



# Synthesis of new chiral macrocycles-based glycolipids and its application in asymmetric Michael addition

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## Abstract

A series of new mix aza- and thia-macrocyclic glycolipids (**9**, **10**, **16** and **17**) have been synthesized and their enantiomeric selectivity was studied. The synthesis of the macrocycles involved a simple protection of two hydroxyl groups of the glycolipids followed by building up the mix-heteroatom macrocyclic in simple sequences. The macrocycles and previously investigated analogues (**18**, **19**, **20** and **21**) have been applied as phase transfer catalysts in the enantioselective Michael addition of 2-nitropropane to chalcone and showed good-to-excellent enantiomer excess (ee). Among the catalysts, the galactose aza-crown ether-based glycolipid **21** proved to be the most effective with 90% ee.

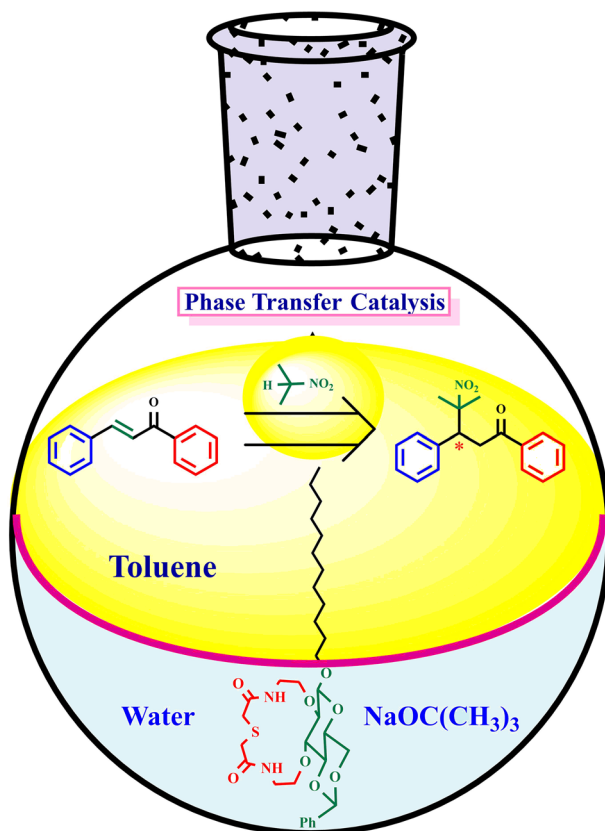
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## Graphic abstract



**Keywords** Glycolipids · Macrocycles · Asymmetric · Michael addition · Aza · Templating

## Introduction

The chiral crown ethers are of interest in various chemical applications, mainly in asymmetric organic reactions [1–4]. The carbohydrate-based crown ether moieties represent an important group of optically active compounds [5, 6]. By containing more than one stereogenic centers as active sites, they can serve as one of the good candidates for chiral recognition [7, 8], asymmetric reactions [9–12], and enantiomers purifications [13–15]. Among carbohydrate-containing macrocycles, the glycolipid involving crown ethers on their constructions representing a new class of lariat chiral crown ethers [16]. From the synthetic aspects, the balance between lipophilicity and hydrophobicity of compound is a crucial factor for micelle formation to act as a phase transfer catalyst [17]. The typical bond formation processes involve

in phase transfer catalyst reaction are asymmetric Michael addition and epoxidation reactions [18–22]. In general, the reaction provides a practical access to a variety of optically active materials, which are useful in the field of medicinal [23], pharmaceutical [24], and agrochemical [25]. In this context, the synthesis of new chiral mix-heteroatoms crown ethers with suitable lariat side arm could be a promising material as phase transfer catalyst in obtaining enantiomer excess (ee) product [26–28].

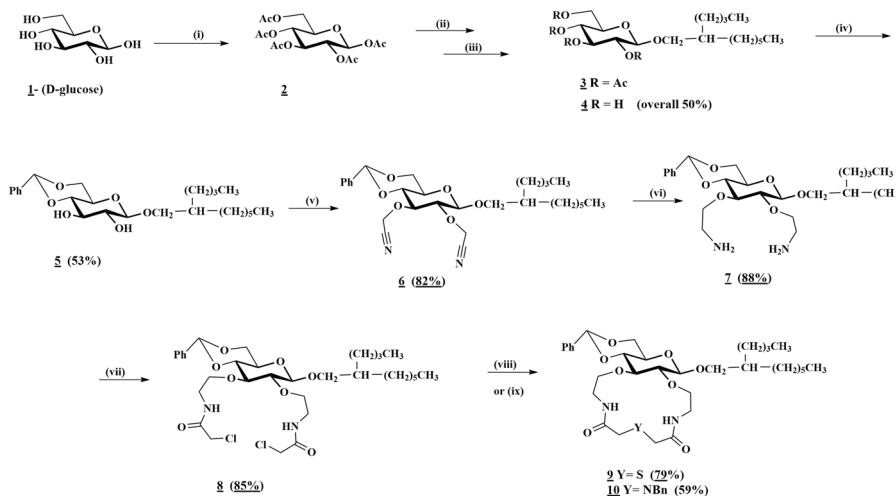
The demands of obtaining stereoselective reactions in the formation of carbon–carbon single bond by the addition of enolates or their analogues to the  $\alpha$ – $\beta$  unsaturated carbonyl compounds have been extensively investigated [29]. Due to its significant relevance in preparing biologically active materials, many researchers focus on carrying out the Michael addition of carbon nucleophiles to conjugated enones using stereoselective approach. A few sugar-based crown ethers which contain carbohydrate moieties as the source of chirality have been successfully used as catalysts in asymmetric Michael addition reactions [9, 30]. Bako et al. reported that the yield and the enantioselectivity of the 1,2-addition reaction of 2-nitropropane to chalcone catalyzed by glucose-based chiral lariat ethers and crown ether derived from D-mannitol was greatly influenced by the substituents on the nitrogen atom of the macrocycle [30].

Recently, our attention was drawn to macrocyclic compounds containing the single chain lauryl glucoside units [31] and the mixed heteroatom thiadiazia and triaza crown ether attached to lauryl galactoside and glucoside [32]. We also previously published on the new sugar-thiacrown-ether appended calix[4]arene, coupled with pyrene units macrocycles and demonstrated the common approaches to the synthesis of these macrocycles [33, 34]. In continuation of our ongoing program to develop innovative procedures to synthesize novel macrocycles, we report here the synthesis of new mix-heteroatoms macrocycles design including those with double chain glycoside units. Also, we anticipated to evaluate how the different position of macrocycles, type of heteroatoms on macrocyclic part, lariat side chain on the anomeric center, alkyl chain type and sugar head influence the stereoselectivity in the reaction of chalcone and 2-nitropropane.

## Results and discussion

### Synthesis

The glycolipid **4** (Scheme 1) was synthesized according to the standard procedure we reported previously [32]. The glucose was treated with acetic anhydride under basic condition to obtain  $\beta$ -glucose pentaacetate, and then reacted with the branched chain alcohol, i.e., 2-butyl-1-octanol under acidic boron trifluoride to obtain a fully acetylated glycolipid **3** with major  $\beta$ -anomer. We carried out the column chromatography in the next reaction sequence as it is more cost-effective and time-saving way to remove the trace of  $\alpha$ -anomer. The deacetylation of protected glycolipids **3** to obtain free hydroxyl groups on the sugar head is necessary to functionalize the material and building the desired macrocycles. Sodium methoxide in methanol has



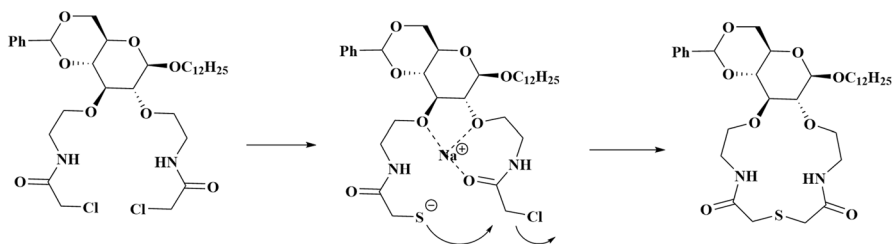
(i) Acetic anhydride, NaOAc, (ii) 2-butyl-1-octanol,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , DCM, (iii)  $\text{NaOCH}_3$ , Methanol, (iv)  $\text{PhCH(OMe)}_2$ , TsOH, DCM, (v)  $\text{BrCH}_2\text{CN}$ , Toluene, NaOH (50%),  $\text{Bu}_4\text{NBr}$ , (vi)  $\text{LiAlH}_4$ , THF, (vii)  $\text{(ClCH}_2\text{CO)}_2\text{O}$ , DCM,  $\text{Et}_3\text{N}$ , (viii)  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ , ethanol, or (ix)  $\text{BnNH}_2$ , Acetonitrile,  $\text{Na}_2\text{CO}_3$ , reflux.

**Scheme 1** Synthesis of aza and thia macrocycles **9** and **10** on 2,3-positions

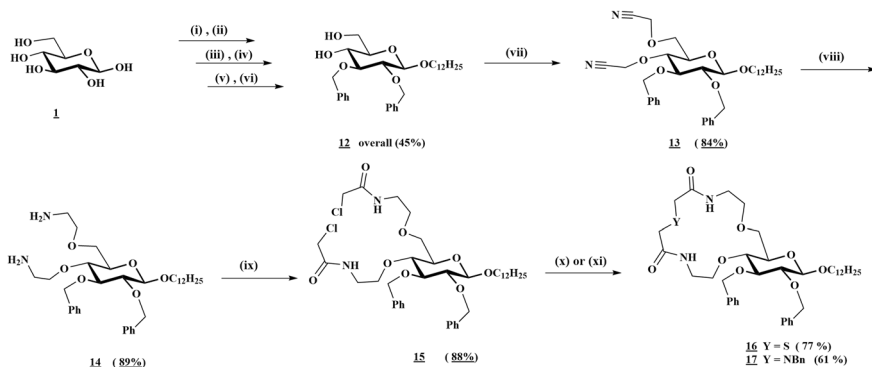
been used as an agent to achieve the clean deprotected glycolipid **4** as a mixture of  $\alpha$ -/ $\beta$ -anomers. Furthermore, the functionalization of glycolipid **4** with benzylidene protecting group enables not only for gaining free diol **5** at 2- and 3-positions, but also to get pure  $\beta$ -anomer after simple crystallization. This was achieved by the reaction of **4** with benzaldehyde dimethyl acetal in the presence of catalytic amount of TsOH in DCM. The diol **5** was introduced with ethylamine arm in two steps, by the treatment of **5** with bromoacetonitrile under phase transfer catalyst in a mixture of toluene and aqueous sodium hydroxide 50%, followed by the reduction of **6** by  $\text{LiAlH}_4$  in dry cyclic ether to get the diamine **7**. The diamine **7** was formed by addition of 2.2 equivalents chloroacetic anhydride in DCM in the presence of triethylamine as base. This procedure allows us to get a pure dichloro precursor **8** which serve as macrocyclic backbones without chromatographic purification. The macrocycle **9** was obtained by the treatment of **8** with  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$  in a mixture of ethanol: water 85:15 ratio in relatively high yield 79%. In the same manner, the benzyl amine was used to form macrocycle **10** by adding it with dichloro derivative **8** in acetonitrile in the presence of sodium carbonate in 59% yield after chromatography.

This extraordinary yield obtained by this approach could be justified in terms of templating effect. Initially, the sulfide attacks the nucleophilic carbon which possessing the chloride by  $\text{S}_{\text{N}}2$  reaction, the free sodium will act as a templating agent to assist the pre-organization of ring formation which allow the other nucleophilic carbon to be in a suitable position to form the macrocycle (Scheme 2).

On the other hand, the macrocycles on 4- and 6-positions of the glucopyranoside ring could be obtained by manipulating the protecting strategy to afford **12** (Scheme 3) [31]. The acid catalytic cleavage of benzylidene group of lauryl 2,3-O-dibenzyl-4,6-benzylidene glucopyranoside furnished **12**. Intermediate **12**



**Scheme 2** Sodium templating-assisted macrocyclization



(i) Acetic anhydride, NaOAc, (ii) 2-butyl-1-octanol,  $\text{BF}_3 \cdot \text{Et}_2\text{O}$ , DCM, (iii)  $\text{NaOCH}_3$ , Methanol, (iv)  $\text{PhCH}(\text{OMe})_2$ , TsOH, DCM, (v)  $\text{BnBr}$ , Toluene,  $\text{NaOH}$  (50%),  $\text{Bu}_4\text{NBr}$ , (vi)  $\text{Me TsOH} \cdot \text{H}_2\text{O}$ , (vii)  $\text{BrCH}_2\text{CN}$ , Toluene,  $\text{NaOH}$  (50%),  $\text{Bu}_4\text{NBr}$ , (viii)  $\text{LiAlH}_4$ , THF, (ix)  $(\text{ClCH}_2\text{CO})_2\text{O}$ , DCM,  $\text{Et}_3\text{N}$ , (x)  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$ , ethanol, or (xi)  $\text{BnNH}_2$ , Acetonitrile,  $\text{Na}_2\text{CO}_3$ .

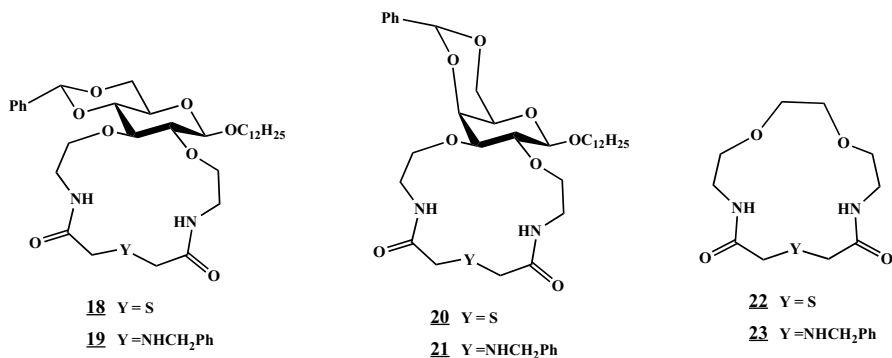
**Scheme 3** Synthesis of thia- and aza-macrocycles **16** and **17** on 4,6-positions

was treated with the same sequence of reactions including alkylation with bromoacetonitrile under phase transfer catalyst condition to produce **13** in good purity with an excellent yield (84%). Subsequently, the diamino **14** was obtained by treatment of **13** with  $\text{LiAlH}_4$  in dry THF. The acylation of **14** with chloroacetic anhydride gave the dichloroamido derivative **15** in almost 90% yield. Finally, the cyclization reactions of intermediate **15** with either  $\text{Na}_2\text{S} \cdot 9\text{H}_2\text{O}$  or  $\text{BnNH}_2$  afforded the macrocycles **16** (77% yield) and **17** (61% yield), respectively. When compared, the yield of macrocycles 4-,6-positions is relatively lower than 2,3-positions analogues.

### Michael addition of 2-nitropropane to chalcone

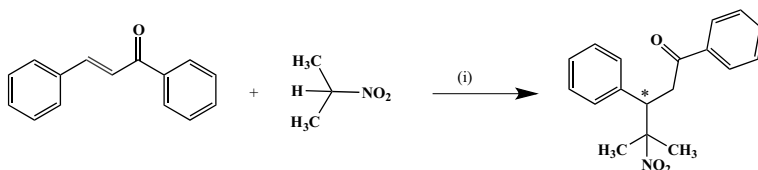
The addition of 2-nitropropane to chalcone was investigated under phase transfer catalytic conditions in the presence of macrocycles **9**, **10**, **16** and **17**. We also include macrocycles **18**, **19**, **20** and **21** (Fig. 1) in which their synthetic procedures have been described in our previous work [32, 33]. Besides, their non-sugar analogues **22** and **23** were also assessed (Fig. 1).

The phase transfer catalytic reaction in solid-liquid phase was carried out at room temperature using dry toluene, 30% of solid sodium tert-butoxide and 5%



**Fig. 1** Macrocycles **18–21** incorporating glucose-based and galactose-based glycolipids, while macrocycles **22** and **23** representing its non-sugar analogs

of the chiral catalysts (Scheme 4). The preparative TLC was used for obtaining the product and the enantiomeric excess (ee %) was determined by <sup>1</sup>H NMR spectroscopy in the presence of Eu(hfc)<sub>3</sub> as a chiral shift reagent. The significant results of asymmetric Michael addition are listed in Table 1. A few factors were addressed here to study the effects of sugar head group, position of macrocycles,



**Scheme 4** Michael addition of 2-nitropropane to chalcone. Reagents and conditions: (i) catalyst (**9,10**) and one of (**16–23**), sodium tert-butoxide and toluene

**Table 1** Asymmetric Michael addition of 2-nitropropane to chalcone catalyzed by mix-heteroatoms macrocycles

Entry	Catalyst	Time (h)	Yield (%) <sup>a</sup>	ee (%) <sup>b</sup>
1	<b>9</b>	2	71	67 (S)
2	<b>10</b>	2	75	72 (S)
3	<b>16</b>	4	66	58 (S)
4	<b>17</b>	4	70	61(S)
5	<b>18</b>	2	75	72 (S)
6	<b>19</b>	2	71	78 (S)
7	<b>20</b>	2	67	80 (S)
8	<b>21</b>	2	74	90 (S)
9	<b>22</b>	2	79	0
10	<b>23</b>	2	82	4(R)

<sup>a</sup>Based on products isolated by preparative TLC

<sup>b</sup>Determined by <sup>1</sup>H NMR spectroscopy

type of heteroatoms on macrocyclic part, the lariat side chain on the anomeric center and the straight vs. branched alkyl chain on the asymmetric addition.

The highest enantiomeric excess (ee) was obtained using catalyst **21**, the galactose-based with benzylamino-residue on the macroring at 2,3-positions, followed by its thia-analogue **20** with ee of 90 and 80%, respectively (entries 7 and 8). This result can be explained by the fact that the benzyl groups on the nitrogen atom of **21** which oriented in a way to block one side of the macrocycle enforce the addition to be mainly from the opposite side compared to that of thia-analogue **20**. Moreover, the benzylidene group on galactose derivatives **20** and **21** at 4-position is axial which make the steric effect in one side is greater than the equatorial orientation at 4-position of glucose analogues **18** and **19**. Furthermore, the lipophilic alkyl chain, i.e., straight and branched hydrocarbon tails on compounds **9**, **10**, **18** and **19** (entries 1, 2, 5 and 6) were found to be less effective in ee with the values of 67–78%. The stereoselectivity of macrocyclic sugar on 4,6-positions **16** and **17** (entries 3 and 4) were 58 and 61% ee, respectively which is less than the 2,3-analogues. This could be explained by the less stereocenters available and less rigidity in the macrocyclic structure of **16** and **17** compared to that of **18** and **19** analogues. Unsurprisingly, the non-sugar macrocyclic analogues **22** and **23** (entries 9 and 10) showed no enantiomeric excess at all. This outcome is expected due to the non-chirality in their structures in contrast to their sugar analogues.

## Conclusion

The new mix-heteroatoms crown ethers glycolipids involving 2,3-positions on glucose with branched tail **9** and **10** and its analogues on 4,6-positions with straight chain **16** and **17** were synthesized successfully in good yields. Their stereoselective toward asymmetric Michael addition of 2-nitropropane to chalcone are investigated beside their galactose (**20**, **21**) and glucose (**18**, **19**) straight chain analog. Among the studied catalysts, the galactose aza-crown ether-based glycolipid **21** exhibits the highest enantiomeric excess (ee) by 90%.

## Experimental

### General methods

All reagents were obtained from commercial sources and used without further purification. Flash column chromatography was carried out on silica gel 60 (230–400 mesh, E. Merck). TLC was performed on pre-coated aluminum plates of Silica Gel 60 F<sub>254</sub> (0.25 mm, E. Merck). NMR spectra were recorded on Bruker Avance and Joel ECA spectrometers at 400 MHz for <sup>1</sup>H and 100 MHz for <sup>13</sup>C, respectively. Chemical shifts were in ppm from Me<sub>4</sub>Si, calibrated using the residual proton and carbon of the deuterated solvent. Proton peak assignments were performed with the aid of 2D NMR techniques (<sup>1</sup>H-<sup>1</sup>H COSY and HSQC/HMQC) the hydrogen multiplicities of carbon peaks were determined using DEPT and PENDANT experiments.

High-resolution mass spectra were recorded on an Agilent Technologies 6530 Accurate Q-TOF LC-MS system, applying MeOH-water eluents. A gas flow of 250 °C hot nitrogen at 5 mL, min and electrospray ionization at 125 eV were applied.

### General procedure for cyanomethylation

The glycolipid **5** or **12** (2 mmol) was dissolved in a mixture of toluene (30 mL), 50% NaOH solution (20 mL) and tetrabutyl ammonium hydrogen sulfate (1 mmol) and stirred at 10 °C for 30 min. Bromoacetonitrile (4 mmol) was added dropwise. The mixture was stirred for 2 h. Hexane (50 mL) was added and the organic layer was separated, filtered through pad of celite, dried over MgSO<sub>4</sub> and the solvent was evaporated. The crude material could be crystallized or purified by column chromatography.

### General procedure of reduction of aminoethyl derivatives

Compound **6** or **13** (1 mmol) was dissolved in THF (50 mL) and was cooled to 0 °C. LiAlH<sub>4</sub> (4 mmol) was added in small portion carefully within 30 min. The mixture was stirred for 1 h. The complete conversion of the reaction was indicated by TLC. Ethyl acetate (10 mL) was added and stirring was continued for 15 min to destroy excess LiAlH<sub>4</sub>. The solid was filtered, and the solvent was evaporated to give the crude amine, which was pure enough to be used without further purification.

### General procedure of amide formation

Compound **7** or **14** (2 mmol) was dissolved in DCM (100 mL) and was cooled to 0 °C. (ClCH<sub>2</sub>CO)<sub>2</sub>O (4.4 mmol) was added in small portion. The mixture was stirred for 2 h at 0 °C and then leave at room temperature overnight. TLC indicated the complete consumption of the starting materials. The mixture was washed with saturated NaHCO<sub>3</sub> solution followed by water. The organic layer was dried over MgSO<sub>4</sub> and the solvent was evaporated to give the reasonable pure diamide which was either used directly or purified by flash chromatography.

### General procedure of thiadiamido crown ether formation

Compound **8** or **15** (1 mmol) was dissolved in EtOH (120 ml) and the reaction was stirred at room temperature for 15 min. Na<sub>2</sub>S·9H<sub>2</sub>O (1 mmol) was added and the mixture was heated at reflux for 1 h followed by Na<sub>2</sub>S·9H<sub>2</sub>O (0.5 mmol) and was continued to reflux for additional 3 h. The EtOH was evaporated when the TLC showed there were no starting materials left. The residue was dissolved in DCM (50 mL), washed with water and dried over MgSO<sub>4</sub>. The solvent was evaporated, and flash chromatography was applied to obtain the pure crown ether.



### General procedure of benzylaza-diamido crown ether formation

Compound **8** or **15** (1.0 mmol) was dissolved in acetonitrile (100 ml) and then  $\text{Na}_2\text{CO}_3$  (10 mmol) was added. Benzyl amine (1.2 mmol) was added and the mixture was heated at reflux for 12 h. When TLC showed there was no starting materials remained, the mixture was cooled down to room temperature, filtered and the solvent was evaporated under reduced pressure. The remaining was dissolved in DCM (50 mL) and washed with water, dried over  $\text{MgSO}_4$ . The solvent was evaporated, and flash chromatography was applied to get the pure macrocycle.

### General procedure of Michael addition of 2-nitropropane to chalcone

The series of macrocycles **9**, **10**, **16**, **17**, **18**, **19**, **20**, **21**, **22** and **23** were subjected to Michael addition reaction of 2-nitropropane to chalcone. The preparative TLC was used for isolating the product after normal workup sequence. The  $^1\text{H}$  NMR spectroscopy was employed to determine the enantiomeric excess (ee %) using  $\text{Eu}(\text{hfc})_3$  as a chiral shift reagent.

### 2-butyloctyl 4,6-O-benzylidene- $\beta$ -D-glucopyranoside **5**

Crude **4** (7.2 g, 20 mmol) and benzaldehyde dimethyl acetal (7.4 mL, 48 mmol) were dissolved in 150 mL DCM. P-TsOH (100 mg) was added according to general benzylidenation procedure, to give pure  $\beta$ -anomer **5** (4.6 g, 53%).  $[\alpha]_{\text{D}} = -38$  ( $c = 0.21$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta = 7.51\text{--}7.24$  (m, 5 H; Ph), 5.52 (s; Ph-CH), 4.34–4.28 (m, 2 H; H-1, H-6 eq), 3.82–3.78 (m, 3 H; H-2, H-3, H-6ax), 3.56–3.35 (m, 4 H; H-4, H-5,  $\alpha$ - $\text{CH}_2$ ), 3.15 (d, 1 H,  $^3J = 8.0$  Hz; OH-3), 2.76 (d, 1 H,  $^3J = 8.0$  Hz; OH-2), 1.62–1.60 (m, 1 H;  $\beta$ -CH), 1.31–1.25 (m, 16 H; bulk- $\text{CH}_2$ ), 0.92–0.86 (m, 6 H;  $2\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta = 137.04$  (Ph-C), 129.24/128.33/126.32 (Ph-CH), 103.48 (C-1), 101.89 (PhCH), 80.64 (C-4), 74.68 (C-2), 73.66 (C-3), 73.64 ( $\alpha$ - $\text{CH}_2$ ), (73.08 CH), 68.70 (C-6), 66.39 (C-5), 38.19 ( $\beta$ ), 31.88/31.86/31.21/31.15/30.88/30.82/29.69/28.96/28.94/26.73/26.68/23.05/ 22.67 (bulk- $\text{CH}_2$ ), 14.12 ( $2\text{CH}_3$ ).

### 2-butyloctyl 4,6-O-benzylidene-2,3-bis-O-[cyanomethyl]- $\beta$ -D-glucopyranoside **6**

Compound **5** (2.7 g, 6.2 mmol) in toluene (40 mL) was treated with aqueous NaOH (25 mL, 50%),  $\text{Bu}_4\text{N.HSO}_4$  (1.4 g, 4 mmol) and  $\text{BrCH}_2\text{CN}$  (3.80 g, 32 mmol) according to general procedure 4.1.2 to give **6** as a white solid (2.61 g, 82%).  $[\alpha]_{\text{D}} = -29.0$  ( $c = 1.2$ ,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta = 7.52\text{--}7.35$  (m, 5 H; Ph), 5.57 (s, 1 H; Ph-CH), 4.56–4.54 (mc, 4 H;  $\text{CH}_2\text{CN}$ ), 4.45 (d, 1 H,  $^3J_{1,2} = 7.5$  Hz; H-1), 4.37 (dd, 1 H,  $^2J_{6\text{eq},6\text{ax}} = 10.8$ , 5.0 Hz; H-6 eq), 3.82 (dt, 2 H,  $^3J = 8.0$ , 5.5 Hz;  $\alpha$ - $\text{CH}_2$ ),

$\alpha$ -CH<sub>2b</sub>), 3.75–3.65 (m, 2 H; H-6ax, H-4), 3.47–3.35 (m, 3 H; H-3,H-5,H-2), 1.63 (mc, 1 H;  $\beta$ -CH), 1.39–1.24 (m, 16 H; bulk-CH<sub>2</sub>), 0.95–0.88 (m, 6 H; 2 CH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 136.68 (Ph-C), 129.31 / 128.37/ 126.08 (Ph-CH), 116.15/ 115.83 (2 C $\equiv$ N), 103.00 (C-1), 101.52 (Ph-CH), 81.91 (C-2), 80.85 / 80.65 (C-3, C-4), 73.45 ( $\alpha$ -CH<sub>2</sub>), 73.38 (CH), 68.55 (C-6), 65.71 (C-5), 57.72/ 57.63 (2 CH<sub>2</sub>C $\equiv$ N), 38.16 ( $\beta$ ), 31.86/ 31.23/ 31.18/30.90/ 30.88/ 29.66/ 28.96 / 28.89 /26.73/26.68 / 23.06/ 22.67 (bulk-CH<sub>2</sub>), 14.10 (2 CH<sub>3</sub>).

HRMS: [M + Na]<sup>+</sup> calcd. for C<sub>29</sub>H<sub>42</sub>N<sub>2</sub>O<sub>6</sub>Na: 537.2941; found: 537.2934.

### 2-butylloctyl 4,6-O-benzylidene-2,3-bis-(2-aminoethyl)- $\beta$ -D-glucopyranoside **7**

Cynomethylated glycolipid **6** (2.0 g, 3.9 mmol) was subjected to general reduction procedure 4.1.2 to give amino-glycolipid **7** as a pale-yellow semisolid (1.78 g, 88%). [ $\alpha$ ]<sub>D</sub> = -50.0 (c = 1.3, CH<sub>2</sub>Cl<sub>2</sub>). The product was subjected to the next reaction without purification.

### 2-butylloctyl 4,6-O-benzylidene-2,3-bis-[2-(2-chloroacetamido)ethyl]- $\beta$ -D-glucopyranoside **8**

Compound **7** (2.08 g, 4.0 mmol) and (ClCH<sub>2</sub>CO)<sub>2</sub>O (1.52 g, 8.8 mmol) were subjected to general procedure 4.1.3 to give diamide **8** as a pale-yellow semisolid (2.28 g, 85%). [ $\alpha$ ]<sub>D</sub> = +3.7 (c = 0.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.39–7.27 (m, 5 H; Ph), 6.82 (t, 1 H, <sup>3</sup>J = 5.5 Hz; CONH), 6.71 (t, 1 H, <sup>3</sup>J = 5.5 Hz; CONH), 5.46 (s; Ph-CH), 4.32 (d, 1H, <sup>3</sup>J<sub>1,2</sub> = 7.8 Hz; H-1), 4.28 (dd, 1 H, <sup>2</sup>J<sub>6eq,6ax</sub> = 10.5, 5.0 Hz; H-6 eq), 4.02–3.98 (m, 1 H; CH<sub>2a</sub>O), 3.94–3.75 (m, 1 H; CH<sub>2a</sub>O), 3.78–3.66 (m, 4 H;  $\alpha$ -CH<sub>2a</sub>, 2 CH<sub>2a</sub>Cl, H-6ax), 3.65–3.48 (m, 4 H; H-3, H-4,  $\alpha$ -CH<sub>2b</sub>), 3.35–3.24 (m, 4 H; H-2, 2 CH<sub>2b</sub>Cl, CH, CH<sub>2</sub>N), 3.23–3.11 (m, 5 H; H-5, CH<sub>2</sub>N), 1.54–1.46 (mc, 1 H;  $\beta$ -CH), 1.30–1.15 (m, 16 H; bulk-CH<sub>2</sub>), 0.92–0.88 (m, 6 H; 2 CH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  = 167.88, 167.81 (C=O), 137.1 (Ph-C), 129.14 / 128.34/ 125.87 (Ph-CH), 104.02 (C-1), 101.19 (Ph-CH), 82.07 (C-2), 80.31/ 79.53 (C-3, C-4), 73.24/ 73.18 (2 CH<sub>2</sub>O), 71.34/ 71.07 ( 2  $\alpha$ -CH<sub>2</sub>), 68.69 (C-6), 65.81 (C-5), 39.72/ 39.58 (2 CH<sub>2</sub>Cl), 38.22 ( $\beta$ ), 36.49/ 36.46 (2 CH<sub>2</sub>N)/ 31.29/31.14/ 30.96/ 30.85/ 29.66/ 29.63/ 29.05/ 28.86 /26.80/26.63 / 23.04/ 23.00/ 22.63 (bulk-CH<sub>2</sub>), 14.07 (2 CH<sub>3</sub>).

HRMS: [M + Na]<sup>+</sup> calcd. for C<sub>33</sub>H<sub>52</sub>Cl<sub>2</sub>N<sub>2</sub>O<sub>8</sub>Na: 697.2998; found: 697.2989.

### 2-butylloctyl 4,6-O-benzylidene-2,3-[15-cr-5]thiadiamido- $\beta$ -D-glucopyranoside **9**

Compound **8** (0.47 g, 0.7 mmol) and Na<sub>2</sub>S $\cdot$ 9H<sub>2</sub>O (0.25 g, 1.06 mmol) were subjected to general procedure 4.1.4 to give **9** as a white semisolid (0.35 g, 79%). [ $\alpha$ ]<sub>D</sub> = -35.0 (c = 0.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  = 7.52–7.34 (m, 5 H; Ph), 7.14 (t, 1 H, <sup>3</sup>J = 5.5 Hz; CONH), 7.02 (t, 1 H, <sup>3</sup>J = 5.5 Hz; CONH), 5.55 (s; Ph-CH), 4.39 (d,

$^1\text{H}$ ,  $^3J_{1,2}=7.8$  Hz; H-1), 4.35 (dd, 1 H,  $^2J_{6\text{eq},6\text{ax}}=10.5$ , 5.0 Hz; H-6 eq), 4.11–4.07 (mc, 1 H; 2  $\text{CH}_{2\text{a}}\text{N}$ ), 4.02–3.87 (mc, 2 H;  $\text{CH}_{2\text{a}}\text{O}$ ), 3.85–3.74 (m, 4 H;  $\alpha\text{-CH}_{2\text{a}}$ ,  $\text{CH}_{2\text{b}}\text{O}$ , H-6ax), 3.70–3.35 (m, 10 H;  $\alpha\text{-CH}_{2\text{b}}$ ,  $\text{CH}_{2\text{b}}\text{N}$ , H-3, H-4, H-5, 2  $\text{CH}_2\text{S}$ ), 3.35 (dd~t, 1 H,  $^3J_{2,3}=9.0$  Hz; H-2), 1.64 (mc, 1 H;  $\beta\text{-CH}_2$ ), 1.38–1.24 (m, 16 H; bulk- $\text{CH}_2$ ), 0.92–0.88 (m, 6 H; 2  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta=166.075$ , 166.01 (C=O), 136.94 (Ph-C), 129.36/128.42/ 126.08 (Ph-CH), 103.91 (C-1), 101.69 (Ph-CH), 82.27 (C-2), 81.06 (C-4), 80.84 (C-3), 73.45/73.39 ( $\alpha\text{-CH}_2$ ), 71.40/71.34 (2  $\text{CH}_2\text{O}$ ), 68.73 (C-6), 66.04 (C-5), 42.66/42.46 (2  $\text{CH}_2\text{NH}$ ), 40.19/39.91 (2  $\text{CH}_2\text{S}$ ), 38.22 ( $\beta$ ), 31.86/ 31.23/ 30.90/30.80/ 29.70/29.67 /28.96/28.90/26.70/(bulk-  $\text{CH}_2$ ), 23.07( $\gamma$ ), 22.65 ( $\omega$ -1), 14.11 (2  $\omega$ ).

HRMS:  $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{33}\text{H}_{52}\text{N}_2\text{O}_8\text{SNa}$ : 659.3342; found: 659.3437.

### 2-butylloctyl 4,6-O-benzylidene-2,3-[15-cr-5]triazadiamido- $\beta$ -D-glucopyranoside **10**

Compound **8** (0.42 g, 0.62 mmol), benzyl amine (0.08 g, 0.74 mmol) and  $\text{Na}_2\text{CO}_3$  (0.63 g, 6.0 mmol) were subjected to general procedure 4.1.5, to give **10** as a yellow semisolid (0.26 g, 59%).  $[\alpha]_{\text{D}}=-44.0$  ( $c=0.2$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta=7.39$ – $7.20$  (m, 11 H; 2 Ph, CONH), 7.10 (br., 1 H; CONH), 5.50 (s; Ph-CH), 4.37 (d, 1H,  $^3J_{1,2}=7.8$ ; H-1), 4.30 (dd, 1 H,  $^2J_{6\text{eq},6\text{ax}}=10.5$ , 5.0; H-6 eq), 4.16–4.02 (m, 2 H,  $\text{CH}_{2\text{a}}\text{O}$ ), 3.81–3.70 (m, 2 H; H-6ax,  $\alpha\text{-CH}_{2\text{a}}$ ), 3.66–3.50 (m, 9 H; H-4, H-3,  $\alpha\text{-CH}_{2\text{b}}$ ,  $\text{CH}_{2\text{b}}\text{O}$ ,  $\text{NCH}_2\text{PH}$ ,  $\text{CH}_{2\text{a}}\text{N}$ ), 3.40–3.28 (m, 2 H;  $\alpha\text{-CH}_{2\text{b}}$ , H-5), 3.24–3.10 (m, 5 H; H-2, 2  $\text{CH}_{2\text{b}}\text{NHCO}$ ,  $\text{CH}_{2\text{b}}\text{N}$ ), 1.52 (mc, 1 H;  $\beta\text{-CH}$ ), 1.32–1.15 (m, 16 H; bulk- $\text{CH}_2$ ), 0.93–0.88 (m, 6 H; 2  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta=169.63/169.61$  (2 C=O), 136.98/136.48 (2 Ph-C), 129.16 /129.06/128.94/128.54/128.37/128.15/126.45/125.86 (Ph-CH), 104.22 (C-1), 101.11 (Ph-CH), 82.19 (C-4), 80.63 (C-2), 79.94 (C-3), 73.53 ( $\alpha\text{-CH}_2$ ), 71.34 /71.02 (2  $\text{CH}_2\text{O}$ ), 68.74 (C-6), 65.73 (C-5), 60.34 ( $\text{PhCH}_2\text{N}$ ), 59.21/ 59.00 (2  $\text{CH}_2\text{CONH}$ ), 39.15/39.05 (2  $\text{CH}_2\text{NH}$ ), 38.21 ( $\beta$ ), 31.87/31.31/ 30.98/ 30.83/ 29.69 / 29.66/29.06/ 28.83/26.62 (bulk-  $\text{CH}_2$ ), 23.07( $\gamma$ ), 22.65 ( $\omega$ -1), 14.20/ 14.11 (2  $\omega$ ).

HRMS:  $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{40}\text{H}_{59}\text{N}_3\text{O}_8\text{Na}$ : 732.4270; found: 732.4290.

### Dodecyl 4,6-O-benzylidene-2,3-di-O-benzyl- $\beta$ -D-glucopyranoside **11**

The glycolipid **4** (4.36 g, 10 mmol) was dissolved in DMF (100 mL) and NaH 60% suspension in paraffin oil (2.4 g, 40 mmol). The mixture was stirred for 1 h and then was cooled to 0 °C. Benzyl bromide (4.08 g, 24 mmol) was added dropwise, and the reaction mixture was stirred for 2 h at room temperature. MeOH (30 mL) was added with stirring followed by water (20 mL) to obtain a white precipitate, which was filtered, washed with MeOH (5×5 mL) and dried. The compound was subjected to column chromatography to give **11** as a yellow syrup (5.54 g, 90%).  $[\alpha]_{\text{D}}=+5.4$  ( $c=1.0$ ,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta=7.44$ – $7.22$  (m, 15 H; Ph), 5.53 (s, 1 H; Ph-CH), 4.84 (d, 2 H; Bn), 4.76–4.66 (2 d, 2 H; Bn), 4.43 (d,

1 H,  $^3J_{1,2}=8.0$  Hz; H-1), 4.28 (dd, 1 H,  $^2J_{\text{H-6 eq,ax}}=11.0$ , 5 Hz; H-6 eq), 3.90–3.82 (dt, 1 H,  $^2J_{\text{CH}_{2\text{a,b}}}=8.0$ , 2.3 Hz;  $\alpha\text{-CH}_{2\text{a}}$ ), 3.77–3.57 (m, 3 H; H-3, H-4, H-6ax), 3.53–3.45 (dt, 1 H,  $^2J_{\text{CH}_{2\text{a,b}}}=8.0$ , 2.3 Hz;  $\alpha\text{-CH}_{2\text{b}}$ ), 3.40 (t~dd, 1 H,  $^3J_{1,2}=9.0$  Hz; H-2), 3.40–3.33 (m, 2H; H-3, H-5), 1.61–1.53 (m, 2 H;  $\beta\text{-CH}_2$ ), 1.35–1.13 (m, 18 H; bulk  $\text{CH}_2$ ), 0.86 (t, 3 H,  $^3J=8.0$  Hz;  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta=138.53/138.37/137.34$  (Ph-C), 128.93/128.33/128.29/128.24/128.12/128.03/127.71/127.61/126.00 (Ph), 104.16 (C-1), 101.11 (Ph-CH), 82.15 (C-2), 81.51/ 80.89 (C-3, C-4), 75.35 / 75.13 (Ph- $\text{CH}_2$ ), 70.66 ( $\alpha\text{-CH}_2$ ), 68.83 (C-6), 66.00 (C-5), 31.93 ( $\beta$ ), 29.78/29.71/29.68/29.64/29.59/28.46/29.37 (bulk- $\text{CH}_2$ ), 26.13 ( $\gamma$ ), 22.70 ( $\omega$ -1), 14.21 ( $\omega$ ).

HRMS:  $[\text{M}+\text{Na}]^+$  calcd. for  $\text{C}_{39}\text{H}_{52}\text{O}_6\text{Na}$ : 639.3662; found: 639.3672.

### Dodecyl 2,3-di-O-benzyl- $\beta$ -D-glucopyranoside **12**

Compound **11** (5.5 g, 10 mmol) was dissolved in  $\text{CHCl}_3$ : MeOH 1:1 (150 mL), and p-toluenesulfonic acid (200 mg) was added. The mixture was stirred for 12 h at room temperature. Water (150 mL) was added and the organic phase was washed with saturated  $\text{NaHCO}_3$  solution ( $2 \times 50$  mL). The organic phase was dried over  $\text{MgSO}_4$  and the solvent was evaporated. Column chromatography of the residue gave **12** as a yellow semisolid (4.38 g, 93%).  $[\alpha]_{\text{D}}^{25} = +4.0$  ( $c=1.0$ ,  $\text{CH}_2\text{Cl}_2$ ).

$^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta=7.38\text{--}7.29$  (m, 10 H; aromatic), 4.90 (2 d, 2 H,  $^2J_{\text{Bn}}=11.0$  Hz; Bn) 4.62 (2d, 2 H,  $^2J_{\text{Bn}}=11.0$  Hz; Bn), 4.38 (d, 1 H,  $^3J_{1,2}=8.0$  Hz; H-1), 3.87 (dt, 1 H,  $^2J_{\alpha\text{-CH}_{2\text{a}},\alpha\text{-CH}_{2\text{b}}}=9.1$  Hz;  $\alpha\text{-CH}_{2\text{a}}$ ), 3.81 (dd, 1 H; H-6 eq), 3.67 (dd, 1 H,  $^2J_{\text{H-6 eq, ax}}=11.0$ , 5.0 Hz; H-6ax), 3.51–3.44 (m, 2 H; H-4,  $\alpha\text{-CH}_{2\text{b}}$ ) 3.38 (t~dd, 1 H,  $^3J_{2,3}=9.0$  Hz; H-2), 3.33 (t~dd, 1 H,  $^3J_{2,3}=9.0$  Hz; H-3), 3.28–3.23 (m, 1 H; H-5), 1.66–1.55 (m, 2 H;  $\beta\text{-CH}_2$ ), 1.37–1.12 (m, 18 H; bulk  $\text{CH}_2$ ); 0.88 (t, 3 H,  $^3J=8.0$  Hz;  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta=138.50/138.32$  (Ph-C), 128.64, 128.41, 128.13, 127.96, 127.76 (Ph), 103.85 (C-1), 83.91 (C-2), 81.90 (C-3), 75.23 / 74.70 ( $\text{CH}_2\text{Ph}$ ), 74.82 (C-5), 70.49 (C-4), 70.47 ( $\alpha\text{-CH}_2$ ), 62.73 (C-6), 31.91 ( $\beta$ ), 29.80 / 29.67 / 29.63 / 29.62 / 29.58 / 29.45 / 29.35 / (bulk- $\text{CH}_2$ ), 26.16 ( $\gamma$ ), 22.69 ( $\omega$ -1), 14.20 ( $\omega$ ).

HRMS:  $[\text{M}+\text{Na}]^+$  calcd. for  $\text{C}_{32}\text{H}_{48}\text{O}_6\text{Na}$ : 551.3349; found: 551.3356.

### Dodecyl 2,3-O-dibenzyl-4,6-bis-O-[cynomethyl]- $\beta$ -D-glucopyranoside **13**

Compound **12** (2.6 g, 5 mmol) was subjected to general procedure 4.1.1 to give **13** as a yellow syrup (2.5 g, 84%).  $[\alpha]_{\text{D}}^{25} = +5.0$  ( $c=1.0$ ,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta=7.38\text{--}7.25$  (m, 10 H; Ph), 4.94 (d, 2 H,  $^2J_{\text{Bn}}=11.0$  Hz; Bn), 4.70–4.63 (2 d, 2 H,  $^2J_{\text{Bn}}=11.0$  Hz; Bn), 4.45–4.36 (dd, 2 H;  $\text{CH}_2\text{C}\equiv\text{N}$ ), 4.37 (d, 1 H  $^3J_{1,2}=8.0$  Hz; H-1), 3.34–3.27 (dd, 2 H  $^2J_{\text{CH}_2\text{C}\equiv\text{N}}=16$  Hz;  $\text{CH}_2\text{C}\equiv\text{N}$ ), 3.96–3.93 (dt, 1 H;  $\alpha\text{-CH}_{2\text{a}}$ ), 3.93–3.86, (dd, 1 H,  $^2J_{\text{H-6a,b}}=11.0$ , 5.0 Hz; H-6 eq), 3.82–3.77 (dd, 1 H,  $^2J_{\text{H-6a,b}}=11.0$ , 6.8 Hz; H-6ax), 3.61 (t~dd, 1 H,  $^3J_{1,2}=8.0$ ,  $^3J_{2,3}=9.0$ ; H-2), 3.54–3.47 (m, 2 H; H-4,  $\alpha\text{-CH}_{2\text{b}}$ ), 3.44–3.37 (m, H-3; H-5), 1.68–1.57 (m, 2 H;  $\beta\text{-CH}_2$ ), 1.40–1.18 (m, 18 H; bulk  $\text{CH}_2$ ), 0.86 (t, 3 H,  $^3J=8.0$  Hz;  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  = 128.64, 128.52, 128.25, 128.07, 127.98 (Ph), 116.28 / 115.91 (2  $\text{C}\equiv\text{N}$ ), 103.72 (C-1), 84.04 (C-2), 82.05 (C-3), 77.45 (C-4), 75.62 / 74.76 ( $\text{CH}_2\text{OR}$ ), 73.17 (C-5), 74.04 / 73.30 (Bn) 70.51 / 69.48 (C-6,  $\alpha$ - $\text{CH}_2$ ), 57.56 / 56.97 ( $\text{CH}_2\text{C}\equiv\text{N}$ ), 32.59 ( $\beta$ ), 30.95, 29.78 / 29.72 / 29.53 / 29.46 / 29.41 / 28.55 (bulk- $\text{CH}_2$ ), 26.17 ( $\gamma$ ), 22.79 ( $\omega$ -1), 14.20 ( $\omega$ ).

HRMS:  $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{36}\text{H}_{50}\text{N}_2\text{O}_6\text{Na}$ : 629.3567; found: 629.3572.

### Dodecyl 2,3-di-O-dibenzyl-4,6-bis-O-[2-aminoethyl]- $\beta$ -D-glucopyranoside **14**

Compound **13** (2.3 g, 3.8 mmol) was subjected to general reduction procedure 4.1.2 to give amino-glycolipid **14** as a yellow syrup (2.07 g, 89%).  $[\alpha]_{\text{D}} = +12$  ( $c = 1.0$ ,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.38–7.25 (m, 10 H; Ph), 4.94 (d, 2 H,  $^2J_{\text{Bn}} = 11.0$  Hz; Bn), 4.72–4.65 (2 d, 2 H,  $^2J_{\text{Bn}} = 11.0$  Hz; Bn), 4.37 (d, 1 H,  $^3J_{1,2} = 8.0$  Hz; H-1), 3.96–3.23 (mc, 12 H, 2  $\text{OCH}_2$ ,  $\alpha$ - $\text{CH}_{2\text{a}}$ , H-6 eq, H-6ax, H-2, H-4,  $\alpha$ - $\text{CH}_{2\text{b}}$ , H-3, H-5), 2.94–2.68 (mc, 4 H;  $\text{CH}_2\text{NH}_2$ ), 1.68–1.57 (m, 2 H;  $\beta$ - $\text{CH}_2$ ), 1.40–1.18 (m, 18 H; bulk- $\text{CH}_2$ ), 0.86 (t, 3 H,  $^3J = 8.0$  Hz;  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  = 138.67, 138.52, 128.64, 128.52, 128.25, 128.07, 127.98 (Ph), 103.83 (C-1), 84.50 (C-2), 82.47 (C-3), 77.46 (C-4), 75.65 / 74.92 ( $\text{CH}_2\text{OR}$ ), 76.62 (C-5), 74.04 / 73.30 (Bn) 70.31 / 70.00 (C-6,  $\alpha$ - $\text{CH}_2$ ), 42.66 / 41.77 ( $\text{CH}_2\text{NH}_2$ ), 32.59 ( $\beta$ ), 30.95, 29.78 / 29.72 / 29.53 / 29.46 / 29.41 / 28.55 (bulk- $\text{CH}_2$ ), 26.17 ( $\gamma$ ), 22.79 ( $\omega$ -1), 14.20 ( $\omega$ ).

HRMS:  $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{36}\text{H}_{58}\text{N}_2\text{O}_6\text{Na}$ : 637.4193; found: 637.4199.

### Dodecyl 2,3-di-O-dibenzyl-4,6-bis-O-[2-(2-chloroacetamido)ethyl]- $\beta$ -D-glucopyranoside **15**

Compound **14** (2.33 g, 3.8 mmol) and chloroacetic anhydride (1.42 g, 8.36 mmol) were subjected to general procedure 4.1.3 to give diamide **15** as a pale-yellow wax (2.55 g, 88%).  $[\alpha]_{\text{D}} = +3.0$  ( $c = 0.2$ ,  $\text{CHCl}_3$ ).  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  = 7.36–7.26 (m, 10 H; Ph), 7.08 (br., 1 H; CONH), 7.02 (br., 1 H; CONH), 4.95 (t~dd, 2 H,  $^2J_{\text{Bn}} = 11.0$  Hz; Bn), 4.69 (2 d, 2 H,  $^2J_{\text{Bn}} = 11.0$  Hz; Bn), 4.38 (d, 1 H,  $^3J_{1,2} = 8.0$  Hz; H-1), 4.05 (s, 2 H;  $\text{CH}_2\text{Cl}$ ), 3.95–3.81 (m, 4 H;  $\text{CH}_2\text{O}$ ,  $\text{CH}_2\text{Cl}$ ), 3.78–3.27 (m, 14 H; H-2, H-3, H-4, H-5, H-6,  $\text{CH}_2\text{O}$ ,  $\alpha$ - $\text{CH}_2$ ,  $\text{CH}_2\text{NHCO}$ ), 1.62 (mc, 2 H;  $\beta$ - $\text{CH}_2$ ), 1.40–1.18 (m, 18 H; bulk- $\text{CH}_2$ ), 0.87 (t, 3 H,  $^3J = 8.0$  Hz;  $\text{CH}_3$ ).

$^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ )  $\delta$  = 166.24, 166.05 (CONH), 138.33, 138.31, 128.54, 128.49, 128.27, 128.06, 127.90, 127.83 (Ph), 103.79 (C-1), 84.28/82.25/77.06 (C-2, C-3, C-4), 75.78/74.84 (Bn), 74.63 (C-5), 70.93/70.40 ( $\text{CH}_2\text{O}$ ), 70.12/69.50 (C-6,  $\alpha$ - $\text{CH}_2$ ), 42.72/42.66 ( $\text{CH}_2\text{Cl}$ ), 40.38/39.63 ( $\text{CH}_2\text{NH}_2$ ), 32.00 ( $\beta$ ), 30.32, 29.85/29.77/29.72/29.69/29.55/29.45/29.41 (bulk- $\text{CH}_2$ ), 26.27 ( $\gamma$ ), 22.79 ( $\omega$ -1), 14.23 ( $\omega$ ).

HRMS:  $[\text{M} + \text{Na}]^+$  calcd. for  $\text{C}_{40}\text{H}_{60}\text{Cl}_2\text{N}_2\text{O}_8\text{Na}$ : 789.3624; found: 789.3632.

**Dodecyl 2,3-di-O-dibenzyl-4,6-[15-cr-5]thiadiamido-β-D-glucopyranoside 16**

Compound **15** (0.40 g, 0.52 mmol) and Na<sub>2</sub>S·9H<sub>2</sub>O (0.19 g, 0.78 mmol) was subjected to general procedure 4.1.4 to give **16** as a white solid (0.29 g, 77%). [α]<sub>D</sub> = +33.0 (c=0.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ = 7.38–7.24 (m, 10 H; Ph), 7.07 (m, 1 H; CONH), 7.03 (m, 1 H; CONH), 5.00 (dd, 2 H, <sup>2</sup>J<sub>Bn</sub> = 11.0, 10.8 Hz; Bn), 4.74 (d, 1 H, <sup>2</sup>J<sub>Bn</sub> = 10.8; Bn), 4.60 (d, 1 H, <sup>2</sup>J<sub>Bn</sub> = 11.0; Bn), 4.32 (d, 1 H, <sup>3</sup>J<sub>1,2</sub> = 8.0 Hz; H-1), 3.90 (dt, 1 H, <sup>2</sup>J<sub>α-CH<sub>2</sub>a,α-CH<sub>2</sub>b</sub> = 9.1, <sup>3</sup>J<sub>α-CH<sub>2</sub>a,β-CH<sub>2</sub>a</sub> = 6.8 Hz; α-CH<sub>2</sub>a), 3.88–3.78 (m, 3 H; CH<sub>2</sub>O, H-6 eq), 3.77–3.63 (m, 4 H; CH<sub>2</sub>O, H-4, H-6ax), 3.60–3.31 (m, 8 H; H-2, H-3, α-CH<sub>2</sub>b, CH<sub>2</sub>NHCO, CH<sub>2</sub>S), 3.2 (m, 1 H; H-5), 3.03 (m, 1 H; CH<sub>2</sub>N), 2.92 (d, 1 H <sup>2</sup>J<sub>CH<sub>2</sub>S</sub> = 8.0 Hz; CH<sub>2</sub>S), 2.58 (d, 1 H, <sup>2</sup>J<sub>CH<sub>2</sub>S</sub> = 8.0 Hz; CH<sub>2</sub>S), 1.63 (mc, 2 H; β-CH<sub>2</sub>), 1.38–1.19 (m, 18 H; bulk-CH<sub>2</sub>), 0.87 (t, 3 H, <sup>3</sup>J = 8.0 Hz; CH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ = 169.26, 168.94 (CONH), 138.35, 137.90, 128.75, 128.55, 128.40, 128.32, 127.89 (Ph), 103.87 (C-1), 84.33/82.37 (C-2, C-3), 78.15 (C-4), 76.30 (Bn), 75.63 (C-5), 74.81 (Bn), 70.59 (α-CH<sub>2</sub>), 70.29/70.27 (CH<sub>2</sub>O), 68.98 (C-6), 4158/40.00 (CH<sub>2</sub>NH), 36.79/36.22 (CH<sub>2</sub>S), 32.00 (β), 29.81, 29.77/29.69/29.66/29.54/29.45/29.41 (bulk-CH<sub>2</sub>), 26.26 (γ), 22.78 (ω-1), 14.22 (ω).

HRMS: [M + Na]<sup>+</sup> calcd. for C<sub>40</sub>H<sub>60</sub>N<sub>2</sub>SO<sub>8</sub>Na: 751.3988; found: 751.4080.

**Dodecyl 2,3-di-O-dibenzyl-4,6-[15-cr-5]triazadiamido-β-D-glucopyranoside 17**

Compound **15** (0.40 g, 0.52 mmol) and benzyl amine (0.07 g, 0.63 mmol) was subjected to general procedure 4.1.5 to give **17** as a pale-yellow wax (0.25 g, 61%). [α]<sub>D</sub> = -7.0 (c=0.2, CHCl<sub>3</sub>). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ = 7.39–7.20 (m, 15 H; Ph), 7.11 (br., 1 H; CONH), 7.03 (br., 1 H; CONH), 4.95 (dd, 2 H, <sup>2</sup>J<sub>Bn</sub> = 11.0, 5.0 Hz; Bn), 4.68 (t≈dd, 2 H, <sup>2</sup>J<sub>Bn</sub> = 11.0, 5.0 Hz; Bn), 4.41 (d, 1 H, <sup>3</sup>J<sub>1,2</sub> = 8.0 Hz; H-1), 3.98–3.91 (m, 2 H; α-CH<sub>2</sub>a, H-6 eq), 3.78 (dd, 1 H, <sup>2</sup>J<sub>H-6 eq-H-6ax</sub> = 11.0 Hz, <sup>3</sup>J<sub>H-6ax-5H</sub> = 8.0 Hz; H-6ax), 3.73–3.44 (m, 8 H; α-CH<sub>2</sub>b, H-2, BnN, CH<sub>2</sub>O), 3.43–3.33 (m, 7 H; H-3, H-4, H-5, CH<sub>2</sub>NH), 3.25–3.02 (m, 4 H; CH<sub>2</sub>NCO), 1.63 (mc, 2 H; β-CH<sub>2</sub>), 1.38–1.19 (m, 18 H; bulk-CH<sub>2</sub>), 0.87 (t, 3 H, <sup>3</sup>J = 8.0 Hz; CH<sub>3</sub>).

<sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ = 169.26, 168.94 (CONH), 138.22, 137.91, 128.97, 128.55, 128.52, 128.28, 127.97, 127.93, 127.89 (Ph), 103.78 (C-1), 84.38/82.32/79.55 (C-2, C-3, C-4), 75.70/74.89 (Bn), 74.66 (C-5), 72.34/71.19 (CH<sub>2</sub>O), 70.46 (α-CH<sub>2</sub>), 70.22 (C-6), 60.34 (BnN), 59.39/58.45 (COCH<sub>2</sub>N), 40.09/38.78 (CH<sub>2</sub>NH), 32.00 (β), 29.87, 29.76/29.72/29.55/29.45 (bulk-CH<sub>2</sub>), 26.26 (γ), 22.78 (ω-1), 14.22 (ω).

HRMS: [M + Na]<sup>+</sup> calcd. C<sub>47</sub>H<sub>67</sub>N<sub>3</sub>O<sub>8</sub>Na: 824.4894; found: 824.4890.

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### Declarations

**Conflict of interest** The authors declare no conflict of interests.

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