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Versatile Routes to C-2- and C-6-Functionalized Glucose Derivatives of Iminodiacetic Acid

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A series of novel D-glucose derivatives, functionalized at the C-2 or the C-6 position with an iminodiacetic acid moiety for transition-metal complexation, has been prepared. The sugar and the metal-chelating parts are separated by either propyl or octyl chains and were introduced by the reaction of bromoalkylamine. Either *N*-1-Boc-3-bromopropylamine (**17**) or *N*-(8-bromooctyl)-phthalimide (**19**) reacted with methyl 3,5,6-*tri*-*O*-benzyl-α-*β*-D-glucofuranoside (**4**) (C-2 position) and 1,2:3,5-(*O*-methylene)-α-D-glucose (**11**) (C-6 position), respectively, in the presence of sodium hydride in DMF at room temperature, affording the desired intermediates. For aminopropyl derivatives, yields varied between 57% and 65%, and for aminooctyl derivatives, yields varied between 40% and 71%. After deprotection of the amine functionality, the metal chelate was built up by dialkylation (**6a**−**c** and **13a,b**) with methyl bromoacetate in the presence of triethylamine under reflux in THF. Yields varied between 56% and 69% for the glucose modified at the C-2 position and between 58% and 62% for the one modified at the C-6 position. All compounds were characterized by ^{1}H or ^{13}C NMR or both, IR, and mass spectroscopy. Final products were isolated as a mixture of α and *β* anomers.

Introduction

Carbohydrates are interesting building blocks for organic chemistry and drug development due to their involvement in various biological systems, water solubility, and optical activity. The latter two characteristics make them interesting, for example, in asymmetric synthesis[1] and in heterogeneous catalysis. Also, several review papers recently appeared summarizing the importance and growing application of carbohydrate-based drugs.[2] On the other hand, the chemistry and application of carbohydrate-based transition-metal complexes in other research areas is strikingly underdeveloped. Carbohydrate-based complexes could be extremely important in research fields such as bioinorganic and bioorganometallic chemistry, where they have attracted considerable attention, for example, in assay development and nuclear medicine.[3−7] The development of new sugar-pendant ligand systems for site-specific transition-metal coordination could significantly extend the scope of these research topics.

With a view to develop novel, metal-based, tumor-targeting radiopharmaceuticals for diagnostic and therapeutic purposes, we previously reported the synthesis and functionalization of *β*-glucose and 2-deoxy-α-glucose at the C-1 position with an *O*-glycosidically linked iminodiacetic acid (IDA) chelating moiety.[8] Reaction of the corresponding glucose and deoxyglucose derivatives with the organometallic precursor $[NEt_4]_2[ReBr_3(CO)_3]$ yielded almost quantitatively highly stable and water-soluble organometallic complexes.

However, to target either glucose transport systems such as, e.g., Glut-1 (often overexpressed on malignant tumors cells) or the active site of the enzyme hexokinase or both, the functionalization of glucose at the C-6[9] or C-2 position for transition-metal coordination would be desirable.[10] In the case of hexokinase, the C-2 position appears to be the sole center where substitution is tolerated without completely losing the biological activity of glucose.[11]

We report here the first systematic synthesis of glucose functionalized at the C-2 or C-6 position with a metal-chelating moiety.

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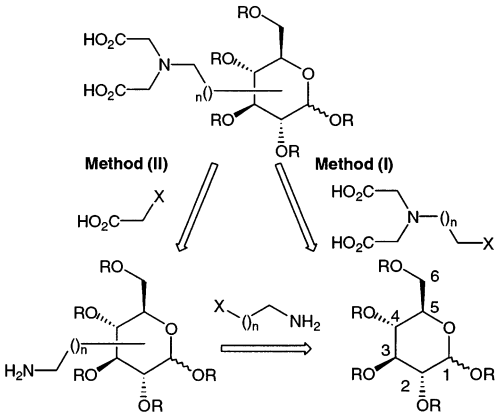
SCHEME 1

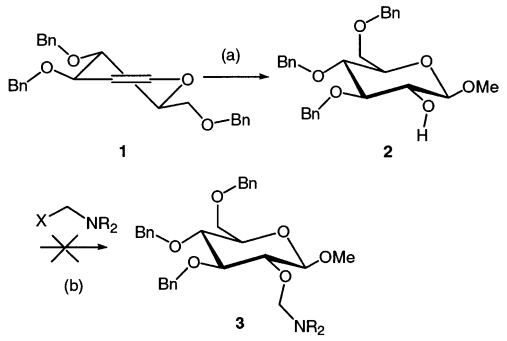


Results and Discussion

In a recent review, Nicolaou[12] presents a list of 20 different general methods to carry out an *O*-glycosylation, which shows the diversity of carbohydrate chemistry. However, syntheses of glucose derivatives at positions other than C-1 with multiple functional groups, including amines, are scarcely reported. Among the other positions, the chemistry of C-6 is the most developed and described due to the relatively easy access to a reactive precursor such as, e.g., 1,2:3,5-(*O*-methylene)-α-D-glucose (**11**).[13] On the other hand, the C-2 position of glucose is exceptionally problematic to *C*-substitute, presumably due to the unreactivity of a C-2 leaving group toward displacement with charged nucleophiles. This fact was attributed to the electron-withdrawing effect of the anomeric carbon atom and the unfavorable dipolar interaction in the transition state of the substitution reaction.[14,15] Last, *O*-substitution of the hydroxyl group at the C-2 position is rarely employed for purposes other than protection. For our approach, we decided to follow the reaction pathway using *O*-substitution, which was also recently utilized to prepare different D-glucose-derivatized bisimidazole compounds.[16]

Two options are reasonable for the retrosynthesis of glucose derivatives at the C-2 and C-6 positions. The first one is a convergent synthesis which includes the coupling of a halogenoalkane already functionalized with the chelating moiety (Scheme 1, method I) to the protected glucose. The second alternative is a linear synthesis. In the latter case, the first step is the *O*-alkylation of the protected glucose by a halogenated primary alkylamine to afford the spacer pendant carbohydrate. The chelating moiety will subsequently be built up by dialkylation of glucose derivative with methyl bromoacetate (Scheme 1, method II). Although method I is straightforward, we found that the basic conditions for the coupling of the ligand system led to uncontrolled hydrolysis of the ester functionalities rather than linkage of the ligand system to glucose. Therefore, we followed method II.

SCHEME 2[a]



[a] Reagents and conditions: (a) *m*-CPBA, MeOH, 64%; (b) different conditions have been tested for this reaction; various bases (KOH, NaOH, NaH), solvents (dioxane, DMF), and desiccants have been used as well as different temperature conditions.

Substitution at the C-2 Position. Methyl 3,4,6-tribenzyl-β-D-glucopyranoside (**2**) seemed to be an ideal starting material for functionalization of glucose at the C-2 position. The commercially available tribenzyl glucal **1** was treated with *m*-CPBA in methanol to afford the desired methyl glucopyranose **2** (Scheme 2) as a mixture of the α and β anomers (ratio 1:20) in 64% yield as described by Danishefsky et al.[17,18]

However, attempts to alkylate the unprotected alcohol at the C-2 position in the presence of different bases (KOH, NaOH, or NaH) in DMF or dioxane with an alkyl bromide or an alkyl tosylate yielded the desired product only in trace amounts even at elevated temperatures. The use of desiccant including Drierite, calcium carbonate, and molecular sieves in the reaction solution did not increase the yields either. Steric hindrance of the OH group due to the bulky benzyl groups particularly in the case of sugars in the pyranose form might be the reason for these synthetic problems. We therefore chose to start from a protected furanose precursor because, in this case, the protecting groups are above and the OH group is below the plane of the furanose ring system. The steric hindrance should thus be reduced and the alkylation at C-2 position facilitated.

The methyl 3,5,6-tri-*O*-benzyl-D-α-β-glucofuranoside (**4**) prepared according to the synthesis reported by Lee et al.[19] has been successively coupled with 3-bromo-*N*-(1-*tert*-butoxycarbonyl)propylamine,[20] *N*-bromooctylphthalimide,[21] and commercially available 1,2-bis(2-chlorethoxy)-ethane in DMF at room temperature in the presence of sodium hydride. The corresponding *N*-protected aminopropyl and aminooctyl sugars **5a** and **5b** were obtained after 14 h with respective yields of 65% and 71%. Compound **5c** was obtained from the alkylation reaction and converted without purification into the azide **5d** in an 87% overall yield. The modified glucoses **5a**−**d** were all present as a mixture of the α and β anomers in a ratio of 1:1, as evident from the ^{1}H NMR spectra. The next

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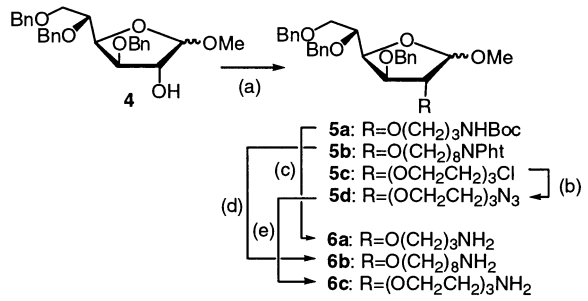
SCHEME 3[a]



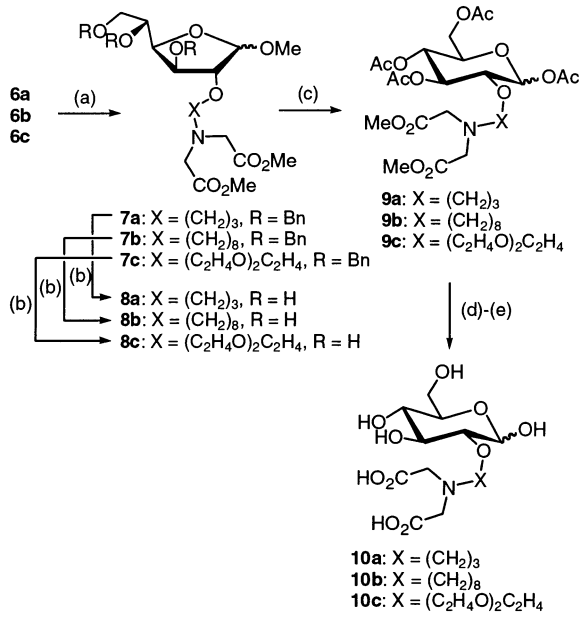
[a] Reagents and conditions: (a) NaH, 3-bromo-*N*-(1-*tert*-butoxycarbonyl)propylamine, *N*-bromooctylphthalimide, or 1,2-bis(2-chlorethoxy)ethane, DMF, rt, 14 h, 65−71%; (b) NaN_3, 2 h, DMF, 100 °C; (c) CF_3CO_2H, CH_2Cl_2, rt, 1 h, 86%; (d) NH_2NH_2, MeOH, rt, 2 h, 77%; (e) $LiAlH_4$, THF, rt, 3 h, 71%. Pht = phthalloyl.

step of the synthesis was the deprotection of the amine functionality to build up the chelating moiety by dialkylation. Compound **6a** was isolated after 1 h of reaction without purification by deprotection of the Boc groups in the presence of trifluoroacetic acid in dichloromethane (Scheme 3). The phthalimide group of the glucose derivative **5b** was removed in the presence of hydrazine in methanol at room temperature to afford the aminoalkyl-D-glucose **6b**. The azide functionality of glucose derivative **5c** was reduced overnight under reflux by the action of $LiAlH_4$ in THF to furnish the free amine derivative **6c**.

The chelating moieties were obtained by double alkylation of the amines of furanoses **6a**−**c** using methyl bromoacetate in THF in the presence of triethylamine to afford the diesters **7a**−**c** with yields of 56−69%. The following three steps led to final deprotections of the sugar and the chelating moiety. The hydrogenolysis of the benzyl groups occurred in methanol in the presence of a catalytic amount of palladium hydroxide to give the deprotected triols **8a**−**c** in excellent yields (>85%). The partial transformation of the furanose in pyranose and the elimination of the methyl at the C-1 position[22] were achieved simultaneously in acetic anhydride in the presence of trimethylsilyl triflate to afford hexaesters **9a**, **9b**, and **9c** (Scheme 4). Hexaesters **9a**−**c** were obtained as a mixture of the α and β anomers of the pyranose form. Traces of the corresponding anomers of the furanose form have also been observed in the ^{1}H NMR spectrum. Transesterification of the four acetates of derivatives **9a**−**c** in methanol with sodium methanolate and the saponification of the methyl ester in an aqueous solution of sodium hydroxide finally yielded the functionalized glucose derivatives **10a**−**c**. Overall yields of derivatives **10a**−**c** were 16%, 23%, and 22% with respect to glucofuranose **4**.

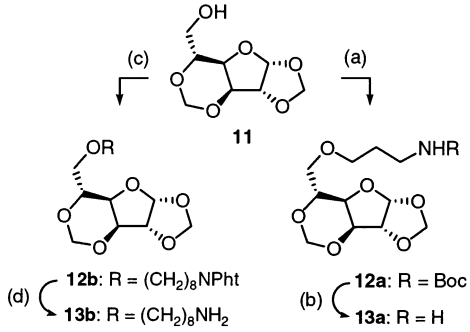
Substitution at the C-6 Position. The starting material for the alkylation at the C-6 position, 1,2:3,5-(*O*-methylene)-α-D-glucose (**11**), was prepared according to the method described by Hough et al.[13] in one step from D-glucopyranose. As for the synthesis of sugar derivatives **10a**−**c**, the substitution at the C-6 position started with the insertion of the linker at the C-6 position. The unprotected alcohol was alkylated in DMF in the presence of sodium hydride with either the protected bro-

SCHEME 4[a]



[a] Reagents and conditions: (a) $BrCH_2CO_2Me$, NEt_3, THF, reflux, 14 h, 56−69%; (b) H_2, $Pd(OH)_2$/C, MeOH, 85−99%; (c) TMSOTf, AcOH, 0 °C, 40 min, 66−90%; (d) NaOMe, MeOH; (e) NaOH (0.091 N), Dowex 50W-X8, 85−89%.

SCHEME 5[a]



[a] Reagents and conditions: (a) NaH, 3-bromo-*N*-(1-*tert*-butoxycarbonyl)propylamine, DMF, rt, 14 h, 57%; (b) CF_3CO_2H, CH_2Cl_2, rt, 1 h, 91%; (c) NaH, *N*-bromooctylphthalimide, DMF, rt, 14 h, 40%; (d) NH_2NH_2, MeOH, rt, 2 h, 81%.

moamine 3-bromo-*N*-(1-*tert*-butoxycarbonyl)propylamine or *N*-bromooctylphthalimide to afford their corresponding amino ethers **12a**,**b** (Scheme 5). The second step of the synthesis is still the deprotection of the amine functionality to allow the preparation of the metal-chelating moiety. Using the same method described for the C-2 position, the amines **12a** and **12b** were respectively deprotected in the presence of trifluoroacetic acid in dichloromethane or hydrazine monohydrate in methanol to afford the corresponding primary amines **13a**,**b**.

The C-6-substituted glucose derivatives **13a**,**b** were dialkylated in the same manner as compounds **7** to yield the corresponding diester derivatives **14a** and **14b** (Scheme 6). Finally, the two glucose derivatives **15a**,**b** were obtained by saponification of the esters of carbohydrates **14a**,**b** in 1 M aqueous NaOH and the deprotection of the acetals by addition of Dowex 50W-X8. Overall yields of derivatives **15a,b** were 23% and 16% with respect to bismethylene-D-glucofuranose **11**.

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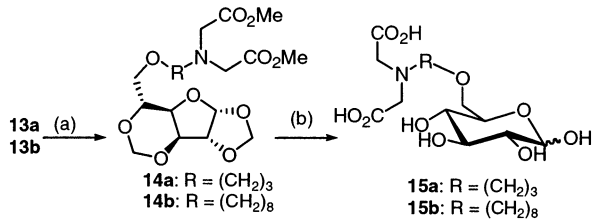
SCHEME 6[a]



[a] Reagents and conditions: (a) $BrCH_2CO_2Me$, NEt_3, THF, reflux, 14 h, 58−62%; (b) NaOH, rt, 2 h, Dowex 50W-X8, 77−78%.

Conclusion

In summary the first practical and versatile method for the substitution of glucose at the C-2 or C-6 position with a functionalized side chain (**10a**−**c** and **15a**,**b**) has been successfully developed. Although this method was set up for D-glucose, it can presumably be extended to the substitution/functionalization of other natural and artificial monosaccharides. The synthetic intermediates **8a**−**c** and **13a,b** may be particularly useful for the preparation of functionalized carbohydrates for linkage to peptides and lipids. They can also be powerful intermediates for the formation of amine-containing ligand systems tailor-made for various transition-metal centers. In vitro evaluation of the bioaffinity of the corresponding ^{99m}Tc-labeled glucose derivatives **10a**−**c** and **15a,b** for hexokinase and Glut-1 are in progress.

Experimental Section

General Procedures. Unless otherwise specified purchased materials were used without further purification. Dry THF was distilled from Na/benzophenone immediately before use. Moisture-sensitive reactions were conducted in oven-dried glassware under a nitrogen atmosphere. All reactions were monitored by thin-layer chromatography performed on precoated silica gel (60 F_{254}) plates and visualized using UV light and applying a solution of potassium permanganate (1% in water). Similarly, amines were detected by ninhydrin (0.5% in methanol). Column chromatography was accomplished on silica gel 60 (0.062−200 mesh). High-resolution mass spectroscopy was done by the MS service of the Department of Organic Chemistry at the Federal Institute of Technology Zurich (ETHZ). The elemental analyses were performed by the Laboratory of Microelementary Analysis from the Department of Organic Chemistry at the ETHZ. The NMR spectra were measured at 300 and 75 MHz for ^{1}H and ^{13}C, respectively. Unless otherwise specified, spectra were recorded in $CDCl_3$ as solvent, and chemical shifts are expressed in parts per million relative to that of residual $CHCl_3$ at 7.27 ppm for ^{1}H and that of $CDCl_3$ at 77.7 ppm for ^{13}C.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-(3-*tert*-butoxycarbonylaminopropyl)-α,*β*-D-glucofuranoside (5a). To a solution of methyl 3,5,6-*tri*-*O*-benzyl-α-*β*-D-glucofuranoside (**4**) (985 mg, 2.12 mmol, 1 equiv) and 3-bromo-*N*-(1-*tert*-butoxycarbonyl)-propylamine (1.51 g, 6.36 mmol, 3 equiv) in DMF (30 mL) at 0 °C was added portionwise NaH (60% in oil) (340 mg, 8.5 mmol, 4 equiv). The obtained suspension was stirred overnight with increasing temperature from 0 °C to rt. The excess of NaH was then destroyed by addition of methanol (0.32 mL) and water (0.63 mL) at 0 °C. The solvents were removed by distillation to afford a brown oil, which was diluted in dichloromethane and washed two times with water. The organic layer was dried over Na_2SO_4, filtered, and evaporated to dryness to provide a brown oil, which was purified by chromatography on silica gel, CH_2Cl_2/acetone (95:5): yield 65%; R_f 0.27 (AcOEt/nHex, 1:3); ^{1}H NMR δ 7.20−7.11 (m, 15H), 5.01 (d, J = 4.7 Hz, 0.5H), 4.86−4.67 (m, 2H), 4.66−4.50 (m, 5.5H), 4.38−4.28 (m, 1H), 4.17 (dd, J = 5.6, J = 3.5 Hz, 1H), 4.13−3.80 (m, 1.5H), 3.82−3.66 (m, 1.5H), 3.58−3.49 (m, 1H), 3.48−3.35 (m, 4H), 3.30−3.19 (m, 2H), 1.80−1.62 (m, 2H), 1.44 (s, 9H); HRMS *m*/*z* calcd for $C_{36}H_{47}NO_8$ 621.3302, found 621.3307.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-(8-phthalimidooctyl)-α,*β*-D-glucofuranoside (5b). Compound **5b** was prepared from **4** and *N*-bromooctylphthalimide according to the preparation of **5a**: yield 71%; R_f 0.45 (AcOEt); IR (neat) 1748, 1372, 1222 cm^{-1}; ^{1}H NMR δ 7.88−7.79 (m, 1H), 7.74−7.65 (m, 1H), 7.40−7.19 (m, 17H), 5.04 (d, J = 4.8 Hz, 0.5H), 4.97 (d, J = 4.0 Hz, 0.5H), 4.81 (d, J = 11.6 Hz, 1H), 4.75−4.48 (m, 6H), 4.39−4.18 (m, 2H), 4.18−3.99 (m, 2H), 3.97−3.84 (m, 1H), 3.83−3.62 (m, 2H), 3.60−3.30 (m, 2H), 3.47 (s, 1.5H), 3.42 (s, 1.5H), 1.78−1.40 (m, 4H), 1.40−1.18 (m, 8H); ^{13}C NMR δ 179.9 (2C), 139.6, 139.3, 138.6, 132.8 (2C), 128.9 (4C), 128.8 (3C), 128.6 (2C), 128.3 (4C), 128.2 (3C), 128.0 (2C), 127.9, 109.3, 86.9, 81.1, 80.8, 77.5, 77.2, 74.0, 73.0, 72.8, 71.5, 70.6, 30.2, 29.9, 29.7, 27.4, 26.6. Anal. Calcd for $C_{44}H_{51}NO_8$ (721.36): C, 73.21; H, 7.12; N, 1.94. Found: C, 73.44; H, 7.48; N, 2.31.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-[2-(2-azidoethoxy)ethoxy]-ethyl-α,*β*-D-glucofuranoside (5d). To a solution of methyl 3,5,6-*tri*-*O*-benzyl-α-*β*-D-glucofuranoside (**4**) (1 g, 2.1 mmol, 1 equiv) and 1,2-bis(2-chlorethoxy)ethane (3.4 mL, 21.5 mmol, 10.2 equiv) in DMF (50 mL) at 0 °C was added portionwise NaH (60% in oil) (430 mg, 10.8 mmol, 5.1 equiv). The obtained suspension was stirred overnight with increasing temperature from 0 °C to rt. The excess of NaH was then destroyed by addition of methanol (0.5 mL) and water (1.5 mL) at 0 °C. The solvents were removed by distillation to afford a yellow oil, which was diluted in AcOEt (50 mL) and washed two times with water (50 mL). The organic layer was dried over Na_2SO_4, filtered, and evaporated to dryness to provide an oil (1.2 g) composed of a mixture of **5c** and 1,2-bis(2-chlorethoxy)-ethane in a ratio of 2:3. To a solution of this oil in DMF (25 mL) was added at rt NaN_3 (252 mg, 4.48 mmol, 2 equiv). The resulting suspension was heated at 100 °C for 4 h. After cooling, brine (188 mL) was added, and the mixture was extracted with Et_2O (3 × 110 mL). The combined organic layers were dried over Na_2SO_4 and evaporated to dryness to afford a brown oil, which was purified by chromatography on silica gel, AcOEt/nHex (1:3): yield 87%; R_f 0.60 (AcOEt/nHex, 1:3); IR (neat) 2106, 1110, 1062 cm^{-1}; ^{1}H NMR δ 7.57−7.19 (m, 15H), 5.09 (d, J = 4.3 Hz, 0.2H), 4.97 (s, 0.8H), 4.93−4.84 (m, 1H), 4.77−4.58 (m, 5H), 4.41 (dd, J = 9.0, 4.8 Hz, 1H), 4.23−4.08 (m, 2H), 4.01 (dd, J = 10.5, 1.9 Hz, 1H), 3.98 (s large, 1H), 3.82 (dd, J = 10.5, 5.2 Hz, 1H), 3.81−3.63 (m, 10H), 3.52 (s, 0.6H), 3.49 (s, 2.4H), 3.54−3.43 (m, 2H); ^{13}C NMR δ 139.6, 139.3, 138.6, 129.9 (2C), 129.5, 129.2 (3C), 128.7 (2C), 128.4, 128.0 (2C), 127.7 (2C), 127.4 (2C), 110.3, 109.9, 108.2, 88.6, 87.3, 87.2, 81.3, 80.8, 80.2, 74.0, 72.8, 71.5, 71.4, 71.1, 70.0, 51.3; MS *m*/*z* 644.5 (MNa^+). Anal. Calcd for $C_{34}H_{43}N_3O_8$ (621.73): C, 65.68; H, 6.97; N, 6.76. Found: C, 65.68; H, 6.98; N, 6.68.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-(8-aminooctyl)-α,*β*-D-glucofuranoside (6b). To a solution of **5b** (279 mg, 0.39 mmol, 1 equiv) in methanol (6 mL) was added at rt hydrazine (24% in water) (0.41 mL, 3.1 mmol, 8 equiv). After one night of stirring the solvent was removed and the crude oil directly used in the following step without any purification: yield 77%; R_f 0.10 (AcOEt/nHex, 2:1); IR (neat) 1702, 1580, 1494 cm^{-1}; ^{1}H NMR δ 7.35−7.19 (m, 15H), 4.84−4.71 (m, 2H), 4.65−4.45 (m, 5H), 4.28 (dd, J = 9.0, 4.5 Hz, 1H), 4.12−4.03 (m, 1H), 3.98 (d, J = 4.8 Hz, 1H), 3.89 (dd, J = 10.5, 2.1 Hz, 1H), 3.77 (s large, 1H), 3.70 (dd, J = 10.5, 5.4 Hz, 1H), 3.36 (s, 3H), 3.31 (t, J = 6.6 Hz, 2H), 3.24−3.31 (m, 2H), 1.52−1.35 (m, 4H), 1.29−1.14 (m, 8H); HRMS *m*/*z* calcd for $C_{36}H_{49}NO_6$ 591.3560, found 591.3555.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-[2-(2-aminoethoxy)ethoxy]ethyl-α,*β*-D-glucofuranoside (6c). To a solution of **5c** (1.83 g, 2.95 mmol, 1 equiv) in THF (25 mL) was added at rt

a solution of $LiAlH_4$ (2.3M) in THF (1.3 mL, 2.95 mmol, 1 equiv). After 3 h of reflux the resulting solution cooled, and the excess $LiAlH_4$ was destroyed by successive addition of water (22 μL), NaOH (3.75 M, 221 μL), and water (620 μL). The resulting suspension was filtered over a Celite pad and the filtrate evaporated to dryness to afford a colorless oil: yield 50%; R_f 0.26 (AcOEt/nHex, 5:1); IR (neat) 1108, 1062 cm^{-1}; ^1H NMR δ 7.60−7.21 (m, 15H), 5.09 (d, J = 4.0 Hz, 0.4H), 4.97 (s, 0.6H), 4.88 (dd, J = 11.4, 6.0 Hz, 1H), 4.82−4.59 (m, 5.4H), 5.13−4.37 (m, 1H), 4.35−4.28 (m, 0.6H), 4.23−4.08 (m, 2H), 4.05−3.95 (m, 2H), 3.89−3.64 (m, 10H), 3.62−3.55 (m, 2H), 3.52 (s, 1.2H), 3.49 (s, 1.8H); HRMS m/z calcd for $C_{34}H_{45}NO_8$ 595.3145, found 595.3137.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-[bis-*N*-[(1-methoxycarbonyl)methyl]aminopropyl]-α,*β*-D-glucofuranoside (7a). To a solution of **5a** (857 mg, 1.38 mmol, 1 equiv) in CH_2Cl_2 (5 mL) was added at rt TFA (0.85 mL, 16.8 mmol, 8 equiv). The resulting solution was stirred for 1 h and then washed with water (10 mL) and a saturated solution of $NaHCO_3$ (10 mL). The organic layer was dried over Na_2SO_4 and evaporated to afford **6a** as a crude oil directly used in the following step: R_f 0.26 (CH_2Cl_2). Triethylamine (0.35 mL, 2.5 mmol, 2.1 equiv) and methyl bromoacetate (0.23 mL, 2.5 mmol, 2.1 equiv) were added to a solution of **6a** (617 mg, 1.19 mmol, 1 equiv) in THF (8 mL), and the solution was refluxed overnight. After cooling, the mixture was filtered; the filtrate was diluted with CH_2Cl_2 (15 mL) and washed with water (15 mL). The organic layer was dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel, AcOEt/nHex (1:2): yield 59% from **5a**; R_f 0.34 (AcOEt/nHex, 1:3); IR (neat) 1710, 1452, 1364, 1206 cm^{-1}; ^1H NMR δ 7.36−7.23 (m, 15H), 4.82 (s, 1H), 4.77 (d, J = 11.4 Hz, 1H), 4.61−4.54 (m, 4H), 4.52 (d, J = 11.1 Hz, 1H), 4.32−4.20 (m, 1H), 4.12−4.04 (m, 1H), 4.01−3.98 (m, 1H), 3.96−3.84 (m, 1H), 3.84−3.62 (m, 2H), 3.68 (s, 6H), 3.53 (s, 4H), 3.43 (t, J = 6.3 Hz, 2H), 3.38 (s, 3H), 2.75 (t, J = 7.2 Hz, 2H), 1.74−1.64 (m, 2H); MS m/z 688.5 (MNa^+). Anal. Calcd for $C_{37}H_{47}NO_{10}$ (665.32): C, 66.75; H, 7.12; N, 2.10. Found: C, 66.70; H, 7.09; N, 1.74.

Methyl 3,5,6-Tri-*O*-benzyl-2-*O*-[bis-*N*-[(1-methoxycarbonyl)methyl]aminooctyl]-α,*β*-D-glucofuranoside (7b). Compound **7b** was prepared from **6b** according to the preparation of **7a**: yield 56%; R_f 0.52 (AcOEt/nHex, 5:3); ^1H NMR δ 7.38−7.21 (m, 15H), 4.83−4.74 (m, 2H), 4.63−4.48 (m, 5H), 4.28 (dd, J = 9.1, 4.6 Hz, 1H), 4.08 (ddd, J = 9.0, 5.4, 1.8 Hz, 1H), 3.99 (d, J = 4.5 Hz, 1H), 3.90 (dd, J = 10.5, 1.8 Hz, 1H), 3.77 (s, 1H), 3.73 (d, J = 5.4 Hz, 1H), 3.70 (s, 6H), 3.55 (s, 4H), 3.38 (s, 3H), 3.32 (t, J = 6.6 Hz, 2H), 2.68 (m, Hz, 2H), 1.54−1.39 (m, 4H), 1.32−1.20 (m, 8H); ^{13}C NMR δ 172.4 (2C), 139.9, 139.5, 138.8, 129.0 (3C), 128.9 (2C), 128.8 (2C), 128.6 (2C), 128.3, 128.2 (3C), 128.0, 127.9, 109.3, 86.9, 81.2, 80.8, 77.5, 74.0, 73.1, 72.8, 71.6, 70.7, 56.6, 55.6 (2C), 55.2 (2C), 52.2, 30.3, 30.1, 30.0, 28.5, 27.8, 26.6; MS m/z 736.3 (MH^+). Anal. Calcd for $C_{42}H_{57}NO_{10}$ (735.40): C, 68.55; H, 7.81; N, 1.90. Found: C, 68.29; H, 7.94; N, 1.64.

Methyl 3,5,6-Tri-*O*-benzyl-2-O-[2-[bis-*N*-[(1-methoxycarbonyl)methyl]aminoethoxy]ethoxy]ethyl-α,*β*-D-glucofuranoside (7c). Compound **7c** was prepared from **6c** according to the preparation of **7a**: yield 62%; R_f 0.24 (AcOEt/nHex, 1:1); ^1H NMR δ 7.55−7.25 (m, 15H), 4.96 (s, 1H), 4.88 (d, J = 11.4 Hz, 1H), 4.84−4.58 (m, 4H), 4.62 (d, J = 11.4 Hz, 1H), 4.40 (dd, J = 9.0, 4.8 Hz, 1H), 4.18 (ddd, J = 9.0, 5.7, 2.1 Hz, 1H), 4.14 (d, J = 4.5 Hz, 1H), 4.08−3.46 (m, 12H), 4.01 (dd, J = 10.5, 2.1 Hz, 1H), 3.8 (s, 6H), 3.73 (4H), 3.49 (s, 3H), 3.06 (t, J = 5.7 Hz, 2H). Anal. Calcd for $C_{40}H_{53}NO_{12}$ (739.36): C, 65.03; H, 7.09; N, 1.90. Found: C, 65.01; H, 6.94; N, 1.51.

Methyl 2-*O*-[Bis-*N*-[(1-methoxycarbonyl)methyl]aminopropyl]-α,*β*-D-glucofuranoside (8a). To a solution of **7a** (450 mg, 0.67 mmol, 1 equiv) in methanol (15 mL) was added at rt $Pd(OH)_2$/C (10% by weight) (45 mg). The resulting suspension was stirred under 1 atm of hydrogen till the TLC showed no more starting material. The suspension was then filtered over a Celite pad, and the solution was evaporated to dryness to afford a colorless oil used without purification in the following step: yield 85%; R_f 0.52 (AcOEt); IR (neat) 1748 cm^{-1}; (**7aα**) ^1H NMR (D_2O) δ 5.94 (d, J = 3.9 Hz, 1H), 5.04−4.87 (m, 5H), 4.71−4.64 (m, 1H), 4.47 (d, J = 3.9 Hz, 1H), 4.43−3.35 (m, 1H), 4.24−4.01 (m, 2H), 4.00−3.70 (m, 6H), 3.68−3.40 (m, 5H), 3.29 (t, J = 6.9 Hz, 2H), 1.80−1.69 (m, 2H); (**7a*β***) ^1H NMR (CD_3OD) δ 5.32 (d, J = 3.3 Hz, 1H), 4.54 (d, J = 7.8 Hz, 1H), 4.48−4.24 (m, 4H), 4.17−4.04 (m, 1H), 4.03−3.48 (m, 6H), 3.87 (s, 9H), 3.43−3.20 (m, 2H), 2.13−1.99 (m, 2H); HRMS m/z calcd for $C_{16}H_{29}NO_{10}$ 395.1791, found 395.1788.

Methyl 2-*O*-[Bis-*N*-[(1-methoxycarbonyl)methyl]aminooctyl]-α,*β*-D-glucofuranose (8b). Compound **8b** was prepared from **7b** according to the preparation of **8a**: yield 99%; R_f 0.30 (AcOEt/nHex, 5:3); IR (neat) 1750, 1656 cm^{-1}; ^1H NMR (CD_3OD) δ 4.97 (d, J = 4.7 Hz, 1H), 4.72 (s large, 1H), 4.15 (d, J = 3.9 Hz, 1H), 3.99−3.64 (m, 6H), 3.79 (s, 6H), 3.62−3.43 (m, 4H), 3.36−3.21 (m, 2H), 3.28 (s, 3H), 1.74−1.42 (m, 4H), 1.38−1.22 (m, 8H); ^{13}C NMR (CD_3OD) δ 168.8 (2C), 110.1, 90.9, 83.5, 75.8, 72.6, 71.9, 65.9, 58.9, 56.6, 56.1 (2C), 54.6 (2C), 31.6, 31.0, 30.9, 28.2, 27.9, 26.0; HRMS m/z calcd for $C_{21}H_{40}NO_{10}$ 465.2652, found 465.2652 (MH^+).

Methyl 2-*O*-[2-[Bis-*N*-[(1-methoxycarbonyl)methyl]aminoethoxy]ethoxy]ethyl-α,*β*-D-glucofuranoside (8c). Compound **8c** was prepared from **7c** according to the preparation of **8a**: yield quantitative; R_f 0.31 (AcOEt); ^1H NMR δ 4.83−4.76 (m, 1H), 4.71 (d, J = 11.8 Hz, 0.5H), 4.51 (d, J = 11.8 Hz, 0.5H), 4.34−4.28 (m, 0.5H), 4.17−4.05 (m, 1.5H), 3.99−3.64 (m, 3H), 3.71−3.47 (m, 10H), 3.65 (s, 6H), 3.63 (s, 4H), 3.33 (s, 1.5H), 3.32 (s, 1.5H), 2.98−2.86 (m, 2H); ^{13}C NMR δ 172.2, 172.1, 108.5, 107.8, 88.8, 87.8, 82.7, 81.7, 79.8, 75.0, 72.7 (2C), 71.6, 71.3, 71.2, 71.0, 70.9 (2C), 70.8, 70.7, 70.6 (2C), 70.6, 70.3 (2C), 70.1 (2C), 69.9, 64.7, 64.6, 56.2, 56.0, 55.9, 55.8, 54.1, 54.0, 52.2, 52.0; MS m/z 492.2 (MNa^+). Anal. Calcd for $C_{19}H_{35}NO_{12}$ (469.22): C, 48.61; H, 7.51; N, 2.98. Found: C, 48.95; H, 7.11; N, 2.99.

1,3,5,6-Tetra-*O*-acetyl-2-*O*-[bis-*N*-[(1-methoxycarbonyl)methyl]]aminopropyl-α,*β*-D-glucopyranose (9a). To a suspension of **8a** (130 mg, 0.28 mmol, 1 equiv) in anhydride acetic (3 mL) was added at 0 °C and under nitrogen flux TMSOTf (49 μL, 0.28 mmol, 1 equiv). After 40 min of stirring at 0 °C, the solution was diluted in dichloromethane and poured into a $NaHCO_3$/ice mixture. The biphasic solution was stirred, and $NaHCO_3$ was added until a constant basic pH was reached. The layers were separated, and the aqueous one was extracted two times with dichloromethane. The combined organic layers were then dried over Na_2SO_4, filtered, and evaporated to dryness to afford a yellow oil, which was purified by chromatography on silica gel, AcOEt/nHex (2:1). The desired product was obtained as a colorless oil with a yield of 90%: R_f 0.36 (AcOEt/nHex, 2:1); IR (neat) 1750, 1436, 1370 cm^{-1}; ^1H NMR δ 6.34 (d, J = 3.9 Hz, 0.2H), 5.55 (d, J = 8.0 Hz, 0.3H), 5.34−5.25 (m, 0.5H), 5.18−4.92 (m, 1H), 4.30−4.20 (m, 1H), 4.12−3.99 (m, 1H), 3.82−3.35 (m, 5H), 3.67 (s, 6H), 3.49 (s, 4H), 2.74−2.64 (m, 2H), 2.06 (s, 3H), 2.04 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.68−1.55 (m, 2H); HRMS m/z calcd for $C_{23}H_{36}NO_{14}$ 550.2136, found 550.2136 (MH^+).

1,3,5,6-Tetra-*O*-acetyl-2-*O*-[bis-*N*-[(1-methoxycarbonyl)methyl]aminooctyl]-α,*β*-D-glucopyranose (9b). Compound **9b** was prepared from **8b** according to the preparation of **9a**: yield 66%; R_f 0.38 (AcOEt/nHex, 2:1); ^1H NMR δ 6.35 (d, J = 4.8 Hz, 0.03H), 6.17 (s, 0.18H), 5.86 (d, J = 5.1 Hz, 0.34H), 5.81 (d, J = 4.5 Hz, 0.45H), 5.54−5.33 (m, 1.7H), 5.28−5.19 (m, 0.3H), 4.74−4.50 (m, 0.5H), 4.42−4.32 (m, 0.5H), 4.21−4.12 (m, 1H), 3.93−3.44 (m, 4H), 3.77 (s, 6H), 3.61 (s, 4H), 2.78−2.69 (m, 2H), 2.19−2.06 (m, 12H), 1.66−1.48 (m, 4H), 1.39−1.28 (m, 8H); ^{13}C NMR δ 172.2 (2C), 171.2, 170.6, 170.3, 169.6, 94.2, 89.9, 79.3, 74.8, 73.1, 72.3, 71.4, 70.3, 69.9, 68.7, 62.3 (2C), 55.4 (2C), 52.2, 51.8, 51.6, 29.3, 29.0, 21.6, 21.4, 21.3; MS m/z 620.2 (MH^+). Anal. Calcd for $C_{28}H_{45}NO_{14}$ (619.28): C, 54.27; H, 7.32; N, 2.26. Found: C, 54.13; H, 7.37; N, 2.38.

1,3,5,6-Tetra-*O*-acetyl-2-*O*-[2-[bis-*N*-[(1-methoxycarbonyl)methyl]aminoethoxy]ethoxy]ethyl-α,*β*-D-glucopyranose (9c). Compound **9c** was prepared from **8c** according to the preparation of **9a**: yield 41%; R_f 0.44 (AcOEt); ^{1}H NMR δ 6.24 (dd, J = 8.5, 4.3 Hz, 0.06H), 6.04 (d, J = 11.4 Hz, 0.27H), 5.86 (d, J = 5.5 Hz, 0.17H), 5.74 (d, J = 5.2 Hz, 0.27H), 5.74 (d, J = 8.2 Hz, 0.23H), 5.41−5.17 (m, 2H), 5.13−5.06 (m, 0.5H), 4.81−4.36 (m, 1.5H), 4.33−4.19 (m, 0.8H), 4.17−3.96 (m, 2.2H), 3.89−3.41 (m, 10.99H), 3.63 (s, 6H), 3.39 (s, 0.81H), 3.36 (s, 0.69H), 3.28 (s, 0.51H); 2.93−2.83 (m, 2H), 2.09−1.94 (m, 12H); MS *m*/*z* 646.2 (MNa^+). Anal. Calcd for $C_{26}H_{41}NO_{16}$ (623.61): C, 50.08; H, 6.63; N, 2.25. Found: C, 50.17; H, 6.37, N, 2.29.

2-*O*-[Bis(carboxymethyl)aminopropyl]-α,*β*-D-gluco pyranose (10a). NaOMe (13.4 mg, 0.25 mmol, 1 equiv) was added to a solution of **9a** (137.2 mg, 0.25 mmol, 1 equiv) in dry methanol (1 mL) at rt under nitrogen flux. After 3 h of reaction the solvent was removed, and the product was dissolved in NaOH (0.091 N, 1 mL) and stirred overnight. The solution was neutralized by addition of Dowex 50W-X8 till pH 7 was attained. The solution was then filtered and evaporated to afford an oil: yield 85%; IR (neat) 1632, 1402 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.44 (m, 0.5H), 4.72 (d, J = 8.1 Hz, 0.5H), 4.26−3.59 (m, 8H), 3.56−3.45 (m, 2H), 3.39−3.10 (m, 1H), 3.21−3.18 (m, 0.5H), 3.06−2.92 (m, 0.5H), 2.28−2.01 (m, 2H), 1.56−1.40 (m, 2H); MS *m*/*z* 357.0 (MH_4^+). Anal. Calcd for $C_{13}H_{23}NO_{10}$ (353.13): C, 44.19; H, 6.56; N, 3.96. Found: C, 43.83; H, 6.57; N, 3.62.

2-*O*-[Bis(carboxymethyl)aminooctyl]-α,*β*-D-glucopyranose (10b). Compound **10b** was prepared from **9b** according to the preparation of **10a**: yield 89%; IR (neat) 1596, 1354 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.37 (d, J = 3.3 Hz, 0.5H), 4.64−4.59 (m, 0.5H), 4.12−3.56 (m, 9H), 3.52−3.45 (m, 1H), 3.39−3.34 (m, 1H), 3.34−3.22 (m, 2.5H), 3.01 (dd, J = 8.7, 8.1 Hz, 0.5H), 1.89−1.78 (m, 2H), 1.76−1.65 (m, 2H), 1.57−1.40 (m, 8H); MS *m*/*z* 423.2 (M). Anal. Calcd for $C_{18}H_{33}NO_{10}$ (423.21): C, 51.05; H, 7.85; N, 3.31. Found: C, 51.00; H, 7.88; N, 3.46.

2-*O*-[2-[Bis(carboxymethyl)aminoethoxy]ethoxy]ethyl-α,*β*-D-glucopyranose (10c). Compound **10c** was prepared from **9c** according to the preparation of **10a**: yield 81%; ^{1}H NMR (CD_3OD) δ 5.48−5.35 (m, 0.45H), 5.26−5.10 (m, 0.55H), 4.60−4.49 (m, 0.5H), 4.08−3.81 (m, 2H), 3.76−3.48 (m, 1.5H), 3.36−3.10 (m, 3H), 3.10−2.75 (m, 13H), 2.39−2.25 (m, 2H); MS *m*/*z* 427.3 (M). Anal. Calcd for $C_{16}H_{29}NO_{12}$ (427.17): C, 44.96; H, 6.84; N, 3.28. Found: C, 44.89; H, 6.82; N, 3.15.

6-*O*-(3-*tert*-Butoxycarbonylaminopropyl)-1,2:3,5-(*O*-methylene)-α-D-glucofuranose (12a). Compound **12a** was prepared from 1,2:3,5-(*O*-methylene)-α-D-glucofuranose (**11**) and 3-bromo-*N*-(1-*tert*-butoxycarbonyl)propylamine according to the preparation of **5a**: yield 57%; R_f 0.38 (CH_2Cl_2/acetone, 95:5); $[\alpha]_D^{20}$ = +0.7, *c* 0.008, MeOH; IR (neat), 2922, 1710 cm^{-1}; ^{1}H NMR δ 6.01 (d, J = 3.9 Hz, 1H), 5.12−4.97 (m, 4H), 4.82 (dd, J = 9.4, 5.9 Hz, 1H), 4.46 (dd, J = 9.4, 3.9 Hz, 1H), 4.32 (dd, J = 6.5, 2.4 Hz, 1H), 4.15−4.08 (m, 1H), 4.03−3.99 (m, 1H), 3.76 (dd, J = 10.5, 3.9 Hz, 1H), 3.66 (dd, J = 10.5, 4.8 Hz, 1H), 3.59−3.41 (m, 2H), 3.28−3.11 (m, 2H), 1.82−1.70 (m, 2H), 1.42 (s, 9H); MS *m*/*z* 384.3 (MNa^+). Anal. Calcd for $C_{16}H_{27}NO_8$ (361.17): C, 53.18; H, 7.53; N, 3.88. Found: C, 53.17; H, 7.26; N, 4.01.

1,2:3,5-(*O*-Methylene)-6-*O*-(8-phthalimidooctyl)-α-D-glucofuranose (12b). Compound **12b** was prepared from **11** and *N*-bromooctylphthalimide according to the preparation of **5a**: yield 40%; R_f 0.33 (CH_2Cl_2/acetone, 95:5), $[\alpha]_D^{20}$ = +18.0, *c* 0.0183, MeOH; IR (neat) 1772, 1712, 1400 cm^{-1}; ^{1}H NMR δ 8.08−7.89 (m, 2H), 7.57−7.34 (m, 2H), 5.97 (d, J = 3.6 Hz, 1H), 5.12−4.94 (m, 3H), 4.75 (dd, J = 6.0, 5.7 Hz, 1H), 4.42 (dd, J = 8.4, 3.9 Hz, 1H), 4.30 (dd, J = 12.0, 2.4 Hz, 1H), 4.13−4.02 (m, 1H), 4.00−3.95 (m, 1H), 3.73 (dd, J = 10.5, 3.6 Hz, 1H), 3.62 (dd, J = 10.5, 4.8 Hz, 1H), 3.45−3.26 (m, 4H), 1.69−1.43 (m, 4H), 1.42−1.16 (m, 8H); ^{13}C NMR δ 166.1 (2C), 134.7, 134.2, 132.7 (2C), 124.0, 123.3, 105.0, 104.5, 97.1, 78.1, 76.8, 76.4, 72.7, 72.3, 72.2, 71.8, 30.0, 29.7, 29.6, 29.1, 27.3, 26.6; MS *m*/*z* 484.3(MNa^+). Anal. Calcd for $C_{24}H_{31}NO_8$ (461.206): C, 62.46; H, 6.77; N, 3.04. Found: C, 62.47; H, 6.82; N, 3.20.

1,2:3,5-(*O*-Methylene)-6-*O*-(3-aminopropyl)-α-D-glucofuranose (13a). Compound **13a** was prepared from **12a** according to the preparation of **6a**: yield 91%; R_f 0.15 (CH_2Cl_2/acetone, 95:5); $[\alpha]_D^{20}$ = +13.4, *c* 0.047, MeOH; ^{1}H NMR δ 5.99 (d, J = 3.6 Hz, 1H), 5.04 (d, J = 4.8 Hz, 1H), 5.01 (d, J = 4.8 Hz, 1H), 4.88 (s, 2H), 4.53 (d, J = 3.3 Hz, 1H), 4.24−4.22 (m, 1H), 4.05−4.01 (m, 2H), 3.83−3.74 (m, 3H), 3.65−3.57 (m, 1H), 3.30−3.19 (m, 2H), 2.04−1.99 (m, 2H); ^{13}C NMR δ 105.1 (t), 104.9 (t), 97.0 (d, 2C), 88.5 (t, 2C), 84.2 (t), 84.0 (t), 71.6 (d), 66.4 (d). Anal. Calcd for $C_{11}H_{19}NO_6$ (261.12): C, 50.57; H, 7.33; N, 5.36. Found: C, 50.25; H, 7.00; N, 5.63.

1,2:3,5-(*O*-Methylene)-6-*O*-(8-aminooctyl)-α-D-glucofuranose (13b). Compound **13b** was prepared from **12b** according to the preparation of **6b**: yield 81%; R_f 0.33 (CH_2Cl_2/acetone, 95:5); $[\alpha]_D^{20}$ = −12, *c* 0.00084, MeOH; IR (neat) 1708, 1634 cm^{-1}; ^{1}H NMR δ 6.13 (d, J = 3.9 Hz, 1H), 5.23 (d, J = 6.0 Hz, 1H), 5.20−5.10 (m, 2H), 4.88 (d, J = 6.0 Hz, 1H), 4.56 (d, J = 4.8 Hz, 1H), 4.46 (d, J = 2.4 Hz, 1H), 4.29−4.20 (m, 1H), 4.17−4.09 (m, 1H), 3.92−3.81 (m, 1H), 3.81−3.70 (m, 1H), 3.56−3.45 (m, 2H), 2.96−2.84 (m, 2H), 2.90−1.05 (m, 12H); ^{13}C NMR δ 105.2, 104.8, 97.2, 84.5, 76.9, 76.6, 72.8, 72.5, 72.3, 72.0, 32.3, 30.2, 29.9, 27.4, 26.8, 23.3; MS *m*/*z* 332.3 (MH^+). Anal. Calcd for $C_{16}H_{29}NO_6$ (331.20): C, 57.99; H, 8.82; N, 4.23. Found: C, 58.37; H, 8.56; N, 4.34.

6-*O*-[Bis-*N*-[(1-methoxycarbonyl)methyl]aminopropyl]-1,2:3,5-(*O*-methylene)-α-D-glucofuranose (14a). Compound **14a** was prepared from **13a** according to the preparation of **7a**, AcOEt/nHex (1:2): yield 58%; R_f 0.87 (CH_2Cl_2/acetone, 95:5); $[\alpha]_D^{20}$ = −37.9, *c* 0.0380, MeOH; ^{1}H NMR δ 5.88 (d, J = 3.7 Hz, 1H), 5.04−4.89 (m, 3H), 4.79−4.67 (m, 1H), 4.39 (dd, J = 8.7, 3.7 Hz, 1H), 4.23 (dd, J = 12.7, 1.7 Hz, 1H), 4.08−4.01 (m, 1H), 3.95−3.90 (m, 1H), 3.72−3.54 (m, 2H), 3.62 (s, 6H), 3.56−3.34 (m, 2H), 3.47 (s, 4H), 2.77−2.68 (m, 2H), 1.75−1.61 (m, 2H); ^{13}C NMR δ 146.4, 140.0, 105.1, 104.9, 97.3, 97.2, 88.9, 88.5, 84.3, 76.6, 76.4 (2C), 72.2, 72.1, 68.6 (2C), 68.5; MS *m*/*z* 428.3 (MNa^+). Anal. Calcd for $C_{17}H_{27}NO_{10}$ (405.16): C, 50.37; H, 6.71; N, 3.46. Found: C, 50.56; H, 6.37; N, 3.48.

6-*O*-[Bis-*N*-[(1-methoxycarbonyl)methyl]aminooctyl]-1,2:3,5-(*O*-methylene)-α-D-glucofuranose (14b). Compound **14b** was prepared from **13b** according to the preparation of **7a**: yield 62%; $[\alpha]_D^{20}$ = +122, *c* 0.0043, MeOH; IR (neat) 1746, 1660 cm^{-1}; ^{1}H NMR δ 6.15 (d, J = 3.9 Hz, 1H), 5.25 (d, J = 6.0 Hz, 1H), 5.21−5.19 (m, 1H), 5.19−5.16 (m, 1H), 4.90 (d, J = 5.7 Hz, 1H), 4.58 (d, J = 3.9 Hz, 1H), 4.48 (d, J = 1.8 Hz, 1H), 4.24−4.20 (m, 1H), 4.18−4.15 (m, 1H), 3.86−3.82 (m, 1H) 3.81 (s, 6H), 3.80−3.76 (m, 1H), 3.66 (s, 4H), 3.59−3.50 (m, 2H), 2.79 (dd, J = 7.5, 5.4 Hz, 2H), 1.73−1.29 (m, 12H); MS *m*/*z* 498.6 (MNa^+); HRMS *m*/*z* calcd for $C_{22}H_{37}NO_{10}$ 475.2417, found 475.2426.

6-*O*-[Bis(carboxymethyl)aminopropyl]-α,*β*-D-glucopyranose (15a). Compound **14a** (117 mg, 0.29 mmol, 1 equiv) was dissolved in a 1 M solution of NaOH (1 mL). After 2 h of stirring at rt, the solution was neutralized by addition of Dowex 50W-X8 till pH 5−6 was attained. The solution was then filtered and evaporated to afford an oil: yield 78%; IR (neat) 1716, 1654, 1560 cm^{-1}; ^{1}H NMR (CD_3OD) δ 5.94 (d, J = 3.9 Hz, 0.5H), 5.09 (d, J = 6.3 Hz, 0.5H), 5.07−5.02 (m, 1H), 5.01−4.96 (m, 1H), 4.70 (d, J = 6.6 Hz, 0.5H), 4.54−4.39 (m, 0.5H), 4.39−4.28 (m, 0.5H), 4.17−3.92 (m,1.5H), 3.86−3.65 (m, 1H), 3.76 (s, 2H), 3.74 (s, 2H), 3.56−3.47 (m, 2H), 3.43−2.30 (m, 2H), 1.89−1.76 (m, 2H); MS *m*/*z* 356.1 (MH_3^+). Anal. Calcd for $C_{13}H_{23}NO_{10}$ (353.13): C, 44.19; H, 6.56; N, 3.96. Found: C, 44.05; H, 6.61; N, 4.08.

6-*O*-[Bis(carboxymethyl)aminooctyl]-α,*β*-D-glucopyranose (15b). Compound **15b** was prepared from **14b** according to the preparation of **9a**: yield 77%; IR (neat) 1602, 1402 cm^{-1}; ^{1}H NMR (CD_3OD) δ 6.14 (d, J = 6.5 Hz, 0.6H), 5.18−5.09 (m, 2.4H), 4.70−4.64 (m, 1H), 4.59 (s large, 1H), 4.39−4.32 (m, 1H), 4.13−3.98 (s large, 1H), 4.08−3.96 (m, 1H), 3.85 (s large, 1H), 3.81−3.59 (m, 4H), 3.34−3.02 (m, 2H), 1.84−1.32 (m,

12H); MS *m*/*z* 423.1 (M). Anal. Calcd for $C_{18}H_{33}NO_{10}$ (423.21): C, 51.05; H, 7.85; N, 3.31. Found: C, 50.98; H, 7.88; N, 3.39.

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Supporting Information Available: ^{1}H NMR spectra of all the products and ^{13}C NMR spectra of **5b**, **5d**, **7b**, **7c**, **8c**, **9c**, **12b**, and **14a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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