Concise Synthesis and Antidiabetic Effect of Three Natural Triterpenoid Saponins Isolated from *Fadogia ancylantha* (Makoni tea)

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The first concise synthesis of the bidesmosidic oleanolic acid saponins **1**–**3** isolated from *Fadogia ancylantha* (Makoni tea) have been accomplished through a 'one-pot sequential glycosylation' strategy with two glycosyl 1-(trichloroacetimidate)s as glycosyl donors. The synthesized natural products **1**–**3** were then evaluated for their inhibitory activities against α-glucosidase, α-amylase, and lipase. Among the assayed compounds **1**–**3**, compound **1** showed strong α-glucosidase and α-amylase inhibition, with IC_{50} values of 160 and 180 μM, respectively. Moreover, compounds **2** and **3** showed strong inhibition against α-glucosidase and lipase, with the respective IC_{50} values of 170 and 190 μM, and 190 and 200 μM.

Introduction. – For individuals with postprandial hyperglycemia, there is a growing health risk, such as coronary heart disease, angina pectoris, myocardial infarction, and other cardiovascular diseases. In order to reduce the incidence of the cardiovascular diseases associated with high blood glucose level, the conventional approach to treat diabetic patients and individuals with impaired glucose tolerance focuses on the control of blood glucose level [1]. α-Glucosidase is a glucohydrolase enzyme at the brush-border surface membrane of intestinal cells, that hydrolyses the cleavage of D-glucose of disaccharides and oligosaccharides from dietary complex carbohydrates. α-Glucosidase inhibitors postpone the digestion of dietary complex carbohydrates into monosaccharides in the intestine and reduce the postprandial insulin and glucose level [2][3]. Consequently, synthetic α-glucosidase inhibitors, such as acarbose, voglibose, and miglitol effectively make up defective early phase insulin release through inhibiting post-prandial absorption of monosaccharides, and have been formulated and launched for clinical use of the treatment of type 2 diabetes in the last two decades [4–6].

Considerable efforts have been made in the development of potent and effective small-molecule α-glucosidase inhibitors from natural products and artificial synthetic compounds for the treatment of type 2 diabetes [7–15]. Our program was carried out with carbohydrate-based modification on natural products. In a series of studies on *in vitro* α-glucosidase-inhibiting principles from synthetic natural products and deriva-

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tives, we previously reported four hederagenin glycosides, two natural benzophenone *O*-glycosides, and ten derivatives by efficient artificial synthesis. The structure–activity relationships (SAR) of these carbohydrate-based modifications on hederagenin and benzophenone showed that the sugar moiety strongly influenced α-glucosidase inhibitory activity[16][17].

Glycosides of oleanolic acid with one sugar chain attached through an ester linkage at C(28) and another through an ether linkage at C(3), constitute more than half of the triterpeniod saponins, which are widely distributed in plants and in some marine organisms [18–20]. They have been reported to possess important biological and pharmacological activities, including anti-inflammatory [21], anti-HIV [22], antifungal [23], antitumor [24–26], and inhibition against α-glucosidase [12][27–29]. The plant, *Fadogia ancylantha* HIERN. (Rubiaceae), commonly known as 'Makoni' or 'marange', is a wild perennial shrub growing in the Eastern Highlands area of Zimbabwe. Its leaves are used as a folk medicine for the treatment of topical ulcers. By investigating the chemical constituents of Makoni tea, *Mencherini et al.* recently reported the isolation and structural characterization of three oleanolic acid saponins **1**–**3** (*Fig.*) [30]. Attracted by the specific structure and potent biological properties of oleanolic acid saponins **1**–**3**, we report here a facile synthesis of these metabolites. The three saponins **1**–**3** were also evaluated for *in vitro* inhibition activities against α-glucosidase, α-

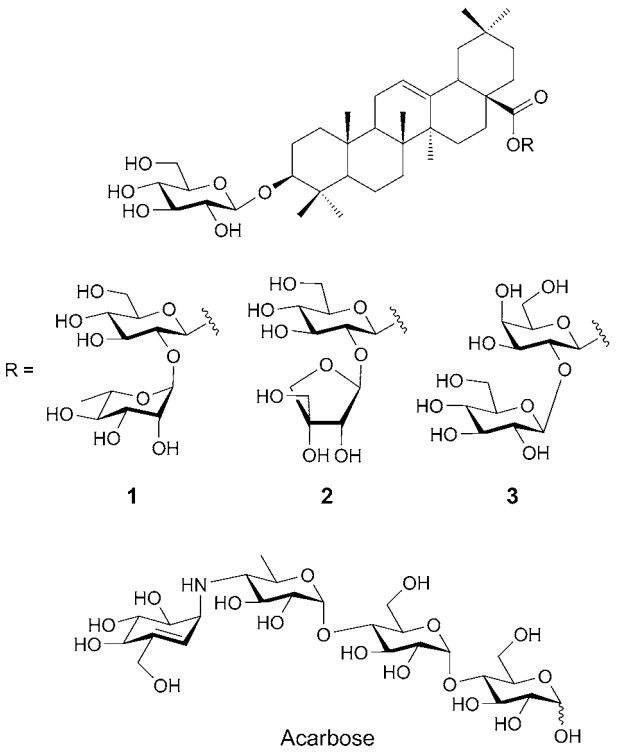


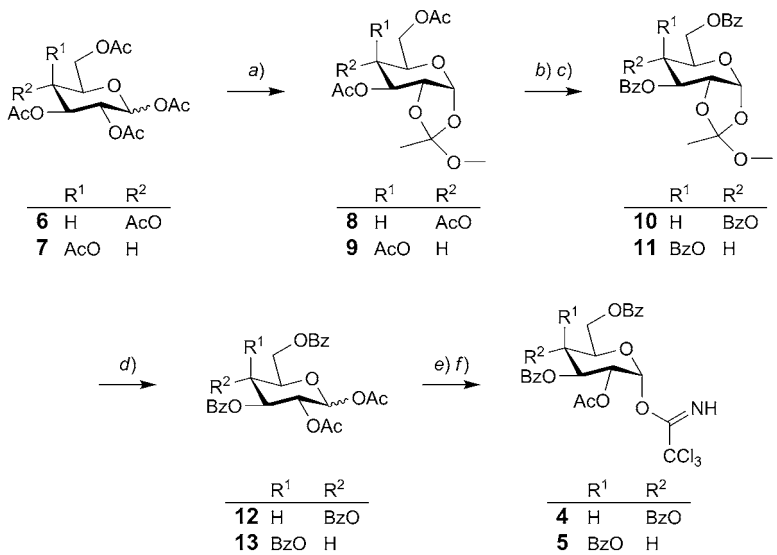
Figure. *Structures of oleanolic acid saponins* **1**–**3** *and Acarbose*

amylase, and lipase. These investigations would be useful for designing and preparing novel stronger α-glucosidase inhibitors and elucidate the structure–activity relationship in the inhibition process of α-glucosidase for the treatment of type 2 diabetes.

Results and Discussion. – Recently, we have successfully completed the synthesis of several bidesmosidic oleanolic acid saponins *via* applying the 'one-pot sequential glycosylation' strategy [17][31–35]. Encouraged by these accomplishments, we decided to adopt the similar strategy with two glycosyl 1-(trichloroacetimidate)s as glycosyl donors to synthesize the new bidesmosidic oleanolic acid saponins **1**–**3** in the present study.

Synthesis of Target Compounds **1**–**3**. Firstly, the two trichloroacetimidate donors **4** and **5** were prepared as depicted in *Scheme 1*, respectively. Treatment of the known 1,2,3,4,6-penta-*O*-acetyl-α/β-D-glucopyranose **6** [36] or 1,2,3,4,6-penta-*O*-acetyl-α/β-D-galactopyranose **7** [37] with 33% HBr in AcOH in the presence of lutidine afforded 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-α-D-glucopyranose **8** (95%) and 3,4,6-tri-*O*-acetyl-1,2-*O*-(1-methoxyethylidene)-α-D-galactopyranose **9** (94%), respectively. Removal of the Ac groups with MeONa in CH_2Cl_2/MeOH, followed by benzoylation with BzCl in pyrdine, gave 3,4,6-tri-*O*-benzoyl-1,2-*O*-(1-methoxyethylidene)-α-D-glucopyranose **10** (80%) or 3,4,6-tri-*O*-benzoyl-1,2-*O*-(1-methoxyethylidene)-α-D-galactopyranose **11** (83%). Treatment of **10** or **11** with AcOH afforded the desired 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α/β-D-glucopyranose **12** (97%) or 1,2-di-*O*-acetyl-3,4,6-tri-*O*-benzoyl-α/β-D-galactopyranose **13** (96%). Then, regioselective removal of

Scheme 1



	R^1	R^2
6	H	AcO
7	AcO	H

	R^1	R^2
8	H	AcO
9	AcO	H

	R^1	R^2
10	H	BzO
11	BzO	H

	R^1	R^2
12	H	BzO
13	BzO	H

	R^1	R^2
4	H	BzO
5	BzO	H

a) 33% HBr in AcOH, lutidine, MeOH/CH_2Cl_2, 95% for **8**, 94% for **9**. *b*) MeONa, MeOH/CH_2Cl_2. *c*) BzCl, pyrdine, 80% for **10** (two steps), 83% for **11** (two steps). *d*) AcOH, 97% for **12**, 96% for **13**. *e*) $NH_2NH_2 \cdot AcOH$, DMF. *f*) $CNCCl_3$, DBU, CH_2Cl_2, 78% for **4** (two steps), 81% for **5** (two steps).

Ac group at C(1) of **12** or **13** with $NH_2NH_2 \cdot AcOH$ in DMF, followed by trichloroacetimidation ($CNCCl_3$, DBU), furnished the trichloroacetimidate donors **4** (78%) and **5** (81%) over two steps.

With oleanolic acid aglycon acceptor **14** [38] and trichloroacetimidate donors **4**, **5**, and **15** in hand, we next turned our attention to a 'one-pot sequential glycosylation' strategy for the efficient synthesis of natural oleanolic acid saponins **1**–**3** using two glycose 1-(trichloroacetimidate) donors (*Scheme 2*). Herein, condensation of oleanolic ester **14** with 2,3,4,6-tetra-*O*-benzoyl-α-D-glucopyranosyl trichloroacetimidate **15** under the promotion of trimethylsilyl trifluoromethanesulfonate (TMSOTf, 0.3 equiv.) at $-78°$ for 30 min afforded the desired intermediate. Removal of the trityl group by warming to ambient temperature for 30 min led to the expected product. After addition of a CH_2Cl_2 solution of trichloroacetimidate **4** or **5** to the above mixture at 0°, the desired product **18** or **19** was obtained. Removal of the Ac group of compound **18** or **19** using 1% AcCl in $MeOH/CH_2Cl_2$ furnished the required product **20** or **21**, respectively. Glycosylation between acceptor **20** (or **21**) and the known donor, **15**, 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl trichloroacetimidate **16**, or the peracetyl apioside donor **17** with the promotion of the reaction by TMSOTf generated the desired product **22**, **23**, or **24** in satisfactory yield. Finally, removal of the Bz and Ac groups on the sugar residues with MeONa in MeOH and CH_2Cl_2 afforded the expected natural products **1**–**3** in satisfactory yields, whose analytical data were identical with those reported in the literature [30].

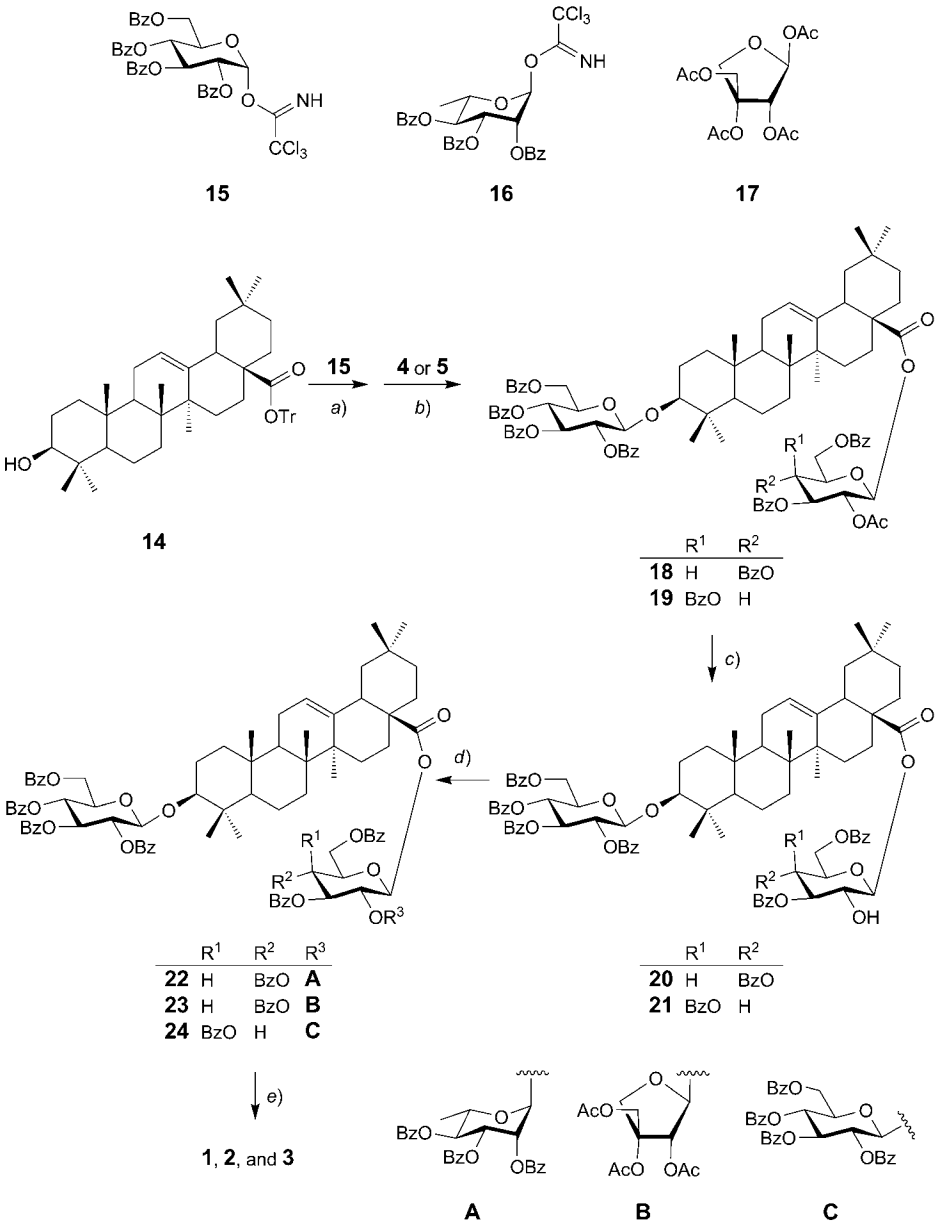
Inhibition of α-Glucosidase, α-Amylase, and Lipase. The inhibitory activities of the synthesized compounds **1**–**3** against α-glucosidase, α-amylase, and lipase were evaluated, and the results are summarized in the *Table*. The data indicated that three bidesmosidic oleanolic acid saponins were active. Among the assayed triterpenoids, compound **1** showed strong α-glucosidase and α-amylase inhibition, with IC_{50} values of 160 and 180 μM, respectively. Notably, the α-glucosidase inhibitory activity of saponin **1** was three-fold stronger than acarbose, a widely used clinically useful drug, used as a positive control. Compounds **2** and **3** showed strong inhibition against α-glucosidase and lipase, with the respective IC_{50} values of 170, 190 μM and 190, 200 μM, however, exhibited no inhibitory activity against α-amylase. In this study, compound **1** showed weaker inhibitory activity against lipase. These results demonstrated that α-L-rhamnopyranosyl moiety with glycosyl fragment is favorable to enhance the inhibitory activity

Table. *Inhibitory Activities of Compounds* **1**–**3** *for α-Glucosidase, α-Amylase, and Lipase*

Compounds	IC_{50} [μM][a])		
	α-Glucosidase	α-Amylase	Lipase
1	160 ± 19	180 ± 19	790 ± 49
2	170 ± 25	NA[b])	190 ± 25
3	190 ± 24	NA	200 ± 27
Acarbose[d])	450 ± 40	600 ± 31	–[c])
Orlistat[d])	–	–	140 ± 25

[a]) The IC_{50} values in μM were calculated from the dose response curve of six concentrations of each test compound in triplicate. [b]) NA: not active. [c]) '–': not determined. [d]) Positive control.

Scheme 2



a) TMSOTf, CH_2Cl_2, −78°; 0°, CH_2Cl_2, 89% for **18**, 87% for **19**. *b*) 0°, CH_2Cl_2. *c*)1% AcCl in MeOH, CH_2Cl_2, 90% for **20**, 91% for **21**. *d*) TMSOTf, CH_2Cl_2, 0°, 87% for **22**, 90% for **23**, 89% for **24**. *e*) MeONa, MeOH/CH_2Cl_2, 93% for **1**, 90% for **2**, 91% for **3**.

against α-amylase, and the specific configuration of apioside seems to have a beneficial effect on the lipase inhibitory activities.

Conclusions. – In conclusion, a concise synthesis of the bidesmosidic oleanolic acid saponins **1**–**3** isolated from *Fadogia ancylantha* (Makoni tea) has been accomplished, and their inhibitory activities against α-glucosidase, α-amylase, and lipase were evaluated. On the basis of our results, the synthetic compounds **1**–**3** exhibited positive response against α-glucosidase, α-amylase, and lipase. In terms of structure–activity relationships, we can conclude that: *i*) the α-L-rhamnopyranosyl moiety with glycosyl fragment is favorable to enhance their inhibitory activity against α-amylase; *ii*) the specific configuration of apioside seems to have a beneficial effect on the lipase inhibitory activities. Thus, our study indicates that bidesmosidic oleanolic acid saponins represent an interesting class of compounds for further pharmacological studies and preclinical developments.

Experinental Part

General. Commercial reagents were used without further purification unless specialized. Solvents were dried and redistilled prior to use in the usual way. Thin-layer chromatography (TLC): precoated *E. Merck* Silica Gel *60* F_{254} plates. Flash column chromatography: silica gel (SiO_2; 200–300 mesh). Optical rotations: *PerkinElmer Model 241 MC* polarimeter. ^{1}H- and ^{13}C-NMR spectra: *JEOL JNM-ECP 600* spectrometer with tetramethylsilane as the internal standard, and chemical shifts are recorded in δ values. Mass spectra: *Q-TOF Global* mass spectrometer.

Compounds **8** *and* **9***: Typical Procedure.* To a soln. of **6** or **7** (2.43 g, 6.23 mmol) in dry CH_2Cl_2 (20 ml) was added a soln. of 33% HBr in glacial AcOH (6.6 ml). The mixture was stirred for 1 h at ambient temp. The mixture was poured into a 100 ml beaker containing crushed ice and diluted with CH_2Cl_2, and neutralized with a sat. aq. $NaHCO_3$ soln. The aq. soln. was extracted with CH_2Cl_2, and the org. extract was successively washed with $NaHCO_3$ soln. and brine. The org. layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure to provide the bromide as light yellow syrup. The crude bromide was immediately dissolved in dry CH_2Cl_2 (8 ml) and dry MeOH (8 ml), and 2,6-lutidine (1.2 ml) was added over the course of 5 min. The mixture was stirred at ambient temp. for 12 h. The soln. was diluted with CH_2Cl_2 and washed with a cold sat. aq. $NaHCO_3$ soln., a sat. aq. $CuSO_4$ soln. and brine. The org. layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude solid was recrystallized from Et_2O to afford the colorless crystalline **8** or **9**.

3,4,6-Tri-O*-acetyl-1,2*-O*-(1-methoxyethylidene)-α*-D*-glucopyranose* (**8**). Colorless crystalline. Yield 95%. ^{1}H-NMR ($CDCl_3$, 600 MHz): 5.75 (*d*, *J* = 3.0, 1 H, H–C(1)); 5.18 (*t*, *J* = 9.6, 1 H, H–C(3)); 4.93 (*dd*, *J* = 9.6, 2.8, 1 H, H–C(2)); 4.54 (*t*, *J* = 9.6, 1 H, H–C(4)); 4.37 (*dd*, *J* = 11.9, 3.6, 1 H, H_a–C(6)); 4.22–4.24 (*m*, 1 H, H–C(5)); 3.97 (*dd*, *J* = 11.9, 5.7, 1 H, H_b–C(6)); 3.27 (*s*, 3 H, MeO); 2.13, 2.09, 2.07 (3*s*, 3 H each, 3 Me); 1.71 (*s*, 3 H, Me). HR-ESI-MS: 385.1147 ($[M+Na]^+$, $C_{15}H_{22}NaO_{10}^+$; calc. 385.1105).

3,4,6-Tri-O*-acetyl-1,2*-O*-(1-methoxyethylidene)-α*-D*-galactopyranose* (**9**). Colorless crystalline. Yield 94%. ^{1}H-NMR ($CDCl_3$, 600 MHz): 5.87 (*d*, *J* = 4.7, 1 H, H–C(1)); 5.41 (*dd*, *J* = 9.3, 4.8, 1 H, H–C(2)); 5.09 (*dd*, *J* = 9.3, 3.7, 1 H, H–C(3)); 4.58 (*t*, *J* = 3.6, 1 H, H–C(4)); 4.39–4.42 (*m*, 1 H, H–C(5)); 4.21 (*dd*, *J* = 11.3, 4.6, 1 H, H_a–C(6)); 4.08 (*dd*, *J* = 11.3, 5.7, 1 H, H_b–C(6)); 3.25 (*s*, 3 H, MeO); 2.09, 2.01, 1.99 (3*s*, 3 H each, 3 Me); 1.63 (*s*, 3 H, Me); HR-ESI-MS: 385.1139 ($[M+Na]^+$, $C_{15}H_{22}NaO_{10}^+$; calc. 385.1105).

Compounds **10** *and* **11**: *Typical Procedure.* MeONa (140 mg, 2.48 mmol) was added to a stirred soln. of **8** or **9** (3.0 g, 0.82 mmol) in MeOH (20 ml). The mixture was stirred for 1 h and then concentrated under reduced pressure to afford the triol, quantitatively, which was used in the next step without further purification. The triol and DMAP (cat.) were dissolved in dry pyridine (5 ml) and BzCl (6 equiv., 0.04 mol, 5 ml) was added at 0° and stirring was continued for 12 h. The mixture was poured into ice water. The precipitate was dissolved in CH_2Cl_2, and was washed sequentially with 1 mol/l aq. HCl soln.,

$NaHCO_3$ (sat.) soln., NaCl (sat.) soln., dried (Na_2SO_4), and filtered. The solvent was evaporated to yield orange syrup. Recrystallization from AcOEt/hexane gave the tribenzoate **10** (or **11**) as colorless crystalline.

3,4,6-Tri-O-*benzoyl-1,2*-O-*(1-methoxyethylidene)*-α-D-*glucopyranose* (**10**). Colorless crystalline. Yield 80%. ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.35–8.02 (*m*, 15 arom. H); 5.95 (*t*, *J* = 9.6, 1 H, H–C(4)); 5.83 (*t*, *J* = 9.6, 1 H, H–C(3)); 5.76 (*d*, *J* = 2.9, 1 H, H–C(1)); 4.87 (*dd*, *J* = 9.6, 2.9, 1 H, H–C(2)); 4.67 (*dd*, *J* = 12.0, 3.2, 1 H, H_a–C(6)); 4.45 (*dd*, *J* = 12.0, 4.9, 1 H, H_b–C(6)); 4.15–4.18 (*m*, 1 H, H–C(5)); 3.26 (*s*, 3 H, MeO); 1.73 (*s*, 3 H, Me). HR-ESI-MS: 571.1593 ($[M+Na]^+$, $C_{30}H_{28}NaO_{10}^+$; calc. 571.1575).

3,4,6-Tri-O-*benzoyl-1,2*-O-*(1-methoxyethylidene)*-α-D-*galactopyranose* (**11**). Colorless crystalline. Yield 83%. ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.37–8.01 (*m*, 15 arom. H), 5.97 (*dd*, *J* = 9.7, 3.7, 1 H, H–C(3)); 5.83 (*t*, *J* = 3.6, 1 H, H–C(4)); 5.79 (*d*, *J* = 4.9, 1 H, H–C(1)); 5.53 (*dd*, *J* = 9.6, 4.9, 1 H, H–C(2)); 4.71 (*dd*, *J* = 12.1, 4.8, 1 H, H_a–C(6)); 4.53 (*dd*, *J* = 12.1, 3.7, 1 H, H_b–C(6)); 4.29–4.33 (*m*, 1 H, H–C(5)); 3.27 (*s*, 3 H, MeO); 1.65 (*s*, 3 H, Me). HR-ESI-MS: 571.1553 ($[M+Na]^+$, $C_{30}H_{28}NaO_{10}^+$; calc. 571.1574).

Compounds **12** *and* **13***: Typical Procedure.* Compound **10** or **11** (3.2 g, 6 mmol) was dissolved in glacial AcOH (20 ml). The soln. was stirred for 1 h at r.t., and then partitioned between AcOEt and H_2O. The org. layer was dried with Na_2SO_4, filtered, and concentrated under reduced pressure to yield **12** or **13** as yellow oil.

1,2-Di-O-*acetyl-3,4,6-tri*-O-*benzoyl*-α/β-D-*glucopyranose* (**12**). Yellow oil. Yield 97%. *Data of the* α*-Anomer:* ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.33–8.05 (*m*, 15 arom. H); 6.47 (*d*, *J* = 3.3, 1 H, H–C(1)); 5.97 (*t*, *J* = 9.7, 1 H, H–C(3)); 5.71 (*t*, *J* = 9.7, 1 H, H–C(4)); 5.37 (*dd*, *J* = 9.7, 3.6, 1 H, H–C(2)); 4.65 (*dd*, *J* = 12.1, 3.3, 1 H, H_a–C(6)); 4.47 (*dd*, *J* = 12.1, 5.1, 1 H, H_b–C(6)); 4.37–4.40 (*m*, 1 H, H–C(5)); 2.25, 1.97 (2*s*, 3 H each, 2 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 169.7; 168.7; 166.1; 165.9; 165.2; 133.7; 133.5; 133.3; 133.1; 132.5; 132.1; 132.0; 130.5; 130.3; 130.1; 129.9; 129.8; 129.7; 129.5; 129.1; 128.9; 128.7; 89.7; 70.8; 70.5; 69.7; 69.3; 62.8; 21.8; 20.6. HR-ESI-MS: 599.1551 ($[M+Na]^+$, $C_{31}H_{28}NaO_{11}^+$; calc. 599.1524).

1,2-Di-O-*acetyl-3,4,6-tri*-O-*benzoyl*-α/β-D-*galactopyranose* (**13**). Yellow oil. Yield 96%. *Data of the* α*-Anomer:* ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.35–8.03 (*m*, 15 arom. H); 6.51 (*d*, *J* = 3.7, 1 H, H–C(1)); 5.93 (*dd*, *J* = 9.9, 3.6, 1 H, H–C(3)); 5.75 (*t*, *J* = 3.6, 1 H, H–C(4)); 5.41 (*dd*, *J* = 9.9, 3.7, 1 H, H–C(2)); 4.71 (*dd*, *J* = 12.3, 3.5, 1 H, H_a–C(6)); 4.45–4.47 (*m*, 1 H, H–C(5)); 4.41 (*dd*, *J* = 12.3, 5.5, 1 H, H_b–C(6)); 2.21, 1.93 (2*s*, 3 H each, 2 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 170.1; 168.9; 166.0; 165.9; 165.1; 133.9; 133.5; 133.2; 133.1; 132.7; 132.1; 131.9; 130.6; 130.3; 130.1; 130.0; 129.9; 129.8; 129.7; 129.3; 129.1; 128.9; 128.5; 89.3; 70.7; 70.6; 69.9; 69.1; 62.5; 21.9; 20.3. HR-ESI-MS: 599.1543 ($[M+Na]^+$, $C_{31}H_{28}NaO_{11}^+$; calc. 599.1524).

Compounds **4** *and* **5***: Typical Procedure.* To a soln. of **12** or **13** (1.00 g, 1.74 mmol) in DMF (10 ml) was added $NH_2NH_2 \cdot AcOH$ (321 mg, 3.48 mmol), and the mixture was stirred for 3 h. Then, the mixture was concentrated to syrup, which was used in the next step without further purification. The syrup was dissolved in CH_2Cl_2 (20 ml) and then cooled to 0°. To this soln. was added $CNCCl_3$ (1.67 ml, 16.6 mmol) and DBU (5 drops). The mixture was stirred for 4 h at 0°, then concentrated. The residue was purified by SiO_2 CC (petroleum ether (PE)/AcOEt) to afford the product **4** or **5**.

2-O-*Acetyl-3,4,6-tri*-O-*benzoyl*-α-D-*glucopyranosyl Trichloroacetimidate* (=*2*-O-*Acetyl-3,4,6-tri*-O-*benzoyl-1*-O-*(2,2,2-trichloroethanimidoyl)*-α-D-*glucopyranose*; **4**). Amorphous white solid. Yield 78%. $[\alpha]_D^{27} = 17.0$ (*c* = 0.8, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 8.57 (br. *s*, 1 H, NH); 7.23–7.97 (*m*, 15 arom. H); 6.75 (*d*, *J* = 3.6, 1 H, H–C(1)); 6.20 (*t*, *J* = 9.9, 1 H, H–C(3)); 5.75 (*t*, *J* = 9.9, 1 H, H–C(4)); 5.41 (*dd*, *J* = 9.9, 3.6, 1 H, H–C(2)); 4.57 (*dd*, *J* = 12.3, 3.1, 1 H, H_a–C(6)); 4.51–4.54 (*m*, 1 H, H–C(5)); 4.41 (*dd*, *J* = 12.3, 5.0, 1 H, H_b–C(6)); 2.01 (*s*, 3 H, Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 169.3 (Me*C*O); 165.9; 165.3; 165.1; 160.3 (C=N); 133.6; 133.3; 133.1; 129.9; 129.8; 129.5; 129.3; 128.3; 128.1; 127.9; 127.7; 127.5; 93.3 (C(1)); 70.6; 70.4; 70.2; 68.7; 62.3; 20.9. HR-ESI-MS: 700.0531 ($[M+Na]^+$, $C_{31}H_{26}Cl_3NNaO_{10}^+$; calc. 700.0515).

2-O-*Acetyl-3,4,6-tri*-O-*benzoyl*-α-D-*galactopyranosyl Trichloroacetimidate* (=*2*-O-*Acetyl-3,4,6-tri*-O-*benzoyl-1*-O-*(2,2,2-trichloroethanimidoyl)*-α-D-*galactopyranose*; **5**). Amorphous white solid. Yield 81%. $[\alpha]_D^{27} = 23.5$ (*c* = 1.3, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 8.69 (*s*, 1 H, NH); 7.25–8.09 (*m*, 15 arom. H); 6.81 (*d*, *J* = 3.6, 1 H, H–C(1)); 6.19 (*t*, *J* = 3.7, 1 H, H–C(4)); 6.01 (*dd*, *J* = 10.0, 3.7, 1 H, H–C(3)); 5.76 (*dd*, *J* = 10.0, 3.6, 1 H, H–C(2)); 4.76–4.80 (*m*, 1 H, H–C(5)); 4.60 (*dd*, *J* = 12.1, 4.6, 1 H,

H_a–C(6)); 4.43 (*dd*, *J* = 12.1, 5.9, 1 H, H_b–C(6)); 2.03 (*s*, 3 H, Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 169.9 (Me*C*O); 165.9; 165.6; 165.3; 160.5 (C=N); 133.9; 133.7; 133.3; 133.2; 129.9; 129.8; 129.7; 129.4; 128.9; 128.7; 128.1; 127.9; 127.8; 127.3; 93.9 (C(1)); 69.9; 68.7; 68.5; 67.7; 62.3; 21.3. HR-ESI-MS: 700.0542 ([*M* + Na]$^+$, $C_{31}H_{26}Cl_3NNaO_{10}^+$; calc. 700.0515).

Compounds **18** *and* **19***: Typical Procedure.* A mixture of oleanolic ester **14** (200 mg, 0.29 mmol), trichloroacetimidate **15** (0.35 mmol, 1.2 equiv.), and powdered 4 Å molecular sieves in dry CH_2Cl_2 (8 ml) were stirred for 30 min at r.t. and then cooled to 0°. TMSOTf (15 µl, 0.09 mmol, 0.3 equiv.) was added slowly. After being stirred at −78° for 30 min, the mixture was warmed up to r.t. for 30 min, and then cooled to 0°. A soln. of **4** or **5** (298 mg, 0.44 mmol, 1.5 equiv.) in dry CH_2Cl_2 (10 ml) was injected slowly. The mixture was stirred at 0° for 30 min, and then warmed up to r.t. for another 30 min. The reaction was quenched by addition of Et_3N and then filtered. The filtrate was concentrated and purified by SiO_2 CC (PE/AcOEt) to afford the product **18** or **19**.

*2-*O*-Acetyl-3,4,6-tri-*O*-benzoyl-1-*O*-{(3β)-28-oxo-3-[(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-oxy]olean-12-en-28-yl}-β-*D*-glucopyranose* (**18**). Amorphous white solid. Yield 89%. $[\alpha]_D^{27} = 16.9$ (*c* = 1.1, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.33–8.05 (*m*, 35 arom. H); 5.99 (*t*, *J* = 9.6, 1 H, H–C(3″)); 5.93 (*d*, *J* = 8.7, 1 H, H–C(1″)); 5.89 (*t*, *J* = 9.9, 1 H, H–C(3′)); 5.75 (*t*, *J* = 9.6, 1 H, H–C(4″)); 5.69 (*dd*, *J* = 9.6, 8.7, 1 H, H–C(2″)); 5.60 (*t*, *J* = 9.9, 1 H, H–C(4′)); 5.55 (*dd*, *J* = 9.9, 7.8, 1 H, H–C(2′)); 5.27 (*t*, *J* = 3.6, 1 H, H–C(12)); 4.87 (*d*, *J* = 7.8, 1 H, H–C(1′)); 4.61 (*dd*, *J* = 11.9, 3.2, 1 H, H_a–C(6′)); 4.55 (*dd*, *J* = 11.9, 2.8, 1 H, H_a–C(6″)); 4.51 (*dd*, *J* = 11.9, 6.7, 1 H, H_b–C(6′)); 4.47 (*dd*, *J* = 11.9, 5.0, 1 H, H_b–C(6″)); 4.22–4.25 (*m*, 1 H, H–C(5″)); 4.16–4.19 (*m*, 1 H, H–C(5′)); 3.10 (*dd*, *J* = 11.9, 4.6, 1 H, H–C(3)); 2.91 (*dd*, *J* = 13.7, 3.7, 1 H, H–C(18)); 2.01 (*s*, 3 H, Me), 0.93, 0.85, 0.81, 0.76, 0.71, 0.62, 0.45 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 178.1 (C(28)); 169.9 (Me*C*O); 165.9; 165.8; 165.5; 165.3; 163.7; 163.5; 163.1; 143.5 (C(13)); 138.5; 138.3; 138.1; 137.9; 137.5; 136.7; 136.3; 136.1; 133.6; 133.3; 132.9; 129.9; 129.8; 129.7; 128.5; 128.3; 122.4 (C(12)); 105.1 (C(1′)); 97.1 (C(1″)); 89.6 (C(3)); 78.5; 77.5; 71.9; 70.6; 70.0; 67.3; 66.7; 66.1; 65.9; 62.7; 55.9; 47.9; 41.7; 39.3; 36.7; 33.6; 31.9; 27.8; 26.7; 25.9; 24.7; 21.2; 17.6; 17.1; 15.6. HR-ESI-MS: 1573.6501 ([*M* + Na]$^+$, $C_{93}H_{98}NaO_{21}^+$; calc. 1573.6493).

*2-*O*-Acetyl-3,4,6-tri-*O*-benzoyl-1-*O*-{(3β)-28-oxo-3-[(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)-oxy]olean-12-en-28-yl}-β-*D*-galactopyranose* (**19**). Amorphous white solid. Yield 87%. $[\alpha]_D^{27} = 41.7$ (*c* = 1.9, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.31–8.03 (*m*, 35 arom. H); 5.96 (*dd*, *J* = 9.9, 3.7, 1 H, H–C(3″)); 5.91 (*d*, *J* = 8.3, 1 H, H–C(1″)); 5.87 (*t*, *J* = 9.9, 1 H, H–C(3′)); 5.71 (*t*, *J* = 3.7, 1 H, H–C(4″)); 5.66 (*dd*, *J* = 9.9, 8.3, 1 H, H–C(2″)); 5.61 (*t*, *J* = 9.9, 1 H, H–C(4′)); 5.57 (*dd*, *J* = 9.9, 7.7, 1 H, H–C(2′)); 5.29 (*t*, *J* = 3.6, 1 H, H–C(12)); 4.89 (*d*, *J* = 7.7, 1 H, H–C(1′)); 4.65 (*dd*, *J* = 12.1, 3.3, 1 H, H_a–C(6′)); 4.55 (*dd*, *J* = 11.9, 2.9, 1 H, H_a–C(6″)); 4.51 (*dd*, *J* = 12.1, 5.7, 1 H, H_b–C(6′)); 4.44 (*dd*, *J* = 11.9, 5.1, 1 H, H_b–C(6″)); 4.25–4.28 (*m*, 1 H, H–C(5″)); 4.17–4.21 (*m*, 1 H, H–C(5′)); 3.12 (*dd*, *J* = 11.9, 3.7, 1 H, H–C(3)); 2.89 (*dd*, *J* = 13.7, 4.3, 1 H, H–C(18)); 2.00 (*s*, 3 H, Me), 0.93, 0.87, 0.81, 0.76, 0.70, 0.62, 0.49 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 177.9 (C(28)); 170.1 (Me*C*O); 165.9; 165.7; 165.5; 165.1; 163.7; 163.6; 163.1; 143.3 (C(13)); 138.9; 138.5; 138.1; 137.9; 137.6; 136.7; 136.3; 136.1; 133.6; 133.1; 132.9; 129.9; 129.8; 129.6; 128.5; 128.1; 122.3 (C(12)); 104.9 (C(1′)); 96.7 (C(1″)); 89.7 (C(3)); 78.3; 77.5; 72.3; 70.6; 69.9; 67.3; 66.9; 66.3; 65.6; 63.0; 55.9; 47.9; 41.7; 39.5; 36.7; 33.6; 31.7; 27.8; 26.7; 25.9; 24.7; 21.0; 17.6; 17.3; 15.6. HR-ESI-MS: 1573.6479 ([*M* + Na]$^+$, $C_{93}H_{98}NaO_{21}^+$; calc. 1573.6493).

Compounds **20** *and* **21***: Typical Procedure.* To a soln. of compound **18** or **19** (180 mg, 0.12 mmol) in dry CH_2Cl_2 (10 ml) was added 1% AcCl in MeOH (1 ml). The mixture was stirred for 5 h, and then, the reaction was quenched by addition of Et_3N. The mixture was concentrated and purified by SiO_2 CC (PE/AcOEt) to afford the product **20** or **21**.

*3,4,6-Tri-*O*-benzoyl-1-*O*-{(3β)-28-oxo-3-[(2,3,4,6-tetra-*O*-benzoyl-β-*D*-glucopyranosyl)oxy]olean-12-en-28-yl}-β-*D*-glucopyranose* (**20**). Amorphous white solid. Yield 90%. $[\alpha]_D^{27} = 13.8$ (*c* = 1.6, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.31–8.07 (*m*, 35 arom. H); 5.97 (*t*, *J* = 9.7, 1 H, H–C(3″)); 5.93 (*d*, *J* = 8.3, 1 H, H–C(1″)); 5.88 (*t*, *J* = 9.9, 1 H, H–C(3′)); 5.73 (*t*, *J* = 9.9, 1 H, H–C(4″)); 5.63 (*t*, *J* = 9.7, 1 H, H–C(4′)); 5.57 (*dd*, *J* = 9.9, 8.3, 1 H, H–C(2″)); 5.53 (*dd*, *J* = 9.7, 7.7, 1 H, H–C(2′)); 5.27 (*t*, *J* = 3.7, 1 H, H–C(12)); 4.89 (*d*, *J* = 7.7, 1 H, H–C(1′)); 4.63 (*dd*, *J* = 12.3, 3.9, 1 H, H_a–C(6′)); 4.55 (*dd*, *J* = 12.1, 2.8, 1 H, H_a–C(6″)); 4.50 (*dd*, *J* = 12.3, 6.5, 1 H, H_b–C(6′)); 4.43 (*dd*, *J* = 12.1, 5.3, 1 H, H_b–C(6″)); 4.25–4.28 (*m*, 1 H, H–C(5″)); 4.17–4.21 (*m*, 1 H, H–C(5′)); 3.11 (*dd*, *J* = 11.9, 3.7, 1 H, H–C(3)); 2.89 (*dd*, *J* = 13.7, 4.3, 1 H, H–C(18)); 0.97, 0.85, 0.80, 0.76, 0.73, 0.62, 0.49 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$,

150 MHz): 178.3 (C(28)); 165.9; 165.8; 165.7; 165.3; 163.9; 163.5; 163.3; 163.1; 143.3 (C(13)); 138.6; 138.3; 138.0; 137.9; 137.7; 136.7; 136.3; 136.0; 133.6; 133.2; 132.9; 129.9; 129.8; 129.7; 128.5; 128.3; 122.3 (C(12)); 105.3 (C(1′)); 97.3 (C(1″)); 89.7 (C(3)); 78.9; 77.3; 71.7; 70.6; 69.7; 67.3; 66.7; 66.3; 65.6; 62.7; 55.7; 47.9; 41.7; 39.3; 36.7; 33.6; 31.9; 27.8; 26.7; 25.9; 24.6; 17.6; 17.1; 15.3. HR-ESI-MS: 1531.6399 ([M + Na]$^+$, $C_{91}H_{96}NaO_{20}^+$; calc. 1531.6387).

3,4,6-Tri-O-*benzoyl-1*-O-*{(3β)-28-oxo-3-[(2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl)oxy]olean-12-en-28-yl}-β*-D-*galactopyranose* (**21**). Amorphous white solid. Yield 91%. $[\alpha]_D^{27} = 27.6$ ($c = 1.8$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.35 – 8.01 (*m*, 35 arom. H); 5.97 (*dd*, $J = 9.7, 3.7$, 1 H, H–C(3″)); 5.89 (*d*, $J = 8.5$, 1 H, H–C(1″)); 5.85 (*t*, $J = 9.7$, 1 H, H–C(3′)); 5.73 (*t*, $J = 3.7$, 1 H, H–C(4″)); 5.65 (*dd*, $J = 9.7, 8.5$, 1 H, H–C(2″)); 5.60 (*t*, $J = 9.7$, 1 H, H–C(4′)); 5.55 (*dd*, $J = 7.9, 9.9$, 1 H, H–C(2′)); 5.31 (*t*, $J = 3.6$, 1 H, H–C(12)); 4.87 (*d*, $J = 7.9$, 1 H, H–C(1′)); 4.66 (*dd*, $J = 12.3, 3.5$, 1 H, H_a–C(6′)); 4.57 (*dd*, $J = 12.0, 3.1$, 1 H, H_a–C(6″)); 4.51 (*dd*, $J = 12.3, 5.3$, 1 H, H_b–C(6′)), 4.44 (*dd*, $J = 12.1, 5.7$, 1 H, H_b–C(6″)); 4.21 – 4.25 (*m*, 1 H, H–C(5″)); 4.15 – 4.18 (*m*, 1 H, H–C(5′)); 3.10 (*dd*, $J = 11.9, 4.3$, 1 H, H–C(3)); 2.87 (*dd*, $J = 13.7, 3.7$, 1 H, H–C(18)); 0.97, 0.89, 0.80, 0.73, 0.69, 0.61, 0.51 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 178.1 (C(28)); 165.9; 165.7; 165.6; 165.0; 163.9; 163.6; 163.5; 143.7 (C(13)); 138.7; 138.5; 138.3; 137.9; 137.5; 136.7; 136.3; 136.1; 133.9; 133.6; 133.3; 132.9; 129.9; 129.8; 129.5; 128.3; 128.0; 122.4 (C(12)); 104.7 (C(1′)); 96.9 (C(1″)); 89.3 (C(3)); 78.1; 76.9; 72.1; 70.9; 69.6; 67.1; 66.5; 66.1; 65.6; 63.1; 55.9; 47.9; 41.7; 39.5; 36.9; 33.6; 31.5; 27.8; 26.7; 25.9; 24.7; 17.6; 17.5; 15.6. HR-ESI-MS: 1531.6361 ([M + Na]$^+$, $C_{91}H_{96}NaO_{20}^+$; calc. 1531.6387).

Compounds **22** – **24**: *Typical Procedure.* A mixture of **20** or **21** (100 mg, 0.07 mmol), trichloroacetimidate **15**, **16**, or **17** (0.084 mmol, 1.20 equiv.) and powdered 4 Å molecular sieves in dry CH_2Cl_2 (5 ml) were stirred for 30 min at r.t. and then cooled to 0°. TMSOTf (5 µl, 0.02 mmol, 0.3 equiv.) was added slowly. After being stirred at 0° for 1 h, the mixture was warmed up to r.t. for 30 min. The reaction was quenched by addition of Et_3N, and then filtered. The filtrate was concentrated and purified by a SiO_2 CC (PE/AcOEt) to afford the products **22** – **24**.

3,4,6-Tri-O-*benzoyl-1*-O-*{(3β)-28-oxo-3-[(2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl)oxy]olean-12-en-28-yl}-2*-O-*(2,3,4-tri*-O-*benzoyl-6-deoxy-α*-L-*mannopyranosyl)-β*-D-*glucopyranose* (**22**). Amorphous white solid. Yield 87%. $[\alpha]_D^{27} = 56.1$ ($c = 0.83$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.27 – 8.09 (*m*, 50 arom. H); 5.95 (*t*, $J = 9.9$, 1 H, H–C(3‴)); 5.91 (*d*, $J = 8.5$, 1 H, H–C(1″)); 5.88 (*dd*, $J = 10.1, 3.2$, 1 H, H–C(3″)); 5.85 (*t*, $J = 9.9$, 1 H, H–C(3′)); 5.81 (*dd*, $J = 5.0, 1.8$, 1 H, H–C(2‴)); 5.77 (br. *s*, 1 H, H–C(1‴)); 5.74 (*t*, $J = 9.9$, 1 H, H–C(4″)); 5.67 (*t*, $J = 10.1$, 1 H, H–C(4‴)); 5.61 (*t*, $J = 9.9$, 1 H, H–C(4′)); 5.55 (*dd*, $J = 9.9, 8.5$, 1 H, H–C(2″)); 5.51 (*dd*, $J = 9.9, 7.9$, 1 H, H–C(2′)); 5.23 (*t*, $J = 3.7$, 1 H, H–C(12)); 4.89 (*d*, $J = 7.9$, 1 H, H–C(1′)); 4.65 (*dd*, $J = 12.1, 3.3$, 1 H, H_a–C(6′)); 4.57 (*dd*, $J = 12.0, 3.1$, 1 H, H_a–C(6″)), 4.50 – 4.55 (*m*, 2 H, H–C(5‴), H_b–C(6′)); 4.41 (*dd*, $J = 12.0, 5.6$, 1 H, H_b–C(6″)); 4.23 – 4.27 (*m*, 2 H, H–C(5′), H–C(5″)); 3.21 (*dd*, $J = 11.9, 4.6$, 1 H, H–C(3)); 2.91 (*dd*, $J = 13.1, 3.2$, 1 H, H–C(18)); 1.36 (*d*, $J = 6.0$, 3 H, H–C(6‴)); 1.13, 0.95, 0.89, 0.80, 0.76, 0.73, 0.63 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 177.6 (C(28)); 165.9; 165.8; 165.7; 165.3; 163.7; 163.5; 163.3; 163.1; 143.8 (C(13)); 138.7; 138.5; 138.3; 138.0; 137.9; 137.8; 136.7; 136.5; 136.1; 133.6; 133.2; 132.9; 129.9; 129.8; 129.7; 128.5; 128.2; 128.1; 122.5 (C(12)); 104.9 (C(1′)); 97.7 (C(1‴)); 97.1 (C(1″)); 89.9 (C(3)); 80.9; 78.1; 75.3; 72.1; 70.7; 70.3; 69.5; 67.3; 66.7; 66.3; 65.9; 65.6; 62.7; 56.0; 47.9; 41.7; 41.5; 39.3; 36.7; 33.6; 31.9; 27.8; 26.7; 25.9; 23.6; 19.3; 17.6; 17.1; 15.3. HR-MALDI-MS: 1989.7771 ([M + Na]$^+$, $C_{118}H_{118}NaO_{27}^+$; calc. 1989.7753).

3,4,6-Tri-O-*benzoyl-2*-O-*{(2*S*,3*R*,4*S*)-3,4-bis(acetyloxy)-4-[(acetyloxy)methyl]tetrahydrofuran-2-yl}-1*-O-*{(3β)-28-oxo-3-[(2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl)oxy]olean-12-en-28-yl}-β*-D-*glucopyranose* (**23**). Amorphous white solid. Yield 90%. $[\alpha]_D^{27} = 95.3$ ($c = 1.2$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.33 – 8.01 (*m*, 35 arom. H); 5.99 (*t*, $J = 9.9$, 1 H, H–C(3″)); 5.95 (*d*, $J = 8.1$, 1 H, H–C(1″)); 5.87 (*t*, $J = 9.7$, 1 H, H–C(3′)); 5.73 (*t*, $J = 9.9$, 1 H, H–C(4″)); 5.60 (*t*, $J = 9.7$, 1 H, H–C(4′)); 5.53 (*dd*, $J = 9.9, 8.1$, 1 H, H–C(2″)); 5.50 (*dd*, $J = 9.7, 7.9$, 1 H, H–C(2′)); 5.29 (*s*, 1 H, H–C(1‴)); 5.21 (*t*, $J = 3.6$, 1 H, H–C(12)); 4.93 (*d*, $J = 7.9$, 1 H, H–C(1′)); 4.67 (*dd*, $J = 12.3, 3.7$, 1 H, H_a–C(6′)); 4.53 (*dd*, $J = 11.9, 3.3$, 1 H, H_a–C(6″)); 4.50 (*d*, $J = 12.5$, 1 H, H_a–C(3‴)); 4.47 (*dd*, $J = 12.3, 5.8$, 1 H, H_b–C(6′)); 4.45 (*d*, $J = 12.5$, 1 H, H_b–C(3‴)), 4.40 (*dd*, $J = 11.9, 5.3$, 1 H, H_b–C(6″)); 4.35 (*d*, $J = 10.7$, 1 H, H_a–C(4‴)); 4.27 – 4.31 (*m*, 1 H, H–C(5′)); 4.19 – 4.22 (*m*, 1 H, H–C(5″)); 4.17 (*d*, $J = 10.7$, 1 H, H_b–C(4‴)); 3.19 (*dd*, $J = 11.9, 4.3$, 1 H, H–C(3)); 2.89 (*dd*, $J = 13.3, 3.7$, 1 H, H–C(18)); 2.17, 2.00, 1.91 (3*s*, 3 H each, 3 Me), 1.12, 0.97, 0.89, 0.83, 0.76, 0.71, 0.62 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 177.9 (C(28)); 170.1; 169.7; 169.3

(Me*C*O); 165.9; 165.7; 165.5; 165.3; 163.9; 163.5; 163.3; 163.0; 143.5 (C(13)); 138.5; 138.2; 138.0; 137.9; 136.7; 136.5; 136.0; 133.5; 133.1; 132.9; 129.9; 129.7; 128.5; 128.1; 122.3 (C(12)); 106.7 (C(1‴)); 104.3 (C(1′)); 97.8 (C(1″)); 89.7 (C(3)); 83.9; 80.3; 78.5; 76.1; 75.3; 73.0; 72.1; 70.5; 69.5; 67.3; 66.4; 65.9; 65.6; 63.1; 56.1; 47.9; 41.9; 41.5; 39.5; 36.7; 33.6; 31.9; 27.9; 26.7; 25.9; 23.6; 20.9; 20.5; 20.1; 19.3; 17.6; 17.1; 15.2. HR-MALDI-MS: 1789.7143 ($[M+Na]^+$, $C_{102}H_{110}NaO_{27}^+$; calc. 1789.7127).

3,4,6-Tri-O-*benzoyl-1*-O-*[(3β)-28-oxo-3-[(2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl)oxy]olean-12-en-28-yl]-2*-O-*(2,3,4,6-tetra*-O-*benzoyl-β*-D-*glucopyranosyl)-β*-D-*galactopyranose* (**24**). Amorphous white solid. Yield 89%. $[\alpha]_D^{27} = 87.9$ ($c = 0.9$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$, 600 MHz): 7.29–8.11 (*m*, 55 arom. H); 5.97 (*dd*, *J* = 9.9, 3.6, 1 H, H–C(3″)); 5.91 (*d*, *J* = 8.3, 1 H, H–C(1″)); 5.85 (*t*, *J* = 9.9, 1 H, H–C(3′)); 5.83 (*t*, *J* = 9.9, 1 H, H–C(3‴)); 5.75 (*t*, *J* = 3.6, 1 H, H–C(4″)); 5.65 (*dd*, *J* = 9.9, 8.3, 1 H, H–C(2″)); 5.59 (*t*, *J* = 9.9, 1 H, H–C(4‴)); 5.56 (*t*, *J* = 9.9, 1 H, H–C(4′)); 5.51 (*dd*, *J* = 9.9, 7.9, 1 H, H–C(2′)); 5.44 (*t*, *J* = 9.1, 1 H, H–C(2‴)); 5.30 (*t*, *J* = 3.7, 1 H, H–C(12)); 5.01 (*d*, *J* = 8.2, 1 H, H–C(1‴)); 4.89 (*d*, *J* = 7.9, 1 H, H–C(1′)); 4.61 (*dd*, *J* = 12.1, 3.7, 1 H, H_a–C(6′)); 4.53 (*dd*, *J* = 12.0, 3.5, 1 H, H_a–C(6″)); 4.49 (*dd*, *J* = 12.1, 5.7, 1 H, H_b–C(6′)); 4.45 (*dd*, *J* = 12.0, 5.0, 1 H, H_b–C(6″)); 4.18–4.23 (*m*, 2 H, H–C(5″), H_a–C(6‴)); 4.13–4.16 (*m*, 1 H, H–C(5′)); 3.81–3.85 (*m*, H–C(5‴), H_b–C(6‴)); 3.12 (*dd*, *J* = 11.9, 3.7, 1 H, H–C(3)); 2.85 (*dd*, *J* = 13.7, 4.6, 1 H, H–C(18)); 1.13, 0.97, 0.83, 0.79, 0.76, 0.69, 0.62 (7*s*, 3 H each, 7 Me). ^{13}C-NMR ($CDCl_3$, 150 MHz): 178.3 (C(28)); 165.9; 165.7; 165.5; 165.0; 164.9; 163.9; 163.7; 163.5; 163.1; 143.9 (C(13)); 138.9; 138.7; 138.5; 138.3; 137.9; 137.7; 136.7; 136.3; 136.0; 133.9; 133.7; 133.6; 133.3; 132.9; 129.9; 129.8; 129.5; 128.3; 128.0; 127.9; 122.3 (C(12)); 104.1 (C(1′)); 99.9 (C(1‴)); 96.7 (C(1″)); 89.6 (C(3)); 78.1; 77.3; 76.9; 74.5; 72.1; 70.9; 70.3; 69.6; 67.5; 67.1; 66.5; 66.1; 65.6; 63.1; 62.9; 55.6; 47.9; 41.7; 39.5; 36.9; 33.6; 32.9; 31.5; 27.8; 26.7; 25.9; 24.7; 17.7; 17.5; 15.6. HR-MALDI-MS: 2109.7981 ($[M+Na]^+$, $C_{125}H_{122}NaO_{29}^+$; calc. 2109.7964).

Compounds **1**–**3**: *Typical Procedure.* To a soln. of fully protected oleanolic acid glycosides **22**–**24** (50 mg) in dry 1:2 CH_2Cl_2/MeOH (10 ml) was added a newly prepared MeONa in MeOH soln. (1.0 mol/l, 0.20 ml). The mixture was stirred at r.t. 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 SiO_2 CC to give the target compounds **1**–**3** as white amorphous solids.

2-O-*(6-Deoxy-α*-L-*mannopyranosyl)-1*-O-*[(3β)-3-(β*-D-*glucopyranosyloxy)-28-oxoolean-12-en-28-yl]-β*-D-*glucopyranose* (**1**). Amorphous white solid. Yield 93%. $[\alpha]_D^{27} = -4.1$ ($c = 0.17$, MeOH). ^{1}H-NMR (CD_3OD, 600 MHz): 5.45 (*d*, *J* = 7.6, 1 H, H–C(1″)); 5.36 (*d*, *J* = 1.4, 1 H, H–C(1‴)); 5.26 (*t*, *J* = 3.6, 1 H, H–C(12)); 4.30 (*d*, *J* = 7.7, 1 H, H–C(1′)); 3.91 (*dd*, *J* = 2.1, 1.4, 1 H, H–C(2‴)); 3.84 (*dd*, *J* = 12.0, 2.6, 1 H, H_a–C(6′)); 3.80 (*dd*, *J* = 12.0, 3.6, 1 H, H_a–(6″)); 3.73–3.76 (*m*, 1 H, H–C(5‴)); 3.69 (*dd*, *J* = 12.0, 4.1, 1 H, H_b–C(6′)); 3.67 (*dd*, *J* = 8.5, 2.0, 1 H, H–C(3‴)); 3.65 (*dd*, *J* = 12.0, 4.5, 1 H, H_b–C(6″)); 3.55 (*dd*, *J* = 9.0, 7.5, 1 H, H–C(2″)); 3.41 (*t*, *J* = 9.0, 1 H, H–C(3″)); 3.39 (*t*, *J* = 8.5, 1 H, H–C(4‴)); 3.37 (*t*, *J* = 9.0, 1 H, H–C(4″)); 3.35 (*t*, *J* = 9.0, 1 H, H–C(3′)); 3.30–3.33 (*m*, 1 H, H–C(5″)); 3.29 (*t*, *J* = 9.0, 1 H, H–C(4′)); 3.23–3.26 (*m*, 1 H, H–C(5′)); 3.19 (*dd*, *J* = 9.0, 7.7, 1 H, H–C(2′)); 3.16 (*dd*, *J* = 11.9, 4.6, 1 H, H–C(3)); 2.83 (*dd*, *J* = 14.0, 3.3, 1 H, H–C(18)); 1.26 (*d*, *J* = 6.6, 3 H, H–C(6‴)); 1.14, 1.03, 0.95, 0.93, 0.90, 0.85, 0.78 (7*s*, 3 H each, 7 Me). ^{13}C-NMR (CD_3OD, 150 MHz): 177.9 (C(28)); 144.8 (C(13)); 122.9 (C(12)); 105.9 (C(1′)); 101.6 (C(1‴)); 94.7 (C(1″)); 90.1 (C(3)); 78.8 (C(2″)); 78.0 (C(3‴)); 77.8 (C(5″)); 77.3 (C(3′)); 76.9 (C(5′)); 75.3 (C(2′)); 73.4 (C(4‴)); 71.7 (C(3‴)); 73.5 (C(2‴)); 70.7 (C(4″)); 70.6 (C(4′)); 69.8 (C(5‴)); 62.2 (C(6″)); 61.8 (C(6′)); 56.3; 48.3; 47.3; 46.5; 42.3; 40.2; 39.6; 39.1; 37.3; 34.0; 33.3; 32.8; 31.9; 30.7; 28.9; 27.8; 25.6; 25.1; 23.3; 23.2; 22.7; 18.4; 17.9 (C(6‴)); 16.8; 16.1. HR-ESI-MS: 949.5123 ($[M+Na]^+$, $C_{48}H_{78}NaO_{17}^+$; calc. 949.5137).

2-O-*[(2*S*,3*R*,4*S*)-Tetrahydro-3,4-dihydroxy-4-(hydroxymethyl)furan-2-yl]-1*-O-*[(3β)-3-(β*-D-*glucopyranosyloxy)-28-oxoolean-12-en-28-yl]-β*-D-*glucopyranose* (**2**). Amorphous white solid. Yield 90%. $[\alpha]_D^{27} = -6.5$ ($c = 0.12$, MeOH). ^{1}H-NMR (CD_3OD, 600 MHz): 5.42 (*d*, *J* = 2.0, 1 H, H–C(1‴)); 5.39 (*d*, *J* = 7.6, 1 H, H–C(1″)); 5.25 (*t*, *J* = 3.6, 1 H, H–C(12)); 4.33 (*d*, *J* = 7.6, 1 H, H–C(1′)); 4.01 (*d*, *J* = 10.0, 1 H, H_a–C(4‴)); 3.96 (*d*, *J* = 2.0, 1 H, H–C(2‴)); 3.83 (*dd*, *J* = 12.1, 3.5, 1 H, H_a–C(6″)); 3.81 (*dd*, *J* = 12.1, 2.5, 1 H, H_a–C(6′)); 3.72 (*d*, *J* = 10.0, 1 H, H_b–C(4‴)); 3.67 (*dd*, *J* = 12.1, 4.0, 1 H, H_b–C(6′)); 3.64 (*dd*, *J* = 12.1, 4.5, 1 H, H_b–C(6″)); 3.53 (*dd*, *J* = 9.0, 7.6, 1 H, H–C(2″)); 3.51 (br. *s*, 1 H, H–C(5‴)); 3.38 (*t*, *J* = 9.0, 1 H, H–C(3″)); 3.36 (*t*, *J* = 9.0, 1 H, H–C(4″)); 3.33 (*t*, *J* = 9.0, 1 H, H–C(3′)); 3.30–3.33 (*m*, 1 H, H–C(5″)); 3.27 (*t*, *J* = 9.0, 1 H, H–C(4′)); 3.22–3.26 (*m*, 1 H, H–C(5′)); 3.17 (*dd*, *J* = 9.0, 7.6, 1 H, H–C(2′)); 3.15 (*dd*, *J* = 11.9, 4.3, 1 H, H–C(3)); 2.83 (*dd*, *J* = 14.0, 3.7, 1 H, H–C(18)); 1.14, 1.02, 0.95,

0.93, 0.91, 0.85, 0.76 (7*s*, 3 H each, 7 Me). ^{13}C-NMR (CD_3OD, 150 MHz): 177.8 (C(28)); 144.8 (C(13)); 122.9 (C(12)); 106.9 (C(1′)); 110.7 (C(1‴)); 94.7 (C(1″)); 90.1 (C(3)); 79.8 (C(3‴)); 79.1 (C(2″)); 77.9 (C(3′)); 77.8 (C(2‴)); 77.3 (C(5′)); 77.1 (C(5″)); 76.6 (C(3″)); 75.3 (C(2′)); 74.7 (C(4‴)); 73.3 (C(4″)); 71.2 (C(4′)); 64.7 (C(5‴)); 62.2 (C(6″)); 62.1 (C(6′)); 56.3; 48.3; 47.2; 46.5; 42.3; 40.1; 39.6; 39.2; 37.3; 34.1; 33.3; 32.8; 31.9; 30.6; 28.9; 27.9; 25.6; 25.1; 23.3; 23.2; 22.7; 18.5; 16.8; 16.1. HR-ESI-MS: 935.5383 ([*M* + Na]$^+$, $C_{47}H_{76}NaO_{17}^+$; calc. 935.5361).

2-O-*β*-D-*Glucopyranosyl-1*-O-*[(3β)-3-(β*-D-*glucopyranosyloxy)-28-oxoolean-12-en-28-yl]-β*-D-*galactopyranose* (**3**). Amorphous white solid. Yield 91%. $[\alpha]_D^{27} = -4.1$ ($c = 0.11$, MeOH). ^{1}H-NMR (CD_3OD, 600 MHz): 5.45 (*d*, *J* = 7.5, 1 H, H–C(1″)); 4.81 (*d*, *J* = 7.6, 1 H, H–C(1‴)); 5.24 (*t*, *J* = 3.7, 1 H, H–C(12)); 4.31 (*d*, *J* = 7.6, 1 H, H–C(1′)); 3.91 (*dd*, *J* = 12.0, 2.5, 1 H, H_a–C(6‴)); 3.89 (*dd*, *J* = 9.9, 7.5, 1 H, H–C(2″)); 3.81 (*dd*, *J* = 12.0, 2.5, 1 H, H_a–C(6′)); 3.79 (*dd*, *J* = 11.9, 7.5, 1 H, H_a–C(6″)); 3.69 (*dd*, *J* = 11.9, 4.5, 1 H, H_b–C(6″)); 3.67 (*dd*, *J* = 9.9, 3.2, 1 H, H–C(3‴)); 3.65 (*dd*, *J* = 12.0, 4.0, 1 H, H_b–C(6′)); 3.62 (*dd*, *J* = 12.0, 4.0, 1 H, H_b–C(6‴)); 3.55 – 3.58 (*m*, 1 H, H–C(5″)); 3.37 (*t*, *J* = 9.0, 1 H, H–C(4‴)); 3.35 (*d*, *J* = 3.2, 1 H, H–C(4″)); 3.31 (*d*, *J* = 9.0, 1 H, H–C(3′)); 3.27 – 3.30 (*m*, 1 H, H–C(5‴)); 3.28 (*t*, *J* = 9.0, 1 H, H–C(4′)); 3.21 – 3.25 (*m*, 1 H, H–C(5′)); 3.21 (*t*, *J* = 9.0, 1 H, H–C(3‴)); 3.17 (*dd*, *J* = 9.0, 7.6, 1 H, H–C(2′)); 3.14 (*dd*, *J* = 9.0, 7.6, 1 H, H–C(2‴)); 3.16 (*dd*, *J* = 12.3, 4.3, 1 H, H–C(3)); 2.81 (*dd*, *J* = 14.3, 3.7, 1 H, H–C(18)); 1.13, 1.02, 0.96, 0.93, 0.91, 0.83, 0.76 (7*s*, 3 H each, 7 Me). ^{13}C-NMR (CD_3OD, 150 MHz): 177.8 (C(28)); 144.7 (C(13)); 122.9 (C(12)); 106.3 (C(1′)); 102.7 (C(1‴)); 94.4 (C(1″)); 90.1 (C(3)); 78.1 (C(5″)); 77.8 (C(3′)); 77.5 (C(5′)); 77.4 (C(2″)); 77.1 (C(5‴)); 77.0 (C(3‴)); 75.2 (C(2′)); 72.9 (C(5‴)); 71.6 (C(2‴)); 71.4 (C(4′)); 71.0 (C(3‴)); 70.0 (C(4″)); 62.7 (C(5‴)); 62.3 (C(6′)); 61.2 (C(6″)); 56.4; 48.3; 47.2; 46.5; 42.3; 40.0; 39.6; 39.2; 37.2; 34.1; 33.3; 32.8; 31.9; 30.7; 28.9; 27.9; 25.6; 25.1; 23.3; 23.2; 22.7; 18.5; 16.8; 16.1. HR-ESI-MS: 965.5041 ([*M* + Na]$^+$, $C_{48}H_{78}NaO_{18}^+$; calc. 965.5061).

Assay for α-Glucosidase Inhibitory Activities. Inhibitory *α*-glucosidase activities were determined spectrophotometrically in a 96-well microtiter plate based on *p*-nitrophenyl *α*-D-glucopyranoside (PNPG) as a substrate. In brief, 20 µl of enzyme soln. (0.8 U/ml *α*-glucosidase in 0.01M potassium phosphate buffer (pH 6.8) containing 0.2% of BSA) and 120 µl of the synthetic compound in 0.5% DMSO of 0.01M potassium phosphate buffer were mixed, and was preincubated at 37° prior to initiation of the reaction by adding the substrate. After 15 min of preincubation, PNPG soln. (20 µl) (5.0 mM PNPG in 0.1M potassium phosphate buffer (pH 6.8) was added and then incubated together at 37°. After 15 min of incubation, 0.2M Na_2CO_3 (80 µl) in 0.1M potassium phosphate buffer was added to the test tube to stop the reaction. Acarbose was used as positive control. The increment in absorption at 410 nm due to the hydrolysis of PNPG by *α*-glucosidase was monitored continuously with an auto multi-functional microplate reader (BIORAD680).

Assay for α-Amylase Inhibitory Activities. The *α*-amylase inhibitory activities were measured with the method reported by *Xiao et al.* and *Yoshikawa et al.* with slight modifications [39][40]. Substrate was prepared by heating starch (250 mg) in 12 ml of 0.4M NaOH soln. for 5 min at 100°, and then cooled to 0° and adjusted to pH 7 with 2M HCl. Sample solns. were prepared by dissolving each soln. in acetate buffer (pH 6.5). The sample (20 µl) and the substrate (40 µl) were mixed in a microplate well. After preincubation at 37° for 15 min, 5 mg/ml *α*-amylase soln. (20 ml) was added and the soln. was incubated at 37° for 15 min. The reaction was stopped by adding 50 ml 1M HCl, and then 50 ml I_2 soln. was added. The absorbances were measured at 650 nm by a microplate reader. Acarbose was used as positive control.

Assay for Lipase Inhibitory Activities. Lipase inhibitory activities were measured according to the method of *Han et al.* with slight modifications [41]. Substrate was prepared by sonication of a mixture of glyceryl trioleate (80 mg), lecithin (10 mg), and sodium cholate (5 mg) suspended in 9 ml of 0.1M TES buffer (pH 7.0). Samples were prepared by dissolving each sample in 0.1M TES buffer. The sample (20 µl) and the substrate (20 µl) were mixed in microplate wells. After preincubated for 5 min, 10 µl of lipase soln. (20 µg/ml) was added to each mixture and incubated for 30 min at 37°. The amount of released fatty acid was measured at 405 nm. Inhibition of lipase activity was expressed as the percentage decrease in the absorbance when porcine pancreatic lipase was incubated with the test compounds. Orlistat was used as positive control.

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