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Synthesis of Functionalized Amphiphilic Glycoconjugates and Glycoclusters

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Glycolipids are involved in many cellular recognition processes, so there is a need for their synthesis as well as for the design and preparation of glycolipid mimetics. In addition to the application of glycolipid mimetics in a glycobiological context, they are also of interest in many other fields of research, due to their amphiphilic characters. Our goal was to elaborate a series of known orthogonally functionalized glycomimetics and cluster glycosides into glycomimetics of a glycolipid type, so monosaccharide building blocks such as **3**, glycodendrons such as **19**, and branched cluster glycosides of the type **24** were ligated with lipophilic molecules by peptide coupling, this conjugation providing a new class of complex amphiphilic glycoconjugates with high molecular diversity.

Introduction

Glycoconjugates[1] are natural products in which complex carbohydrates are covalently linked to various aglycon moieties, such as, for example, in cardiac glycosides or enediyne antibiotics. An especially prominent class of glycoconjugates, involved in many cellular recognition processes, consists of glycoproteins on one hand and glycolipids on the other.[2] Several hundred naturally occurring glycolipids have been isolated and characterized to date, demonstrating that they, unlike glycoproteins, are structurally diverse in their core carbohydrates while their oligosaccharide portions are typically smaller than those found in glycoproteins.

Glycolipids often exhibit high biological activity – as inhibitors of microbial adhesion, for example – because they can interact both with polar and with nonpolar regions in their receptors.[3] Galactosylsphingolipid, for example, has been reported to interact with the HIV-1 virus,[4] while the potency of multivalent sialic acid conjugates as inhibitors of influenza adhesion has been improved through the introduction of a nonpolar residue.[5]

Moreover, as amphiphilic glycoconjugates, glycolipids can form supramolecular structures such as micelles or liposomes,[6] and this feature may be employed for drug-delivery approaches[7] or to enhance biological activity through multivalent presentation of carbohydrate ligands.[8]

Because of their structural complexity the synthesis of glycoconjugates, including glycosphingolipids, is highly demanding[9] and so relatively simple mimetics of the natural example structures[10] have been sought and targeted for goals involving various applications in glycobiology,[11] biotechnology,[12] or in the contexts of liquid crystals,[13] surfactants,[14] or immunomodulation.[15]

Because of the high relevance and exceptional potential of glycolipids and glycolipid mimetics, we set ourselves the goal of utilizing our experience with multivalent glycomimetics and glycoclusters for the synthesis of amphiphilic glycoconjugates. Use of a combination of functionalized oligosaccharide mimetics and various hydrophobic moieties according to a molecular building block system approach should allow modular and facile access to lipophilically functionalized glycoconjugates of high molecular diversity. The results of this endeavor are reported in this contribution.

Results and Discussion

Our first approach to the synthesis of amphiphilic glycomimetics was based on the design of so-called "mixed glycoclusters", which we had elaborated earlier.[16] This approach utilizes the potential for bifunctionalization of 6-amino-6-deoxy glycosides by addressing the terminal amino group in a manner analogous to a Michael reaction. Firstly, through the use of a stoichiometric amount of freshly distilled methyl acrylate in methanol, the 6-amino-functionalized mannoside **1**[17] was converted into ester **2**, which can be used as a carbohydrate scaffold for the subsequent syntheses of glycolipid mimetics (Scheme 1). Methyl ester **2** could be deprotected to yield the corresponding acid **3**, while on the other hand it could also be modified by HATU-mediated[18] peptide coupling with lauric acid to furnish glycoconjugate **4** in 72% yield. Deprotection of **4** furnished **5** in high yield.

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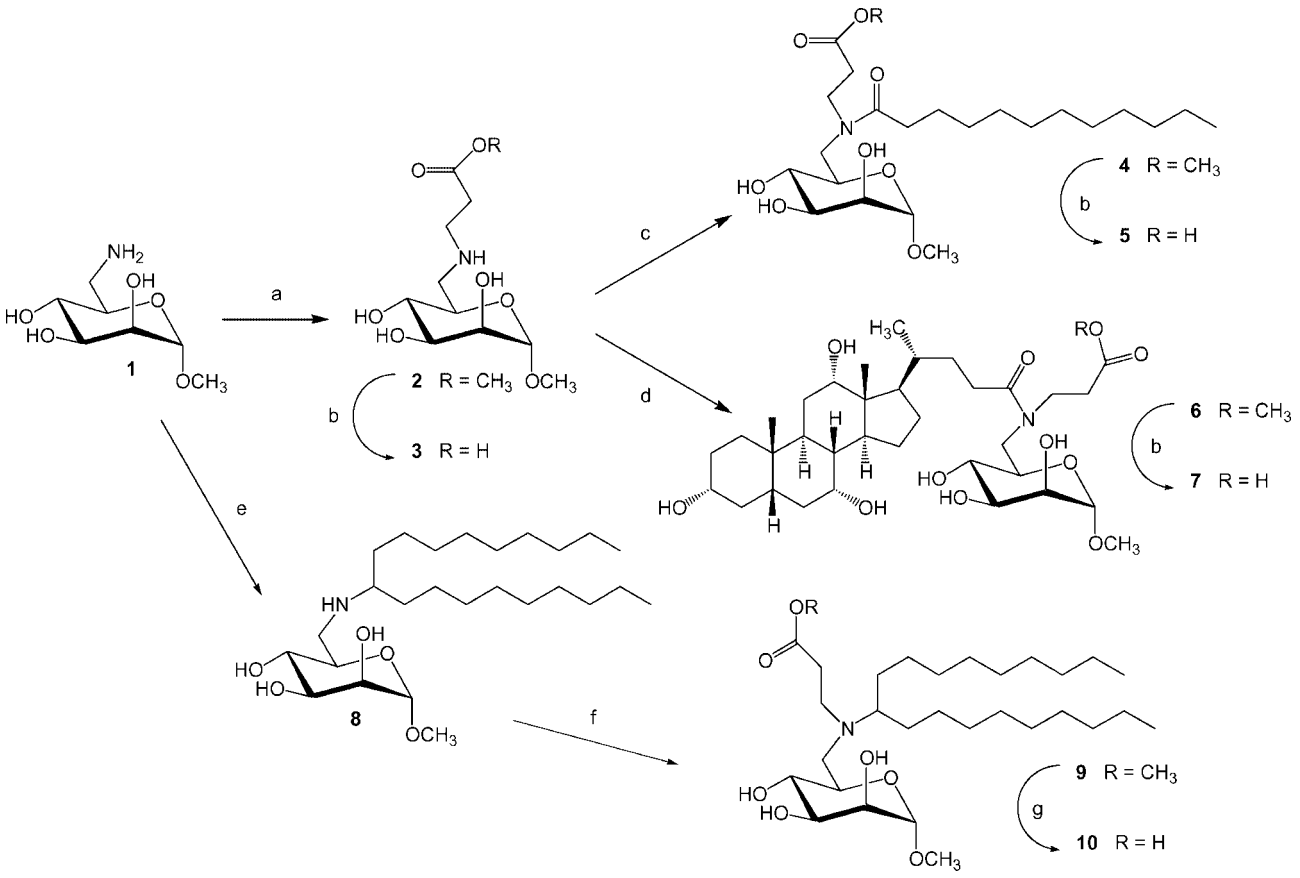


Scheme 1. a) Methyl acrylate, MeOH, 0 °C→room temp., 12 h, 70%. b) LiOH·H_2O, H_2O/MeOH (2:1), 0 °C, 12 h, 92% for **3**; 88% for **5**; 90% for **7**. c) Lauric acid, HATU, DIPEA, DMF, 40 °C, 6 h, 72%. d) Cholic acid, HATU, DIPEA, DMF, 40 °C, 6 h, 63%. e) Nonadecan-10-one, $NaCNBH_3$, MeOH/THF (1:1), 60 °C, 12 h, 48%. f) Methyl acrylate, room temp., 6 h, 62%. g) LiOH·H_2O, *i*PrOH/H_2O (2:1), room temp., 12 h, 80%.

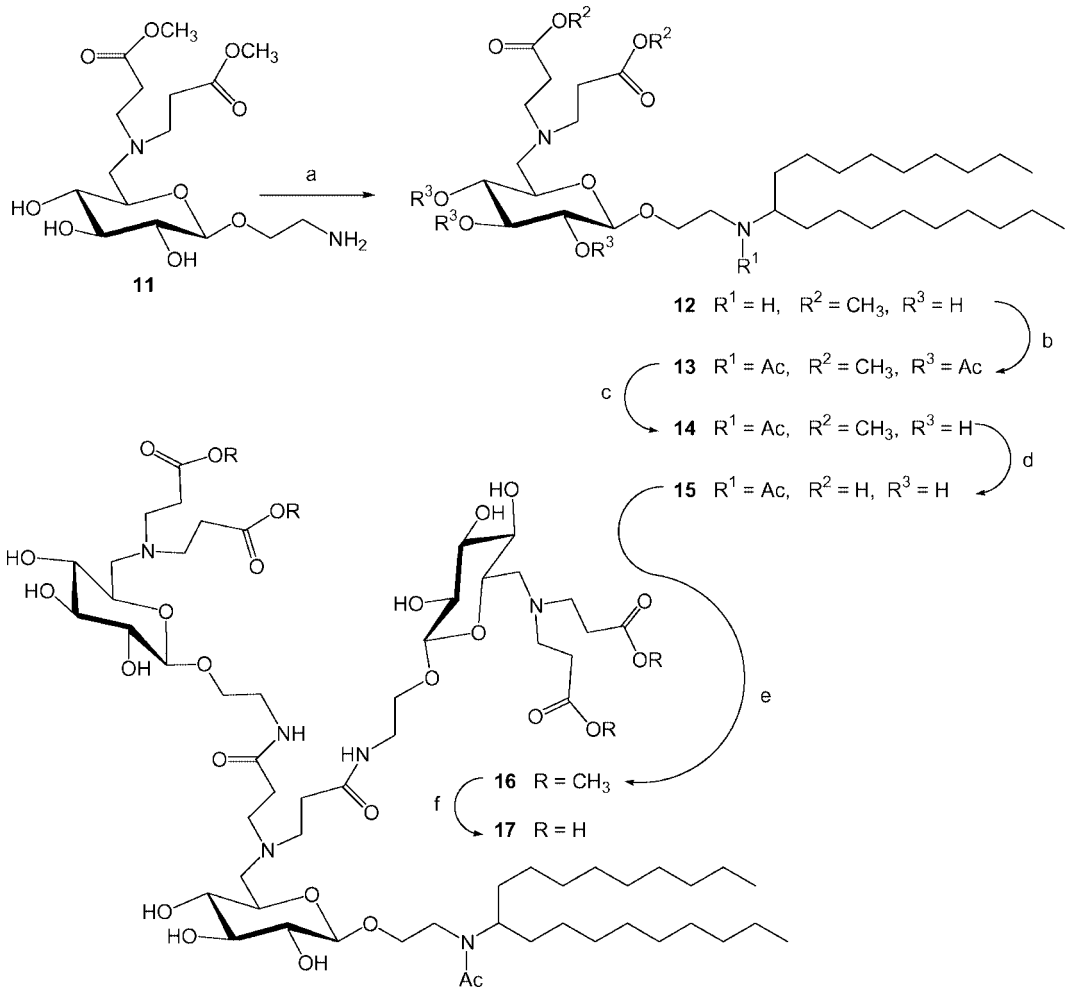
We selected cholic acid for the analogous reaction with amide **2**, to demonstrate the conjugation of a steroid[19] to saccharides. Treatment of **2** with cholic acid proceeded almost equally well as with lauric acid, delivering the glycomodified steroid **6**. Saponification of the glycoconjugates **4** and **6** was carried out with lithium hydroxide in a methanol/water mixture (1:2), affording the amphiphilic derivatives **5** and **7**, respectively, in almost quantitative yields.

We next tried to attach two lipophilic side chains to the secondary amine **2** by reductive amination of nonadecan-10-one, but all our attempts to produce the target molecule **9** by this approach failed. Only minor amounts of the mannoside **8** were detected in this reaction, most probably due to a retro-Michael reaction occurring during reductive amination. When the reductive amination of nonadecan-10-one was carried out with the aminoglycoside **1**, however, the sodium cyanoborohydride-mediated reaction gave **8** in acceptable yield, while subsequent treatment with methyl acrylate afforded the desired ester **9**. As the bilipid glycoconjugate **9** is insoluble in methanol/water (1:2), ester hydrolysis was in this case carried out in a propan-2-ol/water mixture (2:1), giving the free acid **10** in 80% yield.

The prepared mannosides **3**, **5**, **7**, and **10** can be regarded as functionalized glycolipid mimetics, which are amenable to subsequent modifications such as, for example, peptide coupling.

Then it became our goal to utilize the potential of carbohydrate building blocks of an AB_2-type, previously employed for the synthesis of dendritic glycopeptides,[20] to elaborate them into various sugar amphiphiles. Starting with the trifunctional carbohydrate scaffold **11**,[21] reductive amination of nonadecan-10-one with sodium cyanoborohydride in MeOH/THF (1:1) was first carried out at an elevated temperature to afford the monomeric bilipid conjugate **12** (Scheme 2). Protection of the secondary amino function in **12** was necessary prior to possible peptide coupling reactions, so the crude product was fully acetylated to give **13**, and Zemplén deesterification[22] was then performed to cleave the acetate esters chemoselectively and to yield the desired product **14** in 23% yield over three consecutive steps. The methyl diester **14** was then hydrolyzed with LiOH hydrate to give the dicarboxylic acid **15**, and subsequent peptide coupling of **15** with the amino-functionalized building block **11** in the presence of HATU and DIPEA yielded the branched glycolipid mimetic **16**, which could be deprotected to provide the amphiphilic product **17**.

As an alternative, the branched glycopeptide building block **18**[20] was synthesized first and deprotected at the ter-



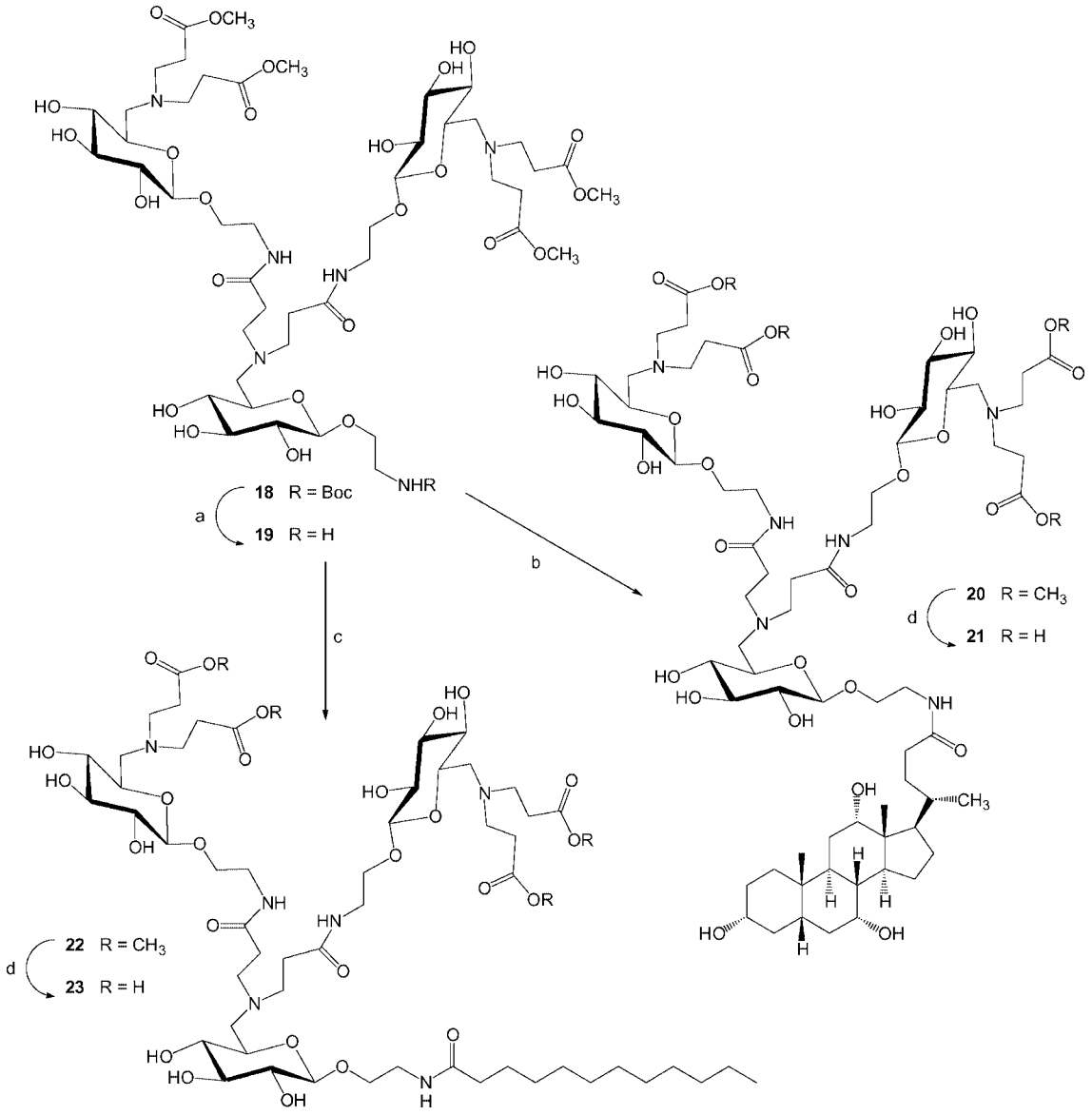
Scheme 2. a) Nonadeca-10-one, $NaCNBH_3$, H_2O/MeOH (1:1), 60 °C, 6 h. b) Ac_2O, pyridine, DMAP, 3 h. c) NaOMe/MeOH, 0 °C, 3 h, 23% over three steps. d) LiOH·H_2O, H_2O/MeOH (2:1), 0 °C, 12 h, 92%. e) **11**, HATU, DIPEA, DMF, room temp., 12 h, 27%. f) LiOH·H_2O, H_2O/MeOH (2:1), room temp., 12 h, 79%.

minal amino function by use of a TFA/DMS mixture (1:1) to yield the glycopeptide dendron **19** possessing a terminal primary amino function (Scheme 3). This was subjected to peptide coupling with cholic acid on one hand and lauric acid on the other, forming the glycolipid conjugates **20** and **22**, respectively, in good yields, these methyl esters next being saponified with LiOH to provide the corresponding carboxylic acids **21** and **23**. NMR and MS analysis allows unequivocal confirmation of the product structures. A quick indication of ester hydrolysis can be obtained from the disappearance in the NMR spectrum of the singlet signals corresponding to the methyl ester groups at about 3.67 ppm.

A third synthetic sequence was dedicated to functionalization of the carbohydrate-centered cluster mannoside **24**[23] to give amphiphilic neoglycoconjugates (Scheme 4). HATU-mediated peptide coupling with lauric acid with this complex molecule was tried first, providing the alkyl oligosaccharide mimetic **25** in high yield. The analogous reaction with cholesterol furnished the trihydroxy-cholanyl glycocluster **26**.

Fluorescing glycoconjugates have been reported to be valuable tools in glycobiology,[24] while we have envisaged that, in addition to the use of fluorescence dyes, coloring of glycoconjugates could be a favorable modification for carbohydrate-binding studies. Furthermore, many lectins such as bacterial FimH[25] or concanavaline A,[26] possess hydrophobic areas in or close to their carbohydrate recognition domains, so we reasoned that the introduction of a hydrophobic dye into a neoglycoconjugate might facilitate both the lectin affinity of a given glycoconjugate and the assaying of binding. We utilized the CSP (chromophore-supported parallel synthesis) strategy employing azulene derivatives, as recently published,[27] and the guajazulene derivative 3-(7-isopropyl-1-methylazulen-4-yl)propanoic acid could indeed be attached to **24** by peptide coupling techniques, providing the deep blue amphiphile **27**.

NMR analysis of products **25**, **26**, and **27** shows that the NMR spectra do not differ significantly with regard to the cluster mannoside substructure. This is due to the hexyl aglycon of **24**, which acts as a spacer to distance the cluster mannoside from the introduced lipophilic moiety. In addition, the chemical shifts of the introduced lipophilic moieties are not significantly influenced by the peptide coupling reaction with **24**. The chemical shifts of the rather compli-



Scheme 3. a) F_3CCO_2H/SMe_2 (2:1), 0 °C, 3 h, 84%. b) Cholic acid, HATU, DIPEA, room temp., 12 h, 58%. c) Lauric acid, HATU, DIPEA, room temp., 12 h, 66%. d) $LiOH·H_2O$, H_2O/MeOH (2:1), 0 °C, 72% for **21**, 79% for **23**.

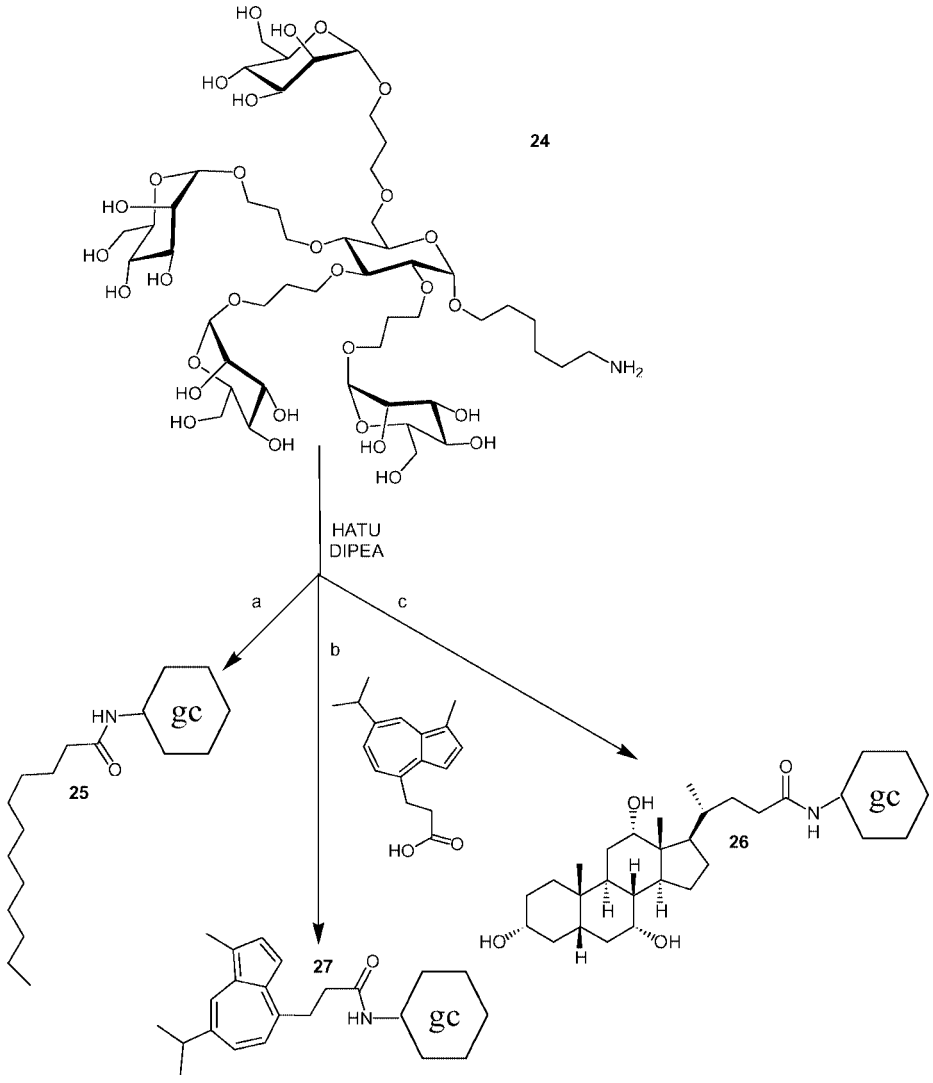
cated steroid part in **26**, as well as in all other glycosteroids described here, are in good agreement with published extensive NMR studies on steroids.[28]

Conclusions

It has been shown that rather complex glycolipid mimetics can be synthesized by peptide coupling techniques in a molecular building block system approach, sometimes in excellent yields. The reported examples offer many options for diverse modifications, including further functionalization, multimerization, or attachment to solid phase. We will further evaluate this potentially very useful chemistry in the context of our studies on the glycocalyx function.

Experimental Section

General Remarks: Optical rotations were measured with a Perkin–Elmer polarimeter (20 °C, 589 nm, length of cuvette: 1 dm). Reactions were monitored by TLC on silica gel GF_{254} (Merck), with detection under UV and by charring with 10% sulfuric acid in ethanol and subsequent heating. Flash column chromatography was performed on silica gel 60 (40–63 μm, Merck). NMR spectra were recorded on Bruker AMX 400 or Bruker DRX 500 instruments. Chemical shifts are relative to TMS or the (residual) solvent peaks of $CDCl_3$ (δ = 7.24 ppm ^1H, 77.0 ppm ^{13}C) or [D_6]acetone (δ = 2.04 ppm ^1H, 29.3 ppm ^{13}C). Where necessary, assignments were based on COSY and HSQC experiments. Assignments indexed with an asterisk (*) are interchangeable. IR spectra were taken with a Perkin–Elmer FT-IR Paragon 1000 (KBr). MALDI-TOF mass spectra were measured with a Bruker Biflex III with 19 kV acceleration voltage. DHB (c = 10 μg μL^{-1} in 40% acetonitrile/water, 0.1%



Scheme 4. a) Lauric acid, DMF, 0 °C→room temp., 8 h, 96%. b) 3-(7-Isopropyl-1-methylazulen-4-yl)propanoic acid, DMF, 0 °C→room temp., 8 h, 79%. c) Cholic acid, DMF, 0 °C→room temp., 8 h, 86% (gc = glycocluster moiety derived from **24**).

TFA) was used as the matrix. Ionization was effected with a nitrogen laser at 337 nm. ESI mass spectra were measured with an Applied Biosystems Mariner ESI-TOF 5280.

Methyl 6-Deoxy-6-[(2-methoxycarbonylethyl)amino]-α-D-mannopyranoside (2): A mixture of the amine **1**[17] (0.84 g, 4.35 mmol) and freshly distilled methyl acrylate (0.39 mL, 4.35 mmol) in dry methanol (5 mL) was stirred in the dark for 12 h at room temp. It was then concentrated and the residue was purified by flash chromatography ($MeOH/CH_2Cl_2$ 1:1) to afford the Michael adduct **2** (0.85 g, 3.05 mmol, 70%) as a colorless syrup. R_f = 0.2 (α-naphthol; $MeOH/CH_2Cl_2$ 1:1). $[a]_D^{20}$ = +60.7 (*c* = 1.95 in MeOH). ^1H NMR (500 MHz, [D$_4$]MeOH): δ = 4.62 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1-H), 3.77 (dd, $J_{1,2}$ = 1.7, $J_{2,3}$ = 3.4 Hz, 1 H, 2-H), 3.67 (s, 3 H, CO_2CH_3), 3.63 (dd, $J_{2,3}$ = 3.4, $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 3.58 (m_c, 1 H, 5-H), 3.47 (t, $J_{4,3}$ = 9.4 Hz, 1 H, 4-H), 3.38 (s, 3 H, OCH_3), 2.98 (dd, $J_{5,6a}$ = 2.9, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6a-H), 2.88 (m_c, 2 H, $NHCH_2$), 2.76 (dd, $J_{5,6b}$ = 8.2, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6b-H), 2.56 (t, *J* = 6.6 Hz, 2 H, $CH_2CO_2CH_3$) ppm. ^{13}C NMR (75.46 MHz, [D$_4$]-MeOH): δ = 174.5 (CO_2CH_3), 102.7 (C-1), 72.3 (C-3), 71.9 (C-2), 71.8 (C-5), 70.7 (C-4), 55.4 (OCH_3), 52.1 (CO_2CH_3), 51.7 (C-6), 45.8 (NCH_2), 34.5 ($CH_2CO_2CH_3$) ppm. MALDI-TOF MS: *m*/*z* = 280.2 $[M + H]^+$, 302.2 $[M + Na]^+$ and 318.2 $[M + K]^+$ observed for $C_{11}H_{21}NO_7$ (279.13).

Methyl 6-[(2-Carboxyethyl)amino]-6-deoxy-α-D-mannopyranoside (3): A mixture of the methyl ester **2** (0.05 g, 0.17 mmol) and $LiOH·H_2O$ (15 mg, 0.35 mmol) was dissolved in $MeOH/H_2O$ (1:2; 1 mL) and stored at 4 °C for 12 h. The pH of the basic reaction mixture was then adjusted to a value of 6 by careful addition of an aq. HCl (2 N) solution at 0 °C. The mixture was lyophilized and the freeze-dried crude product was then desalted by gel permeation chromatography on Bio-gel P-2 with water as the eluent to provide the pure carboxylic acid **3** (43 mg, 0.16 mmol, 92%) as a white lyophilizate. R_f = 0.1 (α-naphthol; $MeOH/CH_2Cl_2$ 1:2.5). $[a]_D^{20}$ = +38.4 (*c* = 2.0 in H_2O). ^1H NMR (300 MHz, [D$_4$]MeOH): δ = 4.62 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1-H), 3.77 (dd, $J_{1,2}$ = 1.7, $J_{2,3}$ = 3.3 Hz, 1 H, 2-H), 3.63 (dd, $J_{2,3}$ = 3.3, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.58 (m_c, 1 H, 5-H), 3.48 (t, $J_{3,4}$ = 9.4 Hz, 1 H, 4-H), 3.35 (s, 3 H, OCH_3), 2.98 (dd, $J_{5,6a}$ = 3.0, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6a-H), 2.88 (m_c, 2 H, NCH_2), 2.76 (dd, $J_{5,6b}$ = 8.2, $J_{6a,6b}$ = 12.3 Hz, 1 H, 6b-H), 2.56 (t, *J* = 6.6 Hz, 2 H, CH_2CO_2H) ppm. ^{13}C NMR (75.46 MHz, [D$_4$]-MeOH): δ = 174.6 (CO_2H), 102.9 (C-1), 72.4 (C-3), 72.0 (C-2), 72.0 (C-5), 70.8 (C-4), 55.5 (OCH_3), 51.9 (C-6), 45.9 (NCH_2), 34.6

(CH_2CO_2H) ppm. MALDI-TOF MS: m/z = 267.3 $[M + H]^+$ and 288.3 $[M + Na]^+$ observed for $C_{10}H_{19}NO_7$ (265.11).

Methyl 6-Deoxy-6-[(dodecanoyl)(2-methoxycarbonylethyl)amino]-α-D-mannopyranoside (4): The secondary amine **3** (0.10 g, 0.35 mmol), lauric acid (0.08 g, 0.43 mmol), and HATU (0.16 g, 0.43 mmol) were dissolved in dry DMF (3 mL) under argon, DIPEA (0.18 mL, 1.07 mmol) was then added, and the reaction mixture was stirred at 45 °C for 12 h. After evaporation in vacuo, purification of the resulting crude product by flash chromatography ($MeOH/CH_2Cl_2$ 1:9) afforded the pure laurylamide **4** (0.12 g, 0.25 mmol, 72%) as a colorless syrup. R_f = 0.5 (α-naphthol; $MeOH/CH_2Cl_2$ 1:10). $[\alpha]_D^{20}$ = +75.7 (c = 1.50 in MeOH). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 4.61 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1-H), 3.85 (dd, 1 H, 6a-H), 3.83–3.71 (m, 3 H, 2-H, NCH_a, 3-H), 3.67 (s, 3 H, CO_2CH_3), 3.67–3.40 (m, 4 H, NCH_b, 6b-H, 5-H, 4-H), 3.30 (s, 3 H, OCH_3), 2.63 (t, J = 7.2 Hz, 2 H, $CH_2CO_2CH_3$), 2.46 (m_c, 2 H, CH_2CON), 1.60 (m_c, 2 H, CH_2CH_2CON), 1.33–1.25 (m, 16 H, 8×CH_2), 0.90 (t, J = 6.5 Hz, 3 H, alkyl-CH_3) ppm. ^{13}C NMR (125.84 MHz, [D$_4$]MeOH): δ = 176.5 (CONH), 173.9 (CO_2CH_3), 102.6 (C-1), 73.4 (C-5), 72.3 (C-3), 71.6 (C-2), 69.9 (C-4), 55.3 (OCH_3), 52.1 (CO_2CH_3), 51.1 (C-6), 44.5 (NCH_2), 33.9 (CH_2CO), 32.9 ($CH_2CO_2CH_3$), 30.6, 30.5, 30.4, 30.3, 30.2 (5 CH_2), 26.5 (CH_2CH_2CO), 23.6 (2×CH_2), 14.4 (alkyl-CH_3) ppm. MALDI-TOF MS: m/z = 462.4 $[M + H]^+$, 484.4 $[M + Na]^+$ observed for $C_{23}H_{43}NO_8$ (461.29).

Methyl 6-[(2-Carboxyethyl)(dodecanoyl)amino]-6-deoxy-α-D-mannopyranoside (5): The methyl ester **4** (40 mg, 0.08 mmol) was saponified with LiOH·H_2O (7.0 mg, 0.16 mmol) in a MeOH/H_2O solution (1:2, 2 mL) by an experimental procedure similar to that used in the case of **3**. Purification of the crude desalted product by gel permeation chromatography on Bio-gel P-2 with water as eluent afforded the title compound **5** (34 mg, 0.07 mmol, 88%) in the form of a white lyophilizate. R_f = 0.3 (α-naphthol; $MeOH/CH_2Cl_2$ 1:10). $[\alpha]_D^{20}$ = +22.1 (c = 2.75 in H_2O). ^{1}H NMR (300 MHz, D_2O): δ = 4.65 (d, $J_{1,2}$ = 1.7 Hz, 1 H, 1-H), 4.0–3.84 (m, 2 H, 6a-H, 2-H), 3.84–3.63 (m, 3 H, NCH_a, 3-H, NCH_b), 3.61–3.45 (m, 2 H, 5-H, 6b-H), 3.30–3.20 (m, 4 H, 4-H, OCH_3), 2.63–2.30 (m, 4 H, CH_2CO_2H, CH_2CON), 1.59 (m_c, 2 H, CH_2CH_2CON), 1.30–1.15 (m, 16 H, 8×CH_2), 0.85 (t, J = 6.5 Hz, 3 H, alkyl-CH_3) ppm. ^{13}C NMR (75.46 MHz, D_2O): δ = 178.1 (CO_2H), 177.6 (CON), 103.2 (C-1), 74.2 (C-5), 72.9 (C-3), 72.4 (C-2), 71.6 (C-4), 56.8 (OCH_3), 45.0 (C-6), 35.4 (NCH_2), 34.3 (CH_2CO), 32.2 (CH_2CO_2H, 2×CH_2), 32.2, 32.1, 31.8 (4×CH_2), 27.8 (CH_2CH_2CO), 25.0 (2×CH_2), 14.6 (alkyl-CH_3) ppm. MALDI-TOF MS: m/z = 448.5 $[M + H]^+$, 470.5 $[M + Na]^+$, 486.5 $[M + K]^+$ observed for $C_{22}H_{41}NO_8$ (447.28).

Methyl 6-Deoxy-6-[(2-methoxycarbonylethyl)(3α,7α,12α-trihydroxy-5β-cholan-24-oyl)amino]-α-D-mannopyranoside (6): DIPEA (0.18 mL, 1.07 mmol) was added under argon to a mixture of mannoside **3** (0.10 g, 0.35 mmol), cholic acid (0.17 g, 0.43 mmol), and HATU (0.16 g, 0.43 mmol) dissolved in dry DMF (3 mL), and the reaction mixture was stirred at 45 °C for 12 h. After concentration of the reaction mixture in vacuo, the resulting crude product was purified by flash chromatography ($MeOH/CH_2Cl_2$ 1:5) to afford pure **6** (0.15 g, 0.22 mmol, 63%) as a colorless syrup. R_f = 0.6 (α-naphthol, $MeOH/CH_2Cl_2$ 1:5). $[\alpha]_D$ = +46.2 (c = 1.60 in MeOH). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.64 (d, $J_{1,2}$ = 1.3 Hz, 1 H, 1-H), 3.96–3.91 (m, 2 H, 2-H, 6a-H), 3.95 (m_c, 1 H, 12-H_{chol}), 3.81–3.75 (m, 2 H, NCH_a, 3-H), 3.79 (m_c, 1 H, 8-H_{chol}), 3.66 (s, 3 H, CO_2CH_3), 3.67–3.59 (m, 2 H, NCH_b, 5-H), 3.45–3.35 (m, 2 H, 6b-H, 4-H), 3.31 (m_c, 1 H, 3-H_{chol}), 3.28 (s, 3 H, OCH_3), 2.64 (t, J = 7.2 Hz, 2 H, $CH_2CO_2CH_3$), 2.29 (m_c, 3 H, 20-H_{chol}, 4-H_{chol}, 10-H_{chol}), 2.11 (ddd, J = 6.6, 9.6, 13.9 Hz, 1 H, 20′-H_{chol}), 1.96 (m_c, 3 H, 7-H_{chol}, 16-H_{chol}, 14-H_{chol}), 1.85 (m_c, 1 H, 17-H_{chol}), 1.80 (m_c, 1 H, 1-H_{chol}), 1.75 (m_c, 2 H, 15-H_{chol}, 19-H_{chol}), 1.65 (m_c, 1 H, 4′-H_{chol}), 1.55 (m_c, 5 H, 2-H_{chol}, 11-H_{chol}, 11′-H_{chol}, 9-H_{chol}, 7′-H_{chol}), 1.40 (m_c, 4 H, 2′-H_{chol}, 18-H_{chol}, 19′-H_{chol}, 5-H_{chol}), 1.29 (m_c, 1 H, 16′-H_{chol}), 1.10 (m_c, 1 H, 15′-H_{chol}), 1.02 (d, J = 6.40 Hz, 3 H, 3×18-H_{chol}), 0.97 (m_c, 1 H, 1′-H_{chol}), 0.91 (s, 3 H, 3×6-H_{chol}) 0.71 (s, 3 H, 3×13-H_{chol}) ppm. ^{13}C NMR (125.75 MHz, $CDCl_3$): δ = 175.4 (NCO), 172.9 (CO_2CH_3), 101.1 (C-1), 74.1 (C-12$_{chol}$), 72.9 (C-3$_{chol}$), 72.2 (C-5), 70.6 (C-2), 69.1 (C-8$_{chol}$), 68.4 (C-3), 68.2 (C-4), 54.9 (OCH_3), 51.7 (CO_2CH_3), 48.0 (C-17$_{chol}$), 47.5 (C-13$_{chol}$), 47.0 (C-6), 43.2 (C-5$_{chol}$), 43.1 (C-14$_{chol}$), 42.0 (NCH_2), 41.1 (C-9$_{chol}$), 40.5 (C-4$_{chol}$), 37.0 (C-18$_{chol}$), 36.5 (C-1$_{chol}$), 35.93 (C-7$_{chol}$), 35.91 (C-6$_{chol}$), 34.1 (C-20$_{chol}$), 32.3 (C-19$_{chol}$), 31.8 ($CH_2CO_2CH_3$), 31.2 (C-2$_{chol}$), 29.6 (C-11$_{chol}$), 28.8 (C-16$_{chol}$), 27.9 (C-10$_{chol}$), 24.3 (C-15$_{chol}$), 23.2 (6-CH_3), 17.8 (C-18$_{chol}$), 13.1 (C-13$_{chol}$) ppm. MALDI-TOF MS: m/z = 670.5 $[M + H]^+$, 692.6 $[M + Na]^+$ observed for $C_{35}H_{59}NO_{11}$ (669.40).

Methyl 6-[(2-Carboxyethyl)(3α,7α,12α,trihydroxy-5β-cholan-24-oyl)amino]-6-deoxy-α-D-mannopyranoside (7): The methyl ester **6** (70 mg, 0.10 mmol) was saponified with LiOH·H_2O (9.0 mg, 0.21 mmol) in a MeOH/H_2O solution (1:2, 2 mL) by an experimental procedure similar to that used in the case of **3**. Gel permeation chromatography on Bio-gel P-2 with water as eluent afforded the pure carboxylic acid **7** (60 mg, 0.09 mmol, 90%) as a white lyophilizate. R_f = 0.2 (α-naphthol, $MeOH/CH_2Cl_2$ 1:5). $[\alpha]_D^{20}$ = +35.4 (c = 2.04 in H_2O). ^{1}H NMR (300 MHz, D_2O): δ = 4.64 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1-H), 4.01 (m_c, 1 H, 12-H_{chol}), 4.0–3.78 (m, 3 H, 6a-H, 2-H, NCH_a), 3.87 (m_c, 1 H, 8-H_{chol}), 3.77–3.65 (m, 2 H, 3-H, NCH_b), 3.56 (m_c, 1 H, 5-H), 3.51–3.30 (m, 3 H, 4-H, 6b-Hb, 3-H_{chol}), 3.29 (s, 3 H, OCH_3), 2.50 (t, J = 7.2 Hz, 2 H, CH_2CO_2H), 2.32 (m_c, 1 H, 20-H_{chol}), 2.17 (m_c, 1 H, 10-H_{chol}), 2.10 (m_c, 1 H, 4-H_{chol}), 2.06 (m_c, 1 H, 4′-H_{chol}), 1.95 (m_c, 1 H, 20′-H_{chol}), 1.95 (m_c, 2 H, 7-H_{chol}, 16-H_{chol}), 1.81 (m_c, 2 H, 14-H_{chol}, 17-H_{chol}), 1.72 (m_c, 3 H, 1-H_{chol}, 15-H_{chol}, 19-H_{chol}), 1.55 (m_c, 5 H, 2-H_{chol}, 11-H_{chol}, 11′-H_{chol}, 9-H_{chol}, 7′-H_{chol}), 1.38 (m_c, 4 H, 2′-H_{chol}, 18-H_{chol}, 19′-H_{chol}, 5-H_{chol}), 1.23 (m_c, 2 H, 16′-H_{chol}, 15′-H_{chol}), 1.10 (m_c, 1 H, 1′-H_{chol}), 0.98 (d, J = 5.58 Hz, 3 H, 3×18-H_{chol}), 0.89 (s, 3 H, 3×6-H_{chol}), 0.69 (s, 3 H, 3×13-H_{chol}) ppm. ^{13}C NMR (75.46 MHz, D_2O): δ = 180.8 (CO_2H), 174.7 (NCO), 104.46 (C-1), 74.3 (C-5), 73.04 (C-12$_{chol}$), 69.65 (C-3$_{chol}$), 72.7 (C-2), 71.7 (C-3), 71.1 (C-4), 68.27 (C-8$_{chol}$), 58.2 (OCH_3), 49.8 (C-6), 48.91 (C-17$_{chol}$), 46.37 (C-13$_{chol}$), 45.31 (C-4$_{chol}$), 43.2 (NCH_2), 41.60 (C-5$_{chol}$), 41.08 (C-14$_{chol}$), 35.17 (C-9$_{chol}$), 35.0 (CH_2CO_2H), 34.91 (C-6$_{chol}$), 34.86 (C-8$_{chol}$), 33.91 (C-1$_{chol}$), 32.65 (C-7$_{chol}$), 31.81 (C-19$_{chol}$), 29.50 (C-2$_{chol}$), 29.26 (C-20$_{chol}$), 27.78 (C-11$_{chol}$), 27.34 (C-16$_{chol}$), 26.38 (C-10$_{chol}$), 23.00 (C-15$_{chol}$), 22.13 (C-6$_{chol}$), 16.77 (C-18$_{chol}$), 12.18 (C-13$_{chol}$) ppm. MALDI-TOF MS: m/z = 656.4 $[M + H]^+$, 678.5 $[M + Na]^+$ observed for $C_{34}H_{57}NO_{10}$ (655.39).

Methyl 6-Deoxy-6-[(1-nonyldecyl)amino]-α-D-mannopyranoside (8): A mixture of the amino-functionalized mannoside **1** (0.14 g, 0.46 mmol), nonadecan-10-one (0.26 g, 0.92 mmol), and $NaCNBH_3$ (0.14 g, 2.31 mmol) was dissolved in MeOH/THF (1:1, 2 mL) under argon at room temp. and was then heated at 60 °C for 6 h. The reaction mixture was then dried in vacuo and redissolved in MeOH (1 mL) to precipitate the unreacted ketone. The suspension was filtered off, the filtrate was concentrated, and the residue was redissolved in $CHCl_3$ and washed successively with H_2O and brine. After drying over anhydr. Na_2SO_4, it was filtered and washed, the filtrate was concentrated, and the crude product was purified by flash chromatography ($MeOH/CH_2Cl_2$ 1:5), to afford pure **8** (0.10 g, 0.22 mmol, 48%) as a colorless syrup. R_f = 0.5 (α-naphthol, $MeOH/CH_2Cl_2$ 1:5). ^{1}H NMR (500 MHz, [D$_4$]-

MeOH): δ = 4.68 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1-H), 3.83 (dd, $J_{2,1}$ = 1.6, $J_{2,3}$ = 3.3 Hz, 1 H, 2-H), 3.74 (m_c, 1 H, 5-H), 3.67 (dd, $J_{2,3}$ = 3.3, $J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 3.53 (t, $J_{3,4}$ = 9.5 Hz, 1 H, 4-H), 3.42 (s, 3 H, OCH_3), 3.34 (dd, 1 H, 6a-H), 3.16–3.08 (m, 2 H, NCH, 6b-H), 1.67 [m_c, 4 H, NCH(CH_2)$_2$], 1.35–1.24 (m, 28 H, 14×CH_2), 0.90 (t, J = 6.9 Hz, 6 H, 2×alkyl-CH_3) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 103.2 (C-1), 71.9 (C-3), 71.8 (C-2), 70.1 (C-5), 69.9 (C-4), 59.9 (NCH), 56.1 (OCH_3), 47.3 (C-6), 33.0 (4×CH_2), 31.9, 31.4 [NCH(CH_2)$_2$], 30.6, 30.5, 30.4, 26.3, 26.2, 23.7 (10×CH_2), 14.4 (2×alkyl-CH_3) ppm. MALDI-TOF MS: m/z = 460.4 [M + H]$^+$, 682.5 [M + Na]$^+$, 698.5 [M + K]$^+$ observed for $C_{26}H_{53}NO_5$ (459.39).

Methyl 6-Deoxy-6-[(2-methoxycarbonylethyl)(1-nonyldecyl)amino]-α-D-mannopyranoside (9): The secondary amine **8** (100 mg, 0.21 mmol) was dissolved in freshly distilled methyl acrylate (2 mL) and the reaction mixture was stirred in the dark for 12 h at room temp. It was then concentrated and the residue was purified by flash chromatography (MeOH/CH_2Cl_2 1:5) to afford the Michael adduct **9** (73 mg, 0.13 mmol, 62%) as a colorless syrup. R_f = 0.6 (α-naphthol, MeOH/CH_2Cl_2 1:5). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 4.57 (d, $J_{1,2}$ = 1.6 Hz, 1 H, 1-H), 3.75 (dd, $J_{2,1}$ = 1.6, $J_{2,3}$ = 3.3 Hz, 1 H, 2-H), 3.64 (s, 3 H, CO_2CH_3), 3.64 (dd, $J_{2,3}$ = 3.3 Hz, 1 H, 3-H), 3.46–3.43 (m, 2 H, 4-H, 5-H), 3.37 (s, 3 H, OCH_3), 2.92 (dd, $J_{5,6a}$ = 2.4, $J_{6a,6b}$ = 13.9 Hz, 1 H, 6a-H), 2.82 (t, J = 7.0 Hz, 2 H, NCH_2), 2.57 (dd, $J_{5,6b}$ = 6.8, $J_{6a,6b}$ = 13.8 Hz, 1 H, 6b-H), 2.54–2.44 (m, 3 H, $CH_2CO_2CH_3$, NCH), 1.47 [m_c, 4 H, NCH(CH_2)$_2$], 1.30–1.23 (m, 28 H, 14×CH_2), 0.90 (t, J = 7.0 Hz, 6 H, 2×alkyl-CH_3) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 175.1 (CO_2CH_3), 102.8 (C-1), 73.5 (C-3), 72.5 (C-2), 72.0 (C-5), 71.6 (C-4), 63.0 (NCH), 55.6 (OCH_3), 54.6 (C-6), 52.0 (CO_2CH_3), 48.3 (NCH_2), 35.5 ($CH_2CO_2CH_3$), 33.1 [NCH(CH_2)$_2$], 32.1, 31.5, 31.0, 30.9, 30.8, 30.5, 28.7, 28.6, 23.8 (14×CH_2), 14.5 (2×alkyl-CH_3) ppm. MALDI-TOF MS: m/z = 546.6 [M + H]$^+$, 568.6 [M + Na]$^+$, 584.6 [M + K]$^+$ observed for $C_{30}H_{59}NO_7$ (545.42).

Methyl 6-[(2-Carboxyethyl)(1-nonyldecyl)amino]-6-deoxy-α-D-mannopyranoside (10): The methyl ester **9** (30 mg, 0.05 mmol) was dissolved in propan-2-ol/H_2O (2:1; 1 mL) and treated with LiOH·H_2O (5.0 mg, 0.12 mmol) at room temp. for 12 h. The basic reaction mixture was then neutralized (to pH = 6) at 0 °C by the careful addition of an aq. HCl (2 N) solution and the solvent was evaporated. The obtained crude product was purified by flash chromatography (MeOH/CH_2Cl_2 1:5), and silica gel impurities were then removed by passing the mixture through a short column of Sephadex LH-20 in MeOH/CH_2Cl_2 (1:1) to provide the pure carboxylic acid **10** (22 mg, 0.04 mmol, 80%) as a white lyophilizate. R_f = 0.2 (α-naphthol, MeOH/CH_2Cl_2 1:5). ^{1}H NMR (300 MHz, [D$_4$]MeOH): δ = 4.52 (dd, $J_{1,2}$ = 1.3 Hz, 1 H, 1-H), 3.60 (dd, $J_{1,2}$ = 1.3 Hz, 1 H, 2-H), 3.62–3.48 (m, 3 H, 5-H, 3-H, 4-H), 3.28 (s, 3 H, OCH_3), 3.18 (dd, 1 H, 6a-H), 3.03 (m_c, 2 H, NCH_2), 3.00–2.85 (m, 2 H, NCH, 6b-H), 2.37 (m_c, 2 H, CH_2CO_2H), 1.70–1.52 (m, 2 H, NCHCH_2), 1.45–1.28 (m, 2 H, NCHCH_2), 1.20–1.10 (m, 28 H, 14×CH_3), 0.75 (t, J = 6.5 Hz, 6 H, 2×alkyl-CH_3) ppm. ^{13}C NMR (75.46 MHz, [D$_4$]MeOH): δ = 175.4 (CO_2H), 102.7 (C-1), 72.2 (C-3), 71.6 (C-2), 71.4 (C-5), 69.6 (C-4), 63.5 (NCH), 55.8 (OCH_3), 52.5 (C-6), 49.7 (NCH_2), 32.6 (CH_2CO_2H), 31.3 {NCH(CH_2)$_2$}, 30.5, 30.4, 30.3, 30.2, 30.0, 27.8, 27.7, 23.3 (14×CH_2), 14.3 (2×alkyl-CH_3) ppm. MALDI-TOF MS: m/z = 554.5 [M + Na]$^+$, 570.4 [M + K]$^+$ observed for $C_{29}H_{57}NO_7$ (531.41).

2-[Acetyl(1-nonyldecyl)amino]ethyl 6-[Bis(2-methoxycarbonylethyl)-amino]-6-deoxy-β-D-glucopyranoside (14): A suspension of aminoglycoside **11** (389 mg, 0.986 mmol), nonadecan-10-one (554 mg, 1.96 mmol), and $NaCNBH_3$ (185 mg, 2.94 mmol) in MeOH/THF (1:1, 5 mL) was heated at 60 °C for 6 h. When the clear homogeneous reaction mixture had cooled to room temp. and been diluted with methanol (5 mL), the excess of unreacted ketone precipitated and could be filtered off. The filtrate was concentrated in vacuo, redissolved in CH_2Cl_2 (10 mL), and washed with water (3×5 mL). The organic layer was then dried with anhydrous Na_2SO_4, filtered, and washed, and the filtrate was concentrated to provide the crude bilipid adduct **12**. This was then treated at 0 °C with Ac_2O (2 mL), together with a catalytic amount of DMAP (10 mg), in a pyridine/CH_2Cl_2 mixture (1:1, 6 mL) . After 3 h at room temp. the reaction mixture was cooled in an ice bath and the excess of Ac_2O was quenched with methanol (ca. 1 mL). The reaction mixture was evaporated to deliver the fully acetylated derivative **13**. This crude intermediate was then treated with a freshly prepared solution of NaOMe (1 M, 1 mL) in methanol (5 mL) and stirred for 3 h at 0 °C, the basic mixture was then neutralized with aqueous HCl (5%) solution, and concentration and silica gel column chromatographic purification (MeOH/CH_2Cl_2 1:20) afforded the title compound **14** (159 mg, 0.226 mmol, 23% over three steps) as a colorless syrup. R_f = 0.6 (MeOH/CH_2Cl_2 1:9). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 0.90 (t, J = 7.1 Hz, 6 H, 2×CH_3), 1.27 (m_c, 28 H, 14×CH_2), 1.54 [m_c, 4 H, NCH(CH_2)$_2$], 2.08 (s, 3 H, $NCOCH_3$), 2.49 (t, J = 7.0 Hz, 4 H, 2×$CH_2CO_2CH_3$), 2.64 (dd, J = 6.6, 14.3 Hz, 1 H, 6a-H), 2.88 (m_c, 4 H, 2×NCH_2), 2.95 (dd, J = 2.5, 14.3 Hz, 1 H, 6b-H), 3.12 (m_c, 1 H, 4-H), 3.16 (m_c, 1 H, 2-H), 3.45 (m_c, 3 H, 5-H, NCH_aH_b), 3.49 (t, J = 6.5 Hz, 1 H, NCH_aH_b), 3.65 (s, 6 H, 2×CO_2CH_3), 3.67 (m_c, 1 H, AcNCH), 3.88 (t, J = 6.2 Hz, 1 H, OCH_aH_b), 3.93 (t, J = 6.9 Hz, 1 H, OCH_aH_b), 4.23 (d, J = 7.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 14.5 (2×CH_3), 22.5 ($NCOCH_3$), 23.7, 30.5, 30.7, 30.7, 30.8, 33.1, 34.2 (2×$CH_2CO_2CH_3$, 14×CH_2), 34.9 [2×NCH(CH_2)$_2$], 41.9 (CH_2NCO), 49.3 (2×NCH_2), 51.4 (2×CO_2CH_3), 55.9 (C-6), 60.5 (AcNCH), 68.5 (OCH_2), 73.7 (C-4), 73.8 (C-2), 76.0 (C-5), 78.0 (C-3), 104.4 (C-1), 174.1 ($NCOCH_3$), 174.6 (2×CO_2CH_3) ppm. MALDI-TOF MS (positive mode): m/z = 703.47 [M + H]$^+$ 725.30 [M + Na]$^+$, observed for $C_{37}H_{70}N_2O_{10}$ (702.50).

2-[Acetyl(1-nonyldecyl)amino]ethyl 6-[Bis(2-carboxyethyl)amino]-6-deoxy-β-D-glucopyranoside (15): A homogeneous reaction mixture containing glycoconjugate **14** (116 mg, 0.165 mmol) and lithium hydroxide monohydrate (1.4 mg, 0.33 mmol) in methanol/water (1:2, 3 mL) was stored in the refrigerator for 12 h. The basic reaction mixture was worked up in a similar way as described for **3**, and the obtained crude product was subjected to purification on Bio-gel P-2 with doubly distilled water as the eluent to provide the pure title compound **15** (103 mg, 0.152 mmol, 92%) as a white solid after lyophilization. R_f = 0.3 (propan-2-ol/water/aq. ammonia 8:1:1). This product was used for the following peptide coupling reactions without further characterization.

1-Nonyldecyl-Modified Glycodendron 16: A mixture of the dicarboxylic acid **15** (60 mg, 88.90 μmol), the aminoglycoside **11** (88 mg, 0.22 mmol), and HATU (85 mg, 0.22 mmol) was dissolved in dry DMF (2 mL) and treated with DIPEA (0.15 mL, 0.89 mmol) at ambient temperature under argon. The reaction mixture was stirred overnight at room temp. and then concentrated to dryness, yielding a brown syrup, which was subjected to gel permeation chromatography on Sephadex LH-20 with methanol as the eluent to deliver the title compound **16** (35 mg, 24.51 μmol, 27%) as a white lyophilizate. R_f = 0.3 (propan-2-ol/water/aq.ammonia 7:3:1). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 0.89 (t, 6 H, 2×CH_3), 1.27 (m_c, 28 H, 14×CH_2), 1.50 [m_c, 4 H, NCH(CH_2)$_2$], 2.09 (s, 3 H, $NCOCH_3$), 2.40 (m_c, 4 H, 2×CH_2CONH), 2.50 (t, J = 7.0 Hz, 8 H, 4×$CH_2CO_2CH_3$), 2.63 (dd, J = 7.0, 14.1 Hz, 2 H, 2×6-H), 2.73 (dd, J = 6.6, 14.2 Hz, 1 H, 6-H), 2.86 (m_c, 12 H, 6×NCH_2), 2.96

(dd, J = 2.3, 11.7 Hz, 3 H, 3×6-H), 3.12 (dd≈t, J = 9.5 Hz, 3 H, 3×4-H), 3.20 (m_c, 3 H, 3×2-H), 3.30 (m_c, 2 H, 2×CH_aH$_b$NHCO), 3.38 (m_c, 3 H, 3×3-H), 3.40 (m_c, 3 H, 3×5-H), 3.49 (m_c, 2 H, 2×CH$_a$$H_b$NHCO), 3.60 ($m_c$, 3 H, 3×OCH$_a$$H_b$), 3.65 (s, 12 H, 4×CO$_2CH_3$), 3.66 ($m_c$, 3 H, AcNC$H$, C$H_2$NAc), 3.90 ($m_c$, 3 H, 3×OC$H_aH_b$), 4.25 (d, J = 7.7 Hz, 2 H, 2×1-H), 4.28 (d, J = 7.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 14.5 (2×CH$_3$), 22.4 (NCOCH_3), 23.7, 23.8, 27.6, 27.7, 30.4, 30.5, 30.6, 30.7, 30.8, 33.1, 33.2 (14×CH$_2$), 33.4 (4×CH$_2$CO$_2$Me), 34.6 [NCH(CH_2)$_2$], 34.8 (2×CH$_2$CONH), 40.4 (2×CH$_2$NHCO), 51.3, 52.0 (6×NCH$_2$), 52.2 (4×CO$_2$$CH_3$), 56.0 (3×C-6), 61.0 ($CH_2$NAc), 68.2, 69.4 (3×OCH$_2$), 72.7 (AcN$CH$), 73.8, 73.9 (3×C-4), 75.0 (3×C-2), 75.6, 75.7 (3×C-5), 77.9, 78.0 (3×C-3), 104.1, 104.2, 104.3 (3×C-1), 174.1, 174.7 (4×CO$_2$Me), 174.8, 174.9 (2×CONH, NCOCH$_3$) ppm. MALDI-TOF MS (positive mode): m/z = 1450.40 [M + Na]$^+$ observed for $C_{67}H_{122}N_6O_{26}$ (1426.84).

1-Nonyldecyl-Modified Glycodendron 17: A solution of bilipid conjugate **16** (21 mg, 14.71 μmol) and lithium hydroxide monohydrate (2.5 mg, 58.84 μmol) in methanol/water (1:2, 5 mL) was allowed to stand at room temp. for 12 h. The reaction mixture was processed as in the case of **3** and the obtained crude product was subjected to gel permeation chromatography on Bio-gel P-2 with doubly distilled water as the eluent. Pure fractions containing the product were collected and freeze-dried to provide the tetracarboxylic acid **17** (16 mg, 11.66 μmol, 79%) as a white lyophilizate. ^{1}H NMR (500 MHz, D$_2$O): δ = 0.86 (m_c, 6 H, 2×CH$_3$), 1.25 (m_c, 28 H, 14×CH$_2$), 1.65 [m_c, 4 H, NCH(CH_2)$_2$], 2.10 (s, 3 H, NCOCH$_3$), 2.20 (m_c, 4 H, 2×CH_2CONH), 2.65 (m_c, 8 H, 4×CH_2CO$_2$H), 3.27 (m_c, 15 H, 3×2-H, 3×4-H, 6×NCH$_a$$H_b$, 3×6-H), 3.43 ($m_c$, 2 H, 2×C$H_aH_b$NHCO), 3.50, ($m_c$, 15 H, 3×5-H, 3×6-H, 3×3-H, 6×NCH_aH$_b$), 3.65 (m_c, 5 H, 3×OCH$_a$$H_b$, 2×CH$_a$$H_b$NHCO), 3.85 ($m_c$, 3 H, AcNC$H$, C$H_2$NAc), 3.95 ($m_c$, 3 H, 3×OC$H_aH_b$), 4.45 (d, J = 8.3 Hz, 3 H, 3×1-H) ppm. ^{13}C NMR (125.75 MHz, D$_2$O): δ = 15.7 (2×CH$_3$), 24.3, 27.1 (8×CH$_2$), 31.2, 31.4, 31.6 (4×CH$_2$CO$_2$H, 6×CH$_2$), 33.1 [NCH(CH_2)$_2$], 33.6 (2×CH$_2$CONH), 40.3 (2×CH$_2$NHCO), 45.1 (NCOCH_3), 53.4, 53.5 (6×NCH$_2$), 62.6 (3×C-6), 70.1 (CH_2NAc), 71.2 (3×OCH$_2$), 71.4 (3×C-4), 72.7 (AcNCH), 72.8 (3×C-2), 74.6 (3×C-5), 76.8 (3×C-3), 103.5 (3×C-1), 172.8 (4×CO$_2$H), 173.2 (2×CONH), 175.2 (NCOCH$_3$) ppm. MALDI-TOF MS (negative mode): m/z = 1371.79 [M + H]$^+$, 1392.10 [(M-H)+Na]$^+$, observed for $C_{63}H_{114}N_6O_{26}$ (1370.77).

Aminoethyl-Modified Glycodendron 19: The Boc-protected glycodendron **18**[20] (200 mg, 164.03 μmol) was dissolved in a freshly prepared solution of dimethylsulfide and trifluoroacetic acid (1:2, 1 mL) and stirred for 3 h at 0 °C. The reaction mixture was concentrated to dryness under high vacuum with the bath temperature not exceeding 30 °C, last traces of TFA were neutralized with ammonium hydroxide (25%, 0.5 mL), and the residue was loaded onto a gel permeation desalting column (Bio-gel P-2) with doubly distilled water as the eluent to provide the desired amino-functionalized dendron **19** (156 mg, 139.39 μmol, 84%) as a pale yellow lyophilizate. This was used in the following peptide coupling reaction without further characterization.

2-[(3α,7α,12α-Trihydroxy-5β-cholan-24-oyl)amino]ethyl-Modified Glycodendron 20: In an experimental procedure similar to that used for the preparation of glycodendron **16**, a mixture of cholic acid (88.3 mg, 216.23 μmol), the glycocedron **19** (110 mg, 98.28 μmol), and HATU (82.2 mg, 216.23 μmol) was dissolved in dry DMF (2 mL), and this solution was allowed to react in the presence of DIPEA (0.17 mL, 0.98 mmol) to provide the crude product as a brown syrup. This was subjected to gel permeation chromatography on Sephadex LH-20 with MeOH as the eluent to provide the title steroid conjugate **20** (86 mg, 57.57 μmol, 58%) as a pale yellow glass. R_f = 0.5 (propan-2-ol/water/aq.ammonia 8:1:1). $[\alpha]_D^{20}$ = +2.2 (c = 1.45 in methanol). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 0.71 (s, 3 H, 13-H$_{chol}$), 0.91 (s, 3 H, 3×6-H$_{chol}$), 0.97 (m_c, 1 H, 1-H$_{chol}$), 1.02 (d, J = 6.4 Hz, 3 H, 3×18′-H$_{chol}$), 1.10 (m_c, 1 H, 15′-H$_{chol}$), 1.29 (m_c, 1 H, 16′-H$_{chol}$), 1.40 (m_c, 4 H, 2′-H$_{chol}$, 18-H$_{chol}$, 19′-H$_{chol}$, 5-H$_{chol}$), 1.55 (m_c, 4 H, 2-H$_{chol}$, 11-H$_{chol}$, 9-H$_{chol}$, 7′-H$_{chol}$), 1.65 (m_c, 1 H, 4-H$_{chol}$), 1.75 (m_c, 2 H, 15-H$_{chol}$, 19-H$_{chol}$), 1.80 (m_c, 1 H, 1-H$_{chol}$), 1.85 (m_c, 1 H, 17-H$_{chol}$), 1.96 (m_c, 3 H, 7-H$_{chol}$, 16-H$_{chol}$, 14-H$_{chol}$), 2.11 (ddd, J = 6.6, 9.6, 13.9 Hz, 1 H, 20′-H$_{chol}$), 2.29 (m_c, 3 H, 20-H$_{chol}$, 4-H$_{chol}$, 10-H$_{chol}$), 2.41 (m_c, 4 H, 2×CH_2CONH), 2.50 (m_c, 8 H, 4×CH_2CO$_2$CH$_3$), 2.62 (dd, J = 7.2, 14.3 Hz, 2 H, 2×6-H), 2.70 (dd, J = 7.0, 14.4 Hz, 1 H, 6-H), 2.84 (m_c, 6 H, 6×NCH$_a$$H_b$), 2.88 ($m_c$, 6 H, 6×NC$H_aH_b$), 2.96 (dd, J = 2.6, 14.3 Hz, 2 H, 2×6-H), 2.98 (dd, J = 2.5, 9.5 Hz, 1 H, 6-H), 3.12 (dd, J = 9.7, 8.8 Hz, 3 H, 3×4-H), 3.20 (m_c, 3 H, 3×2-H), 3.31 (m_c, 3 H, 3×CH$_a$$H_b$NHCO), 3.36 ($m_c$, 3 H, 3×3-H), 3.44 ($m_c$, 3 H, 3×C$H_aH_b$NHCO), 3.51 ($m_c$, 3 H, 3×5-H), 3.59 ($m_c$, 3 H, 3×OCH$_a$$H_b$), 3.66 (s, 12 H, 4×CO$_2CH_3$), 3.79 ($m_c$, 1 H, 8-H$_{chol}$), 3.89 ($m_c$, 3 H, 3×OC$H_aH_b$), 3.95 ($m_c$, 1 H, 12-H$_{chol}$), 4.27 (d, J = 7.7 Hz, 2 H, 2×1-H), 4.29 (d, J = 7.9 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 13.1 (C-13$_{chol}$), 17.8 (C-18$_{chol}$), 23.2 (C-6$_{chol}$), 24.3 (C-15$_{chol}$), 27.9 (C-10$_{chol}$), 28.8 (C-16$_{chol}$), 29.6 (C-11$_{chol}$), 31.2 (C-2$_{chol}$), 32.3 (C-19$_{chol}$), 33.4 (4 C, 4×CH$_2$CO$_2$CH$_3$), 34.1 (C-20$_{chol}$), 34.7 (2 C, CH$_2$CONH), 35.9 (C-6$_{chol}$), 35.9 (C-7$_{chol}$), 36.5 (C-1$_{chol}$), 37.0 (C-18$_{chol}$), 40.4 (2 C, CH$_2$NHCO), 40.5 (C-4$_{chol}$, CH$_2$NHCO), 41.0 (C-9$_{chol}$), 43.0 (C-14$_{chol}$), 43.2 (C-5$_{chol}$), 47.5 (C-13$_{chol}$), 48.0 (C-17$_{chol}$), 51.3 (2×NCH$_2$), 52.2 (4×CO$_2$CH_3), 55.7 (C-6), 56.1 (2×C-6), 59.3 (4×NCH$_2$), 69.1 (C-8$_{chol}$), 69.4, 69.4 (3×OCH$_2$), 72.9 (C-3$_{chol}$), 73.9, 73.8 (3×C-4), 74.0 (C-12$_{chol}$), 75.0 (3×C-2), 75.5 (3×C-5), 77.8 (3×C-3), 104.0 (2×C-1), 104.1 (C-1), 174.7 (4×CO$_2$CH$_3$), 174.9 (2×CONH), 176.9 (CONH) ppm. MALDI-TOF MS (positive mode): m/z = 1532.30 [M + Na]$^+$, observed for $C_{70}H_{120}N_6O_{29}$ (1508.80).

2-[(3α,7α,12α-Trihydroxy-5β-cholan-24-oyl)amino]ethyl-Modified Glycodendron 21: For deprotection, a homogeneous mixture of **20** (29 mg, 19.21 μmol) and lithium hydroxide monohydrate (4 mg, 96.05 μmol) in methanol/water (1:2, 5 mL) was allowed to stand in the refrigerator overnight. The reaction mixture was processed as in the case of **3**, and the crude product was subjected to purification on Bio-gel P-2 with doubly distilled water as the eluent to deliver the pure tetracarboxylic acid **21** (22 mg, 15.13 μmol, 79%) as a white solid after lyophilization. $[\alpha]_D^{20}$ = +21.4 (c = 1.70 in water). ^{1}H NMR (500 MHz, D$_2$O): δ = 0.69 (s, 3 H, 3×13-H$_{chol}$), 0.89 (s, 3 H, 3×6-H$_{chol}$), 0.98 (d, J = 5.6 Hz, 3 H, 3×18′-H$_{chol}$), 1.10 (m_c, 1 H, CH$_a$$H_b$), 1.23 ($m_c$, 2 H, 16′-H$_{chol}$, 15′-H$_{chol}$), 1.38 ($m_c$, 4 H, 2′-H$_{chol}$, 18-H$_{chol}$, 19′-H$_{chol}$, 5-H$_{chol}$), 1.55 ($m_c$, 4 H, 2-H$_{chol}$, 11-H$_{chol}$, 9-H$_{chol}$, 7′-H$_{chol}$), 1.72 ($m_c$, 3 H, 1-H$_{chol}$, 15-H$_{chol}$, 19-H$_{chol}$), 1.81 ($m_c$, 2 H, 14-H$_{chol}$, 17-H$_{chol}$), 1.95 ($m_c$, 2 H, 7-H$_{chol}$, 16-H$_{chol}$), 1.98 ($m_c$, 1 H, 20′-H$_{chol}$), 2.06 ($m_c$, 1 H, 4-H$_{chol}$), 2.10 ($m_c$, 1 H, 4′-H$_{chol}$), 2.17 ($m_c$, 1 H, 10-H$_{chol}$), 2.32 ($m_c$, 1 H, 20-H$_{chol}$), 2.84 ($m_c$, 4 H, 2×C$H_2CO_2$H), 2.90 ($m_c$, 4 H, 2×C$H_2CO_2$H), 2.95 ($m_c$, 4 H, 2×C$H_2$CONH), 3.00 ($m_c$, 2 H, C$H_2$CONH), 3.32 ($m_c$, 10 H, 3×6-H, 3-H$_{chol}$, 6×NCH$_a$$H_b$), 3.47 ($m_c$, 9 H, 3×6-H, 6×NC$H_aH_b$), 3.53 ($m_c$, 6 H, 3×2-H, 3 5-H), 3.67 (m_c, 6 H, 3×5-H, 3×3-H), 3.70 (m_c, 6 H, 3×CH_2NHCO), 3.87 (m_c, 1 H, 8-H$_{chol}$), 3.92 (m_c, 6 H, OCH$_2$), 4.01 (m_c, 1 H, 12-H$_{chol}$), 4.51 (d, J = 8.1 Hz, 2 H, 2×1-H), 4.55 (d, J = 7.9 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, D$_2$O): δ = 12.2 (C-13$_{chol}$), 16.7 (C-18$_{chol}$), 22.1 (C-6$_{chol}$), 23.0 (C-15$_{chol}$), 26.4 (C-10$_{chol}$), 27.3, 27.8 (C-11$_{chol}$, C-16$_{hol}$), 29.2, 29.3 (C-20$_{chol}$, 6×CH$_2$CO), 29.5 (C-2$_{chol}$), 31.8 (C-19$_{chol}$),

32.6 (C-7_{chol}), 33.9 (C-1_{chol}), 34.8 (C-18_{chol}), 34.9 (C-6_{chol}), 35.2 (C-9_{chol}), 38.4 (CH_2NHCO), 39.1 (2×CH_2NHCO), 41.1 (C-14_{chol}), 41.6 (C-5_{chol}), 45.3 (C-4_{chol}), 46.3 (C-13_{chol}), 48.9 (C-17_{chol}), 51.2, 51.4 (6×NCH_2), 54.8, 55.5 (3×C-6), 68.2 (C-8_{chol}), 68.3, 68.5 (3×OCH_2), 69.5 (3×C-4), 69.6 (C-3_{chol}), 71.1, 71.5 (3×C-2), 72.8 (3×C-5), 73.0 (C-12_{chol}), 75.2 (3×C-3), 101.9 (2×C-1), 102.0 (C-1), 172.0 (4×CO_2H), 175.0 (2×CONH), 171.5 (CONH) ppm. MALDI-TOF MS (negative mode): m/z = 1474.2 $[(M-H)+Na]^+$, observed for $C_{66}H_{112}N_6O_{29}$ (1452.74).

Laurylamidoethyl-Modified Glycodendron 22: A mixture of the amine **19** (120 mg, 107.22 μmol), lauric acid (49.3 mg, 246.10 μmol), and HATU (93.5 mg, 245.85 μmol) was dissolved in dry DMF (2 mL) and treated under argon at room temperature with DIPEA (0.1 mL, 0.53 mmol). The colorless reaction mixture turned pale yellow. The reaction mixture was stirred overnight at room temp. and was then evaporated to dryness, the brown residual syrup was filtered through a membrane filter, which was washed with methanol, and the filtrate was subjected to GPC on Sephadex LH-20 with methanol as eluent. Pure fractions containing the product were collected and concentrated to provide the title compound **22** (93 mg, 71.46 μmol, 66%) as a pale yellow, transparent glass. R_f = 0.45 (propan-2-ol/water/ammonium hydroxide 8:1:1). $[\alpha]_D^{20}$ = –8.54 (c = 1.17 in methanol). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 0.90 (t, J = 7.0 Hz, 3 H, CH_3), 1.30 (m_c, 16 H, 8×CH_2), 1.60 (m_c, 2 H, NHCOCH_2CH_2), 2.19 (dd≈t, J = 7.3 Hz, 2 H, NHCOCH_2), 2.41 (m_c, 4 H, 2×CH_2CONH), 2.51 (m_c, 8 H, 4×C$H_2$$CO_2CH_3$), 2.62 (dd, J = 7.3, 14.3 Hz, 2 H, 2×6-H), 2.71 (dd, J = 6.6, 14.1 Hz, 1 H, 6-H), 2.87 (m_c, 12 H, 6×NCH_2), 2.96 (dd, J = 6.6, 14.3 Hz, 2 H, 2×6-H), 3.01 (dd, J = 2.3, 11.7 Hz, 1 H, 6-H), 3.13 (m_c, 3 H, 3×4-H), 3.21 (m_c, 3 H, 3×2-H), 3.32 (m_c, 3 H, 3×CH_aH_bNHCO), 3.37 (m_c, 3 H, 3×3-H), 3.41 (m_c, 3 H, 3×5-H), 3.50 (m_c, 3 H, 3×C$H_a$$H_b$NHCO), 3.59 ($m_c$, 3 H, 3×$OCH_aH_b$), 3.66 (s, 12 H, 4×$CO_2CH_3$), 3.89 ($m_c$, 3 H, 3×OC$H$-$_a$$H_b$), 4.27 (d, J = 7.7 Hz, 2 H, 2×1-H), 4.28 (d, J = 7.7 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, [D$_4$]MeOH): δ = 14.4 (CH_3), 30.7, 30.6, 30.5, 30.4, 30.3, 27.0 23.7 (8×CH_2), 33.0 (NHCOCH_2CH_2), 33.4 (4×C$H_2$$CO_2$Me), 37.1, 34.6 (3×C$H_2$CONH), 40.4 ($CH_2$NH), 40.4 (2×C$H_2$NHCO), 51.9, 51.3 (6×$NCH_2$), 52.2, 52.1 (4×$CO_2CH_3$), 55.9, 55.6 (3×C-6), 69.3, 69.3 (3×OCH_2), 73.8 (3×C-4), 75.1, 75.0, 74.9 (3×C-2), 75.6 (3×C-5), 77.8, 77.7 (3×C-3), 104.1, 104.0 (3×C-1), 174.7, 174.6 (4×CO_2Me), 176.4, 174.9 (3×CONH) ppm. MALDI-TOF MS (positive mode): m/z = 1324.4 $[M + Na]^+$, observed for $C_{58}H_{104}N_6O_{26}$ (1300.70).

Laurylamidoethyl-Modified Glycodendron 23: For deprotection, a solution of **22** (36 mg, 27.66 μmol) and lithium hydroxide monohydrate (4.6 mg, 110.64 μmol) in methanol/water (1:1, 5 mL) was allowed to stand at 0 °C for 12 h. The basic reaction mixture was worked up and the product was purified as in the case of **3** to furnish the tetracarboxylic acid **23** (25 mg, 200.74 μmol, 72%) as a white, hygroscopic solid. $[\alpha]_D^{20}$ = +13.11 (c = 1.64 in water). ^{1}H NMR (500 MHz, D_2O): δ = 0.85 (t, J = 7.0 Hz, 3 H, CH_3), 1.25 (m_c, 16 H, 8×CH_2), 1.55 (m_c, 2 H, 2×NHCOCH_2CH_2), 2.23 (m_c, 2 H, NHCOCH_2), 2.74 (m_c, 4 H, 2×CH_2CONH), 2.83 (m_c, 8 H, 4×C$H_2$$CO_2$H), 3.40 ($m_c$, 18 H, 3×$CH_aH_b$NHCO, 3×6-H, 6×$NCH_aH_b$, 3×2-H, 3×4-H), 3.60 (15 H, 3×C$H_a$$H_b$NHCO, 3×6-H, 6×NC$H_a$$H_b$, 3×3-H), 3.74 ($m_c$, 3 H, 3×$OCH_aH_b$), 3.91 ($m_c$, 3 H, 3×5-H), 4.00 ($m_c$, 3 H, 3×OC$H_a$$H_b$), 4.50 (d, J = 7.9 Hz, 2 H, 2×1-H), 4.55 (d, J = 7.8 Hz, 1 H, 1-H) ppm. ^{13}C NMR (125.75 MHz, D_2O): δ = 16.2 (CH_3), 31.9, 31.9, 31.8, 31.6, 31.3, 31.2, 30.0, 24.9 (8×CH_2), 34.1 (4×C$H_2$$CO_2$H), 41.6, 38.4, 38.3 (3×CH_2CONH), 51.3 (6×NCH_2), 54.2, 53.2 (3×CH_2NHCO), 57.2 (3×C-6), 71.0, 70.6 (3×OCH_2), 72.3, 72.1 (3×C-5), 73.6, 73.5 (3×C-4), 75.3 (3×C-2), 77.6 (3×C-3), 104.3 (3×C-1), 174.2 (3×CONH), 178.8 (4×CO_2H) ppm. MALDI-TOF MS (negative mode): m/z = 1268.0 $[M + Na]^+$, observed for $C_{54}H_{96}N_6O_{26}$ (1244.63).

6-(Dodecanoylamino)hexyl 2,3,4,6-Tetrakis-*O*-[3-(α-D-mannopyranosyloxy)propyl]-β-D-glucopyranoside (25): The amine **24** (27 mg, 0.023 mmol), lauric acid (6.1 mg, 0.03 mmol), and DIPEA (0.02 mL, 0.12 mmol) were dissolved in dry DMF (5 mL) under argon, cooled to 0 °C, and treated with HATU (11.6 mg, 0.03 mmol). The reaction mixture was stirred at 0 °C for 2 h and for another 6 h at room temp., the mixture was passed over a Sephadex LH-20 column, and the product was eluted with MeOH and obtained in the form of a colorless syrup (29 mg, 0.022 mmol, 96%). $[\alpha]_D^{20}$ = +42.9 (c = 0.17 in MeOH). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 4.81, 4.80, 4.80, 4.78 (each d, $J_{1,2man}$ = 1.5 Hz, 4 H, 4×1-H_{man}), 4.30 (d, $J_{1,2glc}$ = 7.7 Hz, 1 H, 1-H_{glc}), 3.98–3.82 [m, 17 H, 4×2-H_{man}, 4×6-H_{man}, 5×(glc)OCHH, 4×(man)OCHH], 3.79–3.52 [m, 27 H, 4×3-H_{man}, 4×4-H_{man}, 4×5-H_{man}, 4×6′-H_{man}, 6-H_{glc}, 6′-H_{glc}, 5×(glc)OCHH, 4×(man)OCHH], 3.36–3.32 (m, 1 H+MeOH, 5-H_{glc}), 3.31–3.25 (m, 2 H, 3-H_{glc}, 4-H_{glc}), 3.20 (t, J = 7.0 Hz, 2 H, CH_2NHCO), 3.02 (dd≈t, $J_{2,3glc}$ = 8.8 Hz, 1 H, 2-H_{glc}), 2.21 (t, J = 7.5 Hz, 2 H, NHCOCH_2), 1.97–1.86 (m, 8 H, 4×OCH_2CH_2CH_2O), 1.71–1.30 [m, 26 H, (C-1_{glc})-$OCH_2CH_2CH_2CH_2CH_2CH_2$NH, 18×$H_{alkyl\ chain}$] 0.94 (t, J = 6.8 Hz, 3 H, CH_3) ppm. ^{13}C NMR (125.76 MHz, [D$_4$]MeOH): δ = 177.5 (NHCO), 105.9 (C-1_{glc}), 102.8 (4×C-1_{man}), 87.2 (C-3_{glc}), 84.9 (C-2_{glc}), 80.4 (C-4_{glc}), 77.0 (C-5_{glc}), 75.8 (4×C-5_{man}), 73.8 (4×C-3_{man}), 73.4 (4×C-2_{man}), 72.8, 72.0–71.8, 70.4 [5×(glc)OCH$_2$, C-6_{glc}], 69.8 (3×), 69.7 (4×C-4_{man}), 66.8, 66.7, 66.5 (2×) [4×(man)-OCH$_2$], 64.1 (4×C-6_{man}), 41.6, 38.3, 34.2 (CH_2CH_2CONHCH$_2$), 32.9, 32.7 (2×), 32.1–31.5 (9×) [4×OCH$_2$CH_2CH$_2$O, (C-1_{glc})OCH$_2$CH_2CH$_2$CH$_2$CH_2CH$_2$NH, 6×$C_{alkyl\ chain}$], 29.0, 28.3, 28.1 [(C-1_{glc})OCH$_2$CH$_2$CH_2CH_2, $C_{alkyl\ chain}$], 25.0 ($C_{alkyl\ chain}$), 15.7 (CH_3) ppm. MALDI-TOF MS: m/z = 1364.7 $[M + Na]^+$ (1341.71 calcd. for $C_{60}H_{111}NO_{31}$).

6-[(3α,7α,12α-Trihydroxy-5β-cholan-24-oyl)amino]hexyl 2,3,4,6-Tetrakis-*O*-[3-(α-D-mannopyranosyloxy)propyl]-β-D-glucopyranoside (26): The amine **24** (34 mg, 0.029 mmol), cholic acid (13.2 mg, 0.032 mmol), and DIPEA (0.02 mL, 0.12 mmol) were dissolved in dry DMF (3 mL), the mixture was cooled to 0 °C, and HATU (13 mg, 0.034 mmol) was added. The reaction mixture was stirred for 2 h at 0 °C and for another 6 h at room temp. and was then purified by GPC on Sephadex LH-20 with methanol as the eluent to provide the title compound as a colorless syrup (39 mg, 0.025 mmol, 86%). $[\alpha]_D^{20}$ = +43.3 (c = 0.27 in MeOH). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 4.81, 4.81, 4.80, 4.78 (each d, $J_{1,2man}$ = 1.3 Hz, 4 H, 4×1-H_{man}), 4.30 (d, $J_{1,2glc}$ = 7.7 Hz, 1 H, 1-H_{glc}), 3.97–3.82 [m, 19 H, 4×2-H_{man}, 4×6-H_{man}, 5×(glc)OCHH, 4×(man)OCHH, 7-H_{chol}, 12-H_{chol}], 3.79–3.53 [m, 27 H, 4×3-H_{man}, 4×4-H_{man}, 4×5-H_{man}, 4×6′-H_{man}, 6-H_{glc}, 6′-H_{glc}, 5×(glc)OCHH, 4×(man)OCHH], 3.42–3.28 (m, 2 H + MeOH, 5-H_{glc}, 3-H_{chol}), 3.30–3.25 (m, 2 H, 3-H_{glc}, 4-H_{glc}), 3.20 (t, J = 7.0 Hz, 2 H, CH_2NHCO), 3.03 (dd≈t, J = 8.2 Hz, 1 H, 2-H_{glc}), 2.34–2.06 (m, 4 H, NHCOCH_2, NHCOCH_2, 4-H_{chol}, 9-H_{chol}), 2.02–1.74 (m, 15 H, 4×OCH_2CH_2CH_2O, 6-H_{chol}, 14-H_{chol}, 16-H_{chol}, 1-H_{chol}, 15-H_{chol}, 17-H_{chol}, 22-H_{chol}), 1.71–1.28 [m, 19 H, (C-1_{glc})-$OCH_2CH_2CH_2CH_2CH_2CH_2$NH, 2-$H_{chol}$, 4′-$H_{chol}$, 6′-$H_{chol}$, 8-$H_{chol}$, 11-$H_{chol}$, 11′-$H_{chol}$, 2′-$H_{chol}$, 5-$H_{chol}$, 16′-$H_{chol}$, 20-$H_{chol}$, 22′-$H_{chol}$], 1.12 (m, 1 H, 15′-$H_{chol}$), 1.06–0.95 (m, 4 H, 1′-H_{chol}, 3×21-H_{chol}), 0.95 (s, 3 H, 3×19-H_{chol}), 0.71 (s, 3 H, 3×18-H_{chol}) ppm. ^{13}C NMR (125.76 MHz, [D$_4$]MeOH): δ = 178.0 (NHCO), 105.9 (C-1_{glc}), 102.8 (4×C-1_{man}), 87.2 (C-3_{glc}), 84.9 (C-2_{glc}), 80.4 (C-4_{glc}), 77.0 (C-5_{glc}), 75.8 (4×C-5_{man}), 75.3 (C-12_{chol}), 74.1 (C-3_{cholan}), 73.8

(4×C-3$_{man}$), 73.4 (4×C-2$_{man}$), 72.8, 72.0–71.8 (4×), 70.5 [4×(glc)-OCH$_2$, (C-1$_{glc}$)OCH$_2$, C-6$_{glc}$], 70.2 (C-7$_{chol}$), 69.8 (3×), 69.7 (4×C-4$_{man}$), 66.9, 66.8, 66.6 (2×) [4×(man)OCH$_2$], 64.1 (4×C-6$_{man}$), 49.2 (C-17$_{chol}$), 48.7 (C-13$_{chol}$), 44.4 (C-5$_{chol}$), 44.2 (C-14$_{chol}$), 42.2 (C-8$_{chol}$), 41.6 (CH$_2$NHCO, C-4$_{chol}$), 38.1 (C-20$_{chol}$), 37.7 (C-1$_{chol}$), 37.1 (C-6$_{chol}$, C-10$_{chol}$), 35.4 (C-23$_{chol}$), 34.7 (C-22$_{chol}$), 32.4 (C-2$_{chol}$), 30.8 (C-11$_{chol}$), 32.9, 32.7, 32.7, 32.1, 31.9, 31.7 ([C-1$_{glc}$]-OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH, 4×OCH$_2$CH$_2$CH$_2$O), 30.0 (C-16$_{chol}$), 29.0 (C-9$_{chol}$), 29.0, 28.2 [(C-1$_{glc}$)OCH$_2$CH$_2$CH$_2$CH$_2$], 25.5 (C-15$_{chol}$), 24.4 (C-19$_{chol}$), 18.9 (C-21$_{chol}$), 14.3 (C-18$_{chol}$) ppm. MALDI-TOF MS: *m*/*z* = 1572.8 [M + Na]$^+$ (1549.8 calcd. for $C_{72}H_{127}NO_{34}$).

6-{[3-(7-Isopropyl-1-methylazulen-4-yl)propanoyl]amino}hexyl 2,3,4,6-Tetrakis-*O*-[3-(α-D-mannopyranosyloxy)propyl]-β-D-glucopyranoside (27): The amine **24** (7.5 mg, 0.029 mmol), the guajazulene derivative 3-(7-isopropyl-1-methylazulen-4-yl)propanoic acid,[27] and DIPEA (0.015 mL, 0.09 mmol) were dissolved in dry DMF (5 mL), and the mixture was cooled to 0 °C under argon and then treated with HATU (11.8 mg, 0.03 mmol). The reaction mixture was stirred at 0 °C for 2 h and for another 6 h at room temp. Purification was performed on Sephadex LH-20 with MeOH as the eluent to obtain the blue title compound in the form of a syrup (32 mg, 0.023 mmol, 79%). ^{1}H NMR (500 MHz, [D$_4$]MeOH): δ = 8.22 [d, *J* = 1.5 Hz, 1 H, (Me$_2$C)CCHCR$_2$], 7.66 [d, *J* = 3.5 Hz, 1 H, C(CMe)CHCH], 7.50 [dd, *J* = 1.8, 10.8 Hz, 1 H, (Me$_2$C)-CCHCH], 7.37 [d, *J* = 3.7 Hz, 1 H, C(CMe)CHCH], 7.10 [d, *J* = 10.8 Hz, 1 H, (Me$_2$C)CCHCH], 4.81, 4.80, 4.80, 4.78 (each d, $J_{1,2man}$ = 1.7 Hz, 4 H, 4×1-H$_{man}$), 4.27 (d, $J_{1,2glc}$ = 7.9 Hz, 1 H, 1-H$_{glc}$), 3.97–3.82 [m, 17 H, 4×2-H$_{man}$, 4×6-H$_{man}$, 5×(glc)OCHH, 4×(man)OCHH], 3.79–3.45 [m, 29 H, 4×3-H$_{man}$, 4×4-H$_{man}$, 4×5-H$_{man}$, 4×6′-H$_{man}$, 6-H$_{glc}$, 6′-H$_{glc}$, 5×(glc)OCHH, 4×(man)-OCHH, CH$_2$CH$_2$CONH], 3.32–3.21 (m, 3 H, 5-H$_{glc}$, 3-H$_{glc}$, 4-H$_{glc}$), 3.14 (m, 3 H, CH$_2$NHCO, CHMe$_2$), 3.00 (dd≈t, $J_{2,3glc}$ = 8.9 Hz, 1 H, 2-H$_{glc}$), 2.72–2.65 (m, 5 H, CH$_2$CONH, CCH$_3$), 1.97–1.82 (m, 8 H, 4×OCH$_2$CH$_2$CH$_2$O), 1.70–1.23 [m, 14 H, (C-1$_{glc}$)-OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH, 2×CH(CH$_3$)$_2$] ppm. ^{13}C NMR (125.76 MHz, [D$_4$]MeOH): δ = 176.3 (NHCO), 149.2 (CCH$_2$CH$_2$CON), 142.4 (Me$_2$CHC), 139.5, 139.0 (R$_2$CCR$_2$), 139.0 [C(CMe)CH], 137.3 [(Me$_2$C)CCHCH], 135.1 [(Me$_2$C)CCHCR$_2$], 127.6 (CMe), 126.6 [(Me$_2$C)CCHCH], 114.6 (CHCHCMe), 105.9 (C-1$_{glc}$), 102.8 (4×C-1$_{man}$), 87.1 (C-3$_{glc}$), 84.9 (C-2$_{glc}$), 80.4 (C-4$_{glc}$), 77.0 (C-5$_{glc}$), 75.8 (4×C-5$_{man}$), 73.8 (4×C-3$_{man}$), 73.4 (4×C-2$_{man}$), 72.8, 72.0–71.8 (4×), 70.4 [5×(glc)OCH$_2$, C-6$_{glc}$], 69.8 (3×), 69.7 (4×C-4$_{man}$), 66.8, 66.7, 66.5 (2×) [4×(man)OCH$_2$], 64.1 (4×C-6$_{man}$), 41.6 (CONHCH$_2$), 40.6 [CH(CH$_3$)$_2$], 39.9 (CH$_2$CONH), 36.4 (CH$_2$CH$_2$CONH), 32.9, 32.7, 32.7, 32.1, 31.9 [4×OCH$_2$CH$_2$-CH$_2$O, (C-1$_{glc}$)OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH], 31.4 (CH$_2$CH$_2$-NH), 28.8, 28.1 [(C-1$_{glc}$)OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$NH], 26.4 [CH(CH$_3$)$_2$], 14.2 (CCH$_3$) ppm. MALDI-TOF MS: *m*/*z* = 1420.7 [M + Na]$^+$ (1397.68 calcd. for $C_{65}H_{107}NO_{31}$).

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