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Facile synthesis of three bidesmosidic oleanolic acid saponins with strong inhibitory activity on pancreatic lipase

Tiantian Guo, Qingchao Liu, Peng Wang, Lei Zhang, Wei Zhang, Yingxia Li *

Key Laboratory of Marine Drugs, The Ministry of Education of China, School of Medicine and Pharmacy, Ocean University of China, Qingdao 266003, China

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ABSTRACT

The first synthesis of scabiosaponins E (**1**), F (**2**), and G (**3**), three new oleanolic acid saponins with strong inhibitory activity on pancreatic lipase isolated from the Chinese traditional medicinal herb *Scabiosa tschiliensis*, was efficiently achieved in an one-pot strategy under the combined use of glycosyl trichloroacetimidates and *p*-toluene 1-thioglycosides (STol) as donors.

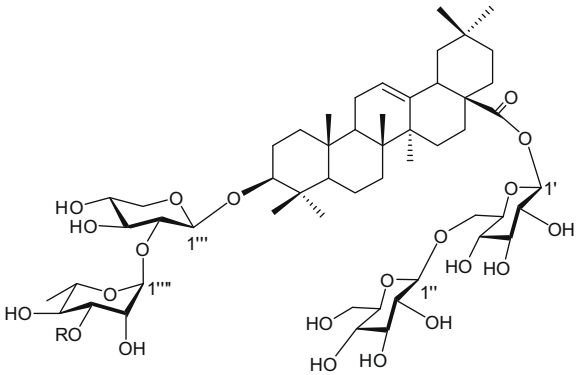
1. Introduction

Saponins, glycosides of steroids and triterpenes, which are widely distributed in plants and in some marine organisms,[1,2] possess a broad spectrum of interesting biomedical activities, including antitumor, anti-HIV, anti-inflammatory, antifungal, ion channel-blocking, and immune-stimulating activities.[3–5] Besides, it has been reported that oleanane-type, lupine-type, and dammarane-type triterpenoid saponins exhibit inhibitory activity upon pancreatic lipase and prevent the increase of body weight because of a high-fat diet.[6–8] Obesity is widely recognized as a major public health problem, which can result in cardiovascular-related diseases such as type II diabetes, hypertension, hyperlipidemia, and coronary heart disease (CHD).[9] The application of a pancreatic lipase inhibitor has been considered as an effective therapeutic means for diet-induced obesity in humans. Orlistat, first approved in 1998, is a pancreatic lipase inhibitor that suppresses the development of obesity and hyperlipidemia.[10,11]

Scabiosaponins E–G (**1–3**), three new bidesmosidic oleanolic acid saponins (Fig. 1), were isolated from *Sacbiosa tschiliensis* Grun. (Dipsacaceae), a perennial herb used for the treatment of headache, fever, cough, and jaundice in Inner Mongolia, and they showed remarkable inhibition activity against pancreatic lipase.[12] The formidable task of isolating these compounds turns out to be a great obstacle for further pharmacological research, so it is worthwhile to exploit an efficient approach to afford this kind of saponin for further SAR investigation. Herein we report the first, convenient synthesis of the three bidesmosidic oleanolic acid saponins, which overcomes the problem of the scarceness of this type of saponins in nature.

2. Results and discussion

So far few facile synthetic approaches toward bidesmosidic oleanane-type saponins bearing the distinctive disaccharide, the α-L-



Scabiosaponin E (1): R = Xyl

Scabiosaponin F (2): R = Glc

Scabiosaponin G (3): R = Glc (1 → 4) Glc

Figure 1. Structures of scabiosaponins E–G (**1–3**).

* Corresponding author. Tel.: +86 532 82032150; fax: +86 532 82033054.
E-mail address: liyx417@ouc.edu.cn (Y. Li).

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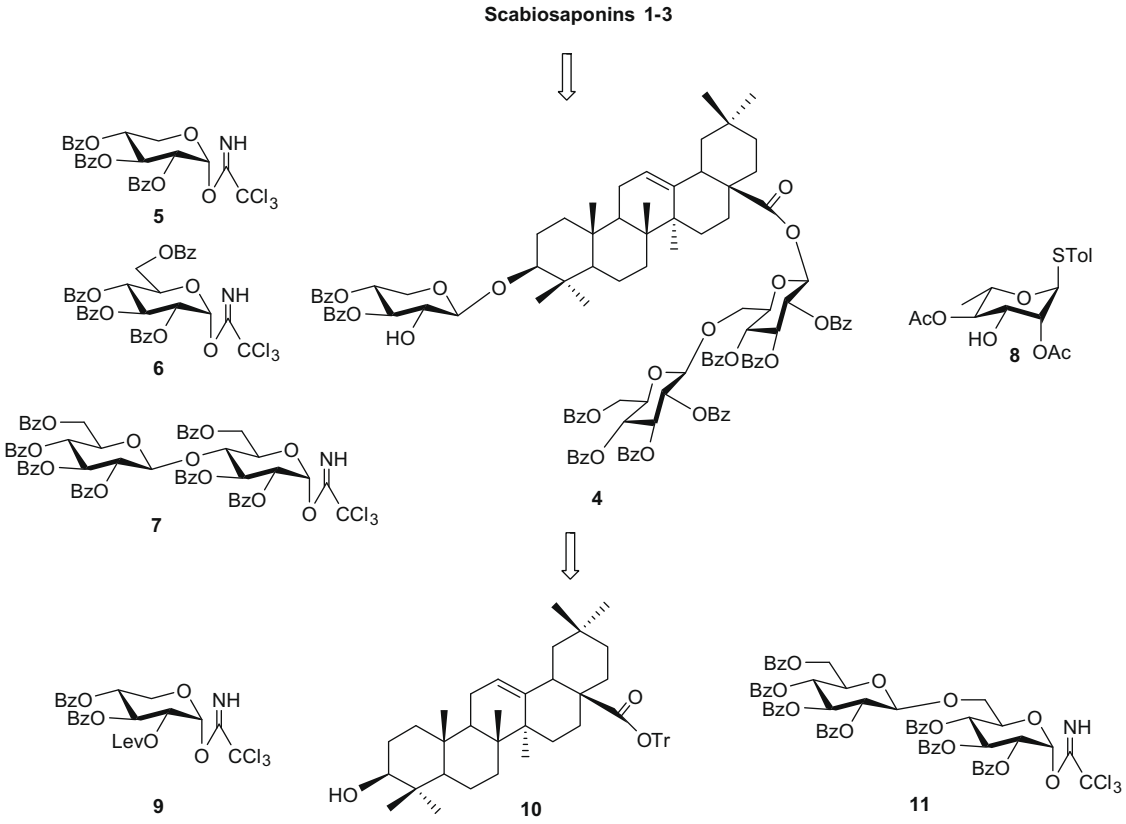
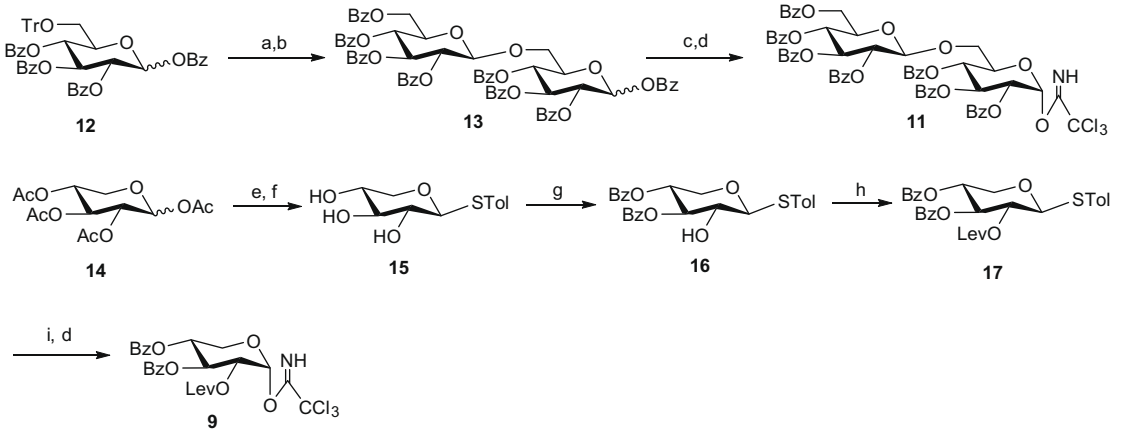


Scheme 1. Retrosynthesis of scabiosaponins **1–3**.

rhamnopyranosyl-(1→2)-β-D-xylopyranosyl moiety, have been reported.[13] Fortunately, the successful synthesis of many natural saponins has provided us with a gratifying experience,[14] especially since the application of a one-pot protocol makes the synthetic route more concise and efficient.[15] The one-pot approach with the combined use of glycosyl trichloroacetimidates and thioglycosides was developed by Takahashi et al.,[16] and then Yu and coworkers applied it to the synthesis of natural saponins.[15g,15i] In this approach, thioglycosides employed by them were either ethyl 1-thioglycosides or phenyl 1-thioglycosides; herein we decided to adopt the one-pot sequential glycosylation strategy employing the *p*-toluene 1-thioglycosides to complete the assembly of the 3- and 28-glycosyl residues in the target compounds. Such an approach would allow us to rapidly obtain a variety of structural analogues of bidesmosidic oleanolic acid saponin.

As shown in Scheme 1, saponins **1–3** were retrosynthetically disconnected into three glycosyl trichloroacetimidate donors **5**,[17] **6**,[18] and **7**,[19] a thioglycoside acceptor **8**,[20] and a triterpene saponin acceptor **4**. The latter could be assembled from three readily accessible building blocks **9**, **10**[15h], and **11** through two successive glycosylation steps in a one-pot reaction.

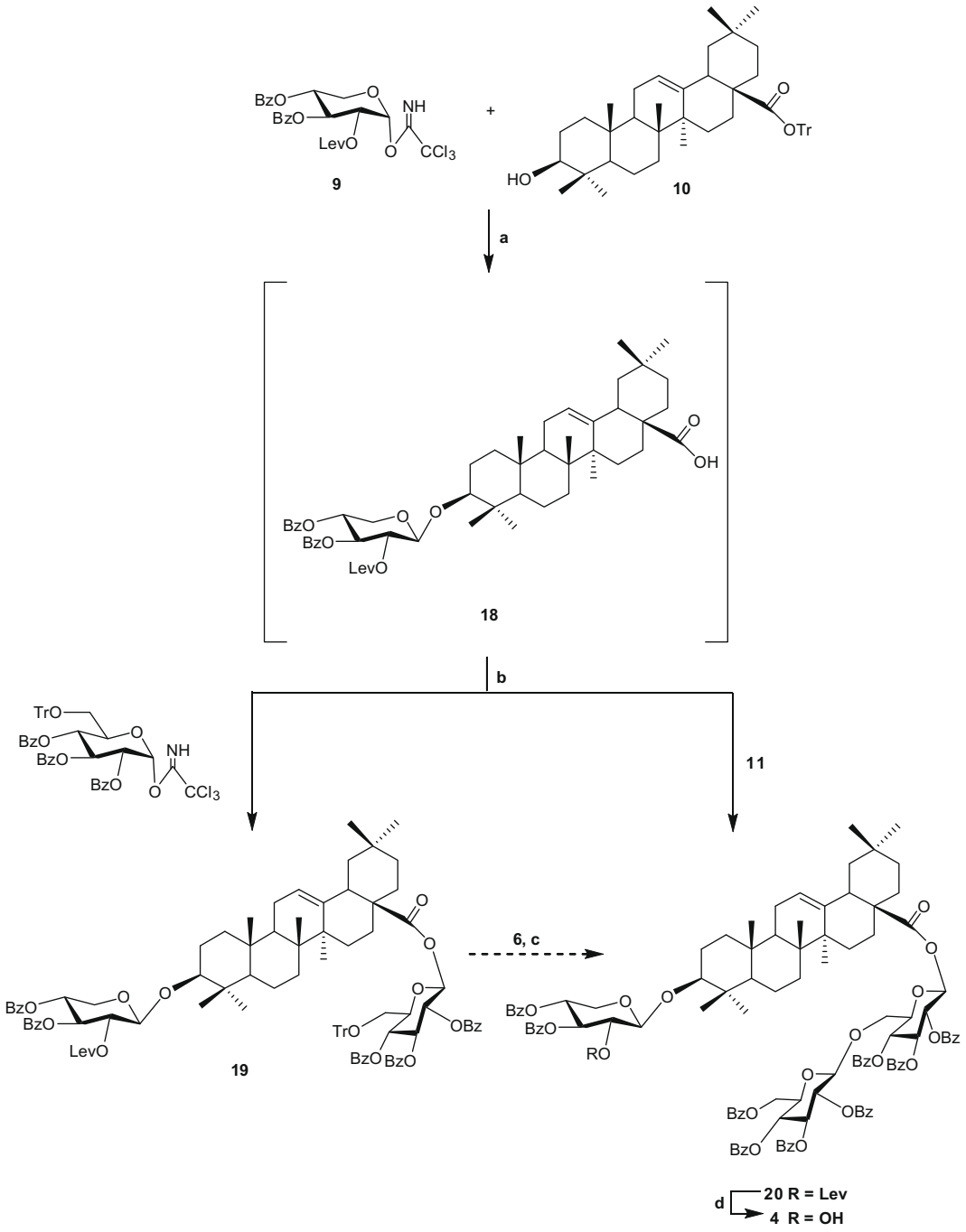
Disaccharide trichloroacetimidate donor **11** was readily prepared in a straightforward manner as depicted in Scheme 2. Herein, 1,2,3,4-tetra-*O*-benzoyl-6-*O*-trityl-α,β-D-glucopyranoside (**12**)[15h] was



Scheme 2. Reagents and conditions: (a) $FeCl_3·6H_2O$, CH_2Cl_2, 88%; (b) **6**, TMSOTf (0.1 equiv), CH_2Cl_2, 4 Å MS, 0 °C, 94%; (c) CH_3NH_2–$HOCH_3$, THF, 94%; (d) $CNCCl_3$, DBU, CH_2Cl_2, 87% (for **11**); 79% (for **9**); (e) *p*-thiocresol, $BF_3·Et_2O$, CH_2Cl_2, 0 °C→ rt, 85%; (f) MeONa, MeOH, rt, 99%; (g) Bu_2SnO, toluene, reflux; then BzCl (2.0 equiv), 0 °C, 94%; (h) levulinic acid, DCC, DMAP, CH_2Cl_2, rt, 85%; (i) NBS, 9:1 CH_3COCH_3–H_2O, −20 °C, 78%.

treated with $FeCl_3 \cdot 6H_2O$ in CH_2Cl_2 at room temperature,[21] to afford 1,2,3,4-tetra-*O*-benzoyl-D-glucopyranoside, which was coupled with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl trichloroacetimidate (**6**) in anhydrous CH_2Cl_2 in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) to provide the corresponding β-selective disaccharide **13** in 94% yield. Treatment of **13** with $MeNH_2$ in CH_3OH, followed by trichloroacetonitrile (Cl_3CCN) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dry CH_2Cl_2, afforded the corresponding imidate **11** in a yield of 87% over two steps. The ^1H NMR data for compound **11** were in good agreement with those from the natural product.[19] The product's integrity was further substantiated by the observation of a single spot by TLC analysis.

The preparation of donor **9** began with acetyl-protected xyloside **14**.[22] The latter was treated with *p*-thiocresol and $BF_3 \cdot Et_2O$ in CH_2Cl_2 to introduce the 4-tolylthio group,[23] and subsequently the acetyl groups were deprotected by treatment with a catalytic amount of sodium methoxide in methanol to afford *p*-tolyl 1-thio-β-D-xylopyranoside (**15**)[24] in 84% overall yield. Typically, the regioselectivity is difficult to control due to the similar reactivity of the secondary 2-, 3- and 4-hydroxyl groups in xylose. Although a series of useful techniques for access to differentially protected xylose building blocks have been developed, the laborious protecting manipulation results in notoriously low yields.[14e,f,25] We completed the synthesis of compound **16** with satisfactory regioselectivity achieved by employing a dibutyltin oxide-mediated reaction[26] that gave no traces of monosubstituted, 2,3- or 2,4-disubstituted byproducts. In the ^1H NMR spectrum of **16**, the H-3 and H-4 signals all appeared downfield at δ 5.56 and 5.27, which

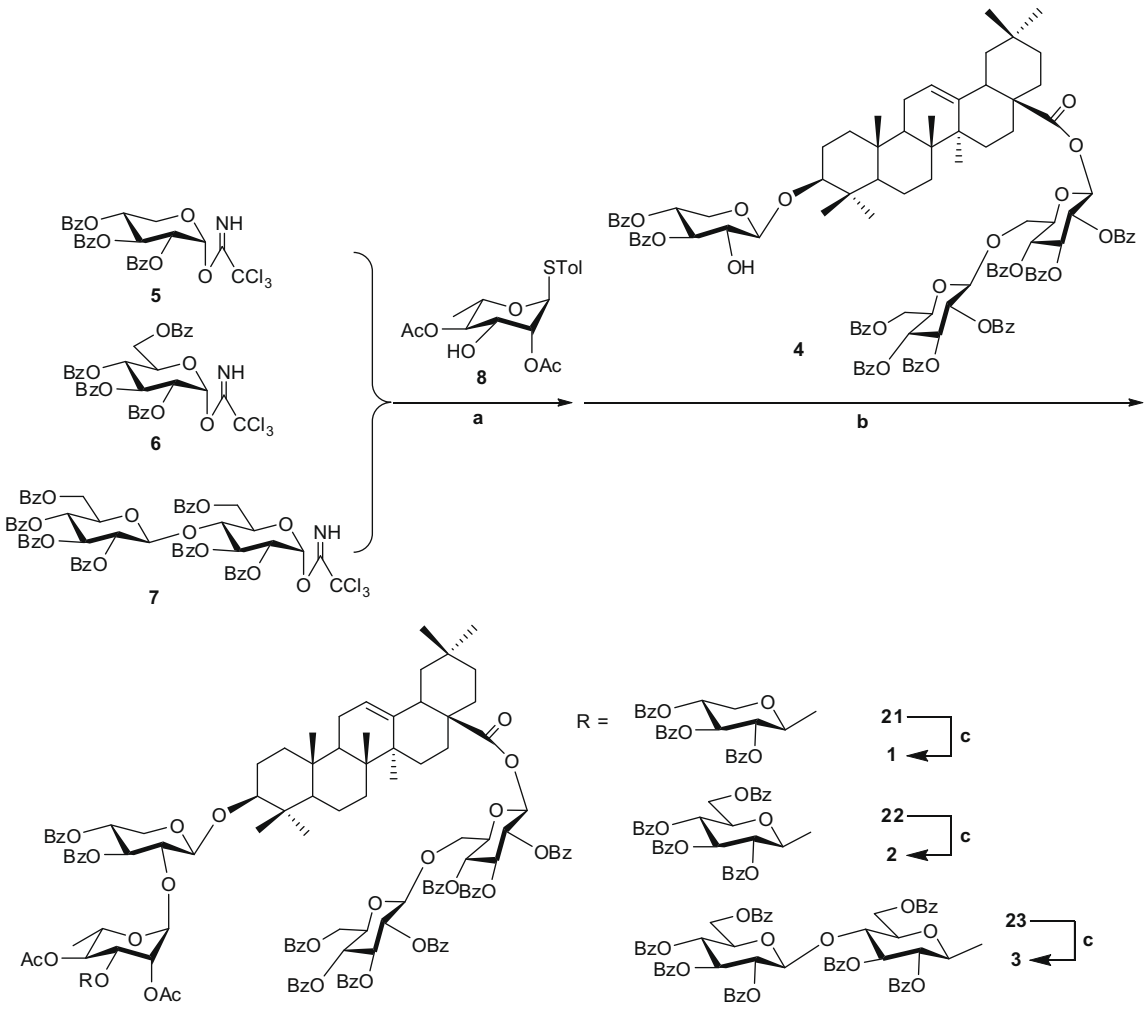


Scheme 3. Reagents and conditions: (a) TMSOTf (0.3 equiv), CH_2Cl_2, 4 Å MS, −78 °C→rt; (b) **11** (1.6 equiv), CH_2Cl_2, 4 Å MS, 0 °C, 66% (overall yields based on **10**); (c) catalyst (1.5 equiv), CH_2Cl_2, 4 Å MS; (d) $NH_2NH_2 \cdot HOAc$, 1:1CH_2Cl_2–CH_3OH, 83%.

clearly proved the selectivity. As it was desirable to have a distinguishable 2-O-protecting group that would allow selective cleavage in the presence of an acyl-protecting group and at the same time ensure stereoselectivity in forming the 1,2-*trans* glycosidic linkages, the levulinoyl (Lev) group[27] was chosen. The Lev group was introduced by treatment of **16** with levulinic acid and DCC–DMAP to prepare **17** in 85% yield. The anomeric 4-tolylthio group of **17** was removed with NBS in 9:1 acetone–H_2O in 15 min to obtain the hemiacetal, which was then converted into the corresponding trichloroacetimidate donor **9** in satisfactory yield.

The key intermediate **4** was efficiently prepared as shown in Scheme 3. The initial focus of this work was to employ three successive glycosylation steps based on Yu's methodology[15h] for the synthesis of **4**. Herein, condensation of oleanolic ester **10** with trichloroacetimidate **9** under the promotion of TMSOTf in −78 °C for 30 min provided the desired product, which was then transformed into compound **18** by warming to ambient temperature for 30 min. Following addition of a CH_2Cl_2 solution of 2,3,4-tri-*O*-benzoyl-6-*O*-trityl-α-D-glucopyranosyl trichloroacetimidate to the above mixture at 0 °C, the glycoside **19** was obtained. After the next trichloroacetimidate **6** was subsequently added to the reaction mixture in the presence of TMSOTf and *N*-iodosuccinimide (NIS) at 0 °C, a complicated mixture of products was unfortunately observed by TLC. The spots were close to each other, and were inseparable by column chromatography. To address the problem, we then turned our attention to the reaction conditions, including alteration of the amount of reagents, temperature, and catalysts ($BF_3{\cdot}Et_2O$ and TfOH). We also tried other known donors, such as 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate,[28] *p*-tolyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside,[29] and *p*-tolyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-glucopyranoside.[30] Finally, we found that the catalyst amount had a key effect on the reaction. If the amount of catalyst had decreased, Tr was not totally deprotected, while if the amount of catalyst was increased, Lev was cleaved to generate a free OH, which could be coupled with donors, providing the undesired by-products. For this reason, we decided to utilize the two sequential glycosylation steps for the synthesis of **4**. With the above-synthesized **11** in hand, we added the CH_2Cl_2 solution of **11** to the reaction mixture of **18** in the presence of TMSOTf at 0 °C, and after 30 min the desired glycoside **20** was smoothly obtained. Removing the Lev protecting group by treatment with $NH_2NH_2{\cdot}HOAc$ in CH_2Cl_2–CH_3OH finished the synthesis of **4** in 83% yield.

With an effective synthetic access to the key intermediate **4**, we then set about our final assembly of the target natural products, scabiosaponins **1–3** by a one-pot sequential glycosylation with the combined use of glycosyl trichloroacetimidates and *p*-toluene 1-thioglycosides (STol) donors (Scheme 4). Readily accessible trichloroacetimidates **5–7** and *p*-toluene 1-thioglycoside **8** were, respectively, coupled with promotion by TMSOTf at −78 °C, afford-



Scheme 4. Reagents and conditions: (a) TMSOTf (0.2 equiv), CH_2Cl_2, 4 Å MS, −78 °C; (b) −10 °C, NIS (1.0 equiv), 30 min, 68% for **21**, 65% for **22**, 65% for **23**; (c) NaOMe, 1:1 CH_2Cl_2–CH_3OH, 89% for **1**, 87% for **2**, 90% for **3**.

ing the corresponding three glycosides. These products were then glycosylated in order with saponin **4** dissolved in a CH_2Cl_2 solution under the presence of TMSOTf and NIS at −10 °C, and the fully protected saponin derivatives **21–23** were obtained in good yields (60–70%). Finally, removal of the acetyl and benzoyl groups with NaOMe in MeOH–CH_2Cl_2 afforded the target scabiosaponins **1–3** in 87–90% yields. All the analytical data for the synthesized triterpene saponins **1–3** are identical in all respects to those reported in the literature.[12]

In summary, the completion of the first synthesis of scabiosaponins **1–3** was reported in an efficient, practical one-pot sequential glycosylation, which paves the way to easy access to bidesmosidic triterpene saponins and their diversified analogues.

3. Experimental

3.1. General methods

Solvents were purified in the usual way. TLC was performed on precoated E. Merck Silica Gel 60 F_{254} plates. Flash column chromatography was performed on silica gel (200–300 mesh, Qingdao, China). Optical rotations were determined with a JASCO P-1020 polarimeter. Melting points were determined with a Yanaco apparatus and were uncorrected. NMR spectra were recorded on a Jeol JNM-ECP 600-MHz spectrometer with Me_4Si as the internal standard, and chemical shifts are reported as δ values. Mass spectra were obtained on a Q-TOF GIOBAL mass spectrometer.

3.2. *p*-Tolyl 3,4-di-*O*-benzoyl-1-thio-β-D-xylopyranoside (16)

Compound **15** (2.56 g, 10 mmol) and dibutyltin oxide (2.50 g, 1.03 equiv) were suspended in benzene (350 mL), and the mixture was stirred at reflux overnight with the azeotropic removal of water. The resulting hazy-to-clear solution was cooled under N_2 in an ice-water bath and stirred while BzCl (2.4 mL, 2.05 equiv) was added via a syringe. After addition was complete, the flask was removed from the ice-water bath and was allowed to reach room temperature. After completion of the reaction (monitored by TLC), the reaction mixture was quenched with CH_3OH, concentrated under reduced pressure, and the crude mixture was purified by column chromatography (5:1 petroleum ether–EtOAc) to afford **16** as a white solid (4.35 g, 94%): $[\alpha]_D^{23}$ −106.6 (*c* 1.90, $CHCl_3$); R_f 0.45 (3:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3486, 3066, 2957, 2860, 1731, 1606, 1494, 1447, 1276, 1077, 805, 707 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.17–8.02 (m, 14H, Ph-*H*), 5.56 (t, 1H, *J* 8.4 Hz, H-3), 5.27 (td, 1H, *J* 9.0, 4.8 Hz, H-4), 4.71 (d, 1H, *J* 8.4 Hz, H-1), 4.45 (dd, 1H, *J* 11.4, 4.8 Hz, H-5-1), 3.72 (t, 1H, *J* 8.4 Hz, H-2), 3.58 (dd, 1H, *J* 11.4, 9.0 Hz, H-5-2), 2.38 (s, 3H, SPhC*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 166.4, 165.7, 139.5, 134.2, 134.0, 130.2, 130.1, 129.9, 129.8, 128.7, 128.6, 89.3 (C-1), 74.5, 70.5, 69.5, 66.2, 21.4; HRESIMS: Calcd for $C_{26}H_{24}O_6NaS$ [M+Na^+]: *m/z* 487.1191; found: *m/z* 487.1210.

3.3. *p*-Tolyl 3,4-di-*O*-benzoyl-2-*O*-levulinoyl-1-thio-β-D-xylopyranoside (17)

To a solution of compound **16** (300 mg, 0.61 mmol) in dry CH_2Cl_2 (5 mL), levulinic acid (142 mg, 1.22 mmol), DCC (252 mg, 1.22 mmol), and DMAP (7.5 mg, 0.06 mmol) were added under argon. The mixture was stirred for 5 h, diluted with CH_2Cl_2 (20 mL), washed with H_2O (5 mL), 1 M HCl (2 × 5 mL), satd aq $NaHCO_3$ (2 × 5 mL), and brine (2 × 5 mL), dried over Na_2SO_4, and concentrated. The residue was purified by silica gel column chromatography (2:1 petroleum ether–EtOAc) to give **17** (307 mg, 85%) as a white solid: $[\alpha]_D^{23}$ −77.9 (*c* 2.15, $CHCl_3$); R_f 0.30 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3066, 2949, 2867, 1719, 1603, 1490, 1447, 1264, 1147, 1089, 1061, 813, 707 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.15–8.01 (m, 14H, Ph-*H*), 5.62 (t, 1H, *J* 7.8 Hz, H-3), 5.20–5.24 (m, 1H, H-4), 5.17 (t, 1H, *J* 7.8 Hz, H-2), 4.93 (d, 1H, *J* 7.8 Hz, H-1), 4.55 (dd, 1H, *J* 11.9, 4.1 Hz, H-5-1), 3.63–3.67 (m, 1H, H-5-2), 2.49–2.69 (m, 4H, $CH_3COCH_2CH_2$–), 2.36 (s, 3H, Ph–CH_3), 2.06 (s, 3H, CH_3CO–); ^{13}C NMR ($CDCl_3$): δ 205.9, 171.4, 165.6, 139.2, 133.8, 133.6, 130.2, 130.1, 130.0, 129.9, 129.2, 128.6, 86.6 (C-1), 71.9, 70.0, 69.1, 62.0, 38.0, 29.8, 28.1, 21.4; HRESIMS: Calcd for $C_{31}H_{30}O_8NaS$ [M+Na^+]: *m/z* 585.1559; found: *m/z* 585.1563.

3.4. 3,4-Di-*O*-benzoyl-2-*O*-levulinoyl-β-D-xylopyranosyl trichloroacetimidate (9)

To a solution of compound **17** (622 mg, 1.05 mmol) in 10 mL of 9:1 acetone–H_2O, NBS (487 mg, 2.74 mmol) was added at −20 °C. The mixture was stirred for 5 min, and quenched with satd aq $NaHCO_3$.The reaction mixture was concentrated, and the residue was diluted with EtOAc (20 mL), washed with satd aq $NaHCO_3$ (2 × 5 mL), brine (2 × 5 mL), dried over Na_2SO_4, and concentrated. A solution of the above-obtained product, $CNCCl_3$ (0.52 mL, 5.30 mmol) and DBU (0.12 mL, 0.33 mmol) in dry CH_2Cl_2 (8 mL) was stirred for 3 h at room temperature, then the solvent was evaporated in vacuo to give a residue, which was purified by silica gel flash column chromatography (3:1 petroleum ether–EtOAc) to afford **9** as a colorless oil (261 mg, 66% two steps): $[\alpha]_D^{23}$ −8.7 (−2.25, $CHCl_3$); R_f = 0.57 (1:1 petroleum ether–EtOAc); ^1H NMR ($CDCl_3$): δ 8.73 (s, 1H, N*H*), 7.39–7.98 (m, 10H, Ph-*H*), 6.58 (d, 1H, *J* 3.3 Hz, H-1), 6.05 (t, 1H, *J* 9.9 Hz, H-3), 5.41 (ddd, 1H, *J* 9.9, 6.0, 4.4 Hz, H-4), 5.35 (dd, 1H, *J* 9.9, 3.3 Hz, H-2), 4.24 (dd, 1H, *J* 11.5, 6.0 Hz, H-5-1), 3.98 (dd, 1H, *J* 11.5, 4.0 Hz, H-5-2), 2.58–2.69 (m, 2H, Lev-C*H*$_2$), 2.44–2.52 (m, 2H, Lev-C*H*$_2$), 1.58 (s, 3H, Lev-C*H*$_3$); ^{13}C NMR ($CDCl_3$): δ 206.0, 171.9, 165.8, 165.7, 161.1, 133.7, 133.6, 130.1, 130.0, 129.3, 128.6, 93.6 (C-1), 70.3, 69.8, 69.7, 61.3, 37.8, 29.8, 27.9; HRESIMS: Calcd for $C_{26}H_{25}O_9NCl_3$ [M+H^+]: *m/z* 600.0595; found: *m/z* 600.0583.

3.5. 3-*O*-(3,4-Di-*O*-benzoyl-2-*O*-levulinoyl-β-D-xylopyranosyl)-oleanolic acid, 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl ester (20)

A mixture of **10** (200 mg, 0.29 mmol), **9** (206 mg, 0.34 mmol, 1.2 equiv), and 4 Å MS (400 mg) in dry CH_2Cl_2 (3 mL) was stirred at room temperature for 30 min and then cooled to −78 °C. TMSOTf (15 μL, 0.09 mmol, 0.3 equiv) was added slowly. After stirring at −78 °C for 30 min, the reaction mixture was warmed to room temperature for 30 min, and then cooled to 0 °C. A solution of **11** (520 mg, 0.43 mmol, 1.5 equiv) in dry CH_2Cl_2 (3 mL) was added slowly by injection. The reaction mixture was stirred at 0 °C for 30 min, and then warmed up to room temperature for another 30 min. The reaction was quenched by addition of Et_3N (0.3 mL), and then filtered. The filtrate was concentrated and purified by a silica gel column chromatography (3:1 petroleum ether–EtOAc) to afford **20** (370 mg, 66% based on acceptor **10**): mp 133–135 °C; $[\alpha]_D^{23}$ +16.6 (*c* 3.16, $CHCl_3$); R_f 0.35 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3065, 2949, 1735, 1598, 1450, 1260, 1061, 711 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.25–8.16 (m, 45H, Ph-*H*), 5.86 (d, 1H, *J* 8.0 Hz, H-1′), 5.84 (t-like, 1H, *J* 9.9, 9.6 Hz, H-3‴), 5.81 (t-like, 1H, *J* 8.8, 8.5 Hz, H-3′), 5.62 (t-like, 1H, *J* 8.8, 8.4 Hz, H-3″), 5.57 (dd, 1H, *J* 9.9, 8.4 Hz, H-2′), 5.54 (t-like, 1H, *J* 9.5, 9.2 Hz, H-4′), 5.46 (dd, 1H, *J* 9.5, 8.0 Hz, H-2‴), 5.39–5.42 (m, 1H, H-5‴-1), 5.35 (t-like, 1H, *J* 4.4, 4.0 Hz, H-12), 5.24–5.28 (m, 1H, H-5″), 5.21 (dd, 1H, *J* 8.8, 7.0 Hz, H-2″), 5.06 (d, 1H, *J* 8.0 Hz, H-1‴), 4.66 (d, 1H, *J* 6.6 Hz, H-1″), 4.56 (dd, 1H, *J* 12.1, 3.3 Hz, H-6′-1), 4.46 (dd, 1H, *J* 12.1, 5.5 Hz, H-6′-2), 4.31–4.36 (m, 2H, H-4″, H-6″-1), 4.05–4.10 (m, 1H, H-4‴), 3.99–4.03 (m, 1H, H-5′), 3.93–

3.98 (m, 1H, H-5‴-2), 3.47 (dd, 1H, *J* 14.0, 7.0 Hz, H-6″-2), 3.11 (dd, 1H, *J* 11.3, 4.4 Hz, H-3), 2.89 (dd, 1H, *J* 14.3, 4.0 Hz, H-18), 0.96, 0.90, 0.87, 0.87, 0.85, 0.74, 0.48 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR ($CDCl_3$): δ 205.9, 175.6 (C-28), 171.2, 166.1, 165.7, 165.6, 165.5, 165.3, 165.2, 165.1, 164.6 (C=O), 142.9 (C-13), 133.4, 133.2, 133.1, 133.0, 130.1, 129.9, 129.8, 129.7, 129.6, 129.4, 129.2, 129.1, 128.9, 128.8, 128.7, 128.4, 128.3, 128.2, 122.8 (C-12), 102.8 (C-1″), 100.1 (C-1‴), 91.9 (C-1′), 89.9 (C-3), 75.3, 72.9, 72.7, 72.2, 71.8, 71.7, 71.3, 70.3, 69.9, 69.7, 69.3, 66.5, 63.1, 62.0, 55.4, 47.5, 46.8, 45.7, 41.5, 41.0, 38.9, 38.4, 37.8, 36.7, 33.8, 32.9, 31.9, 31.7, 30.5, 29.6, 27.8, 25.8, 25.7, 25.4, 23.6, 23.4, 22.6, 18.1, 16.4, 15.3; HRMALDI-MS: Calcd for $[M+Na]^+$ $C_{115}H_{118}O_{28}$: *m/z* 1969.7682; found: *m/z* 1969.7702.

3.6. 3-*O*-(3,4-Di-*O*-benzoyl-β-D-xylopyranosyl)oleanolic acid, 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl ester (4)

To a stirred solution of **20** (300 mg, 0.16 mmol) in CH_2Cl_2 (50 mL) and CH_3OH (50 mL) was added $NH_2NH_2{\cdot}HOAc$ (50 mg, 0.5 mmol). After 2 h, the solution was concentrated, and the residue was purified by silica gel column chromatography (3:1 petroleum ether–EtOAc) to afford **4** (250 mg, 83%) as a white solid: mp 141–143 °C; $[\alpha]_D^{23}$ +17.7 (*c* 3.10, $CHCl_3$); R_f 0.41 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3066, 2941, 1731, 1603, 1447, 1264, 1085, 704 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.22–8.15 (m, 45H, Ph-*H*), 5.86 (t-like, 1H, *J* 9.9, 9.5 Hz, H-3‴), 5.85 (d, 1H, *J* 8.4 Hz, H-1′), 5.82 (t-like, 1H, *J* 8.5, 8.4 Hz, H-3′), 5.59 (t-like, 1H, *J* 8.5, 8.4 Hz, H-3′), 5.57 (t, 1H, *J* 9.9 Hz, H-2′), 5.54 (t-like, 1H, *J* 9.5, 9.4 Hz, H-4′), 5.46 (dd, 1H, *J* 9.9, 8.0 Hz, H-2‴), 5.39–5.42 (m, 1H, H-5‴-1), 5.35 (t-like, 1H, *J* 4.4, 3.7 Hz, H-12), 5.27–5.31 (m, 1H, H-5″), 5.06 (d, 1H, *J* 7.7 Hz, H-1‴), 4.55 (dd, 1H, *J* 12.1, 3.3 Hz, H-6′-1), 4.53 (d, 1H, *J* 6.6 Hz, H-1″), 4.46 (dd, 1H, *J* 12.1, 5.5 Hz, H-6′-2), 4.29–4.32 (m, 2H, H-4″, H-6″-1), 4.05–4.08 (m, 1H, H-4‴), 3.94–4.03 (m, 3H, H-5′, H-2″, H-5‴-2), 3.51 (dd, 1H, *J* 11.7, 9.5 Hz, H-6″-2), 3.19 (dd, 1H, *J* 11.7, 4.4 Hz, H-3), 2.89 (dd, 1H, *J* 13.9, 4.0 Hz, H-18), 0.97, 0.96, 0.88, 0.86, 0.85, 0.80, 0.48 (s each, 3H each, $CH_3 \times 7$); 13C NMR ($CDCl_3$): δ 175.6 (C-28), 166.2, 166.1, 165.6, 165.3, 165.1, 164.6 (C=O), 142.9 (C-13), 133.4, 133.2, 133.1, 133.0, 130.1, 129.9, 129.8, 129.7, 129.6, 129.4, 129.1, 128.9, 128.8, 128.7, 128.5, 128.4, 128.2, 122.8 (C-12), 105.2 (C-1″), 100.1 (C-1‴), 91.9 (C-1′), 89.8 (C-3), 75.2, 73.6, 72.9, 72.7, 72.5, 72.2, 71.8, 70.3, 69.9, 69.7, 69.3, 66.5, 63.2, 62.4, 55.4, 47.5, 46.8, 45.7, 41.5, 41.0, 38.9, 38.4, 36.7, 33.8, 32.9, 31.9, 31.7, 30.5, 28.2, 27.9, 25.9, 25.4, 23.6, 23.4, 22.6, 18.1, 16.7, 16.5, 15.4; HRMALDI-MS: Calcd for $[M+Na]^+$ $C_{110}H_{112}O_{26}$: *m/z* 1871.7356; found: *m/z* 1871.7334.

3.7. Typical procedure for the one-pot synthesis of triterpene saponins 21–23

A solution of thioglycoside **8** (40 mg, 0.11 mmol) and 4 Å MS (80 mg) in CH_2Cl_2 (5 mL) was stirred at room temperature under argon for 30 min and then cooled to −78 °C. At this temperature, a solution of TMSOTf (0.2 equiv) in dry CH_2Cl_2 was injected, and after 10 min trichloroacetimidate **5**, **6**, or **7** (2.1 equiv) in dry CH_2Cl_2 was added. The resulting mixture was stirred for additional 30 min and then warmed to −10 °C. To the above mixture was added a solution of saponin acceptor **4** (200 mg, 0.11 mmol, 1.0 equiv) in CH_2Cl_2 (2 mL), followed by NIS (50 mg, 0.11 mmol, 2.0 equiv). After stirring for 1 h, the reaction mixture was quenched with Et_3N, and then filtered through a pad of Celite. The filtrate was concentrated. The residue was purified by silica gel column chromatography (2.5:1 petroleum ether–EtOAc) to give the fully protected saponin. The amounts of the reactants and the yields of the saponin products were calculated based on saponin accepter **4**.

3.7.1. 3-*O*-(2,3,4-Tri-*O*-benzoyl-β-D-xylopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-β-D-xylopyranosyl)oleanolic acid, 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl ester (21)

Yield 68%; mp 156–158 °C; $[\alpha]_D^{23}$ −1.97 (*c* 2.35, $CHCl_3$); R_f 0.38 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3062, 2938, 1735, 1603, 1451, 1264, 1093, 707 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.27–8.06 (m, 60H, Ph-*H*), 5.87 (t, 1H, *J* 9.7 Hz, H-3′), 5.85 (t, 1H, *J* 9.6 Hz, H-3″), 5.81 (d, 1H, *J* 8.8 Hz, H-1′), 5.53–5.59 (m, 5H, H-3‴, H-3⁗, H-4′, H-4″, H-4‴), 5.46 (dd, 1H, *J* 9.9, 7.7 Hz, H-2‴), 5.41 (t, 1H, *J* 9.6 Hz, H-4⁗), 5.35 (t, 1H, *J* 3.7 Hz, H-12), 5.20–5.22 (m, 2H, H-4⁗, H-5‴-1), 5.13–5.16 (m, 2H, H-5′, H-5″), 5.07 (s, 1H, H-1⁗), 5.05 (d, 1H, *J* 7.7 Hz, H-1″), 5.04 (t, 1H, *J* 9.6 Hz, H-3⁗), 4.79 (d, 1H, *J* 7.2 Hz, H-1⁗), 4.57 (d, 1H, *J* 8.0 Hz, H-1‴), 4.55 (m, 1H, H-5⁗-1), 4.46 (dd, 1H, *J* 12.1, 5.5 Hz, H-6″-1), 4.39 (dd, 1H, *J* 13.2, 4.4 Hz, H-6′-1), 4.07–4.10 (m, 2H, H-2′, H-2⁗), 3.99–4.03 (m, 3H, H-5″-2, H-5⁗, H-5⁗-2), 3.93–3.96 (m, 2H, H-2″, H-2⁗), 3.65 (dd, 1H, *J* 12.6, 6.0 Hz, H-6′-2), 3.31 (dd, 1H, *J* 12.7, 6.1 Hz, H-6″-2), 3.11 (dd, 1H, *J* 11.5, 4.4 Hz, H-3), 2.87 (dd, 1H, *J* 14.8, 3.8 Hz, H-18), 2.05, 1.95 (s each, 3H each, Ac × 2), 1.14 (d, 3H, *J* 6.6 Hz, H-6‴), 0.96, 0.92, 0.91, 0.88, 0.86, 0.71, 0.49 (s each, 3 H each, $CH_3 \times 7$); ^{13}C NMR ($CDCl_3$): δ 175.7 (C-28), 170.0, 169.8, 165.7, 165.6, 165.5, 165.3, 165.2, 142.9 (C-13), 133.5, 133.3, 133.2, 129.9, 129.8, 129.7, 129.5, 128.4, 122.9 (C-12), 102.9 (C-1⁗), 101.1 (C-1‴), 100.3 (C-1″), 97.8 (C-1⁗), 92.0 (C-1′), 89.4 (C-3), 75.9, 75.3, 73.1, 72.8, 72.3, 71.9, 71.3, 70.4, 70.2, 69.9, 69.5, 68.9, 67.2, 63.2, 60.8, 60.5, 55.6, 47.6, 46.9, 45.8, 41.7, 41.1, 39.2, 39.0, 38.7, 36.8, 33.9, 33.1, 32.0, 31.8, 30.6, 29.8, 28.1, 27.9, 25.9, 25.5, 23.7, 23.5, 22.7, 20.9, 20.6, 18.2, 17.5, 16.6, 16.5, 15.6, 14.3. HRMALDI-MS: Calcd for $[M+Na]^+$ $C_{146}H_{146}O_{39}$: *m/z* 2545.9355; found: *m/z* 2545.9334.

3.7.2. 3-*O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-β-D-xylopyranosyl)oleanolic acid, 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl ester (22)

Yield 65%; mp 160–162 °C; $[\alpha]_D^{23}$ +27.3 (*c* 2.10, $CHCl_3$); R_f 0.35 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3062, 2941, 1727, 1603, 1447, 1264, 1085, 1062, 1027, 704 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.27–8.08 (m, 65H, Ph-*H*), 5.87 (t, 1H, *J* 9.6 Hz, H-3″), 5.85 (t, 1H, *J* 9.6 Hz, H-3⁗), 5.82 (d, 1H, *J* 8.2 Hz, H-1′), 5.53–5.61 (m, 4H, H-2‴, H-3′, H-3⁗⁗, H-4⁗⁗), 5.50 (t, 1H, *J* 9.8 Hz, H-3‴), 5.46 (dd, 1H, *J* 9.9, 7.7 Hz, H-2′), 5.41 (t, 1H, *J* 9.9 Hz, H-2″), 5.36–5.39 (br s, 2H, H-12, H-2⁗), 5.12–5.16 (m, 2H, H-4′, H-4⁗), 5.06 (s, 1H, H-1⁗), 5.05 (d, 1H, *J* 8.0 Hz, H-1″), 4.98 (t, 1H, *J* 9.6 Hz, H-4″), 4.70 (d, 1H, *J* 5.6 Hz, H-1⁗⁗), 4.57 (dd, 1H, *J* 12.4, 3.4 Hz, H-6′-1), 4.46 (dd, 1H, *J* 12.1, 4.0 Hz, H-6″-1), 4.34–4.38 (m, 2H, H-6″-2, H-6⁗⁗-1), 4.28 (d, 1H, *J* 7.7 Hz, H-1‴), 4.24 (dd, 1H, *J* 12.1, 3.8 Hz, H-5‴-1), 4.04–4.08 (m, 1H, H-4‴), 4.01–4.03 (m, 1H, H-5″), 3.92–3.97 (m, 3H, H-4⁗⁗, H-5⁗, H-6′-2, H-6⁗⁗-2), 3.87 (t-like, 1H, *J* 6.6, 5.5 Hz, H-2⁗⁗), 3.56 (dd, 1H, *J* 12.1, 6.6 Hz, H-5‴-2), 3.31–3.34 (m, 1H, H-6⁗⁗-2), 3.09 (dd, 1H, *J* 11.6, 4.4 Hz, H-3), 2.89 (dd, 1H, *J* 13.8, 3.7 Hz, H-18), 2.04, 1.88 (s each, 3H each, Ac × 2), 1.07 (d, 3H, *J* 6.0 Hz, H-6⁗), 0.97, 0.90, 0.87, 0.86, 0.85, 0.72, 0.50 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR ($CDCl_3$): δ 175.7 (C-28), 170.0, 169.7, 166.1, 165.6, 165.2, 165.0, 164.7, 142.9 (C-13), 133.5, 133.3, 133.2, 129.9, 129.8, 128.5, 128.4, 122.9 (C-12), 103.3 (C-1⁗⁗), 101.0 (C-1″), 100.3 (C-1⁗), 97.7 (C-1‴), 92.1 (C-1′), 89.0 (C-3), 75.7, 75.3, 72.8, 72.3, 71.9, 71.8, 71.7, 70.4, 70.1, 69.9, 69.6, 69.4, 68.8, 67.0, 66.6, 63.2, 62.4, 60.9, 60.5, 55.6, 47.6, 46.9, 45.8, 41.7, 41.1, 39.1, 39.0, 38.7, 36.8, 33.9, 33.1, 32.0, 31.9, 30.6, 29.8, 28.0, 25.5, 23.7, 23.4, 22.7, 21.2, 20.8, 20.2, 18.2, 17.5, 16.6, 16.4,

15.5, 14.2; HRMALDI-MS: Calcd for $[M+Na]^+$ $C_{154}H_{152}O_{41}$: *m/z* 2679.9672; found: *m/z* 2679.9701.

3.7.3. 3-*O*-(2,3,4,6-Tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzoyl-β-D-glucopyranosyl-(1→3)-2,4-di-*O*-acetyl-α-L-rhamnopyranosyl-(1→2)-3,4-di-*O*-benzoyl-β-D-xylopyranosyl)oleanolic acid, 2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-D-glucopyranosyl ester (23)

Yield 65%; mp 161–163 °C; $[\alpha]_D^{23}$ +29.4 (*c* 2.15, $CHCl_3$); R_f 0.31 (2:1 petroleum ether–EtOAc); IR (KBr) ν_{max} 3062, 2922, 2852, 1735, 1603, 1451, 1268, 1097, 704 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.23–8.13 (m, 80H, Ph-*H*), 5.87 (t, 1H, *J* 9.4 Hz, H-3‴″), 5.82 (d, 1H, *J* 8.8 Hz, H-1′), 5.67 (t, 1H, *J* 9.7 Hz, H-3′), 5.58 (dd, 1H, *J* 9.9, 8.2 Hz, H-2′), 5.50–5.56 (m, 3H, H-2‴, H-2‴″, H-3‴″), 5.47 (dd, 1H, *J* 9.9, 7.7 Hz, H-4″), 5.41 (t, 1H, *J* 9.9 Hz, H-3″), 5.36–5.38 (m, 2H, H-12, H-1‴), 5.31 (t, 1H, *J* 9.9 Hz, H-4′), 5.26 (dd, 1H, *J* 9.8, 7.7 Hz, H-2‴), 5.16 (m, 1H, H-5″), 5.06 (d, 1H, *J* 7.8 Hz, H-1‴″), 4.90–4.97 (m, 3H, H-2‴″, H-3‴, H-4‴), 4.74 (d, 1H, *J* 8.2 Hz, H-1‴″), 4.68 (d, 1H, *J* 6.5 Hz, H-1″), 4.56 (dd, 1H, *J* 12.4, 3.3 Hz, H-5‴-1), 4.46 (dd, 1H, *J* 12.6, 5.4 Hz, H-5‴-2), 4.37 (dd, 1H, *J* 11.6, 3.3 Hz, H-6″-1), 4.26 (m, 2H, H-5‴″, H-6‴″-1), 4.08 (m, 1H, H-4‴), 4.00–4.04 (m, 2H, H-5‴″, H-6‴″-2), 3.94–3.99 (m, 5H, H-1‴, H-6′-1, H-4‴″, H-6‴″-2, H-6‴″-2), 3.89 (dd, 1H, *J* 9.9, 6.1 Hz, H-5‴″), 3.82–3.87 (m, 2H, H-2″, H-5‴), 3.68 (m, 1H, H-5′), 3.58 (dd, 1H, *J* 12.1, 5.5 Hz, H-6″-2), 3.53 (dd, 1H, *J* 11.6, 6.6 Hz, H-6′-2), 3.10 (dd, 1H, *J* 12.0, 4.4 Hz, H-3), 2.89 (dd, 1H, *J* 13.7, 3.9 Hz, H-18), 2.06, 2.05 (s each, 3H each, Ac × 2), 1.06 (d, 3H, *J* 6.0 Hz, H-6‴″), 0.96, 0.89, 0.88, 0.87, 0.87, 0.67, 0.49 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR ($CDCl_3$): δ 175.7 (C-28), 169.9, 169.8, 165.8, 165.7, 165.6, 165.5, 165.4, 165.3, 142.9 (C-13), 133.9, 133.5, 133.3, 133.2, 129.9, 129.8, 128.5, 128.4, 122.9 (C-12), 103.3 (C-1″), 100.9 (C-1‴), 100.5 (C-1‴″), 100.3 (C-1‴″), 98.1 (C-1‴′), 92.1 (C-1′), 88.9 (C-3), 75.4, 73.1, 73.0, 72.4, 72.3, 71.9, 69.9, 69.5, 67.0, 66.6, 63.2, 62.7, 61.8, 60.9, 60.5, 55.6, 47.6, 46.9, 45.8, 41.7, 41.1, 39.1, 39.0, 38.7, 36.7, 33.9, 33.1, 32.0, 31.9, 30.6, 29.8, 27.9, 26.0, 25.5, 23.7, 23.5, 22.7, 21.2, 20.7, 20.1, 18.2, 17.4, 16.6, 16.3, 15.5, 14.3; HRMALDI-MS: Calcd for $[M+Na]^+$ $C_{181}H_{174}O_{49}$: *m/z* 3154.1015; found: *m/z* 3154.1016.

3.8. Typical procedure for removal of the protecting groups of triterpene saponins 21–23

To a solution of fully protected triterpene saponins **21–23** (100 mg) in dry 1:2 CH_2Cl_2–MeOH (20 mL) was added a newly prepared NaOMe in MeOH solution (1.0 mol/L, 0.20 mL). The mixture was stirred at rt for 5 h and neutralized with Dowex H^+ resin to pH 7 and then filtered. The filtrate was concentrated, and the resulting residue was subjected to a silica gel column chromatography (1:20:0.1 MeOH–$CHCl_3$–H_2O) to give the natural products **1–3** as white amorphous solids.

3.8.1. 3-*O*-(β-D-Xylopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl)oleanolic acid, β-D-glucopyranosyl-(1→6)-β-d-glucopyranosyl ester (1)

Yield 89%; mp 213–215 °C; $[\alpha]_D^{25}$ −17.1 (*c* 0.70, CH_3OH); R_f 0.31 (1:20:0.1 MeOH–$CHCl_3$–H_2O); IR (KBr) ν_{max} 3401, 2938, 1731, 1642, 1459, 1361, 1050 cm^{-1}; ^1H NMR (C_5D_5N): δ 6.63 (br s, 1H, H-1‴′), 6.29 (d, 1H, *J* 8.3 Hz, H-1′), 5.44 (t, 1H, *J* 3.7 Hz, H-12), 5.42 (d, 1H, *J* 7.8 Hz, H-1‴″), 5.07 (d, 1H, *J* 7.7 Hz, H-1″), 5.04 (br s, 1H, H-2‴′), 4.86 (d, 1H, *J* 7.3 Hz, H-1‴), 4.84 (dd, 1H, *J* 9.2, 3.2 Hz, H-3‴′), 4.81 (dq, 1H, *J* 9.6, 5.9 Hz, H-5‴′), 4.75 (dd, 1H, *J* 11.4, 1.8 Hz, H-6′-1), 4.58 (t-like, 1H, *J* 9.6, 9.2 Hz, H-4‴′), 4.50 (dd, 1H, *J* 11.9, 2.3 Hz, H-6″-1), 4.36–4.40 (m, 4H, H-5‴-1, H-5‴′-1, H-6′-2, H-6″-2), 4.29 (t-like, 1H, *J* 8.6, 7.7 Hz, H-2‴), 4.26 (m, 1H, H-4′), 4.21–4.25 (m, 4H, H-3′, H-3′, H-4″, H-4‴″), 4.17–4.20 (m, 3H, H-2′, H-3‴, H-3‴″), 4.10–4.15 (m, 3H, H-2‴″, H-4‴, H-5′), 4.05 (t, 1H, *J* 8.2 Hz, H-2″), 3.92 (m, 1H, H-5″), 3.78 (d, 1H, *J* 10.1 Hz, H-5″-2), 3.75 (d, 1H, *J* 9.1 Hz, H-5‴″-2), 3.36 (dd, 1H, *J* 11.5, 4.1 Hz, H-3), 3.23 (dd, 1H, *J* 13.7, 4.1 Hz, H-18), 1.68 (d, 3H, *J* 5.9 Hz, H-6‴′), 1.41, 1.29, 1.27, 1.12, 0.92, 0.91, 0.91 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR (C_5D_5N): δ 176.9 (C-28), 144.6 (C-13), 123.2 (C-12), 107.8 (C-1‴″), 106.4 (C-1‴), 105.5 (C-1″), 101.7 (C-1‴′), 96.0 (C-1′), 88.9 (C-3), 83.2 (C-3‴′), 80.1, 79.0, 78.8, 78.7, 78.6, 78.3, 77.2, 75.9, 75.4, 74.2, 73.2, 72.2, 71.8 (C-3‴), 71.4, 71.1, 70.0, 69.6, 67.8, 67.3, 62.9, 56.4, 48.4, 47.3, 46.5, 42.4, 42.0, 40.2, 39.9, 39.3, 37.4, 33.4, 32.8, 31.1, 28.5, 27.2, 26.4, 24.1, 24.0, 18.9, 17.8, 17.6, 16.0; HRESIMS: Calcd for $C_{58}H_{94}O_{25}Na$ $[M+Na^+]$: *m/z* 1213.5982; found: *m/z* 1213.6011.

3.8.2. 3-*O*-(β-D-Glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl)oleanolic acid, β-D-glucopyranosyl-(1→6)-β-D-glucopyranosyl ester (2)

Yield 87%; mp 222–224 °C; $[\alpha]_D^{25}$ −13.1 (*c* 0.25, CH_3OH); R_f 0.29 (1:20:0.1 MeOH–$CHCl_3$–H_2O); IR (KBr) ν_{max} 3401, 2938, 1735, 1645, 1455, 1365, 1073 cm^{-1}; ^1H NMR (C_5D_5N): δ 6.55 (br s, 1H, H-1‴′), 6.30 (d, 1H, *J* 8.2 Hz, H-1′), 5.55 (d, 1H, *J* 7.8 Hz, H-1‴″), 5.46 (t, 1H, *J* 3.6 Hz, H-12), 5.13 (br s, 1H, H-2‴′), 5.08 (d, 1H, *J* 7.7 Hz, H-1″), 4.93 (dd, 1H, *J* 9.9, 3.2 Hz, H-3‴′), 4.86 (d, 1H, *J* 6.8 Hz, H-1‴), 4.81 (dq, 1H, *J* 9.6, 5.9 Hz, H-5‴′), 4.77 (dd, 1H, *J* 9.6, 4.7 Hz, H-5‴-1), 4.60 (t-like, 1H, *J* 9.7, 9.6 Hz, H-4‴′), 4.50–4.55 (m, 2H, H-6″-1, H-6‴″-1), 4.38–4.45 (m, 4H, H-6′-1, H-6′-2, H-6″-2, H-6‴″-2), 4.33–4.35 (m, 2H, H-3‴, H-4‴), 4.30 (t, 1H, *J* 9.1 Hz, H-4′), 4.25–4.28 (m, 3H, H-2‴, H-3‴″, H-4‴″), 4.14–4.24 (m, 6H, H-2′, H-3′, H-5′, H-3″, H-4″, H-2‴″), 4.07 (t-like, 1H, *J* 8.3, 8.2 Hz, H-2″), 4.03 (m, 1H, H-5‴″), 3.94 (m, 1H, H-5″), 3.76 (t, 1H, *J* 10.1 Hz, H-5‴-2), 3.36 (dd, 1H, *J* 11.9, 3.7 Hz, H-3), 3.23 (dd, 1H, *J* 13.7, 3.7 Hz, H-18), 1.68 (d, 3H, *J* 5.9 Hz, H-6‴′), 1.44, 1.30, 1.27, 1.13, 0.94, 0.93, 0.93 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR (C_5D_5N): δ 176.9 (C-28), 144.5 (C-13), 123.2 (C-12), 107.1 (C-1‴″), 106.6 (C-1‴), 105.5 (C-1″), 101.9 (C-1‴′), 96.0 (C-1′), 89.0 (C-3), 83.5 (C-3‴′), 79.8, 79.0, 78.8, 78.7, 78.3, 77.5, 76.3, 76.2, 76.1, 75.5, 74.2, 73.3, 71.9 (C-3‴), 71.2, 70.1, 69.6, 67.3, 62.9, 62.8, 56.4, 48.4, 47.4, 46.6, 42.5, 42.0, 40.2, 40.0, 39.3, 37.4, 35.3, 33.5, 32.8, 31.1, 28.5, 27.2, 26.4, 24.1, 24.0, 23.7, 19.0, 18.8, 17.8, 17.6, 16.0; HRESIMS: *m/z* Calcd for $C_{59}H_{96}O_{26}Na$ $[M+Na^+]$: 1243.6088; found: 1243.6119.

3.8.3. 3-*O*-(β-D-Glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→3)-α-L-rhamnopyranosyl-(1→2)-β-D-xylopyranosyl)oleanolic acid, β-D-glucopyranosyl-(1→6)-*O*-β-D-glucopyranosyl ester (3)

Yield 90%; mp 229–231 °C; $[\alpha]_D^{25}$ −17.8 (*c* 1.20, CH_3OH); R_f 0.21 (1:20:0.1 MeOH–$CHCl_3$–H_2O); IR (KBr) ν_{max} 3416, 2941, 1731, 1638, 1377, 1062 cm^{-1}; ^1H NMR (C_5D_5N): δ 6.51 (br s, 1H, H-1‴′), 6.28 (d, 1H, *J* 8.2 Hz, H-1′), 5.48 (d, 1H, *J* 7.8 Hz, H-1‴″), 5.47 (br s, 1H, H-12), 5.22 (d, 1H, *J* 7.8 Hz, H-1‴″), 5.05 (d, 1H, *J* 7.8 Hz, H-1″), 4.86 (dd, 1H, *J* 9.6, 3.0 Hz, H-3‴′), 4.80 (d, 1H, *J* 7.2 Hz, H-1‴), 4.78 (dq, 1H, *J* 9.6, 5.0 Hz, H-5‴′), 4.73 (d, 1H, *J* 10.9 Hz, H-6′-1), 4.53–4.58 (m, 3H, H-4‴, H-6‴″-1, H-6‴″-1), 4.50 (dd, 1H, *J* 9.7, 3.0 Hz, H-6″-1), 4.43 (dd, 1H, *J* 10.1, 3.2 Hz, H-6‴″-2), 4.35–4.40 (m, 5H, H-4′, H-4‴″, H-5‴-1, H-6″-2, H-6‴″-2), 4.28–4.31 (m, 2H, H-3‴″, H-3‴″), 4.21–4.26 (m, 5H, H-2‴, H-3′, H-3″, H-4″, H-4‴), 4.16–4.20 (m, 5H, H-2′, H-3‴, H-2‴″, H-5′, H-6′-2), 4.11–4.14 (m, 2H, H-2‴″, H-3‴″), 4.09 (t, 1H, *J* 7.2 Hz, H-2″), 4.03 (m, 1H, H-5‴″), 3.96 (m, 1H, H-5‴″), 3.90 (m, 1H, H-5″), 3.72 (t, 1H, *J* 9.2 Hz, H-5‴-2), 3.32 (dd, 1H, *J* 11.9, 3.2 Hz, H-3), 3.19 (dd, 1H, *J* 13.3, 3.7 Hz, H-18), 1.66 (d, 3H, *J* 5.0 Hz, H-6‴′), 1.38, 1.27, 1.23, 1.10, 0.90, 0.90, 0.90 (s each, 3H each, $CH_3 \times 7$); ^{13}C NMR (C_5D_5N): δ 177.0 (C-28), 144.6 (C-13), 122.9 (C-12), 106.7 (C-1‴″), 106.5 (C-1‴), 105.5 (C-1″), 105.3 (C-1‴″), 101.8 (C-1‴′), 96.0 (C-1′), 88.9 (C-3), 83.7 (C-3‴′), 81.5, 79.3, 79.0, 78.8, 78.7, 78.6, 78.3, 77.6, 77.1, 75.7, 75.5, 75.2, 74.3, 73.2, 71.9 (C-3‴), 71.2, 70.1, 69.7, 67.4, 64.8, 62.9, 62.8, 62.1, 56.5, 48.5, 47.4, 46.6, 42.5, 42.1,

40.3, 40.0, 39.4, 37.4, 34.4, 33.5, 32.9, 31.1, 30.3, 28.7, 28.6, 27.3, 26.5, 24.2, 24.1, 23.8, 19.0, 18.9, 17.9, 17.7, 16.1; HRESIMS: Calcd for $C_{65}H_{107}O_{31}$ [M+H$^+$]: *m/z* 1383.6796; found: *m/z* 1383.6826.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.carres.2009.04.024.

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