Synthesis of a Typical Glucuronide-Containing Saponin, 28-*O*-β-D-Glucopyranosyl Oleanate 3-*O*-β-D-Galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside

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Abstract: 28-*O*-β-D-Glucopyranosyl oleanate 3-*O*-β-D-galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (**1**), a structurally typical glucuronide-containing triterpene saponin isolated from *Aralia dasyphylla*, was concisely synthesized in linear nine steps and 26% overall yield. The key features of the synthesis are: (1) attachment of the 28-glucosyl ester ahead of assembly of the 3-*O*-sugar chain; (2) elaboration of the glucuronide residue at a later stage via the TEMPO-mediated selective oxidation; (3) installation of 2-(azidomethyl)benzoyl group as a benzoylic neighboring participating group which is selectively removed afterwards for synthesis of the 1→2 sugar linkage.

Keywords: triterpene saponin, glucuronide, synthesis, glycosylation, oxidation

28-*O*-β-D-Glucopyranosyl oleanate 3-*O*-β-D-galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (**1**) was isolated from *Aralia dasyphylla* Miq. (Araliaceae), a Chinese folk medicinal plant used for treatment of hepatitis and diabetes.[1] This compound was claimed to be highly cytotoxic, with IC_{50} values of 1.2 μg/mL and 0.02 μg/mL against two cultured human cancer cell lines, KB and Hela-S_3 cells, respectively.[1] In fact, an early report has mentioned the same structure being isolated from *Polyscias fruticosa* (L.) Harms. (Araliaceae).[2] However, two reports provided quite different ^1H and ^{13}C NMR data as well as the optical rotation value for this compound.[1,2] Structurally, saponin **1** represents a typical member of the family termed glucuronide oleanane-type triterpene carboxylic acid 3,28-*O*-bisdesmoside (GOTCAB).[3] We have recently reported the first synthesis of a GOTCAB saponin, ginsenoside Ro [28-*O*-β-D-glucopyranosyl oleanate 3-*O*-β-D-glucopyranosyl-(1→2)-β-D-glucuronopyranoside].[4] Here we report a full account on the synthesis of saponin **1** (Figure 1).

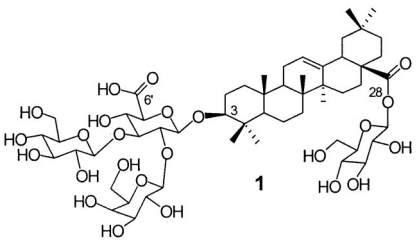

Figure 1

Adopting the common tactic for introduction of uronate residues in the synthesis of complex oligosaccharides and glycoconjugates,[5] we scheduled to elaborate the 6′-carboxyl function via a selective oxidation of the primary 6′-OH of **2** (Scheme 1) at a later stage after assembly of the tetrasaccharide. Therefore, the sequence for assembly of the four glucose and galactose residues determines the synthetic route toward saponin **1**. Highly selective glycosylation of the 28-COOH of an oleanolic triterpene with a glycosyl bromide, in the presence of the 3-OH, has been demonstrated.[6] A convergent manner would therefore call for the subsequent assembly of the remaining 3-OH with a trisaccharide donor. However, the 3-*O*-trisaccharide bearing a 1→2 linkage, which is a common pattern in triterpene saponins,[3] precludes the use of a trisaccharide donor with a neighboring participating group to ensure a stereospecific glycosylation. We thus planned to assemble a Glu-(1→3)-Glu donor installed with a participating group at the 2-OH, and then follow with a selective removal of the 2-*O*-group and a subsequent glycosylation with a galactosyl donor (e.g., **5**). For construction of the 1,2-*trans*-glycosidic bond at the 3-OH of triterpenoids and steroids, the glycosylation conditions have been optimized,[7] where glycosyl trichloroacetimidate (or trifluoroacetimidate)[8] donors with a benzoyl group at 2-OH and TMSOTf as catalyst are required. Thus, disaccharide trifluoroacetimidate donor **4** was designed: the 2-(azidomethyl)benzoyl (AZMB) group, a benzoylic group capable of selective removal under reductive conditions,[9] was chosen as the 2-*O*-group; the 4,6-*O*-acetyl groups were expected to be removed in the presence of benzyl groups at a later stage for introduction the 6′-carboxylic function.[10] Benzoyl group was selected as the permanent protecting group, which could be taken off under alkaline conditions without affecting the robust 28-glycosyl ester linkage.[11]

Disaccharide trifluoroacetimidate **4** was readily prepared as shown in Scheme 2. Regioselective glycosylation of the 2,3-diol **6** (allyl 4,6-*O*-benzylidene-α-D-glucopyranoside) with 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl

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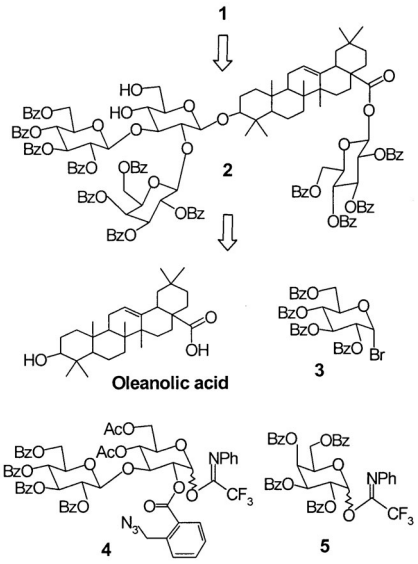
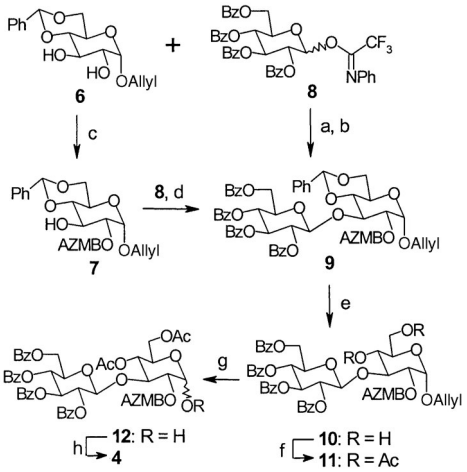


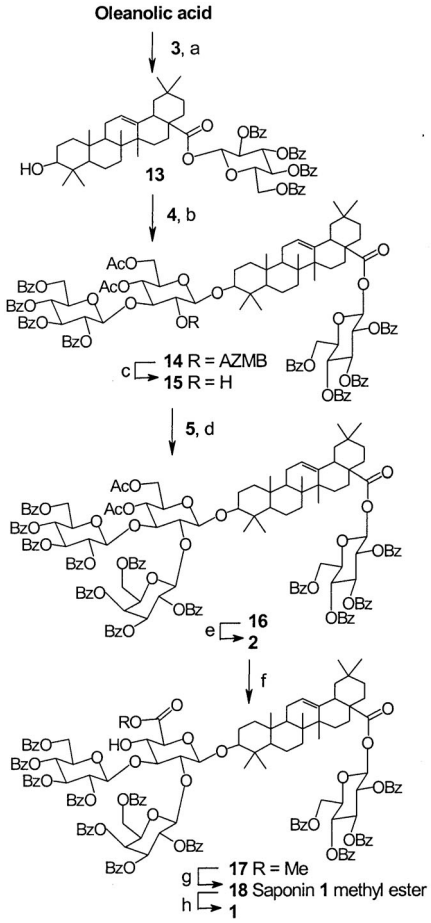
Scheme 1 Retrosynthetic plan



Scheme 2 Preparation of the disaccharide donor **4**: *Reagents and conditions:* (a) **8** (1.0 equiv), TMSOTf (0.06 equiv), CH_2Cl_2, 4 Å MS, 0 °C–r.t., 92% (for a mixture of the 2-*O*- and 3-*O*-glycosylated isomers). (b) AZMBCl, DMAP, CH_2Cl_2, r.t., 66% (for **9**, 2 steps). (c) AZMBCl, pyridine–CH_2Cl_2, 0 °C, 78%. (d) **8** (2.0 equiv), TMSOTf (0.1 equiv), CH_2Cl_2, 4 Å MS, r.t., 62%. (e) *p*-TsOH, MeOH–CH_2Cl_2, reflux, 97%. (f) Ac_2O, pyridine–CH_2Cl_2, r.t., 98%. (g) $PdCl_2$ (0.7 equiv), MeOH–CH_2Cl_2, r.t., 84%. (h) PhN=CClCF$_3$, K_2CO_3, acetone, r.t., 91%.

trichloroacetimidate to give the 1→3 linked disaccharide has been reported.[12] However, under similar reaction conditions (0.06 equiv of TMSOTf, CH_2Cl_2, 4 Å MS, 0 °C–r.t.), coupling of **6** with **8** (or its trichloroacetimidate counterpart) gave a mixture of the 2-*O*- and 3-*O*-glycosylated isomers, which are inseparable on silica gel. Subsequent acylation with AZMBCl provided the corresponding regioisomers in a ratio of 3.5:1 in favor of the desired 3-*O*-glycosylated isomer **9** (66% yield for two steps). Alternatively, regioselective benzoylation (and pivaloylation) of the 2-OH of **6** is feasible.[13] Treatment of **6** with AZMBCl in pyridine–CH_2Cl_2 at 0 °C provided the 2-*O*-AZMB product **7** [δ = 5.03 (dd, *J* = 9.6, 3.6 Hz, H-2)] in a satisfactory yield (78%) with an easy purification. And the 2,3-di-*O*-AZMB product [δ = 5.33 (overlapped H-2), δ = 6.09 (t, *J* = 9.9 Hz, H-3)] was isolated in 6% yield. Glycosylation of the hindered 3-OH of **7** with trifluoroacetimidate **8** in the presence of a catalytic amount of TMSOTf (0.1 equiv) afforded the desired disaccharide **9** in a compromised 62% yield. In comparison, coupling of **7** with 2,3,4,6-tetra-*O*-benzoyl-D-glucopyranosyl trichloroacetimidate under similar conditions was examined, providing **9** in 52% yield. To avoid problems associated with cleavage of the anomeric allyl group,[14] the 4,6-benzylidene **9** was converted to the 4,6-di-*O*-acetate **11**. Treatment of **11** with $PdCl_2$ in MeOH–CH_2Cl_2 at room temperature provided the corresponding hemiacetal **12** in 84% yield,[15] which was directly subjected to addition with *N*-phenyl-2,2,2-trifluoroacetimidoyl chloride (K_2CO_3, acetone, r.t.),[8] affording the desired trifluoroacetimidate **4** in 91% yield.

Expectedly, treatment of oleanolic acid with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl bromide (**3**) under the slightly modified literature conditions (K_2CO_3, Bu_4NBr, CH_2Cl_2–H_2O, reflux)[6] provided the 28-glucosyl ester **13** in 90% yield (Scheme 3). The anomeric proton appeared at δ = 5.96 ppm (d, *J* = 8.1 Hz). Next, glycosylation of **13** with **4** in the presence of a catalytic amount of TMSOTf (0.1 equiv) afforded the desired β-bismoside **14** (H-1′, 4.44 ppm, d, *J* = 7.4 Hz) in high yield (89%). Selective removal of the 2′-*O*-AZMB group with PBu_3 in the presence of acetyl and benzoyl groups was achieved,[9] providing **15** in 90% yield. Subsequent glycosylation of the resulting 2′-OH of **15** with galactosyl trifluoroacetimidate **5** in the presence of TBSOTf (0.4 equiv) afforded the β-glycosylated tetrasaccharide **16** in an excellent yield (90%). Here, the use of TBSOTf as the catalysis in place of TMSOTf improved the glycosylation yield by avoiding the production of the corresponding 2′-*O*-TMS ether. Selective removal of the 4′,6′-*O*-acetate on **16** with 1% HCl in MeOH in the presence of 12 benzoyl groups met with no problem, providing 4′,6′-diol **2** in 88% yield.[10] Diol **2** was then subjected to selective oxidation with a modified oxidation protocol of TEMPO/KBr/Ca(ClO)$_2$ under phase-transfer aqueous conditions.[16] In order to facilitate purification and characterization, the resulting 6′-carboxylic acid derivative was directly subjected to methylation with CH_2N_2 to provide methyl ester **17** in 72% isolated yield. Finally, removal of the benzoyl groups with NaOMe in MeOH–CH_2Cl_2 gave the methyl ester of saponin **1** (**18**) in 85% yield. Further treatment of **18** with aq NaOH (0.5 N) afforded the target saponin **1** (78%). All the analytical data of **1** are in full agreement with those reported for the saponin isolated from *Aralia dasyphylla*.[1]



Scheme 3 Synthesis of saponin **1**: *Reagents and conditions*: (a) K_2CO_3, Bu_4NBr, CH_2Cl_2–H_2O, reflux, 90%. (b) TMSOTf (0.1 equiv), CH_2Cl_2, 4 Å MS, r.t., 89%. (c) Bu_3P, THF–H_2O, r.t., 90%. (d) TBSOTf (0.4 equiv), CH_2Cl_2, 4 Å MS, r.t., 90%. (e) 1% AcCl, MeOH–CH_2Cl_2, 0 °C–r.t., 88%. (f) TEMPO, $Ca(ClO)_2$, KBr, Bu_4NBr, $CHCl_3$–H_2O, 0 °C; then CH_2N_2, Et_2O, 0 °C, 72%. (g) NaOMe, MeOH–CH_2Cl_2, r.t., 85%. (h) aq. NaOH (0.5 N), MeOH–CH_2Cl_2, r.t., 78%.

In summary, 28-*O*-β-D-glucopyranosyl oleanate 3-*O*-β-D-galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (**1**), a structurally typical glucuronide-containing triterpene saponin isolated from *Aralia dasyphylla*, was concisely synthesized in linear nine steps and 26% overall yield. The key features of the synthesis are: (1) attachment of the 28-glucosyl ester before assembly of the 3-*O*-sugar chain; (2) elaboration of the glucuronide residue at a later stage via the TEMPO-mediated selective oxidation; (3) installation of AZMB as a benzoylic neighboring participating group in a glycosyl donor and removal of AZMB selectively afterwards for assembly of the 1→2 sugar linkage.

Solvents were purified in the usual way. TLCs were performed on precoated plates of silica gel HF254 (0.5 mm, Yantai, China). Flash column chromatography was performed on silica gel H (10–40 μM, Yantai, China). Optical rotations were determined with a Perkin Elmer Model 241 MC polarimeter. NMR spectra were recorded on a Bruker AM 300 spectrometer with Me_4Si as the internal standard. *J* values are given in Hz. Mass spectra were obtained on a HP5989A or a VG Quatro mass spectrometer. Elemental analyses were performed on a Perkin Elmer Model 2400 instrument.

Allyl 2-*O*-(2-azidomethyl)benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (7)

To a stirred solution of compound **6** (450 mg, 1.46 mmol) in anhyd CH_2Cl_2 (4 mL) at 0 °C under Ar was added anhyd pyridine (2 mL), followed by a solution of AZMBCl (2.0 equiv) in CH_2Cl_2. After being stirred at 0 °C for 2 h, the reaction was quenched with water and diluted with CH_2Cl_2. The organic phase, after being washed with aq 2 N HCl and brine, was dried over Na_2SO_4, and then concentrated in vacuo. The residue was applied to a silica gel column chromatography (petroleum ether–EtOAc, 5:1) to give **7** as a yellow syrup (529 mg, 78%); $[\alpha]_D$ +68.6 (*c* = 1.17, $CHCl_3$).

IR (film): 3459, 2870, 2104, 1720, 1602, 1580, 1453, 1379, 1333, 1263, 1144, 1120, 1085, 1035, 995, 927, 752, 700 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.10 (d, *J* = 7.5 Hz, 1 H), 7.60–7.37 (m, 8 H), 5.85 (m, 1 H), 5.60 (s, 1 H), 5.28 (dd, *J* = 10.5, 1.5 Hz, 1 H), 5.26 (d, *J* = 3.9 Hz, 1 H), 5.18 (dd, *J* = 10.5, 1.5 Hz, 1 H), 5.03 (dd, *J* = 9.6, 3.6 Hz, 1 H), 4.89 (d, *J* = 13.5 Hz, 1 H), 4.66 (d, *J* = 14.1 Hz, 1 H), 4.40 (t, *J* = 9.5 Hz, 1 H), 4.32 (dd, *J* = 5.4, 4.8 Hz, 1 H), 4.22 (dt, *J* = 15.0, 3.9 Hz, 1 H), 4.06–3.93 (m, 2 H), 3.80 (t, *J* = 10.4 Hz, 1 H), 3.68 (t, *J* = 9.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.2, 136.9, 133.3, 133.0, 131.8, 131.6, 130.0, 129.5, 129.2, 128.5, 128.2, 127.9, 126.2, 117.7, 101.9, 95.7, 81.2, 74.5, 68.7, 68.6, 68.5, 62.3, 53.2.

ESI–MS: *m*/*z* = 490.1 [M + Na^+].

Anal. Calcd for $C_{24}H_{25}N_3O_7$: C, 61.66; H, 5.39; N, 8.99. Found: C, 61.35; H, 5.41; N, 9.68.

Allyl 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-2-*O*-(2-azidomethyl)benzoyl-4,6-*O*-benzylidene-α-D-glucopyranoside (9)

To a mixture of **7** (86 mg, 0.18 mmol), **8** (282 mg, 0.37 mmol), and 4 Å molecular sieves in anhyd CH_2Cl_2 (2 mL) was added TMSOTf in CH_2Cl_2 (0.10 equiv) under Ar at r.t. After being stirred for 3 h, the mixture was neutralized with Et_3N, and then filtered and concentrated. The residue was purified by a flash column chromatography on silica gel (petroleum ether–EtOAc, 3:1) to give **9** (118 mg, 62%) as a white foam; $[\alpha]_D$ +56.8 (*c* = 0.97, $CHCl_3$).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.4 Hz, 2 H), 7.89 (d, *J* = 7.5 Hz, 1 H), 7.82 (d, *J* = 8.7 Hz, 2 H), 7.70 (d, *J* = 8.4 Hz, 2 H), 7.59–7.25 (m, 18 H), 7.20 (t, *J* = 6.6 Hz, 2 H), 7.06 (t, *J* = 7.5 Hz, 2 H), 5.78 (t, *J* = 9.9 Hz, 1 H), 5.75 (m, 1 H), 5.65 (s, 1 H), 5.64 (t, *J* = 9.6 Hz, 1 H), 5.49 (t, *J* = 8.1 Hz, 1 H), 5.20 (dt, *J* = 17.4, 1.2 Hz, 1 H), 5.16–5.08 (m, 4 H), 4.68 (d, *J* = 15 Hz, 1 H), 4.52–4.41 (m, 2 H), 4.35–4.22 (m, 3 H), 4.14 (m, 1 H), 4.02–3.91 (m, 3 H), 3.86 (t, *J* = 9.3 Hz, 1 H), 3.82 (t, *J* = 9.3 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 165.7, 165.2, 165.0, 164.8, 138.0, 137.1, 133.3, 133.1, 133.0, 132.7, 131.1, 129.7, 129.6, 129.3, 129.2, 129.1, 128.8, 128.7, 128.3, 128.2, 128.0, 127.4, 126.0, 118.0, 101.5, 101.0, 95.6, 79.8, 76.4, 73.1, 73.0, 72.2, 71.9, 69.7, 68.8, 63.1, 62.6, 52.7.

ESI–MS: *m*/*z* = 1068.3 [M + Na^+].

Anal. Calcd for $C_{58}H_{51}N_3O_{16}\cdot H_2O$: C, 65.51; H, 5.02; N, 3.97. Found: C, 65.89; H, 4.87; N, 3.96.

Allyl 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-2-*O*-(2-azidomethyl)benzoyl-α-D-glucopyranoside (10)

A solution of compound **9** (1.40 g, 1.3 mmol) and *p*-TsOH (254 mg, 1.3 mmol) in MeOH–CH_2Cl_2 (10 mL:10 mL) was refluxed for 5 h. The mixture was then neutralized with Et_3N and concentrated. The residue was purified by a flash column chromatography on silica gel

(3:2 petroleum ether–EtOAc) to yield **10** (1.24 g, 97%) as a white foam; $[\alpha]_D$ +45.2 (*c* = 1.05, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.7 Hz, 2 H), 7.90 (d, *J* = 8.4 Hz, 2 H), 7.85 (d, *J* = 7.5 Hz, 1 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.61–7.18 (m, 15 H), 6.94 (t, *J* = 7.8 Hz, 2 H), 5.88 (t, *J* = 9.9 Hz, 1 H), 5.70 (m, 1 H), 5.62 (t, *J* = 10.0 Hz, 1 H), 5.52 (t, *J* = 8.9 Hz, 1 H), 5.18 (d, *J* = 17.1 Hz, 1 H), 5.06 (m, 3 H), 4.95 (dd, *J* = 9.3, 3.9 Hz, 1 H), 4.81 (d, *J* = 11.7 Hz, 1 H), 4.65 (d, *J* = 15.3 Hz, 1 H), 4.41 (dd, *J* = 11.7, 6.6 Hz, 1 H), 4.28 (m, 1 H), 4.19–4.02 (m, 3 H), 3.98–3.85 (m, 3 H), 3.84–3.70 (m, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 166.1, 165.6, 165.1, 164.9, 164.7, 138.0, 133.6, 133.3, 133.2, 132.9, 132.7, 131.1, 129.9, 129.8, 129.5, 129.1, 129.0, 128.4, 128.3, 128.2, 127.9, 126.8, 117.8, 101.7, 94.7, 82.5, 72.7, 72.4, 72.2, 71.6, 71.1, 69.36, 69.2, 68.4, 62.6, 52.7.

ESI–MS: *m*/*z* = 975.4 [M + NH_4^+].

Anal. Calcd for $C_{51}H_{47}N_3O_{16}\cdot H_2O$: C, 62.77; H, 5.06; N, 4.32. Found: C, 63.15; H, 4.28; N, 3.94.

Allyl 2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-acetyl-2-*O*-(2-azidomethyl)benzoyl-α-D-glucopyranoside (11)

To a solution of compound **10** (1.09 g, 1.14 mmol) in anhyd pyridine (10 mL) at 0 °C was added acetic anhydride (1.15 mL, 11.4 mmol) dropwise. The mixture was stirred at r.t. for 2 h. After a conventional workup, the residue was subjected to a column chromatography on silica gel (petroleum ether–EtOAc, 2:1) to yield **11** (1.17 g, 98%) as a white solid; $[\alpha]_D$ +33.3 (*c* = 0.70, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.08 (m, 3 H), 7.87 (d, *J* = 8.4 Hz, 2 H), 7.72 (d, *J* = 8.1 Hz, 2 H), 7.76–7.19 (m, 15 H), 7.04 (t, *J* = 7.0 Hz, 2 H), 5.84–5.63 (m, 3 H), 5.46 (t, *J* = 8.4 Hz, 1 H), 5.20 (d, *J* = 17.1 Hz, 1 H), 5.18–5.07 (m, 4 H), 4.95 (dd, *J* = 9.9, 2.9 Hz, 1 H), 4.68 (m, 2 H), 4.50 (dd, *J* = 12.1, 4.6 Hz, 1 H), 4.38 (t, *J* = 10.0 Hz, 1 H), 4.24–4.15 (m, 2 H), 4.14–4.05 (m, 3 H), 3.98–3.89 (m, 2 H), 2.10 (s, 3 H), 1.97 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 169.3, 166.1, 165.7, 165.1, 164.9, 164.8, 138.4, 133.4, 133.3, 133.0, 132.8, 131.1, 129.8, 129.7, 129.6, 129.5, 129.3, 128.8, 128.7, 128.6, 128.4, 128.2, 128.0, 127.0, 118.3, 101.5, 94.7, 76.7, 73.6, 72.9, 72.0, 69.5, 68.8, 68.0, 67.7, 63.1, 62.1, 52.7, 20.7, 20.6.

ESI–MS: *m*/*z* = 1064.3 [M + Na^+].

Anal. Calcd for $C_{55}H_{51}N_3O_{18}$: C, 63.40; H, 4.93; N, 4.03. Found: C, 63.32; H, 5.02; N, 3.97.

2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-acetyl-2-*O*-(2-azidomethyl)benzoyl-α/β-D-glucopyranoside (12)

A dark suspension of $PdCl_2$ (165 mg, 0.94 mmol) and compound **11** (1.4 g, 1.34 mmol) in methanol–CH_2Cl_2 (10 mL:10 mL) was stirred at r.t. until TLC (petroleum ether–EtOAc, 1.5:1) indicated that the reaction completed. The mixture was filtered through a bed of celite. The filtrates were concentrated in vacuo to give a dark syrup, which was purified by a flash column chromatography on silica gel (petroleum ether–EtOAc, 2:1) to give **12** (α and β mixture) as a white solid (1.13 g, 84%).

12α

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (m, 3 H), 7.87 (d, *J* = 7.1 Hz, 2 H), 7.71 (d, *J* = 7.4 Hz, 2 H), 7.69–7.30 (m, 13 H), 7.22 (t, *J* = 7.7 Hz, 2 H), 7.05 (t, *J* = 7.8 Hz, 2 H), 5.82 (t, *J* = 9.6 Hz, 1 H), 5.65 (t, *J* = 9.6 Hz, 1 H), 5.49 (s, 1 H), 5.46 (t, *J* = 9.6 Hz, 1 H), 5.15 (t, *J* = 9.6 Hz, 1 H), 5.10 (d, *J* = 7.8 Hz, 1 H), 4.97 (dd, *J* = 10.2, 3.6 Hz, 1 H), 4.70 (d, *J* = 15.1 Hz, 1 H), 4.64 (dd, *J* = 12.0, 3.0 Hz, 1 H), 4.50 (dd, *J* = 12.1, 5.2 Hz, 1 H), 4.44 (t, *J* = 9.6 Hz, 1 H), 4.23–4.09 (m, 5 H), 3.11 (brs, 1 H), 2.09 (s, 3 H), 1.97 (s, 3 H).

^{13}C NMR (75 MHz,$CDCl_3$): δ = 166.1, 165.7, 135.1, 164.9, 164.8, 138.3, 133.4, 133.3, 132.8, 131.2, 129.7, 129.6, 129.5, 129.3, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.0, 127.0, 101.5, 89.8, 76.3, 73.8, 72.9, 72.0, 69.5, 67.9, 67.5, 63.1, 62.2, 52.8, 20.7, 20.5.

ESI-MS: *m*/*z* = 1019.1 [M + NH_4^+].

Anal. Calcd for $C_{52}H_{47}N_3O_{18}\cdot 1/2H_2O$: C, 61.78; H, 4.79; N, 4.17. Found: C, 61.63; H, 4.75; N, 4.01.

2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-acetyl-2-*O*-(2-azidomethyl)benzoyl-α/β-D-glucopyranosyl *N*-(Phenyl)trifluoroacetimidate (4)

To a stirred mixture of **12** (1.05g, 1.04 mmol) and K_2CO_3 (468 mg, 3.0 equiv) in acetone (20 mL) under Ar at r.t. was added *N*-(phenyl)trifluoroacetimidoyl chloride (185 L, 1.2 equiv). After being stirred at r.t. for 7 h, the mixture was filtered and concentrated. The residue was purified by a flash column chromatography on silica gel (petroleum ether–EtOAc, 5:2) to afford **4** (α and β mixture, 1.11 g, 91%) as a white solid.

4α (Major)

$[\alpha]_D$ +26.6 (*c* = 0.91, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.0 Hz, 3 H), 7.90 (d, *J* = 6.9 Hz, 2 H), 7.72 (d, *J* = 7.1 Hz, 3 H), 7.69–7.51 (m, 2 H), 7.50–7.28 (m, 10 H), 7.24 (t, *J* = 7.8 Hz, 2 H), 7.09 (t, *J* = 7.4 Hz, 2 H), 6.99 (t, *J* = 8.0 Hz, 3 H), 6.56 (br s, 1 H), 6.25 (d, *J* = 7.4 Hz, 2 H), 5.86 (t, *J* = 9.7 Hz, 1 H), 5.68 (t, *J* = 9.7 Hz, 1 H), 5.49 (dd, *J* = 9.9, 8.0 Hz, 1 H), 5.28 (t, *J* = 9.7 Hz, 1 H), 5.19 (dd, *J* = 9.9, 3.6 Hz, 1 H), 5.11 (d, *J* = 8.0 Hz, 1 H), 4.68 (dd, *J* = 12.2, 2.9 Hz, 1 H), 4.53 (dd, *J* = 12.4, 5.2 Hz, 1 H), 4.45–4.26 (m, 3 H), 4.23–4.16 (m, 2 H), 4.14–4.03 (m, 2 H), 2.11 (s, 3 H), 2.00 (s, 3 H).

4β (Minor)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.1 Hz, 2 H), 7.98 (d, *J* = 7.7 Hz, 1 H), 7.88 (d, *J* = 7.1 Hz, 2 H), 7.72 (d, *J* = 7.1 Hz, 2 H), 7.68 (d, *J* = 7.7 Hz, 1 H), 7.61–7.31 (m, 12 H), 7.29–7.05 (m, 7 H), 6.64 (d, *J* = 7.7 Hz, 2 H), 5.81 (t, *J* = 9.6 Hz, 2 H), 5.65 (t, *J* = 9.8 Hz, 1 H), 5.48 (t, *J* = 8.0 Hz, 1 H), 5.45 (t, *J* = 7.7 Hz, 1 H), 5.25 (t, *J* = 9.3 Hz, 1 H), 5.06 (d, *J* = 8.0 Hz, 1 H), 4.64 (dd, *J* = 3.0, 12.4 Hz, 1 H), 4.57–4.85 (m, 2 H), 4.28–4.10 (m, 5 H), 3.70 (br s, 1 H), 2.09 (s, 3 H), 2.00 (s, 3 H).

ESI–MS: *m*/*z* = 1024.2 [M + Na^+ – C(=NPh)CF_3].

Anal. Calcd for $C_{60}H_{51}F_3N_4O_{18}\cdot H_2O$: C, 60.51; H, 4.32; N, 4.70. Found: C, 60.36; H, 4.51; N, 4.43.

2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate (13)

To a solution of oleanolic acid (195 mg, 0.43 mmol) and bromide **3** (377 mg, 1.3 equiv) in CH_2Cl_2 (5.0 mL) were added K_2CO_3 (151 mg, 2.5 equiv), water (5.0 mL), and Bu_4NBr (56 mg, 0.4 equiv). The resulting mixture was refluxed for 6 h, and then diluted with CH_2Cl_2. The organic phase, after being washed with water and brine, was dried over Na_2SO_4, and then concentrated in vacuo. The residue was purified by a flash column chromatography on silica gel (toluene–EtOAc, 25:1) to give **13** (398 mg, 90%) as a white foam; $[\alpha]_D$ +67.0 (*c* = 1.0, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (d, *J* = 7.2 Hz, 2 H), 7.97 (d, *J* = 7.5 Hz, 2 H), 7.90 (d, *J* = 7.2 Hz, 2 H), 7.83 (d, *J* = 7.2 Hz, 2 H), 7.59–7.28 (m, 12 H), 5.99 (t, *J* = 9.6 Hz, 1 H), 5.96 (d, *J* = 8.1 Hz, 1 H), 5.78–5.69 (m, 2 H), 5.28 (s, 1 H), 4.56 (dd, *J* = 12.3, 3.0 Hz, 1 H), 4.46 (dd, *J* = 9.3, 5.4 Hz, 1 H), 4.26 (m, 1 H), 3.14 (m, 1 H), 2.79 (m, 1 H), 0.97, 0.94, 0.86, 0.83, 0.76, 0.74, 0.45 (7 × s, 7 × CH_3).

ESI–MS: *m*/*z* = 1057.9 [M + Na^+].

Anal. Calcd for $C_{64}H_{74}O_{12}$: C, 74.25; H, 7.21. Found: C, 74.29; H, 7.34.

28-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate 3-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-acetyl-2-*O*-(2-azidomethyl)benzoyl-β-D-glucopyranoside (14)

A mixture of imidate **4** (1.0 g, 0.85 mmol), acceptor **13** (806 mg, 0.78 mmol), and powered 4 Å molecular sieves in anhyd CH_2Cl_2 was stirred at r.t. under Ar for 1 h. A solution of TMSOTf in CH_2Cl_2 (0.1 equiv) was added dropwise. After being stirred at r.t. overnight, the mixture was neutralized with Et_3N, and then filtered and concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether–EtOAc, 2:1) to give **14** (1.4 g, 89%) as a white solid.; $[\alpha]_D$ +40.8 (*c* = 0.93, $CHCl_3$).

IR (film): 2952, 2104, 1737, 1603, 1585, 1492, 1452, 1369, 1316, 1265, 1178, 1106, 1093, 1069, 1027, 977, 709, 687 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.03 (t, *J* = 6.9 Hz, 3 H), 7.94 (m, 9 H), 7.67 (t, *J* = 8.0 Hz, 2 H), 7.58–7.09 (m, 30 H), 5.97 (t, *J* = 9.8 Hz, 1 H), 5.94 (d, *J* = 8.2 Hz, 1 H), 5.79–5.68 (m, 3 H), 5.62 (t, *J* = 9.6 Hz, 1 H), 5.42 (t, *J* = 8.5 Hz, 1 H), 5.25 (s, 1 H), 5.23 (t, *J* = 7.7 Hz, 1 H), 5.09 (t, *J* = 9.5 Hz, 1 H), 5.00 (d, *J* = 7.7 Hz, 1 H), 4.65 (dd, *J* = 12.1, 3.0 Hz, 1 H), 4.60–4.40 (m, 5 H), 4.29–4.20 (m, 1 H), 4.19–4.09 (m, 4 H), 4.02 (d, *J* = 16.2 Hz, 1 H), 3.51 (m, 1 H), 2.89 (dd, *J* = 11.0, 4.1 Hz, 1 H), 2.78 (d, *J* = 9.9 Hz, 1 H), 2.07, 1.99, 0.90, 0.84, 0.81, 0.68, 0.48, 0.43, 0.38 (9 × s, 9 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.6, 170.7, 169.2, 166.0, 165.6, 165.1, 164.7, 163.7, 142.9, 139.2, 133.5, 133.2, 133.0, 132.8, 130.4, 129.8, 129.6, 129.5, 129.1, 128.7, 128.4, 128.3, 128.0, 127.6, 127.0, 122.7, 103.0, 101.3, 91.9, 90.3, 79.2, 73.3, 72.9, 72.0, 71.6, 70.3, 69.6, 69.3, 68.8, 63.1, 62.7, 62.5, 55.3, 52.8, 47.4, 46.8, 45.7, 41.5, 40.9, 38.8, 38.5, 38.3, 36.5, 33.7, 32.9, 31.8, 30.5, 29.7, 27.6, 25.6, 25.4, 23.4, 22.6, 20.8, 20.6, 17.9, 16.4, 16.1, 15.1.

ESI–MS: *m*/*z* = 2040.8 [M + Na^+].

Anal. Calcd for $C_{116}H_{119}N_3O_{29}·H_2O$: C, 68.40; H, 5.94; N, 2.06. Found: C, 68.07; H, 5.69; N, 1.60.

28-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate 3-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-4,6-di-*O*-acetyl-β-D-glucopyranoside (15)

To a solution of **14** (1.20 g, 0.60 mmol) in THF (6 mL) at r.t. was added water (270 μL, 25 equiv), followed by Bu_3P (446 μL, 3 equiv). After being stirred for 1 h, the mixture was diluted with CH_2Cl_2 and washed with sat. aq $NaHCO_3$ and water. The organic layer was dried over Na_2SO_4, and then filtered and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (petroleum ether–EtOAc, 2:1) to yield **15** (995 mg, 90%) as a white foam; $[\alpha]_D$ +43.6 (*c* = 1.0, $CHCl_3$).

IR (film): 3066, 2952, 1737, 1603, 1585, 1492, 1453, 1369, 1317, 1266, 1178, 1094, 1069, 1027, 853, 802, 709, 683, 503 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.07–7.78 (m, 15 H), 7.59–7.18 (m, 25 H), 5.95 (t, *J* = 9.6 Hz, 1 H), 5.92 (d, *J* = 8.2 Hz, 1 H), 5.86 (t, *J* = 9.6 Hz, 1 H), 5.76–5.68 (m, 2 H), 5.66 (t, *J* = 9.7 Hz, 1 H), 5.45 (dd, *J* = 9.0, 8.0 Hz, 1 H), 5.25 (s, 1 H), 5.20 (t, *J* = 8.0 Hz, 1 H), 4.83 (t, *J* = 9.6 Hz, 1 H), 4.60 (dd, *J* = 12.2, 2.8 Hz, 1 H), 4.52 (dd, *J* = 12.4, 2.9 Hz, 1 H), 4.43 (dd, *J* = 12.2, 4.8 Hz, 2 H), 4.28–4.16 (m, 2 H), 4.15–3.97 (m, 3 H), 3.76 (t, *J* = 9.2 Hz, 1 H), 3.49 (m, 1 H), 3.31 (t, *J* = 7.1 Hz, 1 H), 3.00 (dd, *J* = 11.5, 4.4 Hz, 1 H), 2.76 (d, *J* = 11.0 Hz, 1 H), 2.00, 1.87, 0.93, 0.86, 0.82, 0.79, 0.70, 0.66, 0.42 (9 × s, 9 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7, 170.6, 169.4, 166.0, 165.8, 165.6, 165.1, 164.9, 164.7, 143.0, 133.2, 133.0, 129.9, 129.7, 128.7, 128.4, 128.3, 122.7, 104.5, 101.5, 91.9, 89.9, 81.0, 74.8, 72.9, 72.2, 72.0, 71.6, 70.4, 69.6, 69.3, 68.4, 62.9, 62.7, 62.6, 55.3, 47.4, 46.8, 45.7, 41.5, 40.9, 38.9, 38.8, 38.3, 36.6, 33.7, 32.9, 31.8, 30.5, 28.2, 27.7, 25.6, 25.5, 23.4, 22.6, 20.7, 20.5, 18.1, 16.6, 16.5, 15.1.

HRESI–MS: *m*/*z* calcd [M + Na^+] for $C_{108}H_{114}O_{28}Na$: 1881.7389; found: 1881.7356.

2,3,4,6-Tetra-*O*-benzoyl-α/β-D-galactopyranosyl *N*-(Phenyl)trifluoroacetimidate (5)

To a stirred mixture of 2,3,4,6-tetra-*O*-benzoyl-α/β-D-galactose (600 mg, 1.0 mmol) and K_2CO_3 (416 mg, 3.0 mmol) in acetone (20 mL) was added *N*-(phenyl)trifluoroacetimidoyl chloride (175 μL, 1.2 mmol) under Ar at r.t. After being stirred overnight, the mixture was filtered. The filtrates were concentrated. The residue was purified by flash column chromatography on silica gel (petroleum ether–EtOAc, 5:1) to produce **5** (α/β mixture, 721 mg, 94%) as a white foam; $[\alpha]_D$ +115.6 (**5α**, *c* = 1.08, $CHCl_3$).

^1H NMR (300 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 7.4 Hz, 2 H), 8.03 (d, *J* = 7.1 Hz, 2 H), 8.00 (d, *J* = 7.4 Hz, 2 H), 7.81 (d, *J* = 7.4 Hz, 2 H), 7.66–7.36 (m, 10 H), 7.28 (t, *J* = 7.7 Hz, 2 H), 7.12 (t, *J* = 7.1 Hz, 2 H), 7.02 (t, *J* = 7.4 Hz, 1 H), 6.89 (br s, 1 H), 6.45 (d, *J* = 6.6 Hz, 2 H), 6.17 (d, *J* = 2.2 Hz, 1 H), 6.06 (dd, *J* = 10.7, 3.0 Hz, 1 H), 5.95 (dd, *J* = 10.7, 3.3 Hz, 1 H), 4.81 (m, 1 H), 4.65 (dd, *J* = 11.4, 6.9 Hz, 1 H), 4.44 (dd, *J* = 11.4, 5.9 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.9, 165.6, 165.5, 165.4, 142.8, 133.7, 133.3, 133.2, 129.9, 129.8, 129.7, 129.3, 128.8, 128.7, 128.6, 128.4, 128.3, 124.4, 119.1, 93.0, 69.8, 68.5, 68.2, 67.6, 62.2.

Anal. Calcd for $C_{42}H_{32}F_3NO_{10}·1/2H_2O$: C, 64.95; H, 4.28; N, 1.81. Found: C, 64.93; H, 4.02; N, 1.62.

28-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate 3-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→2)-[2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)]-4,6-di-*O*-acetyl-β-D-glucopyranoside (16)

A mixture of acceptor **15** (381 mg, 0.20 mmol), donor **5** (472 mg, 3 equiv), and powered 4 Å molecular sieves in anhyd CH_2Cl_2 (15 mL) was stirred for 1 h at r.t. under Ar. A solution of TBSOTf in CH_2Cl_2 (0.2 equiv) was added. The mixture was stirred for 3 h. Et_3N was added, and the mixture was filtered. The filtrates were concentrated to give a residue, which was applied to a flash column chromatography on silica gel (petroleum ether–EtOAc, 5:2–2:1) to provide **16** (447 mg, 90%) as a white solid; $[\alpha]_D$ +85.1 (*c* = 1.13, $CHCl_3$).

^1H NMR (300 MHz, $CDCl_3$): δ = 8.24 (d, *J* = 7.4 Hz, 2 H), 8.16 (d, *J* = 7.4 Hz, 2 H), 8.07 (d, *J* = 7.4 Hz, 2 H), 8.05–7.78 (m, 18 H), 7.72–7.18 (m, 36 H), 5.98 (t, *J* = 9.6 Hz, 1 H), 5.94 (d, *J* = 8.2 Hz, 1 H), 5.87 (t, *J* = 9.9 Hz, 1 H), 5.78–5.68 (m, 2 H), 5.65–5.06 (m, 2 H), 5.48–5.39 (m, 3 H), 3.27 (s, 1 H), 4.85 (t, *J* = 9.5 Hz, 1 H), 4.72 (d, *J* = 7.4 Hz, 2 H), 4.54 (dd, *J* = 12.2, 2.6 Hz, 1 H), 4.48 (dd, *J* = 12.2, 4.8 Hz, 1 H), 4.38 (dd, *J* = 11.3, 6.3 Hz, 1 H), 4.29–4.19 (m, 4 H), 4.18–3.98 (m, 5 H), 3.79 (m, 2 H), 3.35 (m, 1 H), 2.98 (dd, *J* = 11.5, 4.4 Hz, 1 H), 2.78 (d, *J* = 11.6 Hz, 1 H), 2.42 (m, 1 H), 2.32 (t, *J* = 7.0 Hz, 1 H), 2.04, 1.90, 1.22, 0.99, 0.86, 0.84, 0.79, 0.74, 0.42 (9 × s, 9 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.6, 170.6, 169.3, 166.0, 165.6, 165.5, 165.0, 164.7, 142.9, 134.7, 134.7, 133.5, 133.3, 133.0, 130.2, 129.8, 128.6, 128.3, 122.8, 103.5, 100.1, 91.9, 90.7, 80.0, 72.9, 72.4, 71.3, 70.9, 70.6, 70.4, 69.6, 69.3, 68.6, 67.8, 62.7, 60.6, 55.6, 47.5, 46.8, 45.8, 41.6, 41.0, 39.2, 39.0, 38.6, 36.6, 33.7, 33.0, 31.8, 30.6, 29.7, 27.9, 25.8, 25.5, 23.4, 22.7, 20.8, 18.1, 16.5, 15.2.

HRESI–MS: *m*/*z* [M + Na^+] calcd for $C_{142}H_{140}O_{37}Na$: 2459.8966, found: 2459.8973.

28-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate 3-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→2)-[2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)]-β-D-glucopyranoside (2)

To a solution of **16** (390 mg, 0.16 mmol) in anhyd MeOH (15 mL) and CH_2Cl_2 (8 mL) was added acetyl chloride (0.4 mL) at 0 °C. The solution was stirred at r.t. until TLC (petroleum ether–EtOAc, 1:1) showed that the starting material disappeared. The solution was then neutralized with Et_3N, and concentrated to dryness. The residue was passed through a short silica gel column (petroleum ether–

EtOAc, 3:2) to give **2** (336 mg, 88%) as a white foam; $[\alpha]_D$ +81.4 (c = 0.67, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.29–7.74 (m, 24 H), 7.72–7.18 (m, 36 H), 5.99 (t, J = 9.6 Hz, 1 H), 5.93 (d, J = 8.2 Hz, 1 H), 5.89 (t, J = 9.0 Hz, 1 H), 5.79–5.66 (m, 2 H), 5.64–5.55 (m, 2 H), 5.53–5.36 (m, 3 H), 5.28 (s, 1 H), 4.79 (dd, J = 11.4, 9.3 Hz, 1 H), 4.69 (dd, J = 11.4, 7.5 Hz, 1 H), 4.59–4.12 (m, 7 H), 4.04 (m, 1 H), 3.92–3.67 (m, 3 H), 3.59 (t, J = 8.3 Hz, 1 H), 3.50 (t, J = 9.6 Hz, 1 H), 3.44 (s, 1 H), 3.22 (m, 1 H), 3.02 (m, 1 H), 2.79 (m, 1 H), 2.62 (m, 1 H), 2.46 (m, 1 H), 2.33 (m, 1 H), 1.24, 0.99, 0.87, 0.86, 0.83, 0.70, 0.44 (7 × s, 7 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.6, 166.0, 165.9, 165.7, 165.6, 165.3, 165.2, 165.0, 164.9, 164.8, 164.6, 142.8, 133.8, 133.6, 133.4, 133.2, 133.0, 130.2, 129.9, 129.7, 129.5, 129.2, 128.6, 128.5, 128.3, 122.7 103.5, 100.4, 99.8, 91.8, 90.1, 85.8, 74.7, 72.9, 72.1, 71.9, 71.7, 71.0, 70.8, 70.4, 69.5, 69.3, 69.0, 67.6, 63.1, 62.7, 61.8, 60.4, 55.5, 47.4, 46.8, 45.7, 41.5, 40.9, 39.2, 38.9, 38.5, 36.5, 33.7, 32.9, 31.8, 30.5, 27.8, 26.2, 25.4, 25.4, 23.4, 22.7, 18.1, 16.4, 15.1.

ESI–MS: m/z = 2375.5 [M + Na^+].

Anal. Calcd for $C_{138}H_{136}O_{35}$: C, 70.40; H, 5.82. Found: C, 69.72; H, 6.01.

Methyl 28-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl Oleanate 3-*O*-2,3,4,6-Tetra-*O*-benzoyl-β-D-galactopyranosyl-(1→2)-[2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (17)

A solution of calcium hypochlorite (12 mg, 2 equiv), KBr (1.1 mg, 0.2 equiv), and Bu_4NBr (1.0 mg, 0.07 equiv) in sat. aq $NaHCO_3$ (0.7 mL) at 0 °C was added dropwise to a cooled solution of **2** (107 mg, 44.7 μmol, 1.0 equiv) and TEMPO (0.14 mg, 0.02 equiv) in $CHCl_3$ (0.7 mL). The mixture was stirred at 0 °C for 3 h, and then diluted with water and quenched with Na_2SO_3.The solution was acidified to pH = 3 with HOAc and then extracted with EtOAc twice. The organic phase was washed with brine, dried over Na_2SO_4, and concentrated. The residue was dissolved in THF (1.5 mL). CH_2N_2 (3.0 equiv) in Et_2O (3 mL) was added to the solution at 0 °C. After being stirred for 0.5 h at 0 °C, the mixture was concentrated to give a residue, which was purified by silica gel column chromatography (2:1 petroleum ether–EtOAc, 2:1) to provide **17** (76 mg, 72%) as a white foam; $[\alpha]_D$ +72.8 (c = 0.91, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.23–8.16 (m, 4 H), 8.09–7.66 (m, 22 H), 7.64–7.19 (m, 34 H), 5.97 (t, J = 9.6 Hz, 1 H), 5.94 (d, J = 8.5 Hz, 1 H), 5.90 (t, J = 9.8 Hz, 1 H), 5.78–5.69 (m, 2 H), 5.58 (t, J = 8.4 Hz, 2 H), 5.52–5.43 (m, 2 H), 5.38 (d, J = 3.6 Hz, 1 H), 5.27 (s, 1 H), 4.68 (d, J = 7.7 Hz, 1 H), 4.60 (d, J = 8.0 Hz, 1 H), 4.56 (dd, J = 12.4, 2.8 Hz, 1 H), 4.45 (dd, J = 12.2, 4.8 Hz, 1 H), 4.42–4.30 (m, 2 H), 4.28–4.16 (m, 2 H), 4.03 (dd, J = 11.0, 7.7 Hz, 1 H), 3.88–3.75 (m, 2 H), 3.78 (s, 3 H), 3.70 (d, J = 9.6 Hz, 1 H), 3.58 (t, J = 8.6 Hz, 1 H), 3.53 (s, 1 H), 3.02 (dd, J = 15.7, 4.2 Hz, 1 H), 2.78 (d, J = 9.0 Hz, 1 H), 2.62 (m, 1 H), 2.33 (t, J = 6.9 Hz, 1 H), 1.16, 1.02, 0.98, 0.95, 0.86, 0.82, 0.42 (7 × s, 7 × CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 175.7, 168.5, 166.1, 165.6, 165.4, 164.9, 164.8, 142.9, 133.5, 133.3, 133.0, 129.8, 129.5, 129.3, 128.6, 128.4, 122.8, 103.8, 100.4, 100.0, 91.9, 90.3, 85.3, 74.8, 72.9, 72.2, 71.9, 71.0, 70.4, 69.9, 69.3, 69.1, 67.6, 62.7, 62.1, 60.6, 55.5, 52.5, 47.5, 46.8, 45.8, 41.5, 41.0, 39.3, 38.9, 36.5, 33.7, 33.0, 31.8, 30.6, 29.7, 27.8, 25.5, 23.4, 22.7, 18.1, 16.4, 15.2.

ESI–MS: m/z = 2403.3 [M + Na^+].

Anal. Calcd for $C_{139}H_{136}O_{36}$: C, 70.07; H, 5.75. Found: C, 69.79; H, 6.09.

Methyl 28-*O*-β-D-Glucopyranosyl Oleanate 3-*O*-β-D-galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (18)

To a solution of **17** (43 mg, 18.1 mol) in MeOH–CH_2Cl_2 (2:1, 9 mL) was added NaOMe (5% in MeOH, 0.35 mL). The mixture was stirred for 2 h at r.t., and then neutralized with Dowex 50-X8 (H^+) resin. The resin was filtered off and washed with MeOH. The filtrate and washings were combined and concentrated. The residue was purified with a silica gel column chromatography (CH_2Cl_2–MeOH, 3:2) to give **18** (17 mg, 85%) as a white solid; $[\alpha]_D$ +20 (c = 0.21, MeOH).

^{1}H NMR (300 MHz, C_5D_5N–D_2O): δ = 6.10 (d, J = 7.7 Hz, 1 H), 5.30 (d, J = 7.7 Hz, 1 H), 5.18 (s, 1 H), 5.10 (d, J = 7.4 Hz, 1 H), 4.70 (d, J = 7.1 Hz, 1 H), 4.49 (s, 1 H), 4.45–3.87 (m, 15 H), 3.84–3.68 (m, 4 H), 3.46 (s, 3 H), 3.0 (m, 2 H), 1.07, 1.02, 0.87, 0.85, 0.68, 0.65, 0.57 (7 × s, 7 × CH_3).

^{13}C NMR (100 MHz, C_5D_5N–D_2O): δ = 176.6, 170.1, 144.2, 105.3, 104.82, 104.75, 95.9, 89.9, 87.6, 79.4, 79.3, 79.0, 78.7, 76.8, 76.4, 75.5, 74.3, 73.9, 71.8, 71.7, 69.9, 62.4, 61.8, 56.0, 52.3, 47.2, 42.3, 41.9, 40.0, 39.7, 38.8, 37.0, 34.1, 33.3, 32.7, 30.9, 30.6, 30.1, 28.4, 28.2, 26.6, 26.2, 23.9, 23.8, 23.6, 18.9, 17.6, 16.8, 15.7.

HRESI–MS: m/z [M + Na^+] calcd for $C_{55}H_{88}O_{24}Na$: 1155.5558; found 1155.5579.

28-*O*-β-D-Glucopyranosyl Oleanate 3-*O*-β-D-Galactopyranosyl-(1→2)-[β-D-glucopyranosyl-(1→3)]-β-D-glucuronopyranoside (1)

Compound **18** (33 mg, 29 μmol) was dissolved in MeOH–CH_2Cl_2 (2:1, 9 mL), and aq NaOH (0.5 M, 1.2 mL) was added dropwise at r.t. The resulted solution was stirred for 4 h, and then acidified with HOAc to pH = 7.0, and with Dowex 50-X8 (H^+) resin to pH = 3.0. The filtrates were concentrated and purified with a silica gel column chromatography (CH_2Cl_2–MeOH–H_2O, 30:10:1) to give **1**[1] (25 mg, 78%) as a white solid; $[\alpha]_D$ +17 (c = 0.39, MeOH).

^{13}C NMR (100 MHz, C_5D_5N–D_2O): δ = 178.8, 145.3, 124.4, 105.7, 104.6, 104.4, 96.5, 92.3, 86.8, 79.6, 79.5, 78.7, 78.6, 78.4, 77.8, 75.8, 75.5, 74.5, 74.0, 72.9, 72.0, 71.7, 70.9, 64.7, 63.3, 62.9, 57.0, 49.0, 48.4, 47.44, 43.2, 42.8, 40.9, 40.7, 39.5, 37.9, 35.0, 34.3, 34.1, 33.5, 31.8, 30.8, 29.3, 29.0, 27.2, 24.8, 24.7, 24.4, 19.5, 18.5, 17.7, 16.5.

HRESI–MS: m/z [M + Na^+] calcd for $C_{54}H_{86}O_{24}Na$: 1141.5401; found 1141.5392.

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