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Synthesis of peracetylated chacotriose

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Abstract

Steroidal glycoalkaloids of many *Solanum* species have recognized biological activities, especially those containing the glycosyl moiety α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→4)]-D-glucopyranose (chacotriose) whose peracetate is here synthesized and characterized by complete ^{1}H and ^{13}C NMR assignment.

Keywords: *Solanum*; Glycoalkaloid; Chacotriose; L-Rhamnose

1. Introduction

Steroidal glycoalkaloids[1] are secondary metabolites frequently found in species of *Solanum*, conferring on them resistance to insects and other pests.[2,3] Most *Solanum* species contain two major glycoalkaloids which share the same aglycone, bound either to chacotriose, α-L-rhamnopyranosyl-(1→2)-[α-L-rhamnopyranosyl-(1→4)]-β-D-glucopyranose, or solatriose, α-L-rhamnopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-galactopyranose. It has been demonstrated that *Solanum* steroidal glycoalkaloids have antineoplasic,[4] antifungal,[5] as well as trypanolytic and trypanocidal activities.[6] Glycosides containing chacotriose are consistently more active than their solatriose containing counterparts.

Inactivation of *Herpes simplex* virus by *Solanum* glycoalkaloids has been reported by Thorne et al.[7] who demonstrated that α-chaconine, the glycoside of solanidine with chacotriose, was the most effective, whereas the corresponding aglycone was inactive. The low activity of the aglycones indicates that the role of the carbohydrate moiety is very important. The biological activity of *Solanum* glycoalkaloids is believed to depend on the interaction of the carbohydrate moiety with membrane sugar receptors, which allow penetration of the steroidal alkaloid and subsequent disruption of the cell metabolism of the pathogen.[8] *Solanum americanum* Miller is a herbaceous plant that grows abundantly in Venezuela.[9] The expressed fruits and leaves of this plant, commonly called 'yerbamora', are used by the rural population to treat skin injuries caused by *Herpes zoster*. The main steroidal glycoalkaloids in the fruits of this plant are α-solamargine and α-solasonine.[10]

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Clinical tests carried out with a hydrophilic cream containing either a crude extract of *S. americanum* fruits or α-solamargine, applied topically, healed patients suffering from *H. zoster*, *H. simplex*, and *H. genitalis* after 3–10 days.[11]

Glycoalkaloids containing chacotriose are known to be the most active of such alkaloids, and such compounds as α-chaconine and α-solamargine are not easily obtained in large quantities. Since the glycosidic moiety, chacotriose, is important for biological activity, it was decided to make it more readily available by chemical synthesis as its peracetate. Peracetylated chacotriose is more stable than unprotected chacotriose and it could be readily transformed into α-chaconine or α-solamargine on a commercial scale for inclusion into antiviral creams, which could prove cheaper alternatives to antiviral drugs already on the market. Moreover, chacotriose could be bound to other aglycones in the search for new biologically active glycosides, or be obtained as labeled derivatives which could be used to study its mechanism of action in biological systems.

2. Results and discussion

Peracetylated chacotriose was synthesized starting from D-glucose. The strategy adopted was to partially protect the glucose leaving only the 2- and 4-hydroxyl groups available for glycosidic bond formation with two L-rhamnopyranose units. The synthetic sequence started from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose[12] (**1**). 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**3**) was prepared by the procedure of Goueth et al.[13] in two steps from **1** in 62% yield. Compound **3** was treated with *p*-toluenesulfonyl chloride in 1:1 toluene–C_5H_5N at 4 °C to give 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-tosyl-α-D-glucofuranose (**4**) in 90% yield; the presence of the tosyl group at C-6 was confirmed in the ^{13}C NMR spectrum by the characteristic aryl signals. Compound **4** was treated with 2.2 equivalents of NaOH[13] in 9:1 dioxane–water and the crude product was purified on silica gel to give 5,6-anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**5**) in 76% yield; the formation of the anhydro group was ascertained by signals at 46.9 ppm (C-6) and 48.1 ppm (C-5) in the ^{13}C NMR spectrum. 3,6-Di-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**7**) was prepared by condensing compound **5** with benzyl alcohol (5 equiv) in the presence of KOH (6 equiv) in 1:1 toluene–Me_2SO; to facilitate its extraction, the crude product was acetylated to separate the corresponding 5-*O*-acetyl derivative **6** (76% yield) which treated with NaOMe in MeOH gives pure compound **7**. Subsequently, **7** was treated with 9:1 CF_3CO_2OH–water[14] and the crude product purified on silica gel to give 3,6-di-*O*-benzyl-D-glucopyranose (**8**) in 86% yield; the ^{13}C NMR spectrum showed signals at 92.8 ppm (C-1α) and 97.1 ppm (C-1β) which indicated that the anomeric hydroxyl was free. Acetylation of **8** gave 1,2,4-tri-*O*-acetyl-3,6-di-*O*-benzyl-D-glucopyranose (**9**) in 86% yield. To obtain glucose in the required protected form for attachment of two rhamnose units at the 2- and 4-hydroxyl groups, **9** was initially benzylated at the anomeric position by reaction with benzyl alcohol in dry CH_2Cl_2 in the presence of $SnCl_4$[15] to give benzyl 2,4-di-*O*-acetyl-3,6-di-*O*-benzyl-β-D-glucopyranoside (**10**) as the sole anomer in 60% yield. The ^{13}C NMR spectrum of **10** showed the signal of the anomeric carbon at 99.9 ppm (C-1β). Compound **10** was then treated with NaOMe in MeOH to give benzyl 3,6-di-*O*-benzyl-β-D-glucopyranoside (**11**) in 98% yield without purification. The ^{13}C NMR data of **11** showed a signal for the anomeric carbon at 102.1 ppm. The intermediate **11** was thus obtained from 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose in an overall yield of 14%.

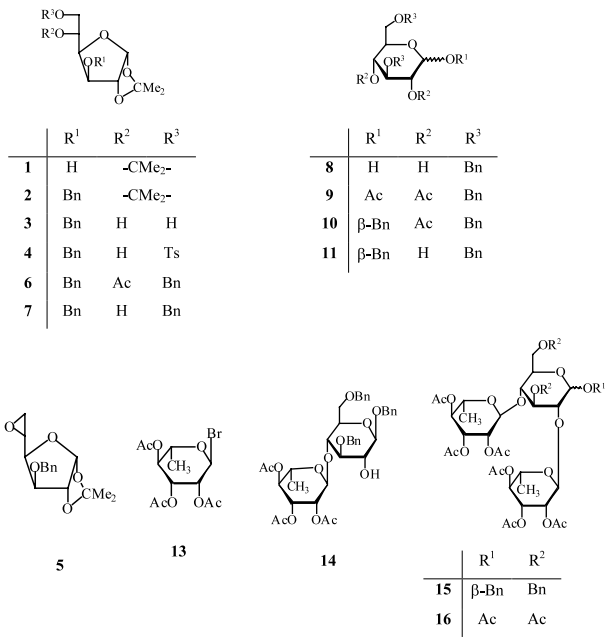
L-Rhamnose was first peracetylated with Ac_2O–C_5H_5N to give, after silica-gel chromatography, 1,2,3,4-tetra-*O*-acetyl-L-rhamnopyranose (**12**) in 67% yield. The anomeric carbon of **12** appeared at 90.3 (C-1β) and 90.6 ppm (C-1α) in the ^{13}C NMR spectrum. Compound **12** was treated with 4.5 equivalents of HBr (33% in glacial acetic acid)[16,17] to obtain 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl bromide (**13**) in 94% yield; the anomeric carbon appeared at 83.7 ppm in ^{13}C NMR. Compound **11** was mixed with four

equivalents of **13** in dry CH_2Cl_2 at 0 °C, in the presence of tetramethylurea and silver triflate.[18–20] The product was purified on silica gel to give benzyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)-3,6-di-*O*-benzyl-β-D-glucopyranoside (**14**) (30%) and benzyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)]-3,6-di-*O*-benzyl-β-D-glucopyranoside (**15**) (65%). The ^{13}C NMR spectrum of **15** showed three anomeric carbons at 97.2, 97.7, and 100.3 ppm, while the spectrum of **14** showed only two at 97.4 and 98.6 ppm. A HMQC experiment indicated a correlation between C-1 of the rhamnose unit and H-4 of the glucose unit indicating (1→4) glycosylation in **14**. Compound **15** was subjected to catalytic hydrogenolysis to remove the benzyl protecting groups and subsequently acetylated to obtain the desired peracetylated chacotriose **16** in 24% yield (Scheme 1).

3. Experimental

General methods.—Melting points were determined on an electrothermal automatic apparatus, and are uncorrected. Optical rotations for solutions in $CHCl_3$ or MeOH were measured with a JASCO digital polarimeter model DIP-370 using a sodium lamp at 25 °C. NMR spectra were recorded with a Bruker WB-300 instrument for solutions in $CDCl_3$ (internal Me_4Si). All compounds were characterized by acquisition of ^1H, ^{13}C, DEPT, ^1H–^1H COSY, and ^1H–^{13}C correlated experiments. Electron (EI-MS) and fast-atom bombardment (FAB-MS) ionizations were accomplished on an AutoSpec (Micromass, UK), high-resolution mass spectrometer. Electrospray ionization (ESI-MS) was performed on a SSQ710 (ThermoFinnigan, USA), simple quadrupole mass spectrometer. For the positive ESI-MS experiments, the compound was dissolved in 100:400:0.02 water–MeOH–$CH_3CO_2NH_4$ at a concentration of 0.02 mg mL^{-1} and then introduced into the ion source (Analytica of Branford, USA) at a flow rate of 3 μL min^{-1}. Reactions were monitored by either high-performance liquid chromatography (HPLC) (Waters 721) using reverse-phase column RP-18 (E. Merck), or CPG (Girdel) with OV-17 columns. Analytical thin-layer chromatography (TLC) was performed on E. Merck aluminum-backed silica gel (Silica Gel F254). Column chromatography was performed on silica gel (60 mesh, Matrex) by gradient elution with hexane–acetone or hexane–EtOAc (in each case the ratio of silica gel to product mixture to be purified was 30:1).

3-O-*Benzyl-1,2*-O-*isopropylidene-6*-O-*tosyl*-α-D-*glucofuranose* (**4**).—To a stirred solution of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-glucofuranose (**3**)[13] (37 g, 119 mmol) in 1:1 toluene–pyridine (370 mL) was added, at −10 °C, tosyl chloride (27.3 g, 143 mmol) in toluene (50 mL). After 72 h at 6 °C, the mixture was filtered and the filtrate concentrated under reduced pressure. The residue was purified by column chromatography eluting with 4:1 hexane–acetone to give **4** in 90% yield as an oil; $[\alpha]_D + 73.2°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.90–7.11 (m, 9 H, Ph, C_6H_4), 5.60 (d, 1 H, $J_{1,2}$ 3.3 Hz, H-1), 4.58 (d, 1 H, $J_{2,3}$0.0 Hz, H-2), 4.50 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 4.30 (dd, 1 H, $J_{6a,6b}$ 10.0 Hz, H-6a), 4.20 (m, 1 H, $J_{5,6a}$ 1.8 Hz, H-5), 4.10 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 4.00 (m, 1 H, $J_{4,5}$ 4.0 Hz, H-4), 2.37 (s, 3 H, $CH_3C_6H_4$), 1.20, 1.30 (2s, 6 H, CMe_2); ^{13}C NMR ($CDCl_3$, 75.5



Scheme 1.

MHz): δ 144.9 (C_{ipso}), 137.0–127.8 (CH_2Ph), 132.4–129.8 (C_6H_4), 111.8 (CMe_2), 105.0 (C-1), 81.9 (C-2), 81.8 (C-3), 81.6 (C-4), 79.1 (CH_2Ph), 72.2 (C-5), 67.1 (C-6), 26.7, 26.1 (CMe_2). Anal. Calcd for $C_{23}H_{28}O_8S$: C, 59.47; H, 6.08; S, 6.90. Found: C, 59.29; H, 5.98; S, 7.05.

*5,6-Anhydro-3-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**5**).—To a stirred solution of **4** (58 g, 125 mmol) in 9:1 1,4-dioxane–water (580 mL) was added powdered NaOH (11 g, 275 mmol). After 2 h at rt, the mixture was neutralized with satd aq NH_4Cl and extracted with toluene. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography eluting with 9:1 hexane–acetone to give **5** in 76% yield as an oil; $[\alpha]_D$ −9.7° (*c* 1.3, $CHCl_3$); lit.[21] $[\alpha]_D$ −8.6° (*c* 1.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33–7.23 (m, 5 H, Ph, C_6H_4), 5.92 (d, 1 H, d, $J_{1,2}$ 3.7 Hz, H-1), 4.63 (2d, 2 H, CH_2Ph), 4.61 (d, 1 H, $J_{2,3}$0.0 Hz, H-2), 4.05 (d, 1 H, $J_{3,4}$ 3.2 Hz, H-3), 3.73 (dd, 1 H, $J_{4,5}$ 7.1 Hz, H-4), 3.28 (m, 1 H, $J_{5,6a}$ 3.9 Hz, H-5), 2.89 (dd, 1 H, $J_{6a,6b}$ 5.1 Hz, H-6a), 2.75 (dd, 1 H, $J_{5,6b}$ 2.5 Hz, H-6b), 1.28, 1.43 (2s, 6 H, CMe_2). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 127.5–137.3 (Ph), 111.8 (CMe_2), 105.2 (C-1), 82.6 (C-2), 82.0 (C-3), 81.6 (C-4), 72.3 (CH_2Ph), 48.1 (C-5), 46.9 (C-6), 26.8, 26.2 (CMe_2). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.89. Found: C, 65.89; H, 7.01.

*5-*O*-Acetyl-3,6-di-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**6**).—To a stirred solution of **5** (26 g, 89 mmol) and benzyl alcohol (48 g, 445 mmol) in 1:1 toluene–Me_2SO (260 mL) was added powdered KOH (30 g, 534 mmol). After 48 h at rt, the mixture was filtered and the filtrate neutralized with satd aq NH_4Cl. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. A solution of the residue (59.3 g) in pyridine (593 mL) was treated with Ac_2O (41.7 mL) for 24 h at rt. Dichloromethane was added and the mixture was then washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by column chromatography eluting with 4:1 hexane–acetone to give **6** isolated in 76% yield as an oil; $[\alpha]_D$ −87.9° (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.30–7.20 (m, 10 H, Ph, C_6H_4), 5.85 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1), 5.35 (m, 1 H, $J_{5,6a}$ 8.8 Hz, H-5), 4.61–4.40 (4d, 4 H, CH_2Ph), 4.51 (d, 1 H, $J_{2,3}$0.0 Hz, H-2), 4.40 (dd, 1 H, $J_{4,5}$ 6.0 Hz, H-4), 3.90 (d, 1 H, $J_{3,4}$ 2.9 Hz, H-3), 3.75 (dd, 1 H, $J_{6a,6b}$ 11.1 Hz, H-6a), 3.65 (dd, 1 H, $J_{5,6b}$ 9.4 Hz, H-6b), 1.91 (s, 3 H, CH_3CO), 1.27, 1.49 (2s, 6 H, CMe_2). ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.6 (CO), 138.2–127.4 (CH_2Ph), 111.8 (CMe_2), 105.1 (C-1), 81.6 (C-2), 80.8 (C-3), 77.6 (C-4), 71.9, 73.0 (CH_2–Ph), 69.6 (C-6), 69.0 (C-5), 26.7, 26.3 (CMe_2), 21.0 (CH_3CO). Anal. Calcd for $C_{25}H_{30}O_7$: C, 67.86; H, 6.83. Found: C, 67.69; H, 6.98.

*3,6-Di-*O*-benzyl-1,2-*O*-isopropylidene-α-*D*-glucofuranose* (**7**).—To a stirred solution of **6** (29.8 g, 74 mmol) in MeOH (239 mL) was added NaOMe (290 mg, 6 mmol). After 24 h at rt, the mixture was neutralized with satd aq NH_4Cl and extracted with CH_2Cl_2. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure to give **7** without further purification in 99% yield as an oil; $[\alpha]_D$ −24.9° (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35–7.23 (m, 10 H, Ph), 5.90 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 4.67–4.49 (4d, 4 H, CH_2Ph), 4.57 (d, 1 H, $J_{2,3}$0.0 Hz, H-2), 4.09 (d, 1 H, $J_{3,4}$ 2.6 Hz, H-3), 4.17–4.08 (m, 2 H, H-4, H-5), 3.72 (dd, 1 H, $J_{5,6a}$ 2.5, $J_{6a,6b}$ 9.7 Hz, H-6a), 3.58 (dd, 1 H, $J_{5,6b}$ 5.5 Hz, H-6b), 2.72 (d, 1 H, $J_{5,OH}$ 5.3 Hz, OH-5), 1.47, 1.29 (2s, 6 H, C-Me_2); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 138.0–127.8 (Ph), 111.7 (CMe_2), 105.1 (C-1), 82.3 (C-2), 82.0 (C-3), 79.8 (C-4), 73.4 (C-6), 72.3, 72.1 (CH_2Ph), 68.0 (C-5), 26.8, 26.3 (CMe_2). Anal. Calcd for $C_{23}H_{28}O_6$: C, 68.98; H, 7.05. Found: C, 69.11; H, 6.97.

*3,6-Di-*O*-benzyl-*D*-glucopyranose* (**8**).—The monoacetal derivative **7** (27 g, 67 mmol) was added to a stirred solution of 9:1 CF_3CO_2OH–water (54 mL). After 30 min, at rt, the solution was concentrated under reduced pressure. The residue was purified by column chromatography eluting with 3:2 hexane–EtOAc to give **8** in 86% yield as an oil, α/β 3:2; $[\alpha]_D$ +31.6° (*c* 1.8, MeOH); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ **8α** 139.0, 138.0

(C_{ipso}), 129.4–128.4 (Ph), 92.8 (C-1), 82.5 (C-3), 75.2, 74.2 (CH_2Ph), 72.8 (C-2), 71.2 (C-4), 70.5 (C-5), 70.4 (C-6); **8β** 139.0, 138.0 (C_{ipso}), 129.4–128.4 (Ph), 97.1 (C-1), 84.3 (C-3), 75.2, 74.2 (CH_2Ph), 74.0 (C-2), 71.2 (C-4), 70.5 (C-5), 70.4 (C-6). Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.41; H, 6.52.

1,2,4-Tri-O-*acetyl-3,6-di*-O-*benzyl*-D-*glucopyranose* (**9**).—To a stirred solution of **8** (20.8 g, 57 mmol) in pyridine (276 mL) was added Ac_2O (27 mL, 288 mmol). After 24 h at rt, the mixture was diluted with CH_2Cl_2 and washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. Compound **9** was isolated without further purification in 86% yield as an oil, α/β 13:1; $[\alpha]_D$ +28° (*c* 1.1, $CHCl_3$); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 169.5, 169.2, 168.8 CH_3CO), 137.9–127.4 (Ph), 92.0 (C-1β), 89.4 (C-1α), 79.9 (C-3β) 77.4 (C-3α) 76.9 (C-2β) 76.5 (C-2α) 74.5, 73.5 (CH_2Ph) 71.5 (C-5) 70.7 (C-4) 69.6 (C-6). Anal. Calcd for $C_{26}H_{30}O_9$: C, 64.19; H, 6.21. Found: C, 64.38; H, 6.14.

Benzyl 2,4-di-O-*acetyl-3,6-di*-O-*benzyl-β*-D-*glucopyranoside* (**10**).—To a stirred solution of **9** (24 g, 49 mmol) and benzyl alcohol (5.6 g, 54 mmol) in CH_2Cl_2 (240 mL) was added $SnCl_4$ (6.35 mL, 54 mmol). After 24 h at rt, the mixture was filtered and the filtrate neutralized with solid $NaHCO_3$. The solution was concentrated under reduced pressure. The residue was purified by column chromatography eluting with 22:3 hexane–acetone to give **10** in 60% yield as white crystals; mp 73–74 °C, $[\alpha]_D$ −30.9° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.39–7.26 (m, 10 H, Ph), 5.15 (dd, 1 H, $J_{2,3}$ 9.4 Hz, H-2), 5.14 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.93–4.60 (CH_2Ph), 4.49 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 3.70 (t, 1 H, $J_{3,4}$ 9.4 Hz, H-3), 3.61 (m, 3 H, H-5, H-6), 2.03 1.92 (2s, 6 H, CH_3CO); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 170.0–169.7 (CH_3CO), 138.3–128.2 (Ph), 99.9 (C-1), 80.6 (C-3), 73.9 (C-2), 73.0 (C-4), 71.2 (C-5), 70.1 (C-6), 74.1, 70.8 (CH_2Ph), 21.3 (CH_3CO). Anal. Calcd for $C_{31}H_{34}O_8$: C, 69.65; H, 6.41. Found: C, 69.41; H, 6.17.

Benzyl 3,6-di-O-*benzyl-β*-D-*glucopyranoside* (**11**).—To a stirred solution of **10** (5.7 g, 105 mmol) in MeOH (45 mL) was added NaOMe (45 mg, 6 mmol). After 3 h at rt, the mixture was neutralized with AcOH and concentrated under reduced pressure. The residue was purified by column chromatography eluting with 17:3 hexane–acetone to give **11** in 98% yield as an oil; $[\alpha]_D$ −51.9° (*c* 0.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.21–7.12 (m, 10 H, Ph), 4.78–4.45 (CH_2Ph), 4.20 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 3.59 (m, 2 H, $J_{6a,6b}$ 10.5 Hz, H-6), 3.45 (t, 1 H, $J_{4,5}$ 9.4 Hz, H-4), 3.45 (dd, 1 H, $J_{2,3}$ 9.1 Hz, H-2), 3.30 (m, 1 H, $J_{5,6a}$ and $J_{5,6b}$ 5.2 Hz, H-5), 3.23 (t, 1 H, $J_{3,4}$ 8.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ 138.3–128.2 (Ph), 102.1 (C-1), 84.2 (C-3), 75.1, 74.1, 71.0 (CH_2Ph), 74.9 (C-2), 74.7 (C-4), 71.6 (C-5), 70.6 (C-6). Anal. Calcd for $C_{27}H_{30}O_6$: C, 71.98; H, 6.71. Found: C, 72.15; H, 6.82.

Benzyl 2,3,4-tri-O-*acetyl-α*-L-*rhamnopyranosyl-(1→4)-3,6-di*-O-*benzyl-β*-D-*glucopyranoside* (**14**) *and benzyl 2,3,4-tri*-O-*acetyl-α*-L-*rhamnopyranosyl-(1→2)-[(2,3,4-tri*-O-*acetyl-α*-L-*rhamnopyranosyl-(1→4)]-3,6-di*-O-*benzyl-β*-D-*glucopyranoside* (**15**).—To a stirred solution of bromide derivative **13** (8.6 g, 24 mmol) and benzyl derivative **11** (2.5 g, 6 mmol) in anhyd CH_2Cl_2 (66 mL) was added, at 0 °C in the dark, tetramethylurea (2.65 mL, 24 mmol) and CF_3SO_3Ag (4.28 g, 84 mmol). After 48 h at rt in the dark, the mixture was filtered and extracted with CH_2Cl_2–water. The organic phase was separated, washed with water (twice), dried (Na_2SO_4) and concentrated under reduced pressure. Column chromatography eluting with hexane–acetone allowed to obtain first **14** in 30% yield as an oil; $[\alpha]_D$ −12° (*c* 1.2, $CHCl_3$); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ *glucose* 137.9–127.2 (Ph), 98.6 (C-1), 81.8 (C-3), 75.6, 74.0, 71.4 (CH_2Ph), 74.6 (C-4), 73.5 (C-2), 70.9 (C-5), 68.6 (C-6), *rhamnose (1→4)* 170.7–170.3 (CH_3CO), 97.4 (C-1), 70.6 (C-4), 70.5 (C-2), 69.5(C-3), 67.1 (C-5), 21.2 (CH_3CO), 17.3 (C-6). Anal. Calcd for $C_{39}H_{46}O_{13}$: C, 64.81; H, 6.41. Found: C, 65.09; H, 6.37. Mass spectrometry: FAB-MS; $[M+Li]^+$ *m/z* 729, $C_{12}H_{17}O_7^+$ *m/z* 273. Benzyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1→4)]-3,6-di-*O*-benzyl-β-D-glucopyranoside (**15**) was obtained next in 65% yield as an oil; $[\alpha]_D$ −69° (*c* 0.8, $CHCl_3$); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ *glucose* 137.4–127.7 (Ph), 100.3 (C-1), 81.0 (C-3), 79.6 (C-2),

75.8, 73.5, 69.7 (CH_2Ph), 75.4 (C-4), 70.9 (C-5), 68.5 (C-6), *rhamnose(1→4)* 170.6–169.9 (CH_3CO), 97.2(C-1), 71.2 (C-4), 70.5 (C-2), 69.3(C-3), 67.2 (C-5), 21.2 (CH_3CO), 17.3 (C-6), *rhamnose(1→2)* 170.6–169.9 (CH_3CO), 97.7(C-1), 71.2 (C-4), 70.0 (C-2), 69.3(C-3), 67.2 (C-5), 21.2 (CH_3CO), 17.3 (C-6). Anal. Calcd for $C_{51}H_{62}O_{20}$: C, 61.56; H, 6.28. Found: C, 61.28; H, 6.03. Mass spectrometry: FAB-MS; $[M + Li]^+$ m/z 1001, $C_{12}H_{17}O_7^+$ m/z 273.

2,3,4-Tri-O-acetyl-α-L-rhamnopyranosyl-(1→2)-[2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl-(1→4)]-1,3,6-tri-O-acetyl-D-glucopyranose (**16**).—A mixture of prehydrogenated 5% Pd–C catalyst (263 mg) in EtOH and **15** (606 mg, 0.61 mmol) dissolved in EtOH (20 mL) was shaken in a hydrogen atmosphere (1 atm) during 96 h. The catalyst was filtered off and EtOH evaporated under vacuum to give an oil. The mixture was dissolved in pyridine (1 mL) and was added Ac_2O (1 mL). After 12 h at rt, iced water was added and the product extracted with EtOAc. The organic layer was washed several times with water, dried (Na_2SO_4) and evaporated under reduced pressure several times with toluene. The residue was purified by column chromatography eluting with 13:7 hexane–EtOAc to give **16** in 24% yield as an oil, α/β 2:1; $[\alpha]_D$ 1.5° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{36}H_{50}O_{23}$: C, 50.82; H, 5.92. Found: C, 51.09; H, 5.94. Mass spectrometry: EI-MS; $[M - CH_3CO_2H]^{+\bullet}$ m/z 790, $C_{12}H_{16}O_7^{+\bullet}$ m/z 272, $[C_{12}H_{16}O_7 - 2CH_3CO_2H]^{+\bullet}$ m/z 152. ESI-MS; $[M + NH_4]^+$ m/z 868, $C_{12}H_{17}O_7^+$ m/z 273. **16α** anomer. ^1H NMR ($CDCl_3$, 300 MHz): δ *Glucose* 6.27 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.51 (t, 1 H, $J_{3,4}$ 9.3 Hz, H-3), 4.38 (dd, 1 H, $J_{5,6a}$ 1.9, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.34 (dd, 1 H, $J_{5,6b}$ 3.3 Hz, H-6b), 4.03 (ddd, 1 H, H-5), 3.79 (t, 1 H, $J_{4,5}$ 9.9 Hz, H-4), 3.76 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-2), *rhamnose (1→4)* 5.23 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 10.1 Hz, H-3), 5.06 (t, 1 H, H-4), 5.02 (dd, 1 H, $J_{1,2}$ 1.7 Hz, H-2), 4.83 (d, 1 H, H-1), 3.88 (dq, 1 H, $J_{4,5}$ 9.6, $J_{5,6}$ 6.2 Hz, H-5), 1.18 (d, 3 H, H-6), *rhamnose (1→2)* 5.16 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 5.04 (t, 1 H, H-4), 5.02 (dd, 1 H, H-2), 4.82 (d, 1 H, $J_{1,2}$ 1.6 Hz, H-1), 3.80 (dq, 1 H, $J_{4,5}$ 9.5, $J_{5,6}$ 6.2 Hz, H-5), 1.18 (d, 3 H, H-6). 2.27, 2.17 (2 s, 6 H, 2 CH_3CO), 2.14 (s, 6 H, 2 CH_3CO), 2.12 (s, 3 H, CH_3CO), 2.05 (s, 6 H, 2 CH_3CO), 2.01, 1.99 (2 s, 6 H, 2 CH_3CO); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ *glucose* 89.9 (C-1), 77.2 (C-4), 76.6 (C-2), 71.8 (C-3), 70.3 (C-5), 61.7 (C-6), *rhamnose (1→4)* 99.5 (C-1), 70.6 (C-4), 70.2 (C-2), 68.4 (C-3), 67.8 (C-5), 17.2 (C-6), *rhamnose (1→2)* 99.1 (C-1), 70.6 (C-4), 70.0 (C-2), 68.2 (C-3), 67.3 (C-5), 17.2 (C-6). 170.5–168.5 (CH_3CO), 21.1–20.4 (CH_3CO). **16β** anomer. ^1H NMR ($CDCl_3$, 300 MHz): δ *Glucose* 5.68 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1), 5.33 (t, 1 H, $J_{3,4}$ 8.8 Hz, H-3), 4.43 (dd, 1 H, $J_{5,6a}$ 1.4, $J_{6a,6b}$ 12.6 Hz, H-6a), 4.33 (dd, 1 H, $J_{5,6b}$ 3.4 Hz, H-6b), 3.81 (t, 1 H, $J_{4,5}$ 10.8 Hz, H-4), 3.78 (ddd, 1 H, H-5), 3.64 (dd, 1 H, $J_{2,3}$ 9.3 Hz, H-2), *rhamnose (1→4)* 5.19 (dd, 1 H, $J_{3,4}$ 10.2 Hz, H-3), 5.05 (t, 1 H, $J_{4,5}$ 9.7 Hz, H-4), 5.01 (dd, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 4.83 (d, 1 H, $J_{1,2}$ 2.1 Hz, H-1), 3.86 (dq, 1 H, $J_{5,6}$ 6.2 Hz, H-5), 1.17 (d, 3 H, H-6), *rhamnose (1→2)* 5.11 (dd, 1 H, $J_{3,4}$ 10.2 Hz, H-3), 5.07 (dd, $J_{2,3}$ 3.4 Hz, 1 H, H-2), 5.04 (t, 1 H, $J_{4,5}$ 9.3 Hz, H-4), 4.85 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 3.91 (dq, 1 H, $J_{5,6}$ 6.3 Hz, H-5), 1.16 (d, 3 H, H-6). 2.20, 2.15 (2 s, 6 H, 2 CH_3CO), 2.14 (s, 6 H, 2 CH_3CO), 2.12, 2.05, 2.04, 2.00, 1.97 (5s, 15 H, 5 CH_3CO); ^{13}C NMR ($CDCl_3$, 75.5 MHz): δ glucose 92.5 (C-1), 78.7 (C-2), 77.0 (C-4), 74.0 (C-3), 73.1 (C-5), 61.7 (C-6), *rhamnose (1→4)* 99.5 (C-1), 70.5 (C-4), 70.1 (C-2), 68.4 (C-3), 67.9 (C-5), 17.1 (C-6), *rhamnose (1→2)* 98.6 (C-1), 70.5 (C-4), 69.8 (C-2), 68.7 (C-3), 67.2 (C-5), 17.2 (C-6), 170.5–168.5 (CH_3CO), 21.1–20.4 (CH_3CO).

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