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Synthesis of Diterpene Glycosides

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Summary. Mono-, di-, and linear triglycosides of a diterpene alcohol, derived from abietic acid and glucose have been synthesized employing peracetylbromo-α-*D*-glucose (**4**) and maltose derivatives **5** and **8** as glycosyl donors. The triglycoside **14** exhibits slight haemolytic activity.

Keywords. Abietic acid; Diterpenes; Glycoside synthesis; Saccharide donors.

Synthese von Diterpenglycosiden

Zusammenfassung. Es wird die Synthese von Mono-, Di-, und linearen Triglycosiden aus einem von Abietinsäure abgeleiteten Diterpenalkohol beschrieben. Als Glycosyldonoren wurden neben Peracetobrom-α-*D*-glucose (**4**) die Maltosederivate **5** und **8** verwendet. Das Triglycosid **14** zeigt schwache hämolytische Aktivität.

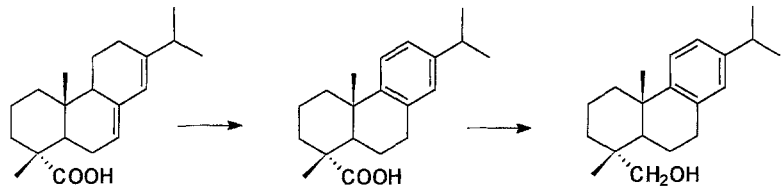
Introduction

Many terpene glycosides exhibit biological activities which are closely related to their structures and configurations. Saponins, for example, which are triterpene glycosides with complex oligosaccharide structures, have several important biological and pharmacological activities such as cancer related activity, antiphlogistic and antiallergic, immunomodulating, antihepatotoxic, antiviral, haemolytic, antifungal, and molluscidal activities [1–7]. Determination of structure-activity relationships within this class of compounds is difficult, because only a limited amount of substance can be isolated and the oligosaccharide structure as well as the structure of the terpene residue has to be modified by partial synthesis. Only few approaches of partial syntheses of terpene glycosides appear in the literature [8–10], and only in one case information about a relation between structure and haemolytic activity has been reported [11]. The aim of this study was to investigate if the title compounds show haemolytic activity and how this activity is related to the length of the glycosidic chain. We have used the *Koenigs-Knorr* method to condense acetobromo glucose and di- and triglycosyl donors, respectively with a diterpene alcohol to obtain terpene glycosides. The diterpene alcohol has been derived from abietic acid.

Results and Discussion

Synthesis of the terpene residue

Dehydroabietic acid (**2**) was obtained from abietic acid (**1**) in the usual way [12, 13]. Reduction of **2** with $LiAlH_4$ gave the desired diterpene alcohol **3**.



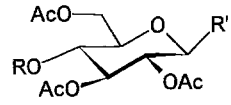
1 2 3

Scheme 1

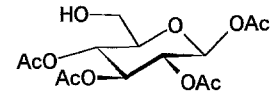
Synthesis of glycosyl donors

We used acetobromo-α-*D*-glucose (**4**), acetobromo-α-maltose (**5**) [14], and 6-maltosido-β-*D*-glucopyranosylbromide decaacetate (**7**) as glycosyl donors. The latter was prepared by condensation of β-*D*-glucose-1,2,3,4-tetraacetate (**6**) [15] with acetobromo-α-maltose (**5**) giving 6-maltosido-β-*D*-glucose undecaacetate (**8**) [16]. Subsequent treatment of **8** with hydrogen bromide in glacial acetic acid [17] yielded the trisaccharid donor **7** as a white amorphous solid.

7 is very sensitive against moisture and was immediately used for glycosylation. Its structure was characterized mainly by ^1H and ^{13}C NMR spectro-



4 R = Ac, R' = Br
5 R = Tetraacetyl-α-D-glucopyranosyl, R' = Br



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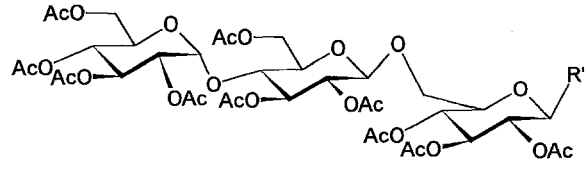


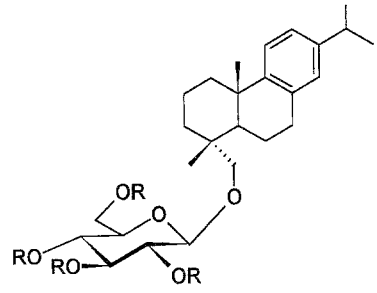
7 R' = Br
8 R' = OAc

Scheme 2

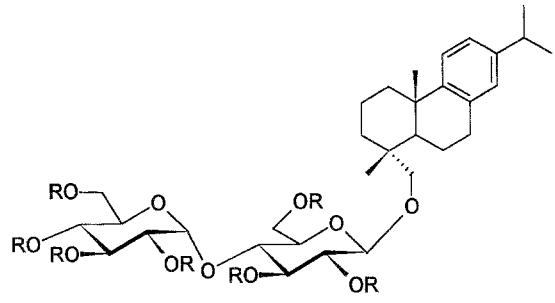
scopy. The introduction of bromine at position 1 was indicated by a low field shift of the anomeric proton (0.9 ppm) and a high field shift of C-1 (5 ppm).

Synthesis of the glycosides

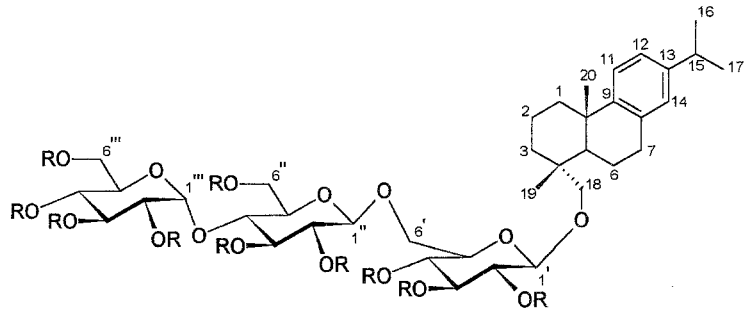
For the glycosylation, we used drierite [18] as dehydrating agent. The reaction was catalyzed by silver oxide which was prepared according to the method of *Helferich*



9 R = Ac
10 R = H



11 R = Ac
12 R = H



13 R = Ac
14 R = H

Scheme 3

and *Klein* [15]. Iodine was added to the reaction mixture following the procedure of *Helferich*, *Bohm*, and *Winkler* [19] affording the terpene carbohydrate derivates **9**, **11**, and **13**. Cleavage of the ester groups with sodium methoxide [20] yielded the diterpeneglycosides **10**, **12**, and **14** in yields between 30 and 75% after chromatographic purification. Only **14** was sufficiently soluble in water to allow determination of its haemolytic activity. The haemolytic index was 3000, indicating that triglycoside **14** has moderate activity. We consider this to be due to the diterpene residue which is too small to induce pronounced activity.

Experimental

Analytical methods

Melting points: melting point apparatus Dr. Tottoli, uncorrected; optical rotation: polarimeter 241 MC (Perkin Elmer); MS: Varian MAT 711 spectrometer, 70 eV electron impact and field desorption; IR spectra: infrared spectrometer System 2000 FT (Perkin Elmer); UV/Vis: Lambda 17 UV/Vis-spectrometer (Perkin Elmer); NMR spectra: Varian Inova 400, 600 (300 K), 5 mm tubes, solvent resonance as internal standard. ^{1}H and ^{13}C resonances were assigned using ^{1}H, ^{1}H and ^{1}H, ^{13}C correlation spectra and are numbered as given in formulae **13** and **14**. Preparative TLC: Chromatotron Harrison Research, USA; 1 mm Kieselgel 60 PF_{254} containing gypsum (Merck) elementary analyses: Laboratory for Microanalysis, Institute of Physical Chemistry, University of Vienna; Column chromatography (CC): silica gel Kieselgel 60 (Merck) (70–230 mesh), pore diameter 60 Å; thin-layer chromatography (TLC): TLC plates (Merck) Kieselgel 60 F_{254} 0.2 mm, 200 × 200 mm; the substances were detected in UV light at 254 nm and by spraying with methanol/sulfuric acid (9:1) and subsequent heating with a hot air gun.

General methods

Glycosidation (according to Ref. [15])
A solution of 9 mmol aglycon in dry $CHCl_3$ was stirred with 13 mmol freshly prepared Ag_2O and 10 g drierite for 90 minutes at room temperature in an argon atmosphere. Then, 2 mmol of iodine and a solution of 9 mmol acetobromo carbohydrate in 13 ml $CHCl_3$ were added dropwise within one hour. The reaction mixture was stirred overnight at room temperature. After filtration and evaporation of the solvent at room temperature, the solid residue was purified as described below.

Deacetylation

2 mmol of the acetylated terpene glycoside were dissolved in 16 ml of dry $CHCl_3$. For each ester group, 4 ml of a 1 *M* solution of sodium methylate in dry methanol were added at −20°C. The course of the reaction was monitored by TLC. The reaction mixture was poured on ice and neutralized with diluted hydrochloric acid. The chloroform solution was separated, and the aqueous layer extracted five times with $CHCl_3$. The combined organic phases were dried over sodium sulfate, filtered, and evaporated *in vacuo*. Further purification of the product is described below.

6-Maltosido-β-D-glucopyranosylbromide decaacetate (**7**)

Prepared according to the method of *Brauns* [17]; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.97, 1.89, 2.00, 2.01, 2.02, 2.05, 2.05, 2.05, 2.06, 2.11$ (10s, 30H, CH_3CO), 3.56 (dd, $J = 11.2, 3.2$ Hz, 1H, 6′-H), 3.60–3.66 (m, 1H, 5″-H), 3.91–4.03 (m, 4H, 6′-H, 5‴-H, 4″-H, 6‴-H), 4.16–4.26 (m, 3H, 6″-H,

6‴-H, 5′-H), 4.43 (dd, $J = 12$, 2.4 Hz, 1H, 6′-H), 4.52 (d, $J = 7.6$ Hz, 1H, 1″-H), 4.73–4.84 (m, 3H, 2′-H, 2″-H, 2‴-H), 5.01 (dd, $J = 10$, 10 Hz, 1H, 4‴-H), 5.05 (dd, $J = 10$, 10 Hz, 1H, 4′-H), 5.21 (dd, $J = 9.2$, 9.2 Hz, 1H, 3″-H), 5.32 (dd, $J = 10$, 10 Hz, 1H, 3‴-H), 5.37 (d, $J = 4$ Hz, 1H, 1‴-H), 5.49 (dd, $J = 9.6$, 9.6 Hz, 1H, 3′-H), 6.58 (d, $J = 3.6$ Hz) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.58$, 20.64, 20.80, 20.86 (CH_3CO), 61.47 (C-6‴), 62.70 (C-6″), 66.71 (C-6′), 67.38 (C-4′), 67.97 (C-4‴), 68.46 (C-5‴), 69.27 (C-3‴), 69.94 (C-2‴), 70.20 (C-3′), 70.50 (C-2′), 71.73 (C-2″), 72.19 (C-5″), 72.58 (C-4″), 73.00 (C-5′), 75.16 (C-3″), 86.61 (C-1′), 95.47 (C-1‴), 100.24 (C-1″), 169.17, 169.66, 170.14, 170.48 (CH_3CO) ppm.

6-Maltosido-α-D-glucose undecaacetate (**8**)

Melting point: as in Ref. [16]; IR (KBr): $\tilde{\nu} = 2900$ (w), 1750 (s), 1625 (w), 1450 (w), 1375 (m), 1225 (s), 1100 (m), 1050 (s), 900 (w) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 2.00$, 2.01, 2.02, 2.02, 2.03, 2.03, 2.04, 2.05, 2.11, 2.11, 2.15 (11s, 33H, CH_3CO), 3.56 (dd, $J = 11.6$, 5.6 Hz, 1H, 6′-H), 3.64–3.70 (m, 1H, 5″-H), 3.77–3.81 (m, 1H, 5′-H), 3.93 (dd, $J = 11.2$, 2.4 Hz, 1H, 6′-H), 3.96–4.00 (m, 2H, 4″-H, 5‴-H), 4.04 (dd, 12.8, 2 Hz, 1H, 6‴-H), 4.19–4.27 (m, 2H, 6″-H, 6‴-H), 4.48 (dd, $J = 12$, 2.4 Hz, 1H, 6″-H), 4.55 (d, $J = 7.6$ Hz, 1H, 1″-H), 4.82 (dd, $J = 8$, 8 Hz, 1H, 2″-H), 4.86 (dd, $J = 10.4$, 3.6 Hz, 1H, 2‴-H), 4.98–5.11 (m, 3H, 4′-H, 4‴-H, 2′-H), 5.20–5.25 (m, 2H, 3′-H, 3‴-H), 5.35 (dd, $J = 10.2$, 10.2 Hz, 1H, 3‴-H), 5.40 (d, $J = 4$ Hz, 1H, 1‴-H), 5.68 (d, $J = 8.4$ Hz, 1H, 1′-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.54$, 20.65, 20.80, 20.86, (CH_3CO), 61.48 (C-6‴), 62.70 (C-6″), 67.60 (C-6′), 67.98 (C-4‴), 68.31 (C-4′), 68.46 (C-5‴), 69.30 (C-3‴), 69.94 (C-2‴), 70.21 (C-2′), 71.78 (C-2″), 72.18 (C-5″), 72.65 (C-4″), 72.87 (C-3′), 73.69 (C-5′), 75.24 (C-3″), 91.57 (C-1′), 95.51 (C-1‴), 100.18 (C-1″), 169.27, 170.43 (CH_3CO) ppm.

[1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl peracetyl-(O-β-D-glucopyranosid) (**9**)

2.55 g (9 mmol) **3** were treated with Ag_2O, drierite, I_2, and 3.67 g (9 mmol) acetobromo-α-*D*-glucose in $CHCl_3$ as described above. The yellowish resin was dissolved in acetone and crystallized upon cooling.

White needles; 2.15 g (38.7%); m.p.: 145–148°C; $R_f = 0.48$ (dichlormethane); $[\alpha]_D^{20} = 13.5°$, $[\alpha]_{546}^{20} = 16.0°$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 2950$ (m), 1750 (s), 1600 (w), 1500 (w), 1450 (w), 1350 (m), 1250 (s), 1150 (w), 1100 (m), 1050 (s), 950 (w), 900 (w), 850 (w), 700 (w) cm^{-1}; UV (MeOH): λ (log ε) = 215 (4.248), 265 (2.916), 275 (2.900) nm; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 0.89$ (s, 3H, 19-H), 1.20 (s, 3H, 20-H), 1.23 (d, $J = 6.8$ Hz, 6H, $CH(CH_3)_2$), 1.30–1.50 (m, 3H, 3-H, 1-H_{ax}), 1.60–1.80 (m, 6H, 2-H, 5-H, 6-H), 1.97, 1.99, 2.03, 2.11 (4s, 12H, CH_3CO), 2.26 (d, br, $J = 16$ Hz, 1H, 1-H_{eq}), 2.80–2.85 (m, 3H, 7-H, 15-H), 3.09 (d, $J = 9.2$ Hz, 1H, 18-H), 3.67–3.71 (m, 1H, 5′-H), 3.71 (d, $J = 9.2$ Hz, 1H, 18H), 4.15 (dd, $J = 12.4$, 2.4 Hz, 1H, 6′-H), 4.27 (dd, $J = 12.4$, 4.6 Hz, 1H, 6′-H), 4.48 (d, $J = 8$ Hz, 1H, 1′-H), 4.97 (dd, $J = 9.6$, 8 Hz, 1H, 2′-H), 5.08 (dd, $J = 9.6$, 9.6 Hz, 1H, 4′-H), 5.20 (dd, $J = 9.6$, 9.6 Hz, 1H, 3′-H), 6.88 (d, $J = 2$ Hz, 1H, 14-H), 6.98 (dd, $J = 8.2$ Hz, 1H, 12-H), 7.16 (d, $J = 8$ Hz, 1H, 11-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.3$ (C-19), 18.6 (C-2), 18.9 (C-6), 20.49, 20.57, 20.58, 20.73 (CH_3CO), 23.95 (C-16, C-17), 25.30 (C-20), 30.12 (C-7), 33.42 (C-15), 35.43 (C-3), 37.28 (C-10), 37.44 (C-4), 38.36 (C-1), 44.29 (C-5), 62.04 (C-6′), 68.58 (C-4′), 71.33 (C-2′), 71.61 (C-5′), 72.78 (C-3′), 79.34 (C-18), 101.25 (C-1′), 123.72 (C-12), 124.22 (C-11), 126.74 (C-14), 134.78 (C-8), 145.43 (C-13), 147.13 (C-9), 169.07, 169.34, 170.31, 170.64 (CH_3CO) ppm; MS (70 eV): *m/z* (%) = 616 (0.9) [M$^+$], 538 (0.6), 496 (0.6), 436 (0.5), 331 (25.9), 300 (1.5), 285 (3.7), 271 (10.4), 253 (22.2), 211 (8.1), 169 (100.0), 115 (6.7), 109 (13.3), 98 (5.9), 43 (68.9); $C_{34}H_{48}O_{10}$ (616.75); calc. C 66.31, H 7.84; found: C 66.42, H 7.83.

[1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10,10a-octahydro-1, 4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl-β-D-glucopyranosid (**10**)

1.29 g (2 mmol) **9**, dissolved in 16 ml $CHCl_3$, were treated with 0.3 g Na in 16.1 ml dry MeOH as described above. After evaporation of the solvent, a white residue was obtained which was purified by CC (dichlormethane/methanol = 9:1).

0.41 g (41.5%); m.p.: 90–100°C; $R_f = 0.34$ (dichlormethane/methanol = 9:1); $[\alpha]_D^{20} = 16.97°$, $[\alpha]_{546}^{20} = 19.56°$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\nu = 3450$ (s), 2950 (s), 1750 (w), 1700 (w), 1635 (m), 1500 (m), 1450 (m), 1350 (m), 1300 (w), 1250 (m), 1200 (w), 1150 (m), 1075 (s), 1025 (s), 900 (w), 800 (m), 750 (w), 635 (m) cm^{-1}; UV (MeOH): λ (log ε) = 267 (3.458), 275 (3.423) nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.90$ (s, 3H, 19-H), 1.17 (s, 3H, 20-H), 1.20 (d, $J = 6.8$ Hz, 6H, $CH(CH_3)_2$), 1.30–1.50 (m, 3H, 3-H, 1-H_{ax}), 1.60–1.75 (m, 6H, 2-H, 5-H, 6-H), 2.22 (d, br, $J = 11.2$ Hz, 1H, 1-H_{eq}), 2.78–2.85 (m, 3H, 7-H, 15-H), 3.13 (d, $J = 9.2$ Hz, 1H, 18-H), 3.18 (d, br, $J = 8.8$ Hz, 1H, 5′-H), 3.30–3.34 (m, 1H, 2′-H), 3.46 (dd, $J = 8.8$, 8.8 Hz, 1H, 3′-H), 3.53 (dd, $J = 8.8$, 8.8 Hz, 1H, 4′-H), 3.65 (d, $J = 9.2$ Hz, 1H, 18-H), 3.68–3.78 (m, 2H, 6′-H), 4.16 (d, $J = 8$ Hz, 1H, 1′-H), 6.86 (s, 1H, 14-H), 6.96 (d, $J = 8.4$ Hz, 1H, 12-H), 7.14 (d, $J = 8.4$ Hz, 1H, 11-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.41$ (C-19), 18.61 (C-2), 19.05 (C-6), 24.00 (C-6, C-17), 25.35 (C-20), 30.12 (C-7), 33.42 (C-15), 35.65 (C-3), 37.30 (C-10), 37.56 (C-4), 38.37 (C-1), 44.57 (C-5), 61.63 (C-6′), 69.73 (C-4′), 73.54 (C-2′), 75.34 (C-5′), 76.13 (C-3′), 79.90 (C-18), 103.75 (C-1′), 123.75 (C-12), 124.23 (C-11), 126.77 (C-14), 134.72 (C-8), 145.44 (C-13), 147.25 (C-9) ppm; MS (70 eV): *m/z* (%) = 448 (1.5) [M^+], 415 (0.8), 334 (0.8), 328 (5.9), 327 (9.6), 286 (53.3), 271 (39.3), 253 (56.3), 239 (8.9), 211 (13.3), 185 (15.6), 173 (100.0), 159 (18.2), 131 (11.1), 117 (5.9), 97 (1.5), 73 (3.0), 60 (5.9); $C_{26}H_{40}O_6$ (448.60); calc.: C 69.61, H 8.99; found: C 69.37, H 9.04.

[1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10,10a-Octahydro-1, 4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl-peracetyl-α-D-glucopyranosyl-(1 →4)-β-D-glucopyranosid (**11**)

1.77 g (6 mmol) **3** dissolved in 7.5 ml $CHCl_3$ were treated with 7 g drierite, 2.5 g Ag_2O, 0.36 g iodine, and 4.3 g (6 mmol) acetobromo-α-maltose in 18 ml $CHCl_3$.

3.47 g (77.4%); yellow resin; 100 mg were purified by preparative TLC (CH_2Cl_2): 60 mg; m.p:. 85–90°C; $R_f = 0.42$ (CH_2Cl_2); $[\alpha]_D^{20} = 49°$, $[\alpha]_{546}^{20} = 60.4°$ ($c = 0.5$, $CHCl_3$); IR (KBr): $\bar{\nu} = 2950$ (m), 2900 (m), 2850 (w), 1750 (s), 1650 (w), 1500 (w), 1450 (w), 1375 (m), 1225 (s), 1175 (w), 1125 (w), 1050 (s), 950 (w), 900 (w) 810 (w) cm^{-1}; UV (MeOH): λ (log ε) = 215 nm (4.402), 267.5 (3.304), 275 (3.263) nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.87$ (s, 3H, 19-H), 1.19 (s, 3H, 20-H), 1.22 (d, $J = 6.8$ Hz, 6H, $CH(CH_3)_2$) 1.33–1.42 (m, 3H, 3-H, 1-H_{ax}), 1.63–1.78 (m, 6H, 2-H, 5-H, 6-H), 1.94, 1.97, 2.00, 2.03, 2.04, 2.11, 2.16 (7s, 21-H, CH_3CO), 2.25 (d, br, $J = 12.8$ Hz, 1H, 1-H_{eq}), 2.78–2.87 (m, 3H, 7-H, 15-H), 3.05 (d, $J = 9.2$ Hz, 1H, 18-H), 3.63–3.77 (m, 2H, 18-H, 5′-H), 3.94–4.00 (m, 2H, 4′-H, 5″-H), 4.04 (dd, $J = 12.4$, 2 Hz, 1H, 6″-H), 4.21–4.29 (m, 2H, 6′-H, 6″-H), 4.47 (dd, $J = 12.2$, 8 Hz, 1H, 6′-H), 4.49 (d, $J = 7.6$ Hz, 1H, 1′-H), 4.80 (dd, $J = 9.2$, 7.6 Hz, 1H, 2′-H), 4.85 (dd, $J = 9.6$, 4.4 Hz, 1H, 2″-H), 5.05 (dd, $J = 9.6$, 9.6 Hz, 1H, 4″-H), 5.23 (dd, $J = 9.2$, 9.2 Hz, 1H, 3′-H), 5.36 (dd, $J = 9.6$, 9.6 Hz, 1H, 3″-H), 5.40 (d, $J = 4$ Hz, 1H, 1″-H), 6.84 (d, $J = 1.6$ Hz, 1H, 14-H), 6.97 (dd, $J = 8$, 6 Hz, 1H, 12-H), 7.15 (d, $J = 8$ Hz, 1H, 11-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.36$ (C-19), 18.56 (C-2), 18.84 (C-6), 20.46, 20.55, 20.58, 20.67, 20.86 (CH_3CO), 23.96 (C-16, C-17), 25.28 (C-20), 30.10 (C-7), 33.41 (C-15), 35.38 (C-3), 37.26 (C-10), 37.39 (C-4), 38.35 (C-1), 44.11 (C-5), 61.49 (C-6″), 62.86 (C-6′), 68.01 (C-4″), 68.42 (C-5″), 69.33 (C-3″), 69.97 (C-2″), 71.90 (C-5′), 72.15 (C-2′), 72.83 (C-4′), 75.32 (C-3′), 79.14 (C-18), 95.46 (C-1″), 100.66 (C-1′), 123.74 (C-12), 124.22 (C-11), 126.69 (C-14), 134.75 (C-8), 145.44 (C-13), 147.15 (C-9), 169.39, 169.93, 170.23, 170.43, 170.48 (CH_3CO) ppm; MS (70 eV): *m/z* (%) = 904 (0.04) [M^+], 784 (0.6), 683 (0.6), 619 (8.2), 561 (2.2), 559 (17.0), 331 (54.8), 289 (5.9), 271 (13.3), 253 (17.8), 211 (8.9), 169 (100.0), 109 (17.0); $C_{46}H_{64}O_{18}$) (905.00); calc.: C 61.05, H 7.13; found: C 61.14, H 7.42.

1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl-α-D-glucopyranosyl-(1→4)-β-D-glucopyranosid (**12**)

200 mg (2 mmol) **11** dissolved in 4 ml $CHCl_3$ were treated as described above at −20°C, the residue was purified by preparative TLC (CH_2Cl_2/MeOH = 8:2)

15 mg (11.1%); m.p.: 90–100°C; $R_f = 0.47$ (dichlormethane/methanol = 8:2); $[\alpha]_D^{20} = 87.9°$, $[\alpha]_{546}^{20} = 102°$ ($c = 0.7$, $CHCl_3$); IR (KBr): $\bar{\nu} = 3450$ (s), 2900 (m), 1625 (w), 1550 (w), 1450 (w), 1375 (m), 1325 (w), 1250 (w), 1150 (m), 1025 (s), 900 (m), 850 (w), 825 (w), 800 (w), 750 (w) cm^{-1}; UV (MeOH): λ (log ε) = 265 (3.439), 275 (3.404) nm; ^1H NMR (400 MHz, CD_3OD): $\delta = 0.86$ (s, 3H, 19-H), 1.12 (d, $J = 6.8$ Hz, 6H, $CH(CH_3)_2$), 1.13 (s, 3H, 20-H), 1.30–1.35 (m, 2H, 1-H_{ax}, 3-H), 1.56–1.85 (m, 7H, 2-H, 3-H, 5-H, 6-H), 2.21 (d, br, $J = 12.8$ Hz, 1H, 1-H_{eq}), 2.71 (sept, $J = 6.8$ Hz, 1H, $CH(CH_3)_2$), 2.75–2.79 (m, 2H, 7-H), 2.98 (d, $J = 9.2$ Hz, 1H, 18-H), 3.13–3.22 (m, 2H, 2′-H, 4″-H), 3.26–3.30 (m, 1H, 5′-H), 3.37 (dd, $J = 9.6$, 3.6 Hz, 1H, 2″-H), 3.45 (dd, $J = 9.2$, 9.2 Hz, 1H, 4′-H), 3.50–3.65 (m, 4H, 3′-H, 3″-H, 5″-H, 6″-H), 3.72–3.78 (m, 3H, 6″-H, 6′-H), 3.80 (d, $J = 9.2$ Hz, 1H, 18-H), 4.16 (d, $J = 8$ Hz, 1H, 1′-H), 5.09 (d, $J = 4$ Hz, 1H, 1″-H), 6.76 (s, 1H, 14-H), 6.85 (d, $J = 8.4$ Hz, 1H, 12-H), 7.07 (d, $J = 8$ Hz, 1H, 11-H) ppm; ^{13}C NMR (100 MHz, CD_3OD): $\delta = 18.42$ (C-19), 20.09 (C-2), 20.19 (C-6), 24.84 (C-16, C-17), 26.03 (C-20), 31.47 (C-7), 35.15 (C-15), 36.87 (C-3), 38.72 (C-10), 38.85 (C-4), 40.00 (C-1), 45.36 (C-5), 62.60 (C-6′), 63.06 (C-6″), 71.80 (C-4″), 74.47 (C-2″), 75.06 (C-2′, C-5″), 75.39 (C-3″), 76.91 (C-5′), 78.24 (C-3′), 80.22 (C-18), 81.68 (C-4′), 103.18 (C-1″), 105.46 (C-1′), 124.88 (C-12), 125.50 (C-11), 127.92 (C-14), 136.42 (C-8), 146.89 (C-13), 149.03 (C-9) ppm; MS (LSIMS, 4.5 kV): *m/z* (%) = 610 (37.1) [M^+], 609 (100.0), 589 (4.5), 559 (2.2), 517 (4.5), 463 (2.2), 447 (7.6), 427 (3.0), 339 (6.0), 265 (4.5), 221 (6.0), 179 (14.4), 158 (18.2), 118 (55.3), 71 (47.0), 59 (40.2), 45 (9.1); $C_{32}H_{50}O_{11}$ (610.74).

Peracetyl-[1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10,10a-octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl-α-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosid (**13**)

0.65 g (2 mmol) **3** in 7.1 ml $CHCl_3$ were glycosylated with 2 g (2 mmol) of 6-maltosido-β-D-glucopyranosylbromide decaacetate in 10 ml $CHCl_3$. The product, a yellowish residue, was purified by CC (CH_2Cl_2/EtOH = 97:3) yielding 1.97 g (72.7%).

M.p.: 155–162°C (EtOH); $R_f = 0.21$ (CH_2Cl_2/EtOH = 97:3); $[\alpha]_D^{20} = 40.19°$, $[\alpha]_{546}^{20} = 46.99°$ (= 0.5 $CHCl_3$); IR (KBr): $\bar{\nu} = 2950$ (m), 1750 (s), 1625 (w), 1500 (w), 1450 (w), 1375 (m), 1225 (s), 1175 (w), 1125 (w), 1050 (s), 950 (w), 900 (w), 825 (w), 800 (w) cm^{-1}; UV (MeOH): λ (log ε) = 215 (4.246), 267 (3.298), 274 (3.263) nm; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 0.86$ (s, 3H, 19-H), 1.16 (s, 3H, 20-H), 1.19 (d, $J = 7$ Hz, 6H, $CH(CH_3)_2$), 1.24–1.40 (m, 3H, 1-H_{ax}, 3-H), 1.56–1.77 (m, 6H, 2-H, 5-H, 6-H), 1.90, 1.95, 1.96, 1.97, 1.98, 1.99, 2.00, 2.01, 2.07, 2.11 (10s, 30H, CH_3CO), 2.22 (d, br, $J = 12.8$ Hz, 1H, 1-H_{eq}), 2.74–2.87 (m, 3H, 7-H, 15-H), 3.02 (d, $J = 9.4$ Hz, 1H, 18-H), 3.50–3.70 (m, 3H, 5′-H, 5″-H, 6′-H), 3.69 (d, $J = 9.4$ Hz, 1H, 18-H), 3.81 (d, $J = 9.4$ Hz, 1H, 6′-H), 3.88–4.03 (m, 3H, 4″-H, 5″-H, 6‴-H), 4.15–4.24 (m, 2H, 6″-H, 6‴-H), 4.40 (d, $J = 7.8$ Hz, 1H, 1′-H), 4.45 (dd, $J = 12.1$, 2.5 Hz, 1H, 6″-H), 4.59 (d, $J = 7.8$ Hz, 1H, 1″-H), 4.76–4.94 (m, 4H, 2′-H, 2″-H, 2‴-H, 4′-H), 5.02 (dd, $J = 9.8$, 9.8 Hz, 1H, 4‴-H), 5.14 (dd, $J = 9.5$, 9.5 Hz, 1H, 3′-H), 5.20 (dd, $J = 9.8$, 9.8 Hz, 1H, 3″-H), 5.33 (dd, $J = 9.8$, 9.8 Hz, 1H, 3‴-H), 5.38 (d, $J = 3.8$ Hz, 1H, 1‴-H), 6.85 (s, 1H, 14-H), 6.93 (d, $J = 8$ Hz, 1H, 12-H), 7.11 (d, $J = 8$ Hz, 1H, 11-H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 17.33$ (C-19), 18.58 (C-2), 18.97 (C-6), 20.58, 20.64, 20.80 (CH_3CO) 23.96 (C-16, C-17), 25.29 (C-20), 30.12 (C-7), 33.41 (C-15), 35.56 (C-3), 37.29 (C-10), 37.51 (C-4), 38.39 (C-1), 44.45 (C-5), 61.46 (C-6‴), 62.63 (C-6″), 67.98 (C-4‴), 68.18 (C-6′), 68.47 (C-5‴), 69.14 (C-4′), 69.29 (C-3‴), 69.92 (C-2‴), 71.34 (C-2′), 71.94 (C-2″), 72.25 (C-5″), 72.57 (C-4″), 72.70 (C-3′), 73.24 (C-5′), 75.28 (C-3″), 79.39 (C-18), 95.51 (C-1‴), 100.23 (C-1″), 101.30 (C-1′), 123.69 (C-12), 124.19 (C-11), 126.77 (C-14), 134.70 (C-8), 145.42 (C-13), 147.05 (C-9), 169.07, 169.38, 169.86,

170.04, 170.25, 170.49 (CH_3CO) ppm; MS (70 eV): *m/z* (%) = 1192 (3.5) [M^+], 1134 (8.8), 1132 (52.6), 1090 (1.8), 1073 (8.8), 1072 (2.8), 1013 (14.0), 1012 (24.6), 971 (35.1), 928 (14.0), 907 (49.1), 848 (10.5), 845 (100.0), 826 (45.6), 789 (15.8), 784 (38.6), 745 (1.8), 742 (26.3), 725 (26.3), 683 (45.6), 682 (26.3), 619 (80.7), 577 (3.5), 559 (71.9), 517 (3.5), 457 (3.5), 436 (1.6), 397 (1.6), 339 (1.6), 331 (98.2), 317 (8.8), 289 (29.8), 271 (52.6), 229 (21.1), 211 (14.0), 173 (71.9), 169 (98.2), 127 (10.5), 109 (40.3), 97 (5.3), 43 (52.6), 39 (1.8); $C_{58}H_{80}O_{26}$ (1193.26).

[1R-(1α, 4aβ, 10aα)]-1,2,3,4,4a,9,10,10a-Octahydro-1,4a-dimethyl-7-(1-methylethyl)-1-phenanthrenmethyl-α-D-glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-β-D-glucopyranosid (**14**)

500 mg (4 mmol) **13** in 7 ml $CHCl_3$ were deacetylated as described above; 92 mg (29.7%) **14** were obtained by preparative TLC (MeOH).

M.p.: 158°C (EtOH); R_f = 0.65 (CH_2Cl_2/MeOH = 9 : 1); $[\alpha]_D^{20} = 52.0°$, $[\alpha]_{546}^{20} = 56.4°$ (*c* = 0.25, $CHCl_3$); IR (KBr): $\bar{\nu}$ = 3400 (s), 2900 (m), 1750 (w), 1600 (w), 1550 (w), 1450 (w), 1400 (w), 1350 (w), 1250 (w), 1200 (w), 1050 (s), 1025 (s), 950 (w), 900 (w), 825 (w), 775 (w) cm^{-1}; UV (MeOH): λ (log ε) = 215 ((4.402), 265 (3.360), 275 (3.330) nm, ^1H NMR (600 MHz, CD_3OD): δ = 0.89 (s, 3H, 19-H), 1.16 (d, *J* = 6.8 Hz, 6H, $CH(CH_3)_2$), 1.16 (s, 3H, 20-H), 1.30–1.45 (m, 2H, 1-H_{ax}, 3-H), 1.60–1.95 (m, 7H, 2-H, 3-H, 5-H, 6-H), 2.25 (d, *J* = 12.8 Hz, 1H, 1-H_{eq}), 2.78 (sept, *J* = 6.8 Hz, 1H, $CH(CH_3)_2$), 2.79–2.84 (m, 2H, 7-H), 3.01 (d, *J* = 9.2 Hz, 1H, 18-H), 3.12–3.14 (m, 1H, 2′-H), 3.25 (dd, *J* = 9.6, 9.6 Hz, 1H, 4‴-H), 3.26 (dd, *J* = 8.4, 8.4 Hz, 1H, 2″-H), 3.28–3.37 (m, 2H, 3′-H, 5″-H), 3.39–3.44 (m, 2H, 2‴-H, 4′-H), 3.51 (dd, *J* = 9.6, 9.6 Hz, 1H, 4″-H), 3.57–3.81 (m, 8H, 3″-H, 3‴-H, 5′-H, 5‴-H, 6′-H, 6‴-H), 3.81 (d, *J* = 9.2 Hz, 1H, 18-H), 3.88 (dd, *J* = 12, 2 Hz, 1H, 6″-H), 4.10 (dd, *J* = 12, 2 Hz, 1H, 6′-H), 4.19 (d, *J* = 8.2 Hz, 1′-H), 4.40 (d, *J* = 7.6 Hz, 1H, 1″-H), 5.11 (d, *J* = 3.5 Hz, 1‴-H), 6.81 (d, *J* = 1.6 Hz, 1H, 14-H), 6.89 (dd, *J* = 8, 1.6 Hz, 1H, 12-H), 7.10 (d, *J* = 8 Hz, 1H, 11-H) ppm; ^{13}C NMR (150 MHz, CD_3OD): δ = 18.51 (C-19), 20.07 (C-2), 20.21 (C-6), 24.83 (C-16, C-17), 26.04 (C-20), 31.49 (C-7), 35.11 (C-15), 36.85 (C-3), 38.71 (C-10), 38.84 (C-4), 40.00 (C-1) 45.17 (C-5), 62.50 (C-6″), 63.01 (C-6‴), 70.20 (C-6′), 71.80 (C-4‴, C-5′), 74.43 (C-2‴), 74.96 (C-2″), 75.07 (C-5‴), 75.36 (C-3‴), 75.40 (C-2′), 77.02 (C-5″), 77.28 (C-4′), 78.04 (C-3″), 78.37 (C-3′), 80.02 (C-18), 81.71 (C-4″), 103.28 (C-1‴), 105.13 (C-1″), 105.27 (C-1′), 124.83 (C-12), 125.48 (C-11), 127.96 (C-14), 136.45 (C-8), 146.89 (C-13), 149.01 (C-9) ppm; MS (LSIMS, 4.5 kV): *m/z* (%) = 771 (88.6) [M^+], 755 (9.1), 679 (6.1), 625 (3.8), 609 (33.3), 591 (9.1), 517 (6.1), 447 (16.7), 409 (6.8), 382 (12.1), 280 (11.4), 263 (12.9), 221 (34.8), 179 (41.7), 140 (42.4), 119 (96.2), 71 (100.0), 59 (87.1); $C_{38}H_{60}O_{16}$ (772.88).

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