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Synthesis of three diosgenyl saponins: dioscin, polyphyllin D, and balanitin 7

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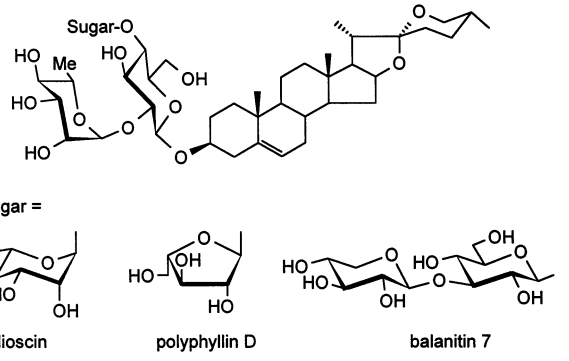
Abstract

Dioscin, polyphyllin D, and balanitin 7, which belong to a group of structurally similar diosgenyl saponins with promising bioactivities, were synthesized by stepwise glycosylation. © 1999 Elsevier Science Ltd. All rights reserved.

Keywords: Diosgenyl 2,4-di-*O*-α-L-rhamnopyranosyl-β-D-glucopyranoside (dioscin); Diosgenyl α-L-rhamnopyranosyl-(1→2)-(α-L-arabinofuranosyl)-(1→4)-β-D-glucopyranoside (polyphyllin D); Diosgenyl [β-D-xylopyranosyl-(1→3)-β-D-glucopyranosyl]-(1→4)-(α-L-rhamnopyranosyl)-(1→2)-β-D-glucopyranoside (balanitin 7); Saponin; Synthesis

1. Introduction

Saponins are a structurally and biologically diverse class of glycosides of steroids and triterpenes that are widely distributed in terrestrial plants and in some marine organisms. The structural diversity of saponins lies mainly in their sugar moieties [1]. Diosgenyl saponins are the most abundant existing steroid saponins. A typical structural pattern of the sugar chain in this family is one with a β-D-glucopyranoside as the first sugar attached to diosgenin, which in turn has an α-L-rhamnopyranose substituted at 2-OH and another sugar or sugar chain at 4-OH. Dioscin, polyphyllin D, and balanitin 7 belong to this group. Dioscin exists widely in the plant kingdom, including many species intensively used in traditional Chinese herbal medicines that exhibit cardiovascular and antifungal activities [2]. Polyphyllin D has been isolated from *Paris polyphylla* and other species and shows very promising cardiovascular and cytotoxic activities [3]. Balanitin 7 is one of the cytostatic saponins isolated from the east African medicinal plant *Balanites aegyptica* [4]. Herein we wish to report a general approach to synthesizing these three saponins [5].



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2. Results and discussion

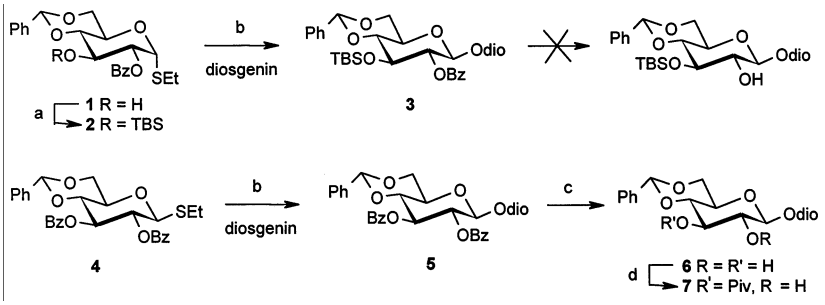
The common diosgenyl disaccharide building block (**11**) for the target saponins was synthesized as shown in Schemes 1 and 2.

Glycosylation of diosgenin with thioglycoside **2**, which was prepared from ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**1**) [6a] under promotion by NIS–AgOTf [6,7] gave the desired glycoside **3** in moderate yield (55%). Surprisingly, the 2-OBz on **3** was found to be highly inert to any cleaving reagents, such as NaOMe, NaOH, *t*-KOBu–H_2O [8a], DIBAL-H [8b], MeMgI [8c], and $LiAlH_4$ [8d]. Therefore, diosgenyl glycoside **5** was prepared from ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**) [9]. Removal of the two benzoyl groups afforded the diol **6**. It has been documented that it is quite difficult to selectively protect one of the OH groups of the 2,3-diol of a D-glucopyranoside, especially when it is in the β-form [5b]. Fortunately, treatment of **6** with pivaloyl chloride predominantly gave the 3-*O*-Piv product **7** in satisfactory yield (64%), which was readily separated by chromatography from the corresponding 2-*O*-Piv product **7a** (9.6%) and 2,3-di-*O*-Piv product **7b** (4.7%) (Scheme 1).

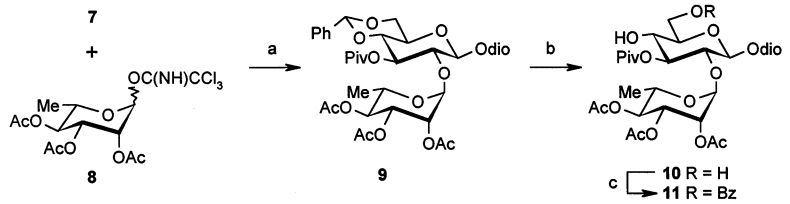
Glycosylation of **7** with tri-*O*-acetyl-L-rhamnopyranosyl trichloroacetimidate **8** [10] under the promotion of a catalytic amount of $BF_3{\cdot}OEt_2$ afforded the diosgenyl disaccharide **9** in almost quantitative yield, which was then treated with TsOH to remove the 4,6-benzylidene to give diol **10** (75%). Selective benzoylation of **10** with benzoyl chloride then provided **11** (75%). Diosgenyl disaccharide **11**, having a single free OH at the 4′ position, is the key building block for the preparation of the target saponins.

2,3,5-Tri-*O*-acetyl-α-L-arabinofuranosyl trichloroacetimidate (**15**) was prepared from tetra-*O*-acetyl-α-L-arabinofuranose (**13**) [11]. Treatment of **13** with ammonia in THF–MeOH or hydrazine acetate gave the corresponding hemiacetal **14** in poor yield (~20%). Nevertheless, treatment of **13** with HBr–HOAc in CH_2Cl_2, after silica gel column chromatography, provided **14** quantitatively. Glycosylation of **11** with the donor imidates **8** and **15** efficiently afforded the corresponding glycosides **12** (89%) and **16** (93%), respectively (Scheme 3). Removal of all of the acyl groups with sodium hydroxide furnished dioscin (100%), and polyphillin D (85%), whose data were virtually identical to those reported [2,3].

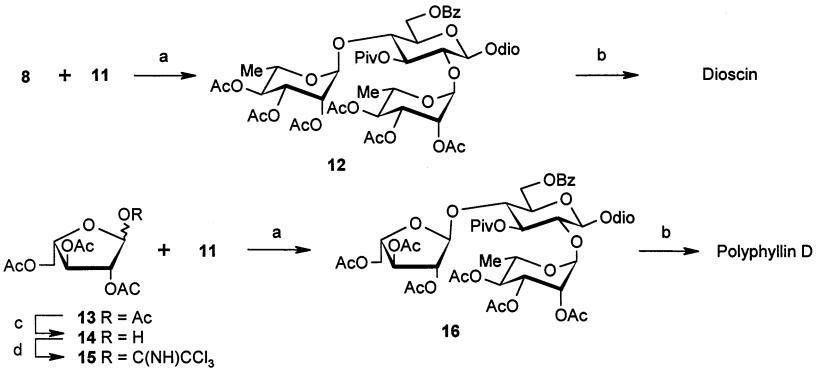
The synthesis of the tetrasaccharide saponin balanitin 7 was completed by glycosylation of



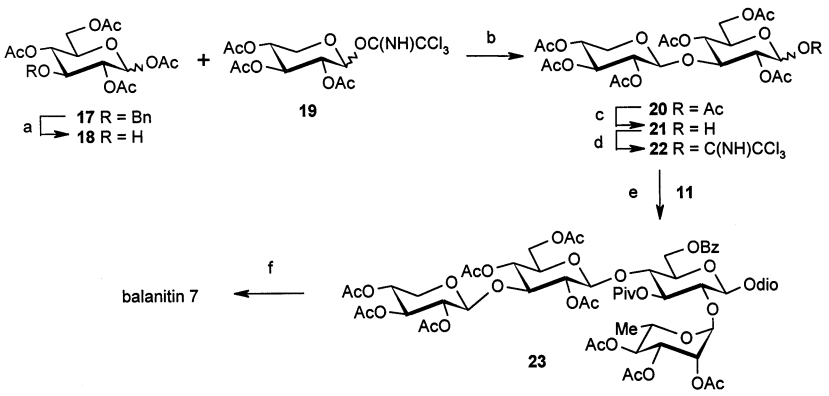
Scheme 1. Reagents and conditions: (a) TBSCl, imidazole, DMF, 50 °C, 5 h, 100%; (b) NIS, AgOTf, 4 Å MS, CH_2Cl_2, −30 °C, 1 h, 55% (for **3**), 50% (for **5**); (c) NaOMe, CH_2Cl_2, MeOH, 50 °C, 85%; (d) PivCl, Py, rt, 64%.



Scheme 2. Reagents and conditions: (a) $BF_3{\cdot}OEt_2$, 4 Å MS, CH_2Cl_2, −40 °C, 100%; (b) $TsOH{\cdot}H_2O$, MeOH, CH_2Cl_2, 80%; (c) BzCl, Py, CH_2Cl_2, −20 °C, 75%.



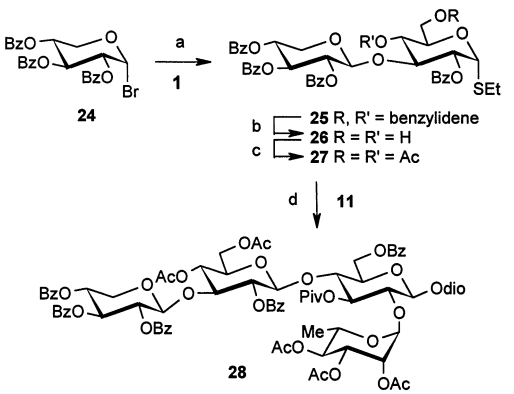
Scheme 3. Reagents and conditions: (a) $BF_3{\cdot}OEt_2$, 4 Å MS, CH_2Cl_2, 89% (for **12**), 93% (for **16**); (b) NaOH, 100% (for dioscin), 85% (for polyphyllin D); (c) HBr–HOAc, CH_2Cl_2, rt, 100%; (d) CCl_3CN, DBU, CH_2Cl_2, 100%.



Scheme 4. Reagents and conditions: (a) Pd–C, H_2, 88%; (b) $BF_3{\cdot}OEt_2$, 4 Å MS, CH_2Cl_2, 100%; (c) $NH_2NH_2{\cdot}HOAc$, DMF, 50 °C, 73%; (d) CCl_3CN, DBU, CH_2Cl_2, 96%; (e) $BF_3{\cdot}OEt_2$, 4 Å MS, CH_2Cl_2, 31%; (f) NaOH, 75%.

the diosgenyl disaccharide **11** with the appropriate disaccharide donor (Schemes 4 and 5). Glycosylation of **18** (which was readily prepared from 1,2,4,6-tetra-*O*-acetyl-3-*O*-benzyl-β-D-glucopyranose (**17**) [12] by hydrogenolysis) with 2,3,4-tri-*O*-acetyl-β-D-xylopyranosyl trichloracetimidate (**19**) [13] in the presence of a catalytic amount of $BF_3{\cdot}OEt_2$ gave disaccharide **20** quantitatively. Heptaacetate **20** was further exposed to hydrazine acetate to afford the desired hemiacetal **21** (73%). Subsequent treatment of **21** with CCl_3CN–DBU [14] gave disaccharide imidate **22** in excellent yield (96%). The coupling of imidate **22** with disaccharide saponin **11** in the presence of $BF_3{\cdot}OEt_2$ gave the desired tetrasaccharide **23** in a quite low yield (31%), along with 66% of the acceptor **11** recovered. Finally, removal of all of the acyl groups on **23** with sodium hydroxide provided balanitin 7 (75%), whose data were in good accordance with those reported by Pettit [4].

Alternatively, an ethyl 1-thio-disaccharide donor (**27**) was prepared and applied to the final glycosylation (Scheme 5). Treatment of bromide **24** [15] and thioglycoside **1** with AgOTf provided the disaccharide **25** in excellent yield (98%). Removal of the 4,6-benzylidene group and subsequent acetylation of the



Scheme 5. Reagents and conditions: (a) AgOTf, collidine, 4 Å MS, CH_2Cl_2, 98%; (b) 70% HOAc, 80 °C; (c) Ac_2O, Py, 86%, two steps; (d) NIS, AgOTf, 4 Å MS, CH_2Cl_2, 66%.

resulting diol afforded peracylated disaccharide **27** (86%, two steps). Glycosylation of **11** with ethyl thioglycoside **27** under the promotion of NIS–AgOTf [6,7] gave the desired tetrasaccharide saponin **28** in better yield (66%) than that in the previous glycosylation with the imidate donor **22** (31%). The low yield of this glycosylation could probably contribute to the steric hindrance of the 4′-OH in **11** and the mismatching of the two rings of the glucopyranosides (donor and acceptor) via the β-(1→4)-glycosidic bond. Recently, it has been shown that the glycosylation between hindered acceptor and donor with thioglycoside instead of imidate would give a more satisfactory result [16].

3. Experimental

General methods.—See Ref. [5b].

Ethyl 2-O-*benzoyl-4,6*-O-*benzylidene-3*-O-tert-*butyldimethylsilyl-1-thio-α*-D-*glucopyranoside* (**2**).—A solution of ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (**1**) (3.0 g, 7.2 mmol), *tert*-butylchlorodimethylsilane (TBDMSCl, 1.63 g, 10.8 mmol) and imidazole (1.23 g, 18.0 mmol) in dry DMF (15 mL) was stirred at 50 °C for 5 h, then diluted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Chromatography of the residue on a silica gel column (10:1 to 3:1 petroleum ether–EtOAc) gave **2** (3.84 g, 100%) as a colorless solid: R_f 0.82 (6:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–7.40 (m, 10 H), 5.68 (d, 1 H, $J_{1,2}$ 5.8, H-1), 5.58 (s, 1 H, PhCH), 5.29 (dd, 1 H, $J_{2,3}$ 9.3, H-2), 4.40–4.17 (m, 3 H, H-6, H-5, H-3), 3.82 (t, 1 H, H-6′), 3.62 (t, 1 H, H-4), 2.54 (m, 2 H), 1.23 (t, 3 H, J 7.4), 0.71 (s, 9 H), 0.01 and −0.06 (each s, each 3 H); EIMS (m/z): 473, 411, 367, 351, 105. Anal. Calcd for $C_{28}H_{38}O_6SSi$: C, 63.36; H, 7.22. Found: C, 63.52; H, 7.39.

Diosgenyl 2-O-*benzoyl-4,6*-O-*benzylidene-3*-O-tert-*butyldimethylsilyl-β*-D-*glucopyranoside* (**3**).—A suspension of **2** (3.19 g, 6.0 mmol), diosgenin (2.07 g, 5.0 mmol) and 4 Å MS (2.0 g) in dry CH_2Cl_2 (20 mL) was stirred under Ar at room temperature for 0.5 h, then cooled to −30 °C. NIS (1.69 g, 7.5 mmol) was added, followed by immediate addition of a solution of AgOTf (514 mg, 0.4 mmol) in dry toluene (15 mL). After being stirred for 1 h at room temperature, the mixture was quenched with a satd $Na_2S_2O_3$ solution, then diluted with EtOAc, and filtered. The organic layer was washed with satd $Na_2S_2O_3$ solution and brine, dried over $MgSO_4$, and concentrated. Chromatography of the residue on a silica gel column (20:1 to 15:1 petroleum ether–EtOAc) afforded **3** (2.41 g, 55%) as a white solid: $[\alpha]_D^{22}$ −38.7° (*c* 1.62, $CHCl_3$); R_f 0.69 (5:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–7.30 (m, 10 H), 5.55 (s, 1 H, PhCH), 5.20 (m, 2 H, H-6, H-2′), 4.70 (d, 1 H, $J_{1',2'}$ 8.7, H-1′), 4.41–4.30 (m, 2 H, H-16, H-6′), 4.01 (t, 1 H, $J_{2,3}$ $J_{3,4}$ 8.9, H-3′), 3.83 (t, 1 H, H-6′), 3.61 (t, 1 H, H-4′), 3.53–3.30 (m, 4 H, H-5′, H-3, H-26a, H-26b), 0.69 (s, 9 H), −0.06 and −0.11 (each s, each 3 H); EIMS (m/z): 881, 826, 469, 397 (base).

Diosgenyl 2,3-di-O-*benzoyl-4,6*-O-*benzylidene-β*-D-*glucopyranoside* (**5**).—A procedure similar to that for the preparation of **3** was employed. Ethyl 2,3-di-*O*-benzoyl-4,6-*O*-benzylidene-1-thio-β-D-glucopyranoside (**4**) (625 mg, 1.2 mmol) and diosgenin (414 mg, 1.0 mmol) were treated with NIS (337 mg, 1.50 mmol) and AgOTf (103 mg, 0.4 mmol) to afford **5** (439 mg, 50%) as a white solid: $[\alpha]_D^{22}$ 8.5° (*c* 1.2, $CHCl_3$); R_f 0.50 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00–7.30 (m, 15 H), 5.75 (t, 1 H, $J_{2,3}$ $J_{3,4}$ 9.5, H-3′), 5.53 (s, 1 H, PhCH), 5.43 (dd, 1 H, $J_{1,2}$ 7.9, H-2′), 5.22 (d, 1 H, J 5.2, H-6), 4.89 (d, 1 H, H-1′), 4.41 (dd, 1 H, J 4.9, 9.7, H-16), 4.34 (t, 1 H, H-4′), 4.26 (dd, 1 H, $J_{5,6}$ 4.9, $J_{6'a,6'b}$ 12.8, H-6′a), 3.99 (t, 1 H, H-6′b), 3.67 (m, 1 H, H-5′), 3.60–3.40 (m, 3 H, H-3, H-26a, H-26b); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.73, 165.28, 140.34, 136.93, 133.21, 133.12, 129.90, 129.84, 129.79, 129.60, 129.57, 129.07, 128.44, 128.36, 128.26, 126.20, 125.98, 121.87, 109.35, 101.53, 100.58, 80.87, 80.15, 78.92, 72.80, 72.64, 72.33, 72.27, 68.82, 66.93, 66.72, 66.05, 62.21, 56.55, 50.14, 41.69, 40.34, 39.82, 38.86, 37.24, 36.88, 32.12, 31.91, 31.47, 30.38, 29.59, 28.89, 20.90, 19.38, 17.20, 16.32, 14.58; EIMS (m/z): 872, 459, 105 (base). Anal. Calcd for $C_{54}H_{64}O_{10}$: C, 74.29; H, 7.39. Found: C, 74.47; H, 7.18.

Diosgenyl 4,6-O-benzylidene-β-D-glucopyranoside (**6**).—A solution of **5** (111 mg, 0.127 mmol) and NaOMe (catalytic) in CH_2Cl_2 (6 mL) and MeOH (6 mL) was stirred at 50 °C overnight. The mixture was then neutralized with Dowex-50 (H^+ form), and filtered. The filtrate was concentrated, and the resulting residue was purified by column chromatography to afford diol **6** (71 mg, 85%) [5b].

Diosgenyl 4,6-O-benzylidene-3-O-pivaloyl-β-D-glucopyranoside (**7**), *diosgenyl 4,6-O-benzylidene-2-O-pivaloyl-β-D-glucopyranoside* (**7a**), *and diosgenyl 4,6-O-benzylidene-2,3-di-O-pivaloyl-β-D-glucopyranoside* (**7b**).—To a solution of **6** (723 mg, 1.09 mmol) in pyridine (4 mL) was slowly added pivaloyl chloride (0.27 mL, 2.19 mmol) at room temperature. After being stirred for 2 h, the mixture was quenched with MeOH and concentrated. Chromatography of the residue on a silica gel column (6:1 to 4:1 petroleum ether–EtOAc) gave **7** (511 mg, 64%) as a white foam, **7a** (77 mg, 9.6%), **7b** (41 mg, 4.7%) and recovered **6** (82 mg, 11.3%). **7**: $[\alpha]_D^{22}$ −91.9° (*c* 0.48, $CHCl_3$); R_f 0.43 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.30 (m, 5 H), 5.52 (s, 1 H, PhCH), 5.39 (d, 1 H, *J* 4.7, H-6), 5.20 (t, 1 H, $J_{2,3}$ $J_{3,4}$ 9.3, H-3′), 4.59 (d, 1 H, $J_{1',2'}$ 7.7, H-1′), 4.40 (m, 1 H, H-16), 4.36 (dd, 1 H, $J_{5',6'a}$ 4.7, $J_{6'a,6'b}$ 10.6, H-6′a), 3.80 (t, 1 H, $J_{5',6'b}$ 10.2, H-6′b), 3.67 (t, 1 H, $J_{4',5'}$9.6, H-4′), 3.60–3.30 (m, 5 H, H-2′, H-3, H-5′, H-26a, H-26b), 1.23 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 178.71, 140.26, 137.15, 129.00, 128.28, 126.01, 122.17, 109.38, 102.10, 101.23, 80.92, 79.53, 78.70, 73.71, 73.64, 68.83, 66.96, 66.54, 66.08, 62.25, 56.61, 50.21, 41.74, 40.39, 39.05, 37.30, 36.97, 32.20, 31.96, 31.53, 31.28, 30.42, 29.73, 28.93, 27.20, 20.98, 19.48, 17.25, 16.39, 16.25, 14.64; EIMS (*m*/*z*): 747, 397, 282, 253, 139 (base). HREIMS Calcd for $C_{45}H_{63}O_9$: 747.4472. Found: 747.4476 [M^+ − H]. **7a**: $[\alpha]_D^{21}$ −84.1° (*c* 0.59, $CHCl_3$); R_f 0.30 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50–7.20 (m, 5 H), 5.54 (s, 1 H, PhCH), 5.35 (d, 1 H, *J* 4.9, H-6), 4.86 (dd, 1 H, $J_{1',2'}$ 8.0, $J_{2',3'}$ 8.8, H-2′), 4.65 (d, 1 H, H-1′), 4.41 (q, 1 H, *J* 7.5, H-16), 4.33 (dd, 1 H, $J_{5',6'a}$ 5.0, $J_{6'a,6'b}$ 10.5, H-6′), 3.87 (t, 1 H, *J* 11.8, H-26a), 3.80 (t, 1 H, $J_{5',6'b}$ 10.4, H-6′b), 3.60 (t, 1 H, $J_{3',4'}$ $J_{4',5'}$ 9.3, H-4′), 3.57–3.32 (m, 4 H, H-3′, H-5′, H-3, H-26b), 1.24 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.69, 140.15, 136.78, 128.95, 128.04, 126.00, 121.56, 109.04, 101.49, 99.57, 80.70, 80.54, 79.06, 74.16, 72.43, 68.40, 66.59, 65.85, 61.87, 56.24, 49.84, 41.35, 40.02, 39.49, 38.64, 36.91, 36.62, 31.82, 31.58, 31.17, 30.02, 29.32, 28.54, 26.92, 20.58, 19.07, 16.87, 16.01, 14.25; FABMS (*m*/*z*): 749 [M + 1], 747, 663, 607, 397 (base). Anal. Calcd for $C_{45}H_{64}O_9 \cdot H_2O$: C, 70.47; H, 8.67. Found: C, 70.52; H, 8.80. **7b**: $[\alpha]_D^{21}$ −73.9° (*c* 0.57, $CHCl_3$); R_f 0.71 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5 H), 5.51 (s, 1 H, PhCH), 5.34 (m, 2 H, H-6, H-3′), 5.03 (dd, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 8.9, H-2′), 4.71 (d, 1 H, H-1′), 4.45–4.27 (m, 2 H, H-16, H-6′a), 3.81 (t, 1 H, $J_{6'a,6'b}$ 10.3, $J_{5',6'b}$ 10.1, H-6′b), 3.71 (t, 1 H, *J* 9.3, H-4′), 3.56–3.34 (m, 4 H, H-5′, H-3, H-26a, H-26b), 1.18 (s, 9 H), 1.16 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.95, 176.25, 140.04, 136.73, 128.60, 127.88, 125.59, 121.62, 108.99, 100.80, 99.89, 80.54, 79.19, 78.53, 71.46, 71.13, 68.41, 66.57, 66.03, 61.89, 56.22, 49.82, 41.35, 40.02, 39.49, 38.64, 38.47, 36.89, 36.60, 31.82, 31.58, 31.17, 30.03, 29.30, 28.56, 26.97, 26.83, 20.58, 19.07, 16.87, 16.01, 14.26; FABMS (*m*/*z*): 833 [M + 1], 831, 662, 397 (base). Anal. Calcd for $C_{50}H_{72}O_{10}$: C, 72.08; H, 8.71. Found: C, 71.95; H, 8.98.

Diosgenyl 2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-4,6-O-benzylidene-3-O-pivaloyl-β-D-glucopyranoside (**9**).—To a suspension of **8** (1.68 g, 3.87 mmol), **7** (833 mg, 1.13 mmol) and 4 Å MS (2 g) in dry CH_2Cl_2 (10 mL) at −40 °C was added a solution of $BF_3 \cdot OEt_2$ (0.55 mL, 0.1 M) in CH_2Cl_2. After being stirred for 1 h, the reaction was quenched with NEt_3 (0.5 mL), filtered, and concentrated. Chromatography of the residue on a silica gel column (5:1 to 4:1 petroleum ether–EtOAc) gave **9** (1.13 g, 100%) as a white solid: $[\alpha]_D^{22}$ −61.9° (*c* 1.41, $CHCl_3$); R_f 0.47 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.20 (m, 5 H), 5.44 (brs, 1 H, PhCH), 5.44–5.36 (m, 2 H, H-6, H-3″), 5.21 (dd, 1 H, $J_{2'',3''}$ 3.3, $J_{3'',4''}$ 9.9, H-3″), 5.16 (dd, 1 H, $J_{1'',2''}$ 1.5, H-2″), 5.03 (t, 1 H, $J_{4'',5''}$ 10.0, H-4″), 4.90 (d, 1 H, H-1″), 4.72 (d, 1 H, $J_{1',2'}$ 7.7, H-1′), 4.48–4.30 (m, 2 H, H-5″, H-16a), 3.80–3.30 (m, 7 H), 2.09,

2.01 and 1.95 (each s, each 3 H), 1.20 (d, 3 H, *J* 6.1), 1.12 (s, 9 H), 1.00 (s,), 0.95 (d, 3 H, *J* 6.9), 0.77 (m, 6 H); EIMS (*m*/*z*): 1019, 962, 608, 153 (base); Anal. Calcd for $C_{57}H_{80}O_{16}\cdot H_2O$: C, 65.88; H, 7.95. Found: C, 65.68; H, 7.95.

*Diosgenyl 2-*O*-(2,3,4-tri-*O*-acetyl-α-*L*-rhamnopyranosyl)-3-*O*-pivaloyl-β-*D*-glucopyranoside* (**10**).—A solution of **9** (1.13 g, 1.11 mmol) and $TsOH\cdot H_2O$ (1.0 g) in CH_2Cl_2 (20 mL) and MeOH (20 mL) was stirred at rt for 2 h, then diluted with CH_2Cl_2. The organic layer was washed with satd $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated. Chromatography of the residue on a silica gel column (2:1 to 1:1 petroleum ether–EtOAc) gave **10** (826 mg, 80%) as a white solid: $[\alpha]_D^{22}$ −72.4° (*c* 1.3, $CHCl_3$); R_f 0.35 (1.5:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.39 (d, 1 H, *J* 4.9, H-6), 5.22–5.16 (m, 2 H), 5.07 (dd, 1 H, $J_{2'',3''}$ 3.2, $J_{3'',4''}$ 9.2, H-3″), 5.03 (m, 1 H, H-4″), 4.97 (d, 1 H, $J_{1'',2''}$ 1.1, H-1″), 4.62 (d, 1 H, $J_{1',2'}$ 7.7, H-1′), 4.48 (m, 1 H, H-5″), 4.41 (m, 1 H, H-16), 3.90 (dd, 1 H, $J_{5',6'a}$ 3.0, $J_{6'a,6'b}$ 12.4, H-6′a), 3.79 (dd, 1 H, $J_{5',6'b}$ 4.7, H-6′b), 3.72 (dd, 1 H, $J_{2',3'}$ 9.2, H-2′), 3.68–3.60 (m, 1 H, H-5′), 3.58 (t, 1 H, $J_{3',4'}$ $J_{4',5'}$ 9, H-4′), 3.50–3.32 (m, 3 H, H-3, H-26a, H-26b), 2.10, 2.01 and 1.95 (each s, each 3 H), 1.20 (d, 3 H, *J*6.3), 1.17 (s, 9 H); EIMS (*m*/*z*): 934, 519, 440, 397, 273, 153 (base). Anal. Calcd for $C_{50}H_{76}O_{16}\cdot 0.5H_2O$: C, 63.74; H, 8.24. Found: C, 63.88; H, 8.14.

*Diosgenyl 2-*O*-(2,3,4-tri-*O*-acetyl-α-*L*-rhamnopyranosyl)-6-*O*-benzoyl-3-*O*-pivaloyl-β-*D*-glucopyranoside* (**11**).—To a cooled (−20 °C) solution of **10** (551 mg, 0.59 mmol) in pyridine (5 mL) and CH_2Cl_2 (5 mL) was added BzCl (78 μL, 0.67 mmol). After being stirred for 1 h, another portion of BzCl (78 μL, 0.67 mmol) was added. The mixture was stirred for another 1 h, then quenched with MeOH, and concentrated. Chromatography of the residue on a silica gel column (5:1 petroleum ether–EtOAc) gave **11** (461 mg, 75%) as a white solid: $[\alpha]_D^{22}$ −26.8° (*c* 1.90, $CHCl_3$); R_f 0.25 (4:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–7.30 (m, 5 H), 5.34 (d, 1 H, *J* 4.9, H-6), 5.20 (m, 2 H, H-2″, H-3″), 5.12–5.00 (m, 2 H, H-4″, H-3′), 4.97 (s, 1 H, H-1‴), 4.60 (m, 3 H, H-1′, H-6′), 4.50–4.40 (m, 2 H, H-5″, H-16), 3.76 (t, 1 H, $J_{1',2'}$ 7.9, $J_{2',3'}$ 9.0, H-2′), 3.70–3.44 (m, 4 H), 3.37 (t, 1 H, *J* 10.8, H-26a), 2.11, 2.02 and 1.96 (each s, each 3 H), 1.18 (s, 9 H), 0.79 (d, 3 H, *J* 6.4); ^{13}C NMR (75 MHz, $CDCl_3$): δ 179.73, 169.94, 169.87, 169.65, 166.61, 140.14, 133.11, 129.81, 128.37, 121.93, 109.28, 99.66, 97.67, 80.79, 79.37, 78.80, 74.80, 74.15, 71.11, 70.82, 69.46, 69.06, 66.85, 66.45, 63.85, 62.14, 56.50, 50.05, 41.63, 40.27, 39.77, 38.98, 38.39, 37.02, 36.80, 32.08, 31.83, 31.40, 30.29, 29.72, 28.82, 26.92, 20.80, 20.68, 19.21, 17.21, 17.11, 16.26, 14.50; FABMS (*m*/*z*): 1036 [M$^+$], 623, 397, 273, 111 (base). Anal. Calcd for $C_{57}H_{80}O_{17}\cdot H_2O$: C, 64.88; H, 7.83. Found: C, 64.93; H, 7.80.

*Diosgenyl 2,4-di-*O*-(2,3,4-tri-*O*-acetyl-α-*L*-rhamnopyranosyl)-6-*O*-benzoyl-3-*O*-pivaloyl-β-*D*-glucopyranoside* (**12**).—To a suspension of **8** (180 mg, 0.414 mmol), **11** (200 mg, 0.193 mmol) and 4 Å MS (200 mg) in dry CH_2Cl_2 (5 mL) at −40 °C, was added $BF_3\cdot OEt_2$ (7.3 μL, 0.058 mmol). After being stirred for 1 h, the reaction was quenched with NEt_3 (0.5 mL), filtered, and concentrated. Chromatography of the residue on a silica gel column (3:1 to 2.5:1, petroleum ether–EtOAc) gave **12** (224 mg, 89%) as a white foam: $[\alpha]_D^{17}$ −76.3° (*c* 0.85, $CHCl_3$); R_f 0.34 (2.5:1 petroleum ether–EtOAc); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.10–7.40 (m, 5 H), 5.32 (d, 1 H, *J* 5.6, H-6), 5.32 (dd, 1 H, $J_{2',3'}$ 7.9, $J_{3',4'}$ 8.3, H-3′), 5.23–5.17 (m, 3 H, H-3″, H-3‴, H-2″), 5.12 (dd, 1 H, $J_{1'',2''}$ 2.0, $J_{2'',3''}$ 2.9, H-2″), 5.03 (t, 1 H, $J_{3'',4''}$ $J_{4'',5''}$ 9.9, H-4″), 5.01 (t, 1 H, $J_{3''',4'''}$ $J_{4''',5'''}$ 9.7, H-4‴), 4.95 (brs, 1 H, H-1‴), 4.85 (brs, 1 H, H-1″), 4.73 (dd, 1 H, $J_{5',6'a}$ 2.4, $J_{6'a,6'b}$ 11.9, H-6′a), 4.61 (d, 1 H, $J_{1',2'}$ 7.3, H-1′), 4.52 (dd, 1 H, $J_{5',6'b}$ 6.1, H-6′b), 4.42 (dd, 1 H, *J* 7.3, 15.2, H-16), 4.35 (m, 1 H, H-5″), 3.95 (m, 1 H, H-5‴), 3.90 (ddd, H-5′), 3.83 (t, 1 H, $J_{4',5'}$ 9.4, H-4′), 3.67 (t, 1 H, H-2′), 3.52 (m, 1 H, H-3), 3.48 (m, 1 H, H-26a), 3.38 (t, 1 H, *J* 11.0, H-26b), 2.11, 2.09, 2.04, 2.01, 1.96 and 1.94 (each s, each 3 H), 1.20–1.16 (m, 15 H), 0.98 (d, 3 H, *J* 7.0), 0.93 (s, 3 H), 0.79 (d, 3 H, *J* 6.4), 0.78 (s, 3 H); EIMS (*m*/*z*): 1021, 897, 634, 273 (base). Anal. Calcd for $C_{69}H_{96}O_{24}$: C, 63.28; H, 7.39. Found: C, 63.02; H, 7.56.

Diosgenyl 2,4-di-O-(α-L-rhamnopyranosyl)-β-D-glucopyranoside (dioscin).—A solution of **12** (100 mg, 0.076 mmol) and NaOH (49 mg, 1.23 mmol) in H_2O (2 mL), MeOH (2 mL) and THF (2 mL) was stirred at 45 °C for 5 h, then neutralized with Dowex-50 (H^+ form), filtered, and concentrated. Chromatography of the residue on a silica gel column (6:1 to 5:1 CH_2Cl_2–MeOH) gave dioscin (66 mg, 100%) as a white solid: $[\alpha]_D^{22}$ −113.6° (*c* 1.1, MeOH), Lit. −121° (*c* 1.0, MeOH) [2].; R_f 0.28 (5:1 CH_2Cl_2–MeOH); ^{1}H NMR (600 MHz, C_5D_5N): δ 6.38 (brs, 1 H, H-1‴), 5.83 (brs, 1 H, H-1″), 5.31 (brd, 1 H, H-6), 5.00–4.85 (m, 3 H, H-1′, H-2′, H-4′), 4.81 (brs, 1 H), 4.66 (brs, 1 H), 4.61 (dd, 1 H, *J* 3.4, 9.3), 4.57–4.50 (m, 2 H), 4.40–4.30 (m, 3 H), 4.20 (m, 3 H), 4.09 (dd, 1 H, $J_{5',6'a}$ 3.1, $J_{6'a,6'b}$ 12.2, H-6′a), 3.87 (m, 1 H, H-3), 3.63 (m, 1 H), 3.57 (m, 1 H, H-26a), 3.50 (t, 1 H, H-26b), 2.79 (dd, 1 H, *J* 2.9, 13.0), 2.71 (t, 1 H), 1.76 (d, 3 H, *J* 6.3), 1.62 (d, 3 H, *J* 5.9), 1.13 (d, 3 H, *J* 6.7), 1.04 (s, 3 H), 0.82 (s, 3 H), 0.69 (d, 3 H, *J* 5.5, H-27); ^{13}C NMR (75 MHz, C_5D_5N): δ 140.95, 121.99, 109.44, 103.09, 102.23, 100.45, 81.28, 78.70, 78.22, 78.15, 77.95, 77.14, 74.32, 74.13, 73.02, 72.94, 72.75, 70.60, 69.72, 67.04, 63.06, 61.44, 56.80, 50.46, 42.14, 40.63, 40.02, 39.15, 37.67, 37.32, 32.48, 32.40, 32.00, 31.85, 30.78, 30.34, 29.45, 21.28, 19.59, 18.85, 18.70, 17.51, 16.52, 15.23; IR (KBr): 3423, 2935, 1458, 1380, 1243, 1135, 1043, 981, 918, 899; FABMS (*m*/*z*): 870 [M + 2], 868 [M].

Diosgenyl 4-O-(tri-O-acetyl-α-L-arabinofuranosyl)-2-O-(2,3,4-tri-O-acetyl-α-L-rhamnopyranosyl)-6-O-benzoyl-3-O-pivaloyl-β-D-glucopyranoside (**16**).—To a cooled solution (0 °C) of tetraacetyl α-L-arabinofuranose (**13**) (0.21 g, 0.66 mmol) in dry CH_2Cl_2 (10 mL) was added HBr–HOAc (30%, 0.5 mL). After being stirred at rt for 3 h, the mixture was concentrated and applied to a silica gel column (2:1 petroleum ether–EtOAc) to give **14** (0.18 g, 100%) as a syrup. A solution of **14** (150 mg, 0.54 mmol), CCl_3CN (0.27 mL, 2.7 mmol) and DBU (1 drop) in CH_2Cl_2 (3 mL) was stirred at 0 °C for 30 min, then concentrated. Chromatography of the residue on a silica gel column (5:1 to 3:1 petroleum ether–EtOAc, with 1% Et_3N) afforded **15** (228 mg, 100%) as a colorless syrup, which was used in the next step without further characterization.

To a suspension of **15** (170 mg, 0.40 mmol), **11** (150 mg, 0.14 mmol) and 4 Å MS (250 mg) in dry CH_2Cl_2 (3 mL) at 0 °C, was slowly added a solution of $BF_3{\cdot}OEt_2$ (0.1 mL, 0.1 M) in CH_2Cl_2. After being stirred for 30 min, the reaction was quenched with NEt_3 (0.5 mL), filtered, and concentrated. Chromatography of the residue on a silica gel column (4:1 to 2.5:1 petroleum ether–EtOAc) gave **16** (174 mg, 93%): $[\alpha]_D^{22}$ −106.4° (*c* 0.30, $CHCl_3$); R_f 0.60 (2:1 petroleum ether–EtOAc); ^{1}H NMR (600 MHz, DQFCOSY, $CDCl_3$): δ 8.10–7.40 (m, 5 H), 5.37–5.32 (m, 2 H, H-6, H-3′), 5.20 (dd, 1 H, $J_{2'',3''}$ 3.4, H-3″), 5.19 (m, 2 H, H-4″, H-2‴), 5.04–5.00 (m, 2 H, H-4″, H-1‴), 4.95 (dd, 1 H, $J_{2''',3'''}$ 1.5, $J_{3''',4'''}$ 4.4, H-3‴), 4.90 (s, 1 H, H-1″), 4.75 (dd, 1 H, $J_{5',6'a}$ 2.0, $J_{6'a,6'b}$ 12.0, H-6′a), 4.61 (d, 1 H, *J* 7.6, H-1′), 4.46 (dd, 1 H, $J_{5',6'b}$ 6.0, H-6′b), 4.42 (dd, 1 H, H-16), 4.40 (m, 1 H, H-5″), 4.31 (dd, 1 H, $J_{4''',5'''}$ 3.7, H-5‴), 4.30 (m, 1 H, H-4‴), 4.16 (dd, 1 H, $J_{4''',5'''a}$ 4.7, $J_{5'''a,5'''b}$ 11.1, H-5‴a), 3.89 (ddd, 1 H, H-5′), 3.79 (t, 1 H, $J_{3',4'}$ 9.1, $J_{4',5'}$ 9.7, H-4′), 3.74 (t, 1 H, *J* 8.0, H-2′), 3.55 (m, 1 H, H-3), 3.48 (m, 1 H, H-26a), 3.38 (t, 1 H, *J* 9.0, 11.0, H-26b), 2.11, 2.10, 2.04, 2.04, 2.02 and 1.95 (each s, each 3 H), 1.19 (d, 3 H, $J_{5'',6''}$ + 6.3, H-6″), 1.17 (s, 9 H), 0.98 (d, 3 H, *J* 6.9), 0.96 (s, 3 H), 0.79 (d, 3 H, *J* 6.4), 0.78 (s, 3 H); IR (KBr): 2954, 1752, 1454, 1371, 1224, 1134, 1050, 920, 900; FABMS (*m*/*z*): 1276, 1257, 1018, 882, 397, 41 (base). Anal. Calcd for $C_{68}H_{94}O_{24}$: C, 63.05; H, 7.31. Found: C, 62.74; H, 7.50.

Diosgenyl α-L-rhamnopyranosyl-(1→2)-[(α-L-arabinofuranosyl)-(1→4)]-β-D-glucopyranoside (polyphyllin D).—A solution of **16** (70 mg, 0.054 mmol) and NaOH (45 mg, 1.12 mmol) in H_2O (1.5 mL), MeOH (1.5 mL) and THF (1.5 mL) was stirred at 45 °C overnight, then neutralized with Dowex-50 (H^+ form), filtered, and concentrated. Chromatography of the residue on a silica gel column (6:1 to 5:1 CH_2Cl_2–MeOH) gave polyphyllin D (45 mg, 85%) as a white solid: $[\alpha]_D^{22}$ −116.3° (*c* 0.52, MeOH), Lit. −113° (*c* 0.53, MeOH) [3]; R_f 0.40 (5:1 CH_2Cl_2–MeOH); ^{1}H NMR (600 MHz, DQFCOSY, C_5D_5N): δ 6.25

(brs, 1 H, H-1″), 5.90 (brs, 1 H, H-1‴), 5.30 (d, 1 H, *J* 4.8, H-6), 5.00–4.80 (m, 4 H, H-1′, H-2′, H-4′, H-2‴), 4.76 (d, 1 H, H-2‴), 4.58 (dd, 1 H, $J_{2'',3''}$ 3.5, $J_{3'',4''}$ 9.2, H-3″), 4.53 (m, H-16), 4.35–4.10 (m, 9 H), 3.86 (m, 1 H, H-3), 3.75 (m, 1 H, H-5″), 3.57 (dd, 1 H, *J* 2.8, 10.3, H-26a), 3.49 (t, 1 H, *J* 10.3, H-26b), 2.77 (dd, 1 H, *J* 2.9, 13), 2.70 (t, 1 H), 1.74 (d, 3 H, *J* 6.2, H-6″), 1.12 (d, 3 H, *J* 6.9), 1.04 (s, 3 H), 0.82 (s, 3 H), 0.68 (d, 3 H, *J* 5.7); ^{13}C NMR (150 MHz, C_5D_5N): δ 140.81, 121.79, 109.64, 109.26, 101.90, 100.18, 86.71, 82.67, 81.11, 78.16, 77.91, 77.69, 77.46, 77.12, 76.71, 74.13, 72.78, 72.43, 69.47, 66.88, 62.92, 62.51, 61.42, 56.66, 50.32, 41.99, 40.48, 39.88, 38.97, 37.51, 37.15, 32.32, 32.23, 31.85, 31.71, 30.61, 30.17, 29.28, 21.12, 19.41, 18.65, 17.32, 16.34, 14.99; IR (KBr): 3400, 2932, 1456, 1378, 1243, 1137, 1052, 982, 919, 900; FABMS (*m*/*z*): 856 [M + 1], 185 (base).

1,2,4,6-Tetra-O-*acetyl*-α,β-D-*glucopyranose* (**18**).—A suspension of **17** (2.0 g, 4.56 mmol) and 10% Pd–C (0.8 g) in EtOAc (20 mL) was stirred at 50 °C and H_2 atmosphere (60 atm) for 2 days, then filtered, and concentrated. Chromatography of the residue on a silica gel column (1:1 to 1:2 petroleum ether–EtOAc) gave **18** (1.39, 88%) as a white solid: $[\alpha]_D^{22}$ −4.9° (*c* 0.88, $CHCl_3$); Anal. Calcd for $C_{14}H_{20}O_{10}$: C, 48.28; H, 5.79. Found: C, 48.13; H, 5.70.

1,2,4,6-Tetra-O-*acetyl*-3-O-*(2,3,4-tri*-O-*acetyl*-β-D-*xylopyranosyl)*-β-D-*glucopyranose* (**20**).—To a suspension of **19** (1.74 g, 4.14 mmol), **18** (1.21 g, 3.49 mmol) and 4 Å MS (500 mg) in dry CH_2Cl_2 (10 mL) at 0 °C, was slowly added a solution of $BF_3{\cdot}OEt_2$ (5.8 mL, 0.07 M). After being stirred for 30 min, the reaction was quenched with NEt_3 (0.5 mL), filtered, and concentrated. Chromatography of the residue on a silica gel column (1.5:1 to 1:1 petroleum ether–EtOAc) gave **20** (2.12 g, 100%) as a white foam: $[\alpha]_D^{22}$ −9.0° (*c* 1.1, $CHCl_3$); R_f 0.36 (1:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.60 (d, 1 H, $J_{1,2}$ 8.4, H-1), 5.14–5.00 (m, 3 H, H-2, H-4, H-3′), 4.87 (dt, 1 H, H-4′), 4.78 (dd, 1 H, $J_{1',2'}$ 3.3, $J_{2',3'}$ 7.9, H-2′), 4.57 (d, 1 H, H-1′), 4.24–4.04 (m, 3 H, H-6, H-5′), 3.87 (t, 1 H, H-3, $J_{2,3}$ $J_{3,4}$ 9.4), 3.78–3.72 (ddd, 1 H, H-5), 3.35 (dd, 1 H, $J_{4',5'a}$ 8.0, $J_{5'a,5''b}$ 12.0, H-5′a), 2.10–2.00 (7s, 21 H); EIMS (*m*/*z*): 606, 444, 394, 229, 43 (base). Anal. Calcd for $C_{25}H_{34}O_{17}{\cdot}0.5H_2O$: C, 48.78; H, 5.73. Found: C, 48.83; H, 5.60.

1,2,4,6-Tetra-O-*acetyl*-3-O-*(2,3,4-tri*-O-*acetyl*-β-D-*xylopyranosyl)*-β-D-*glucopyranosyl trichloroacetimidate* (**22**).—A solution of **20** (1.15 g, 1.89 mmol) and $NH_2NH_2{\cdot}HOAc$ (209 mg, 2.27 mmol) in DMF (10 mL) was stirred at 50 °C for 30 min, then poured into brine and extracted with EtOAc. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated. Chromatography of the residue on a silica gel column (1:1.2 to 1:1.5 petroleum ether–EtOAc) gave **21** (783 mg, 73.4%) as a white solid. A solution of **21** (111 mg, 0.197 mmol), CCl_3CN (0.1 mL, 1 mmol) and DBU (1 drop) in CH_2Cl_2 (2 mL) was stirred at 0 °C for 1 h, then concentrated. Chromatography of the residue on a silica gel column (1:1 petroleum ether–EtOAc, with 1% Et_3N) afforded **22** (140 mg, 100%) as a white foamy solid: $[\alpha]_D^{22}$ +26.0° (*c* 0.83, $CHCl_3$); R_f 0.67 (1:1.5 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.69 (brs, 1 H, NH), 6.47 (brd, 1 H, H-1), 5.14 (t, 1 H, $J_{2',3'}$ 8.5, $J_{3',4'}$ 9.7, H-3′), 5.08 (t, 1 H, *J* 8.0, H-4), 5.07 (dd, 1 H, $J_{1,2}$ 3.8, $J_{2,3}$ 9.7, H-2), 4.89 (m, H-4′), 4.83 (dd, 1 H, H-2′, $J_{1',2'}$ 6.5, $J_{2',3'}$ 8.4), 4.68 (d, 1 H, H-1′), 4.20 (dd, 1 H, $J_{5,6a}$ 4.0, $J_{6a,6b}$ 12.8, H-6a), 4.16–4.08 (m, 3 H, H-6b, H-3, H-5′a), 3.40 (dd, 1 H, $J_{4',5'b}$ 8.0, $J_{5'a,5'b}$ 12.0, H-5′b), 2.09, 2.08, 2.07, 2.05, 2.02, 2.00 (each s, each 3 H); EIMS (*m*/*z*): 649, 547, 432, 259, 43 (base). Anal. Calcd for $C_{25}H_{32}Cl_3NO_{16}$: C, 42.36; H, 4.55; N, 1.98. Found: C, 42.08; H, 4.53; N, 1.96.

Diosgenyl [(2,3,4-tri-O-*acetyl*-β-D-*xylopyranosyl)*-(1→3)-*(2,4,6-tri*-O-*acetyl*-β-D-*glucopyranosyl)]*-(1→4)-*2*-O-*(2,3,4-tri*-O-*acetyl*-α-L-*rhamnopyranosyl)*-*6*-O-*benzoyl*-*3*-O-*pivaloyl*-β-D-*glucopyranoside* (**23**).—To a suspension of **22** (536 mg, 0.76 mmol), **11** (214 mg, 0.21 mmol) and 4 Å MS (500 mg) in dry CH_2Cl_2 (10 mL) at 0 °C, was slowly added a solution of $BF_3{\cdot}OEt_2$ (3 mL, 0.07 M). After being stirred for 30 min, the reaction was quenched with NEt_3 (0.5 mL), filtered, and concentrated. Chromatography of the residue on a silica gel column (1.5:1 to 1:1 petroleum ether–EtOAc) gave **23** (102 mg, 31%) as a white foam and recovered **11** (142

mg, 66%): $[\alpha]_D^{22}$ −62.4° (*c* 0.60, $CHCl_3$); R_f 0.46 (1:1 petroleum ether–EtOAc); ^{1}H NMR (600 MHz, DQFCOSY, $CDCl_3$): δ 8.10–7.40 (m, 5 H), 5.33 (d, 1 H, *J* 4.7, H-6), 5.29 (t, 1 H, *J* 9.0), 5.20 (dd, 1 H, $J_{2'',3''}$ 3.3, $J_{3'',4''}$ 10.0, H-3″), 5.17 (br, 1 H, H-1″), 5.03 (t, 1 H, *J* 8.4, 11.7, H-3‴), 5.02 (dd, 1 H, $J_{4'',5''}$ 14.0, H-4″), 4.90–4.83 (m, 4 H), 4.74 (brd, 1 H, H-2⁗), 4.71 (brd, 1 H, H-6′a), 4.61 (d, 1 H, H-1′, $J_{1',2'}$ 7.7), 4.48 (d, 1 H, $J_{1''',2'''}$ 6.4, H-1‴), 4.43–4.36 (m, 4 H), 4.14 (dd, 1 H, *J* 5.5, 12.3), 4.06–4.02 (m, 2 H), 3.92 (t, 1 H, *J* 9.4), 3.78 (m, 1 H), 3.72 (t, 1 H), 3.70 (t, 1 H, *J* 9.4), 3.54 (m, 1 H, H-3), 3.50–3.44 (m, 2 H), 3.38 (t, 1 H, *J* 11.0, H-26a), 3.32 (dd, 1 H, *J* 8.1, 11.9), 2.40 (brd, 1 H), 2.23 (t, 1 H), 2.10, 2.09, 2.06, 2.04, 2.03, 2.02, 2.00, 1.99, 1.95 (each s, each 3 H), 1.18 (s, 9 H), 0.98 (d, 3 H, *J* 6.7), 0.95 (s, 3 H), 0.79 (d, 3 H, *J* 6.4), 0.78 (s, 3 H); EIMS (*m*/*z*): 1021, 547, 397, 273 (base).

*Diosgenyl [β-*D*-xylopyranosyl-(1→3)-β-*D*-glucopyranosyl]-(1→4)-[(α-*L*-rhamnopyranosyl)]-(1→2)-β-*D*-glucopyranoside (balanitin 7).*—A solution of **23** (58 mg, 0.037 mmol) and NaOH (38 mg, 0.95 mmol) in H_2O (1 mL), MeOH (1 mL) and THF (1 mL) was stirred at 50 °C for 6 h, then neutralized with Dowex-50 (H^+ form), filtered, and concentrated. Chromatography of the residue on a silica gel column (5:1 to 4:1 CH_2Cl_2–MeOH) gave balanitin 7 (32 mg, 86%) as a white solid: $[\alpha]_D^{16}$ −84.6° (*c* 0.80, pyridine), Lit −83° (*c* 0.83, pyridine) [4]; R_f 0.53 (4:1 CH_2Cl_2–MeOH); ^{13}C NMR (75 MHz, C_5D_5N): δ 140.43, 121.44, 108.91, 105.94, 104.20, 101.45, 99.62, 86.98, 81.14, 80.76, 77.84, 77.80, 77.26, 76.95, 75.91, 74.96, 73.76, 73.64, 72.41, 72.08, 70.56, 69.12, 68.68, 67.04, 66.52, 62.55, 61.38, 61.14, 56.28, 49.95, 41.63, 40.12, 39.51, 38.58, 37.15, 36.78, 31.96, 31.88, 31.49, 31.34, 30.25, 29.80, 28.93, 20.76, 19.06, 18.30, 16.97, 15.99, 14.68.

*Ethyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-(2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl)-1-thio-α-*D*-glucopranoside* (**25**).—To a suspension of **24** (2.1 g, 4.0 mmol), **1** (1.265 g, 3.04 mmol), collidine (0.53 mL, 4.05 mmol) and 4 Å MS (4 g) in dry CH_2Cl_2 (30 mL) at −20 °C under Ar, was added a solution of AgOTf (1.02 g, 3.97 mmol) in dry PhMe (10 mL). After being stirred for 2 h, the mixture was filtered, and concentrated. Chromatography of the residue on a silica gel column (6:1 to 5:1 petroleum ether–EtOAc) afforded **25** (2.55 g, 98%) as a syrup: $[\alpha]_D^{22}$ +49.3° (*c* 1.07, $CHCl_3$); R_f 0.36 (petroleum ether–EtOAc 4:1);^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–7.10 (m, 25 H), 5.74 (d, 1 H, $J_{1,2}$ 5.8, H-1), 5.63 (s, 1 H, PhCH), 5.55 (t, 1 H, $J_{2',3'}$ 5.0, $J_{3',4'}$ 5.3, H-3′), 5.33 (dd, 1 H, $J_{2,3}$ 9.7, H-2), 5.28 (d, 1 H, $J_{1',2'}$ 2.9, H-1′), 5.18 (dd, 1 H, H-2′), 5.15 (m, 1 H, H-4′), 4.64 (dd, 1 H, $J_{5,6a}$ 3.1, $J_{6a,6b}$ 13.1, H-6a), 4.48 (t, 1 H, $J_{3,4}$ 9.6, H-3), 4.45–4.30 (m, 2 H, H-5, H-5′a), 3.90–3.60 (m, 3 H, H-5′b, H-6b, H-4), 2.52 (m, 2 H), 1.20 (t, 3 H, *J* 7.4). FABMS (*m*/*z*): 883 [M + Na], 861, 860 [M], 799, 445, 323, 201, 105. Anal. Calcd for $C_{48}H_{44}O_{13}S$: C, 66.97; H, 5.15. Found: C, 66.89; H, 5.12.

*Ethyl 4,6-di-*O*-acetyl-2-*O*-benzoyl-3-*O*-(2,3,4-tri-*O*-benzoyl-β-*D*-xylopyranosyl)-1-thio-α-*D*-glucopyranoside* (**27**).—A solution of **25** (2.29 g, 2.66 mmol) in 70% HOAc (100 mL) was stirred at 80 °C until a clear solution appeared. The mixture was then concentrated, and traces of HOAc and water were coevaporated with toluene several times. The residue was dissolved in Ac_2O (10 mL) and pyridine (10 mL) and then stirred overnight at rt. The reaction was quenched with MeOH, then concentrated. The residue was diluted with EtOAc, washed with diluted HCl, satd $NaHCO_3$ solution, and brine, respectively. The organic layer was dried over $MgSO_4$, then concentrated. Chromatography of the residue on a silica gel column (5:1 petroleum ether–EtOAc) gave **27** (1.97 g, 86%): $[\alpha]_D^{22}$ +44.4° (*c* 1.14, $CHCl_3$); R_f 0.68 (3:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.00–7.10 (m, 20 H), 5.73 (d, 1 H, $J_{1,2}$ 6.0, H-1), 5.62 (t, 1 H, *J* 6.7, 7.4, H-3′), 5.25–5.10 (m, 4 H, H-2, H-4, H-2′, H-4′), 5.06 (d, 1 H, $J_{1',2'}$ 4.6, H-1′), 4.45–4.23 (m, 4 H, H-3, H-6, H-5), 4.13 (dd, 1 H, $J_{4',5'}$ 3.0, $J_{5'a,5'b}$ 12.6, H-5′a), 3.73 (dd, 1 H, H-5′b, $J_{4',5'b}$ 6.5), 2.50 (m, 2 H), 2.14, 2.11 (2 × s, 2 × 3 H), 1.18 (t, 3 H, *J* 7.4 Hz); FABMS (*m*/*z*): 879 [M + Na], 795, 663, 647, 445, 105 (base); Anal. Calcd for $C_{45}H_{44}O_{15}S{\cdot}0.5H_2O$: C, 62.42; H, 5.24. Found: C, 62.64; H, 5.16.

Diosgenyl [2,3,4-tri-O-*benzoyl-β*-D-*xylopyranosyl*-*(1→3)*-*2*-O-*benzoyl*-*4,6*-O-*acetyl-β*-D-*glucopyranosyl]*-*(1→4)*-*[(2,3,4-tri*-O-*acetyl*-*α*-L-*rhamnopyranosyl)]*-*(1→2)*-*6*-O-*benzoyl-3*-O-*pivaloyl-β*-D-*glucopyranoside* (**28**).—To a suspension of **27** (124 mg, 0.145 mmol), **11** (48 mg, 0.046 mmol) and 4 Å MS (100 mg) in dry CH_2Cl_2 (2 mL) at −20 °C under Ar, was added NIS (39 mg, 0.17 mmol), followed by immediate addition of a solution of AgOTf (17 mg, 0.066 mmol) in dry PhMe (0.5 mL). After being stirred for 1 h, the mixture was quenched with NEt_3, then filtered, and concentrated. Chromatography of the residue on a silica gel column (3:1 to 1:1 petroleum ether–EtOAc) afforded **28** (56 mg, 66%) and recovered **11** (12 mg, 25%): $[\alpha]_D^{29}$ −17.9° (*c* 0.55, $CHCl_3$); R_f 0.20 (3:1 petroleum ether–EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.10–7.05 (m, 25 H), 5.61 (t, 1 H, *J* 7.0), 5.37 (d, 1 H, *J* 3.7, H-6), 2.08, 2.07, 2.05, 1.99, 1.94 (each s, each 3 H), 1.62, 1.24 (each s, each 3 H), 1.13 (d, 3 H, *J* 6.1), 1.05 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 176.38, 170.55, 169.88, 169.53, 169.47, 166.02, 165.52, 165.20, 164.99, 164.66, 142.10, 133.35, 132.80, 129.81, 129.63, 129.39, 129.20, 128.87, 128.52, 128.38, 128.02, 121.83, 109.27, 100.74, 97.73, 97.11, 94.85, 80.70, 80–68 (multiple), 49.96, 42–14 (multiple).

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