = 9.0$, 3.6 Hz, H-2′), 3.04 (t, $J = 9.6$ Hz, H-4′), 2.34 (m, H-4$_a$), 2.24 (m, H-4$_b$), 1.96 (m, H-12$_a$), 1.92 (m, H-7$_a$), 1.86 (m, H-2$_a$), 1.80 (m, H-1$_a$), 1.79 (m, H-16), 1.54 (m, H-15$_a$), 1.50 (m, H-25), 1.49 (m, H-7$_b$), 1.48 (m, H-11$_a$), 1.40 (m, H-8, H-11$_b$), 1.38 (m, H-2$_b$), 1.35 (m, H-20), 1.32 (m, H-22$_a$), 1.31 (m, H-23$_a$), 1.22 (m, H-16$_b$), 1.14 (m, H-12$_b$, H-23$_b$), 1.11 (m, H-24$_a$, H-24$_b$), 1.08 (m, H-17), 1.05 (m, H-15$_b$), 0.98 (m, H-1$_b$, H-22$_b$), 0.97 (m, H-14), 0.96 (s, H-19), 0.90 (d, $J = 6.6$ Hz, H-21), 0.89 (m, H-9), 0.84 (d, $J = 6.6$ Hz, H-26, H-27), 0.65 (s, H-18) ppm; ^{13}C NMR (150 MHz, *DMSO*-d$_6$): $\delta = 140.6$ (C-5), 121.0 (C-6), 96.8 (C-1′), 76.3 (C-3), 73.1 (C-3′), 72.8 (C-5′), 71.8 (C-2′), 70.1 (C-4′), 60.9 (C-6′), 56.1 (C-14), 55.5 (C-17), 49.5 (C-9), 41.8 (C-13), 39.6 (C-4), 39.2 (C-12), 38.8 (C-24), 36.5 (C-1), 36.1 (C-10), 35.5 (C-22), 35.1 (C-20), 31.3 (C-7, C-8), 27.7 (C-16), 27.4 (C-2), 27.3 (C-25), 23.8 (C-15), 23.1 (C-23), 22.6* (C-27), 22.3* (C-26), 20.5 (C-11), 19.0 (C-19), 18.5 (C-21), 11.6 (C-18) ppm.

13*β*: Mp 258–260°C, $R_f = 0.38$ (*Et*OA*c*/*Et*OH = 2/1); ^{1}H NMR (600 MHz, *DMSO*-d$_6$): $\delta = 5.32$ (s, H-6), 4.21 (d, $J = 7.8$ Hz, H-1′), 3.65 (dd, $J = 11.4$, 6.0 Hz, H-6′$_a$), 3.46 (m, H-3), 3.41 (d, $J = 11.4$ Hz, H-6′$_b$), 3.13 (t, $J = 9.0$ Hz, H-3′), 3.07 (m, H-5′), 3.03 (t, $J = 9.0$ Hz, H-4′), 2.90 (m, H-2′), 2.36 (m, H-4$_a$), 2.14 (m, H-4$_b$), 1.96 (m, H-12), 1.92 (m, H-7$_a$), 1.82 (m, H-2$_a$), 1.79 (m, H-1$_a$), 1.78 (m, H-16$_a$), 1.54 (m, H-15$_a$), 1.50 (m, H-25), 1.49 (m, H-7$_b$, H-11$_a$), 1.48 (m, H-2$_b$), 1.40 (m, H-8, H-11$_b$), 1.34 (m, H-20), 1.31 (m, H-22$_a$, H-23$_a$), 1.23 (m, H-16$_b$), 1.14 (m, H-12$_b$), 1.13 (m, H-23$_b$), 1.11 (m, H-24$_a$, H-24$_b$), 1.07 (m, H-17), 1.04 (m, H-15$_b$), 0.99 (m, H-1$_b$, H-22$_b$), 0.98 (m, H-14), 0.96 (s, H-19), 0.90 (d, $J = 6.6$ Hz, H-21), 0.89 (m, H-9), 0.84 (d, $J = 6.6$ Hz, H-26, H-27), 0.65

(s, H-18) ppm; ^{13}C NMR (150 MHz, *DMSO*-d_6): $\delta = 140.4$ (C-5), 121.1 (C-6), 100.7 (C-1′), 76.9 (C-3), 76.7 (C-3′), 76.6 (C-5′), 73.4 (C-2′), 70.3 (C-4′), 61.0 (C-6′), 56.1 (C-14), 55.5 (C-17), 49.5 (C-9), 41.8 (C-13), 39.2 (C-12), 38.9 (C-24), 38.3 (C-4), 36.8 (C-1), 36.1 (C-10), 35.6 (C-22), 35.1 (C-20), 31.4 (C-8), 31.3 (C-7), 29.2 (C-2), 27.7 (C-16), 27.3 (C-25), 23.8 (C-15), 23.1 (C-23), 22.6* (C-27), 22.3* (C-26), 20.5 (C-11), 19.0 (C-20), 18.5 (C-21), 11.6 (C-18) ppm.

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