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Carbohydrate Research 303 (1997) 51–65

CARBOHYDRATE RESEARCH

Generation of molecular diversity on *N*-acetyllactosamine via *O*-cyanomethyl ethers

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Received 10 March 1997; accepted 5 May 1997

Abstract

The ability to generate molecular diversity around a natural carbohydrate ligand taking advantage of the rich chemistry of the nitrile functional group was demonstrated by synthesizing 24 derivatives of *N*-acetyllactosamine (LacNAc). The disaccharides prepared carried carboxymethyl, amidinomethyl, aminoethyl, and carbamoylmethyl substituents projecting from each of the six OH groups. The resulting LacNAc derivatives present new structural features with either negatively charged, positively charged, or polar-neutral small substituents sampling the entire periphery of the molecule. These new derivatives should be useful probes for studying carbohydrate–protein interactions in general, and for designing inhibitors of *N*-acetyllactosamine-binding proteins in particular. © 1997 Elsevier Science Ltd.

Keywords: *N*-acetyllactosamine; Sugar-analogs; Molecular diversity

1. Introduction

Multivalency, weak binding to the monovalent oligosaccharides, and usually lack of structural information of the receptor-binding site are the main difficulties confronted by medicinal chemists in the development of inhibitors of carbohydrate-binding proteins. Despite an enormous amount of work in the area of oligosaccharide analogue synthesis, only marginal improvements in binding affinity with respect to the natural epitopes have been generally achieved [1]. Two notable exceptions are a 100-fold improvement in the affinity of a trisaccharide binding to an antibody [2] and the rational design of a sialic acid based inhibitor for influenza hemaglutinin [3] (10 000-fold improvement) based on a crystal structure of the protein containing the bound ligand. In the more common situations where such structural information is unavailable, the development of inhibitors of carbohydrate-binding proteins still relies on the preparation of a large number of analogues of the natural target oligosaccharides.

A general characteristic of the mode of binding of oligosaccharides to proteins is summarized schematically in Fig. 1(A). The carbohydrate combining site is often a cleft or groove on the protein surface [4]. Critical hydrogen-bonding interactions generally involve a limited number of the sugar OH groups which become involved in intricate H-bonding networks that can include water molecules. Van der Waals contacts with nonhydroxylated surfaces on the oligosaccharides also frequently occur. As shown in Fig. 1(B), in principle, it could be possible to enlarge the natural epitope by adding appropriate molecular

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PII S0008-6215(97)00142-0

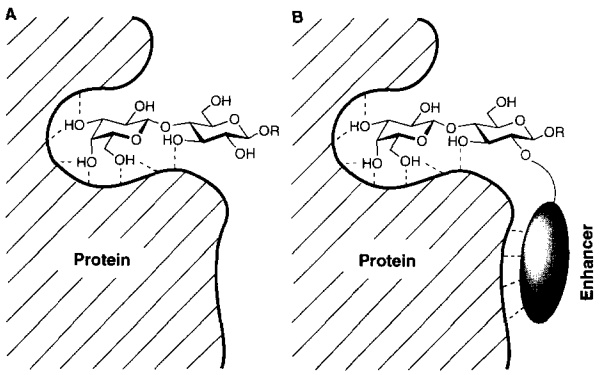


Fig. 1. (A) A schematic representation of a disaccharide bound to a protein indicating the OH groups that are directly involved in complex formation. (B) Molecular structure has been added to the ligand to enhance the affinity of the complex by interacting with a protein structure adjacent to the combining site.

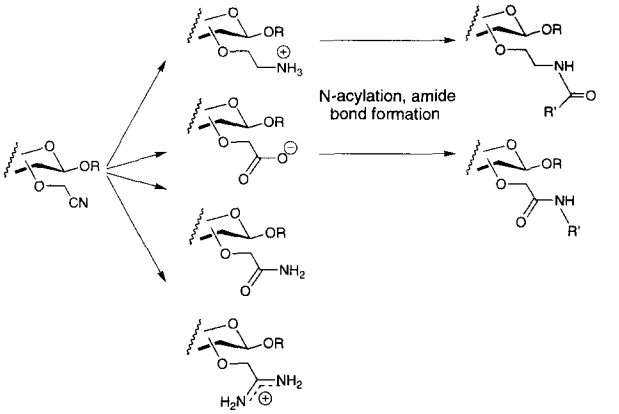


Fig. 2. Versatile transformations of the *O*-cyanomethyl group.

structure to the carbohydrate ligand through the hydroxyl groups that are not directly involved in binding. Furthermore, since most of the amino acids on the surface of proteins are polar and highly solvated, the introduction of polar residues with enhanced hydrogen-bonding abilities may potentially lead to an increase in binding, both for enthalpic (hydrogen bonding) and entropic reasons (return of water molecules solvating the protein surface and the carbohydrate ligand to the bulk solvent).

We have recently reported [5] on the potential of *O*-cyanomethyl ethers of carbohydrates as versatile intermediates for the generation of molecular diversity around a core carbohydrate structure. The nitrile group can be readily converted to an array of different functional groups under conditions that do not cause degradation of glycosidic linkages or other hydroxyl groups of the carbohydrate moiety. Amines, carboxylic acids, amides, and amidines are the immediate products. In addition, the resulting amines and carboxylic acids can be used as handles for further coupling to an array of acylating agents, amino acids or peptides, expanding the possibilities for future development of combinatorial approaches for the preparation of larger libraries of compounds (Fig. 2). Finally, since the effect of the introduction of a given substituent on a carbohydrate OH group not directly involved in binding is *a priori* difficult or impossible to predict [6], this synthetic methodology will provide easy access to families of compounds to evaluate the effects in binding upon addition of a polar-nonionic (amide), anionic (carboxylate), or cationic (amine/amidine salt) residue in the vicinity of any OH group.

The aim of this paper is to show that this strategy, previously developed on simple monosaccharides [5], can be extended in a systematic way to complex systems. *N*-acetyllactosamine was chosen as a model

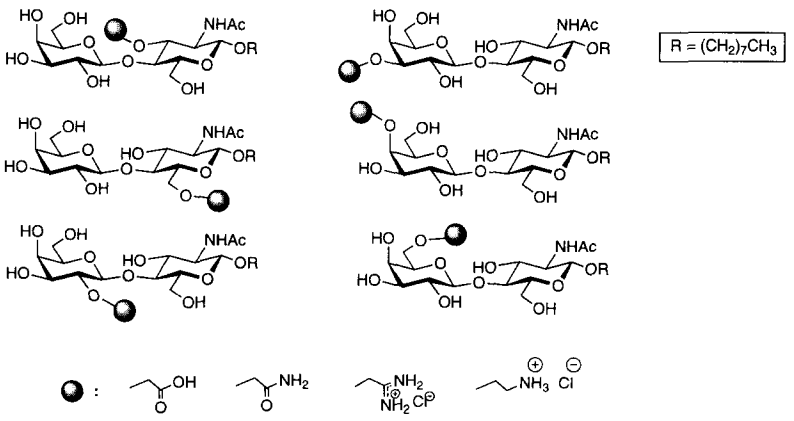
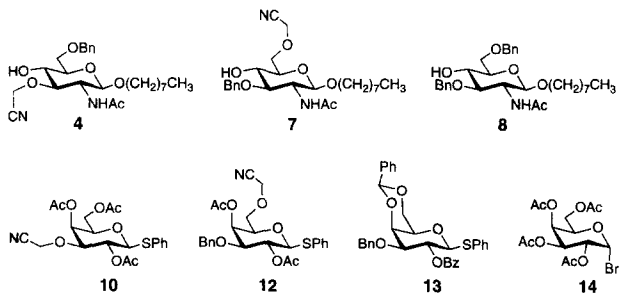


Fig. 3. Derivatives of *N*-acetyllactosamine carrying *O*-carboxymethyl, *O*-carbamoylmethyl, *O*-amidinomethyl, and *O*-(2-aminoethyl) substituents.

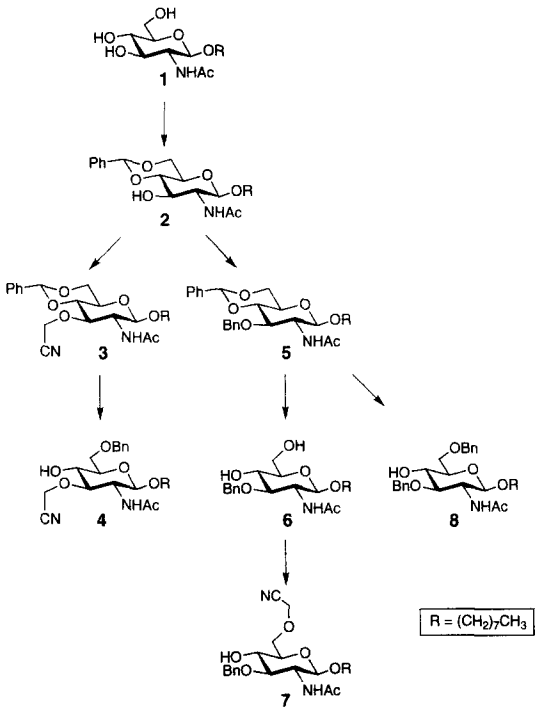
since this disaccharide is the essential epitope recognized by several readily available lectins, and the acceptor substrate for several glycosyltransferases. The compounds prepared can thus be readily evaluated in a variety of carbohydrate-binding protein systems. Cyanomethylation of each of the six hydroxyl groups of this disaccharide and further transformation of the cyano group to the corresponding aminomethyl, carboxy, carbamoyl, and amidino groups afforded the 24 derivatives shown in Fig. 3. The disaccharides were prepared as the octyl glycosides because this hydrophobic aglycon simplifies the purification of the final compounds by reversed-phase column chromatography and allows easy separation and quantitation of product formation and measurement of enzyme activity in future glycosyltransferase assays [7].

2. Results and discussion

The three monosaccharide glycosyl acceptors **4**, **7**, and **8** and the four appropriately functionalized glycosyl donors **10**, **12**, **13**, and **14** (Scheme 1) were used as building blocks for the synthesis of the entire family of *N*-acetyllactosamine analogues described in this paper. Compounds **4**, **7**, **10**, and **12**, the building blocks required for the preparation of the final 3-*O*-, 6-*O*-, 3′-*O*-, and 6′-*O*-cyanomethyl disaccharides, could be prepared in a straightforward and efficient manner. On the other hand, preliminary experiments had shown the cyanomethyl group to be nonparticipating, and 2-*O*-cyanomethylated glycosyl donors invariably gave α/β mixtures of anomers in model glycosylation reactions. To avoid this problem, the 2-position of the galactopyranose unit was modified at the disaccharide level. The use of donor **13** offers the additional advantage of allowing easy manipulation of both the 2′-*O*- and 4′-*O*-positions after glycosylation of acceptor **8**, thus simplifying the synthesis



Scheme 1.

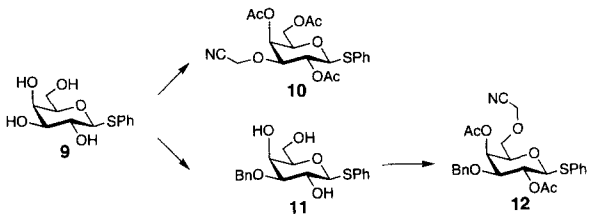


Scheme 2.

of the corresponding cyanomethyl ethers from a common disaccharide intermediate.

Octyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (**2**), prepared in 93% yield from the octyl glycoside **1** [8], was the common precursor for the preparation of the glycosyl acceptors **4**, **7**, and **8** (Scheme 2). Cyanomethylation of **2** using bromoacetonitrile and sodium hydride in acetonitrile yielded **3** (73%), which was subjected to conventional reductive ring opening with sodium cyanoborohydride [9] to afford derivative **4** with OH-4 unmasked. Similarly, low-temperature benzylation of **2** and regioselective ring opening of the benzylidene acetal gave **8** in 60% overall yield. Finally, the 6-*O*-cyanomethyl ether **7** was prepared in two steps from **5** via acid hydrolysis of the benzylidene group (70%), stannylation of the resulting diol **6** with dibutyltin oxide, and regioselective alkylation with bromoacetonitrile (61%).

The 3-*O*-cyanomethyl-1-thio-β-D-galactopyranoside donor **10** was synthesized in 42% overall yield by regioselective stannylation of phenyl 1-thio-β-D-galactopyranoside (**9**) with dibutyltin oxide, followed by *O*-alkylation with bromoacetonitrile and acetylation with acetic anhydride in pyridine. Similarly, two consecutive cycles of stannylation–alkylation of **9**, first with benzyl bromide and finally with bromoacetonitrile, afforded the 6-*O*-cyanomethyl derivative **12**

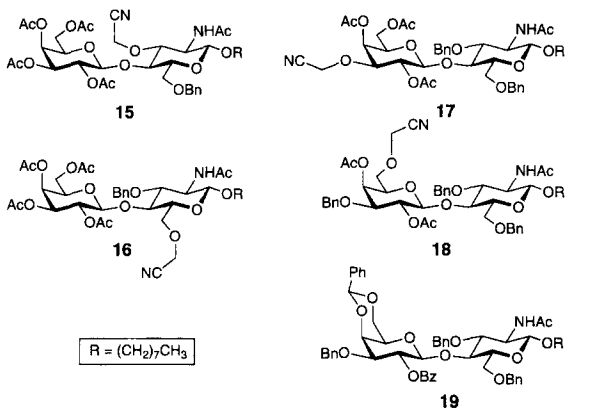


Scheme 3.

in a simple and straightforward way, although only in a moderate overall yield (15%) (Scheme 3).

The results of the disaccharide-forming reactions between the donors **10**, **12**, **13**, and **14** and the acceptors **4**, **7**, and **8** are summarized in Table 1. Silver trifluoromethanesulfonate was used as a promoter for the reaction between 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**14**) and the 3-*O*- and 4-*O*-cyanomethyl acceptors **4** and **7** using dichloromethane as solvent. Disaccharide **16** was obtained in 64% yield, while compound **15** was isolated in 71% yield as a 15:85 α/β mixture. No improvement in the yield or selectivity was observed by changing the promoter to $Hg(CN)_2$ or $Hg(CN)_2/HgBr_2$, lowering the temperature (as low as −40 °C), or changing the solvent (benzene or acetonitrile). A pure sample of the desired β-disaccharide was obtained in 46% yield after careful separation by column chromatography. On the other hand, glycosylation using the phenyl 1-thio-β-D-galactopyranosyl donors **10**, **12**, and **13** with the common acceptor **8** using bromine and silver trifluoromethanesulfonate as promoter [10] afforded the disaccharides **17**, **18**, and **19** in 57–67% yield (Scheme 4).

Disaccharide **19** could be converted to the corresponding 2′-*O*- and 4′-*O*-cyanomethyl derivatives **22** and **24** as shown in Scheme 5. Transesterification with methanolic sodium methoxide, followed by *O*-alkylation with bromoacetonitrile and sodium hydride in acetonitrile, afforded **21**, which on hydrolysis of the benzylidene group yielded **22**. Alternatively, reductive ring opening of the benzylidene acetal with



Scheme 4.

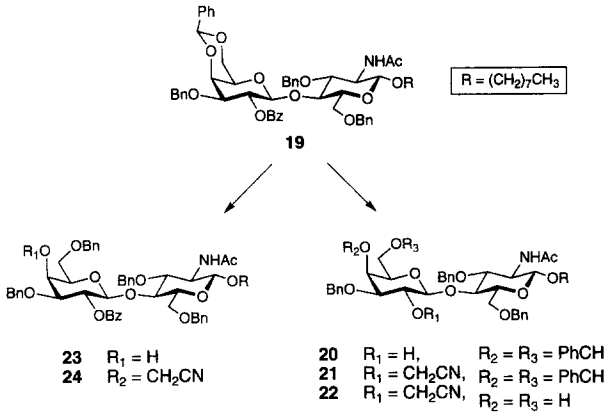
sodium cyanoborohydride, followed by low-temperature alkylation of the 4-OH group of **23**, afforded the 4-*O*-cyanomethyl derivative **24** in 65% yield (based on consumed starting material).

The spectroscopic and physical data for the *O*-cyanomethyl disaccharides **15**–**18**, **22**, and **24** were in accordance with the proposed structures. The ^1H NMR spectra of these compounds showed a characteristic AB system centered at δ 4.3 ± 0.2 ppm with $J \approx 16$ Hz corresponding to the two geminal protons in the cyanomethyl ether and a doublet at δ 4.6 ± 0.2 ppm with $J \approx 8$ Hz confirming the β stereochemistry of the galactopyranosyl unit. A second doublet at δ 4.5 ± 0.2 ppm with coupling constants ranging from 5.5 to 7.5 Hz is characteristic of the *N*-acetyl-β-D-glucopyranosyl residue. The low J values are likely a consequence of the time-averaged interconversion between $^1C_4$ and $^{3,0}B$ conformations for this unit in nonprotic solvents [11].

Table 2 shows the yields in isolated product on transformation of the six protected cyanomethyl disaccharides to the final 24 carboxymethyl, carbamoylmethyl, amidinomethyl, and aminoethyl disaccharides. Basic hydrolysis of the nitrile group with aqueous sodium hydroxide in refluxing methanol gave the corresponding carboxylic acids in essentially quantitative yield, with simultaneous saponification

Table 1
Glycosidation reactions between donors **10**, **12**, **13**, and **14**, and acceptors **4**, **7**, and **8**

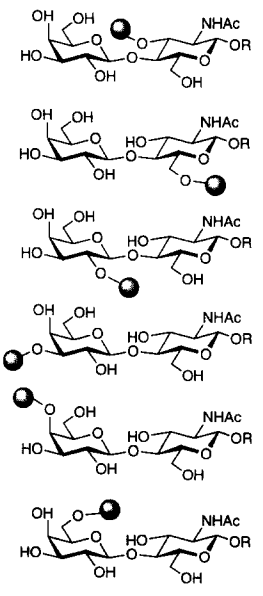
Donor	Acceptor	Product	Promoter	Solvent, T (°C)	Yield (%)
14 (2 eq)	**4**	**15**	AgOTf	CH_2Cl_2, −10 to 0	71 (α/β 15:85)
14 (2 eq)	**7**	**16**	AgOTf	CH_2Cl_2, −10 to 0	64
10 (1.5 eq)	**8**	**17**	Br_2, AgOTf	CH_2Cl_2, −30	63
12 (1.5 eq)	**8**	**18**	Br_2, AgOTf	CH_2Cl_2, −30	67
13 (1.5 eq)	**8**	**19**	Br_2, AgOTf	CH_2Cl_2, −30	57



Scheme 5.

of the ester groups but without *N*-deacetylation. Hydrogenolysis of the remaining benzyl ethers using 10% Pd–C afforded compounds **25a**, **26a**, **27a**, **28a**, **29a**, and **30a** isolated in over more than 90% yield in each case. Treatment of the *O*-cyanomethyl disaccharides with anhydrous methanolic sodium methoxide yielded the corresponding methyl imidates with simultaneous transesterification of the ester groups [5,12]. The resulting imidates were not isolated but directly hydrolyzed to the corresponding amides or trapped with excess ammonium chloride to yield the parent amidinium salts. After removal of the remaining benzyl protecting groups, the final carbamoylmethyl derivatives **25b**, **26b**, **27b**, **28b**, **29b**, and **30b** were isolated in 46 to 68% yield, and the amidinomethyl salts **25c**, **26c**, **27c**, **28c**, **29c**, and **30c** in 58 to 82% yield. Finally, simultaneous debenzylation and reduction of the cyano group by catalytic hydrogenation using Pd–C in methanol or ethanol containing 1.5 equivalents of hydrochloric acid, followed by Zemplén deacetylation, yielded the aminoethyl derivatives **25d**, **26d**, **27d**, **28d**, **29d**, and **30d** in 38 to 75% yields. It should be noted that higher and more reproducible yields have been reported in the reduction of nitriles using metal hydrides or borane complexes [5,13]. The presence of the hydride-labile *N*-acetyl group, however, precludes the use of such reagents in this case. Nevertheless, for oligosaccharide systems that do not contain a GlcNAc moiety, reduction with borane · methyl sulfide complex in refluxing tetrahydrofuran is the common method of choice for converting cyanomethyl ethers to the cor-

Table 2
Conversion of the *O*-cyanomethyl disaccharides to carboxymethyl, carbamoylmethyl, amidinomethyl, and 2-aminoethyl derivatives



Starting cyanomethyl disaccharide	● : OH	NH2	NH2 NH2 Cl⊖	NH3 Cl
15	**25a** (93%)	**25b** (50%)	**25c** (58%)	**25d** (68%)
16	**26a** (90%)	**26b** (57%)	**26c** (72%)	**26d** (75%)
22	**27a** (97%)	**27b** (66%)	**27c** (79%)	**27d** (48%)
17	**28a** (98%)	**28b** (68%)	**28c** (65%)	**28d** (38%)
24	**29a** (97%)	**29b** (46%)	**29c** (59%)	**29d** (72%)
18	**30a** (98%)	**30b** (68%)	**30c** (82%)	**30d** (43%)

R = (CH2)7CH3

responding amine derivatives in yields consistently greater than 70% [5].

3. Conclusions

The methodology presented in this paper allowed the facile transformation of each of the hydroxyl groups of *N*-acetyllactosamine to the corresponding *O*-carboxymethyl, *O*-amidinomethyl, *O*-aminoethyl, and *O*-carbamoylmethyl derivatives. The common *O*-cyanomethyl precursors were shown to be compatible with standard glycosylation procedures and protection–deprotection strategies employed in carbohydrate synthesis. It is expected that similar protocols can be extended to other oligosaccharide core structures. The resulting functionalized carbohydrates bearing either a negative charge, a positive charge, or a polar-neutral small substituent in the vicinity of each of the OH groups are currently being evaluated as potential inhibitors of an extensive series of *N*-acetyllactosamine-binding proteins.

4. Experimental

General methods.—Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 22 ± 2 °C. Melting points were measured with a Fisher–Johns melting point apparatus. TLC was performed on Silica Gel 60-F_{254} (E. Merck, Darmstadt) with detection by charring with H_2SO_4. The following solvent systems were used as mobile phases for checking the purity of the final compounds: (A) 10:4:3 EtOAc–MeOH–H_2O; (B) 20:4:3 EtOAc–MeOH–H_2O; (C) 5:3:1:1 EtOAc–MeOH–H_2O–AcOH; (D) 4:1 MeOH–5% aq NH_3. Column chromatography was performed on Silica Gel 60 (40–63 μm, E. Merck, Darmstadt) or on 10% C_{18}–SiO_2 (Toronto Research Chemicals). ^{1}H NMR spectra were recorded at 360 MHz (Bruker AMR 360) with internal $(CH_3)_4Si$ (δ 0) or external acetone (δ 2.225). ^{13}C NMR spectra were recorded at 75 MHz (Bruker AM 300) using $CDCl_3$ (δ 77.0 ppm) or internal dioxane (δ 67.4 ppm) as the references. The following common signals for the octyl aglycon were observed in $CDCl_3$ soln: ^{1}H NMR δ 1.60–1.40 (m, 2 H, OCH_2CH_2), 1.40–1.10 (m, 10 H, $OCH_2CH_2(CH_2)_5CH_3$), 0.85 (t, 3 H, *J* 7 Hz, octyl CH_3); ^{13}C NMR δ 31.8, 29.6, 29.4, 29.3, 26.0, 22.7 ($OCH_2(CH_2)_6CH_3$), 14.1 (octyl CH_3). Only partial NMR data are reported for the final compounds, as the other data were in accord with the proposed structures. FAB mass spectra were recorded on a Kratos AEIMS9 instrument using glycerol as the matrix. HRMS (FAB) are reported for a representative sample of the final disaccharides. Elemental analyses were carried out on a Carlo Erba EA 1108 instrument. Octyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**1**) was prepared from 3,4,6-tri-*O*-acetyl-2-acetamido-2-deoxy-α-D-glucopyranosyl chloride [14] and *n*-octanol, followed by transesterification with NaOMe in MeOH (90% overall yield) as described for the parent 8-ethoxycarbonyloctyl glycoside [8]a. The physical and spectroscopic data for **1** were in accordance with those previously reported [8]b.

Octyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranoside (**2**).—To a soln of **1** (9.04 g, 27.1 mmol) in dry CH_3CN (350 mL) were added α,α-dimethoxytoluene (8.2 mL, 55 mmol) and *p*-toluenesulfonic acid monohydrate (100 mg). After stirring overnight at room temperature, Et_3N (1 mL) was added and the reaction mixture was concd to ~ 100 mL. Compound **2** crystallized out of the soln as colorless needles (10.6 g, 93%): mp 255–257 °C (MeOH); $[\alpha]_D$ −63.8° (*c* 1, 1:1 $CHCl_3$–MeOH). ^{1}H NMR (1:1 $CDCl_3$–CD_3OD): δ 7.42–7.26 (m, 5 H, Ph), 5.46 (s, 1 H, PhCH), 4.48 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.23 (dd, 1 H, $J_{6a,6b}$ 10.5, $J_{5,6a}$ 5.0 Hz, H-6a), 3.70–3.82 (m, 2 H, H-6b, OCH_2CH_2), 3.71 (t, 1 H, $J_{2,3} = J_{3,4} = 10.0$ Hz, H-3), 3.60 (dd, 1 H, $J_{1,2}$ 8.3, $J_{2,3}$ 10.0 Hz, H-2), 3.45 (t, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.45–3.30 (m, 2 H, H-5, OCH_2CH_2), 1.92, (s, 3 H, CH_3CO), 1.53–1.42 (m, 2 H, OCH_2CH_2), 1.30–1.10 (m, 10 H, octyl CH_2), 0.89 (t, 3 H, *J* 7.0 Hz, octyl CH_3). ^{13}C NMR (1:1 $CDCl_3$–CD_3OD): δ 172.0 (CO), 136.8, 128.5, 127.6, 125.8 (Ph), 101.3, 101.2 (C-1, PhCH), 81.2, 70.7, 69.6, 68.1, 65.8 (C-3, C-4, C-5, C-6, OCH_2CH_2), 56.7 (C-2), 31.3, 29.0, 28.7, 25.3, 22.0, 21.9 (octyl CH_2), 23.0 ($COCH_3$), 13.2 (octyl CH_3). Anal. Calcd for $C_{23}H_{35}NO_6$: C, 65.53; H, 8.37; N, 3.32. Found: C, 65.26; H, 8.49; N, 3.25.

Octyl 2-acetamido-4,6-O-benzylidene-3-O-cyanomethyl-2-deoxy-β-D-glucopyranoside (**3**).—Sodium hydride (4.9 g, 160 mmol, 80% in mineral oil) was added to a suspension of **2** (13.8 g, 32.7 mmol) in dry CH_3CN (190 mL), and heat was applied until evolution of gas began. The mixture was further stirred at room temperature for 2 h, then cooled to −20 °C, and bromoacetonitrile (10.9 mL, 164 mmol) was added dropwise. The thick reaction mixture was vigorously stirred between −20 and −15 °C for 5 h (mechanical stirrer) and finally

allowed to reach room temperature overnight. The resulting brown mass was concd, resuspended in CH_2Cl_2, and filtered. Evaporation of the solvent followed by flash chromatography (CH_2Cl_2, then 50:1, 30:1 CH_2Cl_2–MeOH) and trituration with Et_2O yielded **3** (11.0 g, 73%): mp 222–224 °C (MeOH); $[\alpha]_D$ +5.8° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.47–7.34 (m, 5 H, Ph), 5.69 (d, 1 H, $J_{NH,2}$ 7.4 Hz, NH), 5.51 (s, 1 H, PhCH), 5.00 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 4.48, 4.40 (AB system, 2 H, *J* 16.2 Hz, OCH_2CN), 4.34 (dd, 1 H, $J_{6a,6b}$ 10.2, $J_{5,6a}$ 4.9 Hz, H-6a), 4.33 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 3.82 (dt, 1 H, *J* 9.7, 6.4 Hz, OCH_2CH_2), 3.76 (t, 1 H, $J_{5,6b} = J_{6a,6b} = 10.2$ Hz, H-6b), 3.62 (t, 1 H, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 3.52 (m, 1 H, H-5), 3.48 (dt, 1 H, *J* 9.7, 6.9 Hz, OCH_2CH_2), 3.23 (ddd, 1 H, $J_{1,2}$ 8.2, $J_{2,3}$ 9.2, $J_{NH,2}$ 7.4 Hz, H-2), 2.03 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.9 (CO), 137.0, 129.2, 128.3, 126.1 (Ph), 116.6 (CN), 101.5, 101.4 (C-1, PhCH), 82.0, 78.5, 65.5 (C-3, C-4, C-5), 70.3 (OCH_2CH_2), 68.7 (C-6), 57.7 (OCH_2CN) 56.8 (C-2), 23.6 ($COCH_3$). Anal. Calcd for $C_{25}H_{36}N_2O_6$: C, 65.20; H, 7.88; N, 6.08. Found: C, 65.02; H, 7.90; N, 6.02.

*Octyl 2-acetamido-6-*O*-benzyl-3-*O*-cyanomethyl-2-deoxy-β-*D*-glucopyranoside* (**4**).—To a suspension of **3** (7.80 g, 16.9 mmol), $NaCNBH_3$ (11.7 g, 186 mmol), powdered 4 Å molecular sieves (8 g), and a crystal of methyl orange in THF (200 mL) kept at −5 °C was added a satd soln of HCl in Et_2O until a persistent pink color was observed in the reaction mixture. Stirring at −5 °C was continued for 2 h, and finally at room temperature overnight. The solids were removed by filtration and washed with CH_2Cl_2 (400 mL). The organic layer was washed with aq $NaHCO_3$ and water, concd, and purified by flash chromatography (30:1 CH_2Cl_2) to yield **4** as an amorphous solid (6.57 g, 84%): $[\alpha]_D$ −3.1° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.88 (br d, 1 H, $J_{NH,2}$ 8 Hz, NH), 7.40–7.20 (m, 5 H, Ph), 5.52 (br d, 1 H, $J_{OH,4}$ 6 Hz, OH), 4.48 (s, 2 H, $PhCH_2$), 4.46, 4.55 (AB system, 2 H, *J* 16.5 Hz, OCH_2CN), 4.34 (d, 1 H, $J_{1,2}$ 8.1, Hz, H-1), 3.68 (dd, 1 H, $J_{6a,6b}$ 11.0, $J_{5,6a}$ 1.5 Hz, H-6a), 3.62 (dt, 1 H, *J* 9.9, 6.0 Hz, OCH_2CH_2), 3.51 (dd, 1 H, $J_{5,6b}$ 5.9, $J_{6a,6b}$ 11.0 Hz, H-6b), 3.46–3.28 (m, 4 H, H-2, H-3, H-5, OCH_2CH_2), 3.25 (br t, 1 H, H-4), 1.80 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 171.3 (CO), 137.6, 128.3, 127.7, 127.5 (Ph), 117.2 (CN), 99.9 (C-1), 82.3, 73.6, 73.2 (C-3, C-4, C-5), 73.5, 70.3, 69.7, ($PhCH_2$, OCH_2CH_2, C-6), 57.7 (CH_2CN), 55.7 (C-2), 23.4 ($COCH_3$). Anal. Calcd for $C_{25}H_{38}N_2O_6$: C, 64.91; H, 8.28; N, 6.06. Found: C, 64.76; H, 8.60; N, 6.10.

*Octyl 2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-*D*-glucopyranoside* (**5**).—A soln of **2** (11.9 g, 28.2 mmol) and benzyl bromide (6.7 mL, 56 mmol) in dry Me_2NCHO (200 mL) was cooled to 0 °C. Sodium hydride (80% in mineral oil) was added in portions (250 mg, 8.3 mmol each time) every 30 min until the starting material had been consumed as monitored by TLC (~ 1.8 g, 60 mmol was added in total). The reaction was quenched by carefully adding the mixture to 1 L of cold water and stirring for 10 min. The resulting precipitate was isolated by filtration, washed with water, and recrystallized from MeOH to yield **5** (12.5 g, 86%): mp 224–225 °C (MeOH); $[\alpha]_D$ −0.6° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.50–7.25 (m, 10 H, Ph), 5.56 (s, 1 H, PhCH), 5.48 (d, 1 H, $J_{NH,2}$ 7.3 Hz, NH), 4.99 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 4.88 (d, 1 H, J_{gem} 11.7 Hz, $PhCH_2$), 4.63 (d, 1 H, J_{gem} 11.7 Hz, $PhCH_2$), 4.33 (dd, 1 H, $J_{6a,6b}$ 10.3, $J_{5,6a}$ 5.0 Hz, H-6a), 4.31 (t, 1 H, $J_{2,3} = J_{3,4} = 9.2$ Hz, H-3), 3.81 (dt, 1 H, *J* 9.7, 6.5 Hz, OCH_2CH_2), 3.77 (t, 1 H, $J_{5,6b} = J_{6a,6b} = 10.3$ Hz, H-6b), 3.64 (t, $J_{3,4} = J_{4,5} = 9.2$ Hz, H-4), 3.51 (m, 1 H, H-5), 3.46 (dt, 1 H, *J* 9.7, 6.8 Hz, OCH_2CH_2), 3.19 (m, 1 H, H-2), 1.87 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.3 (CO), 138.5, 137.4, 128.9, 128.4, 128.3, 127.8, 126.1 (Ph), 101.2, 100.4 (PhCH, C-1), 82.8, 76.5, 65.9 (C-3, C-4, C-5), 74.5, ($PhCH_2$), 70.2 (OCH_2CH_2), 68.9 (C-6), 58.1 (C-2), 23.5 ($COCH_3$). Anal. Calcd for $C_{30}H_{41}NO_6$: C, 70.42; H, 8.08; N, 2.74. Found: C, 70.11; H, 7.95; N, 2.65.

*Octyl 2-acetamido-3-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**6**).—A suspension of **5** (12.0 g, 23.5 mmol) in 60% AcOH (500 mL) was stirred at 65 °C for 12 h. After evaporation of the solvent under reduced pressure, the residue was triturated with Et_2O (100 mL) and finally purified by flash chromatography (20:1, then 10:1 CH_2Cl_2–MeOH) to yield **6** (6.95 g, 70%): $[\alpha]_D$ −4.9° (*c* 1, MeOH). ^1H NMR (CD_3OD): δ 7.34–7.21 (m, 5 H, Ph), 4.86 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.64 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.42 (d, 1 H, $J_{1,2}$ 8.4 Hz, H-1), 3.87 (dd, 1 H, $J_{6a,6b}$ 11.9, $J_{5,6a}$ 2.5 Hz, H-6a), 3.87 (dt, 1 H, *J* 9.7, 6.4 Hz, OCH_2CH_2), 3.72 (br t, 1 H, *J* 9 Hz, H-2), 3.68 (dd, 1 H, $J_{5,6b}$ 5.9, $J_{6a,6b}$ 11.9 Hz, H-6b), 3.47–3.54 (m, 2 H, H-3, H-4), 3.44 (dt, 1 H, *J* 9.7, 6.4 Hz, OCH_2CH_2), 3.27 (m, 1 H, H-5), 1.86 (s, 3 H, CH_3CO), 1.56–1.48 (m, 2 H, OCH_2CH_2), 1.40–1.23 (m, 10 H, octyl CH_2), 0.89 (t, 3 H, *J* 7.0 Hz, octyl CH_3). ^{13}C NMR (CD_3OD): δ 173.1 (CO), 140.2,

129.2, 128.8, 128.4 (Ph), 102.5 (C-1), 84.1, 77.9, 72.1 (C-3, C-4, C-5), 75.5 ($PhCH_2$), 70.5 (OCH_2CH_2), 62.7 (C-6), 56.4 (C-2), 32.9, 30.6, 30.4, 27.1, 23.7 (octyl CH_2), 23.0 ($COCH_3$), 14.4 (octyl CH_3). Anal. Calcd for $C_{23}H_{37}NO_6$: C, 65.22; H, 8.80; N, 3.31. Found: C, 65.29; H, 8.81; N, 3.28.

*Octyl 2-acetamido-3-*O*-benzyl-6-*O*-cyanomethyl-2-deoxy-β-*D*-glucopyranoside* (**7**).—Compound **6** (5.05 g, 11.9 mmol) and Bu_2SnO (3.56 g, 14.3 mmol) in benzene (100 mL) were heated at reflux with continuous removal of water (Dean–Stark trap) for 24 h. The resulting soln was cooled to 60 °C, and Bu_4NI (4.40 g, 11.9 mmol) and bromoacetonitrile (2.4 mL, 36 mmol) were added. After stirring at 60 °C for 24 h, more bromoacetonitrile (2.4 mL) was added, and stirring was continued for an additional 40 h. The mixture was cooled to room temperature and filtered through a short pad of SiO_2 (40:1 CH_2Cl_2–MeOH). After evaporation of the solvent the residue was purified by flash chromatography (5:2 hexane–acetone) to yield **7** (3.35 g, 61%): mp 139–140 °C (hexane–EtOAc); $[\alpha]_D$ −12.3° (*c* 1, $CHCl_3$). ^{1}H NMR (Me_2SO-d_6): δ 7.86 (d, 1 H, $J_{NH,2}$ 8.9 Hz, NH), 7.33–7.20 (m, 5 H, Ph), 5.45 (d, 1 H, $J_{OH,4}$ 6.6 Hz, OH), 4.76 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.55 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.53, 4.47 (AB system, 2 H, J_{gem} 16.4 Hz, CH_2CN), 4.35 (d, 1 H, $J_{1,2}$ 8.2 Hz, H-1), 3.82 (dd, 1 H, $J_{6a,6b}$ 10.8, $J_{5,6a}$ 1.3 Hz, H-6a), 3.71–3.60 (m, 2 H, H-6b, OCH_2CH_2), 3.53 (br q, 1 H, *J* 8 Hz, H-2), 3.42 (t, *J* 8.5 Hz, H-3), 3.40–3.33 (m, 2 H, H-5, OCH_2CH_2), 3.27 (m, 1 H, converted to t, *J* 8.5 Hz after shaking with D_2O, H-4), 1.76 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.7 (CO), 138.4, 128.7, 128.1, 128.0 (Ph), 116.0 (CN), 99.8 (C-1), 80.5, 74.6, 70.9 (C-3, C-4, C-5), 74.3, 70.6, 70.0 ($PhCH_2$, C-6, OCH_2CH_2), 57.6 (C-2), 57.0 (CH_2CN), 23.6 ($COCH_3$). Anal. Calcd for $C_{25}H_{38}N_2O_6$: C, 64.91; H, 8.28; N, 6.06. Found: C, 64.60; H, 8.45; N, 6.09.

*Octyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**8**).—To a mixture of **5** (11.1 g, 21.7 mmol), $NaCNBH_3$ (15.0 g, 239 mmol), powdered 4 Å molecular sieves (10 g), and a crystal of methyl orange in THF (250 mL) kept at −5 °C was added a satd soln of HCl in Et_2O until a persistent pink color was observed. Stirring at −5 °C was continued for 2 h, and finally at room temperature overnight. The solids were removed by filtration, washed with CH_2Cl_2, and the resulting soln was extracted with aq $NaHCO_3$ and water. The residue was concd, filtered through a short pad of SiO_2 (40:1 CH_2Cl_2–MeOH), and finally purified by flash chromatography (3:1, 2:1, 1:1 toluene–EtOAc) to yield **8** (7.82 g, 70%); $[\alpha]_D$ −7.1° (*c* 1, $CHCl_3$). ^{1}H NMR (Me_2SO-d_6): δ 7.85 (d, 1 H, $J_{NH,2}$ 9.0 Hz, NH), 7.34–7.26 (m, 10 H, Ph), 5.36 (d, 1 H, $J_{OH,4}$ 6.3 Hz, OH), 4.75 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.54 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.53 (s, 2 H, $PhCH_2$), 4.34 (d, 1 H, $J_{1,2}$ 8.3 Hz, H-1), 3.75 (dd, 1 H, $J_{6a,6b}$ 10.9, $J_{5,6a}$ 1.4 Hz, H-6a), 3.60–3.50, 3.45–3.30 (m, 5 H, H-2, H-3, H-5, H-6b, OCH_2CH_2), 3.26 (m, 1 H, converted to dd, *J* 9.5, 8.5 Hz after shaking with D_2O, H-4), 1.76 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.4 (CO), 138.7, 137.8, 128.6, 128.5, 128.1, 127.8 (Ph), 99.8 (C-1), 80.3, 73.6 (C-3, C-4, C-5), 74.3, 73.7 ($PhCH_2$) 70.8, 69.8 (C-6, OCH_2CH_2), 57.4 (C-2), 23.6 ($COCH_3$). Anal. Calcd for $C_{30}H_{43}NO_6$: C, 70.15; H, 8.44; N, 2.73. Found: C, 70.04; H, 8.77; N, 2.74.

*Phenyl 2,4,6-tri-*O*-acetyl-3-*O*-cyanomethyl-1-thio-β-*D*-galactopyranoside* (**10**).—Phenyl 1-thio-β-D-galactopyranoside (**9**) (10.9 g, 40 mmol) and Bu_2SnO (11.0 g, 44.2 mmol) in benzene (300 mL) were heated at reflux with continuous removal of water (Dean–Stark trap) for 14 h. To the resulting soln were added Et_4NBr (8.41 g, 40 mmol) and bromoacetonitrile (10.7 mL, 161 mmol), and refluxing was continued for 4h. The mixture was evaporated, and the residue filtered through a short pad of SiO_2 (200 g, 20:1 CH_2Cl_2–MeOH). After evaporation of the solvent, the residue was stirred overnight with 1:1 Ac_2O–pyridine (100 mL), concd, and crystallized from 95% EtOH (250 mL, 4 °C overnight) to yield **10** as white needles (6.75 g; concn of the mother liquor to 100 mL yielded an additional 0.64 g, 42% overall yield): mp 115–117 °C (EtOH); $[\alpha]_D$ +33.0° (*c* 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.51–7.46 (m, 5 H, Ph), 5.38 (dd 1 H, $J_{3,4}$ 3.5, $J_{4,5}$ 0.9 Hz, H-4), 5.09 (t, 1 H, $J_{1,2} = J_{2,3} = 9.6$ Hz, H-2), 4.67 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.31, 4.27 (AB system, 2 H, *J* 16.5 Hz, CH_2CN), 4.18 (dd, $J_{6a,6b}$ 11.2, $J_{5,6a}$ 7.0 Hz, H-6a), 4.13 (dd $J_{6a,6b}$ 11.2, $J_{5,6b}$ 6.3 Hz, H-6b), 3.85 (br t, *J* 7 Hz, H-5), 3.74 (dd, $J_{2,3}$ 9.6, $J_{3,4}$ 3.5 Hz, H-3), 2.15, 2.09, 2.04 (3 s, 9 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.3, 170.1, 169.3 (CO), 132.4, 132.2, 128.7, 127.9 (Ph), 115.5 (CN), 86.1 (C-1), 78.8, 74.0, 67.7, 65.0, 61.6 (C-2, C-3, C-4, C-5, C-6), 54.6 (CH_2CN), 20.7, 20.4, 20.3 (CH_3CO). Anal. Calcd for $C_{20}H_{23}NO_8S$: C, 54.91; H, 5.30; N, 3.20, S, 7.33. Found: C, 54.73; H, 5.09; N, 3.16; S, 7.43.

*Phenyl 3-*O*-benzyl-1-thio-β-*D*-galactopyranoside* (**11**).—Phenyl 1-thio-β-D-galactopyranoside (**9**, 10.0 g, 36.7 mmol) and Bu_2SnO (10.0 g, 40.2 mmol) in benzene (300 mL) were heated under reflux for 24 h

with continuous removal of water (Dean–Stark trap). After concentrating the resulting soln to 150 mL, Bu_4NI (14.7 g, 39.8 mmol) and benzyl bromide (8.7 mL, 73.1 mmol) were added, and stirring was continued overnight at 65 °C. The reaction mixture was evaporated, and the residue was redissolved in MeOH (400 mL) and stirred with Dowex 50W-X8 (Na^+, 100 g) for 4 h. The resin and insoluble salts were removed by filtration, and the filtrate was concd and purified by flash chromatography (1:1, 2:3 toluene–EtOAc) to yield **11** (5.75 g, 43%): mp 161–163 °C (EtOAc–hexane); $[\alpha]_D$ −8.5° (*c* 1, MeOH). ^1H NMR (Me_2SO-d_6 + D_2O): δ 7.50–7.10 (m, 10 H, Ph), 4.67 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 4.59 (d, 1 H, $J_{1,2}$ 9.3 Hz, H-1), 5.53 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 3.97 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 3.59 (t, 1 H, $J_{1,2} = J_{2,3} = 9.3$ Hz, H-2), 3.55–3.40 (m, 3 H, H-5, H-6a, H-6b), 3.32 (dd, 1 H, $J_{2,3}$ 9.3, $J_{3,4}$ 3.0 Hz, H-3). ^{13}C NMR (Me_2SO-d_6): δ 139.1, 135.3, 129.6, 128.9, 128.1, 127.6, 127.3, 126.3 (Ph), 87.9 (C-1), 82.6, 79.1, 68.3, 65.0 (C-2, C-3, C-4, C-5), 70.4 ($PhCH_2$), 60.6 (C-6). Anal. Calcd for $C_{19}H_{22}O_5S$: C, 62.96; H, 6.12; S, 8.85. Found: C, 62.80; H, 6.15; S, 8.80.

Phenyl 2,4-di-O-acetyl-3-O-benzyl-6-O-cyanomethyl-1-thio-β-D-galactopyranoside (**12**).—Compound **11** (5.00 g, 13.8 mmol) and Bu_2SnO (3.7 g, 14.9 mmol) in benzene (150 mL) were heated under reflux for 24 h with continuous removal of water (Dean–Stark trap). The soln was concd to 70 mL, Bu_4NI (5.10 g, 13.8 mmol) and bromoacetonitrile (3.7 mL, 56 mmol) were added, and the mixture stirred at 80 °C. After 12 h, more bromoacetonitrile (3.7 mL) was added, and stirring was continued at 80 °C for a total period of 24 h. The mixture was concd, and the residue was redissolved in MeOH (200 mL) and treated with Dowex 50W-X8 (Na^+, 50 g). The resin and insoluble salts were removed by filtration, and the filtrate was concd and purified by flash chromatography (4:1, 1:1 toluene–EtOAc) to yield 1.56 g of a yellowish solid and recovered unreacted starting material (1.68 g, 34%). The product was stirred overnight with Ac_2O–pyridine (50 mL), concd, and purified again by flash chromatography (7:1 toluene–EtOAc) to yield **12** (1.80 g, 27% overall yield): $[\alpha]_D$ +42.3° (*c* 2, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.50–7.20 (m, 10 H, Ph), 5.51 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 0.9 Hz, H-4), 5.14 (t, 1 H, $J_{1,2} = J_{2,3} = 9.6$ Hz, H-2), 4.66 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 4.63 (d, 1 H, $J_{1,2}$ 9.6 Hz, H-1), 4.38 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 4.21, 4.19 (AB system, 2 H, *J* 16.2 Hz, CH_2CN), 3.76 (dt, 1 H, $J_{5,6a} = J_{5,6b} = 6.0$ Hz, $J_{4,5}$ 0.9 Hz, H-5), 3.68 (dd, $J_{6a,6b}$ 10.0, $J_{5,6a}$ 6.0 Hz, H-6a), 3.65 (dd $J_{6a,6b}$ 10.0, $J_{5,6b}$ 6.0 Hz, H-6b), 3.54 (dd, $J_{2,3}$ 9.6, $J_{3,4}$ 3.4 Hz, H-3), 2.15, 2.04 (2 s, 6 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.4, 169.4 (CO), 137.3, 132.7, 132.4, 129.0, 128.4, 128.0, 127.9 (Ph), 115.5 (CN), 86.7 (C-1), 77.5, 75.9, 68.9, 66.2 (C-2, C-3, C-4, C-5), 71.3, 69.7 (C-6, $PhCH_2$), 56.8 (CH_2CN), 21.0, 20.8 (CH_3CO). Anal. Calcd for $C_{25}H_{27}NO_7S$: C, 61.84; H, 5.60; N, 2.88, S, 6.60. Found: C, 61.63; H, 5.49; N, 3.00; S, 6.43.

Phenyl 2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-1-thio-β-D-galactopyranoside (**13**).—Phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside [15] (4.74 g, 10.5 mmol) and benzoyl chloride (2.5 mL, 22 mmol) in pyridine (100 mL) were stirred overnight at room temperature. The reaction mixture was concd, redissolved in CH_2Cl_2, washed with aq $NaHCO_3$, dried (Na_2SO_4), and purified by flash chromatography (CH_2Cl_2) to yield **13** (5.30 g, 91%): $[\alpha]_D$ −5.3° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.00–7.10 (m, 20 H, Ph), 5.55 (t, 1 H, $J_{1,2} = J_{2,3} = 9.8$ Hz, H-2), 5.47 (s, 1 H, PhCH), 4.79 (d, 1 H, $J_{1,2}$ 9.8 Hz, H-1), 4.61 (d, 1 H, J_{gem} 12.7 Hz, $PhCH_2$), 4.54 (d, 1 H, J_{gem} 12.7 Hz, $PhCH_2$), 4.37 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{5,6a}$ 1.6 Hz, H-6a), 4.22 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 0.9 Hz, H-4), 4.01 (dd, 1 H, $J_{6a,6b}$ 12.3, $J_{5,6b}$ 1.6 Hz, H-6b), 3.75 (dd, 1 H, $J_{2,3}$ 9.8, $J_{3,4}$ 3.4 Hz, H-3), 3.48 (m, 1 H, H-5). ^{13}C NMR ($CDCl_3$): δ 164.9 (CO), 137.7–126.6 (Ph), 101.3 (PhCH), 85.5 (C-1), 78.3, 73.2, 70.1, 69.1 (C-2, C-3, C-4, C-5), 71.1, 69.3 (C-6, $PhCH_2$). Anal. Calcd for $C_{33}H_{30}O_6S$: C, 71.46; H, 5.45; S, 5.78. Found: C, 71.33; H, 5.42; S, 6.03.

Octyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-6-O-benzyl-3-O-cyanomethyl-2-deoxy-β-D-glucopyranoside (**15**).—Octyl 2-acetamido-6-*O*-benzyl-3-*O*-cyanomethyl-2-deoxy-β-D-glucopyranoside (**4**, 0.96 g, 2.08 mmol) and powdered 4 Å molecular sieves (2 g) in CH_2Cl_2 (8 mL) were stirred under Ar for 2 h. Silver trifluoromethanesulfonate (1.07 g, 4.16 mmol) was added, the soln was cooled to −10 °C, and 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl bromide (**14**, 1.72 g, 4.18 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise. The soln was allowed to warm to 0 °C, stirred at this temperature for 3 h, and filtered. The filtrate was washed with aq $NaHCO_3$, dried (Na_2SO_4), and concd. Flash chromatography (1:3 → 2:5 acetone–hexane) yielded a white foam that was treated overnight with 1:1 Ac_2O–pyridine (10 mL), concd, and purified again by column chromatography (2:5 acetone–hexane). The resulting compound (1.17 g, 71%) contained ~15% (^1H NMR) of the corresponding α

anomer. Further purification by column chromatography (1.5% EtOH in $CHCl_3$) afforded the pure β anomer **15** (760 mg, 46%): $[\alpha]_D$ +8.2° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.40–7.28 (m, 5 H, Ph), 5.76 (d, 1 H, $J_{NH,2}$ 7.8 Hz, NH), 5.27 (dd, 1 H, $J_{3,4}$ 3.3, $J_{4,5}$ 0.8 Hz, H-4′), 5.01 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.4 Hz, H-2′), 4.83 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1′), 4.79 (dd, 1 H, $J_{2,3}$ 10.4, $J_{3,4}$ 3.3 Hz, H-3′), 4.73 (d, 1 H, J_{gem} 12.1 Hz, $PhCH_2$), 4.44 (d, 1 H, $J_{1,2}$ 7.4 Hz, H-1), 4.43 (d, 1 H, J_{gem} 12.1 Hz, $PhCH_2$), 4.47, 4.40 (AB, 2 H, *J* 16.3 Hz, CH_2CN), 4.19 (dd, 1 H, $J_{6a,6b}$ 11.3, $J_{5,6a}$ 6.9 Hz, H-6′a), [4.03–3.96 (m, 2 H), 3.87–3.76 (m, 2 H), 3.70–3.59 (m, 2 H), 3.46–3.37 (m, 2 H), H-2, H-3, H-4, H-5, H-6a, H-6b, H-5′, H-6′b, OCH_2CH_2], 3.22 (dt, 1 H, *J* 9.3, 7.9 Hz, OCH_2CH_2), 2.11, 2.03, 2.01, 1.95, 1.94 (5 s, 15 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.9, 170.4, 170.2, 169.9, 169.1 (CO), 137.8, 128.7, 128.1 (Ph), 117.1 (CN), 100.4, 99.6 (C-1, C-1′), 79.9, 77.4, 74.0, 70.8, 70.7, 69.1, 67.0 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.7, 69.9, 67.5, 60.9 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 57.9 (CH_2CN), 56.4 (C-2), 23.7, 20.7–20.5 (CH_3CO). Anal. Calcd for $C_{39}H_{56}N_2O_{15}$: C, 59.08; H, 7.12; N, 3.53. Found: C, 59.03; H, 7.37; N, 3.50.

*Octyl 2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-3-*O*-benzyl-6-*O*-cyanomethyl-2-deoxy-β-*D*-glucopyranoside* (**16**).— Octyl 2-acetamido-3-*O*-benzyl-6-*O*-cyanomethyl-2-deoxy-β-D-glucopyranoside (**7**, 1.04 g, 2.25 mmol) and powdered 4 Å molecular sieves (2 g) in CH_2Cl_2 (10 mL) were stirred under Ar for 2 h. Silver trifluoromethanesulfonate (1.16 g, 4.51 mmol) was added, the soln was cooled to −10 °C, and 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl bromide (**14**, 1.85 g, 4.50 mmol) in dry CH_2Cl_2 (6 mL) was added dropwise. The soln was stirred at 0 °C for 2 h, then dild with CH_2Cl_2, filtered, washed with aq $NaHCO_3$, concd, and dried (Na_2SO_4). Purification by flash chromatography (6:1 toluene–EtOAc), followed by crystallization from EtOAc–hexane, afforded **16** (1.14 g, 64%): $[\alpha]_D$ −18.0° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.32–7.25 (m, 5 H, Ph), 5.91 (d, 1 H, $J_{NH,2}$ 8.5 Hz, NH), 5.35 (dd, 1 H, $J_{3,4}$ 3.4, $J_{4,5}$ 0.7 Hz, H-4′), 5.16 (dd, 1 H, $J_{1,2}$ 7.9, $J_{2,3}$ 10.5 Hz, H-2′), 5.02 (dd, 1 H, $J_{2,3}$ 10.5, $J_{3,4}$ 3.4 Hz, H-3′), 4.73 (d, 1 H, $J_{1,2}$ 5.4 Hz, H-1), 4.71, 4.67 (AB, 2 H, *J* 11.5 Hz, $PhCH_2$), 4.57 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1′), 4.32, 4.22 (AB, 2 H, *J* 16.1 Hz, CH_2CN), 4.06–3.62 (m, 10 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-5′, H-6′a, H-6′b, OCH_2CH_2), 3.38 (dt, 1 H, *J* 9.4, 6.7 Hz, OCH_2CH_2), 2.11, 2.07, 1.99, 1.96, 1.92 (5 s, 15 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.3, 170.2, 170.1, 170.0, 169.9 (CO), 138.4, 128.4, 127.7 (Ph), 115.8 (CN), 100.1, 100.0 (C-1, C-1′), 76.4, 75.3, 73.5, 70.9, 70.6, 69.3, 66.8 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.1, 70.2, 69.8, 60.7 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 56.8 (CH_2CN), 52.7 (C-2), 23.3, 20.9, 20.6, 20.5 (CH_3CO). Anal. Calcd for $C_{39}H_{56}N_2O_{15}$: C, 59.08; H, 7.12; N, 3.53. Found: C, 59.02; H, 7.20; N, 3.44.

*Octyl 2,4,6-tri-*O*-acetyl-3-*O*-cyanomethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**17**).—Phenyl 2,4,6-tri-*O*-acetyl-3-*O*-cyanomethyl-β-D-galactopyranoside (**10**, 1.50 g, 3.43 mmol), octyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**8**, 1.18 g, 2.30 mmol), and powdered 4 Å molecular sieves (3 g) in CH_2Cl_2 (30 mL) were stirred under Ar for 2 h. Silver trifluoromethanesulfonate (1.32 g, 5.14 mmol) was added, the mixture was cooled to −30 °C, and bromine (0.18 mL, 3.5 mmol) was added dropwise. Stirring at −30 °C was continued for 1 h, the mixture was then warmed to room temperature, and Et_3N (1 mL) was added. After diluting with CH_2Cl_2, the solids were removed by filtration, and the soln was washed with aq $NaHCO_3$, dried (Na_2SO_4), and concd. Column chromatography (2:1 toluene–EtOAc) afforded **17** (1.21 g, 63%): $[\alpha]_D$ −0.6° (*c* 1.5, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.40–7.25 (m, 10 H, Ph), 5.79 (d, 1 H, $J_{NH,2}$ 8.3 Hz, NH), 5.24 (br d, 1 H, $J_{3,4}$ 3.0 Hz, H-4′), 4.96 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.9 Hz, H-2′), 4.74 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.73 (d, 1 H, $J_{1,2}$ 6.1 Hz, H-1), 4.66 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 4.62 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.45 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1′), 4.44 (d, 1 H, J_{gem} 12.0 Hz, $PhCH_2$), 4.26 (s, 2 H, CH_2CN), 4.48–3.48 (m, 11 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b, OCH_2CH_2), 3.39 (dt, 1 H, *J* 9.5, 6.8 Hz, OCH_2CH_2), 2.09, 2.07, 2.01, 1.90 (4 s, 12 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.6, 170.2, 169.9 (CO), 138.7, 138.1, 128.6, 128.3, 128.0, 127.8, 127.6 (Ph), 115.6 (CN), 99.9, 99.7 (C-1, C-1′), 77.9, 75.7, 74.3, 70.5, 69.9, 64.8 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.6, 73.5, 69.7, 68.8, 60.9 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 54.9 (CH_2CN), 53.5 (C-2), 23.4, 20.9, 20.7 (CH_3CO). Anal. Calcd for $C_{44}H_{60}N_2O_{14}$: C, 62.84; H, 7.19; N, 3.33. Found: C, 62.45; H, 7.14; N, 3.36.

*Octyl 2,4-di-*O*-acetyl-3-*O*-benzyl-6-*O*-cyanomethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-*D*-glucopyranoside* (**18**).—Phenyl 2,4-di-*O*-acetyl-3-*O*-benzyl-6-*O*-cyanomethyl-β-D-galactopyranoside (**12**, 1.97 g, 4.06 mmol), octyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-gluco-

pyranoside (**8**, 1.34 g, 2.61 mmol), and powdered 4 Å molecular sieves (4 g) in CH_2Cl_2 (25 mL) were stirred under Ar for 2 h. Silver trifluoromethanesulfonate (1.34 g, 5.22 mmol) was added, the mixture was cooled to −30 °C, and bromine (90 μL, 1.76 mmol) was added dropwise. The reaction mixture was stirred for 1 h at −30 °C and then processed as described for the synthesis of **17**. Column chromatography (12:1 CH_2Cl_2–acetone) afforded **18** (1.56 g, 67%): $[\alpha]_D$ +7.5° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.36–7.18 (m, 15 H, Ph), 5.86 (br d, 1 H, $J_{NH,2}$ 8 Hz, NH), 5.40 (d, 1 H, $J_{3,4}$ 3.5 Hz, H-4′), 5.02 (dd, 1 H, $J_{1,2}$ 8.1, $J_{2,3}$ 10.0 Hz, H-2′), 4.75 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.69 (d, 1 H, $J_{1,2}$ 6.0 Hz, H-1), 4.65 (2 d, 2 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.61 (d, 1 H, J_{gem} 11.9 Hz, $PhCH_2$), 4.38 (d, 1 H, J_{gem} 11.9 Hz, $PhCH_2$), 4.36 (d, 1 H, $J_{1,2}$ 8.1 Hz, H-1′), 4.35 (d, 1 H, J_{gem} 11.5 Hz, $PhCH_2$), 4.15, 4.02 (AB system, 2 H, *J* 16.1 Hz, CH_2CN), 3.96–3.32 (m, 12 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b, OCH_2CH_2), 2.14, 1.99, 1.92 (3 s, 9 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.3, 169.8 (CO), 138.8, 138.1, 137.5, 128.4–127.6 (Ph), 115.7 (CN), 100.0, 99.9 (C-1, C-1′), 76.3, 75.5, 74.3, 72.1, 70.9, 66.0 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.5, 73.3, 71.3, 69.6, 69.1, 69.0 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 56.8 (CH_2CN), 53.5 (C-2), 23.4, 21.0, 20.9 (CH_3CO). Anal. Calcd for $C_{49}H_{64}N_2O_{13}$: C, 66.20; H, 7.26; N, 3.15. Found: C, 65.95; H, 7.20; N, 3.18.

Octyl 2-O-benzoyl-3-O-benzyl-4,6-O-benzylidene-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**19**).—Phenyl 2-*O*-benzoyl-3-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranoside (**13**, 2.06 g, 3.71 mmol), octyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**8**, 1.27 g, 2.47 mmol), and powdered 4 Å molecular sieves (4 g) in CH_2Cl_2 (25 mL) were stirred under Ar for 2 h. Silver trifluoromethanesulfonate (1.27 g, 4.94 mmol) was added, the mixture was cooled to −30 °C, and bromine (100 μL, 1.95 mmol) was added dropwise. After stirring for 1 h at −30 °C, the mixture was processed as described above for the synthesis of **17** and **18**. Column chromatography (15:1, 10:1 CH_2Cl_2–acetone) afforded **19** (1.35 g, 57%); $[\alpha]_D$ +1.5° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 8.00–7.15 (m, 25 H, Ph), 5.88 (br d, 1 H, $J_{NH,2}$ 8 Hz, NH), 5.56 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.0 Hz, H-2′), 5.48 (s, 1 H, PhCH), 4.81, 4.71 (AB system, 2 H, *J* 11.8 Hz, $PhCH_2$), 4.67, 4.58 (AB system, 2 H, *J* 12.5 Hz, $PhCH_2$), 4.55 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1′), 4.50, 4.32 (AB system, 2 H, *J* 11.9 Hz, $PhCH_2$), 4.36 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 4.23 (d, 1 H, $J_{6a,6b}$ 12.5 Hz, H-6′a), 4.14 (d, $J_{3,4}$ 3.6 Hz, H-4′), 4.02–3.43 (m, 9 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-6′b, OCH_2CH_2), 3.08 (m, 1 H, H-5′), 2.99 (dt, 1 H, *J* 9.5, 6.8 Hz, OCH_2CH_2), 1.93 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.1, 165.6 (CO), 138.8–126.4 (Ph), 101.2, 100.6, 99.8 (C-1, C-1′, PhCH), 78.4, 75.2, 74.8, 73.0, 71.3, 66.7 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.5, 73.4, 70.9, 69.5, 69.3, 69.0 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 53.3 (C-2), 23.4 (CH_3CO). Anal. Calcd for $C_{57}H_{67}NO_{12}$: C, 71.45; H, 7.05; N, 1.46. Found: C, 71.35; H, 6.96; N, 1.47.

Octyl 3-O-benzyl-4,6-O-benzylidene-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**20**).—Compound **19** (1.67 g, 1.74 mmol) was stirred overnight with 0.1 M NaOMe in MeOH (100 mL) at 45–50 °C. The soln was neutralized with CO_2 (s), filtered, concd, and purified by flash chromatography (10:1 CH_2Cl_2–acetone) to yield **20** (1.34 g, 90%): $[\alpha]_D$ +28.6° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.50–7.10 (m, 20 H, Ph), 5.58 (br d, 1 H, $J_{NH,2}$ 8 Hz, NH), 5.37 (s, 1 H, PhCH), 5.00 (d, J_{gem} 11.7 Hz, $PhCH_2$), 4.78 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1′), 4.73–4.64 (m, 4 H, $PhCH_2$), 4.50 (d, 1 H, J_{gem} 12.1 Hz, $PhCH_2$), 4.48 (d, 1 H, $J_{1,2}$ 7.7 Hz, H-1), 4.14–3.26 (m, 13 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2′, H-3′, H-3′, H-4′, H-6′a, H-6′b, OCH_2CH_2), 2.92 (m, 1 H, H-5′), 1.83 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.3 (CO), 139.0–126.4 (Ph), 103.1, 101.1, 100.1 (C-1, C-1′, PhCH), 79.2, 78.9, 77.7, 74.6, 73.0, 70.7, 66.6 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 74.0, 73.3, 71.4, 69.7, 69.1, 68.8 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 56.4 (C-2), 23.5 (CH_3CO). Anal. Calcd for $C_{50}H_{63}NO_{11}$: C, 70.32; H, 7.44; N, 1.64. Found: C, 70.35; H, 7.56; N, 1.72.

Octyl 3-O-benzyl-2-O-cyanomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**22**).—A mixture of **20** (1.37 g, 1.60 mmol) and NaH (240 mg, 80% dispersion in mineral oil, 8.0 mmol) in CH_3CN (10 mL) was gently heated until evolution of gas began, then stirred at room temperature for 1 h. The resulting suspension was cooled to −20 °C, and dry CH_2Cl_2 (10 mL), followed by bromoacetonitrile (0.54 mL, 8.1 mmol), were added. After stirring at −20 °C for 2 h, the reaction mixture was allowed to warm to room temperature. After addition of more NaH (240 mg), the soln was again stirred for 1 h at room temperature. After cooling to −20 °C, more bromoacetonitrile (0.54 mL) was added dropwise, and the mixture was slowly warmed to room temperature

overnight, dild with CH_2Cl_2, filtered, and concd. The residue was purified by flash chromatography (12:1 CH_2Cl_2–acetone). Two main fractions identified as octyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-cyanomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**21**, 0.88 g) and unreacted starting material (0.54 g, 39%) were recovered. Compound **21** was stirred overnight with 60% aq AcOH (50 mL) at 60 °C, concd, and purified by column chromatography (1:3 toluene–EtOAc) to yield **22** (0.68 g, 53% overall yield): $[\alpha]_D$ +13.4° (*c* 1.5, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.40–7.20 (m, 15 H, Ph), 5.70 (br d, 1 H, $J_{NH,2}$ 7 Hz, NH), 4.86 (d, 1 H, J_{gem} 11.4 Hz, $PhCH_2$), 4.81 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1′), 4.68–4.57 (m, 4 H, $PhCH_2$), 4.45 (d, 1 H, J_{gem} 12.1 Hz, $PhCH_2$), 4.39, 4.35 (AB system, *J* 15.9 Hz, CH_2CN), 4.31 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1), 4.11–3.08 (m, 14 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-2′, H-3′, H-4′, H-5′, H-6′a, H-6′b, OCH_2CH_2), 2.6–2.3 (br s, 2 H, OH), 1.86 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.6 (CO), 138.7–127.7 (Ph), 116.3 (CN), 101.3, 99.8 (C-1, C-1′), 80.6, 80.1, 77.9, 77.2, 74.9. 74.0, 67.0 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 74.4, 73.4, 72.1, 69.8, 68.6 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 57.9 (CH_2CN), 56.7 (C-2), 23.5 (CH_3CO). Anal. Calcd for $C_{45}H_{60}N_2O_{11}$: C, 67.14; H, 7.51; N, 3.48. Found: C, 67.07; H, 7.60; N, 3.61.

Octyl 2-O-benzoyl-3,6-di-O-benzyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**23**).—To a suspension of **19** (4.45 g, 4.64 mmol), $NaCNBH_3$ (3.0 g, 47 mmol), powdered 4 Å molecular sieves (4 g), and a crystal of methyl orange in THF (150 mL) kept at 0 °C was added a satd soln of HCl in Et_2O until a persistent pink color appeared in the reaction mixture. The soln was warmed to room temperature and then stirred for 5 h. The mixture was dild with CH_2Cl_2, filtered, washed with aq $NaHCO_3$, and purified by flash chromatography (2:1 toluene–EtOAc) to yield **23** (3.80 g, 85%); $[\alpha]_D$ −1.5° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.94–7.15 (m, 25 H, Ph), 6.03 (br s, 1 H, NH), 5.42 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 9.8 Hz, H-2′), 4.67 (d, 1 H, J_{gem} 12.2 Hz, $PhCH_2$), 4.66 (s, 2 H, $PhCH_2$), 4.52–4.48 (m, 5 H, $PhCH_2$, H-1′), 4.33 (d, 1 H, J_{gem} 11.8 Hz, $PhCH_2$), 4.31 (d, 1 H, $J_{1,2}$ 5.6 Hz, H-1), 4.12 (d, 1 H, $J_{3,4}$ 3.3 Hz, H-4′), 4.02–3.44 (m, 11 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b, OCH_2CH_2), 2.93 (dt, 1 H, *J* 9.5, 6.8 Hz, OCH_2CH_2), 1.96 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.1, 165.9 (CO), 138.7–127.4 (Ph), 100.6, 99.4 (C-1, C-1′), 78.1, 77.9, 74.9, 74.3, 73.4, 71.8, 65.8 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.8, 73.4, 72.8, 71.3, 69.5, 69.3, 68.4 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 52.8 (C-2), 23.3 (CH_3CO). Anal. Calcd for $C_{57}H_{69}NO_{12}$: C, 71.30; H, 7.24; N, 1.46. Found: C, 71.26; H, 7.20; N, 1.55.

Octyl 2-O-benzoyl-3,6-di-O-benzyl-4-O-cyanomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside (**24**).—Compound **23** (2.80 g, 2.92 mmol) and NaH (0.54 g 80% dispersion in oil, 18 mmol) in anhyd CH_3CN (20 mL) were stirred at room temperature for 2 h. The soln was cooled to −18 °C and CH_2Cl_2 (20 mL) followed by bromoacetonitrile (1.2 mL, 18 mmol) were added. The mixture was warmed to room temperature over a period of 4 h, then dild with CH_2Cl_2, filtered, concd, and purified by column chromatography (20:1, 10:1 CH_2Cl_2–acetone) to yield **24** (1.31 g, 45%) and unreacted starting material (0.86 g, 31%); $[\alpha]_D$ −15.8° (*c* 1, $CHCl_3$). ^1H NMR ($CDCl_3$): δ 7.94–7.15 (m, 25 H, Ph), 5.90 (d, 1 H, $J_{NH,2}$ 8.6 Hz, NH), 5.44 (dd, 1 H, $J_{1,2}$ 8.0, $J_{2,3}$ 10.1 Hz, H-2′), 4.69–4.45 (m, 10 H, $PhCH_2$, CH_2CN, H-1′), 4.33 (d, 1 H, $J_{1,2}$ 7.3 Hz, H-1), 4.32 (d, 1 H, J_{gem} 11.8 Hz, $PhCH_2$), 4.09 (d, 1 H, $J_{3,4}$ 2.7 Hz, H-4′), 3.98–3.43 (m, 11 H, H-2, H-3, H-4, H-5, H-6a, H-6b, H-3′, H-5′, H-6′a, H-6′b, OCH_2CH_2), 2.93 (dt, 1 H, *J* 9.5, 6.8 Hz, OCH_2CH_2), 1.96 (s, 3 H, CH_3CO). ^{13}C NMR ($CDCl_3$): δ 170.1, 165.7 (CO), 138.6–127.4 (Ph), 116.2 (CN), 100.5, 99.4 (C-1, C-1′), 79.3, 78.0, 74.7, 74.5, 73.9, 72.7, 72.1 (C-3, C-4, C-5, C-2′, C-3′, C-4′, C-5′), 73.8, 73.4, 73.0, 72.9, 69.5, 69.2, 67.3 (C-6, C-6′, $PhCH_2$, OCH_2CH_2), 57.4 (CH_2CN), 53.1 (C-2), 23.3 (CH_3CO). Anal. Calcd for $C_{59}H_{70}N_2O_{12}$: C, 70.92; H, 7.06; N, 2.80. Found: C, 70.73; H, 7.11; N, 2.79.

General method for the synthesis of the O-carboxymethyl derivatives.—To a soln of the *O*-cyanomethyl disaccharide (0.2 mmol) in MeOH (6 mL) was added 25% aq NaOH (1.5 mL), and the mixture was stirred under reflux for 4 h. The solvent was removed under reduced pressure and the residue redissolved in 1:1 THF–H_2O (50 mL) and stirred with excess Amberlite IR-120 (H^+) for 10 min. After removal of the resin by filtration and evaporation of the solvent, the residue was redissolved in 1:1 THF–H_2O (10 mL) and stirred overnight under a stream of H_2 in the presence of 10% Pd–C (30 mg). Removal of the catalyst by filtration and evaporation of the solvent yielded a residue that was redissolved in cold H_2O, brought to pH 1 with 0.1 N HCl and loaded onto a small reversed-phase C_{18}–SiO_2 column (10 g). After washing with H_2O, the corresponding acids

were eluted with 2:3 CH_3CN–H_2O. The solvent was removed by evaporation, and an aq soln of the residue was filtered (0.22 μm Millex filter) and freeze-dried to yield compounds **25a–30a** (yield > 90%).

General method for the synthesis of the O-*carbamoylmethyl derivatives.*—A soln of the *O*-cyanomethyl disaccharide (0.2 mmol) in freshly prepared 0.1 M NaOMe in MeOH (5 mL) was stirred overnight at room temperature. The temperature of the mixture was then raised to 50 °C, and a satd aq soln of $NaHCO_3$ (1 mL) was added. Stirring at 50 °C was continued until the reaction was judged complete by TLC (8 h to 4 days). The inorganic salts were removed by filtration and washed with MeOH. The filtrate was concd and purified by flash chromatography (MeOH–H_2O–EtOAc or CH_2Cl_2–MeOH mixtures). The resulting compound was redissolved in MeOH (10 mL) and stirred overnight under a stream of H_2 in the presence of 10% Pd–C (30 mg). After removal of the catalyst by filtration, the solvent was removed under reduced pressure. The residue redissolved in H_2O, filtered (0.22 μm Millex filter), and freeze-dried. Compounds **25b–30b** were obtained in 46 to 68% yield.

General method for the synthesis of the O-*amidinomethyl derivatives.*—A soln of the *O*-cyanomethyl disaccharide (0.2 mmol) in freshly prepared 0.1 M NaOMe in MeOH (5 mL) was stirred overnight at room temperature. Solid NH_4Cl (180 mg, 3.4 mmol) was added and stirring was continued at room temperature for 3 h. The insoluble salts were removed by filtration and washed with MeOH, and the soln was concd under reduced pressure. The residue was redissolved in 0.1 N HCl, loaded onto a C_{18}–SiO_2 column (10 g), washed with H_2O, and eluted with MeOH–H_2O (1:4, then 2:3). Evaporation of the solvent yielded a residue that was redissolved in MeOH (10 mL) and stirred overnight under a stream of H_2 in the presence of 10% Pd–C (30 mg). After removal of the catalyst and evaporation of the solvent under reduced pressure, the residue was redissolved in H_2O, filtered (0.22 μm), and freeze-dried. Compounds **25c–30c** were obtained in 58 to 82% yield.

General method for the synthesis of the O-*(2-aminoethyl) derivatives.*—A soln of the *O*-cyanomethyl disaccharide (0.2 mmol) in MeOH or EtOH (10 mL) containing 1.5 equiv of HCl (300 μL of aq N HCl) was stirred for 24 h under a stream of H_2 in the presence of 10% Pd–C (100 mg). Removal of the catalyst and evaporation of the solvent yielded a residue that was stirred overnight with 0.1 M NaOMe in MeOH (10 mL). After concn of the soln, the reaction mixture was purified by column chromatography (Iatrobeads SiO_2, 4:1 MeOH–5% aq NH_3). The resulting amines were redissolved in 0.1 N aq HCl and purified again over C_{18}–SiO_2 (H_2O, then 3:7 CH_3CN–H_2O). After evaporation of the solvent, filtration (0.22 μm) of the aq soln, and lyophilization, the amine hydrochlorides **25d–30d** were obtained in 38–75% yield.

*Octyl β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-3-*O*-carboxymethyl-2-deoxy-β-*D*-glucopyranoside* (**25a**).—Obtained in 93% yield from **16**. R_f 0.45 (solvent A). ^{1}H NMR (D_2O): δ 4.54 (d, 1 H, *J* 8.3 Hz, H-1/1′), 4.49 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.49 and 4.31 (AB system, 2 H, *J* 16.1 Hz, OCH_2COOH), 2.04 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{43}NO_{13}Na$: *m/z* 576.2632; found: 576.2647

*Octyl β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-6-*O*-carboxymethyl-2-deoxy-β-*D*-glucopyranoside* (**26a**).—Obtained in 90% yield from **16**. R_f 0.42 (solvent A). ^{1}H NMR (D_2O): δ 4.52 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.49 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.20 (s, AB system, 2 H, OCH_2COOH), 2.03 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{43}NO_{13}Na$: *m/z* 576.2632; found: 576.2643.

*Octyl 2-*O*-carboxymethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**27a**).—Obtained in 97% yield from **22**. R_f 0.47 (solvent A). ^{1}H NMR (D_2O): δ 4.57 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.53 (m, 1 H, H-1/1′), 4.29 and 4.15 (AB system, 2 H, *J* 16.3 Hz, OCH_2COOH), 3.40 (dd, 1 H, *J* 9.7, 7.8 Hz, H-2′), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 554 $[M + H]^+$ and 576 $[M + Na]^+$.

*Octyl 3-*O*-carboxymethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**28a**).—Obtained in 98% yield from **17**. R_f 0.42 (solvent A). ^{1}H NMR (D_2O): δ 4.50 (br d, 1 H, *J* 7.2 Hz, H-1/1′), 4.49 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.24 and 4.23 (AB system, 2 H, *J* 17.0 Hz, OCH_2COOH), 4.12 (d, 1 H, *J* 3.0 Hz, H-4′), 2.02 (s, 3 H, CH_3CONH). MS: *m/z* 554 $[M + H]^+$ and 576 $[M + Na]^+$.

*Octyl 4-*O*-carboxymethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**29a**).—Obtained in 97% yield from **24**. R_f 0.45 (solvent A). ^{1}H NMR (D_2O): δ 4.49 (br d, 1 H, *J* 7.9 Hz, H-1/1′), 4.46 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.31 and 4.23 (AB system, 2 H, *J* 16.8 Hz, OCH_2COOH), 2.02 (s, 3 H, CH_3CONH). MS: *m/z* 576 $[M + Na]^+$.

*Octyl 6-*O*-carboxymethyl-β-*D*-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-*D*-glucopyranoside*

(**30a**).—Obtained in 98% yield from **18**. R_f 0.42 (solvent A). ^{1}H NMR (D_2O): δ 4.52 (m, 1 H, H-1/1′), 4.48 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.18 and 4.14 (AB system, 2 H, *J* 16.7 Hz, OCH_2COOH), 2.03 (s, 3 H, CH_3CONH). MS: *m/z* 576 $[M + Na]^+$.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-3-O-carbamoylmethyl-2-deoxy-β-D-glucopyranoside (**25b**).—Obtained in 50% yield from **15**. R_f 0.20 (solvent B). ^{1}H NMR (D_2O): δ 4.56 (d, 1 H, *J* 8.5 Hz, H-1/1′), 4.51 (d, 1 H, *J* 7.7 Hz, H-1/1′), 4.34 and 4.20 (AB system, 2 H, *J* 16.8 Hz, OCH_2CONH_2), 2.05 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{45}N_2O_{12}$: *m/z* 553.2972; found: 553.2983.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-6-O-carbamoylmethyl-2-deoxy-β-D-glucopyranoside (**26b**).—Obtained in 57% yield from **16**. R_f 0.17 (solvent B). ^{1}H NMR (D_2O): δ 4.54 (d, 1 H, *J* 8.0 Hz, H-1/1′), 4.42 (d, 1 H, *J* 7.7 Hz, H-1/1′), 4.13 (s, 2 H, OCH_2CONH_2), 2.04 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{44}N_2O_{12}Na$: *m/z* 575.2792; found: 575.2782.

Octyl 2-O-carbamoylmethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**27b**).—Obtained in 66% yield from **22**. R_f 0.22 (solvent B). ^{1}H NMR (D_2O): δ 4.59 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.52 (m, 1 H, H-1/1′), 4.36 and 4.29 (AB system, 2 H, *J* 16.3 Hz, OCH_2CONH_2), 3.45 (dd, *J* 9.8, 7.7 Hz, H-2′), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 553 $[M + H]^+$ and 575 $[M + Na]^+$.

Octyl 3-O-carbamoylmethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**28b**).—Obtained in 68% yield from **17**. R_f 0.22 (solvent B). ^{1}H NMR (1:1 CD_3OD–D_2O): δ 4.45 (2 d, 2 H, *J* 7.8 Hz, H-1, H-1′), 4.19 and 4.11 (AB system, 2 H, *J* 16.1 Hz, OCH_2CONH_2), 4.06 (d, *J* 3.1 Hz, H-4′), 2.00 (s, 3 H, CH_3CONH). MS: *m/z* 553 $[M + H]^+$ and 575 $[M + Na]^+$.

Octyl 4-O-carbamoylmethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**29b**).—Obtained in 46% yield from **24**. R_f 0.22 (solvent B). ^{1}H NMR (D_2O): δ 4.49 (m, 1 H, H-1/1′), 4.48 (d, 1 H, *J* 7.5 Hz, H-1/1′), 4.23 and 4.19 (AB system, 2 H, *J* 15.8 Hz, OCH_2CONH_2), 2.01 (s, 3 H, CH_3CONH). MS: *m/z* 553 $[M + H]^+$ and 575 $[M + Na]^+$.

Octyl 6-O-carbamoylmethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**30b**).—Obtained in 68% yield from **18**. R_f 0.21 (solvent B). ^{1}H NMR (D_2O): δ 4.53 (m, 1 H, H-1/1′), 4.49 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.10 (s, 2 H, OCH_2CONH_2), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 553 $[M + H]^+$ and 575 $[M + Na]^+$.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-3-O-amidinomethyl-2-deoxy-β-D-glucopyranoside hydrochloride (**25c**).—Obtained in 58% yield from **15**. R_f 0.46 (solvent C). ^{1}H NMR (D_2O): δ 4.58 (d, 1 H, *J* 8.4 Hz, H-1/1′), 4.51 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.77 and 4.59 [AB system, 2 H, *J* 16.1 Hz, $OCH_2C(NH_2)_2^+$], 2.05 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{46}N_3O_{11}$: *m/z* 552.3132; found: 552.3159.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-6-O-amidinomethyl-2-deoxy-β-D-glucopyranoside hydrochloride (**26c**).—Obtained in 72% yield from **16**. R_f 0.38 (solvent C). ^{1}H NMR (D_2O): δ 4.55 (d, 1 H, *J* 7.9 Hz, H-1/1′), 4.42 (d, 1 H, *J* 7.7 Hz, H-1/1′), 4.51 and 4.50 [AB system, 2 H, *J* 16.2 Hz, $OCH_2C(NH_2)_2^+$], 2.04 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{46}N_3O_{11}$: *m/z* 552.3132; found: 552.3131.

Octyl 2-O-amidinomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**27c**).—Obtained in 79% yield from **22**. R_f 0.59 (solvent C). ^{1}H NMR (D_2O): δ 4.64 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.54 (m, 1 H, H-1/1′), 4.75 and 4.67 [AB system, 2 H, *J* 16.8 Hz, $OCH_2C(NH_2)_2^+$], 3.50 (dd, *J* 9.9, 7.7 Hz, H-2′), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 552 $[M - Cl]^+$.

Octyl 3-O-amidinometyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**28c**).—Obtained in 65% yield from **17**. R_f 0.49 (solvent C). ^{1}H NMR (D_2O): δ 4.54 (br d, 1 H, *J* 6.8 Hz, H-1/1′), 4.52 (d, 1 H, *J* 7.6 Hz, H-1/1′), 4.66 and 4.56 [AB system, 2 H, *J* 16.4 Hz, $OCH_2C(NH_2)_2^+$], 4.19 (d, 1 H, *J* 3.0 Hz, H-4′), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 552 $[M - Cl]^+$.

Octyl 4-O-amidinomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**29c**).—Obtained in 59% yield from **24**. R_f 0.54 (solvent C). ^{1}H NMR (D_2O): δ 4.49 (2 d, 2 H, *J* 7.8 Hz, H-1, H-1′), 4.64 and 4.57 [AB system, 2 H, *J* 16.3 Hz, $OCH_2C(NH_2)_2^+$], 2.01 (s, 3 H, CH_3CONH). MS: *m/z* 552 $[M - Cl]^+$.

Octyl 6-O-amidinomethyl-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**30c**).—Obtained in 82% yield from **18**. R_f 0.38 (solvent C). ^{1}H NMR (D_2O): δ 4.52 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.48 (d, 1 H, *J* 7.8 Hz, H-1/1′), 4.48 [s, 2 H, $OCH_2C(NH_2)_2^+$], 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 552 $[M - Cl]^+$.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-3-O-(2-aminoethyl)-2-deoxy-β-D-glucopyranoside hydrochloride (**25d**).—Obtained in 68% yield from **15**. R_f 0.15 (solvent D). ^{1}H NMR (D_2O): δ 4.55 (d, 1 H, *J* 8.5 Hz, H-1/1′), 4.48 (d, 1 H, *J* 7.8 Hz,

H-1/1′), 2.95–2.80 (m, 2 H, $OCH_2CH_2NH_3^+$), 2.05 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{46}N_2O_{11}Na$: *m/z* 561.2999; found: 561.3024.

Octyl β-D-galactopyranosyl-(1 → 4)-2-acetamido-6-O-(2-aminoethyl)-2-deoxy-β-D-glucopyranoside hydrochloride (**26d**).—Obtained in 75% yield from **16**. R_f 0.28 (solvent D). ^1H NMR (D_2O): δ 4.52 (d, 1 H, *J* 7.9 Hz, H-1/1′), 4.42 (d, 1 H, *J* 7.7 Hz, H-1/1′), 2.98–2.84 (m, 2 H, $OCH_2CH_2NH_3^+$), 2.04 (s, 3 H, CH_3CONH). HRMS: Calcd for $C_{24}H_{46}N_2O_{11}Na$: *m/z* 561.2999; found: 561.3007.

Octyl 2-O-(2-aminoethyl)-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**27d**).—Obtained in 48% yield from **22**. R_f 0.26 (solvent D). ^1H NMR (D_2O): δ 4.58 (d, 1 H, *J* 7.7 Hz, H-1/1′), 4.53 (m, 1 H, H-1/1′), 3.32–3.16 (m, 2 H, $OCH_2CH_2NH_3^+$), 3.39 (dd, 1 H, *J* 9.8, 7.7 Hz, H-2′), 2.05 (s, 3 H, CH_3CONH). MS: *m/z* 539 $[M - Cl]^+$.

Octyl 3-O-(2-aminoethyl)-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**28d**).—Obtained in 38% yield from **17**. R_f 0.18 (solvent D). ^1H NMR (D_2O): δ 4.52 (br d, 1 H, *J* 7.9 Hz, H-1/1′), 4.51 (d, 1 H, *J* 7.7 Hz, H-1/1′), 4.17 (d, 1 H, *J* 3.0 Hz, H-4′), 3.32–3.18 (m, 2 H, $OCH_2CH_2NH_3^+$), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 539 $[M - Cl]^+$ and 561 $[M - HCl + Na]^+$.

Octyl 4-O-(2-aminoethyl)-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**29d**).—Obtained in 72% yield from **24**. R_f 0.20 (solvent D). ^1H NMR (D_2O): δ 4.50 (br d, 1 H, *J* 7.4 Hz, H-1/1′), 4.48 (d, 1 H, *J* 7.9 Hz, H-1/1′), 3.28–3.13 (m, 2 H, $OCH_2CH_2NH_3^+$), 2.02 (s, 3 H, CH_3CONH). MS: *m/z* 539 $[M - Cl]^+$ and 561 $[M - HCl + Na]^+$.

Octyl 6-O-(2-aminoethyl)-β-D-galactopyranosyl-(1 → 4)-2-acetamido-2-deoxy-β-D-glucopyranoside hydrochloride (**30d**).—Obtained in 43% yield from **18**. R_f 0.28 (solvent D). ^1H NMR (D_2O): δ 4.53 (d, 1 H, *J* 7.9 Hz, H-1/1′), 4.47 (d, 1 H, *J* 7.8 Hz, H-1/1′), 3.21 (t, 2 H, *J* 5.1, $OCH_2CH_2NH_3^+$), 2.04 (s, 3 H, CH_3CONH). MS: *m/z* 539 $[M - Cl]^+$.

Acknowledgements

This work was supported by the Natural Sciences and Engineering Research Council of Canada and by the Protein Engineering Network for Centers of Excellence.

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