Tethered derivatives of D-glucose and pentacyclic triterpenes for homo/heterobivalent inhibition of glycogen phosphorylase†

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Propargyl esters of the C-28 carboxylic acids of pentacyclic triterpenes (oleanolic, ursolic, and maslinic acids) were coupled with 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl azide as well as *N*-(ω-azido-[C-2, C-6, and C-11]alkanoyl)-β-D-glucopyranosylamines under conditions of copper(I)-catalyzed azide–alkyne cycloaddition (CuAAC) to give tethered D-glucose–triterpene heteroconjugates. The *O*-acetyl protecting groups were removed by base-catalyzed hydrolysis. *N*-(ω-Azido-[C-2, C-6, C-11, and C-16]alkanoyl)-β-D-glucopyranosylamines were also tethered by 1,7-octadiyne under CuAAC conditions to furnish D-glucose homoconjugates. *O*-Deacetylation was carried out by the Zemplén protocol. The new compounds were assayed against rabbit muscle glycogen phosphorylase (RMGP) a or b enzymes. Some of the heteroconjugates inhibited the enzyme in the low micromolar range (IC_{50} values 40–70 μM), while the homoconjugates proved inefficient as inhibitors.

Introduction

Type 2 diabetes mellitus has become a widespread disease afflicting a very large proportion of the population all over the world.[1–3] The diseased state is associated with disorders in glucose metabolism by the liver and periphery resulting in elevated blood glucose levels which, in turn, are responsible for fatal long-term complications.[1,4] An ideal anti-diabetic agent should be capable of lowering blood glucose in both fed and fasted states. Control of the hepatic glycogen metabolism is one of the key events through which insulin maintains blood glucose homeostasis. Among other means for influencing glucose production in the liver, inhibition of glycogen phosphorylase (GP), the rate-limiting enzyme of glycogen degradation, has been regarded as a promising therapeutic approach to the treatment of type 2 diabetes.[5,6] Some GP inhibitors have shown efficacy in lowering blood glucose in animal models and clinical trials.[7,8] In the liver and muscle isoforms of GP enzymes, six binding sites have been identified by X-ray crystallographic studies of enzyme–inhibitor complexes: the catalytic, the inhibitor, the allosteric, the glycogen storage, and the new allosteric sites,[6,9] as well as the recently discovered benzimidazole site.[10]

Among the large variety of compounds tested as GP inhibitors, the most populated class is that of D-glucose derivatives,[11,12] which bind primarily to the catalytic site of the enzyme, as proven by several X-ray crystallographic investigations.[9] These glucose analogue inhibitors of GP are characterized by maintaining an intact hexopyranoid sugar ring with the full OH substitution pattern of D-*gluco* configuration, thus resembling the non-reducing end of the natural substrate glycogen. The modifications are located at the anomeric centre as spirocycles, as well as β-NHCOR, β-NHCONHCOR, and β-*C*-heterocyclic substituents, just to mention the most efficient ones.[5,6]

Pentacyclic triterpenes like **1–3** and related compounds have been reported to represent a new class of glycogen phosphorylase inhibitors.[13–15] X-Ray crystallographic studies revealed the molecular basis of their inhibitory effect, demonstrating that pentacyclic triterpenes such as asiatic and maslinic acids bind to GP at the allosteric site.[16] Oleanolic acid (**1**, OA), ursolic acid (**2**, UA) and maslinic acid (**3**, MA) have recently attracted much attention due to their broad biological activities such as protection of the liver against toxic injury, anti-inflammation, anti-HIV, antitumor, antioxidation, anti-hyperglycemia and cardiovascular activities.[17]

Inhibitors having the potential to bind to more than one site of an enzyme may be significantly more efficient than those with a single binding group (for some tentatively selected examples of bi- or trivalent enzyme inhibitors see ref. 18–23). This principle is well known in the interactions of multivalent carbohydrate derivatives with various proteins, and is frequently called the glycoside cluster effect in that field.[24] Trivalent glucose analogues have very recently been tested for GP inhibition to show a slightly better effect than that of derivatives with a single sugar unit.[25] Homobivalent

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indolcarboxamide[26] as well as cinnamic acid[27,28] derivatives proved very efficient inhibitors of GP.

With these preliminaries in mind, we envisaged conjugation of triterpenes and D-glucose in such a way that both could bind to the site to which they bind on their own, thus providing the first potentially heterobivalent inhibitors of GP. The recently reported triterpene–glucose conjugates were not capable of this because the sugar parts were attached to the triterpene *via* the C-6 position.[29] Furthermore, some new bivalent glucose derivatives are also reported.

Results and discussion

Syntheses

The new triterpene glycoconjugates were designed to include oleanolic, ursolic, and maslinic acids (**1–3**) on one hand and *N*-acyl-β-D-glucopyranosylamines on the other, by connecting them *via* linker chains of different length. The Cu(I)-catalyzed azide–alkyne cycloaddition[30] (CuAAC) was chosen as the linking methodology. The syntheses are summarized in Schemes 1–5.

Direct esterification of oleanolic acid **1**, ursolic acid **2**, and maslinic acid **3** with propargyl bromide (Scheme 1) afforded alkynes **4**,[29] **5**, and **6**, respectively, in excellent yields.

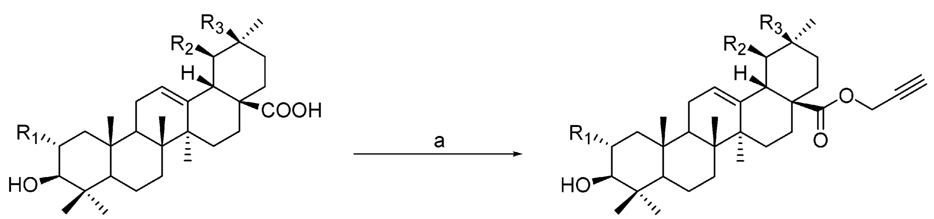
N-Acyl-β-D-glucopyranosylamines with a terminal azide group were synthesized from per-*O*-acetylated-β-D-glucopyranosyl azide[32] **7** (Scheme 2). ω-Bromoalkanoyl derivatives **8–11** were obtained by a 'Staudinger reaction' of **7** with PMe_3, resulting in an intermediate phosphinimine which, without being isolated, was reacted[33] with the corresponding ω-bromoalkanoic acid. Subsequent substitution with NaN_3 in DMF gave compounds **12–15**, respectively. Practically each synthetic step furnished the corresponding product in very good yield.

To perform the CuAAC, an alkyne **4–6** and an azide **7** or **12–14** each were dissolved in CH_2Cl_2–H_2O, followed by the addition of a catalytic amount of sodium L-ascorbate and $CuSO_4{\cdot}5H_2O$. The 'click reactions' proceeded very well at room temperature to afford β-D-glucopyranosyl-1,2,3-triazoles **16–18** (Scheme 3) and the tethered compounds **22–30** (Scheme 4) in good to excellent yields. The *O*-acetyl groups were cleaved with 4 N NaOH/MeOH to give the corresponding deprotected compounds **19–21** (Scheme 3) and **31–37**, respectively (Scheme 4). During deprotection of **28** the desired compound was not obtained; instead compound **38** could be isolated as a result of cleavage of the glucosylamide bond.

For bivalent glucose derivatives the *N*-(ω-azidoalkanoyl)-β-D-glucopyranosylamines **12–15** were reacted with 1,7-octadiyne (**43**) under CuAAC conditions (Scheme 5). The reactions proceeded smoothly to give good to excellent yields of the coupled derivatives **44–47**, which were deprotected under Zemplén conditions to give compounds **48–51** in similarly good yields. In order to make comparisons with monovalent glucose derivatives, azides **12** and **13** were deprotected by the Zemplén protocol to **39** and **41**, respectively, which were further reduced to the ω-amino compounds **40** and **42**.

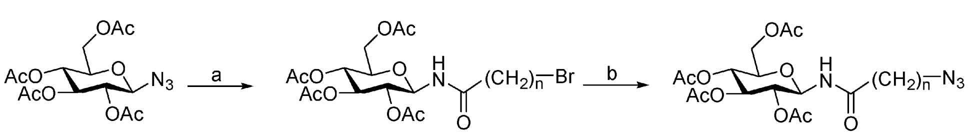
Glycogen phosphorylase inhibition

The above-synthesized derivatives were evaluated in enzyme inhibition assays described previously[35,36] against rabbit muscle glycogen phosphorylase a (RMGPa) or b (RMGPb) which shared considerable sequence similarity with human liver GP (Schemes 1 and 3–5, and Charts 1 and 2). As we found previously,[36] inhibitions of a and b forms of GP showed acceptable similarity.



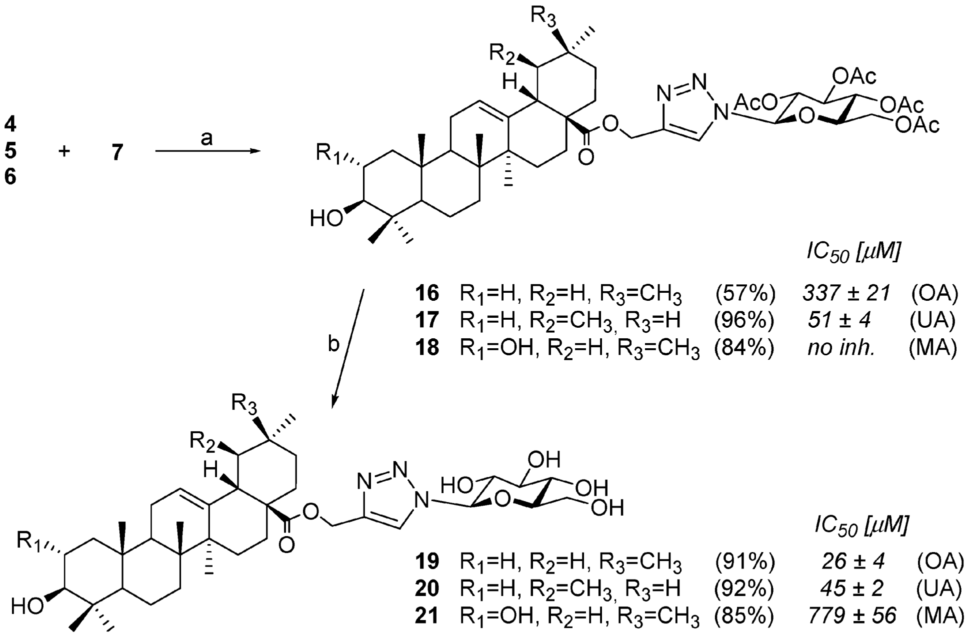
	IC₅₀ [μM]	R^1	R^2	R^3		Yield [%]	*IC₅₀ [μM]*
1 (oleanolic acid, OA)	*14*[14]	H	H	CH_3	**4**	97	*405 ± 30*
2 (ursolic acid, UA)	*9*[13]	H	CH_3	H	**5**	93	*no inh.*
3 (maslinic acid, MA)	*28*[31]	OH	H	CH_3	**6**	87	*no inh.*

Scheme 1 *Reagents and conditions*: (a) K_2CO_3, propargyl bromide, DMF, rt. Inhibition of RMGPa (IC_{50} [μM], values are means of three experiments).

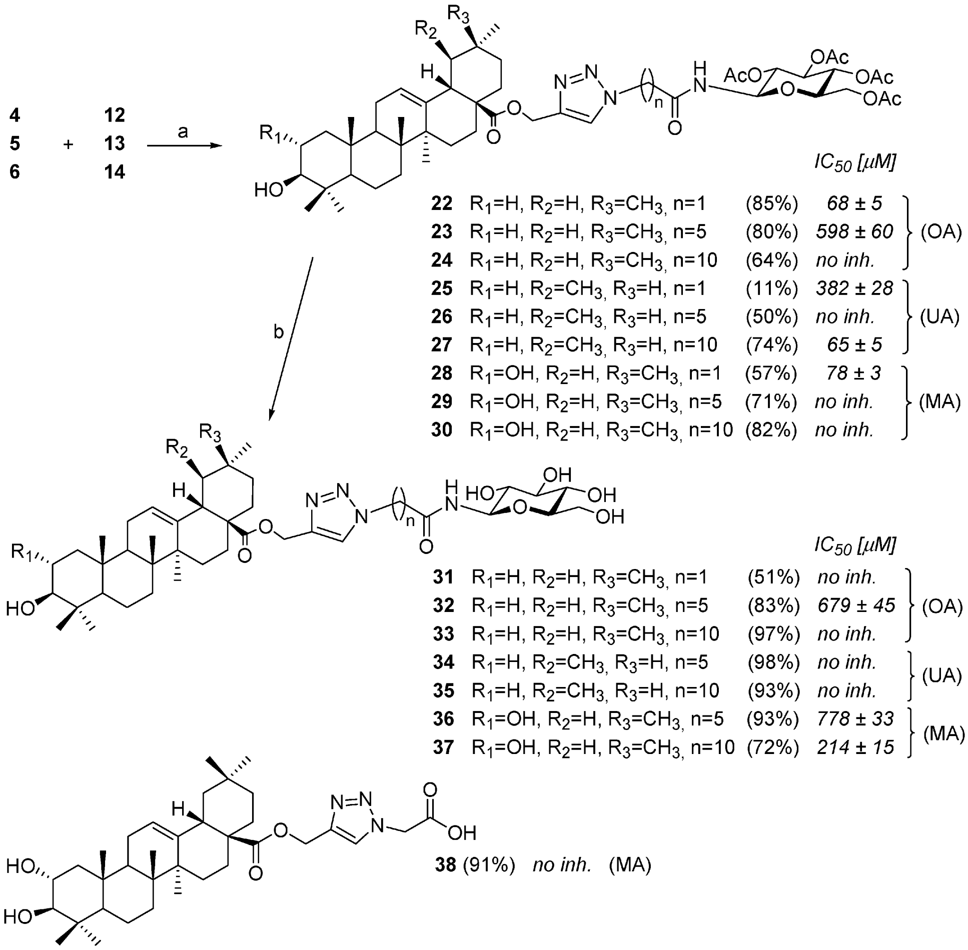


		n	
7	**8** not isolated	1	**12** (63%)
	9 (93%)	5	**13** (85%)
	10 (64%)	10	**14** (88%)
	11 (76%)	15	**15** (81%)

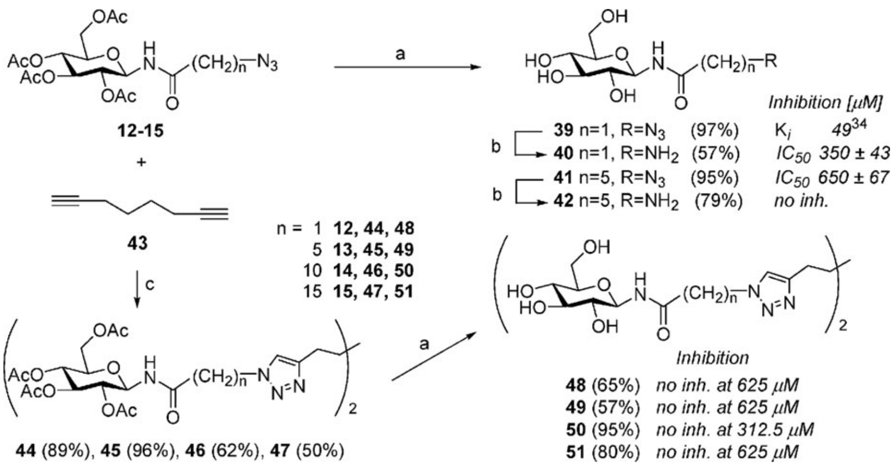
Scheme 2 *Reagents and conditions*: (a) PMe_3, Br–$(CH_2)_n$–COOH, CH_2Cl_2, rt; (b) NaN_3, DMF, rt.



Scheme 3 *Reagents and conditions*: (a) $CuSO_4$, sodium L-ascorbate, CH_2Cl_2–H_2O, rt; (b) NaOH, MeOH, rt. Inhibition of RMGPa (IC_{50} [μM], values are means of three experiments).



Scheme 4 *Reagents and conditions*: (a) $CuSO_4$, sodium L-ascorbate, CH_2Cl_2–H_2O, rt; (b) NaOH, MeOH, rt. Inhibition of RMGPa (IC_{50} [μM], values are means of three experiments).



Scheme 5 *Reagents and conditions*: (a) cat. NaOMe, MeOH rt.; (b) RANEY®-Ni, H_2, MeOH, 70 °C; (c) $CuSO_4$, L-ascorbic acid, CH_2Cl_2–H_2O, rt. Inhibition of RMGPb.

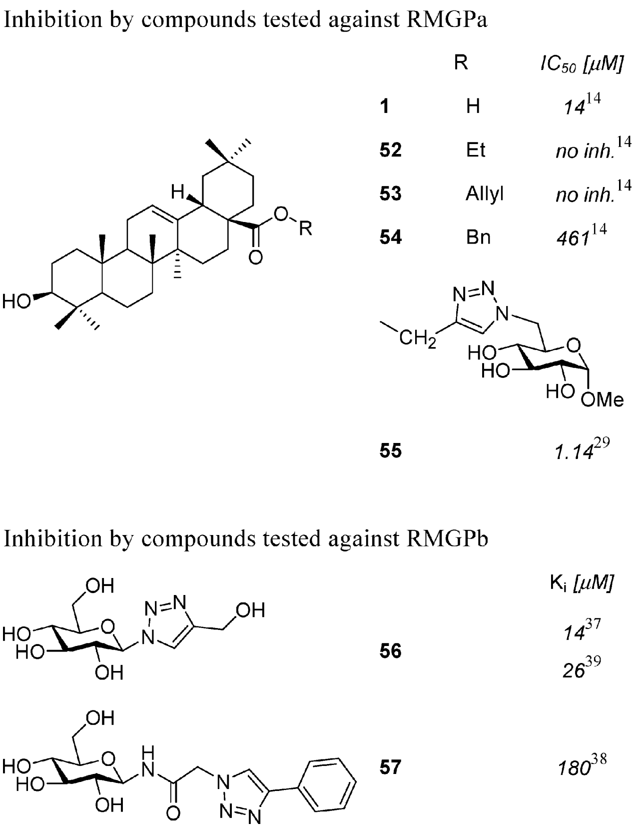


Chart 1 Literature data for some inhibitors of RMGP.

The assay results showed that propargylation of the C-28 carboxyl depressed the GPa enzyme inhibitory activity (compare **1–3** to **4–6** in Scheme 1). This observation is similar to the effect of other esterifications of OA (**52–54**, Chart 1) resulting in a significant loss of activity.[14]

In the sugar-coupled series (Schemes 3 and 4) the activities of OA derivatives were generally better than those of the derivatives of UA and MA (**19** *vs.* **20** and **21**; **22** *vs.* **25** and **28**; **23** *vs.* **26** and **29**; **32** *vs.* **34** and **36**). Deprotection of the sugar part in the 1-β-D-glucopyranosyl-1,2,3-triazole series (Scheme 3) gave better inhibitors with OA (**16** *vs.* **19**) and MA (**18** *vs.* **21**), while no significant change was observed with UA (**17** *vs.* **20**). Appending the sugar to the triazole *via* the C-6 position as in **55** (Chart 1) gave a very good inhibitor, although the *O*-peracetylated analogue had no activity at all.[29]

The effect of the length of the linker between the sugar and the triterpene parts was studied in the ω-triazolylalkanoyl-amide series (Scheme 4): with OA (**22** *vs.* **23** and **24**) and MA (**28** *vs.* **29** and **30**) derivatives the one-carbon linkage was significantly better than the longer ones, while among the UA compounds an opposite effect (**27** *vs.* **25** and **26**) was observed. Removal of the *O*-acetyl protecting groups in the ω-triazolylalkanoyl-amide series (Scheme 4, **31–37**) brought about no obvious difference. Comparison of **19** with the hydroxymethyl-triazole **56** shows that the presence of the OA moiety makes the inhibition somewhat better. However, **56** binds to the catalytic site,[37] while **19** can be expected to occupy the allosteric site.[29] Thus, the comparable inhibitory

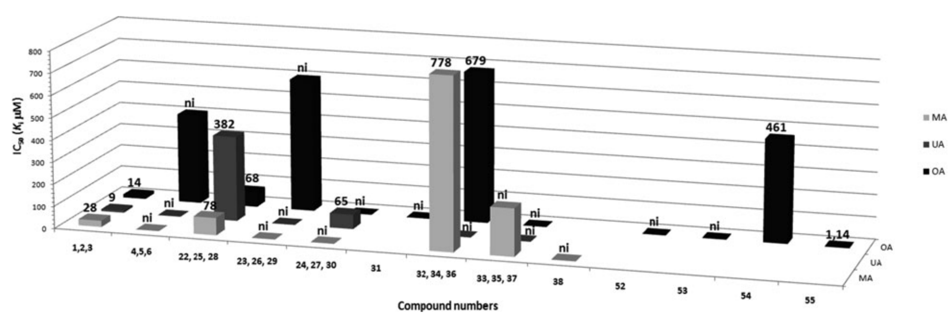


Chart 2 Comparison of inhibition assay results against RMGPa (abbreviations: derivatives of maslinic acid (MA), ursolic acid (UA) and oleanolic acid (OA); ni = no inhibition).

activities may not be directly relevant, except in the as-yet unproven case of a dual binding mode which could be expected to occur between two enzyme dimers.[25] Similar considerations may apply to a comparison of **31** and **57**.

In cases of bivalent glucose derivatives **48–51** (Scheme 5) no inhibition could be observed. Study of analogous monovalent compounds revealed that with an azide as endgroup (**39**, **41**) the inhibitory activity was moderate and decreased with the length of the linker. Bivalent compound **48** can also be compared with the monovalent triazole **57**[38] (Chart 1) to show that the dimeric structures seem to be too large to occupy the catalytic site, and no other interactions exist with the enzyme. In the presence of amine endgroups (**40**, **42**) the inhibition was much weaker, and with the longer linker chain no effect was detected.

Conclusions

Copper(I)-catalyzed azide–alkyne cycloaddition – 'click chemistry' – proved suitable for the synthesis of conjugates of pentacyclic triterpenes and D-glucose derivatives as new, potentially heterobivalent inhibitors of glycogen phosphorylase. Compounds **17** (IC_{50} = 51 μM), **19** (IC_{50} = 26 μM), **20** (IC_{50} = 45 μM), **22** (IC_{50} = 68 μM), **27** (IC_{50} = 65 μM) and **25** (IC_{50} = 78 μM) were the most potent inhibitors of RMGPa. Homobivalent glucose derivatives proved inefficient in RMGPb inhibition assays. The monovalent analogues of both triterpenes and glucose derivatives proved generally more efficient than the bivalent compounds.

Experimental

General methods

All commercially available solvents and reagents were used without further purification. Melting points were measured on a RY-1 or on a Kofler hot-stage melting point apparatus. Column chromatography was carried out on E. Merck Silica Gel 60 (230–400 mesh), on silica gel (200–300 mesh, Qindao Ocean Chemical Company, China), or Kieselgel 60 (Merck, particle size 0.063–0.200 mm). IR spectra were recorded on Shimadzu FTIR-8400S spectrometer. ^{1}H- and ^{13}C-NMR spectra were measured on Bruker AV-300 (300/75 MHz for ^{1}H/^{13}C), Bruker 360 (360/90 MHz for ^{1}H/^{13}C) or Avance DRX 500 (500/125 MHz for ^{1}H/^{13}C) spectrometers. Chemical shifts are reported as values from an internal tetramethylsilane standard. TLC was performed on DC-Alurolle Kieselgel 60 F254 (Merck), and the plates were visualised under UV light and by gentle heating. Mass spectral data were obtained on Agilent 1100 LC/DAD/MSD or Q-Tof Micro MS/MS spectrometers. Optical rotations were measured using a Perkin-Elmer 141 or a Perkin-Elmer 241 polarimeters at rt. PMe_3 (1 M solution in toluene) and 1,7-octadiyne were purchased from Sigma-Aldrich.

Syntheses

General procedure I for the propargylation of oleanolic acid, ursolic acid or maslinic acid

To a solution of a carboxylic acid (**1** or **2** or **3**, 2.2 mmol) in DMF (5 mL), was added propargyl bromide (2.4 mmol) and K_2CO_3 (4.4 mmol). The reaction mixture was stirred at rt for 18 h, then concentrated. The residue was diluted with EtOAc (50 mL), washed successively with 1 N HCl, water, satd. aq. $NaHCO_3$, water and brine, dried ($MgSO_4$), filtered and concentrated. The residue was purified by column chromatography.

Propargyl 3β-hydroxyolean-12-en-28-oate (4)[29]. Prepared from **1** (1 g, 2.2 mmol) and propargyl bromide (0.27 mL, 2.4 mmol) according to General procedure I. The residue was purified by column chromatography (EtOAc–hexane, 1 : 6). Yield: 1.05 g, 97%, white solid, mp 121–122 °C; R_f = 0.33 (EtOAc–hexane, 1 : 4); $[\alpha]_D$ = +67.9 (c = 0.50, CH_2Cl_2). IR (KBr, cm^{-1}): 3308, 2945, 2866, 1731, 1157, 1032, 739; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74, 0.77, 0.92, 0.98, 1.13 (5 s, each 3H, 5 × CH_3), 0.90 (s, 6H, 2 × CH_3), 0.71–2.04 (m, 22H), 2.41 (t, 1H, J = 2.6 Hz, CH), 2.87 (dd, 1H, J = 4.1, 9.5 Hz, H-18), 3.21 (dd, 1H, J = 5.1, 10.7 Hz, H-3), 4.56 (dd, 1H, J = 2.6, 15.4 Hz, CO_2CH_2), 4.68 (dd, 1H, J = 2.6, 15.4 Hz, CO_2CH_2), 5.30 (t, 1H, J = 3.5 Hz, H-12); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.3, 15.6, 17.1, 18.3, 23.0, 23.4, 23.6, 25.8, 27.2, 27.7, 28.1, 30.7, 32.2, 32.8, 33.1, 33.8, 37.0, 38.5, 38.8, 39.4, 41.3, 41.7, 45.9, 46.8, 47.6, 51.6, 55.2, 74.4, 78.1, 79.0, 122.63, 143.4, 176.8. ESI-MS (positive mode) m/z: 517.3 $[M + Na]^+$.

Propargyl 3β-hydroxyurs-12-en-28-oate (5). Prepared from **2** (2.0 g, 4.4 mmol) and propargyl bromide (0.54 mL, 4.8 mmol) according to General procedure I. The residue was purified by column chromatography (EtOAc–hexane, 1 : 5). Yield: 2.0 g, 93%, white solid, mp 129–131 °C; R_f = 0.48 (EtOAc–hexane, 1 : 5). IR (KBr, cm^{-1}): 3309, 2927, 2871, 1729, 1454, 1383, 1221, 1167, 1139, 1106, 1032, 996, 757, 667; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.76, 0.77, 0.91, 0.95, 0.98, 1.08 (6 s, each 3H, 6 × CH_3), 0.87 (d, 3H, J = 6.4 Hz, CH_3), 0.75–2.10 (m, 22H), 2.26 (d, 1H, J = 11.3 Hz, H-18), 2.41 (t, 1H, J = 2.4 Hz, CH), 3.20 (dd, 1H, J = 5.1, 10.7 Hz, H-3), 4.57 and 4.65 (dd, each 1H, J = 2.5, 15.6 Hz, $COOCH_2$), 5.27 (1H, t, J = 3.6 Hz, H-12); ^{13}C NMR (75 MHz, $CDCl_3$): δ 5.5, 15.6, 17.0, 17.2, 18.3, 21.1, 23.3, 23.5, 24.6, 27.3, 28.0, 28.1, 30.6, 33.1, 36.4, 37.0, 38.67, 38.75, 38.8, 39.1, 39.6, 42.1, 47.6, 48.2, 51.6, 52.8, 55.3, 74.3, 78.1, 79.0, 125.9, 137.8, 176.6. ESI-MS (positive mode) m/z: 495.4 $[M + H]^+$.

Propargyl 2α,3β-dihydroxyolean-12-en-28-oate (6). Prepared from **3** (1.4 g, 3.0 mmol) and propargyl bromide (0.37 mL, 3.3 mmol) according to General procedure I. The residue was purified by column chromatography (EtOAc–hexane, 1 : 5). Yield: 1.3 g, 87%, white solid, mp 233–234 °C; R_f = 0.69 (EtOAc–hexane, 1 : 5). IR (KBr, cm^{-1}): 3394, 3309, 2946, 1729, 1463, 1388, 1364, 1259, 1217, 1157, 1121, 1049, 1033, 995, 758, 669, 633; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.74, 0.82, 0.90, 0.92, 0.98, 1.03, 1.13 (7 s, each 3H, 7 × CH_3), 0.75–2.01 (m, 20H), 2.41 (t, 1H, J = 2.4 Hz, CH), 2.87 (dd, 1H, J = 4.3, 13.7 Hz, H-18), 3.01 (d, 1H, J = 9.5 Hz, H-3), 3.65–3.73 (m, 1H, H-2), 4.57 and 4.69 (dd, each 1H, J = 2.4, 15.6 Hz, $COOCH_2$), 5.31 (t, 1H, J = 3.5 Hz, H-12); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.6, 16.7, 17.2, 18.4, 23.0, 23.5, 23.6, 25.9, 27.7, 28.6, 30.7, 32.2, 32.7, 33.1, 33.9, 38.3, 39.2, 39.5, 41.3, 41.8, 45.9, 46.5, 46.8, 47.6, 51.6, 55.4, 69.0, 74.4, 78.1, 84.0, 122.5, 143.5, 176.8. ESI-MS (positive mode) *m/z*: 533.4 $[M + Na]^+$.

General procedure II for the preparation of *N*-(ω-bromoalkanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamines (9–11)

2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl azide (**7**, 0.10 g, 0.27 mmol) was dissolved in dry CH_2Cl_2 (3 mL). To the solution Me_3P (1.1 equiv. of a 1 M solution in toluene) was added in one portion. The mixture was stirred at rt. until nitrogen evolution had ceased and TLC (EtOAc–hexane, 1 : 1) had indicated complete transformation of the azide. This solution was then reacted with an ω-bromoalkanoic acid (1.1 equiv., as indicated with the particular compounds) till the disappearance of the iminophosphorane (TLC, EtOAc–hexane, 1 : 1). Then, it was diluted with CH_2Cl_2 (5 mL) and washed with satd. aq. $NaHCO_3$ solution (2 × 5 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under diminished pressure. The crude product was purified by column chromatography.

***N*-(6-Bromohexanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (9).** Prepared from **7** (0.50 g 1.34 mmol) according to General procedure II. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.65 g, 93%, colourless oil, R_f = 0.35 (EtOAc–hexane, 1 : 1); $[\alpha]_D$ = +22 (c = 0.59, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.42–1.47 (m, 2H, CH_2), 1.60–1.63 (m, 2H, CH_2), 1.83–1.90 (m, 2H, CH_2), 2.02, 2.04, 2.06, 2.08 (4s, 12H, 4 × $OCOCH_3$), 2.21–2.27 (m, 2H, CH_2), 3.39–3.43 (m, 2H, CH_2), 3.86 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 4.08 (dd, 1H, J = 1.2, 11.9 Hz, H-6b), 4.32 (dd, 1H, J = 2.6, 11.9 Hz, H-6a), 4.93, 5.06, 5.29, 5.32 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 6.63 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.3 (3), 20.5 (4 × $OCOCH_3$), 23.9, 27.3, 32.0, 33.3, 35.9 (5 × CH_2), 61.5 (C-6), 67.9, 70.4, 72.5, 73.2 (C-2, C-3, C-4, C-5), 77.7 (C-1), 169.3, 169.6, 170.4, 170.5 (4 × $OCOCH_3$), 172.8 (NHCO). Anal. calcd. for $C_{20}H_{30}BrNO_{10}$ (524.37): C 45.81, H 5.77, N 2.67. Found: C 45.64, H 5.94, N 2.59.

***N*-(11-Bromoundecanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (10).** Prepared from **7** (5.0 g 13.4 mmol) according to General procedure II. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 5.13 g, 64%, white crystalline product, mp 61–63 °C; $[\alpha]_D$ = +15 (c = 0.38, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.28 (bs, 10H, 5 × CH_2), 1.40–1.45 (m, 2H, CH_2), 1.57–1.50 (m, 2H, CH_2), 1.80–1.86 (m, 2H, CH_2), 2.02, 2.04, 2.06, 2.08 (4 s, 12H, 4 × $OCOCH_3$), 2.17–2.21 (m, 2H, CH_2), 3.38–3.43 (m, 2H, CH_2), 3.85 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 4.07 (dd, 1H, J = 1.2, 11.9 Hz, H-6b), 4.32 (dd, 1H, J = 2.6, 11.9 Hz, H-6a), 4.93, 5.06, 5.27, 5.32 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 6.51 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4(3), 20.5 (4 × $OCOCH_3$), 24.8, 25.0, 27.9, 28.4, 28.8, 29.0, 29.1, 32.5, 33.7, 36.3 (10 × CH_2), 61.5 (C-6), 67.9, 70.4, 72.5, 73.3 (C-2, C-3, C-4, C-5), 77.8 (C-1), 169.3, 169.6, 170.4, 170.6 (4 × $OCOCH_3$), 173.3 (NHCO). Anal. calcd. for $C_{25}H_{40}BrNO_{10}$ (594.50): C 50.51, H 6.78, N 2.36. Found: C 50.64, H 6.91, N 2.49.

***N*-(16-Bromohexadecanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (11).** Prepared from **7** (0.50 g 1.34 mmol) according to General procedure II. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.68 g, 76%, white crystalline product, mp 91–93 °C; $[\alpha]_D$ = +10 (c = 0.20, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.28 (m, 18H, 9 × CH_2), 1.36–1.39 (m, 2H, CH_2), 1.48–1.52 (m, 2H, CH_2), 1.57–1.61 (m, 2H, CH_2), 1.84–1.88 (m, 2H, CH_2), 2.03, 2.04, 2.06, 2.08 (4 s, 12H, 4 × $OCOCH_3$), 2.27–2.31 (m, 2H, CH_2), 3.36–3.40 (m, 2H, CH_2), 3.87 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 4.06 (dd, 1H, J = 1.2, 11.9 Hz, H-6b), 4.35 (dd, 1H, J = 2.6, 11.9 Hz, H-6a), 4.98, 5.22, 5.27, 5.32 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 6.50 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.2 (3), 20.3 (4 × $OCOCH_3$), 23.0, 23.4, 24.8, 25.0, 26.0, 26.3, 28.1, 28.8, 29.0, 29.3, 29.4, 32.0, 33.8, 34.5, 36.2, (16 × CH_2), 61.7 (C-6), 68.1, 71.2, 72.5, 74.3 (C-2, C-3, C-4, C-5), 76.8 (C-1), 169.3, 169.6, 170.4, 170.6 (4 × $OCOCH_3$), 172.3 (NHCO). Anal. calcd. for $C_{30}H_{50}BrNO_{10}$ (664.64): C 54.22, H 7.58, N 2.11. Found: C 54.11, H 7.72, N 2.29.

General procedure III for the preparation of *N*-(ω-azidoalkanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamines (12–15)

An *N*-(ω-bromoalkanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (**9–11**) was dissolved in dry DMSO (15 mL/mmol). To the solution NaN_3 (2 equiv.) was added in one portion. The mixture was stirred at rt until the disappearance of the starting bromide (TLC EtOAc–hexane 1 : 1). The solution was diluted with water (150 mL), washed with Et_2O (5 × 25 mL) and water (1 × 25 mL), dried over $MgSO_4$ and the solvent was removed under diminished pressure. The crude product was purified by column chromatography or crystallisation.

***N*-Azidoacetyl-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (12).** To a solution of azide **7** (0.20 g, 0.54 mmol) in dry CH_2Cl_2 (3 mL), PMe_3 (0.54 mL of a 1 M solution in toluene) was added in one portion. The mixture was stirred at rt until nitrogen evolution had ceased, and TLC (EtOAc–hexane, 1 : 1) had indicated complete transformation of **7** (approx. 15 min). This soln was then reacted with bromoacetic acid (0.082 g, 0.59 mmol). When TLC (EtOAc–hexane, 1 : 1) showed no more change (conversions were incomplete), the solvent was evaporated, and the pale yellow oil was dissolved in CH_2Cl_2 (30 mL) and extracted with satd. aq. $NaHCO_3$ solution (2 × 30 mL). The organic phase was dried over $MgSO_4$, concentrated under diminished pressure, then the residue (0.20 g) was dissolved in dry DMF (3 ml) and NaN_3 (0.056 g, 0.82 mmol) was added. The reaction mixture was stirred at rt for 2 h (TLC, EtOAc–hexane, 1 : 1). The mixture was then diluted with water (20 mL) and extracted with Et_2O (5 × 30 mL). The combined organic phase was dried over $MgSO_4$ and the solvent was removed under diminished pressure. The obtained syrup was purified by column chromatography (EtOAc–hexane, 4 : 6) to give **12** as white crystals: 0.15 g, 63%, calcd for **7**; mp 150–152 °C, $[\alpha]_D$ = +39 (c = 0.21, $CHCl_3$), (lit.[40] $[\alpha]_D$ +4.1 (c = 1, $CHCl_3$)); ^1H NMR (360 MHz, $CDCl_3$): δ (ppm) 2.03, 2.04, 2.07, 2.09 (4s, 12H, 4 × $OCOCH_3$), 3.85 (ddd, 1H, J = 2.6, 4.0, 9.2 Hz, H-5), 3.93–4.11 (m, 3H, H-6b, CH_2), 4.30 (dd, 1H J = 2.6, 13.2 Hz, H-6a), 4.99, 5.08, 5.24, 5.33 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 7.19 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.6, 20.5 (4 × $OCOCH_3$), 52.4 (CH_2), 61.5 (C-6)) 67.9, 70.3, 72.5, 73.6 (C-2, C-3, C-4, C-5), 78.0 (C-1), 167.5, 169.5, 169.8, 170.5 (4 × $OCOCH_3$), 170.8 (NH*C*O). Anal. calcd. for $C_{16}H_{22}N_4O_{10}$ (430.37): C, 44.65; H, 5.15; N, 13.02; Found: C, 44.53; H, 5.22; N, 13.12.

***N*-(6-Azidohexanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (13).** Prepared from **9** (2.00 g, 3.81 mmol) according to General procedure III. Yield: 1.57 g, 85%, white crystalline product, mp 135–137 °C; $[\alpha]_D$ = +37 (c = 0.34, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.36–1.44 (m, 2H, CH_2), 1.57–1.68 (m, 4H, 2 × CH_2), 2.02, 2.04, 2.05, 2.08 (4 s, 12H, 4 × $OCOCH_3$), 2.18–2.24 (m, 2H, CH_2), 3.24–3.29 (m, 2H, CH_2), 3.84 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 4.08 (dd, 1H, J = 1.1, 11.9 Hz, H-6b), 4.31 (dd, 1H, J = 11.9, 4.0 Hz, H-6a), 4.92, 5.06, 5.28, 5.31 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 6.57 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4 (3), 20.5 (4 × $OCOCH_3$), 24.4, 26.0, 28.4, 36.1, 51.0 (5 × CH_2), 61.5 (C-6), 68.0, 70.4, 73.4, 72.6 (C-2, C-3, C-4, C-5), 77.9 (C-1), 169.5, 169.7, 170.5, 170.8 (4 × $OCOCH_3$), 173.0 (NH*C*O). Anal. calcd. for $C_{20}H_{30}N_4O_{10}$ (486.48): C 49.38, H 6.22, N 11.52. Found: C 49.46, H 6.14, N 11.59.

***N*-(11-Azidoundecanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (14).** Prepared from **10** (1.00 g, 1.69 mmol) according to General procedure III. Yield: 0.83 g, 88%, white crystalline product, mp 68–70 °C; $[\alpha]_D$ = +13 (c = 0.22, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.25–1.31 (m, 14H, 7 × CH_2), 1.46–1.50 (m, 2H, CH_2), 2.02, 2.04, 2.05, 2.08 (4 s, 12H, 4 × $OCOCH_3$), 2.20–2.25 (m, 2H, CH_2), 2.52–2.56 (m, 2H, CH_2), 3.17 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 3.31 (dd, 1H, J = 1.1, 11.9 Hz, H-6b), 3.53 (dd, 1H, J = 4.0, 11.9 Hz, H-6a), 4.22, 4.29, 4.56, 4.61 (4 pseudo t, 4H, J = 9.2, 10.6 Hz in each, H-1, H-2, H-3, H-4), 7.49 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4 (3), 20.5 (4 × $OCOCH_3$), 25.0, 26.4, 27.9, 28.0, 28.2, 28.3, 30.1, 32.4, 35.0, 50.2 (10 × CH_2), 60.9 (C-6), 67.1, 69.6, 72.2, 72.4 (C-2, C-3, C-4, C-5), 77.9 (C-1), 168.5, 168.6, 168.7, 169.3 (4 × $OCOCH_3$), 173.0 (NH*C*O). Anal. calcd. for $C_{25}H_{40}N_4O_{10}$ (556.62): C 53.95, H 7.24, N 10.07. Found: C 53.76, H 7.04, N 10.19.

***N*-(16-Azidohexadecanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (15).** Prepared from **11** (0.4 g, 0.60 mmol) according to General procedure III. Yield: 0.30 g, 81%, white crystalline product, mp 92–94 °C; $[\alpha]_D$ = +16 (c = 0.22, $CHCl_3$); ^1H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.24–1.28 (m, 18H, 9 × CH_2), 1.36–1.39 (m, 2H, CH_2), 1.47–1.50 (m, 2H, CH_2), 1.56–1.61 (m, 2H, CH_2), 1.84–1.87 (m, 2H, CH_2), 2.02, 2.04, 2.07, 2.08 (4s, 12H, 4 × $OCOCH_3$), 2.27–2.31 (m, 2H, CH_2), 3.38–3.41 (m, 2H, CH_2), 3.21 (ddd, 1H, J = 1.2, 2.6, 10.6 Hz, H-5), 3.29 (1H, dd, J = 1.1, 11.9 Hz, H-6b), 3.52 (dd, 1H, J = 4.0, 11.9 Hz, H-6a), 4.20, 4.25, 4.71, 4.60 (4 pseudo t, 4H, J = 9.2, 10.6 Hz, in each, H-1, H-2, H-3, H-4), 7.48 (d, 1H, J = 9.2 Hz, NH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4 (3), 20.5 (4 × $OCOCH_3$), 23.3, 23.4, 3 24.8, 26.0, 27.1, 27.6, 28.2, 28.5, 29.0, 29.7, 30.4, 31.9, 33.8, 36.5, 49.2 (15 × CH_2), 61.5 (C-6), 68.3, 70.0, 72.1, 72.5 (C-2, C-3, C-4, C-5), 78.7 (C-1), 168.5, 168.6, 168.7, 169.3 (4 × $OCOCH_3$), 172.1 (NH*C*O). Anal. calcd. for $C_{30}H_{50}N_4O_{10}$ (626.75): C 57.49, H 8.04, N 8.94. Found: C 57.23, H 8.24, N 8.82.

General procedures IV for the CuAAC 'click' reaction

(a). To a solution of an alkyne (0.27 mmol) and an azide (0.27 mmol) in CH_2Cl_2 (2 mL) and H_2O (2 mL), was added $CuSO_4{\cdot}5H_2O$ (0.32 mmol) and Na-L-ascorbate (0.64 mmol). The resulting solution was stirred for 12 h at rt. The reaction mixture was diluted with H_2O (10 mL), then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated. The residue was purified by column chromatography.

(b). An *N*-(ω-azidoalkanoyl)-2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamine (0.46 mmol) was added to a 1 : 1 (v/v) mixture of CH_2Cl_2 and water (10 mL/mmol). To the solution 1,7-octadiyne (**43**, 1.0 equiv.), $CuSO_4{\cdot}5H_2O$ (5 mol%) and L-ascorbic acid (15 mol%) were added. The mixture was heated at 50 °C until complete transformation of the starting azide (TLC, EtOAc). The solution was diluted with water (25 mL) and extracted with CH_2Cl_2 (5 × 12 mL). The organic phase was dried over $MgSO_4$ and the solvent was removed under diminished pressure. The crude product was purified by column chromatography or crystallisation.

General procedure V for *O*-deacetylation

To a solution or suspension of an *O*-peracetylated compound (0.081 mmol) in MeOH (3 mL) was added 4 N aq. NaOH (0.4 mL), then stirred at rt for 1 h, and neutralized with 1 N HCl (1.8 mL). The mixture was concentrated *in vacuo* and the residue was taken up in EtOAc (50 mL), washed successively with 1 N HCl (3 × 15 mL), water (3 × 15 mL) and brine (3 × 15 mL), dried (Na_2SO_4), filtered and concentrated. The residue was purified by column chromatography.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (16). Prepared from **4** (0.13 g, 0.27 mmol) and **7** (0.10 g, 0.27 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.13 g, 57%, white solid, mp 124–125 °C. R_f = 0.13 (EtOAc–hexane, 1 : 2). IR (KBr, cm^{-1}): 2947, 2869, 1757, 1460, 1369, 1227, 1036, 758; ^1H NMR (300 MHz, $CDCl_3$): δ 0.66, 0.78, 0.89, 0.90, 0.91, 0.99, 1.13 (7 s, each 3H, 7 × CH_3), 0.67–2.09 (m, 22H), 1.86, 2.03, 2.07, 2.09 (4 s, each 3H, 4 × $OCOCH_3$), 2.86 (dd, 1H, J = 3.8, 13.9 Hz, H-18), 3.18–3.23 (m, 1H, H-3), 3.96–4.02 (m, 1H, H-5-Glc), 4.11–4.16 (m, 1H, H-6a-Glc), 4.33 (dd, 1H, J = 4.8, 12.6 Hz, H-6b-Glc), 5.17 (s, 2H, $COOCH_2$), 5.21–5.27 (m, 1H, H-2-Glc), 5.31 (t, 1H, J = 3.3 Hz, H-12), 5.39–5.43 (m, 2H, overlapping, H-3-Glc and H-4-Glc), 5.84–5.87 (m, 1H, H-1-Glc), 7.81 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$):

δ 15.3, 15.6, 16.9, 18.4, 20.1, 20.5, 20.6, 23.0, 23.4, 23.6, 25.9, 27.2, 27.7, 28.1, 29.7, 30.7, 32.2, 32.7, 33.1, 33.9, 37.1, 38.5, 38.8, 39.3, 41.4, 41.8, 45.9, 46.7, 47.6, 55.3, 57.4, 61.5, 67.7, 70.3, 72.6, 75.3, 79.0, 85.9, 122.0, 122.5, 143.7, 144.0, 168.6, 169.3, 169.9, 170.4, 177.4. ESI-MS (positive mode) *m*/*z*: 890.8 $[M + Na]^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (17). Prepared from **5** (0.13 g, 0.27 mmol) and **7** (0.10 g, 0.27 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 2). Yield: 0.22 g, 96%, white solid, mp 120–122 °C. R_f = 0.20 (EtOAc–hexane, 1 : 2); IR (KBr, cm^{-1}): 2932, 2872, 1757, 1456, 1376, 1228, 1104; ^1H NMR (300 MHz, $CDCl_3$): δ 0.72, 0.81, 0.94, 0.97, 1.01, 1.11 (6 s, each 3H, 6 × CH_3), 0.89 (d, 3H, *J* = 6.3 Hz, CH_3), 0.72–2.13 (m, 22H), 1.89, 2.06, 2.10, 2.13 (4 s, each 3H, 4 × $OCOCH_3$), 2.25 (d, 1H, *J* = 10.8 Hz, H-18), 3.25 (dd, 1H, *J* = 4.3, 10.7 Hz, H-3), 4.00–4.04 (m, 1H, H-5-Glc), 4.14–4.19 (m, 1H, H-6a-Glc), 4.35 (dd, 1H, *J* = 4.5, 12.7 Hz, H-6b-Glc), 5.17 and 5.18 (2 d, each 1H, *J* = 12.8 Hz, $COOCH_2$), 5.23–5.30 (m, 2H, overlapping, H-12 and H-2-Glc), 5.40–5.48 (m, 2H, overlapping, H-3-Glc and H-4-Glc), 5.90 (d, 1H, *J* = 9.2 Hz, H-1-Glc), 7.82 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5, 15.6, 19.96, 17.0, 18.4, 20.1, 20.5, 20.6, 21.1, 23.3, 23.6, 24.2, 27.3, 28.1, 28.2, 30.6, 33.0, 36.4, 37.0, 38.7, 38.8, 38.82, 39.1, 39.6, 42.1, 47.6, 48.1, 52.9, 55.3, 57.3, 61.5, 67.8, 70.4, 72.7, 75.3, 79.1, 86.9, 122.0, 125.8, 138.1, 144.1, 168.6, 169.3, 169.9, 177.3. ESI-MS (positive mode) *m*/*z*: 890.8 $[M + Na]^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (18). Prepared from **6** (0.14 g, 0.27 mmol) and **7** (0.10 g, 0.27 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.20 g, 84%, white solid, mp 158–160 °C, R_f = 0.17 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 3395, 2948, 1758, 1460, 1368, 1227, 1101, 1037, 758; ^1H NMR (300 MHz, $CDCl_3$): δ 0.69, 0.85, 0.92, 0.94, 1.00, 1.06, 1.15 (7 s, each 3H, 7 × CH_3), 0.69–2.12 (m, 20H), 1.88, 2.06, 2.10, 2.12 (4 s, each 3H, 4 × $OCOCH_3$), 2.89 (dd, 1H, *J* = 3.1, 13.2 Hz, H-18), 3.05 (d, 1H, *J* = 9.5 Hz, H-3α), 3.68–3.76 (m, 1H, H-2β), 4.00–4.04 (m, 1H, H-5-Glc), 4.14–4.18 (m, 1H, H-6a-Glc), 4.35 (dd, 1H, *J* = 4.8, 12.6 Hz, H-6b-Glc), 5.19 and 5.20 (2 d, each 1H, *J* = 12.9 Hz, $COOCH_2$), 5.24–5.30 (m, 1H, H-2-Glc), 5.34 (brs, 1H, H-12), 5.43–5.46 (m, 2H, H-3-Glc and H-4-Glc), 5.90 (d, 1H, *J* = 9.2 Hz, H-1-Glc), 7.84 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.9, 17.0, 17.2, 18.6, 20.3, 20.7, 20.9, 23.3, 23.7, 23.9, 26.1, 27.9, 28.8, 30.9, 32.4, 32.9, 33.3, 34.1, 38.6, 39.3, 39.4, 39.7, 41.6, 42.0, 46.1, 46.7, 47.0, 47.9, 55.6, 57.6, 61.8, 68.0, 69.2, 70.6, 72.9, 75.5, 77.4, 84.2, 86.1, 122.2, 122.6, 144.0, 144.3, 168.9, 169.5, 170.1, 170.6, 177.7. ESI-MS (positive mode) *m*/*z*: 906.4 $[M + Na]^+$.

[1-(β-D-Glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxy-olean-12-en-28-oate (19). Prepared from **16** (0.07 g, 0.08 mmol) according to General procedure V. The residue was purified by column chromatography (EtOAc). Yield: 0.05 g, 91%, white solid, mp 178–180 °C, R_f = 0.13 (EtOAc); $[\alpha]_D$ = +45 (*c* = 0.05, MeOH); IR (KBr, cm^{-1}): 3424, 2942, 1712, 1636, 1052, 1033, 1016, 772; ^1H NMR (300 MHz, C_5D_5N): δ 0.82, 0.85, 0.89, 0.93, 1.01, 1.17, 1.21 (7 s, each 3H, 7 × CH_3), 0.82–1.92 (m, 22H), 3.08–3.11 (m, 1H, H-18), 3.39–3.44 (m, 1H, H-3), 4.20–4.22 (m, 1H, H-5-Glc), 4.27–4.41 (m, 3H, overlapping, H-6a-Glc, H-6b-Glc, H-4-Glc), 4.50 (m, 1H, H-2-Glc), 4.79 (t, 1H, *J* = 8.9, 8.9 Hz, H-3-Glc), 5.40 (s, 1H, H-12), 5.47–5.57 (m, 2H, $COOCH_2$), 6.35 (d, 1H, *J* = 9.2 Hz, H-1-Glc), 8.64 (s, 1H, NCH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.7, 16.6, 17.4, 18.8, 23.4, 23.6, 23.8, 26.0, 28.1, 28.8, 30.8, 32.7, 33.1, 33.2, 34.0, 37.4, 39.0, 39.4, 39.8, 41.9, 42.1, 46.1, 47.0, 48.1, 55.9, 58.2, 62.4, 71.1, 73.9, 78.2, 79.1, 82.0, 89.6, 123.0, 124.1, 143.5, 144.0, 177.4. ESI-MS (positive mode) *m*/*z*: 744.3 $[M + HCOO]^+$; HRMS (MALDI) *m*/*z* = $C_{39}H_{61}N_3O_8$ $[M + Na]^+$ calcd. 722.4356, found 722.4371.

[1-(β-D-Glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxy-urs-12-en-28-oate (20). Prepared from **17** (0.14 g, 0.17 mmol) according to General procedure V. The residue was purified by column chromatography (EtOAc). Yield: 0.11 g, 92%, white solid, mp 160–162 °C, R_f = 0.16 (EtOAc); $[\alpha]_D$ = +23 (*c* = 0.1, MeOH); IR (KBr, cm^{-1}): 3381, 2923, 2869, 1723, 1454, 1136, 1098, 1051, 1032, 1016, 772; ^1H NMR (300 MHz, C_5D_5N): δ 0.81 (d, 3H, *J* = 4.7 Hz, CH_3), 0.83, 0.85, 0.89, 0.97, 1.06, 1.17 (6 s, each 3H, 6 × CH_3), 2.34 (d, 1H, *J* = 11.2 Hz, H-18), 0.75–1.94 (m, 22H), 3.38 (m, 1H, H-3), 4.09–4.17 (m, 1H, H-5-Glc), 4.22–4.36 (m, 3H, H-4-Glc and H-6-Glc), 4.46 (d, 1H, *J* = 10.8 Hz, H-2-Glc), 4.75 (t, 1H, *J* = 8.8, 8.8 Hz, H-3-Glc), 5.33 (brs, 1H, H-12), 5.44 (s, 2H, $COOCH_2$), 6.33 (d, 1H, *J* = 9.2 Hz, H-1-Glc), 8.58 (s, 1H, NCH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.8, 16.6, 17.3, 18.8, 19.1, 21.2, 23.7, 23.8, 24.6, 28.2, 28.5, 28.8, 30.8, 33.5, 36.8, 37.3, 39.1, 39.2, 39.3, 39.4, 40.0, 42.4, 48.1, 48.4, 53.4, 55.9, 58.1, 62.4, 71.1, 73.9, 78.2, 79.1, 81.9, 89.6, 124.1, 126.2, 129.3, 138.6, 143.5, 177.1. ESI-MS (positive mode) *m*/*z*: 744.5 $[M + HCOO]^+$; HRMS (MALDI) *m*/*z* = $C_{39}H_{61}N_3O_8$ $[M + Na]^+$ calcd. 722.4356, found 722.4365.

[1-(β-D-Glucopyranosyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (21). Prepared from **18** (0.13 g, 0.15 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 15). Yield: 0.09 g, 85%, white solid, mp 205–207 °C, R_f = 0.18 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +27 (*c* = 0.07, MeOH). IR (KBr, cm^{-1}): 3461, 2945, 2864, 1720, 1642, 1457, 1051, 1031, 1017, 772, 667; ^1H NMR (300 MHz, C_5D_5N): δ 0.82, 0.85, 0.88, 1.03, 1.07, 1.15, 1.25 (7 s, each 3H, 7 × CH_3), 0.82–2.26 (m, 20H), 3.07–3.10 (m, 1H, H-18), 3.29 (d, 1H, *J* = 9.3 Hz, H-3α), 4.09 (m, 1H, H-2β), 4.23–4.31 (m, 1H, H-5-Glc), 4.34–4.42 (m, 3H, overlapping, H-4-Glc and H-6a-Glc, and H-6b-Glc), 4.52 (d, 1H, *J* = 11.0 Hz, H-2-Glc), 4.80 (t, 1H, *J* = 8.9, 8.9 Hz, H-3-Glc), 5.37 (s, 1H, H-12), 5.52 (s, 2H, $COOCH_2$), 6.38 (d, 1H, *J* = 9.2 Hz, H-1-Glc), 8.65 (s, 1H, NCH); ^{13}C NMR (75 MHz, C_5D_5N): δ 17.0, 17.5, 17.7, 18.9, 23.4, 23.6, 23.9, 26.0, 28.1, 29.3, 30.7, 32.7, 33.1, 33.2, 33.9, 38.6, 39.8, 41.9, 42.1, 46.1, 47.0, 47.8, 48.1, 55.9, 58.2, 62.4, 68.6, 71.1, 73.9, 79.1, 81.9, 83.9, 89.6, 122.9, 124.1, 143.5, 144.0, 177.4. ESI-MS (positive mode) *m*/*z*: 716.4 $[M + H]^+$; HRMS (MALDI) *m*/*z* = $C_{39}H_{61}N_3O_9$ $[M + Na]^+$ calcd. 738.4306, found 738.4320.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonylmethyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (22). Prepared from **4** (0.11 g, 0.23 mmol) and **12** (0.10 g, 0.23 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.18 g, 85%, white solid, mp 146–148 °C, R_f = 0.21 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 2947, 2872, 1755, 1552, 1463, 1374, 1230, 1175, 1159, 1045, 759, 667; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.57, 0.78, 0.98, 1.11 (4 s, each 3H, 4 × CH_3), 0.89 (s, 9H, 3 × CH_3), 0.57–2.10 (m, 22H), 2.01, 2.02, 2.03, 2.08 (4 s, each 3H, 4 x$OCOCH_3$), 2.82–2.85 (1H, m, H-18), 3.20 (dd, 1H, *J* = 5.0, 10.4 Hz, H-3), 3.78–3.83 (m, 1H, H-5-Glc), 4.07 (dd, 1H, *J* = 2.1, 12.6 Hz, H-6a-Glc), 4.28 (dd, 1H, *J* = 4.3, 12.5 Hz, H-6b-Glc), 4.90 (t, 1H, *J* = 9.6, 9.6 Hz, H-4-Glc), 4.94–5.32 (m, 8H, overlapping, NCH_2, $COOCH_2$, H-1-Glc, H-2-Glc, H-3-Glc, H-12), 6.78 (d, 1H, *J* = 8.7 Hz, OH), 7.69 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.4, 15.6, 16.7, 18.3, 20.5, 20.7, 23.0, 23.4, 23.6, 26.0, 27.2, 27.6, 28.1, 30.6, 32.3, 32.7, 33.0, 33.8, 37.0, 38.4, 38.7, 39.3, 41.3, 41.7, 45.8, 46.7, 47.5, 52.5, 55.2, 57.3, 61.5, 68.0, 70.3, 72.4, 73.8, 78.5, 79.0, 122.5, 125.4, 143.5, 143.9, 165.4, 169.4, 169.8, 170.5, 171.0, 177.6. ESI-MS (positive mode) *m*/*z*: 947.6 [M + Na]$^+$. HRMS (MALDI) *m*/*z* = $C_{45}H_{72}N_4O_{10}$ [M + Na]$^+$ calcd. 852.0638, found 851.5158.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (23). Prepared from **4** (0.10 g, 0.21 mmol) and **13** (0.10 g, 0.21 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.16 g, 80%, white solid, mp 99–100 °C, R_f = 0.12 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 2947, 2866, 1755, 1537, 1463, 1367, 1229, 1176, 1039, 757, 667; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.55, 0.77, 0.89, 0.97, 1.11 (5 s, each 3H, 5 × CH_3), 0.88 (s, 6H, 2 × CH_3), 0.55–2.07 (m, 28H), 2.02, 2.03, 2.04, 2.07 (4 s, each 3H, 4 × $OCOCH_3$), 2.14–2.18 (m, 2H, CH_2CO), 2.82–2.85 (m, 1H, H-18), 3.20 (dd, 1H, *J* = 4.9, 10.6 Hz, H-3), 3.79–3.84 (m, 1H, H-5-Glc), 4.07 (dd, 1H, *J* = 2.1, 12.5 Hz, H-6a-Glc), 4.28–4.34 (m, 3H, overlapping, NCH_2 and H-6b-Glc), 4.90 (t, 1H, *J* = 9.7, 9.7 Hz, H-4-Glc), 5.06 (t, 1H, *J* = 9.7, 9.7 Hz, H-3-Glc), 5.20 (s, 2H, $COOCH_2$), 5.24–5.34 (m, 3H, overlapping, H-12, H-1-Glc and H-12′), 6.23 (d, 1H, *J* = 9.2 Hz, NH), 7.56 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.3, 15.6, 16.7, 18.3, 20.6, 20.66, 20.7, 22.9, 23.4, 23.6, 24.2, 25.8, 25.9, 27.2, 27.6, 28.1, 29.9, 30.6, 32.3, 32.7, 33.0, 33.8, 36.0, 37.0, 38.4, 38.7, 39.3, 41.3, 41.7, 45.8, 46.7, 47.5, 49.9, 55.2, 57.4, 61.6, 68.1, 70.7, 72.6, 73.6, 77.2, 78.2, 79.0, 122.4, 123.9, 143.1, 143.6, 169.5, 169.8, 170.6, 171.1, 172.7, 177.8. ESI-MS (positive mode) *m*/*z*: 1003.5 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonyldecyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (24). Prepared from **4** (0.09 g, 0.18 mmol) and **14** (0.10 g, 0.18 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.12 g, 64%, white solid, mp 90–92 °C, R_f = 0.22 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 3359, 2922, 2860, 1744, 1693, 1364, 1220, 1049, 1032, 772; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.52, 0.77, 0.87, 0.88, 0.90, 0.98, 1.11 (7 s, each 3H, 7 × CH_3), 0.52–2.07 (m, 38H), 2.02, 2.03, 2.04, 2.07 (4 s, each 3H, 4 × $OCOCH_3$), 2.13–2.23 (m, 2H, CH_2CO), 2.82 (m, 1H, H-18), 3.20 (dd, 1H, *J* = 5.0, 10.9 Hz, H-3), 3.80–3.85 (m, 1H, H-5-Glc), 4.07 (dd, 1H, *J* = 1.9, 12.5 Hz, H-6a-Glc), 4.28–4.34 (m, 3H, overlapping, H-6b-Glc and NCH_2), 4.91 (pseudo t, 1H, *J* = 9.6, 9.7 Hz, H-4-Glc), 5.06 (pseudo t, 1H, *J* = 9.6, 9.7 Hz, H-3-Glc), 5.18 (s, 2H, $COOCH_2$), 5.22–5.34 (m, 3H, overlapping, H-12 and H-1-Glc, H-2-Glc), 6.30 (d, 1H, *J* = 9.3 Hz, NH), 7.56 (s, 1H, s, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ15.4, 15.6, 16.8, 18.3, 20.5, 20.6, 20.7, 23.0, 23.4, 23.6, 25.1, 25.8, 26.5, 27.2, 27.7, 28.1, 29.0, 29.1, 29.2, 29.3, 29.33, 30.2, 30.7, 32.4, 32.7, 33.0, 33.9, 36.6, 37.1, 38.5, 38.8, 39.4, 41.4, 41.7, 45.9, 46.8, 47.6, 50.4, 55.2, 57.5, 61.7, 68.3, 70.7, 72.8, 73.6, 77.2, 78.2, 79.0, 122.4, 123.9, 143.1, 169.5, 170.0, 170.5, 171.0, 173.3, 177.8. ESI-MS (positive mode) *m*/*z*: 1073.9 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonylmethyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (25). Prepared from **5** (0.11 g, 0.23 mmol) and **12** (0.10 g, 0.23 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.024 g, 11%, white solid, mp 116–118 °C, R_f = 0.21 (EtOAc–hexane, 1 : 1); $[\alpha]_D$ = +29 (*c* = 0.05, $CHCl_3$). IR (KBr, cm^{-1}): 3340, 2947, 2871, 1756, 1454, 1377, 1230, 1046, 1033, 997, 758; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.60, 0.78, 0.91, 0.93, 0.98, 1.06 (6 s, each 3H, 6 × CH_3), 0.83 (d, 3H, *J* = 6.4 Hz, CH_3), 0.60–2.01 (m, 22H), 2.01, 2.03, 2.08 (s, 12 H, 4 × $OCOCH_3$), 2.20 (d, 1H, *J* = 11.3 Hz, H-18), 3.22 (dd, 1H, *J* = 4.9, 10.8 Hz, H-3), 3.78–3.83 (m, 1H, H-5-Glc), 4.08 (dd, 1H, *J* = 1.9, 12.7 Hz, H-6a-Glc), 4.28 (dd, 1H, *J* = 4.3, 12.6 Hz, H-6b-Glc), 4.87 (pseudo t, 1H, *J* = 9.5, 9.6 Hz, H-4-Glc), 4.99–5.09 (m, 3H, overlapping, NCH_2CO and H-2-Glc), 5.16 (d, 1H, *J* = 12.7 Hz, $COOCH_2$), 5.19 (d, 1H, *J* = 12.7 Hz, $COOCH_2$), 5.22–5.23 (m, 2H, overlapping, H-1-Glc and H-12), 5.29 (pseudo t, 1H, *J* = 9.5, 9.6 Hz, H-3-Glc), 6.75 (d, 1H, *J* = 8.7 Hz, NH), 7.68 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5, 15.6, 16.9, 17.0, 18.3, 20.5, 20.7, 21.1, 23.3, 23.5, 24.2, 27.3, 28.0, 28.2, 30.6, 33.0, 36.6, 37.0, 38.7, 38.76, 38.84, 39.1, 39.6, 42.1, 47.6, 48.2, 52.6, 52.9, 55.3, 57.2, 61.6, 68.1, 70.4, 72.5, 73.9, 78.5, 79.1, 125.3, 125.8, 138.0, 144.0, 165.3, 169.4, 169.8, 170.5, 171.0, 177.4. ESI-MS (positive mode) *m*/*z*: 947.0 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (26). Prepared from **5** (0.10 g, 0.21 mmol) and **13** (0.10 g, 0.21 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.10 g, 50%, white solid, mp 102–104 °C, R_f = 0.56 (EtOAc–hexane, 2 : 1); IR (KBr, cm^{-1}): 3352, 2940, 2870, 1754, 1534, 1455, 1377, 1228, 1043, 756, 666; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.59, 0.77, 0.90, 0.93, 0.98, 1.06 (6 s, each 3H, 6 × CH_3), 0.83 (d, *J* = 6.4 Hz, 3H, CH_3), 0.59–2.00 (m, 28H), 2.02, 2.03, 2.04, 2.08 (4 s, each 3H, 4 × $OCOCH_3$), 2.14–2.23 (m, 3H, overlapping, H-18 and CH_2CON), 3.21 (dd, 1H, *J* = 4.0, 10.1 Hz, H-3), 3.79–3.84 (m, 1H, H-5-Glc), 4.07 (dd, 1H, *J* = 2.1, 12.7 Hz, H-6a-Glc), 4.29–4.34 (m, 3H, overlapping, H-6b-Glc and NCH_2), 4.90 (pseudo t, 1H, J = 9.5, 9.7 Hz, H-4-Glc), 5.06 (pseudo t, 1H, J = 9.5, 9.7 Hz, H-3-Glc), 5.14 and 5.15 (2 s, each 1H, $COOCH_2$), 5.21–5.34 (m, 3H, overlapping, H-12, H-1-Glc, H-2-Glc), 6.24 (d, 1H, J = 8.8 Hz, NH), 7.54 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 15.5, 15.6, 16.9, 17.0, 18.3, 20.6, 20.67, 20.7, 21.1, 23.3, 23.5, 24.2, 24.22, 25.9, 27.2, 28.0, 28.1, 29.9, 30.6, 33.0, 36.0, 36.6, 37.0, 38.6, 38.7, 38.8, 39.1, 39.5, 42.1, 47.5, 48.1, 49.9, 52.8, 55.2, 57.4, 61.6, 68.2, 70.7, 72.6, 73.6, 77.2, 78.2, 79.0, 123.8, 125.6, 138.0, 143.2, 169.5, 169.8, 170.6, 171.1, 172.7, 177.5. ESI-MS (positive mode) m/z: 1003.6 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonyl-decyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (27). Prepared from **5** (0.09 g, 0.18 mmol) and **14** (0.10 g, 0.18 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 2). Yield: 0.14 g, 74%, white solid, mp 92–93 °C. R_f = 0.30 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 3369, 2928, 2857, 1756, 1693, 1537, 1455, 1376, 1223, 1141, 1102, 1043, 996, 761, 666; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.57, 0.78, 0.90, 0.93, 0.99, 1.06 (6 s, each 3H, 6 × CH_3), 0.83 (d, 3H, J = 6.4 Hz, CH_3), 0.57–2.02 (m, 38H), 2.02, 2.03, 2.04, 2.07 (4 s, each 3H, 4 × $OCOCH_3$), 2.13–2.24 (m, 3H, overlapping, H-18 and CH_2CON), 3.21 (dd, 1H, J = 5.0, 11.0 Hz, H-3), 3.79–3.85 (m, 1H, H-5-Glc), 4.07 (dd, 1H, J = 2.0, 12.5 Hz, H-6a-Glc), 4.29–4.38 (m, 3H, overlapping, H-6b-Glc and NCH_2), 4.92 (pseudo t, 1H, J = 9.6, 9.7 Hz, H-4-Glc), 5.06 (pseudo t, 1H, J = 9.6, 9.7 Hz, H-3-Glc), 5.16 (s, 2H, $COOCH_2$), 5.21–5.23 (m, 1H, H-1-Glc), 5.26–5.34 (m, 2H, overlapping, H-12 and H-2-Glc), 6.30 (d, 1H, J = 9.4 Hz, NH), 7.55 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ15.5, 15.7, 16.9, 17.0, 18.3, 20.5, 20.6, 20.7, 21.1, 23.3, 23.5, 24.2, 25.1, 26.5, 27.3, 28.0, 28.2, 29.0, 29.1, 29.2, 29.3, 29.34, 30.2, 30.7, 33.0, 36.6, 37.0, 38.7, 38.8, 38.84, 39.1, 39.6, 42.1, 47.6, 48.2, 50.4, 52.9, 55.2, 57.4, 60.1, 61.7, 68.3, 70.8, 72.8, 73.6, 77.2, 78.2, 79.0, 123.8, 125.6, 138.1, 143.1, 169.5, 169.8, 170.5, 171.0, 173.3, 177.5. ESI-MS (positive mode) m/z: 1073.5 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonyl-methyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (28). Prepared from **6** (0.12 g, 0.23 mmol) and **12** (0.10 g, 0.23 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.13 g, 57%, white solid, mp 178–180 °C, R_f = 0.39 (EtOAc–hexane, 2 : 1); IR (KBr, cm^{-1}): 3345, 2947, 1755, 1556, 1460, 1371, 1230, 1175, 1160, 1048, 1034, 759; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.58, 0.83, 0.89, 0.90, 0.97, 1.03, 1.12 (7 s, each 3H, 7 × CH_3), 0.83–2.01 (m, 20H), 2.01, 2.02, 2.03, 2.08 (4 s, each 3H, 4 × $OCOCH_3$), 2.84 (dd, 1H, J = 4.1, 9.7 Hz, H-18), 2.99 (d, 1H, J = 9.5 Hz, H-3α), 3.68–3.71 (m, 1H, H-2β), 3.78–3.83 (m, 1H, H-5-Glc), 4.06–4.13 (m, 1H, H-6a-Glc), 4.28 (dd, 1H, J = 4.3, 12.5 Hz, H-6b-Glc), 4.87 (t, 1H, J = 9.6, 9.6 Hz, H-4-Glc), 4.95–5.07 (m, 3H, overlapping, NCH_2CO and H-3-Glc), 5.15–5.21 (m, 3H, overlapping, $COOCH_2$ and H-2-Glc), 5.25–5.32 (m, 3H, overlapping, H-1-Glc and H-12), 6.72 (d, 1H, J = 8.7 Hz, NH), 7.69 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.6, 16.7, 18.3, 20.5, 20.7, 23.0, 23.4, 23.6, 25.8, 27.6, 28.6, 30.6, 32.3, 32.6, 33.0, 33.8, 38.3, 39.2, 39.4, 41.3, 41.8, 45.8, 46.5, 46.7, 52.6, 55.3, 57.4, 61.6, 68.1, 68.9, 70.4, 72.4, 73.9, 78.5, 83.9, 122.3, 125.3, 143.6, 144.0, 165.3, 169.4. ESI-MS (positive mode) m/z: 963.7 [M + Na]$^+$, 979.7 [M + K]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonyl-pentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (29). Prepared from **6** (0.11 g, 0.21 mmol) and **13** (0.10 g, 0.21 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 2 : 1). Yield: 0.15 g, 71%, white solid, mp 160–162 °C, R_f = 0.06 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 3369, 2947, 1794, 1745, 1364, 1228, 1175, 1160, 1046, 757, 666; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.55, 0.82, 0.89, 0.90, 0.95, 1.02, 1.11 (7 s, each 3H, 7 × CH_3), 0.81–2.02 (m, 26H), 2.02, 2.03, 2.04, 2.08 (4 s, each 3H, 4 × $OCOCH_3$), 2.14–2.20 (m, 2H, CH_2CON), 2.85 (dd, 1H, J = 3.7, 10.3 Hz, H-18), 2.98 (d, 1H, J = 9.5 Hz, H-3α), 3.64–3.71 (m, 1H, H-2β), 3.80–3.85 (m, 1H, H-5-Glc), 4.07 (dd, 1H, J = 2.0, 12.5 Hz, H-6a-Glc), 4.28–4.34 (m, 3H, overlapping, NCH_2 and H-6b-Glc), 4.92 (t, 1H, J = 9.6, 9.6 Hz, H-4-Glc), 5.06 (t, 1H, J = 9.7, 9.7 Hz, H-3-Glc), 5.17 (s, 2H, $COOCH_2$), 5.21–5.34 (m, 3H, overlapping, H-12 and H-1-Glc, H-2-Glc), 6.23 (d, 1H, J = 9.3 Hz, NH), 7.55 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.6, 16.7, 16.8, 18.3, 20.5, 20.6, 20.7, 23.0, 23.5, 23.6, 24.3, 25.8, 25.9, 27.6, 28.6, 29.9, 30.6, 32.4, 32.6, 33.0, 33.8, 36.0, 38.3, 39.1, 39.4, 41.3, 41.8, 45.8, 46.4, 46.7, 47.5, 49.9, 55.3, 57.6, 61.7, 68.2, 68.9, 70.8, 72.7, 73.6, 76.7, 77.2, 78.2, 83.9, 114.6, 120.2, 121.8, 122.2, 123.7, 143.2, 143.5, 143.7, 169.5, 169.8, 171.1, 172.6, 177.7. ESI-MS (positive mode) m/z: 1019.4 [M + Na]$^+$.

[1-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosylaminocarbonyl-decyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (30). Prepared from **6** (0.09 g, 0.18 mmol) and **14** (0.10 g, 0.18 mmol) according to General procedure IVa. The residue was purified by column chromatography (EtOAc–hexane, 1 : 1). Yield: 0.16 g, 82%, white solid, mp 110–112 °C, R_f = 0.23 (EtOAc–hexane, 1 : 1); IR (KBr, cm^{-1}): 3374, 2931, 2858, 1795, 1753, 1536, 1461, 1364, 1220, 1175, 1160, 1049, 1034, 770, 667; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.50, 0.81, 0.89, 0.90, 0.95, 1.02, 1.11 (7 s, each 3H, 7 × CH_3), 0.81–2.02 (m, 36H), 2.02, 2.03, 2.04, 2.08 (4 s, each 3H, 4 × $OCOCH_3$), 2.18–2.29 (m, 2H, CH_2CON), 2.84 (dd, 1H, J = 3.5, 13.3 Hz, H-18), 2.97 (d, 1H, J = 9.5 Hz, H-3α), 3.64–3.71 (m, 1H, H-2β), 3.80–3.85 (m, 1H, H-5-Glc), 4.07 (dd, 1H, J = 2.0, 12.5 Hz, H-6a-Glc), 4.28–4.34 (m, 3H, overlapping, NCH_2 and H-6b-Glc), 4.92 (pseudo t, 1H, J = 9.6, 9.7 Hz, H-4-Glc), 5.06 (pseudo t, 1H, J = 9.6, 9.7 Hz, H-3-Glc), 5.16 and 5.17 (2 s, each 1H, $COOCH_2$), 5.22–5.34 (m, 3H, overlapping, H-12 and H-1-Glc, H-2-Glc), 6.32 (d, 1H, J = 9.3 Hz, NH), 7.56 (s, 1H, NCH); ^{13}C NMR (75 MHz, $CDCl_3$): δ 16.7, 16.79, 16.84, 18.4, 20.5, 20.6, 20.7, 23.0, 23.5, 23.6, 25.1, 23.8, 26.6, 27.6, 28.6, 29.0, 29.1, 29.2, 29.3, 30.3, 30.7, 32.5, 32.6, 33.0, 33.9, 36.6, 38.3, 39.2, 39.4, 41.3, 41.8, 45.9, 46.4, 46.7, 47.5, 50.3, 55.3, 57.6, 61.7, 68.3, 68.9, 68.4, 70.8, 72.8, 73.6, 78.2, 83.9, 122.2, 123.8, 143.1, 169.5, 169.8, 171.0, 173.4, 177.8. ESI-MS (positive mode) m/z: 1089.6 $[M + Na]^+$.

[1-(β-D-Glucopyranosylaminocarbonylmethyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (31). Prepared from **22** (0.13 g, 0.14 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 15). Yield: 0.055 g, 51%, white solid, mp 197–199 °C, R_f = 0.09 ($MeOH–CH_2Cl_2$, 1 : 10); $[\alpha]_D$ = +37 (c = 0.11, MeOH); IR (KBr, cm^{-1}): 3407, 2943, 2860, 1705, 1556, 1389, 1161, 1059, 1032, 1018, 772; ^1H NMR (300 MHz, C_5D_5N): δ 0.80, 0.90, 1.03, 1.19, 1.24 (5 s, each 3H, 5 × CH_3), 0.88 (s, 6H, 2 × CH_3), 0.80–1.96 (m, 22H), 3.13 (d, 1H, J = 10.3 Hz, H-18), 3.43 (t, 1H, J = 7.8 Hz, H-3), 4.02–4.11 (m, 2H, overlapping, H-5-Glc and H-6a-Glc), 4.25–4.27 (m, 2H, overlapping, H-4-Glc and H-2-Glc), 4.37 (dd, 1H, J = 4.3, 11.8 Hz, H-6b-Glc), 4.49 (d, 1H, J = 11.5 Hz, H-1′), 5.43 (s, 1H, H-12), 5.48 (s, 2H, NCH_2CO), 5.62 (s, 2H, $COOCH_2$), 5.97 (t, 1H, J = 8.9, 8.9 Hz, H-3-Glc), 8.40 (s, 1H, NCH), 10.60 (d, 1H, J = 8.8 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.6, 16.5, 17.1, 18.7, 23.3, 23.6, 23.7, 26.0, 28.0, 28.1, 28.7, 29.9, 30.7, 32.7, 33.05, 33.1, 33.9, 37.3, 38.9, 39.3, 39.7, 41.9, 42.0, 46.1, 46.9, 48.0, 52.7, 55.8, 58.0, 62.4, 71.5, 74.5, 78.1, 79.5, 80.3, 81.5, 123.1, 123.8, 126.7, 135.8, 143.5, 144.0, 150.2, 166.9, 177.3. ESI-MS (negative mode) m/z: 755.5 $[M - H]^+$; HRMS (MALDI) m/z = $C_{41}H_{64}N_4O_9$ $[M + Na]^+$ calcd. 779.4571, found 779.4594.

[1-(β-D-Glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (32). Prepared from **23** (0.11 g, 0.11 mmol) according to the general procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 15). Yield: 0.076 g, 83%, white solid, mp 164–166 °C, R_f = 0.25 ($MeOH–CH_2Cl_2$, 1 : 10); $[\alpha]_D$ = +42 (c = 0.06, MeOH); IR (KBr, cm^{-1}): 3367, 2939, 2864, 1725, 1663, 1382, 1053, 1032, 1013, 773; ^1H NMR (300 MHz, C_5D_5N): δ 0.81, 0.94, 1.05, 1.20, 1.24 (5 s, each 3H, 5 × CH_3), 0.89 (s, 6H, 2 CH_3), 0.81–1.93 (m, 28H), 2.41 (t, 2H, J = 7.3 Hz, CH_2CO), 3.15 (d, 1H, J = 13.3 Hz, H-18), 3.45 (brs, 1H, H-3), 4.05–4.13 (m, 2H, H-5-Glc and H-6a-Glc), 4.23–4.30 (m, 4H, H-2-Glc, H-4-Glc and NCH_2), 4.37 (dd, 1H, J = 4.6, 11.8 Hz, H-6b-Glc), 4.48 (d, 1H, J = 11.8 Hz, H-1-Glc), 5.43 (s, 1H, H-12), 5.53 and 5.54 (2 d, each 1H, J = 12.6 Hz, $COOCH_2$), 6.01 (t, 1H, J = 9.0, 9.0 Hz, H-3-Glc), 8.13 (s, 1H, NCH), 9.62 (d, 1H, J = 9.1 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.6, 16.5, 17.2, 18.8, 23.3, 23.6, 23.8, 25.1, 26.0, 26.4, 28.0, 28.1, 28.8, 30.3, 30.7, 32.8, 33.1, 33.2, 33.9, 36.3, 37.3, 39.0, 39.4, 39.7, 41.9, 42.0, 46.1, 47.0, 48.0, 50.0, 55.8, 58.1, 62.7, 71.8, 74.6, 78.1, 79.7, 80.1, 81.3, 123.0, 124.6, 143.4, 144.0, 173.6, 177.4. ESI-MS (negative mode) m/z: 811.4 $[M - H]^+$; HRMS (MALDI) m/z = $C_{45}H_{72}N_4O_9$ $[M + Na]^+$ calcd. 835.5197, found 835.5203.

[1-(β-D-Glucopyranosylaminocarbonyldecyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyolean-12-en-28-oate (33). Prepared from **24** (0.083 g, 0.08 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 20). Yield: 0.068 g, 97%, white solid, mp 195–196 °C, R_f = 0.27 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +31 (c = 0.1, MeOH); IR (KBr, cm^{-1}): 3392, 2928, 1727, 1463, 1386, 1158, 1123, 1050, 1032, 1012, 756, 697; ^1H NMR (300 MHz, C_5D_5N): δ 0.59, 0.86, 1.04, 1.10 (4 s, each 3H, 4 × CH_3), 0.74 (s, 9H, 3 × CH_3), 0.59–1.95 (m, 38H), 2.36 (t, 2H, J = 7.3 Hz, CH_2CON), 2.94 (dd, 1H, J = 3.6, 10.0 Hz, H-18), 3.28 (t, 1H, J = 8.0 Hz, H-3), 3.92–3.93 (m, 2H, overlapping, H-5-Glc and H-6a-Glc), 4.04–4.10 (m, 3H, m, overlapping, NCH_2 and H-6b-Glc), 4.26–4.38 (m, 3H, m, overlapping, H-2-Glc, H-3-Glc, and H-4-Glc), 5.26 (s, 1H, H-12), 5.42 (d, 1H, J = 14.1 Hz, $COOCH_2$), 5.46 (d, 1H, J = 14.1 Hz, $COOCH_2$), 5.63 (d, 1H, J = 8.6 Hz, H-1-Glc), 8.18 (s, 1H, NCH), 9.67 (d, 1H, J = 8.8 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.7, 16.6, 17.3, 18.8, 23.4, 23.7, 23.8, 25.9, 26.0, 26.7, 28.1, 28.8, 29.2, 29.6, 29.64, 29.7, 30.6, 30.8, 32.8, 33.1, 33.2, 34.0, 36.9, 37.4, 39.0, 39.4, 39.8, 41.9, 42.1, 46.1, 47.0, 48.0, 50.3, 55.8, 58.1, 62.7, 71.8, 74.5, 78.1, 79.6, 80.0, 81.4, 122.8, 124.7, 143.4, 144.0, 174.1, 177.4. ESI-MS (positive mode) m/z: 917.5 $[M + Cl]^+$; HRMS (MALDI) m/z = $C_{50}H_{82}N_4O_9$ $[M + Na]^+$ calcd. 905.5980, found 905.6013.

[1-(β-D-Glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (34). Prepared from **26** (0.065 g, 0.07 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 20). Yield: 0.053 g, 98%, white solid, mp 214–216 °C, R_f = 0.67 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +26 (c = 0.1, MeOH). IR (KBr, cm^{-1}): 3386, 2924, 2869, 1724, 1657, 1456, 1392, 1049, 1032, 1017; ^1H NMR (300 MHz, C_5D_5N): δ 0.83, 0.91, 0.94, 1.04, 1.13, 1.23 (6 s, each 3H, 6 × CH_3), 0.88 (d, 3H, J = 3.9 Hz, CH_3), 0.83–2.00 (m, 28H), 2.39–2.47 (m, 3H, overlapping, H-18 and CH_2CON), 3.44 (dd, 1H, J = 6.1, 9.8 Hz, H-3), 4.04 (m, 1H, H-5-Glc), 4.16 (t, 1H, J = 9.8, 9.8 Hz, H-4-Glc), 4.24–4.45 (m, 6H, overlapping, NCH_2, H-2-Glc, H-3-Glc and H-6a-Glc, H-6b-Glc), 5.40 (s, 1H, H-12), 5.50 (s, 2H, $COOCH_2$), 5.96 (1H, overlapping, H-1′), 8.13 (s, 1H, NCH), 9.69 (d, 1H, J = 8.2 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.8, 16.6, 17.3, 18.8, 21.2, 23.7, 23.8, 24.6, 25.1, 26.4, 28.1, 28.4, 28.8, 30.0, 30.3, 30.8, 33.5, 36.4, 37.0, 37.3, 39.1, 39.2, 39.3, 39.4, 40.0, 42.4, 48.0, 48.4, 50.1, 53.4, 55.8, 58.0, 62.7, 71.8, 74.5, 78.2, 79.6, 80.0, 81.3, 124.6, 126.2, 138.6, 143.3, 173.7, 177.1. ESI-MS (positive mode) m/z: 847.5 $[M + Cl]^+$. HRMS (MALDI) m/z = $C_{45}H_{72}N_4O_9$ $[M + Na]^+$ calcd. 835.5197, found 835.5206.

[1-(β-D-Glucopyranosylaminocarbonyldecyl)-1*H*-1,2,3-triazol-4-ylmethyl] 3β-hydroxyurs-12-en-28-oate (35). Prepared from **27** (0.10 g, 0.1 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 12). Yield: 0.078 g, 93%, white solid, mp 199–200 °C, R_f = 0.12 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +32 (c = 0.06, MeOH); IR (KBr, cm^{-1}): 3409, 2924, 2861, 1726, 1662, 1453, 1382, 1052, 1032, 1013. ^1H NMR (300 MHz, C_5D_5N): δ 0.81, 0.91, 0.94, 1.03, 1.13, 1.23 (6 s, each 3H, 6 × CH_3), 0.88 (d, 3H, J = 3.6 Hz, CH_3), 0.81–1.99 (m, 38H), 2.43–2.49 (m, 3H, overlapping, H-18 and CH_2CON), 3.44 (dd, 1H, J = 6.8, 9.7 Hz, H-3), 4.04 (m, 1H, H-5-Glc), 4.14 (t, 1H, J = 8.8, 8.8 Hz, H-4-Glc), 4.21–4.33 (m, 2H, NCH_2), 4.35–4.47 (m, 3H, overlapping, H-3-Glc, H-2-Glc and H-1-Glc), 5.39 (brs, 1H, H-12), 5.51 and 5.52 (2 d, each 1H,

J = 12.5 Hz, $COOCH_2$), 8.19 (s, 1H, NCH), 9.62 (d, 1H, J = 9.0 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 15.8, 16.6, 17.3, 17.4, 18.8, 21.2, 23.7, 23.8, 24.6, 26.0, 26.8, 28.2, 28.5, 28.9, 29.3, 29.6, 29.67, 29.7, 30.0, 30.6, 30.8, 33.5, 36.9, 37.0, 37.4, 39.2, 39.3, 39.4, 40.0, 42.4, 48.0, 48.4, 50.3, 53.4, 55.9, 58.1, 62.8, 71.9, 74.6, 78.2, 79.7, 80.0, 81.4, 124.7, 126.2, 143.4, 174.1, 177.2. ESI-MS (positive mode) m/z: 927.5 $[M + HCOO]^+$; HRMS (MALDI) m/z = $C_{50}H_{82}N_4O_9$ $[M + Na]^+$ calcd. 905.5980, found 905.6004.

[1-(β-D-Glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (36). Prepared from **29** (0.10 g, 0.1 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 10). Yield: 0.075 g, 93%, white solid, mp 180–182 °C, R_f = 0.09 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +23 (c = 0.05, MeOH); IR (KBr, cm^{-1}): 3369, 2944, 2873, 1725, 1664, 1546, 1461, 1260, 1159, 1122, 1049, 1033; ^{1}H NMR (300 MHz, C_5D_5N): δ 0.79, 0.90, 1.02, 1.09, 1.16 (5 s, each 3H, 5 × CH_3), 0.87 (s, 6H, 2 × CH_3), 0.79–2.30 (m, 26H), 2.40 (t, 2H, J = 7.3 Hz, CH_2CON), 3.11 (dd, 1H, J = 4.2, 13.5 Hz, H-18), 3.37 (d, 1H, J = 9.3 Hz, H-3α), 4.10 (m, 1H, H-2β), 4.15–4.49 (m, 6H, overlapping, H-1-Glc, H-2-Glc, H-4-Glc, H-5-Glc and H-6-Glc), 5.38 (s, 1H, H-12), 5.52 (s, 2H, $COOCH_2$), 5.99 (t, 1H, J = 9.0, 9.0 Hz, H-3-Glc), 8.11 (s, 1H, NCH), 9.62 (d, 1H, J = 9.0 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 16.9, 17.3, 17.7, 18.9, 23.4, 23.7, 23.9, 25.1, 26.0, 26.5, 28.0, 29.3, 30.0, 30.4, 36.4, 38.6, 39.8, 41.9, 42.1, 46.1, 47.0, 47.8, 48.1, 50.0, 55.9, 58.2, 62.8, 68.6, 71.8, 74.6, 79.7, 80.0, 81.3, 83.8, 122.9, 124.6, 143.3, 144.0, 173.6, 177.4. ESI-MS (positive mode) m/z: 873.5 $[M + HCOO]^+$; HRMS (MALDI) m/z = $C_{45}H_{72}N_4O_{10}$ $[M + Na]^+$ calcd. 851.5146, found 851.5158.

[1-(β-D-Glucopyranosylaminocarbonyldecyl)-1*H*-1,2,3-triazol-4-ylmethyl] 2α,3β-dihydroxyolean-12-en-28-oate (37). Prepared from **30** (0.11 g, 0.1 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 15). Yield: 0.065 g, 72%, white solid, mp 163–165 °C, R_f = 0.18 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +33 (c = 0.07, MeOH), IR (KBr, cm^{-1}): 3377, 2923, 2861, 1725, 1053, 1032, 1015, 772; ^{1}H NMR (300 MHz, C_5D_5N): δ 0.79, 1.04, 1.10, 1.18 (4 s, each 3H, 4 × CH_3), 0.89 (s, 9H, 3 × CH_3), 0.79–2.30 (m, 36H), 2.48 (t, 2H, J = 7.5 Hz, CH_2CON), 3.12 (dd, 1H, J = 3.8, 9.9 Hz, H-18), 3.38 (d, 1H, J = 9.2 Hz, H-3α), 4.05 (m, 1H, H-2β), 4.07–4.51 (m, 8H, overlapping, H-1-Glc, H-2-Glc, H-4-Glc, H-5-Glc, H-6-Glc and NCH_2), 5.40 (s, 1H, H-12), 5.54 and 5.57 (2 d, each 1H, J = 12.6 Hz, $COOCH_2$), 6.03 (t, 1H, J = 9.0, 9.0 Hz, H-3-Glc), 8.12 (s, 1H, NCH), 9.61 (d, 1H, J = 8.9 Hz, NH); ^{13}C NMR (75 MHz, C_5D_5N): δ 17.0, 17.3, 17.7, 18.9, 23.4, 23.9, 25.95, 26.0, 26.8, 28.0, 29.3, 29.4, 29.6, 29.66, 29.7, 30.0, 30.6, 30.8, 32.8, 33.1, 34.0, 36.9, 38.6, 39.9, 41.9, 42.1, 46.1, 47.0, 47.8, 48.1, 50.3, 55.9, 58.2, 62.8, 68.6, 71.9, 74.7, 79.8, 80.1, 81.4, 83.9, 122.9, 124.7, 143.4, 144.1, 174.0, 177.4. ESI-MS (positive mode) m/z: 943.6 $[M + HCOO]^+$; HRMS (MALDI) m/z = $C_{50}H_{82}N_4O_{10}$ $[M + Na]^+$ calcd. 921.5929, found 921.5937.

2-[4-(2α,3β-dihydroxyolean-12-en-28-carbonyloxymethyl)-1*H*-1,2,3-triazol-1-yl] acetic acid (38). Prepared from **28** (0.084 g, 0.09 mmol) according to General procedure V. The residue was purified by column chromatography ($MeOH–CH_2Cl_2$, 1 : 10). Yield: 0.05 g, 91%, white solid, mp 225–227 °C, R_f = 0.06 ($MeOH–CH_2Cl_2$, 1 : 15); $[\alpha]_D$ = +82 (c = 0.06, MeOH); IR (KBr, cm^{-1}): 3403, 2940, 2862, 1724, 1450, 1386, 1229, 1159, 1050, 1033; ^{1}H NMR (300 MHz, C_5D_5N): δ 0.84, 1.02, 1.07, 1.13, 1.17 (5 s, each 3H, 5 × CH_3), 0.87 (s, 6H, 2 × CH_3), 0.84–2.22 (m, 20H), 3.12 (dd, 1H, J = 3.7, 13.5 Hz, H-18), 3.37 (d, 1H, J = 9.4 Hz, H-3α), 4.06–4.14 (m, 1H, H-2β), 5.40 (s, 1H, H-12), 5.54 (s, 2H, NCH_2CO), 5.64 (s, 2H, $COOCH_2$), 5.67 (s, 2H, $COOCH_2$), 8.45 (s, 1H, NCH); ^{13}C NMR (75 MHz, C_5D_5N): δ 16.9, 17.3, 17.7, 18.9, 23.4, 23.7, 23.9, 26.0, 28.1, 29.3, 30.0, 30.8, 32.7, 33.1, 34.0, 38.6, 39.8, 39.9, 41.9, 42.1, 46.1, 47.0, 47.8, 48.1, 52.3, 55.9, 58.2, 68.6, 83.9, 122.6, 126.3, 143.5, 144.0, 177.4. ESI-MS (positive mode) m/z: 634.9 $[M + Na]^+$; HRMS (MALDI) m/z = $C_{35}H_{53}N_3O_6$ $[M + Na]^+$ calcd. 634.3832, found 634.3845.

General procedure VI for the Zemplén-deacetylation

To a solution of an *O*-acetyl-protected compound in dry MeOH 1–2 drops of a ~1 M methanolic NaOMe solution were added, and the reaction mixture was kept at rt until completion of the transformation (TLC, $CHCl_3$–MeOH, 1 : 1). Amberlyst 15 (H^+ form) was then added to remove sodium ions, the resin was filtered off, and the solvent removed *in vacuo*. If the residue was chromatographically non-uniform it was purified by column chromatography or crystallisation.

General procedure VII for reduction

An *N*-(ω-azidoalkanoyl)-β-D-glucopyranosyl-amine was dissolved in dry MeOH (12 mL/mmol). To the solution RANEY®-Ni (~2 mmol) was added, and H_2 gas was bubbled through the mixture at 70 °C until the complete transformation of the starting azide TLC ($CHCl_3$–MeOH, 1 : 1). The solution was filtered over a Celite pad and the solvent was removed *in vacuo*.

***N*-Azidoacetyl-β-D-glucopyranosylamine (39).** Prepared from **12** (0.10 g, 0.23 mmol) according to General procedure VI. The residue was purified by column chromatography ($CHCl_3$–MeOH, 7 : 3). Yield: 0.058 g, 95%, colourless oil, R_f = 0.34 ($CHCl_3$–MeOH, 7 : 3); $[\alpha]_D$ = −12 (c = 0.22, MeOH), (lit.[40] $[\alpha]_D$ = −61 (c = 1, H_2O)); ^{1}H NMR (360 MHz, CD_3OD): δ(ppm) 3.29–3.37 (m, 3H, H-3, H-4, H-5), 3.44 (t, 1H, J = 9.2, 9.2 Hz, H-2), 3.68 (dd, 1H, J = 4.0, 11.9 Hz, H-6b), 3.83–3.99 (m, 3H, CH_2, H-6a), 4.95 (d, 1H, J = 9.2 Hz, H-1). ^{13}C NMR (90 MHz, D_2O): δ(ppm) 52.8 (CH_2), 62.6 (C-6), 71.2, 73.8, 78.8, 79.7 (C-2, C-3, C-4, C-5), 81.0 (C-1), 171.3 (CONH). Analysis: Calcd for $C_8H_{14}N_4O_6$ (262.22): C, 36.64; H, 5.38; N, 21.37. Found: C, 36.73; H, 5.42; N, 21.25.

***N*-Glycyl-β-D-glucopyranosylamine (40).** Prepared from **39** (0.097 g, 0.37 mmol) according to General procedure VII. Yield: 0.07 g, 79%, amorphous oil, R_f = 0.16 (MeOH); $[\alpha]_D$ = +34 (c = 0.08, DMSO); ^{1}H NMR (360 MHz, CD_3OD): δ(ppm) 3.48–3.61 (m, 6H, H-2, H-3, H-4, H-5, CH_2), 3.76 (dd, 1H, J = 5.3, 11.9 Hz, H-6a), 3.90 (dd, 1H, J = 1.2, 11.9 Hz, H-6b), 5.04 (d, 1H, J = 9.2 Hz, H-1). ^{13}C NMR (90 MHz, D_2O): δ(ppm) 44.1 (CH_2), 62.6 (C-6), 69.8, 72.4, 77.1, 78.2 (C-2, C-3, C-4, C-5), 79.9 (C-1), 176.5 (CONH). Analysis: Calcd for $C_8H_{16}N_2O_6$ (236.22): C, 40.68; H, 6.83; N, 11.86. Found: C, 40.75; H, 6.68; N, 11.79.

***N*-(6-Azidohexanoyl)-β-D-glucopyranosylamine (41).** Prepared from **13** (0.50 g, 1.03 mmol) according to General procedure VI. The residue was purified by column chromatography ($CHCl_3$–MeOH, 7 : 3). Yield: 0.31 g (97%) colourless oil, R_f = 0.66 ($CHCl_3$–MeOH, 7 : 3); $[\alpha]_D$ = +13 (c = 0.22, MeOH); ^{1}H NMR (360 MHz, MeOD): δ(ppm) 1.42–1.49 (m, 2H, CH_2), 1.60–1.72 (m, 4H, CH_2), 2.25–2.32 (m, 2H, CH_2), 3.36–3.24 (m, 5H, H-3, H-4, H-5, CH_2), 3.44 (pseudo t, 1H, J = 7.9, 9.2 Hz, H-2), 3.69 (dd, 1H, J = 5.3, 11.9 Hz, H-6b), 3.85 (dd, 1H, J = 1.2, 11.9 Hz, H-6a), 4.92 (d, 1H, J = 7.9 Hz, H-1); ^{13}C NMR (90 MHz, MeOD): δ (ppm) 26.0, 27.4, 29.6, 36.9, 52.3 (5 × CH_2), 62.6 (C-6), 71.4, 73.9, 79.0, 79.5 (C-2, C-3, C-4, C-5), 80.9 (C-1), 177.0 (NH*C*O); Anal. calcd. for $C_{12}H_{22}N_4O_6$ (318.33): C 45.28, H 6.97, N 17.60. Found: C 45.36, H 6.84, N 17.49.

***N*-(6-Aminohexanoyl)-β-D-glucopyranosylamine (42).** Prepared from **41** (0.18 g 0.57 mmol) according to General procedure VII. Yield: 0.09 g (57%) colourless oil, R_f = 0.05 (MeOH); $[\alpha]_D$ = +11 (c =0.15, MeOH); ^{1}H NMR (360 MHz, MeOD): δ(ppm) 1.34–1.38 (m, 2H, CH_2), 1.47–1.51 (m, 2H, CH_2), 1.60–1.64 (m, 2H, CH_2), 2.21–2.27 (m, 2H, CH_2), 2.62–2.68 (m, 2H, CH_2), 3.23–3.35 (m, 3H, H-3, H-4,H-5), 3.38 (t, 1H, J = 7.9, 7.9 Hz, H-2), 3.62 (dd, 1H, J = 5.3, 11.9 Hz, H-6a), 3.81 (dd, 1H, J = 1.2, 11.9 Hz, H-6a), 4.84 (d, 1H, J = 7.9 Hz, H-1); ^{13}C NMR (MeOD, 90 MHz): δ (ppm) 26.2, 27.4, 32.4, 36.9, 41.9 (5 × CH_2), 62.7 (C-6), 71.4, 73.9, 79.0, 79.7 (C-2, C-3, C-4, C-5), 81.0 (C-1), 177.2 (NH*C*O). Anal. calcd. for $C_{12}H_{24}N_4O_6$ (292.33): C 49.30, H 8.28, N 9.58. Found: C 49.36, H 8.18, N 9.45.

1,4-Bis-[1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamino-carbonylmethyl)-1*H*-1,2,3-triazol-4-yl)]butane (44). Prepared from **12** (0.30 g 0.41 mmol) according to General procedure IVb. The residue was purified by column chromatography (EtOAc). Yield: 0.10 g, 89%, white crystalline product, mp 197–199 °C, $[\alpha]_D$ = +35 (c = 0.20, DMSO); ^{1}H NMR (360 MHz, DMSO-d_6): δ(ppm) 1.64 (brs, 4H, 2 × CH_2), 1.93, 1.95, 1.99, 2.00 (4s, 24H, 8 × $OCOCH_3$), 2.65 (brs, 4H, 2 × CH_2), 3.96–4.16 (m, 6H, 2 × H-5-Glc, 2 × H-6a-Glc, 2 × H-6b-Glc), 5.07 (brs, 4H, 2 × CH_2), 4.86, 4.92, 5.34, 5.42 (4t, 8 H, J = 9.2, 9.2 Hz in each, 2 H-1-Glc, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc), 7.78 (s, 2H, 2 triazole CH), 9.20 (d, 2H, J = 9.2 Hz, 2 × NH); ^{13}C NMR (90 MHz, DMSO-d_6): δ(ppm) 20.3, 20.5, (8 × $OCOCH_3$), 24.7, 28.4, 51.3 (6 × CH_2), 61.6 (2 × C-6-Glc), 67.7, 70.5, 72.1, 72.7 (2 C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2 × C-5-Glc), 76.8 (2 × C-1-Glc), 123.4 (2 triazole C-5), 146.4 (2 triazole C-4), 166.4 (2 × *C*ONH), 169.2, 169.3, 169.5, 170.0 (8 × O*C*OCH$_3$). Anal. calcd. for $C_{40}H_{54}N_8O_{20}$ (966.92): C, 49.69; H, 5.63; N, 11.59; Found: C, 49.59; H, 5.71; N, 11.67.

1,4-Bis-[1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamino-carbonylpentyl)-1*H*-1,2,3-triazol-4-yl)]butane (45). Prepared from **13** (0.20 g, 0.41 mmol) according to General procedure IVb. The residue was purified by column chromatography (EtOAc–MeOH, 95 : 5). Yield: 0.21 g, 96%, colourless oil, R_f = 0.32 (EtOAc); $[\alpha]_D$ = +16 (c = 0.16, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.16–1.30 (m, 4H, 2 × CH_2), 1.62–1.74 (m, 4H, 2 × CH_2), 1.85–1.91 (m, 4H, 2 × CH_2), 2.01, 2.03, 2.04, 2.07 (4 s, 24H, 8 × $OCOCH_3$), 2.18–2.22 (m, 4H, 2 × CH_2), 2.52–2.56 (m, 2H, CH_2), 2.72–2.76 (m, 4H, 2 × CH_2), 3.84 (ddd, 2H, J = 1.1, 2.6, 10.6 Hz, 2 × H-5-Glc), 4.13–4.07 (m, 4H, 2 × CH_2), 4.27–4.31 (m, 6H, 2 × H-6a-Glc, 2 × H-6b-Glc, CH_2), 5.28, 5.24, 5.06, 4.93 (4 pseudo t, 8H, J = 9.2, 10.6 Hz in each, 2 × H-1-Glc, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc), 6.57 (d, 2H, J = 7.9 Hz, 2 × NH), 7.34 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.3, 20.4, (8 × OCO*C*H$_3$), 24.1, 25.1, 25.7, 28.6, 29.7, 35.7, 49.5 (14 × CH_2), 61.6 (2 × C-6-Glc), 68.0, 70.4, 72.7, 73.3 (2 × C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2 × C-5-Glc), 77.8 (2 × C-1-Glc), 120.6 (2 triazole C-5), 147.7 (2 triazole C-4), 169.4, 169.6, 170.0, 170.4 (8 × O*C*OCH$_3$), 172.9 (2 × NH*C*O). Anal. calcd. for $C_{48}H_{70}N_8O_{20}$ (1079.13): C 53.43, H 6.54, N 10.38. Found: C 53.49, H 6.62, N 10.45.

1,4-Bis-[1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamino-carbonyldecyl)-1*H*-1,2,3-triazol-4-yl)]butane (46). Prepared from **14** (0.20 g 0.36 mmol) according to General procedure IVb. The residue was purified by column chromatography (EtOAc). Yield: 0.136 g, 62%, colourless oil; $[\alpha]_D$ = +7 (c = 0.62, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 90 MHz): δ (ppm) 1.26 (brs, 24H, 12 × CH_2), 1.56–1.59 (m, 4H, 2 × CH_2), 1.73–1.78 (m, 4H, 2 × CH_2), 1.85–1.89 (m, 4H, 2 × CH_2), 2.02, 2.03, 2.04, 2.08 (4s, 24H, 8 × $OCOCH_3$), 2.10–2.25 (m, 4H, 2 × CH_2), 2.73–2.76 (m, 4H, 2 × CH_2), 3.83 (m, 2H, J = 2.4, 4.3, 9.9 Hz, 2 × H-5-Glc), 4.08 (dd, 2H, J = 2.3, 12.3 Hz, 2 × H-6b-Glc), 4.27–4.34 (m, 6H, 2 × H-6a-Glc, 2 × CH_2), 4.93, 5.06, 5.27, 5.31 (4 pseudo t, 8 H, J = 9.6, 9.9 Hz in each, 2 × H-1-Glc, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc), 6.42 (d, 2H, J = 9.2 Hz, 2 × NH), 7.28 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4, 20.5, 20.6 (8 × OCO*C*H$_3$), 25.0, 25.3, 26.3, 28.7, 28.8, 28.9, 29.0, 29.1, 29.2, 29.6, 30.2, 50.0, (24 × CH_2), 61.6 (2 × C-6-Glc), 68.1, 70.5, 72.6, 73.4 (2 C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2 × C-5-Glc), 78.0 (2 × C-1-Glc), 120.4 (2 triazole C-5), 147.8 (2 triazole C-4), 169.5, 169.8, 170.5, 170.8 (8 × O*C*OCH$_3$), 173.4 (2 × CONH). Anal. calcd. for $C_{58}H_{90}N_8O_{20}$ (1219.38): C, 57.13; H, 7.44; N, 9.19; Found: C, 57.22; H, 7.32; N, 9.30.

1,4-Bis-[1-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylamino-carbonylpentadecyl)-1*H*-1,2,3-triazol-4-yl)]butane (47). Prepared from **15** (0.30 g 0.41 mmol) according to General procedure IV. The residue was purified by column chromatography (EtOAc). Yield: 0.28 g, 50%, white crystalline product, mp 144–146 °C; $[\alpha]_D$ = +14 (c = 0.24, $CHCl_3$); ^{1}H NMR (360 MHz, $CDCl_3$): δ(ppm) 1.20–1.35 (m, 26H, 13CH_2), 1.40–1.50 (m, 8H, 2 × CH_2), 1.60–1.77 (m, 8H, 2 × CH_2), 1.82–1.90 (m, 8H, 2 × CH_2), 2.02, 2.03, 2.05, 2.06 (4 s, 24H, 8 × $OCOCH_3$), 2.32–2.27 (m, 2H, CH_2), 2.60–2.52 (m, 4H, 2 × CH_2), 2.73–2.80 (m, 2H, CH_2), 3.70 (ddd, 2H, J = 1.1, 2.6, 10.6 Hz, 2 × H-5-Glc), 4.11–4.20 (m, 8H, 4 CH_2), 4.37–4.44 (m, 4H, 2 × H-6a-Glc, 2 × H-6b-Glc), 4.94, 5.00, 5.11, 5.19 (4 pseudo t, 8H, J = 9.2, 10.6 Hz in each, 2 × H-1-Glc, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc), 6.73 (d, 2H, J = 7.9 Hz, 2 NH), 7.34 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, $CDCl_3$): δ (ppm) 20.4, 20.5 (8 × OCOCH_3). 22.1, 22.5, 23.0, 23.6,24.8, 25.1, 25.8, 26.1, 26.6, 27.0, 27.5, 29.8, 30.7, 31.7, 35.7, 36.7, 50.1 (32 × CH_2), 60.6 (2 × C-6-Glc), 69.3, 71.0, 72.0, 72.8 (2 × C-2-Glc, 2 × C-3-Glc, 2 × C-4-Clc, 2 xC-5-Glc), 77.6 (2 × C-1-Glc), 121.0 (2 triazole C-5), 146.6 (2 triazole C-4), 169.4, 169.6, 169.9, 170.1 (8 × OCOCH_3), 171.8 (2 × HHCO). Anal. calcd. for $C_{68}H_{110}N_8O_{20}$ (1359.68): C, 60.07; H, 8.15; N, 8.24; Found: C, 60.16; H, 8.22; N, 8.33.

1,4-Bis-[1-(β-D-glucopyranosylaminocarbonylmethyl)-1*H*-1,2,3-triazol-4-yl)]butane (48). Prepared from **44** (0.10 g, 0.10 mmol) according to General procedure VI. Yield: 0.042 g, 65%, white crystalline product, mp 235–236 °C, $[\alpha]_D$ = 42 (c = 0.22, DMSO);^{1}H NMR (360 MHz, D_2O): δ (ppm) 1.64 (brs, 4H, 2 × CH_2), 2.70 (brs, 4H, 2 × CH_2), 3.39–3.57 (8H, m, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc, 2 × H-5-Glc), 3.71 (dd, 2H, J = 5.3 11.9 Hz, 2 × H-6b-Glc), 5.01 (d, 2H, J = 9.2 Hz, 2 × H-1-Glc), 3.85 (dd, 2H, J = <1, 11.9 Hz, 2 × H-6a-Glc), 5.24–5.27 (s, 4H, 2 × CH_2), 7.73 (s, 2H, triazole CH); ^{13}C NMR (90 MHz, DMSO-d_6): δ (ppm) 24.7, 28.4, 51.5 (6 × CH_2), 60.8 (2 × C-6-Glc), 69.9, 72.6, 77.3, 78.7 (2 × C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2 × C-5-Glc), 79.7 (2 × C-1-Glc), 123.5 (2 triazole C-5), 146.5 (2 triazole C-4), 166.1 (2 × CONH). Anal. calcd. for $C_{24}H_{38}N_8O_{12}$ (630.62): C, 45.71; H, 6.07; N, 17.77; Found: C, 45.80; H, 5.97; N, 17.54.

1,4-Bis-[1-(β-D-glucopyranosylaminocarbonylpentyl)-1*H*-1,2,3-triazol-4-yl)]butane (49). Prepared from **45** (0.21 g 0.19 mmol) according to General procedure VI. Yield: 0.09 g, 66%, white crystalline product, mp: 150–152 °C; $[\alpha]_D$ = +14 (c =0.12, MeOH); ^{1}H NMR (360 MHz, D_2O): δ(ppm) 1.20–1.25 (m, 4H, 2 × CH_2), 1.52–1.64 (m, 8H, 4 × CH_2), 1.80–1.88 (m, 4H, 2 × CH_2), 2.22–2.28 (m, 4H, 2 × CH_2), 2.66–2.70 (m, 4H, 2 × CH_2), 3.33–3.42 (m, 6H, 2 × H-3-Glc, 2 × H-4-Glc, CH_2), 3.50 (ddd, 2H, J = 1.2, 5.3, 9.2 Hz, 2 × H-5-Glc), 3.52 (t, 2H, J = 9.2, 9.2 Hz, 2 × H-2-Glc), 3.70 (dd, 2H, J = 5.3, 11.9 Hz, 2 × H-6b-Glc), 3.85 (dd, 2H, J = 1.2, 11.9 Hz, 2 × H-6a-Glc), 4.31–4.37 (m, 4H, 2 × CH_2), 4.91 (d, 2H, J = 9.2 Hz, 2 × H-1-Glc), 7.82 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, D_2O): δ (ppm) 24.0, 24.1, 25.2, 27.8, 29.1, 35.6, 50.4 (14 × CH_2), 60.7 (2 xC-6-Glc) 69.4, 71.9, 76.7, 77.7 (2 × C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2 × C-5-Glc), 79.4 (2x C-1-Glc), 123.8 (2 triazole C-5), 146.2 (2 triazole C-4), 178.1 (2 × NHCO). Anal. calcd. for $C_{32}H_{54}N_8O_{12}$ (742.83): C 51.74, H 7.33, N 15.08. Found: C 51.69, H 7.25, N 15.02.

1,4-Bis-[1-(β-D-glucopyranosylaminocarbonyldecyl)-1*H*-1,2,3-triazol-4-yl)]butane (50). Prepared from **46** (0.07 g, 0.06 mmol) according to General procedure VI. Precipitated from the reaction mixture. Yield: 0.048 g, 95%, white amorphous product; $[\alpha]_D$ = +16 (c = 0.37, DMSO); ^{1}H NMR (360 MHz, DMSO-d_6 + D_2O): δ (ppm) 1.20 (brs, 24H, 12 × CH_2), 1.45, 1.60, 1.75, 2.06, 2.60 (5 brs, 20H, 10 × CH_2), 3.00–3.19 (m, 8H, 2 × H-2-Glc, 2 × H-3-Glc, 2 × H-4-Glc, 2 × H-5-Glc), 3.38 (dd, 2H, J = 4.6, 11.6 Hz, 2 × H-6b-Glc), 3.61 (dd, 2H, J <1.0, 11.2 Hz, 2 × H-6a-Glc), 4.23–4.27 (m, 4H, 2 × CH_2), 4.68 (d, 2H, J = 8.9 Hz, 2 × H-1-Glc),7.80 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, DMSO-d_6 + D_2O): δ (ppm) 24.8, 25.0, 25.9, 28.4, 28.5, 28.9, 29.7, 35.5, 49.2 (24 × CH_2), 60.9 (2 × C-6-Glc), 69.9, 72.3, 77.4, 78.4 (2 × C-2-Glc, 2 × C-3-Glc, 2 × C-4-Glc, 2x C-5-Glc), 79.4 (2 × C-1-Glc), 121.7 (2 triazole C-5), 146.8 (2 triazole C-4), 173.0 (2 × CONH). Anal. calcd. for $C_{42}H_{74}N_8O_{12}$ (883.08): C, 57.12; H, 8.45; N, 12.69; Found: C, 57.23; H, 8.56; N, 12.58.

1,4-Bis-[1-(β-D-glucopyranosylaminocarbonylpentadecyl)-1*H*-1,2,3-triazol-4-yl)]butane (51). Prepared from **47** (0.2 g, 0.147 mmol) according to General procedure VI. Yield: 0.12 g, 80%, white crystalline product, mp 158–160 °C; $[\alpha]_D$ = +25 (c = 0.20, MeOH); ^{1}H NMR (360 MHz, D_2O): δ(ppm) 1.19–1.32 (m, 30H, 15 × CH_2), 1.49–1.70 (m, 4H, 2 × CH_2), 1.91–1.98 (m, 4H, 2 × CH_2), 2.18–2.38 (m, 8H, 4 × CH_2), 2.51–2.90 (m, 20H, 10 × CH_2), 3.32–3.39 (m, 4H, 2 × H-3-Glc, 2x H-4-Glc), 3.45 (ddd, 2H, J = 1.2, 5.3, 9.2 Hz, 2 × H-5-Glc), 3.49 (t, 2H, J = 9.2, 9.2 Hz, 2x H-2-Glc), 3.79 (dd, 2H, J = 5.3, 11.9 Hz, 2 × H-6b-Glc), 3.87 (2H, dd, J = 1.2, 11.9 Hz, 2x H-6a-Glc), 4.41–4.47 (m, 4H, 2 × CH_2), 5.01 (d, 2H, J = 9.2 Hz, 2 × H-1-Glc), 7.67 (s, 2H, 2 triazole CH); ^{13}C NMR (90 MHz, D_2O): δ (ppm) 21.7, 22.9, 23.3, 24.1, 24.8, 25.3, 25.8, 27.1, 27.6, 28.1, 29.5, 31.2, 32.0, 33.1, 36.7, 37.4, 51.2 (34 × CH_2), 61.5 (2 × C-6-Glc), 69.0, 72.1, 76.3, 77.3 (2 × C-2-Glc, 2 × C-3-Glc, 2x C-4-Glc, 2 × C-5-Glc), 78.1 (2 × C-1-Glc), 121.5 (2 triazole C-5), 146.5 (2 triazole C-4), 179.3 (2 × NHCO). Anal. calcd. for $C_{52}H_{94}N_8O_{12}$ (1023.38): C, 61.06; H, 9.26; N, 10.95; Found: C, 61.13; H, 9.36; N, 10.88.

Enzyme assays

(a) Against RMGPa. The inhibitory activity of the prepared compounds against rabbit muscle glycogen phosphorylase a (RMGPa) was monitored using microplate reader (BIO-RAD) based on the published method.[35] In brief, GPa activity was measured in the direction of glycogen synthesis by the release of phosphate from glucose-1-phosphate. Each prepared compound was dissolved in DMSO and diluted to different concentrations for IC_{50} determination. The enzyme was added into 100 μL of buffer containing 50 mM Hepes (pH = 7.2), 100 mM KCl, 2.5 mM $MgCl_2$, 0.5 mM glucose-1-phosphate, 1 mg/ml glycogen and the test compound in 96-well microplates (Costar). After the addition of 150 μL of 1 M HCl containing 10 mg/ml ammonium molybdate and 0.38 mg/ml malachite green, reactions were run at 22 °C for 25 min, and then the phosphate absorbance was measured at 655 nm. The IC_{50} values were estimated by fitting the inhibition data to a dose-dependent curve using a logistic derivative equation.

(b) Against RMGPb. Glycogen phosphorylase b (RMGPb) was prepared from rabbit skeletal muscle according to the method of Fischer and Krebs,[41] using dithiothreitol instead of L-cysteine, and recrystallized at least three times before use. Kinetic experiments were performed in the direction of glycogen synthesis using RMGPb as described.[36,42] IC_{50} values were determined in the presence of 4 mM α-D-glucose-1-phosphate, 1 mM AMP, 1% glycogen and varying concentrations of the inhibitor.[43] Inhibitors were dissolved in dimethyl sulfoxide (DMSO) and diluted in the assay buffer (50 mM triethanolamine, 1 mM EDTA and 1 mM dithiothreitol) so that the DMSO concentration in the assay should be lower than 1%. The means of standard errors for all calculated kinetic parameters averaged to less than 10%.

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