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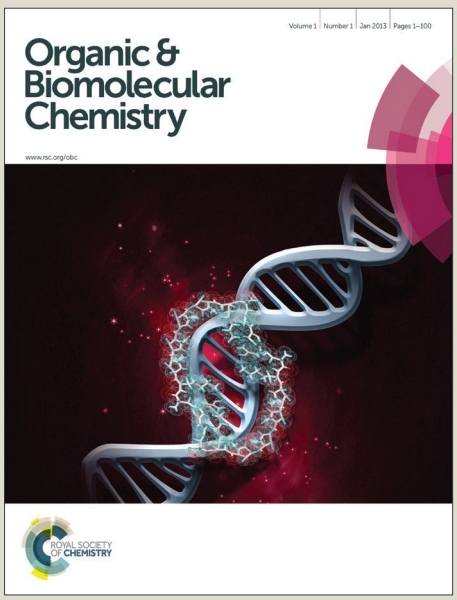

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Synthesis of glycoaminooxy acid and *N*-oxyamide-linked glycolipids

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Aminooxyl sugar derivatives are versatile building blocks for the generation of various glycoconjugates with interesting bioactivities. We report herein a synthetic method for the preparation of orthogonally protected glycoaminooxy acid from the methyl α-D-glycopyranoside in 7 steps. The key steps involves the selective protection, *O*-alkylation and Mitsunobu reaction. Fully deprotected *N*-oxyamide-linked novel glycolipids can be easily generated from the glycoaminooxy ester or from the 2-hydroxy free sugar in 5 or 6 steps.

Introduction

Oligosaccharides and their conjugates like glycolipids and glycopeptides are involved in a variety of important biological, physiological and pathological processes, such as cell-cell interactions, viral and bacterial infections, immune response, cancer progression, etc.[1-5] Recently, synthesis of glycoconjugates and their mimics has attracted increasing research interest for biological and pharmaceutical applications, especially in diagnostics, vaccines and therapeutics.[6-9] Diversely functionalized carbohydrate building blocks could provide a versatile platform for the generation of carbohydrate mimics and various conjugates. Recent studies on aminooxy acids showed that aminooxy acid derived peptides can easily organize into turns and helices structures through intramolecular hydrogen bond formation.[10] This unique property makes *N*-oxyamide linkage attractive for the modification of biomolecules. Furthermore, the *N*-oxy amide linkage is resistant to chemical and enzymatic hydrolysis,[11] and *N*-oxyamide bond could be readily formed using classical amide formation methods. Carbohydrates bearing oxyamine group can be found in *N*- or *O*-glycosyl hydroxylamines and *O*-amino sugar derivatives. *N*-Glycosyl hydroxylamines have become a powerful tool in glycobiology and drug discovery for generating a large neoglycoside-based library through chemoselective neoglycosylation[12-14] and neoglycorandomization.[15-17] *O*-Glycosyl hydroxylamines have been widely employed to prepare various oxime-linked glycolipids,[18] glycopeptides,[19] glycocyclopeptides[20] and glycoproteins.[21-22] Glycosyl aminooxy acids containing an aminooxyl function instead of amino one, have been recently synthesized as glycopeptide mimics.[23-24] Glycoaminooxy acids, with both aminooxyl and carboxyl functions on the sugar frame have also been developed as multifunctional building blocks for the synthesis of *N*-oxyamide-linked oligosaccharide and glycopeptide mimics.[25-28] Our previously developed benzyl-protected 2,6-functionalized pyranoid glucoaminooxy acid has been used for the construction of oligosaccharide mimics.[28] However, due to the sensibility of N-O bond towards the hydrogenation conditions, removal of benzyl groups appeared to be not possible. As a continuing interest in the development of *N*-oxyamide-modified biomolecules,[29-33] we reported herein the synthesis of *para*-methoxybenzyl (PMB) protected glycoaminooxy ester and its use for the preparation of fully deprotected glycolipid derivatives (Figure 1).

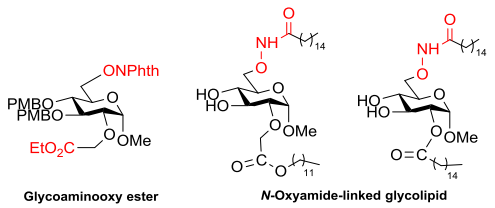

Figure 1 Structure of target glycoaminooxy ester and *N*-oxyamide-linked glycolipids.

Results and discussion

Synthesis of glycoaminooxy acid

In order to functionalise the 2,6-position of the sugar skeleton, selective disilylation was first performed on the methyl α-D-glucopyranoside, by using 2.8 equiv. of TBSCl in pyridine in the presence of catalytic amount of DMAP to give the known 2,6-di-*O*-silylated compound **1**[34] in 86% yield (Scheme 1). Subsequent introduction of the PMB group on the 3- and 4- position appeared to be not trivial. Treatment of compound **1** with NaH (6 equiv.) followed by dropwise addition of PMBCl (4 equiv.) led to a mixture of several products. Alternative addition of NaH (4x1.5 equiv.) and

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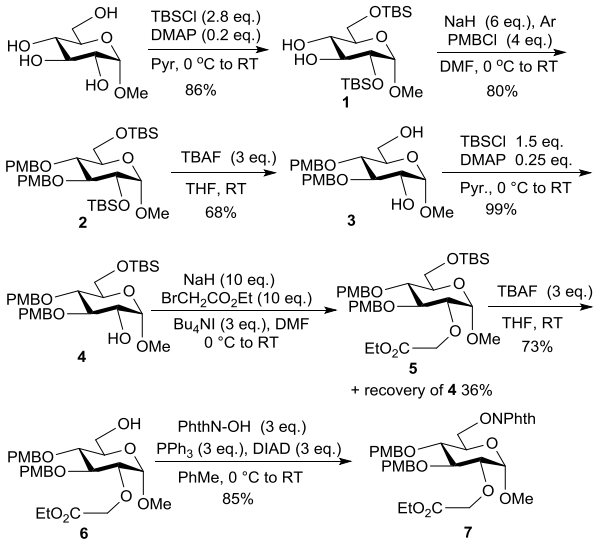
PMBCl (4x1 equiv.) over 40 min at 0 °C followed by reaction at room temperature gave 50 % isolated yield of **2**. The best yield (80%) was obtained by simultaneous addition of 1.5 equiv. NaH and 1 equiv. PMBCl every 20 min (for a total amount of 6 equiv. NaH and 4 equiv. PMBCl) under vigorous stirring under argon. It's to be noticed that PMB group has been previously introduced into the 3,4-positions of methyl 2,6-di-*O*-benzoyl-α-D-glucopyranoside, by using PMB trichloroacetimidate/TfOH in Et_2O,[35] or by heating with PMBCl/DIPEA at 150 °C.[36]



Scheme 1 Synthesis of orthogonally protected glycoaminooxy ester **7**.

Desilylation of **2** followed by selective silylation on the primary alcohol furnished the compound **4** which underwent the *O*-alkylation reaction with ethyl bromoacetate. In our previous work, this reaction worked well with the corresponding 3,4-di-*O*-benzyl derivative (1.5 equiv. each of NaH and $BrCH_2CO_2tBu$ in DMF in 75% yield).[28] In the present case, no reaction occurred when treating compound **4** with up to 5 equiv. each of NaH and $BrCH_2CO_2Et$ (Table 1, Entry 1). Similar difficulty in the *O*-alkylation has been encountered by Xing and Gleason.[37] Hopefully, increasing amount of reagents resulted in 20% conversion (Entry 2). Addition of catalytic imidazole and Bu_4NBr according to Tomaszewski *et al.*[38] improved the conversion to around 30% (Entry 3). Use of Bu_4NI as additive with prolonged reaction time (2 h) before introduction of the electrophile improved further the conversion (Entries 4,5). The best conversion (64%) was obtained by very slow addition of $BrCH_2CO_2Et$ (30 min) after formation of alcoolate (Entry 6). 36% of the **4** was recovered after column chromatography, which led to a corrected yield of 93% for the desired compound **5**. Further investigation with less NaH decreased the conversion ratio (Entries 7,8). Reaction with 5 equiv. each of NaH and $BrCH_2CO_2Et$ in the presence of 3 equiv. Bu_4NI under microwave condition led only to 20% conversion (Entry 9).

Table 1 2-*O*-alkylation of compound **4** in DMF

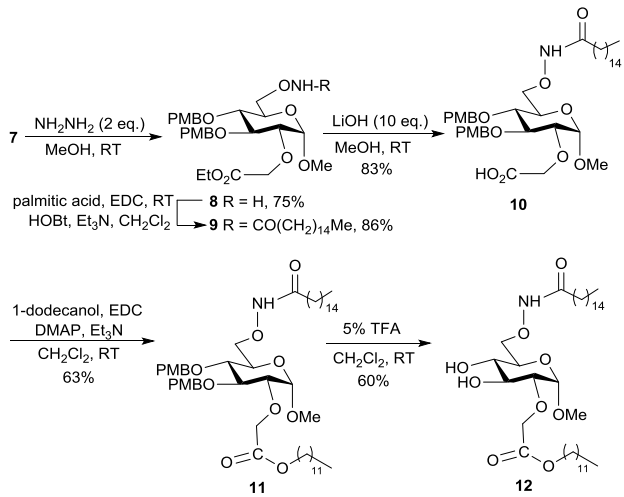
	NaH[a] (equiv.)	Additive (equiv.)	Time[b] (min)	$BrCH_2CO_2Et$ (equiv.)	Conversion[c]
1	5		30	5	0
2	10		30	10	20
3	10	Imidazole (0.2) Bu_4NBr (0.2)	30	10	30
4	10	Bu_4NI (3)	30	10	40
5	10	Bu_4NI (3)	120	10	50
6	10	Bu_4NI (3)	120	10	64[d]
7	5	Bu_4NI (3)	120	10	40
8	2	Bu_4NI (3)	120	10	30
9	5	Bu_4NI (3)		5	20[e]

[a]All the reactions were performed by adding NaH (and additive) to a solution of **4** (50 mg) in DMF (1 mL) at 0 °C, followed by dropwise addition (10 min) of electrophile for 15h reaction at RT; [b]Reaction time with NaH (and additive if used); [c]The conversion was determined by TLC except Entry 6 where the conversion rate was calculated after purification; [d]$BrCH_2CO_2Et$ was introduced during 30 min; [e]Microwave condition: T = 150 °C, P = 2.1-2.3 bars, 45 min.

Removal of TBS group in **5** with TBAF furnished the alcohol **6**. We then employed the Mitsunobu reaction to introduce the phthalimidooxyl function on the 6-position, leading to the target orthogonally protected glycoaminooxy ester **7** in 85% yield.

Synthesis of *N*-oxyaminde-linked glycolipids

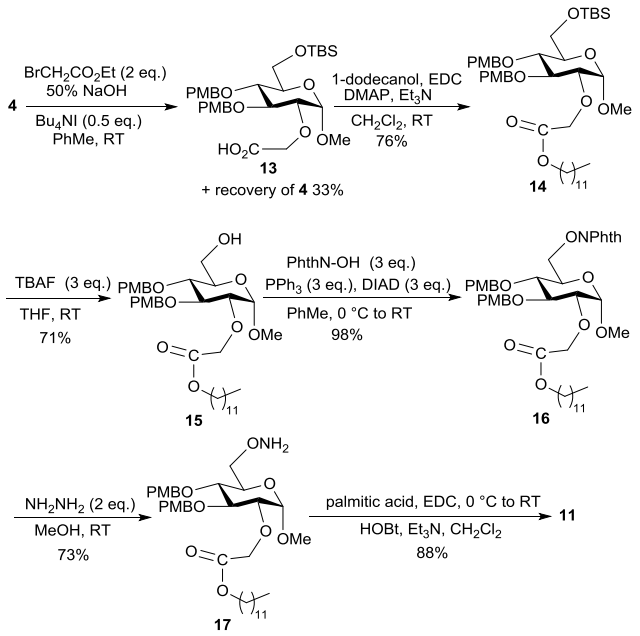
With the glycoaminooxy ester **7** in hand, we envisioned the synthesis of the glycopeptide **12** bearing the lipid chains on the 2- and 6-position of the sugar ring (Scheme 2). The phthaloyl group was firstly removed under hydrazinolysis condition. The obtained oxyamine **8** was then acylated with palmitic acid to afford the glycolipid **9** in 86% yield. The proton of the *N*-oxyamide bond appeared at 8.04 ppm in ^1H NMR spectrum in $CDCl_3$. Deprotection of the carboxylic acid followed by coupling with 1-dodecanol furnished the protected glycolipid **11** in 34% total yield from **7**. The PMB group can be readily removed with 5% TFA in CH_2Cl_2, leading to the deprotected glycolipid **12**.



Scheme 2 Synthesis of glycolipid **12** from glycoaminooxy ester **7**.

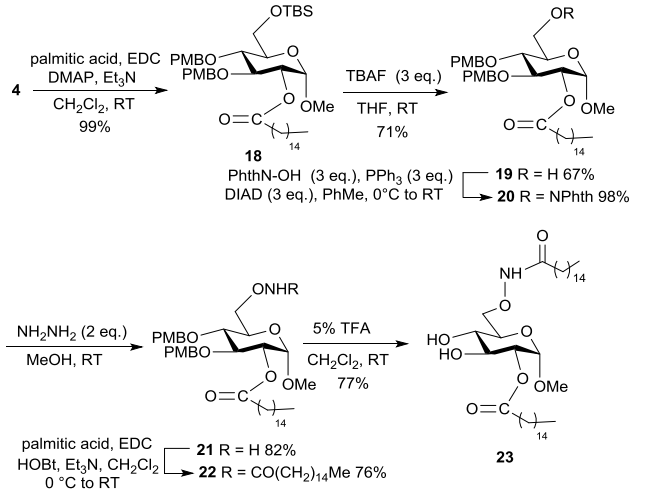
The glycolipid **11** can also be prepared from the intermediate **4**, by introducing the first lipid chain on the 2-position (Scheme 3). Due to the previously encountered difficulty during the *O*-alkylation, we decided to realise the *O*-carboxymethylation under phase transfer conditions in 50% aqueous NaOH/toluene in the presence of 0.5 equiv. Bu_4NI,[39,40] which led to the carboxylic acid **13** with a corrected yield of 74 % (33% of the compound **4** was recovered).

Esterification with 1-dodecanol, followed by desilylation, Mitsunobu reaction with PhthNOH, hydrazinolysis and coupling with palmitic acid furnished the glycolipid **11** in 25% total yields from **4**.



Scheme 3 Alternative synthesis of glycolipid **11** from glucoside **4**.

Lipid chain could also be introduced directly to the alcohol function of the compound **4** (Scheme 4). Esterification of **4** with palmitic acid followed by introduction of the aminooxyl group on the 6-position (by desilylation, Mitsunobu reaction and removal of the phthaloyl group) and acylation readily gave the protected glycolipid **22** which could be deprotected to the glycolipid **23** in 29% total yield in 6 steps.



Scheme 4 Synthesis of glycolipid **23** from glucoside **4**.

Conclusions

The *para*-methoxybenzyl protected glycoaminooxy ester **7** has been synthesized from the methyl α-D-glycopyranoside in 7 steps. Conditions for the introduction of the PMB group on the 3,4-positions and 2-*O*-alkylation reaction have been optimized. Fully deprotected *N*-oxyamide-linked glycolipid could be readily obtained from the glycoaminooxy ester in 6 steps in 20% total yield. We have also demonstrated that *N*-oxyamide-linked glycolipids with the lipid chains on the 2,6-positions can be easily prepared from the orthogonally protected glycopyranoside **4**. We are convinced that the orthogonally protected glycoaminooxy ester could be useful for the generation of various new glycoconjugates.

Experimental

General. All commercial available reagents were used without further purification. Column chromatography was performed on Silica gel 60 (40-60 μm). The solvents for column chromatography were used without purification. The reactions carried out under anhydrous conditions are performed under argon in glassware previously dried in an oven. Methanol is dried over molecular sieves 3Å. THF, DMF, dichloromethane and toluene were previously dried through alumina cartridge using a solvent purificator MBRAUN SPS-800. Reactions were monitored by TLC on Silica Gel 60F-254 plates with detection by UV (254 nm or 365 nm) or by spraying with 10% H_2SO_4 in EtOH and heating about 30 s at 400-600 °C. Melting points were determined with a Kofler melting point apparatus. Optical rotations were measured using a Jasco P-2000 polarmeter at room temperature in a 10 cm, 1 mL cell. NMR spectra were recorded on a JOEL ESC-400 spectrometer in $CDCl_3$ or CD_3OD solution. Chemical shift was given in units of parts per million related to TMS or solvent protons as internal reference. High-resolution mass Spectra (HRMS) were recorded on a Q-TOF MaXis using standard conditions or Bruker Microflex™ MALDI-TOF mass spectrometry.

General procedure for desilylation: To a solution of silylated compound (1 eq.) in anhydrous THF (15 mL/mmol) under argon, was added TBAF (3 eq.). After stirring at room temperature overnight, the solvent was removed under vacuum. The residue was diluted with EtOAc (25 mL/mmol), washed with saturated aq NH_4Cl (10 mL/mmol), H_2O (10 mL/mmol) and brine (10 mL/mmol), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel to afford the silylated compound.

General procedure for the Mitsunobu reaction: To a solution of alcohol (1 eq.), Ph_3P (3 eq.) and PhthNOH (3 eq.) in toluene (20 mL/mmol) at 0 °C under argon, was added DIAD (3 eq.) dropwise. The resulting mixture was stirred at room temperature for 1 h and then extracted with EtOAc (3×30 mL/mmol). The combined organic layers were washed with saturated aq $NaHCO_3$ (3×30 mL/mmol), H_2O (30 mL/mmol) and brine (30 mL/mmol), dried over $MgSO_4$, filtered, evaporated and purified by column chromatography over silica gel to afford the *O*-phthalimido compound.

General procedure for hydrazinolysis: To a solution of *O*-phthalimido compound (1 eq.) in MeOH (20 mL/mmol), was added $N_2H_4{\cdot}H_2O$ (2 eq.). The mixture was stirred at room temperature for 2 h and then extracted with CH_2Cl_2 (3×50 mL/mmol). The combined organic layers were washed with saturated aq $NaHCO_3$ (50 mL/mmol), H_2O (50 mL/mmol) and brine (50 mL/mmol), dried over

$MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel to afford the *O*-amino compound.

General procedure for *N*-oxyamide formation: To a solution of carboxylic acid (1 eq.) in anhydrous CH_2Cl_2 (15 mL/mmol), were added HOBt (2 eq.), EDC·HCl (2 eq.) and Et_3N (2 eq.) under argon at 0 °C. After stirring for 20 min, the oxyamine derivative (1 eq.) was added. The resulting mixture was stirred at room temperature overnight. The solution was diluted with EtOAc (100 mL/mmol), washed with aq HCl (1N, 2×40 mL/mmol), saturated aq $NaHCO_3$ (2×40 mL/mmol) and brine (40 mL/mmol), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel to give the *N*-oxyamide.

General procedure for esrterification: To a solution of carboxylic acid (1 eq.) in anhydrous CH_2Cl_2 (15 mL/mmol), were added EDC·HCl (2 eq.), DMAP (2 eq.) and Et_3N (2 eq.) under argon at 0 °C. After the mixture being stirred for 20 min, the alcohol (1 eq.) was added. The resulting mixture was stirred at room temperature overnight. The solution was diluted with CH_2Cl_2 (50 mL/mmol), washed with aq HCl (1N, 2×40 mL/mmol), saturated aq $NaHCO_3$ (2×40 mL/mmol) and brine (40 mL/mmol), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel to give the ester.

Methyl 2,6-di-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (1).[34] To a solution of methyl *α*-D-glucopyranoside (0.97 g, 5 mmol) in pyridine (10 mL) under argon at 0 °C, were added TBSCl (2.1 g, 14 mmol) and DMAP (0.12 g, 1 mmol). After stirring at room temperature for 16 h, the solvent was removed under vacuum, and the concentrated mixture was partitioned between CH_2Cl_2 (50 mL) and H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography over silica gel (petroleum ether/EtOAc: 10/1) to afford compound **1** (1.82 g, 86.3%) as a colourless paste: R_f = 0.66 (petroleum ether-EtOAc 5/1); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 4.60 (d, *J* = 3.7 Hz, 1H, H-1), 3.87-3.74 (m, 3H, H-3,6), 3.63-3.57 (m, 1H, H-5), 3.55-3.45 (m, 2H, H-2,4), 3.37 (s, 3H, OCH_3), 2.78 (s, 2H, 2×OH), 0.89, 0.89 (2×s, 18H, 2×*t*Bu), 0.12-0.04 (m, 12H, 2×$Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 100.0 (C-1), 74.1 (C-3), 73.6 (C-2), 71.8 (C-4), 70.8 (C-5), 64.1 (CH_2), 55.3 (OCH_3), 26.0, 25.9 (CH_3, *t*Bu); 18.5, 18.3 (C_q, *t*Bu); -4.4, -4.5, -5.3, -5.3 (CH_3, $Si(CH_3)_2$).

Methyl 3,4-di-*O*-(4-methoxybenzyl)-2,6-di-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (2). To a solution of compound **1** (4.5 g, 10.6 mmol) in anhydrous DMF (50 ml) under argon at 0 °C, was added NaH (60%, 2.55 g, 63.8 mmol) and PMBCl (5.8 ml, 42.4 mmol) in portions over 1 h (NaH and PMBCl was added at the same time, 1/4 total amount every 20 min). After addition, the solution was stirred at room temperature for 16 h. Ice was added to destroy the excess NaH, and then the solution was concentrated. The residue was diluted with EtOAc (200 mL), washed with saturated aq NH_4Cl (100 mL), H_2O (100 mL) and brine (100 mL), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel (petroleum ether/EtOAc: 20/1) to afford compound **2** (5.64 g, 80%) as a colourless paste: R_f = 0.48 (petroleum ether-EtOAc 10/1); $[\alpha]_D$ + 36.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.33-7.20 (m, 4H, PMB), 6.90-6.82 (m, 4H, PMB), 4.79-4.40 (m, 4H, 2×OCH_2), 4.33 (d, *J* = 3.6 Hz, 1H, H-1), 3.96 (t, *J* = 8.9 Hz, 1H, H-3), 3.80, 3.78 (2×s, 6H, 2×OCH_3), 3.72-3.59 (m, 2H, H-6), 3.53-3.46 (m, 1H, H-5), 3.31-3.19 (m, 5H, H-2,4, OCH_3), 0.94, 0.85 (2×s, 18H, 2×*t*Bu), 0.13-0.02 (m, 12H, 2×$Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 159.4, 159.1, 130.8, 130.6 (C_q); 130.0, 129.3, 113.8 (CH); 98.0 (C-1), 80.1 (C-2), 79.2 (C-4), 74.6 (CH_2), 74.1 (C-3), 73.3 (CH_2), 71.4 (C-5), 62.6 (CH_2), 55.4, 54.8 (OCH_3); 26.0 (CH_3, *t*Bu); 18.4, 18.3 (C_q, *t*Bu); -3.7, -4.1, -5.0, -5.3 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 685.3562, Calcd for $C_{35}H_{58}NaO_8Si_2$ $[M+Na]^+$ 685.3568.

Methyl 3,4-di-*O*-(4-methoxybenzyl)-*α*-D-glucopyranoside (3).[35-36] Desilylation of compound **2** (5.64 g, 8.52 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **3** (2.53 g, 68.4%) as a white solid: R_f = 0.23 (petroleum ether-EtOAc 1/1); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.33-7.25 (m, 4H, PMB), 6.92-6.85 (m, 4H, PMB), 4.82 (d, *J* = 11.0 Hz, 1H, OCH), 4.67-4.57 (m, 3H, OCH, OCH_2), 4.54 (d, *J* = 3.7 Hz, 1H, H-1), 4.05 (t, *J* = 9.2 Hz, 1H, H-3), 3.81, 3.80 (2×s, 6H, 2×OCH_3), 3.79-3.67 (m, 2H, H-6), 3.62-3.57 (m, 1H, H-5), 3.42 (t, *J* = 9.4 Hz, 1H, H-4), 3.36-3.27 (m, 4H, H-2, OCH_3), 2.43 (s, 1H, OH), 1.67 (s, 1H, OH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 159.7, 159.5, 130.5, 130.1 (C_q); 129.9, 129.9, 114.1, 114.0 (CH); 97.7 (C-1), 79.4 (C-2), 77.0 (C-4), 74.3 (CH_2), 73.5 (C-3), 72.9 (CH_2), 70.3 (C-5), 62.1 (CH_2), 55.4, 55.3 (OCH_3).

Methyl 3,4-di-*O*-(4-methoxybenzyl)-6-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (4). To a solution of compound **3** (2.53 g, 5.82 mmol) in pyridine (40 mL) under argon at 0 °C, were added TBSCl (1.09 g, 7.27 mmol) and DMAP (0.18 g, 1.46 mmol). After stirring at room temperature for 16 h, the solvent was removed under vacuum, and the concentrated mixture was partitioned between CH_2Cl_2 (100 mL) and H_2O (50 mL). The aqueous layer was extracted with CH_2Cl_2 (2×50 mL). The combined organic layers were dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography over silica gel (petroleum ether/EtOAc: 4/1) to afford compound **4** (3.15 g, 98.7%) as a colourless paste: R_f = 0.55 (petroleum ether-EtOAc 2/1); $[\alpha]_D$ + 58.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.32-7.24 (m, 4H, PMB), 6.92-6.84 (m, 4H, PMB), 4.80 (d, *J* = 11.0 Hz, 1H, OCH), 4.66-4.56 (m, 4H, OCH, OCH_2, H-1), 4.04 (t, *J* = 9.2 Hz, 1H, H-3), 3.84-3.73 (m, 8H, 2×OCH_3, H-6), 3.55 (ddd, *J* = 9.9, 4.3, 2.1 Hz, 1H, H-5), 3.41 (t, *J* = 9.4 Hz, 1H, H-4), 3.36-3.27 (m, 4H, H-2, OCH_3), 2.40 (broad s, 1H, OH), 0.90 (s, 9H, *t*Bu), 0.65-0.45 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 159.6, 159.4, 130.9, 130.3 (C_q); 129.8, 129.7, 114.1, 114.0 (CH); 97.4 (C-1), 79.6 (C-2), 77.4 (C-4), 74.3 (CH_2), 73.7 (C-3), 72.8 (CH_2), 71.2 (C-5), 62.5 (CH_2), 55.4, 55.0 (OCH_3); 26.1 (CH_3, *t*Bu), 18.5 (C_q, *t*Bu), -5.0, -5.2 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 571.2698, Calcd for $C_{29}H_{44}NaO_8Si$ $[M+Na]^+$ 571.2703.

Methyl 2-*O*-ethoxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (5). To a solution of compound **4** (200 mg, 0.36 mmol) in DMF (5 mL) under argon at 0 °C, was added NaH (60%, 144 mg, 3.6 mmol)

and TBAI (386 mg, 1.1 mmol). After stirring at 0 °C for 2 h, ethyl bromoacetate (0.4 mL, 3.6 mmol) was added dropwise during 30 min., and the resulting mixture was stirred at room temperature for 15 h. The reaction was quenched with ice, and the mixture extracted with EtOAc (3× 20 mL). The combined organic layers were washed with saturated aq NH_4Cl (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel (petroleum ether/EtOAc: 4/1) to afford compound **4** (72 mg, conversion: 64%) and compound **5** (135 mg, corrected yield: 92.5%) as a colourless paste: R_f = 0.55 (petroleum-EtOAc 3/1); $[\alpha]_D$ + 27.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35-7.23 (m, 4H, PMB), 6.94-6.83 (m, 4H, PMB), 4.86 (d, *J* = 10.5 Hz, 1H, OCH), 4.71-4.47 (m, 6H, OCH, 2×OCH_2, H-1), 4.22 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.88-3.72 (m, 9H, 2×OCH_3, H-3,6), 3.59-3.47 (m, 3H, H-2,4,5), 3.29 (s, 3H, OCH_3), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3), 0.96-0.86 (m, 9H, *t*Bu), 0.09-0.02 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.4 (C=O), 159.5, 159.3, 130.9, 130.4 (C_q); 129.8, 114.0, 113.9 (CH); 97.8 (C-1), 83.7, 79.8, 77.4 (CH); 74.8, 73.0 (CH_2); 71.4 (CH), 71.1, 62.4, 60.8 (CH_2); 55.4, 54.9 (OCH_3); 26.0 (CH_3, *t*Bu), 18.4 (C_q, *t*Bu), 14.4 (CH_3), -5.0, -5.2 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 657.3065, Calcd for $C_{33}H_{50}NaO_{10}Si$ $[M+Na]^+$ 657.3071.

Methyl 2-*O*-ethoxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (6). Desilylation of compound **5** (0.50 g, 0.79 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **6** (0.3 g, 73%) as a colourless paste: R_f = 0.48 (petroleum ether-EtOAc 1/2); $[\alpha]_D$ + 34.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39-7.25 (m, 4H, PMB), 6.95-6.84 (m, 4H, PMB), 4.88 (d, *J* = 11.0 Hz, 1H, OCH), 4.74-4.36 (m, 6H, OCH, 2×OCH_2, H-1), 4.21 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.92-3.77 (m, 7H, 2×OCH_3, H-3), 3.76-3.62 (m, 2H, H-6), 3.60-3.46 (m, 3H, H-2,4,5), 3.29 (s, 3H, OCH_3), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3 (C=O), 159.6, 159.5, 130.5, 130.2 (C_q); 130.0, 129.8, 114.0 (CH); 98.1 (C-1), 83.4, 79.7, 76.5 (CH); 74.7, 73.0, 70.9 (CH_2); 70.5 (CH), 62.0, 60.9 (CH_2); 55.4, 55.2 (OCH_3); 14.3 (CH_3). HRMS (ESI) *m/z* 543.2201, Calcd for $C_{27}H_{36}NaO_{10}$ $[M+Na]^+$ 543.2206.

Methyl 2-*O*-ethoxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-phthalimido-α-D-glucopyranoside (7). The phthalimido group was introduced at the 6-postion of compound **6** (0.3 g, 0.58 mmol) using Mitsunobu reaction according to the general procedure. Purification by column chromatography over silica gel (petroleum ether/EtOAc: 3/1) afforded compound **7** (0.33 g, 85%) as a colourless paste: R_f = 0.47 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 47.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.72 (m, 4H, Phth), 7.35-7.26 (m, 4H, PMB), 6.90-6.82 (m, 4H, PMB), 4.98 (d, *J* = 10.1 Hz, 1H, OCH), 4.81 (d, *J* = 10.5 Hz, 1H, OCH), 4.70 (d, *J* = 11.9 Hz, 1H, OCH), 4.56 (d, *J* = 9.6 Hz, 1H, OCH), 4.55-4.35 (m, 5H, OCH_2, H-1,6), 4.21 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.87-3.72 (m, 9H, 2×OCH_3, H-3,4,5), 3.57 (dd, *J* = 9.3, 3.5 Hz, 1H, H-2), 3.35 (s, 3H, OCH_3), 1.27 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.2, 163.3 (C=O); 159.5, 159.4 (C_q); 134.5 (CH), 130.6, 130.2 (C_q); 130.1, 129.9 (CH); 129.0 (C_q), 123.6, 114.0, 113.9 (CH); 98.2 (C-1), 83.4, 79.2 (CH); 76.5 (CH_2), 76.1 (CH), 74.9, 73.1, 71.0 (CH_2); 69.2 (CH), 60.8 (CH_2), 55.6, 55.3 (OCH_3); 14.3 (CH_3); HRMS (ESI) *m/z* 688.2374, Calcd for $C_{35}H_{39}NaO_{12}$ $[M+Na]^+$ 688.2370.

Methyl 6-*O*-amino-2-*O*-ethoxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-α-D-glucopyranoside (8). Hydrazinolysis of compound **7** (67 mg, 0.1 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **8** (40 mg, 75%) as a colourless paste: R_f = 0.25 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 30.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.22 (m, 4H, PMB), 6.97-6.82 (m, 4H, PMB), 4.91-4.35 (m, 7H, 3×OCH_2, H-1), 4.20 (q, *J* = 7.0 Hz, 2H, OCH_2), 3.93-3.72 (m, 9H, 2×OCH_3, H-3,6), 3.72-3.65 (m, 1H, H-5), 3.57-3.45 (m, 2H, H-2,4), 3.31 (s, 3H, OCH_3), 1.26 (t, *J* = 7.1 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3 (C=O), 159.5, 159.4, 130.6, 130.2 (C_q); 130.0, 129.9, 114.0, 113.9 (CH); 98.0 (C-1), 83.5, 79.5, 76.8 (CH); 74.8, 74.4, 73.0, 70.9 (CH_2); 69.5 (CH), 60.8 (CH_2), 55.4, 55.3 (OCH_3); 14.3 (CH_3); HRMS (ESI) *m/z* 574.2057, Calcd for $C_{27}H_{37}KNO_{10}$ $[M+K]^+$ 574.2055.

Methyl 2-*O*-ethoxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-palmitoylamino-α-D-glucopyranoside (9). Compound **9** was prepared from compound **8** (70 mg, 0.13 mmol) and palmitic acid according to the general procedure for *N*-oxyamide formation. Purification by column chromatography over silica gel (petroleum ether/EtOAc: 3/2) afforded compound **9** (86 mg, 86%) as a white solid: R_f = 0.48 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 39.7 (*c* 0.1, $CHCl_3$); mp 75 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H, NH), 7.39-7.21 (m, 4H, PMB), 6.97-6.81 (m, 4H, PMB), 4.95-4.35 (m, 7H, 3×OCH_2, H-1), 4.20 (q, *J* = 7.0 Hz, 2H, OCH_2), 4.11-3.99 (m, 2H, H-6), 3.88-3.68 (m, 8H, 2×OCH_3, H-3,5), 3.61-3.46 (m, 2H, H-2,4), 3.31 (s, 3H, OCH_3), 2.43-1.92 (m, 2H, CH_2), 1.66-1.54 (m, 2H, CH_2), 1.45-1.17 (m, 27H, 12×CH_2, CH_3) 0.88 (t, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 170.2 (C=O); 159.6, 159.4, 130.3, 130.2 (C_q); 129.8, 114.0, 113.9 (CH); 98.1 (C-1), 83.4, 79.5, 76.3 (CH); 74.7, 73.0, 70.9 (CH_2); 69.5 (CH), 60.9 (CH_2), 55.5, 55.4 (OCH_3); 33.4, 32.0, 29.8, 29.6, 29.5, 25.5, 22.8 (CH_2); 14.3, 14.2 (CH_3); HRMS (ESI) *m/z* 812.4353, Calcd for $C_{43}H_{67}KNO_{11}$ $[M+K]^+$ 812.4351.

Methyl 2-*O*-carboxylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-palmitoylamino-α-D-glucopyranoside (10). To a solution of compound **9** (74 mg, 0.096 mmol) in MeOH (2 mL), was added LiOH (23 mg, 0.96 mmol). The mixture was stirred at room temperature for 48 h and then extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with aq HCl (1N, 10 mL) and brine (10 mL), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel (CH_2Cl_2/MeOH: 25/1) to afford compound **10** (59 mg, 83%) as a white solid: R_f = 0.33 (CH_2Cl_2-MeOH 25/1); $[\alpha]_D$ + 62.0 (*c* 0.1, $CHCl_3$); mp 115 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (s, 1H, NH), 7.35-7.15 (m, 4H), 6.95-6.77 (m, 4H, PMB), 4.82-4.52 (m, 5H, 2×OCH_2, H-1), 4.44 (d, *J* = 17.4 Hz, OCH), 4.36 (d, *J* = 17.4 Hz, OCH), 4.20-3.93 (m, 2H, H-6), 3.81 (s, 3H, OCH_3) 3.79 (s, 3H, OCH_3), 3.76-3.57 (m, 3H, H-3,4,5), 3.49 (dd, *J* = 9.5, 3.1 Hz, 1H, H-2), 3.30 (s, 3H, OCH_3), 2.43-1.95 (m, 2H, CH_2), 1.68-1.52 (m, 2H, CH_2), 1.36-1.06 (m, 24H, 12×CH_2), 0.88 (t, *J* = 6.4 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.1, 171.0 (C=O); 160.0, 159.7

(C_q, PMB); 130.4, 130.2 (CH); 129.5, 128.5 (C_q); 114.2, 114.1 (CH); 97.2 (C-1), 82.2, 78.0, 77.4 (CH); 74.9, 74.3, 72.6, 70.5 (CH_2); 69.5 (CH), 55.6, 55.4 (OCH_3); 33.4, 32.0, 29.8, 29.6, 29.5, 25.4, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 768.4297, Calcd for $C_{41}H_{63}NaNO_{11}$ $[M+Na]^+$ 768.4299.

Methyl 2-*O*-dodecyloxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-palmitoylamino-*α*-D-glucopyranoside (11). Esterification of compound **10** (52 mg, 0.07 mmol) with 1-dodecanol according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 2/1) afforded compound **11** (40 mg, 63%) as a white solid. Compound **11** could also be prepared from compound **16** (20 mg, 0.03 mmol) and palmitic acid according to the general procedure for *N*-oxyamide formation. Purification by column chromatography over silica gel (petroleum ether/EtOAc: 2/1) afforded compound **11** (24 mg, 88%): R_f = 0.56 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 27.3 (*c* 0.1, $CHCl_3$); mp 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.01 (s, 1H, NH), 7.37-7.20 (m, 4H, PMB), 6.96-6.82 (m, 4H, PMB), 4.95-4.36 (m, 7H, 3×OCH_2, H-1), 4.13 (t, *J* = 6.8 Hz, 2H, OCH_2), 4.09-3.89 (m, 2H, H-6), 3.86-3.75 (m, 7H, 2×OCH_3, H-3), 3.74-3.67 (m, 1H, H-5), 3.60-3.44 (m, 2H, H-2,4), 3.30 (s, 3H, OCH_3), 2.41-1.93 (m, 2H, CH_2), 1.69-1.53 (m, 4H, 2×CH_2), 1.40-1.19 (m, 42H, 21×CH_2), 0.93-0.83 (m, 6H, 2×CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.6, 170.3 (C=O); 159.5, 159.4, 130.5, 130.1 (C_q); 130.4, 129.8, 114.0, 113.9 (CH); 98.1 (C-1), 83.4, 79.4, 76.2 (CH); 74.7, 73.1, 70.8 (CH_2); 69.5 (CH), 65.1 (CH_2), 55.5, 55.4 (OCH_3); 33.4, 32.0, 29.8, 29.6, 29.5, 29.4, 28.7, 26.0, 25.5, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 936.6179, Calcd for $C_{53}H_{87}NaNO_{11}$ $[M+Na]^+$ 936.6177.

Methyl 2-*O*-dodecyloxycarbonylmethyl-6-*O*-palmitoylamino-*α*-D-glucopyranoside (12). To a solution of compound **11** (29 mg, 0.03 mmol) in CH_2Cl_2 (1 mL), was added TFA (0.05 mL, 5% in CH_2Cl_2). The mixture was stirred at room temperature for 1 h under argon and then extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, evaporated and purified by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) to afford compound **12** (12 mg, 60%) as a white solid: R_f = 0.44 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 80.0 (*c* 0.1, $CHCl_3$); mp 70 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.74 (s, 1H, NH), 4.80 (d, *J* = 3.2 Hz, 1H, H-1), 4.48 (s, 2H, OCH_2), 4.21-4.08 (m, 4H, OCH_2, H-6), 3.88 (t, *J* = 9.3 Hz, 1H, H-4), 3.76-3.63 (m, 2H, H-2,5), 3.51 (t, *J* = 9.0 Hz, 1H, H-3), 3.42 (s, 3H, OCH_3), 2.09 (t, *J* = 7.4 Hz, 2H, CH_2), 1.70-1.56 (m, 4H, 2×CH_2), 1.38-1.19 (m, 42H, 21×CH_2), 0.92-0.82 (m, 6H, 2×CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 173.8, 171.8 (C=O); 99.7 (C-1), 83.8 (CH), 75.9 (CH_2), 71.8, 70.3 (CH); 69.3, 65.9 (CH_2); 55.6 (OCH_3), 33.3, 32.1, 29.8, 29.7, 29.6, 29.5, 29.4, 29.3, 28.6, 25.9, 25.4, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 696.5025, Calcd for $C_{37}H_{71}NaNO_9$ $[M+Na]^+$ 696.5027.

Methyl 2-*O*-carboxylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (13). To a mixture of compound **4** (0.31g, 0.57 mmol), aqueous NaOH (5 mL, 50%) and TBAI (104 mg, 0.28 mmol) in toluene (10 mL), was added dropwise ethyl bromoacetate (0.13 mL, 1.14 mmol). After stirring at room temperature for 3 days, the solution was concentrated under vacuum. The residue was diluted with EtOAc (50 ml), washed with saturated aq HCl (1N, 3×20 mL), H_2O (20 mL) and brine (20 mL), dried over $MgSO_4$, filtered, evaporated, and purified by column chromatography over silica gel (CH_2Cl_2/MeOH: 100/3) to afford compound **4** (103 mg, conversion: 67%) and compound **13** (170 mg, corrected yield: 74%) as a white powder: R_f = 0.25 (CH_2Cl_2-MeOH 100/3); $[\alpha]_D$ + 64.0 (*c* 0.1, $CHCl_3$); mp 138 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.38-7.20 (m, 4H, PMB), 6.99-6.82 (m, 4H, PMB), 4.79-4.46 (m, 5H, 2×OCH_2, H-1), 4.40 (d, *J* = 17.4 Hz, OCH), 4.32 (d, *J* = 18.4 Hz, OCH), 4.02-3.75 (m, 8H, 2×OCH_3, H-6), 3.71 (t, *J* = 8.9 Hz, H-3), 3.61-3.43 (m, 3H, H-2,4,5), 3.30 (s, 3H, OCH_3), 0.91 (s, 9H, *t*Bu), 0.16-0.02 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.1 (C=O), 159.9, 159.7 (C_q); 130.2, 130.0 (CH); 129.5, 128.6 (C_q); 114.2, 114.1 (CH); 96.8 (C-1), 82.0, 78.5, 77.6 (CH); 74.8, 72.4 (CH_2); 71.5 (CH), 70.5, 61.9 (CH_2); 55.4, 55.1 (OCH_3); 26.0 (CH_3, *t*Bu), 18.4 (C_q, *t*Bu), -5.0, -5.2 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 629.2759, Calcd for $C_{31}H_{46}NaO_{10}Si$ $[M+Na]^+$ 629.2758.

Methyl 2-*O*-dodecyloxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (14). Esterfication of compound **13** (148 mg, 0.24 mmol) with 1-dodecanol according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 5/1) afforded compound **14** (144 mg, 76%) as a white paste: R_f = 0.63 (petroleum ether-EtOAc 4/1); $[\alpha]_D$ + 23.0 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.50-7.19 (m, 4H, PMB), 7.05-6.80 (m, 4H, PMB), 5.00-4.32 (m, 7H, 3×OCH_2, H-1), 4.10 (t, *J* = 6.7 Hz, 2H, OCH_2), 4.04-3.68 (m, 9H, 2×OCH_3, H-3,6), 3.64-3.44 (m, 3H, H-2,4,5), 3.26 (s, 3H, OCH_3), 1.70-1.54 (m, 2H, CH_2), 1.52-1.17 (m, 18H, 9×CH_2), 1.02-0.82 (m, 12H, *t*Bu, CH_3), 0.16-0.02 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.4 (C=O), 159.4, 159.3, 130.7, 130.3 (C_q); 129.8, 113.8 (CH); 97.7 (C-1), 83.6, 79.7, 76.8 (CH); 74.7, 73.0 (CH_2); 71.3 (CH), 70.9, 65.0, 62.3 (CH_2); 55.3, 54.9 (OCH_3); 32.0, 29.7, 29.6, 29.4, 29.3, 28.7 (CH_2); 26.0 (CH_3, *t*Bu), 25.9, 22.8 (CH_2); 18.4 (C_q, *t*Bu), 14.2 (CH_3), -5.1, -5.3 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 797.4639, Calcd for $C_{43}H_{70}NaO_{10}Si$ $[M+Na]^+$ 797.4636.

Methyl 2-*O*-dodecyloxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-*α*-D-glucopyranoside (15). Desilylation of compound **14** (74 mg, 0.096 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **15** (45 mg, 71%) as a colourless paste: R_f = 0.10 (petroleum ether-EtOAc 3/1); $[\alpha]_D$ + 56.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.40-7.22 (m, 4H, PMB), 7.00-6.81 (m, 4H, PMB), 4.91-4.35 (m, 7H, 3×OCH_2, H-1), 4.10 (t, *J* = 6.8 Hz, 2H, OCH_2), 3.91-3.73 (m, 7H, 2×OCH_3, H-3'), 3.73 (dd, *J* = 11.9, 2.8 Hz, 1H, H-6a), 3.65 (dd, *J* = 11.9, 3.2 Hz, 1H, H-6b), 3.57-3.43 (m, 3H, H-2,4,5), 3.26 (s, 3H, OCH_3), 1.79 (s, 1H, OH), 1.65-1.55 (m, 2H, CH_2), 1.40-1.18 (m, 18H, 9×CH_2), 0.85 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.4 (C=O), 159.5, 159.4, 130.4, 130.1 (C_q); 130.0, 129.8, 113.9 (CH); 98.0 (C-1), 83.3, 79.6, 76.4 (CH); 74.7, 73.0, 70.8 (CH_2); 70.5 (CH), 65.0, 61.9 (CH_2); 55.3, 55.2 (OCH_3); 32.0, 29.7, 29.6, 29.4, 29.3, 28.7, 25.9, 22.8 (CH_2); 14.2 (CH_3); HRMS (ESI) *m/z* 683.3775, Calcd for $C_{37}H_{56}NaO_{10}$ $[M+Na]^+$ 683.3771.

Methyl 2-*O*-dodecyloxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-6-*O*-phthalimido-*α*-D-glucopyranoside (16). The phthalimido group was introduced at the 6-postion of compound **15** (55 mg, 0.083 mmol) using Mitsunobu reaction according to the general procedure. Purification by column chromatography over silica gel (petroleum ether/EtOAc: 3/1) afforded the desired compound (66 mg, 98%) as a colourless paste: R_f = 0.77 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 65.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.88-7.72 (m, 4H, Phth), 7.36-7.26 (m, 4H, PMB), 6.91-6.82 (m, 4H, PMB), 4.98 (d, *J* = 10.1 Hz, 1H, OCH), 4.82 (d, *J* = 10.1 Hz, 1H, OCH), 4.75-4.33 (m, 7H, 2×OCH_2, H-1,6), 4.15 (t, *J* = 6.9 Hz, 2H, OCH_2), 3.91-3.72 (m, 9H, 2×OCH_3, H-3,4,5), 3.58 (dd, *J* = 9.1, 3.4 Hz, 1H, H-2), 3.35 (s, 3H, OCH_3), 1.70-1.57 (m, 2H, CH_2), 1.43-1.19 (m, 18H, 9×CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.3, 163.3 (C=O); 159.5, 159.3 (C_q); 134.6 (CH), 130.6, 130.2 (C_q); 130.1, 129.9 (CH); 129.0 (C_q), 123.6 (CH), 113.93, 113.88 (CH); 98.2 (C-1), 83.4, 79.1 (CH); 76.4 (CH_2), 76.0 (CH), 74.9, 73.1, 70.9 (CH_2); 69.1 (CH), 65.1 (CH_2), 55.6, 55.3 (OCH_3); 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 28.7, 26.0, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 844.3678, Calcd for $C_{45}H_{59}KNO_{12}$ $[M+K]^+$ 844.3674.

Methyl 6-*O*-amino-2-*O*-dodecyloxycarbonylmethyl-3,4-di-*O*-(4-methoxybenzyl)-*α*-D-glucopyranoside (17). Hydrazinolysis of compound **16** (58 mg, 0.071 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **17** (35 mg, 73%) as a yellowish paste: R_f = 0.39 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 45.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.34-7.24 (m, 4H, PMB), 6.93-6.84 (m, 4H, PMB), 4.93-4.34 (m, 7H, 3×OCH_2, H-1), 4.13 (t, *J* = 6.8 Hz, 2H, OCH_2), 3.91-3.74 (m, 9H, 2×OCH_3, H-3,6), 3.72-3.65 (m, 1H, H-5), 3.56-3.45 (m, 2H, H-2,4), 3.30 (s, 3H, OCH_3), 1.69-1.57 (m, 2H, CH_2), 1.39-1.17 (m, 18H, 9×CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 170.4 (C=O), 159,5, 159.4, 130.5, 130.2 (C_q); 130.1, 129.9, 114.0, 113.9 (CH); 98.1 (C-1), 83.5, 79.4, 76.7 (CH); 74.8, 74.3, 73.1, 70.9 (CH_2); 69.4 (CH), 65.0 (CH_2), 55.4, 55.3 (OCH_3); 32.0, 29.8, 29.7, 29.6, 29.5, 29.4, 28.7, 26.0, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 698.3884, Calcd for $C_{37}H_{57}NaNO_{10}$ $[M+Na]^+$ 698.3880.

Methyl 3,4-di-*O*-(4-methoxybenzyl)-2-*O*-palmitoyl-6-*O*-*tert*-butyldimethylsilyl-*α*-D-glucopyranoside (18). Esterfication of compound **4** (0.62 g, 1.13 mmol) with palmitic acid according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 8/1) afforded compound **18** (0.88 g, 99%) as a colourless paste: R_f = 0.78 (petroleum ether-EtOAc 3/1); $[\alpha]_D$ + 26.0 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.25-7.14 (m, 4H, PMB), 6.94-6.81 (m, 4H, PMB), 5.53 (t, *J* = 9.6 Hz, 1H, H-3), 4.61-4.47 (m, 5H, 2×OCH_2, H-1), 3.90-3.74 (m, 8H, 2×OCH_3, H-6), 3.68-3.62 (m, 1H, H-5), 3.52 (t, *J* = 9.6 Hz, 1H, H-4), 3.43-3.36 (m, 1H, H-2), 3.33 (s, 3H, OCH_3), 2.26-2.18 (m, 2H, CH_2), 1.68-1.55 (m, 2H, CH_2), 1.50-1.16 (m, 24H, 12×CH_2), 0.98-0.82 (m, 12H, *t*Bu, CH_3), 0.11-0.05 (m, 6H, $Si(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.7 (C=O), 159.4, 159.3, 130.4, 130.3 (C_q); 129.5, 129.4, 113.9 (CH); 97.8 (C-1), 77.7, 76.0 (CH); 73.8 (CH_2), 73.5 (CH), 72.6 (CH_2), 71.2 (CH), 62.2 (CH_2), 55.4, 55.0 (OCH_3); 34.7, 32.1, 29.8, 29.6, 29.5, 29.4 (CH_2); 26.1 (CH_3, *t*Bu), 25.1, 22.8 (CH_2); 18.5 (C_q, *t*Bu), 14.3 (CH_3), -5.0, -5.2 (CH_3, $Si(CH_3)_2$); HRMS (ESI) *m/z* 809.5005, Calcd for $C_{45}H_{74}NaO_9Si$ $[M+Na]^+$ 809.5000.

Methyl 3,4-di-*O*-(4-methoxybenzyl)-2-*O*-palmitoyl-*α*-D-glucopyranoside (19). Desilylation of compound **18** (0.82 g, 1.04 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **19** (0.48 g, 67%) as a white paste: R_f = 0.13 (petroleum ether-EtOAc 3/1); $[\alpha]_D$ + 23.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.26-7.17 (m, 4H, PMB), 6.91-6.82 (m, 4H, PMB), 5.54 (t, *J* = 9.6 Hz, 1H, H-3), 4.62-4.45 (m, 5H, 2×OCH_2, H-1), 3.81, 3.79 (2×s, 6H, 2×OCH_3), 3.77-3.65 (m, 3H, H-5,6), 3.56 (t, *J* = 9.5 Hz, 1H, H-4), 3.40 (dd, *J* = 10.0, 3.5 Hz, 1H, H-2), 3.33 (s, 3H, OCH_3), 2.29-2.21 (m, 2H, CH_2), 1.67-1.56 (m, 2H, CH_2), 1.39-1.18 (m, 24H, 12×CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.7 (C=O), 159.5, 130.2, 130.1 (C_q); 129.7, 129.6, 113.9 (CH); 98.1 (C-1), 77.4, 75.7 (CH); 74.0 (CH_2), 73.4 (CH), 72.7 (CH_2), 70.4 (CH), 61.8 (CH_2), 55.4 (OCH_3), 34.7, 32.1, 29.8, 29.7, 29.5, 29.4, 25.1, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 695.4133, Calcd for $C_{39}H_{60}NaO_9$ $[M+Na]^+$ 695.4135.

Methyl 3,4-di-*O*-(4-methoxybenzyl)-2-*O*-palmitoyl-6-*O*-phthalimido-*α*-D-glucopyranoside (20). The phthalimido group was introduced at the 6-postion of compound **19** (0.43 g, 0.64 mmol) using Mitsunobu reaction according to the general procedure. Purification by column chromatography over silica gel (petroleum ether/EtOAc: 2/1) afforded compound **20** (0.51 g, 98%) as a colourless paste: R_f = 0.62 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 48.3 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.93-7.73 (m, 4H, Phth), 7.35-7.21 (m, 4H, PMB), 6.94-6.81 (m, 4H, PMB), 5.57 (t, *J* = 9.6 Hz, 1H, H-3), 4.83-4.38 (m, 7H, 2×OCH_2, H-1,6), 3.99 (t, *J* = 9.4 Hz, H-4), 3.93-3.84 (m, 1H, H-5), 3.80, 3.77 (2×s, 6H, 2×OCH_3), 3.52 (dd, *J* = 10.1, 3.4 Hz, 1H, H-2), 3.34 (s, 3H, OCH_3), 2.27 (t, *J* = 7.7 Hz, 2H, CH_2), 1.72-1.56 (m, 2H, CH_2), 1.49-1.17 (m, 24H, 12×CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.7, 163.3 (C=O); 159.5, 159.4 (C_q); 134.6 (CH), 130.3 (C_q); 129.8, 129.6 (CH); 129.0 (C_q), 123.7 (CH), 113.9 (CH), 98.3 (C-1), 77.0 (CH), 76.0 (CH_2), 75.2 (CH), 74.2 (CH_2), 73.5 (CH), 72.8 (CH_2), 69.4 (CH), 55.7, 55.4 (OCH_3); 34.7, 32.1, 29.8, 29.7, 29.5, 29.4, 25.1, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 840.4296, Calcd for $C_{47}H_{63}NaNO_{11}$ $[M+Na]^+$ 840.4299.

Methyl 6-*O*-amino-3,4-di-*O*-(4-methoxybenzyl)-2-*O*-palmitoyl-*α*-D-glucopyranoside (21). Hydrazinolysis of compound **20** (0.41 g, 0.50 mmol) according to the general procedure and purification by column chromatography over silica gel (petroleum ether/EtOAc: 1/1) afforded compound **21** (0.28 g, 82%) as a white paste: R_f = 0.25 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 31.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.26-7.17 (m, 4H, PMB), 6.94-6.82 (m, 4H, PMB), 5.52 (t, *J* = 9.6 Hz, 1H, H-3), 4.62-4.45 (m, 5H, 2×OCH_2, H-1), 3.94-3.76 (m, 9H, 2×OCH_3, H-5,6), 3.56-3.47 (m, 1H, H-4), 3.42 (dd, *J* = 10.0, 3.4 Hz, 1H, H-2), 3.34 (s, 3H, OCH_3), 2.30-2.21 (m, 2H, CH_2), 1.69-1.56 (m, 2H, CH_2), 1.42-1.17 (m, 24H, 12×CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.6 (C=O), 159.5, 159.4, 130.1 (C_q); 129.7, 129.6, 113.9 (CH); 98.0 (C-1), 77.4, 76.0 (CH); 74.3, 73.9 (CH_2); 73.3 (CH), 72.7 (CH_2), 69.3 (CH), 55.4 (OCH_3),

34.7, 32.0, 29.8, 29.6, 29.5, 29.4, 25.1, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 726.3936, Calcd for $C_{39}H_{61}KNO_9$ $[M+K]^+$ 726.3983.

Methyl 3,4-di-*O*-(4-methoxybenzyl)-2-*O*-palmitoyl-6-*O*-palmitoylamino-α-D-glucopyranoside (22). Coupling of compound **21** (0.34 g, 0.50 mmol) with palmitic acid according to the general procedure followed by purification by column chromatography over silica gel (petroleum ether/EtOAc: 2/1) afforded compound **22** (0.35 g, 76%) as a white solid: R_f = 0.56 (petroleum ether-EtOAc 1/1); $[\alpha]_D$ + 32.7 (*c* 0.1, $CHCl_3$); mp 90 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.03 (s, 1H, NH), 7.35-7.12 (m, 4H, PMB), 6.95-6.82 (m, 4H, PMB), 5.52 (t, *J* = 9.6 Hz, 1H, H-3), 4.68-4.45 (m, 5H, 2×OCH_2, H-1), 4.20-3.96 (m, 2H, H-6), 3.90-3.75 (m, 7H, 2×OCH_3, H-5), 3.70-3.58 (m, 1H, H-4), 3.45-3.40 (m, 1H, H-2), 3.34 (s, 3H, OCH_3), 2.30-1.94 (m, 4H, 2×CH_2), 1.70-1.54 (m, 4H, 2×CH_2), 1.50-1.15 (m, 48H, 24×CH_2), 0.95-0.84 (m, 6H, 2×CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 172.7 (C=O), 159.6, 130.1, 130.0 (C_q); 129.6, 114.0 (CH); 98.1 (C-1), 77.4, 75.8 (CH); 74.8, 74.0 (CH_2); 73.4 (CH), 72.8 (CH_2), 69.4 (CH), 55.6, 55.4 (OCH_3); 34.7, 33.5, 32.1, 29.8, 29.7, 29.5, 29.4, 25.1, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 948.6542, Calcd for $C_{55}H_{91}NaNO_{10}$ $[M+Na]^+$ 948.6541.

Methyl 2-*O*-palmitoyl-6-*O*-palmitoylamino-α-D-glucopyranoside (23). To a solution of compound **22** (150 mg, 0.16 mmol) in CH_2Cl_2 (4 mL), was added TFA (2 mL, 5% in CH_2Cl_2). The mixture was stirred at room temperature for 1 h under argon and then extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, evaporated and purified by column chromatography over silica gel (CH_2Cl_2/MeOH: 100/3) to afford compound **23** (85 mg, 77%) as a white powder: R_f = 0.28 (CH_2Cl_2-MeOH 100/3); $[\alpha]_D$ + 84.7 (*c* 0.1, $CHCl_3$); mp 96 °C; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 8.55 (s, 1H, NH), 5.14 (t, *J* = 9.7 Hz, 1H, H-3), 4.77 (d, 1H, *J* = 3.6 Hz, 1H, H-1), 4.25-4.13 (m, 2H, H-6), 3.96 (t, *J* = 9.6 Hz, 1H, H-4), 3.83-3.73 (m, 1H, H-5), 3.67-3.56 (m, 1H, H-2), 3.43 (s, 3H, OCH_3), 2.41 (t, *J* = 7.6 Hz, 2H, CH_2), 2.09 (t, *J* = 7.3 Hz, 2H, CH_2), 1.73-1.57 (m, 4H, 2×CH_2), 1.45-1.19 (m, 48H, 24×CH_2), 0.94-0.84 (m, 6H, 2×CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 175.0, 171.9 (C=O); 100.0 (C-1), 75.5 (CH_2), 75.0, 71.4, 70.7, 68.1 (CH); 55.7 (OCH_3), 34.6, 33.2, 32.1, 29.8, 29.6, 29.5, 29.4, 29.2, 25.3, 25.1, 22.8 (CH_2); 14.3 (CH_3); HRMS (ESI) *m/z* 708.5392, Calcd for $C_{39}H_{75}NaNO_8$ $[M+Na]^+$ 708.5390.

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