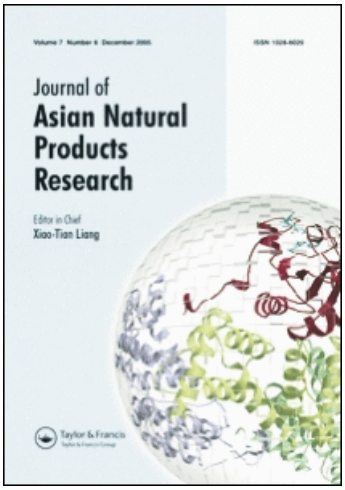

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Synthesis of three natural diosgenyl glycosides

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Synthesis of three natural diosgenyl glycosides

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Three well-known natural diosgenyl glycosides which have the same sugar chains but different sequence, ophipogonin C′, polyphillin C and prosapogenin B, were synthesised by a facile approach. A method using the levulinyl group as a protecting group to selectively mask the C_3–OH of diosgenyl 4,6-*O*-benzylidene-β-D-glucopyranoside is described.

Keywords: Ophipogonin C′; Polyphyllin C; Prosapogenin B; Levulinyl group; Glycosylation

1. Introduction

Ophipogonin C′ [1–3] (figure 1), a steroid glycoside with potent cytostatic activity against human promyelocytic leukaemia HL-60 cells, was first isolated from *Ophiopogon planiscapus*. Polyphyllin C [4–6] has been extracted from *Pairs polyphylla* but showed weak cytotoxicity. Prosapogenin B [7–12] exists widely in the plant kingdom, including many species used in traditional Chinese herbal medicines and which exhibit cardiovascular activity. Recently strong anticancer activity of prosapogenin B was reported. Structurally, these three saponins share a common aglycon and their oligosaccharide chains are made of β-D-glucopyranose and α-L-rhamnopyranose, but the sequence is different. In contrast to the difficulty in isolation of homogeneous saponins from plants, chemical synthesis would provide a realistic route to the availability of saponins. Ophipogonin C′ had been synthesised by us [13] and another group [14] using methods different from that reported herein, but to the best of our knowledge there have been no reports concerning the synthesis of polyphyllin C and prosapogenin B.

2. Results and discussion

Using thioglycoside as donor and NIS–TMSOTf as promoter, protected diosgenyl glycoside **4** was produced [15] (scheme 1). Hydrolysis of **4** with 1 M sodium methoxide in methanol

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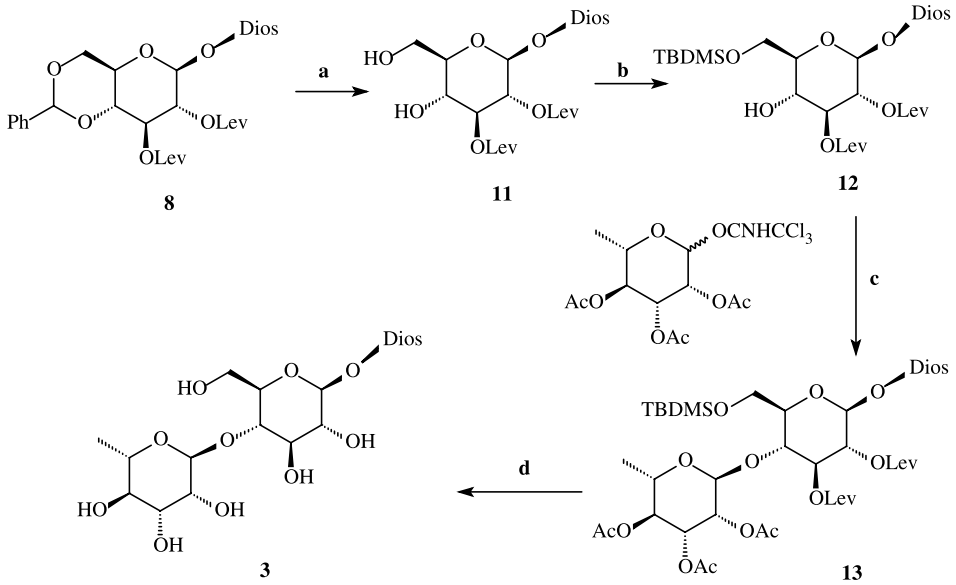
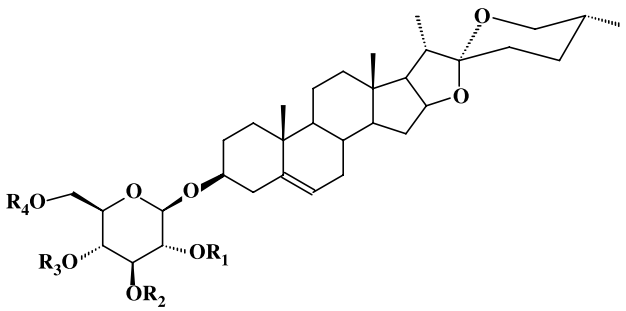


Figure 1. Structure of ophipogonin C′ (**1**), polyphillin C (**2**) and prosapogenin B (**3**).

under reflux gave a glycoside, trillin **5** [16]. Treatment of **5** with benzaldehyde dimethyl acetal and A catalytic amount of *p*-toluenesulfonic acid monohydrate in DMF furnished diosgenyl 4,6-*O*-benzylidene-β-D-glucopyranoside in 87% yield. Though it was difficult to selectively mask one of the hydroxyl groups of the 2,3-diol of a D-glucopyranose [14], the Lev group was introduced by reaction of diosgenyl 4, 6-*O*-benzylidene-β-D-glucopyranoside with levulinic acid and DCC in the presence of a catalytic amount of DMAP, and afforded **6** (73%); at the same time **7** (12%) and **8** (8%) were provided. Glycosylation of ethyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside with **6** and **7** under the promotion of NIS–TMSOTf gave **9** and **10** in yields of 97% and 95%, respectively. The two diosgenyl disaccharides were

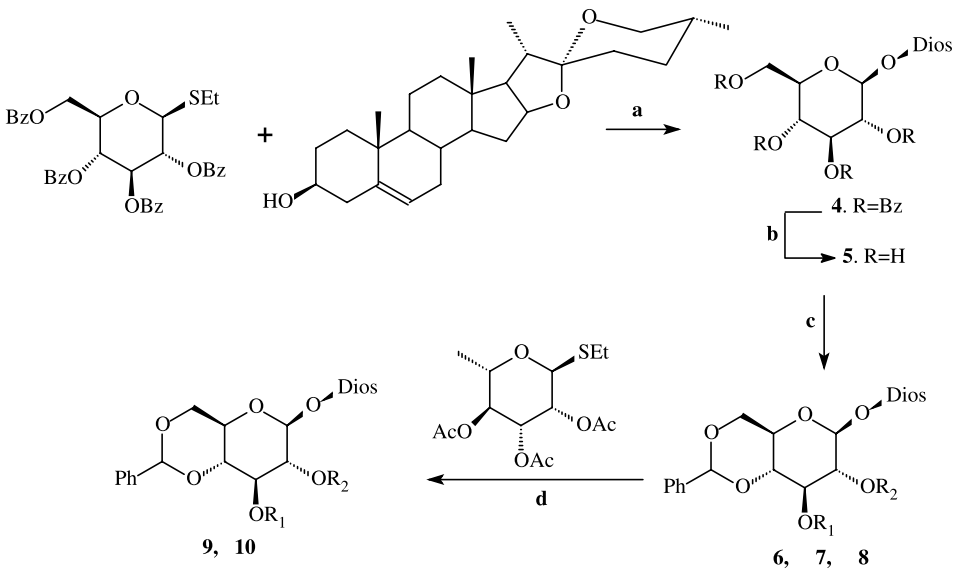


1.: R_1 = α-L-rhamnopyranosyl, $R_2 = R_3 = R_4 = H$
2.: R_2 = α-L-rhamnopyranosyl, $R_1 = R_3 = R_4 = H$
3.: R_3 = α-L-rhamnopyranosyl, $R_1 = R_2 = R_4 = H$

Scheme 1. Synthesis of ophipogonin C′ (**1**) and polyphillin C (**2**). Reagents and conditions: a, NIS–TMSOTf, −15°C 94%. b, 1 M NaOMe in MeOH, reflux, 92%. c, (i) benzaldehyde dimethyl acetal, *p*-toluenesulfonic acid monohydrate, DMF 50°C under aspirator pressure; (ii) levulinic acid, DCC, DMAP, 73% for **6**; 12% for**7**; 8% for **8**. d, NIS–TMSOTf, −30°C 97% for **6** and 95% for **7**. e, (i) 80% HOAc, 70°C; (ii) MeONa/MeOH, 87% for **1** and 89% for **2**.

transformed into corresponding diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1 → 2)-3-*O*-levulinyl-β-D-glucopyranoside (**9a**) and diosgenyl 2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl-(1 → 3)-2-*O*-levulinyl-β-D-glucopyranoside (**10a**) in the presence of 80% HOAc at 70°C. Treatment of these two intermediates with sodium methoxide, followed by neutralisation with Dwex-50W (H^+) ion-exchange resin gave phipogonin C′ (**1**) and polyphyllin C (**2**) in the yields of 87% and 89%, respectively.

With compound **8** in hand, **11** was obtained in a yield of 81% in the presence of 80% acetic acid (scheme 2). Treatment **11** with TBDMSiCl and imidazole furnished **12** in a yield of 94%. Glycosylation of **12** with tri-*O*-acetyl-L-rhamnopyranosyl trichloroacetimidate under the promotion of $BF_3{\cdot}Et_2O$ at −40°C provided protected diosgenyl disaccharide, **13**, in yield



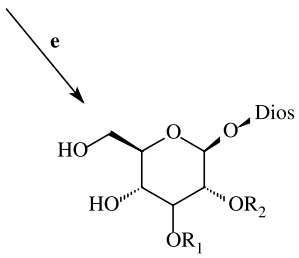
9. R_1=Lev, R_2=2,3,4-tri-O-acetyl-a-L-rhamnopyranosyl

10. R_1=2,3,4-tri-O-acetyl-a-Lrhamnopyranosyl, R_2=Lev

6. R_1=Lev, R_2=H

7. R_1=H, R_2=Lev

8. R_1=R_2=Lev



9(a), 10(a), 1, 2

9(a). R_1=Lev, R_2=2,3,4-tri-O-acetyl-a-L-rhamnopyranosyl

10(a). R_1=2,3,4-tri-O-acetyl-a-Lrhamnopyranosyl, R_2=Lev

1. R_1=H, R_2=a-L-rhamnopyranosyl

2. R_1= a-L-rhamnopyranosyl, R_2=H

Scheme 2. Synthesis of prosapogenin B. Reagents and conditions: a, 80% HOAc, 70°C, 81%. b. TBDMSiCl, imidazole, DMAP, DMF, 94%. c, $BF_3{\cdot}Et_2O$, CH_2Cl_2, −40°C under N_2, 75%. d, (i) 80% HOAc, 70°C, 95%; (ii) MeONa/MeOH, 92%.

of 75%. In the presence of 80% HOAc, THE TBDMS group of **13** was removed within 30 min. On Removal of all the acyl groups with 1 M sodium methoxide, prosapogenin B (**3**) was obtained in yield of 92%.

3. Experimental

3.1 General experimental procedures

Optical rotations were determined at 25°C with a Perkin–Elmer model 241MC automatic polarimeter. Melting points were determined with a 'Yanaco' apparatus. NMR spectra were recorded with Mercury spectrometers. Chemical shifts are referenced to the NMR solvents. Mass spectra were recorded with a VG AutoSpec Ultima-TOF mass spectrometer or a ZAB-2F spectrometer. Thin-layer chromatography was performed on Silica Gel HF_{254} (Qingdao) with detection by charring with 10% (v/v) H_2SO_4 in EtOH. Column chromatography was conducted by elution of a column of silica gel (100–200 mesh, Qingdao), solutions were concentrated at ≤ 60°C under diminished pressure.

3.2 Compounds 6, 7 and 8

To a solution of **5** [10] (1.0 g, 1.7 mmol) and benzaldehyde dimethyl acetal (0.3 ml, 2.0 mmol) in dry DMF (30 ml), *p*-toluene-sulfonic acid monohydrate (50 mg) was added, the mixture was stirred at 50°C under reduced pressure for 2.5 h, then was neutralised with Et_3N (1.5 ml). On removal of most of the solvent at 70°C under reduced pressure, the residue was diluted with EtOAc (100 ml), then washed with brine and dried over anhydrous Na_2SO_4, and concentrated. Chromatography of the residue onto a silica gel column (petroleum ether/acetone = 6:1) afforded diosgenyl 4,6-*O*-benzylidene-β-D-glucopyranoside [14] (1.02 g) as white solid, yield 88%.

DCC (356 mg, 1.72 mmol) and DMAP (20 mg) in dry CH_2Cl_2 (5 ml), were added to a stirred solution of diosgenyl 4,6-*O*-benzylidene-β-D-glucopyranoside (956 mg, 1.44 mmol) and levulinic acid (200 mg, 1.72 mmol) in dry CH_2Cl_2 (15 ml). The reaction mixture became instantaneously cloudy. After stirring for 1.5 h, the precipitated urea was removed by filtration and the filtrate was diluted with CH_2Cl_2 (150 ml), which was washed with water and brine, and dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (CH_2Cl_2/EtOAc = 10:1) to give **6** 803 mg (73%). $[\alpha]_D^{25} = -88.7$ (*c* 1.0, CH_2Cl_2), $R_f = 0.64$ (CH_2Cl_2/EtOAc = 6:1), ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55–7.26 (m, 5H, aromatic), 5.48 (s, 1H, PhCH), 5.37 (brs, 1H, H-6), 5.20 (dd, 1H, J = 8.4, 9.0 Hz, H-3′), 4.56 (d, 1H, J = 7.8 Hz, H-1′), 4.52–4.09 (m, 2H, H-16, H-6_a′), 3.79 (dd, 1H, J = 10.5, 11.1 Hz, H-6_b′), 3.67–3.33 (m, 6H, H-2′, H-4′, H-5′, H-3, H-26), 2.87–2.75 (m, 2H), 2.66–2.56 (m, 2H), 2.42–2.20 (m, 4H), 2.04–2.14 (m, 16H), 2.14 (s, 3H, CH_3CO), 1.25 (s, 3H), 1.02 (s, 3H), 0.97 (d, 3H, J = 5.7 Hz), 0.78 (brs, 6H). ESI-MS: *m/z* 785.5 $(M + Na)^+$.

Compound 7 134 mg (12%). $R_f = 0.53$ (CH_2Cl_2/EtOAc = 6:1) $[\alpha]_D^{25}$ −64.6 (*c* 1.0 CH_2Cl_2), ^{1}H NMR (300 MHz, $CDCl_3$): 7.50–7.35 (m, 5H, aromatic), 5.54 (s, 1H, PhCH), 5.38 (d, J = 4.8 Hz, 1H, H-6), 4.90 (dd, 1H, J = 8.4, 8.7 Hz, H-2′), 4.64 (d, 1H, J = 7.8 Hz, H-1′), 4.44–4.36 (q, 1H, J = 7.8 Hz, H-16), 4.34 (dd, 1H, J = 4.5, 10.2 Hz, H-6_a′), 3.95 (dd, 1H, J = 8.4, 9.6 Hz, H-3′), 3.83 (t, 1H, J = 10.2 Hz, H-6_b′), 3.64 (t, 1H, J = 9.3 Hz, H-4′),

3.49–3.33 (m, 4H, H-5′, H-3, H-26), 2.83–2.79 (m, 2H), 2.64–2.58 (m, 2H), 2.28 (m, 1H), 2.18 (s, 3H, CH_3CO), 1.99–1.09 (m, 20H), 1.04 (s, 3H), 0.97 (d, 3H, $J = 7.2$ Hz), 0.78 (brs, 6H). ESI-MS: *m/z* 785.6 $(M + Na)^+$.

Compound 8 98 mg (8%). $R_f = 0.72$ (CH_2Cl_2/EtOAc = 6:1), ^{1}H NMR (300 MHz, $CDCl_3$): 7.45–7.31 (m, 5H, aromatic), 5.48 (s, 1H, PhCH), 5.37 (d, 1H, $J = 5.4$ Hz, H-6), 5.33 (t, 1H, $J = 9.6$ Hz, H-3′), 4.99 (dd, 1H, $J = 9.6, 7.8$ Hz, H-2′), 4.67 (d, 1H, $J = 7.8$ Hz, H-1′), 4.41–4.31 (m, 2H, H-16, H-6_a′), 3.80 (t, 1H, $J = 10.2$ Hz, H-6_b′), 3.67 (t, 1H, $J = 9.6$ Hz, H-4′), 3.53–3.45 (m, 3H, H-4′, H-26), 3.37 (t, 1H, $J = 10.8$ Hz, H-3), 2.82–2.50 (m, 8H), 2.28–2.20 (m, 1H), 2.17 (s, 3H, CH_3CO), 2.13 (s, 3H, CH_3CO), 2.02–1.93 (m, 3H), 1.89–1.42 (m, 15H), 1.01 (s, 3H), 0.97 (d, 3H, $J = 6.9$ Hz), 0.79 (d, 3H, $J = 4.8$ Hz),0.78 (s, 3H). ESI-MS: *m/z* 883.6 $(M + Na)^+$.

3.3 Compound 9

Ethyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (426 mg, 1.2 mmol) and **6** (756 mg, 0.99 mmol) were dissolved in dry CH_2Cl_2 (20 ml) and stirred with 4-Å molecular sieves (0.2 g) under N_2 at room temperature for 30 min, then cooled to − 30°C. NIS (273 mg, 1.2 mmol) was added followed by addition of TMSOTf (0.04 ml). After 30 min the reaction was quenched with Et_3N (2 ml) and the mixture was diluted with CH_2Cl_2 (100 ml), filtered through Celite and concentrated. The residue was applied onto a silica gel column (toluene/EtOAc = 10:1) and gave **9** as white foam. 1.0 g (97%). $R_f = 0.52$ (PE/AE = 6:1), ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.41–7.33 (m, 5H, aromatic), 5.42 (s, 1H, PhCH), 5.40–5.36 (m, 2H, H-6, H-3′), 5.24 (dd, 1H, $J = 2.4, 10.2$ Hz, H-3″), 5.11–5.04 (m, 3H, H-1″, H-2″, H-4″), 4.70 (d, 1H, $J = 7.8$ Hz, H-1′), 4.48–4.30 (m, 3H, H-16, H-6_a′, H-5″), 3.81–3.37 (m, 7H, H-6_b′, H-5′, H-4′, H-2′, H-3, H-26), 2.79–2.71 (m, 2H), 2.60–2.48 (m, 2H), 2.11 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO), 1.94 (s, 3H, CH_3CO), 1.22 (d, 3H, $J = 6.3$ Hz, H-6″), 1.02 (s, 3H), 0.98 (d, 3H, $J = 6.9$ Hz), 0.79 (d, 3H, $J = 3.9$ Hz), 0.78 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$): δ 206.36, 171.75, 169.97 (2 × C, overlap), 169.81, 139.88, 136.87, 128.92, 128.16, 126.08, 122.25, 109.26, 101.25, 99.70, 97.28, 80.77, 78.65, 75.38, 74.00, 71.21, 69.87, 68.83, 68.60, 66.83, 66.36, 66.13, 62.07, 56.44, 50.05, 41.59, 40.24, 39.72, 38.13, 37.87, 37.14, 36.85, 32.05, 31.82, 31.38, 30.28, 29.59, 29.50, 28.79, 27.79, 21.00, 20.84, 20.74, 19.26, 17.21, 17.11, 16.28, 14.50. ESI-MS: *m/z* 1057.6 $(M + Na)^+$.

3.4 Compound 1

A solution of **9** (200 mg, 0.19 mmol) in 80% HOAc (10 ml) was stirred at 70°C for 4 h. The solvent was removed under vacuum to give a residue, which was dissolved in a mixture of CH_2Cl_2/MeOH (10 ml, v/v = 1) and 1 M MeONa/MeOH (0.5 ml) was added. The solution, kept overnight at room temperature, was neutralised with Dowex-50 (H^+) resin, filtrated and concentrated. The residue was purified by silica gel column chromatography (CH_2Cl_2/-MeOH = 10:1) to give ophipogonin C′ (**1**) 118 mg (87%) as a white solid. Mp: 212–214°C, (lit. [1], 211–213°C), $[\alpha]_D^{25}$ −93.5 (*c* 1.0, pyridine) [lit. [1], $[\alpha]_D^{25}$ −94.3 (*c* 0.72, pyridine)]. ^{1}H NMR (400 MHz, pyridine-d_5): δ 6.37 (brs, 1H), 5.29 (brs, 1H), 5.03–4.98 (m, 2H), 4.79 (s, 1H), 4.63–4.48 (m, 3H), 4.36–4.16 (m, 4H), 3.89 (m, 2H), 3.59–3.48 (m, 2H), 2.73 (m, 1H), 2.13–2.11 (m, 1H), 2.03–1.36 (m, 15H), 1.13 (d, 3H, $J = 6,8$ Hz), 1.04 (s, 3H), 0.81 (s, 3H), 0.68 (d, 3H, $J = 4.4$ Hz). ^{13}C NMR (400 MHz, pyridine-d_5): δ 140.84, 121.73, 109.24, 102.04, 100.34, 81.09, 79.65, 78.27, 77.90, 77.79, 74.15, 72.84, 72.60, 71.79, 69.48, 66.84,

62.88, 62.65, 56.62, 50.27, 41.96, 40.45, 39.85, 38.97, 37.50, 37.14, 32.30, 32.21, 31.82, 31.68, 30.59, 30.18, 29.26, 21.09, 19.41, 18.67, 17.32, 16.33, 15.03. FAB-MS: *m/z* 745 $(M + Na)^+$. HRFAB-MS: *m/z* 745.4108 $(M + Na)^+$ (calcd for $C_{39}H_{62}O_{12}Na$, 745.4138).

3.5 Compound 10a

Ethyl 2,3,4-tri-*O*-acetyl-1-thio-α-L-rhamnopyranoside (427 mg, 1.2 mmol) and **7** (764 mg, 1.0 mmol) were dissolved in dry CH_2Cl_2 (20 ml) and stirred with 4-Å molecular sieves (0.3 g) under N_2 at room temperature for 30 min, then cooled to − 30°C. NIS (275 mg, 1.2 mmol) was added followed by addition of TMSOTf (0.04 ml). After 30 min the reaction was quenched with Et_3N (2 ml) and filtered through Celite. The filtrate was diluted with CH_2Cl_2 (100 ml) washed sequentially with saturated aqueous of $Na_2S_2O_3$, dried over anhydrous Na_2SO_4, and concentrated. The residue was dissolved in 80% HOAc (10 ml) and stirred at 70°C for 6 h. The solvent was removed under vacuum to give a residue. The residue was applied onto a silica gel column (petroleum ether/acetone = 4:1) giving **10a** as white foam (751 mg, 79% overall two steps), $R_f = 0.41$ (petroleum ether/acetone = 2:1), ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36 (d, 1H, $J = 4.5$ Hz, H-6), 5.21–5.17 (m, 2H), 5.07 (t, 1H, $J = 10.2$ Hz), 4.90 (m, 2H), 4.54 (d, 1H, $J = 7.8$ Hz, H-1′), 4.39 (m, 1H, H-16), 4.14–4.09 (m, 1H, H-5″), 3.93–3.88 (dd, 1H, $J = 11.7$, 3.9 Hz, H-6′$_a$), 3.82–3.76 (dd, 1H, $J = 11.7$, 6.0 Hz, H-6′$_b$), 3.61–3.58 (m, 2H, H-5′and H-3′), 3.48–3.33 (m, 4H, H-3, H-26, H-4′), 2.82 (m, 2H, $COCH_2CH_2CO$), 2.60 (m, 2H, $COCH_2CH_2CO$), 2.16 (s, 3H, $COCH_3$), 2.13 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 1.97 (s, 3H, $COCH_3$), 1.24 (d, 3H, $J = 6.3$ Hz, H-6″), 1.01 (s, 3H), 0.97 (d, 3H, $J = 6.9$ Hz), 0.79 (d, 3H, $J = 5.4$ Hz), 0.77 (s, 3H). ESI-MS: *m/z* 969.6 $(M + Na)^+$.

3.6 Compound 2

To the solution of **10a**, 52 mg (0.05 mmol) in a mixture of CH_2Cl_2/MeOH (5 ml, v/v = 1:1), 1 M MeONa/MeOH (0.5 ml) was added. The solution was stirred overnight at room temperature, then neutralised with Dowex-50 (H^+) resin, filtrated and concentrated. The residue was purified onto a silica gel column (CH_2Cl_2/MeOH = 10:1), affording polyphyllin C (**2**) as white foam (33 mg, 89%). Mp: 189–192°C (lit. [4], 185–190°C), $[\alpha]_D^{25}$ − 98.5 (*c* 1.5, pyridine), (lit. [4], $[\alpha]_D^{25}$ − 102 (*c* 0.6, pyridine)). ^{1}H NMR (400 MHz, pyridine-d_5): δ 6.36 (s, 1H), 5.27 (d, $J = 4.4$ Hz, 1H, H-6), 5.13–5.09 (m, 1H), 4.93 (d, $J = 8.0$ Hz, 1H, H-1′), 4.81 (d, $J = 2.0$ Hz, 1H), 4.62–4.59 (dd, $J = 3.2$, 9.2 Hz, 1H), 4.53–4.34 (m, 5H), 4.27 (t, $J = 9.2$ Hz, 1H), 3.90–3.83 (m, 2H), 3.58 (brs, 1H), 3.55 (m, 1H), 3.47 (m, 1H), 2.64 (m, 1H), 2.33 (m, 1H), 2.05–1.99 (m, 2H), 1.73 (d, 3H, $J = 6.4$ Hz, H-6″), 1.12 (d, $J = 6.8$ Hz, 3H), 0.84 (s, 3H), 0.80 (s, 3H), 0.67 (d, 3H, $J = 4.8$ Hz,). ^{13}C NMR (400 MHz, pyridine-d_5): δ 140.67, 121.75, 109.21, 102.84, 102.21, 83.22, 81.04, 78.37, 78.02, 75.75, 74.15, 72.71, 72.59, 69.82, 69.48, 66.79, 62.79, 62.41, 56.55, 50.14, 41.90, 40.38, 39.79, 39.07, 37.34, 36.95, 32.18 (2 × C, overlap), 31.74, 31.55, 30.55, 30.08, 29.21, 21.04, 19.33, 18.71, 17.31, 16.34, 15.03. FAB-MS: *m/z* 745 $(M + Na)^+$. HRFAB-MS: *m/z* 745.4171 $(M + Na)^+$ (calcd for $C_{39}H_{62}O_{12}Na$, 745.4138).

3.7 Compound 12

A solution of **8** (1.2 g, 1.39 mmol) in 80% HOAc (20 ml) was stirred at 70°C for 4 h. The solvent was removed under vacuum to give a residue, which was purified onto a silica gel

column (petroleum ether/acetone = 4:1), and afforded **11** as white foam (874 mg, 81%). To a solution of **11** (874 mg, 1.1 mmol) in dry DMF (15 ml), DMAP (50 mg), imidazole (307 mg, 4.5 mmol) and TBDMSiCl (187 mg, 1.2 mmol) were added. The mixture, stirred at room temperature for 45 min, was then diluted with CH_2Cl_2 (150 ml), washed with brine, dried over Na_2SO_4, and concentrated. Chromatography of the residue on silica gel column (petroleum ether/acetone = 6:1) gave **12** as a white solid (919 mg, 94%). $R_f = 0.72$ (petroleum ether/acetone = 3:1), ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36 (d, 1H, $J = 5.1$ Hz, H-6), 5.09 (dd, 1H, $J = 9.9$, 9.0 Hz, H-3′), 4.87 (dd, 1H, $J = 9.9$, 8.1 Hz, H-2′), 4.55 (d, 1H, $J = 8.1$ Hz, H-1′), 4.40 (m, 1H), 3.88 (d, 2H, $J = 5.1$ Hz, H-6′), 3.67 (t, 1H, $J = 9.3$ Hz, H-4′), 3.49–3.31 (m, 4H), 2.81–2.68 (m, 4H), 2.68–2.45 (m, 4H), 2.16 (s, 6H, CH_3CO), 1.04 (s, 3H), 0.97 (d, 3H, $J = 6.6$ Hz,), 0.89 (s, 9H), 0.79 (d, 3H, $J = 5.7$ Hz,), 0.77 (s, 3H), 0.07 (s, 6H). ESI-MS: *m/z* 909.7 $(M + Na)^+$.

3.8 Compound 13

To a solution of **12** (100 mg, 0.11 mmol) and 4-Å molecular sieves (0.3 g) at −40°C under N_2, was added $BF_3{\cdot}Et_2O$ (0.02 ml), followed by a solution of tri-*O*-acetyl-L-rhamnopyranosyl trichloroacetimidate (97 mg, 0.22 mmol) in CH_2Cl_2 (4 ml). The mixture was stirred at −40°C for 3 h, then quenched with 0.5 ml Et_3N, filtered, and concentrated. The residue was chromatographed on a silica gel column (petroleum ether/EtOAc = 6:1) to afford **13** (94 mg, 75%) as white foam. $R_f = 0.35$ (petroleum ether: EtOAc = 2:1), ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.36 (d, 1H, $J = 4.5$ Hz, H-6), 5.23–5.13 (m, 3H, H-3′, H-2″, H-3″), 5.01 (t, 1H, $J = 9.3$ Hz, H-4″), 4.85 (brs, 1H, H-1″), 4.78 (dd, 1H, $J = 7.5$, 9.3 Hz, H-2′), 4.52 (d, 1H, $J = 7.5$ Hz, H-1′), 4.42 (m, 1H, H-16), 3.86–3.80 (m, 4H, H-4′, H-6′, H-5′), 3.45–3.31 (m, 4H, H-3, H-26, H-5′), 2.80–2.55 (m, 8H, 2 × $COCH_2CH_2CO$), 2.17 (brs, 6H, 2 × $COCH_3$), 2.11 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.21 (s, 3H), 1.16 (d, 3H, $J = 6.0$ Hz, H-6″), 1.00 (s, 3H), 0.98 (d, 3H, $J = 6.6$ Hz), 0.88 (d, 3H), 0.85 (s, 9H, CMe_3), 0.80 (d, $J = 5.1$ Hz, 3H), 0.78 (s, 3H), 0.04 (d, 10.2 Hz, 6H, $SiMe_2$). ESI-MS: *m/z* 1181.6 $(M + Na)^+$.

3.9 Compound 3

A solution of **13** (90 mg, 0.08 mmol) in 80% HOAc (5 ml) was stirred at 70°C for 2 h. The solvent was removed under vacuum to give a residue, which was dissolved in a mixture of CH_2Cl_2/MeOH (5 ml, v/v = 1:1) and 1 M MeONa/MeOH (0.5 ml) was added. The solution, kept overnight at room temperature, was neutralised with Dowex-50 (H^+) resin, filtered and concentrated. The residue was purified by silica gel column chromatography (CH_2Cl_2/-MeOH = 10:1) to give prosapogenin B (**3**) (32 mg) as a white solid. Mp: 230–233°C, (lit. [7], 230–231°C), $[\alpha]_D^{25}$ −92.40 (*c* 1.0, pyridine), [lit. [7], $[\alpha]_D^{25}$ −89 (*c* 0.93, pyridine)]. ^{1}H NMR (400 MHz, pyridine-d_5): δ 5.89 (s, 1H), 5.29 (d, 1H, $J = 4.0$ Hz, H-6), 5.01 (m, 1H), 4.93 (d, 1H, $J = 7.6$ Hz, H-1′), 4.69 (brs, 1H), 4.58–4.43 (m, 3H), 4.34 (t, 1H, $J = 9.6$ Hz), 4.26–4.19 (m, 2H), 4.13–4.10 (dd, 1H), 3.97 (t, 1H, $J = 8.0$ Hz), 3.83 (m, 1H), 3.72 (d, 1H $J = 10.2$ Hz), 3.55 (brs, 1H), 3.45 (m, 1H), 2.70 (m, 1H), 2.43 (m, 1H), 2.07–1.92 (m, 4H), 1.72 (d, 3H, $J = 6.4$ Hz, H-6″), 1.13 (d, 3H, $J = 7.2$ Hz), 0.89 (s, 3H), 0.81 (s, 3H), 0.67 (d, 3H, $J = 4.2$ Hz). ^{13}C NMR (400 MHz, pyridine-d_5): δ 140.85, 121.73, 109.24, 102.68, 102.44, 81.07, 78.25, 78.19, 75.13, 76.70, 75.53, 74.00, 72.82, 72.63, 70.35, 66.84, 62.87,

61.50, 56.53, 50.25, 41.95, 40.44, 39.85, 39.28, 37.42, 37.03, 32.24, 32.17, 31.79, 31.62, 30.58, 30.18, 29.24, 21.10, 19.38, 18.54, 17.31, 16.35, 15.02 FAB-MS: *m/z* 745 $(M + Na)^+$. HRFAB-MS: *m/z* 745.4163 $(M + Na)^+$ (calcd for $C_{39}H_{62}O_{12}Na$, 745.4138).

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