Synthesis of Cluster *N*-Glycosides Based on a β-Cyclodextrin Core

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Abstract: A convenient method for the synthesis of β-D-gluco-, β-D-galacto-, 2-acetamido-2-deoxy-β-D-gluco- and α-D-mannopyranosylamine clusters based on cyclomaltoheptaose (β-cyclodextrin) is presented. The synthesis involves: 1) the one-pot synthesis of the acetylated chloroacetyl *N*-glycoside derivatives of D-glucose, D-galactose, 2-acetamido-2-deoxy-D-glucose and D-mannose from the corresponding glycosyl azides, 2) conversion of the chloroacetyl *N*-glycosides into their isothiouronium derivatives, then 3) attachment of the *N*-glycosides onto heptakis(6-deoxy-6-iodo) and heptakis(6-chloroacetamido-6-deoxy) β-cyclodextrin by means of nucleophilic displacement with caesium carbonate in dimethylformamide, and 4) de-*O*-acetylation of β-cyclodextrin derivatives. The chloroacetyl *N*-glycoside derivatives were easily prepared by mild reduction of the azide function by one of two methods: a) by the Staudinger reaction, with nBu$_3$P, and b) with 1,3-propanedithiol, as reducing reagents.

Keywords: carbohydrates · cluster glycosides · cyclodextrins · glycosylamines · Staudinger reaction

Introduction

The construction of systems that can selectively deliver bioactive molecules to their sites of action within the organism is currently a challenge in therapeutics. In this respect, much effort has been focused on exploitation of the host-guest properties of certain molecules such as cyclodextrins.[1–3] The cyclodextrins (CDs) are cyclomaltooligosaccharides with six (α-CD), seven (β-CD) and eight (γ-CD) α-(1$\rightarrow$4)-D-glucopyranosyl units, respectively, that are formed during the enzymatic degradation of starch.[1, 2] Most applications of CDs are based on their ability to include spatially compatible molecules (guest molecules) in their hydrophobic cavity to yield inclusion complexes[3] without formation of any covalent bonds. This supramolecular property can be used for the solubilization, encapsulation and transport of bioactive molecules by CDs and their derivatives.[4] Nevertheless, CD – drug inclusion complexes exhibit very poor target specificity owing to the lack of biologically recognizable sites. Several researchers are addressing this problem using CDs conjugated with target molecules with promising results, for example, increases in both water solubility and recognition properties of the carrier systems.[5]

Oligosaccharides are known to play important roles in many biological events, for example as cell-surface receptors which enable adhesion of bacteria, parasites, and viruses in the early stages of infection.[6] Therefore, carbohydrates involved in recognition processes are good candidates for targetting molecules. However, unlike protein – protein interactions, carbohydrate – protein interactions usually have low dissociation constants.[7] An effective means to increase binding interactions between carbohydrates and proteins is the use of clusters of carbohydrates.[8] With the aim of achieving much stronger affinity between receptors and saccharides, several authors have reported the synthesis of multivalent glycoconjugates on scaffolds of polymers and oligomers,[9–10] dendrimers,[10–13] calix[4]arenes,[14] crown ethers,[15] surfactant aggregates,[16] and metal complexes.[17]

The well-defined torus-shaped structures of CDs provide a versatile scaffold for the construction of branched structures of bioactive molecules. In our research project we intend to combine the scaffolding potential of the CDs for building multivalent or dendrimerlike molecules with their host – guest properties, in order to develop drug carrier systems. Previously we have reported the synthesis of a variety of persubstituted β-CD derivatives branched with *O*- and *S*-glycosides and their recognition studies towards cell-wall specific lectins.[18]

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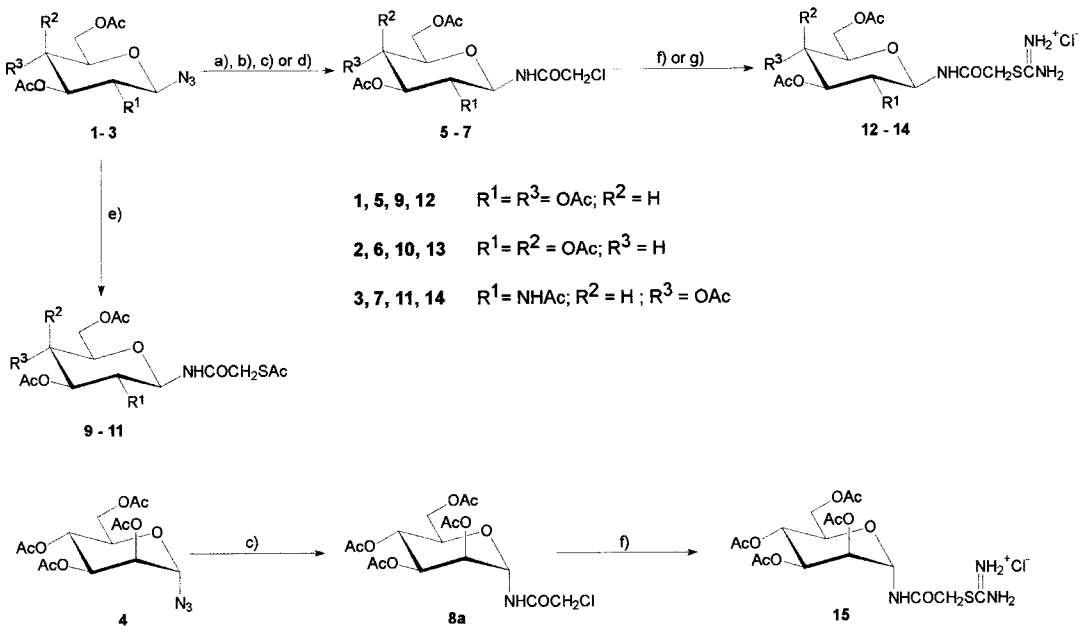


Scheme 1. Synthesis of the glycopyranosylamine derivatives **5**–**15** from the corresponding glycosyl azide derivatives **1**–**4**. Reagents and conditions: a) Bu_3P/CH_2Cl_2, RT, then $(ClCH_2CO)_2O/CH_2Cl_2$, $-80\,^{\circ}C \rightarrow$RT: **5** (68%), **6** (73%); b) Bu_3P/CH_2Cl_2, 1 h, RT, then $(ClCH_2CO)_2O/Et_3N/CH_2Cl_2$, $-80\,^{\circ}C \rightarrow$RT: **7** (36%); c) $(ClCH_2CO)_2O/CH_2Cl_2$, $-80\,^{\circ}C$ then Bu_3P, 3 h $\rightarrow$RT: **7** (67%), **8a** (80%); d) Et_3N/1,3-propanedithiol/MeOH, 3–6 h, then $(ClCH_2CO)_2O$, 2–10 h: **5** (68%), **6** (76%), **7** (74%); e) Bu_3P/CH_2Cl_2, RT, then $(ClCH_2CO)_2O/CH_2Cl_2$, $-80\,^{\circ}C \rightarrow$RT, then AcSH/$Et_3N$, 2–10 h, **9** (88%), **10** (83%), **11** (37%); f) $(NH_2)_2CS/(CH_3)_2CO$, 72 h: **12** (82%), **13** (65%), **15** (80%); g) $(NH_2)_2CS/(CH_3)_2CO/CH_2Cl_2$, 168 h, **14** (78%).

In this paper we describe the synthesis of β-CD persubstituted with glycosyl amide derivatives. Most methods for the synthesis of glycosyl amides involve either the reaction of a nonprotected carbohydrate with aqueous ammonium bicarbonate or the reduction of the corresponding azide derived from a protected glycosyl halide and then acylation of the obtained glycosylamine.[19] Both methods sometimes present problems as a result of the formation of undesired byproducts. The conversion of glycosyl azides into *N*-glycoside derivatives by the Staudinger reaction[20] provides an alternative mild route for the synthesis of *N*-glycosides. For example, glycofuranosyl formamides have been prepared by treatment of phosphinimines derived from the corresponding glycosyl azides with acetic formic anhydride,[21] and sugar ureas have been obtained from glycosyl triphenylphosphinimines by treatment with amines and carbon dioxide.[22]

Our interest in the synthesis of a set of glycosyl amide building blocks suitable for their convenient attachment to β-CD templates led us to explore a more efficient conversion of glycosyl azides into *N*-glycosides, as reported in an earlier communication.[23]

Abstract in Spanish: *Se describe un método práctico para la síntesis de clusters de β-D-gluco-, β-D-galacto-, 2-acetamido-2-desoxi-β-D-gluco- y α-D-manopiranosilaminas unidas a ciclomaltoheptaosa (β-ciclodextrina). La síntesis lleva consigo: 1) la síntesis one-pot de los cloroacetil N-glicósidos acetilados derivados de D-glucosa, D-galactosa, 2-acetamido-2-desoxi-D-glucosa y D-manosa a partir de las correspondientes glicosil azidas; 2) la conversión de los N-glicósidos en sus derivados isotiouronio; a continuación, 3) unión de los N-glicósidos con la heptakis(6-desoxi-6-yodo) y heptakis(6-cloroacetamido-6-desoxi) β-ciclodextrina por medio de una reacción de desplazamiento nucleofílico utilizando carbonato de cesio en dimetilformamida; y 4) des-O-acetilación de los derivados de β-ciclodextrina. Los derivados cloroacetil N-glicósidos se prepararon por reducción suave de la función azida siguiendo dos métodos: a) vía reacción de Staudinger, con nBu3P, y b) utilizando 1,3-propanoditiol, como agentes reductores.*

Results and Discussion

Our synthetic plan involves the preparation of thiolated glycosyl amide building blocks in order to perform attachment to β-CD by a nucleophilic substitution reaction. We first studied the synthesis by the Staudinger reaction of the chloroacetyl *N*-glycosides **5**–**8a** from glycosyl azides **1**–**3**[24] and **4**.[25] Thus, the glucopyranosyl **1** and galactopyranosyl azide **2** derivatives were treated sequentially with $n$$Bu_3P$ at room temperature and chloroacetic anhydride at $-80\,^{\circ}C$ in dry CH_2Cl_2, and the glycosyl amides **5** and **6** in 68 and 73% yields, respectively, were isolated in one pot after chromatographic purification (Scheme 1). We had previously observed that the reaction of **1** with Ph_3P occurred slowly, so we used the more nucleophilic reagent $n$$Bu_3P$. Reaction of the *N*-acetylglucosamine derivative **3** with $n$$Bu_3P$ and chloroacetic anhydride under the same conditions did not yield the glycosyl amide **7**, although TLC showed that the starting material was not present in the reaction mixture after 1 h. We

0947-6539/99/0506-1776 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 6

attributed this particular result to the poor reactivity of the phosphinimine intermediate due to a lower nucleophilicity of the phosphinimine nitrogen. This reactivity decrease might be brought about by a hydrogen bond between that nitrogen and the amide hydrogen. In fact, the addition of triethylamine after chloroacetic anhydride allowed the isolation of the desired *N*-glycoside **7**, although in 36% yield (Scheme 1).

Application of the conditions mentioned above to mannopyranosyl azide derivative **4** gave an approximately 3.1:2 mixture of α anomer **8a** and β anomer **8b** that could not be separated by column chromatography.[23b] When compounds **3** and **4** were treated dropwise with nBu$_3$P in the presence of chloroacetic anhydride at $-80\,^{\circ}$C in dry CH_2Cl_2, the *N*-glycosides **7** and **8a** were isolated in 67 and 80% yields, respectively, after chromatographic purification (Scheme 1). Under these reaction conditions compound **8a** was the only anomer observed by TLC. The configurations at the anomeric positions in **8a** and **8b** could be established from the NMR data obtained from the pure compound **8a** and the mixture **8a** + **8b**.[26] The isomers **8a** and **8b** exhibited $J_{1,2}$ values larger than those normally observed in $^4C_1$ conformations of D-mannopyranosides ($J_{1,2} = 4.8$ and 1.4 Hz for the α anomer **8a** and the β anomer **8b**, respectively). However, $^1J_{C1,H1}$ values of 165 and 156 Hz for **8a** and **8b**, respectively, were in accord with an equatorial H-1 for **8a** and axial H-1 for **8b.** In addition, a NOESY spectrum of the **8a**/**8b** mixture showed a correlation between NH, H-3 and H-5 for the major isomer **8a** and no such correlation for the minor isomer, as well as a correlation between H-1, H-3 and H-5 for **8b** and no such correlation for the major isomer.

We also investigated an alternative method with 1,3-propanedithiol as reducing reagent.[27] We found that reaction of compounds **1–3** with 1,3-propanedithiol and triethylamine in anhydrous methanol followed by treatment with chloroacetic anhydride afforded the *N*-glycosides **5–7** in 68, 76 and 74% yields, respectively (Scheme 1).

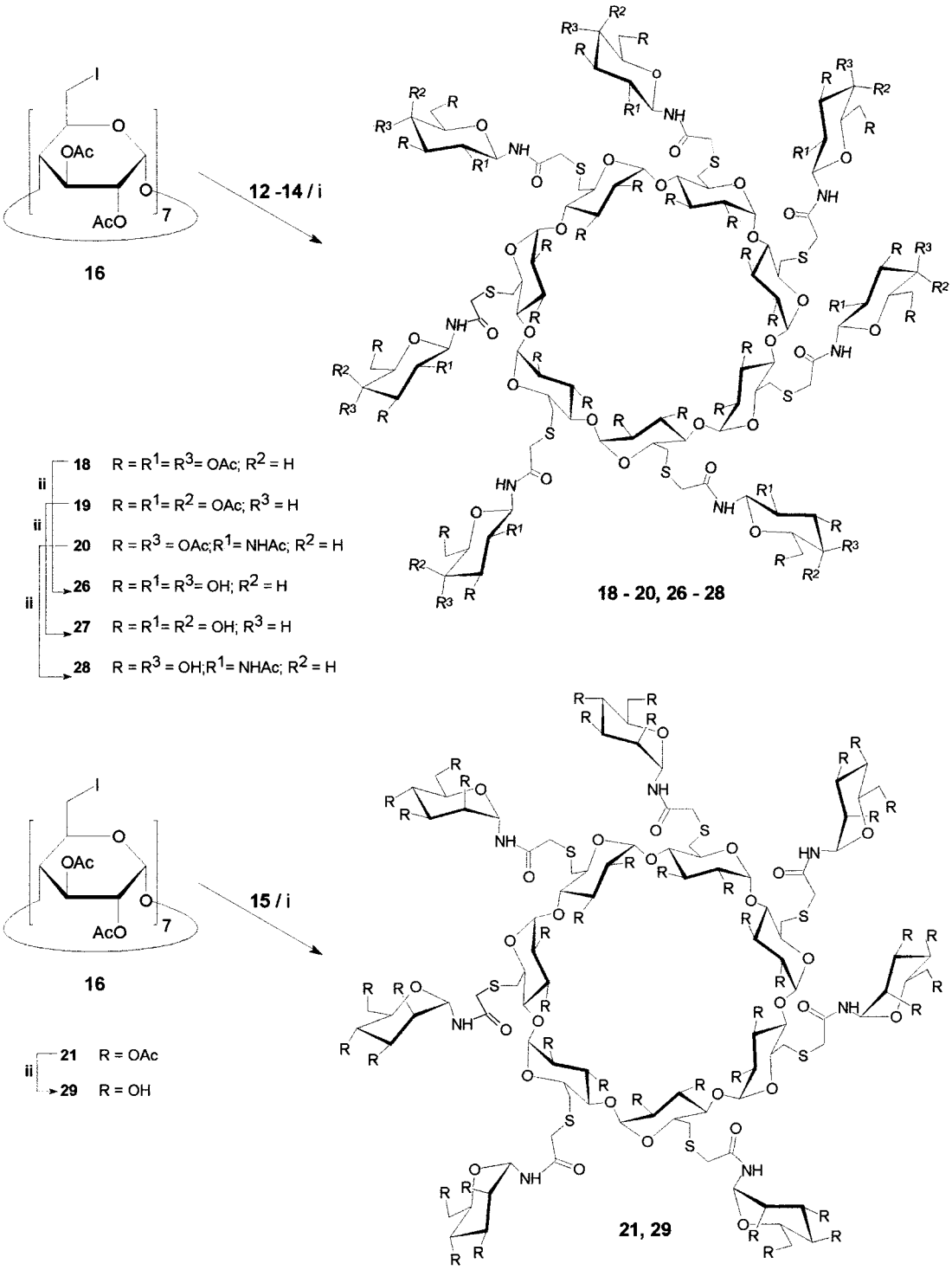
To synthesize the thiolated *N*-glycosides **9–11**, compounds **1–3** were subjected to the reaction conditions described above: first treatment with nBu$_3$P, then chloroacetic anhydride, followed by a subsequent treatment with thioacetic acid and triethylamine after completion of the chloroacetylation reaction monitored by TLC. The *S*-acetylmercaptoacetyl *N*-glycosides **9–11** were then isolated in 88, 83 and 37% yields, respectively (Scheme 1).

First attempts to introduce the *N*-glucopyranosyl moiety in the β-CD involved the de-*O*,*S*-acetylation of **9** under standard Zemplén conditions as well as selective de-*S*-acetylation of **9** with hydrazinium acetate, and then reaction of the resulting products with the β-CD derivative **16** in the presence of DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) or Cs_2CO_3. Both attempts failed, probably owing to the lack of stability of the thiol derivative. In the course of an ongoing parallel research[18] we found that glycosyl isothiouronium salts can be employed as latent thiolate nucleophiles, thus avoiding side reactions. These compounds react with alkyl halides, such as **16** and **17**, in the presence of Cs_2CO_3 to give sulfide derivatives. Therefore *N*-chloroacetylated glycosides **5–8** were transformed into their isothiouronium salts **12–15** by treatment with thiourea. Compounds **12–15** were isolated in 82, 65, 78 and 80% yields, respectively, by precipitation (Scheme 1).

Reaction of the isothiouronium derivatives **12–15** with β-CD derivatives was carried out at room temperature in dry DMF under an argon atmosphere with two molar equivalents of *N*-glycoside and 2–3 equiv of Cs_2CO_3 for every primary halogen group of **16** and **17**. After several days, the reaction led to a mixture of products, as indicated by TLC; then acetic anhydride, pyridine and 4-dimethylaminopyridine (4-DMAP) were added. The peracetylation reaction was kept at 40 °C for 48 h and then the branched β-CD derivatives **18–25** were isolated in excellent yields. Zemplén deacetylation of compounds **18–25** furnished the β-CD derivatives branched with *N*-glycosides through the spacer chain $COCH_2S$ **26–29** in 94–96% yields (Scheme 2) and through the spacer chain $COCH_2SCH_2CONH$ **30–33** in 90–94% yields (Scheme 3).

Branched β-CDs **18–33** were characterized by NMR spectroscopic techniques and FAB mass spectrometry. The room-temperature ^{1}H NMR spectra showed a considerable broadening of the signals; this indicates a restricted mobility on the NMR time scale. When measurements of the NMR data were performed at 80–100 °C, the resolution of the spectra was improved considerably, allowing the assignment of the spectroscopic signals. For the peracetylated compounds **18–25**, the NMR signals were assigned on the basis of COSY and HMQC experiments. The success of the nucleophilic perdisplacement became evident from the seven-fold symmetry of the products as deduced from NMR experiments. Only two anomeric carbon signals were observed at $\delta = 96.1$–101.9 for C-1 and 75.2–80.0 for C-1′ as well as three methylene carbon signals for compounds **18–21** and **26–29** at 33.1–34.9 (C-6), 36.2–37.6 (CH_2S) and 60.4–61.9 (C-6′), and four for compounds **22–25** and **30–33** at 39.1–40.1 (C-6), 34.4–34.9 (2 CH_2S) and 60.4–61.7 (C-6′). From the ^{1}H NMR, the appearance of new signals such as those corresponding to the anomeric H-1′ of the *N*-glycosides ($\delta = 5.34$–5.60) clearly established the assembly of the glycosyl amide building blocks onto the β-CD derivatives.

In summary, we report a very convenient method for the attachment of *N*-glycoside derivatives onto β-CD. The method involves the use of chloroacetyl *N*-glycoside building blocks ready for their conversion into isothiouronium derivatives and then incorporation onto the β-CD by a nucleophilic displacement reaction. The building blocks were also easily prepared by two convenient one-pot syntheses, by the Staudinger reaction or with 1,3-propanedithiol as reducing reagent, from the corresponding glycosyl azides. This methodology could be applied to the rapid preparation of *N*-glycodendrimers from, for example, multivalent *N*-chloroacetylated molecules. The two concepts, that is, the ability to bind guest molecules and multivalency, converge in the structure of the branched β-CDs and therefore constitute potential drug delivery systems. The next stage in our research project is the enhancement of the multivalency by the synthesis of *N*-glycodendrimerlike structures based on CD cores. This is currently under development in our laboratories.

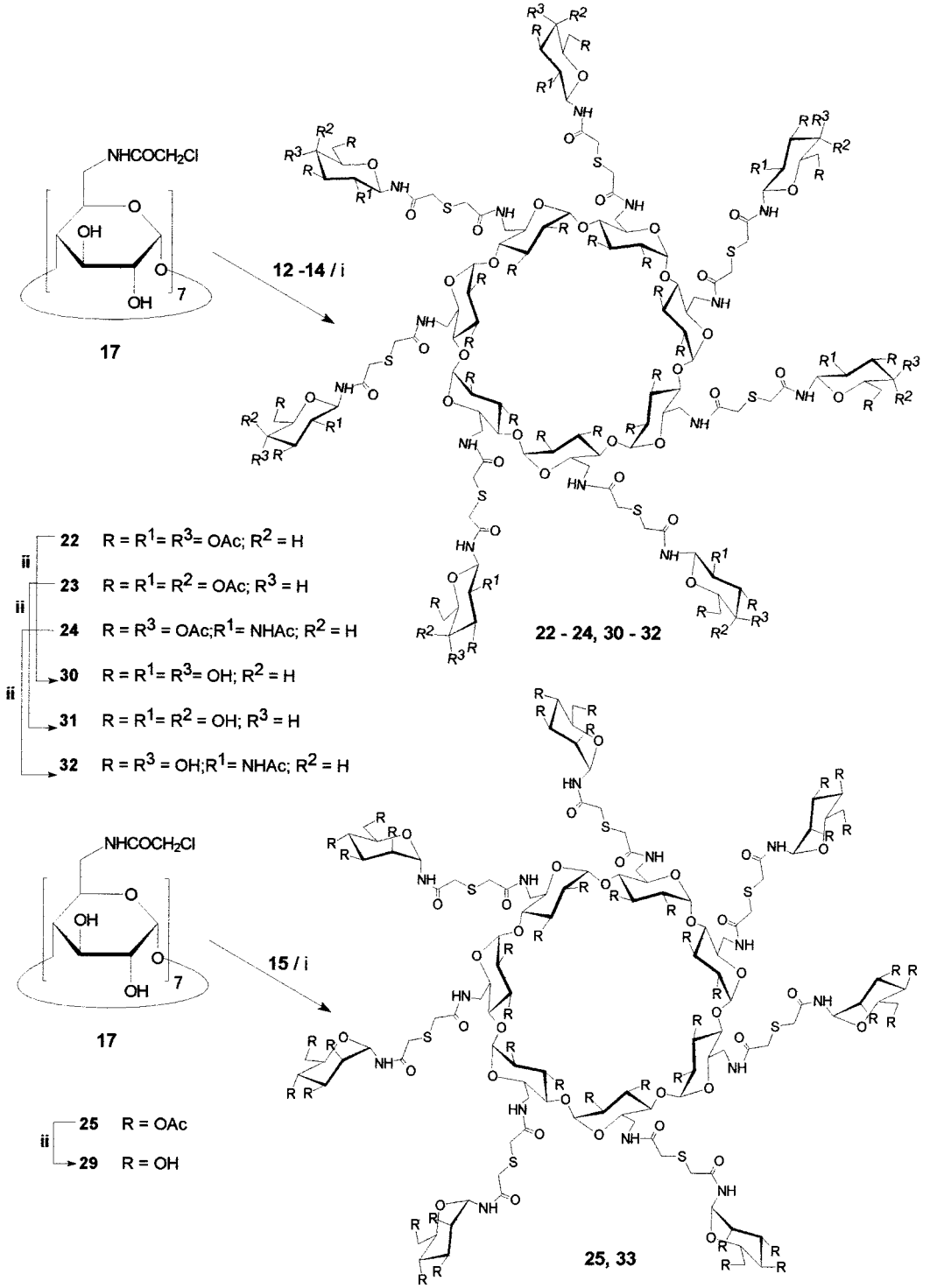


Scheme 2. Synthesis of the branched β-cyclodextrin derivatives **18**–**21** and **26**–**29**. Reagents and conditions: i) a) Cs_2CO_3/DMF, 7 d, RT; b) Ac_2O/Py, 48 h, 40 °C: **18** (92%), **19** (94%), **20** (95%), **21** (87%); ii) NaOMe/MeOH, 10 h, RT: **26** (96%), **27** (94%), **28** (95%), **29** (94%).

Experimental Section

TLC was performed on Merck silica gel $60F_{254}$ aluminium sheets with detection by charring with 5% H_2SO_4 in EtOH, and by UV light when applicable. Flash column chromatography was performed on silica gel Scharlau (230–400 mesh, ASTM). Melting points were measured on a Büchi melting point B-540 apparatus and a Reichter hotplate microscope and are uncorrected. Elemental analyses were carried out with Perkin–Elmer 240C and LECO 932 instruments. Optical rotations were recorded on a Perkin–Elmer 141 polarimeter at room temperature (22 ± 2 °C). IR spectra were recorded on a Perkin–Elmer 983G and ATI Mattson FTIR. ^{1}H and ^{13}C NMR spectra were recorded at room temperature, unless otherwise specified, on a Bruker AM300 and Bruker NMR Avance DPX300 spectrometers. ^{1}H chemical shifts are given in ppm and referenced to internal $CHCl_3$ ($\delta = 7.26$) for $CDCl_3$ solutions, $(CH_3)_2SO$ ($\delta = 2.6$) for $(CD_3)_2SO$ solutions and HOD ($\delta = 4.79$) for D_2O solutions. ^{13}C chemical shifts are given in ppm and referenced to $CDCl_3$ ($\delta = 77.0$), $(CD_3)_2SO$ ($\delta = 39.5$) and external acetone ($\delta = 30.5$) for D_2O solutions. *J* values are given in Hz. Assignments were based on COSY, HMQC,

0947-6539/99/0506-1778 $ 17.50+.50/0 *Chem. Eur. J.* **1999**, *5*, No. 6



Scheme 3. Synthesis of the branched β-cyclodextrin derivatives **22**–**25** and **30**–**33**. Reagents and conditions: i) a) Cs_2CO_3/DMF, 7 d, RT; b) Ac_2O/Py, 48 h, 40 °C: **22** (71 %), **23** (81 %), **24** (84 %), **25** (80 %); ii) NaOMe/MeOH, 10 h, RT: **30** (92 %), **31** (90 %), **32** (94 %), **33** (93 %).

NOESY, DEPT and APT. Mass spectra were recorded on a Micromass Autospec-Q and LC-API-MS spectrometers. Anhydrous solvents were prepared according to standard procedures,[28] and were freshly distilled prior to use.

2,3,4,6-Tetra-*O*-acetyl-*N*-chloroacetyl-β-D-glucopyranosylamine (5):

With nBu_3P (procedure A): nBu_3P (3.26 mL, 13.2 mmol) was added dropwise to a solution of the glycosyl azide **1**[24] (4.06 g, 11.0 mmol) in anhydrous CH_2Cl_2 (40 mL) at room temperature under Ar. Gas evolution was observed to have ceased after 1 h; thereupon, the reaction mixture was cooled to −80 °C, and a solution of chloroacetic anhydride (3.0 g, 17.6 mmol) in anhydrous CH_2Cl_2 (10 mL) was added. The reaction mixture was allowed to warm to room temperature and kept overnight. CH_2Cl_2 (150 mL) was added and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 150 mL) and H_2O (2 × 100 mL). The organic layer was dried ($MgSO_4$), filtered, evaporated, and the crude product chromatographed on silica gel (ether) to give **5** (3.14 g, 68 %) as a solid.

With 1,3-propanedithiol: 1,3-Propanedithiol (0.301 mL, 3.0 mmol) and Et_3N (0.416 mL, 3 mmol) were added to a solution of compound **1** (1.5 mmol) in anhydrous MeOH (8 mL) under Ar. The solution was stirred

at room temperature for 2 h and then, chloroacetic anhydride (1.49 g, 8.7 mmol) was added. After 2 h at room temperature, the solvent was evaporated and the crude product chromatographed on silica gel (ether) to give **5** (431 mg, 68 %).

M.p. 167–168 °C; $[\alpha]_D = +8$ ($c = 1$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.31$ (d, 1 H, $^3J_{NH,1} = 9.2$ Hz, NH), 5.33 (t, 1 H, $^3J = 9.5$ Hz, H-3), 5.21 (dd, 1 H, $^3J_{1,2} = 9.5$ Hz, $^3J = 9.2$ Hz, H-1), 5.09 (dd, 1 H, $^3J_{4,5} = 10.1$ Hz, $J_{3,4} = 9.5$ Hz, H-4), 5.01 (t, 1 H, $^3J = 9.5$ Hz, H-2), 4.31 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6} = 4.4$ Hz, H-6), 4.10 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6'} = 2.1$ Hz, H-6′), 4.07 (d, 1 H, $^2J = 15.4$ Hz, CHCl), 4.00 (d, 1 H, $^2J = 15.4$ Hz, CH′Cl), 3.84 (ddd, 1 H, $^3J_{4,5} = 10.1$ Hz, $^3J_{5,6} = 4.4$ Hz, $^3J_{5,6'} = 2.1$ Hz, H-5), 2.09 (s, 3 H, CH_3CO), 2.06 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 170.9$–166.9 (5 C=O), 78.6 (C-1), 73.9, 72.6, 70.3, 68.1 (C-2, 3, 4, 5), 61.6 (C-6), 42.3 (CH_2Cl), 20.8–20.6 (4 CH_3CO); IR (KBr): $\nu = 3309$ (NH), 1748 (C=O), 1669, 1532 (CONH), 1378, 1225, 1039 (C–O) cm^{-1}; MS (FAB): $m/z = 424$ for $[M+1]$; $C_{16}H_{22}ClNO_{10}$ (423.8): calcd C 45.34, H 5.23, found C 45.00, H 5.28 %.

2,3,4,6-Tetra-*O*-acetyl-*N*-chloroacetyl-β-D-galactopyranosylamine (6):

With nBu_3P (Procedure A): This compound was prepared as described for **5** (Procedure A) with nBu$_3$P (0.94 mL, 3.75 mmol), compound **2**[24] (1.0 g, 2.68 mmol), anhydrous CH_2Cl_2 (20 mL), and chloroacetic anhydride (646 mg, 3.75 mmol) in anhydrous CH_2Cl_2 (5 mL). For the work-up, CH_2Cl_2 (100 mL) was added and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 75 mL) and H_2O (100 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated, and the crude product chromatographed on silica gel (ether) to give **6** (853 mg, 73 %) as a solid.

With 1,3-propanedithiol: Compound **6** was synthesized as described for **5** with the same amount of reagents and solvent. Similar work-up followed by column chromatography (ether) gave **6** (486 mg, 76 %).

M.p. 148–149 °C; $[\alpha]_D = +21$ ($c = 1$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.53$ (d, 1 H, $^3J_{NH,1} = 8.3$ Hz, NH), 5.46 (dd, 1 H, $^3J_{4,5} = 2.8$ Hz, $^3J_{3,4} = 0.8$ Hz, H-4), 5.17 (m, 3 H, H-1,2,3), 4.13 (m, 2 H, H-6,6′), 4.06 (m, 1 H, H-5), 4.09 (d, 1 H, $^2J = 15.5$ Hz, CHCl), 4.01 (d, 1 H, $^2J = 15.5$ Hz, CH′Cl), 2.16 (s, 3 H, CH_3CO), 2.07 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 170.9$–166.7 (5 C=O), 78.6 (C-1), 72.4, 70.6, 67.9, 67.1 (C-2, 3, 4, 5), 61.1 (C-6), 42.2 (1 CH_2Cl), 20.6–20.5 (4 CH_3CO); IR (KBr): $\nu = 3314$ (NH), 1749, 1724 (C=O), 1698, 1549 (CONH), 1370, 1227, 1086 cm^{-1} (C–O); MS (FAB): $m/z = 424$ for $[M+1]$; $C_{16}H_{22}ClNO_{10}$ (423.8): calcd C 45.34, H 5.23, found C 45.25, H 5.60 %.

2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-chloroacetyl-2-deoxy-β-D-glucopyranosylamine (7):

With nBu_3P (Procedure A): nBu$_3$P (0.30 mL, 1.2 mmol) was added dropwise to a solution of the glycosyl azide **3**[24] (372 mg, 1.0 mmol) in anhydrous CH_2Cl_2 (15 mL) at room temperature under Ar. Gas evolution ceased after 1 h; thereupon, the reaction mixture was cooled to −80 °C, and a solution of chloroacetic anhydride (264 mg, 1.5 mmol) in anhydrous CH_2Cl_2 (5 mL) and Et_3N (0.5 mL) was added. The reaction mixture was allowed to warm to room temperature and kept overnight. CH_2Cl_2 (50 mL) was added and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 50 mL) and H_2O (50 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated, and the crude product chromatographed on silica gel (EtOAc) to give **7** (150 mg, 36 %) as a solid.

By Procedure B: nBu$_3$P (4.02 mL, 16.1 mmol) was added dropwise to a solution of chloroacetic anhydride (2.482 g, 14.51 mmol) and glycosyl azide **3** (3.0 g, 8.1 mmol) in anhydrous CH_2Cl_2 (40 mL) at −80 °C under Ar. The reaction mixture was allowed to warm to room temperature and kept overnight. CH_2Cl_2 (150 mL) was added, and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 150 mL) and H_2O (2 × 100 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated, and the crude product chromatographed on silica gel (EtOAc) to give **7** (2.28 g, 67 %).

With 1,3-Propanedithiol: 1,3-Propanedithiol (0.1 mL, 2 mmol) and Et_3N (0.14 mL, 2 mmol) were added to a solution of compound **3** (372 mg, 1 mmol) in anhydrous MeOH (10 mL) under Ar. The solution was stirred at room temperature for 6 h and then chloroacetic anhydride (1.026 g, 6 mmol) was added. After 18 h at room temperature the solvent was evaporated and the crude product chromatographed on silica gel (EtOAc) to give **7** (315 mg, 74 %).

M.p. 162 °C (decomp); $[\alpha]_D = -6$ ($c = 1$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.88$ (d, 1 H, $^3J_{NH,1} = 8.2$ Hz, NH), 6.06 (d, 1 H, $^3J_{NH,2} = 8.2$ Hz, NH), 5.14 (t, 1 H, $^3J = 9.8$ Hz, H-4), 5.07 (t, 1 H, $^3J = 9.8$ Hz, H-3), 5.03 (dd, 1 H, $^3J_{1,2} = 9.8$ Hz, $^3J_{NH,1} = 8.2$ Hz, H-1), 4.30 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6} = 4.2$ Hz, H-6), 4.22 (dt, 1 H, $^3J = 9.8$ Hz, $^3J_{NH,2} = 8.2$ Hz, H-2), 4.09 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6'} = 2.3$ Hz, H-6′), 4.04 (d, 1 H, $^2J = 15.1$ Hz, CHCl), 3.96 (d, 1 H, $^2J = 15.1$ Hz, CH′Cl), 3.78 (ddd, 1 H, $^3J_{4,5} = 9.8$ Hz, $^3J_{5,6} = 4.2$ Hz, $^3J_{5,6'} = 2.3$ Hz, H-5), 2.09 (s, 3 H, CH_3CO), 2.08 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 1.96 (s, 3 H, CH_3CON); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 172.0$–167.4 (5 C=O), 80.6 (C-1), 73.6, 72.7, 67.5 (C-3, 4, 5), 61.6 (C-6), 53.0 (C-2), 42.2 (CH_2Cl), 23.0 (CH_3CON), 20.7–20.6 (3 CH_3CO); IR (KBr): $\nu = 3456$, 3313, 1738, 1693, 1660, 1529, 1376, 1230, 1040 cm^{-1}; MS (FAB): $m/z = 423$ for $[M+1]$; $C_{16}H_{23}ClN_2O_9$ (422.8): calcd C 45.45, H 5.48, found C 45.84, H 5.59 %.

2,3,4,6-Tetra-*O*-acetyl-*N*-chloroacetyl-α-D-mannopyranosylamine (8a): This compound was prepared as described for **8** (Procedure B) with nBu$_3$P (5.12 mL, 20.5 mmol), chloroacetic anhydride (3.161 g, 18.5 mmol), compound **4**[25] (3.83 g, 10.3 mmol), and anhydrous CH_2Cl_2 (60 mL). The mixture was worked up as described and the purification was performed with column chromatography (ether), and **8** was isolated (3.5 g, 80 %) as a solid: m.p. 117 °C; $[\alpha]_D = +29$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.30$ (d, 1 H, $^3J_{NH,1} = 8.4$ Hz, NH), 5.63 (dd, 1 H, $^3J_{NH,1} = 8.4$ Hz, $^3J_{1,2} = 4.8$ Hz, H-1), 5.27 (dd, 1 H, $^3J_{3,4} = 6.2$ Hz, $^3J_{2,3} = 2.2$ Hz, H-3), 5.26 (dd, 1 H, $^3J_{1,2} = 4.8$ Hz, $^3J_{2,3} = 2.2$ Hz, H-2), 5.14 (t, 1 H, $^3J = 6.2$ Hz, H-4), 4.43 (dd, 1 H, $^2J_{6,6'} = 12.1$ Hz, $^3J_{5,6} = 6.6$ Hz, H-6), 4.23 (dd, 1 H, $^2J_{6,6'} = 12.1$ Hz, $^3J_{5,6'} = 4.0$ Hz, H-6′), 4.10 (d, 1 H, $^2J = 15.4$ Hz, CHCl), 4.06 (d, 1 H, $^2J = 15.4$ Hz, CH′Cl), 4.02 (ddd, 1 H, $J_{5,6} = 6.6$ Hz, $J_{4,5} = 6.2$ Hz, $J_{5,6'} = 4.0$ Hz, H-5), 2.11 (s, 3 H, CH_3CO), 2.09 (s, 9 H, 3 CH_3CO); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 170.6$–166.4 (5 C=O), 74.5 (C-1), 72.0 (C-5), 68.5, 67.8 (C-2, 3), 66.9 (C-4), 61.3 (C-6), 42.4 (CH_2Cl), 20.7 (4 CH_3CO); IR (KBr): $\nu = 3454$, 1749, 1684, 1547, 1374, 1227, 1056 cm^{-1}; MS (FAB): $m/z = 424$ for $[M+1]$; $C_{16}H_{22}ClNO_{10}$ (423.8): calcd C 45.34, H 5.23, found C 45.28, H 5.36 %.

2,3,4,6-Tetra-*O*-acetyl-*N*-(*S*-acetylmercaptoacetyl)-β-D-glucopyranosylamine (9): nBu$_3$P (0.94 mL, 3.75 mmol) was added dropwise to a solution of the glycosyl azide **1** (1.0 g, 2.68 mmol) in anhydrous CH_2Cl_2 (20 mL) at room temperature under Ar. Gas evolution ceased after 1 h; thereupon, the reaction mixture was cooled to −80 °C, and a solution of chloroacetic anhydride (0.646 mg, 3.75 mmol) in anhydrous CH_2Cl_2 (15 mL) was added. The reaction mixture was allowed to warm to room temperature and kept overnight. Then AcSH (0.9 mL, 11.26 mmol) and Et_3N (3 mL) were added. After 2 h at room temperature CH_2Cl_2 (150 mL) was added and the organic solution was washed with saturated aqueous $NaHCO_3$ (2 × 150 mL) and H_2O (2 × 100 mL). The organic layer was dried ($MgSO_4$), filtered and evaporated, and the crude product chromatographed on silica gel (hexane/EtOAc 3:2) to give **9** (1.1 g, 88 %) as a solid: m.p. 134–135 °C; $[\alpha]_D = -12$ ($c = 1$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.95$ (d, 1 H, $^3J_{NH,1} = 9.5$ Hz, NH), 5.29 (t, 1 H, $^3J = 9.5$ Hz, H-3), 5.19 (t, 1 H, $^3J = 9.5$ Hz, H-1), 5.06 (t, 1 H, $^3J = 9.5$ Hz, H-4), 4.92 (t, 1 H, $^3J = 9.5$ Hz, H-2), 4.29 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6} = 4.4$, H-6), 4.08 (dd, 1 H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6'} = 2.1$ Hz, H-6′), 3.81 (ddd, 1 H, $^3J_{4,5} = 9.5$ Hz, $^3J_{5,6} = 4.4$ Hz, $^3J_{5,6'} = 2.1$ Hz, H-5), 3.57 (d, 1 H, $^2J = 15.5$ Hz, CHS), 3.49 (d, 1 H, $^2J = 15.5$ Hz, CH′S), 2.44 (s, 3 H, CH_3COS), 2.09 (s, 3 H, CH_3CO), 2.03 (s, 3 H, CH_3CO), 2.01 (s, 3 H, CH_3CO); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 195.1$ (COS), 170.9–168.4 (4 C=O), 78.3 (C-1), 73.7, 72.7, 70.3, 68.2 (C-2, 3, 4, 5), 61.7 (C-6), 32.8 (CH_2S), 30.2 (CH_3COS), 20.8–20.6 (4 CH_3CO); IR (KBr): $\nu = 3339$, 1742, 1695, 1668, 1520, 1375, 1231, 1068, 1041 cm^{-1}; MS (FAB): $m/z = 464$ for $[M+1]$; $C_{18}H_{25}NO_{11}S$ (463.5): calcd C 46.65, H 5.44, found C 46.33, H 5.58 %.

2,3,4,6-Tetra-*O*-acetyl-*N*-(*S*-acetylmercaptoacetyl)-β-D-galactopyranosylamine (10): This compound was prepared as described for **9.** nBu$_3$P (3.24 mL, 12.90 mmol) was added to a solution of compound **2** (4.0 g, 10.72 mmol) in anhydrous CH_2Cl_2 (40 mL). Chloroacetic anhydride (2.75 g, 12.86 mmol) was added in anhydrous CH_2Cl_2 (15 mL). Then AcSH (3.05 mL, 42.88 mmol) and Et_3N (6 mL) were added. After 2 h the mixture was worked up and the product was purified by column chromatography (hexane/ether 1:5), and gave **10** (4.107 g, 83 %) as a solid: m.p. 68 °C; $[\alpha]_D = -7$ ($c = 1$ in chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.96$ (d, 1 H, $^3J_{NH,1} = 9.0$ Hz, NH), 5.38 (br d, 1 H, $^3J_{3,4} = 2.2$ Hz, H-4), 5.14 (t, 1 H, $^3J = 9.0$, H-1), 5.05 (m, 2 H, H-2, 3), 4.13–3.95 (m, 3 H, H-5, 6, 6′), 3.55 (d, 1 H, $^2J = 15.6$ Hz, CHS), 3.45 (d, 1 H, $^2J = 15.6$ Hz, CH′S), 2.40 (s, 3 H, CH_3COS),

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2.11 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.99 (s, 3H, CH_3CO), 1.93 (s, 3H, CH_3CO); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 195.0$ (COS), 170.9–168.2 (5 C=O), 78.4 (C-1), 72.3 (C-5), 70.6, 67.7 (C-2, 3), 67.0 (C-4), 61.1 (C-6), 32.6 (CH_2S), 30.1 (CH_3COS), 20.5–20.4 (4 CH_3CO); IR (KBr): $\nu = 3366$, 1749, 1697, 1532, 1369, 1226, 1084, 1052 cm^{-1}; MS (FAB): $m/z = 464$ for $[M+1]$; $C_{18}H_{25}NO_{11}S$ (463.5): calcd C 46.65, H 5.44, found C 46.44, H 5.27%.

2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-(*S*-acetylmercaptoacetyl)-2-deoxy-β-D-glucopyranosylamine (11): This compound was prepared following a protocol similar to that described for the preparation of **9**. nBu$_3$P (1.6 mL, 6.45 mmol) was added to a solution of **3** (2.0 g, 5.38 mmol) in anhydrous CH_2Cl_2 (25 mL). A solution of chloroacetic anhydride (1.38 g, 8.064 mmol) and Et_3N (0.5 mL) in anhydrous CH_2Cl_2 (15 mL) was added. After addition of AcSH (1.72 mL, 24.2 mmol) and Et_3N (3 mL) the reaction was left for 18 h. The mixture was worked up and the product was purified by column chromatography (EtOAc) to give **11** (927 mg, 37%) as a solid: m.p. 172 °C (decomp); $[\alpha]_D = -7$ ($c = 1$ in chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.47$ (d, 1H, $^3J_{NH,1} = 8.4$ Hz, NH), 6.16 (brs, 1H, NH), 5.1 (m, 3H, H-1, 3, 4), 4.29 (dd, 1H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6} = 4.1$ Hz, H-6), 4.15 (m, 1H, H-2), 4.09 (dd, 1H, $^2J_{6,6'} = 12.5$ Hz, $^3J_{5,6'} = 2.0$ Hz, H-6′), 3.80 (ddd, 1H, $^3J_{4,5} = 9.7$ Hz, $^3J_{5,6} = 4.1$ Hz, $^3J_{5,6'} = 2.0$ Hz, H-5), 3.60 (d, 1H, $^2J = 16.0$ Hz, CHS), 3.52 (d, 1H, $^2J = 16.0$ Hz, CH′S), 2.45 (s, 3H, CH_3COS), 2.09 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 1.93 (s, 3H, CH_3CON); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 171.8–168.8$ (5 C=O), 80.3 (C-1), 73.7, 72.9, 67.9 (C-3, 4, 5), 61.8 (C-6), 52.9 (C-2), 32.8 (CH_2S), 30.4 (CH_3COS), 22.9 (CH_3CN), 20.8–20.6 (3 CH_3CO); IR (KBr): $\nu = 3309$, 1749, 1662, 1535, 1375, 1242, 1047 cm^{-1}; MS (FAB): $m/z = 463$ for $[M+1]$; $C_{18}H_{26}N_2O_{10}S$ (462.5): calcd C 46.75, H 5.67, found C 46.69, H 5.58%.

2,3,4,6-Tetra-*O*-acetyl-*N*-(isothiouronium acetyl)-β-D-glucopyranosylamine hydrochloride (12): To a solution of **5** (2.33 g, 5.50 mmol) in dry acetone (30 mL) was added thiourea (627 mg, 8.25 mmol). The reaction mixture was stirred at room temperature for 72 h. The solution was concentrated to approximately 10 mL under reduced pressure without heating. The precipitated product was filtered off and **12** was isolated as a solid (2.26 g, 82%): m.p. 153 °C (decomp); $[\alpha]_D = +6$ ($c = 0.25$ in methanol); ^1H NMR (300 MHz, $(CD_3)_2SO$): $\delta = 9.44$ (m, 4H, 2 NH_2), 9.40 (d, 1H, $^3J_{NH,1} = 9.6$ Hz, NH), 5.51 (t, 1H, $^3J = 9.6$ Hz, H-1), 5.46 (t, 1H, $^3J = 9.6$ Hz, H-3), 5.00 (t, 1H, $^3J = 9.6$ Hz, H-4), 4.93 (t, 1H, $^3J = 9.6$ Hz, H-2), 4.25 (dd, 1H, $^2J_{6,6'} = 12.0$ Hz, $^3J_{5,6} = 4.7$ Hz, H-6), 4.22 (m, 1H, H-5), 4.21 (d, 1H, $^2J = 15.6$ Hz, CHS), 4.14 (d, 1H, $^2J = 15.6$ Hz, CH′S), 4.06 (dd, 1H, $^2J_{6,6'} = 12.0$ Hz, $^3J_{5,6'} = 3.3$ Hz, H-6′), 2.10 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.02 (s, 3H, CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$): $\delta = 170.0–169.0$ (5 C=O), 167.3 (C=N), 77.1 (C-1), 72.7 (C-3), 72.2 (C-5), 70.5 (C-2), 67.7 (C-4), 61.7 (C-6), 33.7 (CH_2S), 20.6–20.3 (4 CH_3CO); IR (KBr): $\nu = 3330$, 3069, 1742, 1660, 1584, 1433, 1366, 1262, 1047 cm^{-1}; HRMS (FAB): calcd for $C_{17}H_{26}N_3O_{10}SCl$ 464.1339, found 464.1337 for $[M - Cl]^+$.

2,3,4,6-Tetra-*O*-acetyl-*N*-(isothiouronium acetyl)-β-D-galactopyranosylamine hydrochloride (13): To a solution of **6** (1.46 g, 3.46 mmol) in dry acetone (10 mL) was added thiourea (262 mg, 3.456 mmol). The reaction mixture was stirred at room temperature for 120 h and then the precipitated product was filtered off, dissolved in H_2O (10 mL) and concentrated to dryness by lyophilization. Dry acetone (5 mL) was added to the resulting solid; this gave a precipitate that was filtered off, and **13** was isolated (1.295 g, 75%) as a solid: m.p. 134 °C; $[\alpha]_D = +37$ ($c = 0.5$ in methanol); ^1H NMR (300 MHz, $(CD_3)_2SO$): $\delta = 9.44$ (d, 1H, $^3J_{NH,1} = 9.3$ Hz, NH), 9.42 (brs, 4H, 2 NH_2), 5.46 (t, 1H, $^3J = 9.3$ Hz, H-1), 5.40 (dd, 1H, $^3J_{2,3} = 9.3$ Hz, $^3J_{3,4} = 3.5$ Hz, H-3), 5.38 (brs, 1H, H-4), 5.13 (t, 1H, $^3J = 9.3$ Hz, H-2), 4.44 (brt, 1H, H-5), 4.14 (dd, 1H, $^2J_{6,6'} = 11.2$ Hz, $^3J_{5,6} = 6.1$ Hz, H-6), 4.12 (brs, 2H, CH_2S), 4.07 (dd, 1H, $^2J_{6,6'} = 11.2$ Hz, $^3J_{5,6'} = 6.7$ Hz, H-6′), 2.20 (s, 3H, CH_3CO), 2.09 (s, 3H, CH_3CO), 2.08 (s, 3H, CH_3CO), 2.01 (s, 3H, CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$): $\delta = 169.7–169.1$ (5 C=O), 167.3 (C=N), 77.4 (C-1), 71.5 (C-5), 70.6 (C-3 or 4), 68.1 (C-2), 67.5 (C-4 or 3), 61.3 (C-6), 33.5 (CH_2S), 20.3–20.2 (4 CH_3CO); IR (KBr): $\nu = 3335$, 1748, 1653, 1542, 1371, 1231, 1052 cm^{-1}; HRMS (FAB): calcd for $C_{17}H_{26}N_3O_{10}SCl$ 464.1339, found 464.1330 for $[M - Cl]^+$.

2-Acetamido-3,4,6-tri-*O*-acetyl-*N*-(isothiouronium acetyl)-2-deoxy-β-D-glucopyranosylamine hydrochloride (14): To a solution of **7** (1.58 g, 3.74 mmol) in dry acetone (30 mL) and dry CH_2Cl_2 (30 mL) was added thiourea (426 mg, 5.61 mmol). The reaction mixture was stirred at room temperature for 7 d, and then CH_2Cl_2 (15 mL) was added. Filtration of the resulting precipitate gave **14** (1.46, 78%) as a solid: m.p. 149 °C (decomp); $[\alpha]_D = +20$ ($c = 0.25$ in methanol); ^1H NMR (300 MHz, $(CD_3)_2SO$): $\delta = 9.45$ (brs, 4H, 2 NH_2), 9.24 (d, 1H, $^3J_{NH,1} = 9.1$ Hz, NH), 8.11 (d, 1H, $^3J_{NH,2} = 8.8$ Hz, NH), 5.29 (t, 1H, $^3J = 9.4$ Hz, H-1), 5.24 (t, 1H, $^3J = 9.7$ Hz, H-3), 4.92 (t, 1H, $^3J = 9.7$ Hz, H-4), 4.27 (dd, 1H, $^2J_{6,6'} = 12.2$ Hz, $^3J_{5,6} = 4.2$ Hz, H-6), 4.13 (brs, 2H, CH_2S), 4.09 (dd, 1H, $^2J_{6,6'} = 12.2$ Hz, $^3J_{5,6'} = 2.2$ Hz, H-6′), 3.95 (m, 2H, H-5, 2), 2.09 (s, 3H, CH_3CO), 2.05 (s, 3H, CH_3CO), 2.00 (s, 3H, CH_3CO), 1.84 (s, 3H, CH_3CN); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$): $\delta = 170.0–169.3$ (5 C=O), 167.5 (C=N), 78.2 (C-1), 73.0 (C-3), 72.4 (C-5), 68.3 (C-4), 61.7 (C-6), 52.2 (C-2), 33.6 (CH_2S), 22.7 (CH_3CON), 20.6–20.4 (3 CH_3CO); IR(KBr): $\nu = 3228$, 1751.2, 1662, 1535, 1369, 1218, 1049 cm^{-1}; HRMS (FAB): calcd for $C_{17}H_{27}N_4O_9S$ (without Cl) 463.1499, found 463.1498 for $[M - Cl]^+$.

2,3,4,6-Tetra-*O*-acetyl-*N*-(isothiouronium acetyl)-α-D-mannopyranosylamine hydrochloride (15): To a solution of **8** (2.57 g, 6.0 mmol) in dry acetone (30 mL) was added thiourea (786 mg, 10.35 mmol). The reaction mixture was stirred at room temperature for 72 h. The solution was concentrated to approximately 10 mL under reduced pressure without heating. Filtration of the resulting precipitate gave **15** (2.057 g, 80%) as a solid: m.p. 159 °C (decomp); $[\alpha]_D = +54$ ($c = 0.5$ in methanol); ^1H NMR (300 MHz, $(CD_3)_2SO$): $\delta = 9.96$ (d, 1H, $^3J_{NH,1} = 9.1$ Hz, NH), 9.40 (brs, 4H, 2NH_2), 5.65 (dd, 1H, $^3J_{3,4} = 9.7$ Hz, $^3J_{2,3} = 3.6$ Hz, H-3), 5.56 (dd, 1H, $^3J_{NH,1} = 9.1$ Hz, $^3J_{1,2} = 1.7$ Hz, H-1), 5.20 (t, 1H, $^3J = 9.7$ Hz, H-4), 5.18 (dd, 1H, $^3J_{2,3} = 3.6$ Hz, $^3J_{1,2} = 1.7$ Hz, H-2), 4.33 (d, 1H, $^2J = 16.4$ Hz, CHS), 4.27 (d, 1H, $^2J = 16.4$ Hz, CH′S), 4.25 (dd, 1H, $^2J_{6,6'} = 12.0$ Hz, $^3J_{5,6} = 4.5$ Hz, H-6), 4.16 (m, 1H, H-5), 4.08 (dd, 1H, $^2J_{6,6'} = 12.0$ Hz, $^3J_{5,6'} = 2.2$ Hz, H-6′), 2.21 (s, 3H, CH_3CO), 2.12 (s, 3H, CH_3CO), 2.10 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$): $\delta = 170.1–169.4$ (5C=O), 167.0 (C=N), 75.7 (C-1), 69.3 (C-5), 69.0 (C-3), 68.3 (C-2), 65.8 (C-4), 61.8 (C-6), 33.7 (CH_2S), 20.7–20.4 (4 CH_3CO); IR (KBr): $\nu = 3370$, 1755, 1744, 1656, 1551, 1367, 1258, 1224, 1051 cm^{-1}; MS (ES): $m/z = 486$ for $[M - HCl+Na]^+$, 464 for $[M - Cl]$; $C_{17}H_{26}ClN_3O_{10}S$ (499.9): calcd C 40.84, H 5.24, found C 41.18, H 5.60%.

General procedure for the synthesis of *N*-GlycoCDs 18–25: A mixture of **16**[29b] (0.84 mmol for reactions with **12**, **13**, and **15**, 1.01 mmol for reaction with **14**) or **17**[18] (0.84 mmol for reaction with **12**, 1.26 mmol for reactions with **13**–**15**), Cs_2CO_3 (2.5–3.0 equiv) and the *N*-glycoside derivative **12**–**15** (2 equiv) in anhydrous DMF (8–10 mL) was kept under Ar for 7 d at room temperature. After this time, Ac_2O (12 mL), pyridine (8 mL) and DMAP (catalytic amount) were added and the reaction mixture was stirred for 48 h at 40 °C. Then the precipitated material was filtered and the filtrate was poured over ice/H_2O. Aqueous HCl (5%, 100 mL) was added and the aqueous layer extracted with Cl_2CH_2 (2 × 100 mL). The combined organic phases were washed successively with aqueous HCl (5%, 100 mL), saturated aqueous $NaHCO_3$ (2 × 150 mL) and H_2O (2 × 100 mL). The organic solution was dried (Na_2SO_4), filtered, evaporated, and gave a residue that was subjected to column chromatography.

Heptakis{2,3-di-*O*-acetyl-6-*S*-[*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)aminocarbonylmethyl]-6-thio}cyclomaltoheptaose (18): Column chromatography (EtOAc to EtOAc/MeOH 30:1) gave **18** (535 mg, 98%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and compound **18** was obtained (503 mg, 92%): m.p. 155 °C; $[\alpha]_D = +54$ ($c = 0.5$ in chloroform); ^1H NMR (300 MHz, Cl_3CD): $\delta = 7.81$ (d, 7H, $^3J_{NH,1} = 9.3$ Hz, NH), 5.36 (t, 7H, $^3J = 9.3$ Hz, H-3′), 5.34 (t, 7H, $^3J = 9.3$ Hz, H-1′), 5.27 (brdd, 7H, $^3J_{2,3} = 9.7$ Hz, $^3J_{3,4} = 8.6$ Hz, H-3), 5.12 (t, 7H, $^3J = 9.3$ Hz, H-4′), 5.08 (d, 7H, $^3J_{1,2} = 3.7$ Hz, H-1), 5.06 (t, 7H, $^3J = 9.3$ Hz, H-2′), 4.81 (dd, 7H, $^3J_{2,3} = 9.7$ Hz, $^3J_{1,2} = 3.7$ Hz, H-2), 4.36 (dd, 7H, $^3J_{6',6} = 12.5$, $^3J_{5',6} = 4.0$ Hz, H-6′), 4.15 (m, 7H, H-5), 4.09 (m, 7H, H-6′), 3.95 (m, 7H, H-5′), 3.71 (t, 7H, $^3J = 8.6$ Hz, H-4), 3.41 (brs, 14H, CH_2S), 3.20 (brd, 7H, $^3J_{6,6} = 13.5$ Hz, H-6), 3.00 (dd, 7H, $^3J_{6,6} = 13.5$ Hz, $^3J_{5,6} = 6.4$ Hz, H-6), 2.08 (s, 63H, 21 CH_3CO), 2.05 (s, 21H, 7 CH_3CO), 2.03 (s, 21H, 7 CH_3CO), 2.02 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, Cl_3CD): $\delta = 170.7–169.6$ (7 peaks, CO), 96.8 (C-1), 79.7 (C-4), 78.3 (C-1′), 73.7 (C-5′), 73.1(C-3′), 71.8 (C-5), 70.7 (C-2′, 3), 70.4 (C-2), 68.2 (C-4′), 61.9 (C-6′), 37.6 (CH_2S), 34.9 (C-6), 20.8–20.6 (6 peaks, CH_3CO); IR (KBr): $\nu = 3460$, 2940, 1752, 1684, 1532, 1522, 1372, 1230, 1042 cm^{-1}; MS (FAB): $m/z = 4568$ for $[M+Na-2H]^+$, calcd for $C_{182}H_{245}N_7O_{112}S_7$ (4547).

Heptakis{2,3-di-*O*-acetyl-6-*S*-[*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)aminocarbonylmethyl]-6-thio}cyclomaltoheptaose (19): Column

chromatography (EtOAc to EtOAc/MeOH 30:1) gave **19** (530 mg, 97%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **19** (514 mg, 94%): m.p. 163 °C (decomp); $[\alpha]_D = +63$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, Cl_3CD): $\delta = 7.54$ (d, 7H, $^3J_{NH,1} = 9.3$ Hz, NH), 5.52 (d, 7H, $^3J_{3,4} = 3.3$ Hz, H-4′), 5.41 (t, 7H, $^3J = 9.3$ Hz, H-1′), 5.35 (brt, 7H, H-3), 5.30 (dd, 7H, $^3J_{2',3'} = 9.8$ Hz, $^3J_{3',4'} = 3.3$ Hz, H-3′), 5.22 (dd, 7H, $^3J_{2',3'} = 9.8$ Hz, $^3J_{1',2'} = 9.3$ Hz, H-2′), 5.13 (d, 7H, $^3J_{1,2} = 3.6$ Hz, H-1), 4.85 (dd, 7H, $^3J_{2,3} = 9.9$ Hz, $^3J_{1,2} = 3.6$ Hz, H-2), 4.21 (m, 28H, H-5, 5′, 6′, 6′), 3.82 (t, 7H, $^3J_{3,4} = 8.8$ Hz, H-4), 3.48 (d, 7H, $^3J = 16.1$ Hz, CHS), 3.41 (d, 7H, $^3J = 16.1$ Hz, CHS), 3.28 (brd, 7H, $^3J_{6,6} = 14.2$ Hz, H-6), 3.10 (dd, 7H, $^3J_{6,6} = 14.2$ Hz, $^3J_{5,6} = 6.0$ Hz, H-6), 2.22 (s, 21H, 7 CH_3CO), 2.12 (s, 42H, 14 CH_3CO), 2.10 (s, 42H, 14 CH_3CO), 2.03 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, Cl_3CD): $\delta = 170.8 - 169.8$ (7 peaks, CO), 96.6 (C-1), 79.0 (C-4), 78.7 (C-1′), 72.6 (C-5′), 71.5 (C-5), 71.1 (C-3′), 70.8 (C-3), 70.7 (C-2), 68.7 (C-2′), 67.3 (C-4′), 60.9 (C-6′), 37.3 (CH_2S), 34.8 (C-6), 20.9 – 20.6 (6 peaks, CH_3CO); IR (KBr): $\nu = 3611$, 3356, 2935, 1750, 1694.9, 1539, 1423, 1371, 1224, 1044 cm^{-1}; MS (FAB): $m/z = 4570$ for $[M+Na]^+$, calcd for $C_{182}H_{245}N_7O_{112}S_7$ (4547).

Heptakis{2,3-di-*O*-acetyl-6-*S*-[*N*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)aminocarbonylmethyl]-6-thio}cyclomaltoheptaose (20): Column chromatography (EtOAc to EtOAc/MeOH 20:1) gave **20** (644 mg, 98%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **20** (624 mg, 95%): m.p. 181 °C (decomp); $[\alpha]_D = +62$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 373 K): $\delta = 8.5$ (brs, 7H, NH – C-1′), 7.74 (brs, 7H, NH – C-2′), 5.36 (t, 7H, $^3J = 9.9$ Hz, H-1′), 5.31 (t, 7H, $^3J = 9.8$ Hz, H-3), 5.29 (t, 7H, $^3J = 9.7$ Hz, H-3′), 5.17 (d, 7H, $^3J_{1,2} = 3.4$ Hz, H-1), 4.98 (t, 7H, $^3J = 9.7$ Hz, H-4′), 4.86 (dd, 7H, $^3J_{2,3} = 9.8$ Hz, $^3J_{1,2} = 3.4$ Hz, H-2), 4.29 (dd, 7H, $^3J_{6',6''} = 12.5$ Hz, $^3J_{5',6'} = 4.6$ Hz, H-6′), 4.24 (m, 7H, H-5), 4.00 (m, 14H, H-2′, 6′), 3.98 (t, 7H, $^3J = 9.8$ Hz, H-4), 3.95 (m, 7H, H-5′), 3.52 (d, 7H, $^2J = 15.2$ Hz, CHS), 3.43 (d, 7H, $^2J = 15.2$ Hz, CHS), 3.20 (m, 14H, H-6, 6), 2.12 (s, 21H, 7 CH_3CO), 2.10 (s, 42H, 14 CH_3CO), 2.07 (s, 21H, 7 CH_3CO), 2.04 (s, 21H, 7 CH_3CO), 1.93 (s, 14H, 7 CH_3CON); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta = 169.6 - 168.7$ (5 peaks, CO), 96.2 (C-1), 78.3 (C-1′, 4), 73.0 (C-3′), 72.3 (C-5′), 71.2 (C-5), 70.0, 69.8 (C-2, 3), 68.6 (C-4′), 61.7 (C-6′), 52.1 (C-2′), 36.5 (CH_2S), 33.7 (C-6), 22.1 (CH_3CN), 20.0 – 19.8 (4 peaks, CH_3CO); IR (KBr): $\nu = 3474$, 3067, 2928, 1743, 1663, 1540, 1370, 1039 cm^{-1}; MS (FAB): $m/z = 4563$ for $[M+Na]^+$, calcd for $C_{182}H_{252}N_{14}O_{105}S_7$ (4540).

Heptakis{2,3-di-*O*-acetyl-6-*S*-[*N*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)aminocarbonylmethyl]-6-thio}cyclomaltoheptaose (21): Column chromatography (EtOAc to EtOAc/MeOH 30:1) gave **21** (533 mg, 97%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **21** (475 mg, 87%): m.p. 146 °C (decomp); $[\alpha]_D = +106$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 373 K): $\delta = 8.93$ (d, 7H, $^3J_{NH,1'} = 8.5$ Hz, NH – C-1′), 5.61 (m, 14H, H-1′, 3′), 5.33 (t, 7H, $^3J = 9.6$ Hz, H-3), 5.23 (brd, 7H, $^3J_{2',3'} = 3.4$ Hz, H-2′), 5.20 (t, 7H, $^3J = 9.0$ Hz, H-4′), 5.20 (d, 7H, $^3J_{1,2} = 3.6$ Hz, H-1), 4.83 (dd, 7H, $^3J_{2,3} = 9.6$ Hz, $^3J_{1,2} = 3.6$ Hz, H-2), 4.27 (dd, 7H, $^2J_{6',6''} = 12.1$ Hz, $^3J_{5',6'} = 4.9$ Hz, H-6′), 4.27 (m, 7H, H-5), 4.17 (dd, 7H, $^2J_{6',6''} = 12.1$ Hz, $^3J_{5',6'} = 3.0$ Hz, H-6′), 4.12 (m, 7H, H-5′), 4.06 (t, 7H, $^3J = 9.6$ Hz, H-4), 3.55 (d, 7H, $^2J = 14.1$ Hz, CHS), 3.47 (d, 7H, $^2J = 14.1$ Hz, CHS), 3.32 (dd, 7H, $^2J_{6,6} = 14.7$ Hz, $^3J_{5,6} = 3.0$ Hz, H-6), 3.21 (dd, 7H, $^2J_{6,6} = 14.7$ Hz, $^3J_{5,6} = 5.3$ Hz, H-6), 2.19 (s, 21H, 7 CH_3CO), 2.13 (s, 21H, 7 CH_3CO), 2.12 (s, 21H, 7 CH_3CO), 2.11 (s, 21H, 7 CH_3CO), 2.10 (s, 21H, 7 CH_3CO), 2.05 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta = 169.4 - 168.7$ (7 peaks, CO), 96.3 (C-1), 78.0 (C-4), 75.4 (C-1′), 71.2 (C-5), 70.0, 69.9 (C-2, 3), 69.0 (C-5′, C-2′, or 4′), 68.1 (C-3′), 66.2 (C-4′ or 2′), 61.7 (C-6′), 36.2 (CH_2S), 33.6 (C-6), 20.0 – 19.7 (6 peaks, CH_3CO); IR (KBr): $\nu = 3457$, 2940, 1750, 1654, 1540, 1431, 1371, 1229, 1050 cm^{-1}; MS (FAB): $m/z = 4570$ for $[M+Na]^+$, calcd for $C_{182}H_{245}N_7O_{112}S_7$ (4547).

Heptakis{2,3-di-*O*-acetyl-6-amino-*N*-[*S*-(*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)aminocarbonylmethyl)-mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (22): Column chromatography (EtOAc to EtOAc/MeOH 20:1) gave **22** (496 mg, 80%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL), and ether (30 mL) was added. The resulting precipitate was filtered and afforded **22** (439 mg, 71%): m.p. 149 °C; $[\alpha]_D = +22$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 353 K): $\delta = 8.66$ (d, 7H, $^3J_{NH,1'} = 9.5$ Hz, NH – C-1′), 7.80 (brs, 7H, NH – C-6), 5.34 (t, 7H, $^3J = 9.5$ Hz, H-1′), 5.30 (t, 7H, $^3J = 9.5$ Hz, H-3′), 5.20 (t, 7H, $^3J = 9.4$ Hz, H-3), 5.13 (d, 7H, $^3J_{1,2} = 3.0$ Hz, H-1), 4.92 (t, 7H, $^3J = 9.5$ Hz, H-4′), 4.89 (t, 7H, $^3J = 9.5$ Hz, H-2′), 4.81 (dd, 7H, $^3J_{2,3} = 9.4$ Hz, $^3J_{1,2} = 3.0$ Hz, H-2), 4.16 (dd, 7H, $^2J_{6',6''} = 13.1$ Hz, $^3J_{5',6'} = 5.2$ Hz, H-6′), 4.03 (m, 21H, H-5, 5′, 6′), 3.77 (m, 14H, H-4, 6), 3.49 (m, 7H, H-6), 3.37 (d, 7H, $^2J = 14.3$ Hz, CHS), 3.28 (d, 7H, $^2J = 14.3$ Hz, CHS), 3.28 (d, 7H, $^2J = 12.6$ Hz, CHS), 3.23 (d, 7H, $^2J = 12.6$ Hz, CHS), 2.11 (s, 21H, 7 CH_3CO), 2.10 (s, 21H, 7 CH_3CO), 2.08 (s, 21H, 7 CH_3CO), 2.06 (s, 21H, 7 CH_3CO), 2.03 (s, 21H, 7 CH_3CO), 2.01 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta = 169.4 - 168.7$ (7 peaks, CO), 96.1 (C-1), 77.1 (C-1′), 76.7 (C-4), 72.7 (C-3′), 72.2 (C-5′), 70.4 (C-2′), 70.1, 69.8, 69.5 (C-2, 3, 5), 68.0 (C-4′), 61.5 (C-6′), 39.1 (C-6), 34.8 (CH_2S), 34.6 (CH_2S), 20.1 – 19.7 (6 peaks, CH_3CO); IR (KBr): $\nu = 3470$, 2941, 1752, 1663, 1545, 1370, 1229, 1043 cm^{-1}; MS (FAB): $m/z = 4968$ for $[M+Na-1]^+$, calcd for $C_{196}H_{266}N_{14}O_{119}S_7$ (4946).

Heptakis{2,3-di-*O*-acetyl-6-amino-*N*-[*S*-(*N*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)aminocarbonylmethyl)mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (23): Column chromatography (EtOAc to EtOAc/MeOH 40:1) gave **23** (838 mg, 90%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **23** (757 mg, 81%): m.p. 151 °C (decomp); $[\alpha]_D = +35$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 353 K): $\delta = 8.69$ (d, 7H, $^3J_{NH,1'} = 9.3$ Hz, NH-C-1′), 7.79 (brs, 7H, NH – C-6), 5.42 (t, 7H, $^3J = 9.3$ Hz, H-1′), 5.41 (d, 7H, $^3J_{3,4} = 3.4$ Hz, H-4′), 5.35 (dd, 7H, $^3J_{2',3'} = 9.6$ Hz, $^3J_{3',4'} = 3.4$ Hz, H-3′), 5.30 (t, 7H, $^3J = 9.6$ Hz, H-3), 5.24 (d, 7H, $^3J_{1,2} = 3.4$ Hz, H-1), 5.15 (t, 7H, $^3J = 9.6$ Hz, H-2′), 4.91 (dd, 7H, $^3J_{2,3} = 9.6$ Hz, $^3J_{1,2} = 3.4$ Hz, H-2), 4.36 (brt, 7H, $^3J = 6.3$ Hz, H-5′), 4.15 (dd, 7H, $^2J_{6',6''} = 11.2$ Hz, $^3J_{5',6'} = 6.3$ Hz, H-6′), 4.13 (m, 7H, H-5), 4.10 (dd, 7H, $^2J_{6',6''} = 11.2$ Hz, $^3J_{5',6'} = 6.3$ Hz, H-6′), 3.88 (m, 14H, H-4, 6), 3.59 (m, 7H, H-6), 3.47 (d, 7H, $^2J = 14.3$ Hz, CHS), 3.38 (d, 7H, $^2J = 14.3$ Hz, CHS), 3.38 (d, 7H, $^2J = 14.1$ Hz, CHS), 3.32 (d, 7H, $^2J = 14.1$ Hz, CHS), 2.20 (s, 21H, 7 CH_3CO), 2.12 (s, 21H, 7 CH_3CO), 2.09 (s, 21H, 7 CH_3CO), 2.08 (s, 21H, 7 CH_3CO), 2.07 (s, 21H, 7 CH_3CO), 2.01 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta = 169.4 - 168.7$ (6 peaks, CO), 96.1 (C-1), 77.3 (C-1′), 76.6 (C-4), 71.3 (C-5′), 70.6 (C-3′), 70.1 (C-3), 69.8 (C-5), 69.5 (C-2), 68.1 (C-2′), 67.4 (C-4′), 60.9 (C-6′), 39.1 (C-6), 34.8 (CH_2S), 34.5 (CH_2S), 20.0 – 19.7 (6 peaks, CH_3CO); IR (KBr): $\nu = 3470$, 3067, 2938, 1749, 1664, 1542, 1372, 1230, 1050 cm^{-1}, MS (FAB): $m/z = 4969$ for $[M+Na]^+$, calcd for $C_{196}H_{266}N_{14}O_{119}S_7$ (4946).

Heptakis{2,3-di-*O*-acetyl-6-amino-*N*-[*S*-(*N*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)aminocarbonylmethyl)mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (24): Column chromatography (EtOAc/MeOH 20:1 to 5:1) gave **24** (847 mg, 91%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **24** (782 mg, 84%): m.p. 179 °C (decomp); $[\alpha]_D = +55$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 353 K): $\delta = 8.45$ (dd, 7H, $^3J_{NH,1} = 8.8$ Hz, NH – C-1′), 7.80 (m, 14H, 2 NH – C-2′, 6), 5.29 (m, 28H, H-1′, 1, 3′, 3), 4.95 (t, 7H, $^3J = 9.4$ Hz, H-4′), 4.90 (dd, 7H, $^3J_{2,3} = 8.5$ Hz, $^3J_{1,2} = 3.6$ Hz, H-2), 4.27 (dd, 7H, $^3J_{6',6''} = 12.2$ Hz, $^3J_{5',6'} = 4.4$ Hz, H-6′), 4.13 (m, 7H, H-5), 4.11 (dd, 7H, $^3J_{6',6''} = 12.2$ Hz, $^3J_{5',6'} = 3.3$ Hz, H-6′), 4.05 (brdd, 7H, H-2′), 3.92 (m, 7H, H-5′), 3.90 (m, 14H, H-4, 6), 3.60 (brd, 7H, $^3J_{5,6'} = 12.4$ Hz, H-6), 3.45 (d, 7H, $^2J = 14.0$ Hz, CHS), 3.42 (d, 7H, $^2J = 14.5$ Hz, CHS), 3.37 (d, 7H, $^2J = 14.0$ Hz, CHS), 3.35 (d, 7H, $^2J = 14.5$ Hz, CHS), 2.11 (s, 42H, 14 CH_3CO), 2.10 (s, 21H, 7 CH_3CO), 2.07 (s, 21H, 7 CH_3CO), 2.02 (s, 21H, 7 CH_3CO), 1.88 (s, 21H, 7 CH_3CN); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta = 169.4 - 168.7$ (4 peaks, CO), 96.1 (C-1), 78.2 (C-1′), 76.6 (C-4), 73.0 (C-3′), 72.3 (C-5′), 70.1 (C-3), 69.8 (C-5), 69.5 (C-2), 68.6 (C-4′), 61.7 (C-6′), 52.1 (C-2′), 39.1 (C-6), 34.7 ($2 \times CH_2S$), 22.1 (CH_3CN), 20.1 – 19.8 (3 peaks, CH_3CO); IR (KBr): $\nu = 3412$, 3070, 2938, 1750, 1663, 1545, 1371, 1243, 1046 cm^{-1}; MS (FAB): m/z 4961 for $[M+Na-1]^+$, calcd for $C_{196}H_{273}N_{21}O_{112}S_7$ (4939).

Heptakis{2,3-di-*O*-acetyl-6-amino-*N*-[*S*-(*N*-(2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl)aminocarbonylmethyl)mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (25): Column chromatography (EtOAc to EtOAc/MeOH 20:1) gave **25** (829 mg, 89%) as a solid. The isolated solid was dissolved in CH_2Cl_2 (2 mL) and ether (30 mL) was added. The resulting precipitate was filtered and afforded **25** (745 mg, 80%): m.p. 154 °C (decomp); $[\alpha]_D = +72$ ($c = 0.5$ in chloroform); ^{1}H NMR (300 MHz, $(CD_3)_2SO$, 353 K): $\delta = 9.15$ (d, 7H, $^3J_{NH,1'} = 9.0$ Hz, NH – C-1′), 7.80 (brs, 7H, NH – C-6), 5.61 (dd, 7H, $^3J_{3',4'} = 9.4$ Hz, $^3J_{2',3'} = 3.3$ Hz, H-3′), 5.58 (dd, 7H, $^3J_{NH,1'} = 9.0$ Hz, $^3J_{1',2'} = 2.0$ Hz, H-1′), 5.30 (t, 7H, $^3J = 9.7$ Hz, H-3), 5.22 (brd, 7H, $^3J_{2',3'} = 3.3$ Hz, $^3J_{1',2'} = 2.0$, H-2′), 5.19 (d, 7H, $^3J_{1,2} = 3.3$ Hz, H-1), 5.18 (t, 7H, $^3J = 9.4$ Hz, H-4′), 4.90 (dd, 7H, $^3J_{2,3} = 9.7$ Hz, $^3J_{1,2} = 3.3$ Hz, H-2), 4.25 (dd, 7H,

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$^2J_{6',6'}=12.0$ Hz, $^3J_{5',6'}=5.0$ Hz, H-6′), 4.16 (dd, 7H, $^2J_{6',6'}=12.0$ Hz, $^3J_{5',6''}=3.0$ Hz, H-6′), 4.13 (m, 7H, H-5), 4.10 (m, 7H, H-5′), 3.88 (m, 14H, H-4, 6), 3.62 (br d, 7H, $^2J_{6,6}=12.0$ Hz, H-6), 3.52 (d, 7H, $^2J=14.4$ Hz, CHS), 3.45 (br s, 14H, CH_2S), 3.42 (d, 7H, $^2J=14.4$ Hz, CHS), 2.20 (s, 21H, 7 CH_3CO), 2.12 (s, 21H, 7 CH_3CO), 2.11 (s, 42H, 14 CH_3CO), 2.10 (s, 21H, 7 CH_3CO), 2.05 (s, 21H, 7 CH_3CO); ^{13}C NMR (75.5 MHz, $(CD_3)_2SO$, 353 K): $\delta=$ 169.4–168.7 (7 peaks, CO), 96.1 (C-1), 76.7 (C-4), 75.2 (C-1′), 70.1 (C-3), 69.8 (C-5), 69.6 (C-2), 69.0 (C-2′, 5′), 68.1 (C-3′), 66.3 (C-4′), 61.7 (C-6′), 39.1 (C-6), 34.9 (CH_2S), 34.7 (CH_2S), 20.0–19.8 (6 peaks, CH_3CO); IR (KBr): $\nu=$ 3455, 2937, 1748, 1537, 1369, 1227, 1046 cm^{-1}; MS (FAB): $m/z=4970$ for $[M+Na+H]^+$, calcd for $C_{196}H_{266}N_{14}O_{119}S_7$ (4946).

General procedure for the Zemplén de-*O*-acetylation of *N*-glycoCDs 18–25: A solution of compound **18** (387 mg, 0.60 mmol), **19** (377 mg, 0.58 mmol), **20** (371 mg, 0.57 mmol), **21** (334 mg, 0.51 mmol), **22** (375 mg, 0.51 mmol), **23** (361 mg, 0.49 mmol), **24** (364 mg, 0.49 mmol), or **25** (360 mg, 0.48 mmol) in dry MeOH (5–6 mL) was made alkaline to pH 9 (indicator paper) with a methanolic solution of NaOMe (1M). The reaction mixture was stirred overnight at room temperature and the precipitated material was filtered, washed with MeOH and dissolved in H_2O (6 mL). The solution was concentrated by lyophilization and gave a solid.

Heptakis[6-S-(*N*-β-D-glucopyranosylaminocarbonylmethyl)-6-thio]cyclomaltoheptaose (26): Yield 227 mg (96%): m.p. 186 °C (decomp); $[\alpha]_D=+39$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O, 333 K): $\delta=5.46$ (d, 7H, $^3J_{1,2}=3.5$ Hz, H-1), 5.34 (d, 7H, $^3J_{1',2'}=9.9$ Hz, H-1′), 4.39 (m, 7H, H-5), 4.27 (t, 7H, $^3J=9.7$ Hz, H-3), 4.26 (dd, 7H, $^2J_{6',6'}=12.2$ Hz, $^3J_{5',6'}=2.0$ Hz, H-6′), 4.12 (dd, 7H, $^2J_{6',6'}=12.2$ Hz, $^3J_{5',6'}=4.8$ Hz, H-6′), 4.02 (dd, 7H, $^3J_{2,3}=9.7$ Hz, $^3J_{1,2}=3.5$ Hz, H-2), 3.96 (t, 7H, $^3J=9.7$ Hz, H-4), 3.93 (m, 14H, CH_2S), 3.88 (m, 7H, H-5′), 3.86–3.76 (m, 21H, H-2′, 3′, 4′), 3.62 (br d, 7H, $^2J_{6,6}=14.2$ Hz, H-6), 3.39 (dd, 7H, $^2J_{6,6}=14.2$ Hz, $^3J_{5,6}=7.3$ Hz, H-6); ^{13}C NMR (75.5 MHz, D_2O): $\delta=173.5$ (CO), 101.6 (C-1), 83.9 (C-4), 79.6 (C-1′), 77.5, 76.5, 71.8, 69.1 (C-2′, 3′, 4′, 5′), 72.7 (C-3), 71.9 (C-2), 71.7 (C-5), 60.5 (C-6′), 36.2 (CH_2S), 33.7 (C-6); IR (KBr): $\nu=$ 3407, 2920, 1651, 1556, 1361, 1070, 1040.4 cm^{-1}; MS (FAB): $m/z=2803$ for $[M+Na-H]^+$, calcd for $C_{98}H_{161}N_7O_{70}S_7$ (2781).

Heptakis[6-S-(*N*-β-D-galactopyranosylaminocarbonylmethyl)-6-thio]cyclomaltoheptaose (27): Yield 216 mg (94%): m.p. 183 °C (decomp); $[\alpha]_D=+50$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.09$ (d, 7H, $^3J_{1,2}=3.4$ Hz, H-1), 4.92 (d, 7H, $^3J_{1',2'}=8.5$ Hz, H-1′), 4.00 (m, 7H, H-5), 3.97 (d, 7H, $^3J_{3',4'}=2.9$ Hz, H-4′), 3.89 (t, 7H, $^3J=9.3$ Hz, H-3), 3.82–3.44 (m, 63H, H-2, 2′, 3′, 4, 5′, 6′, 6′, CH_2S), 3.23 (br d, 7H, $^2J_{6,6}=14.1$ Hz, H-6), 3.00 (dd, 7H, $^2J_{6,6}=14.1$ Hz, $^3J_{5,6}=7.5$ Hz, H-6); ^{13}C NMR (75.5 MHz, D_2O): $\delta=$ 173.6 (CO), 101.5 (C-1), 83.9 (C-4), 80.0 (C-1′), 76.5, 73.9, 73.3, 72.6, 71.8, 69.3, 68.5 (C-2, 2′, 3, 3′, 4′, 5, 5′), 60.8 (C-6′), 36.2 (CH_2S), 33.6 (C-6); IR (KBr): $\nu=$ 3399, 2918, 1661, 1540, 1374, 1153, 1043 cm^{-1}.

Heptakis{6-S-[*N*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)aminocarbonylmethyl]-6-thio}cyclomaltoheptaose (28): Yield 237 mg (95%): m.p. 201 °C (decomp); $[\alpha]_D=+57$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.04$ (d, 14H, H-1, 1′), 3.99 (m, 7H, H-5), 3.94–3.35 (m, 77H, H-2, 2′, 3, 3′, 4, 4′, 5′, 6′, 6′, CH_2S), 3.16 (br d, 7H, $^2J_{6,6}=14.2$ Hz, H-6), 2.91 (dd, 7H, $^2J_{6,6}=14.2$ Hz, $^3J_{5,6}=7.0$ Hz, H-6), 2.01 (s, 21H, 7 CH_3CN); ^{13}C NMR (75.5 MHz, D_2O): $\delta=174.4$, 173.0 (2 × CO), 101.7 (C-1), 83.8 (C-4), 78.9 (C-1′), 77.5, 74.0, 69.5 (C-3′, 4′, 5′), 72.7, 72.0, 71.7, (C-2, 3, 5), 60.5 (C-6′), 54.2 (C-2′), 36.3 (CH_2S), 33.8 (C-6), 22.1 (CH_3CN); IR (KBr): $\nu=$ 3405, 2919, 1651, 1539, 1373, 1068, 1041 cm^{-1}; MS (FAB) $m/z=3090$ for $[M+Na-2H]^+$, calcd for $C_{112}H_{182}N_{14}O_{70}S_7$ (3069).

Heptakis[6-S-(*N*-α-D-mannopyranosylaminocarbonylmethyl)-6-thio]cyclomaltoheptaose (29): Yield 192 mg (94%): m.p. 190 °C (decomp); $[\alpha]_D=+82$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.47$ (d, 7H, $^3J_{1',2'}=1.3$ Hz, H-1′), 5.07 (d, 7H, $^3J_{1,2}=2.4$ Hz, H-1), 4.10–3.40 (m, 84H, H-2, 2′, 3, 3′, 4, 4′, 5, 5′, 6′, 6′, CH_2S), 3.30 (br d, 7H, $^2J_{6,6}=13.6$ Hz, H-6), 2.90 (dd, 7H, $^2J_{6,6}=13.6$ Hz, $^3J_{5,6}=8.0$ Hz, H-6); ^{13}C NMR (75.5 MHz, D_2O): $\delta=172.6$ (CO), 101.4 (C-1), 84.2 (C-4), 78.8 (C-1′), 74.0, 70.4, 69.6, 66.5 (C-2′, 3′, 4′, 5′), 72.7, 72.3, 71.9 (C-2, 3, 5), 60.8 (C-6′), 35.7 (CH_2S), 33.1 (C-6); IR (KBr): $\nu=$ 3420, 2920, 1667, 1652, 1538, 1406, 1151, 1066, 1043.9 cm^{-1}.

Heptakis{6-amino-*N*-[*S*-(*N*-β-D-glucopyranosylaminocarbonylmethyl)-mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (30): Yield 228 mg (92%): m.p. 188 °C (decomp); $[\alpha]_D=+50$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.06$ (d, 7H, $^3J_{1,2}=3.4$ Hz, H-1), 4.95 (d, 7H, $^3J_{1',2'}=9.0$ Hz, H-1′), 4.10–3.20 (m, 112H, H-2, 2′, 3, 3′, 4, 4′, 5, 5′, 6′, 6′, 6, 6, 2 CH_2S); ^{13}C NMR (75.5 MHz, D_2O): $\delta=172.6$, 171.6 (2 × CO), 101.6 (C-1), 82.5 (C-4), 79.5 (C-1′), 77.5, 76.4, 71.7, 69.1 (C-2′, 3′, 4′, 5′), 72.7, 71.9, 70.1 (C-2, 3, 5), 60.4 (C-6′), 40.0 (C-6), 34.7 (2 × CH_2S); IR (KBr): $\nu=$ 3398, 2919, 1655, 1548, 1418, 1081, 1043 cm^{-1}; MS (FAB): $m/z=3204$ for $[M+Na]^+$, calcd for $C_{112}H_{182}N_{14}O_{77}S_7$ (3181).

Heptakis{6-amino-*N*-[*S*-(*N*-β-D-galactopyranosylaminocarbonylmethyl)-mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (31): Yield 213 mg (90%): m.p. 177 °C (decomp); $[\alpha]_D=+63$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.05$ (d, 7H, $^3J_{1,2}=3.0$ Hz, H-1), 4.90 (d, 7H, $^3J_{1',2'}=8.5$ Hz, H-1′), 4.10–3.30 (m, 112H, H-2, 2′, 3, 3′, 4, 4′, 5, 5′, 6′, 6′, 6, 6, 2 CH_2S); ^{13}C NMR (75.5 MHz, D_2O): $\delta=172.7$, 171.7 (2 × CO), 101.8 (C-1), 82.7 (C-4), 80.0 (C-1′), 76.6, 73.3, 69.3, 68.5 (C-2′, 3′, 4′, 5′), 72.7, 72.1, 70.0 (C-2, 3, 5), 60.8 (C-6′), 40.1 (C-6), 34.7 (2 × CH_2S); IR (KBr): $\nu=$ 3430, 2918, 1654, 1542, 1417, 1082, 1046 cm^{-1}; MS (FAB): $m/z=3203$ for $[M+Na-H]^+$, calcd for $C_{112}H_{182}N_{14}O_{77}S_7$ (3181).

Heptakis{6-amino-*N*-[*S*-(*N*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-aminocarbonylmethyl)mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (32): Yield 244 mg (94%): m.p. 197 °C (decomp); $[\alpha]_D=+71$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.05$ (d, 14H, H-1, 1′), 4.10–3.30 (m, 112H, H-2, 2′, 3, 3′, 4, 4′, 5, 5′, 6′, 6′, 6, 6, 2 CH_2S), 1.98 (s, 21H, 7 CH_3CN); ^{13}C NMR (75.5 MHz, D_2O): $\delta=174.4$, 172.2, 171.4 (3 × CO), 101.9 (C-1), 82.6 (C-4), 78.6 (C-1′), 77.6, 74.0, 69.4 (C-3′, 4′, 5′), 72.7, 72.0, 69.8 (C-2, 3, 5), 60.4 (C-6′), 54.2 (C-2′), 39.9 (C-6), 34.4 (2 × CH_2S), 22.1 (CH_3CN); IR (KBr): $\nu=$ 3411, 2916, 1652, 1547, 1373, 1079, 1046 cm^{-1}; MS (FAB): $m/z=3489$ for $[M+Na]^+$, calcd for $C_{126}H_{203}N_{21}O_{77}S_7$ (3466).

Heptakis{6-amino-*N*-[*S*-(*N*-α-D-mannopyranosylaminocarbonylmethyl)-mercaptoacetyl]-6-deoxy}cyclomaltoheptaose (33): Yield 220 mg (93%): m.p. 193 °C (decomp); $[\alpha]_D=+102$ ($c=0.5$ in water); ^{1}H NMR (300 MHz, D_2O): $\delta=5.44$ (br s, 7H, H-1′), 5.05 (d, 7H, H-1), 4.10–3.20 (m, 112H, H-2, 2′, 3, 3′, 4, 4′, 5, 5′, 6′, 6′, 6, 6, 2 CH_2S); ^{13}C NMR (75.5 MHz, D_2O): $\delta=172.1$, 171.6 (2 × CO), 101.8 (C-1), 82.8 (C-4), 78.8 (C-1′), 74.0, 72.7, 72.0, 70.4, 69.5, 66.5 (C-2, 2′, 3, 3′, 4′, 5, 5′), 60.7 (C-6′), 40.1 (C-6), 34.7 (2 × CH_2S); IR (KBr): $\nu=$ 3424, 2922, 1653, 1540, 1417, 1155, 1046 cm^{-1}.

Supporting information for this article (copies of ^{13}C NMR spectra of compounds **12–15** and **18–33**) is available on the WWW under http://www.wiley-vch.de/home/chemistry/ or from the author.

Acknowledgements

The authors acknowledge the support of the Dirección General de Enseñanza Superior (PB95-1207 and PB96-1505) and the Junta de Andalucía for a scholarship (J.J.G.L.).

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Received: October 19, 1998 [F1400]

  0947-6539/99/0506-1784 $ 17.50+.50/0