Pseudosugars, 40[+]

Synthesis of Ether- and Imino-Linked Octyl *N*-Acetyl-5a′-carba-β-lactosaminides and -isolactosaminides: Acceptor Substrates for α-(1→3/4)-Fucosyltransferase, and Enzymatic Synthesis of 5a′-Carbatrisaccharides[1]

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Synthesis of ether-linked octyl 5a′-carba-β-lactosaminide **3** and -isolactosaminide **5** was carried out in seven steps, starting from the coupling products of 1,2-anhydro-5a-carba-β-D-mannopyranose derivative **7**, and the oxide anions generated from the octyl *N*-acetyl-β-D-glucosaminide derivatives **13** and **16**, respectively, under basic conditions. The 5a-carba-α-D-mannopyranose residues of the coupling products **17** and **26** were transformed into the β-D-*gluco* configuration through epimerization of the respective 2′-oxo derivatives **19** and **28**, and selective reduction, and then into the β-D-*galacto* configuration by direct nucleophilic substitution of their 4′,6′-dimesylates **23** and **31** with an acetate ion. Biological assay has shown that **3** is an acceptor substrate for human-milk α-(1→3/4)-fucosyltransferase and, interestingly, **5** is not. In addition, the imino-linked congeners **4** and **6** have been synthesized by coupling of the 4-amino-4-deoxy- and 3-amino-3-deoxy derivatives **37** and **41** of octyl *N*-acetyl-β-D-glucosaminide**,** and the carba-sugar epoxide **8**, respectively, and subsequent deprotection. Compound **4** is a substrate while **6** is neither a substrate nor an inhibitor for fucosyltransferase. Small-scale enzymatic synthesis was carried out by treatment of **3** and **4** with GDP-fucose and milk fucosyltransferase, which resulted in conversion into the corresponding trisaccharides **47** and **48**, respectively.

In recent years, some human α-(1→3/4)-fucosyltransferases have been extensively studied[3] since they are involved in the last steps of the biosynthesis of Lewis oligosaccharide antigens. These antigens include sialyl Lewis x, which is a tumor-associated structure and a ligand of E-selectin-mediated inflammatory processes.[4] There is interest in developing assays for monitoring enzyme activity and specific fucosyltransferase inhibitors which prevent the synthesis of these antigens. These inhibitors would represent potential anti-inflammatory or anti-tumor agents.[5]

Previously, we described[6] that the carbatrisaccharide β-D-Glc*p*NAc-(1→2)-5a-carba-α-D-Man*p*-(1→6)-β-D-Glc*p*O-$(CH_2)_7CH_3$ was shown to act as a structurally minimum substrate analog for enzyme *N*-(acetylglucosaminyl)-transferase-V, the kinetic parameters being comparable to those of the parent trisaccharide. This paper describes the synthesis of pseudo-*N*-acetyllactosaminides **3** and **4**, and -isolactosaminides **5** and **6**, where the β-D-galactopyranose moieties of the true substrates **1** and **2** are replaced by ether- and imino-linked 5a-carba-β-D-galactopyranose residues, respectively.[6] Since these carbadisaccharides are resistant to enzymatic hydrolysis, they should be useful for a transferase assay or in cell-uptake experiments to study oligosaccharide biosynthesis, provided they are substrates for fucosyltransferases. These disaccharide mimetics have therefore been considered as substrates and inhibitors for the Lewis α-(1→3/4)-fucosyltransferase available from human milk.

Results and Discussion

Synthesis of Ether-Linked Octyl 5a′-Carbalactosaminide (3) and -isolactosaminide (5)

Octyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (**9**) was prepared[7] in 44% yield from D-glucosamine hydrochloride by subsequent per-*N*,*O*-acetylation, and then glycosylation with octanol and ferric chloride in dichloromethane. Zemplén de-*O*-acetylation[8] of **9**, followed by benzylidenation with benzaldehyde in the presence of zinc chloride, gave the (*R*)-4,6-*O*-benzylidene derivative[9] **10** in 88% yield. Benzylation of **10** with benzyl bromide and sodium hydride in DMF gave the 3-*O*-benzyl derivative[9] **11** (82%), which was selectively reduced with sodium cyanoborohydride in THF to afford the 3,6-di-*O*-benzyl derivative **13** (68%). The structure was confirmed by the ^{1}H-NMR spectrum of the 4-acetate **14** derived from **13** by the conventional acetylation. On the other hand, **10** was first converted into the 3-*O*-methoxymethyl derivative **12** (90%), which was subjected to hydrogenolysis with 10% Pd/C cay-

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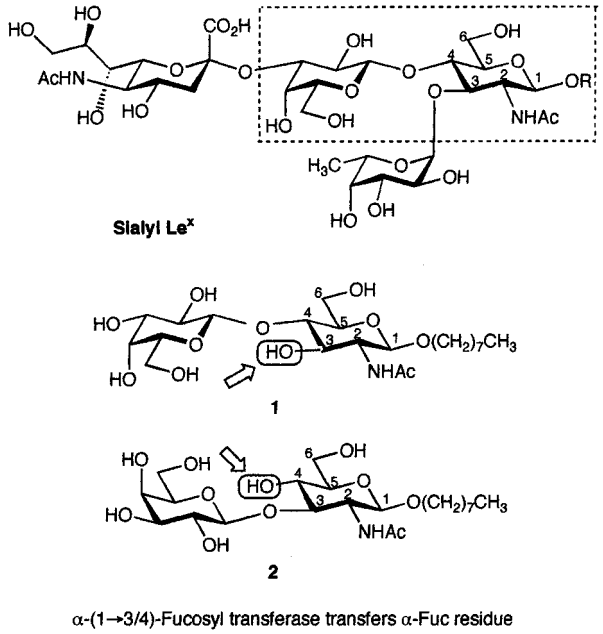
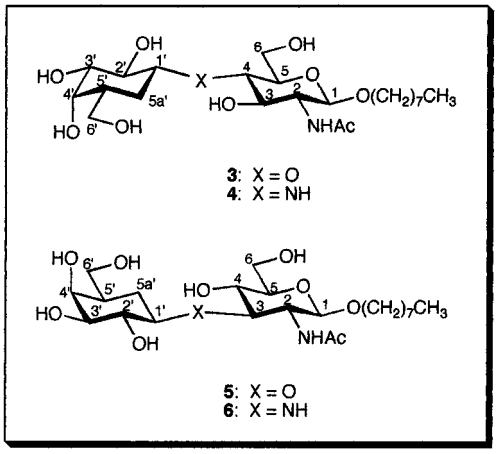
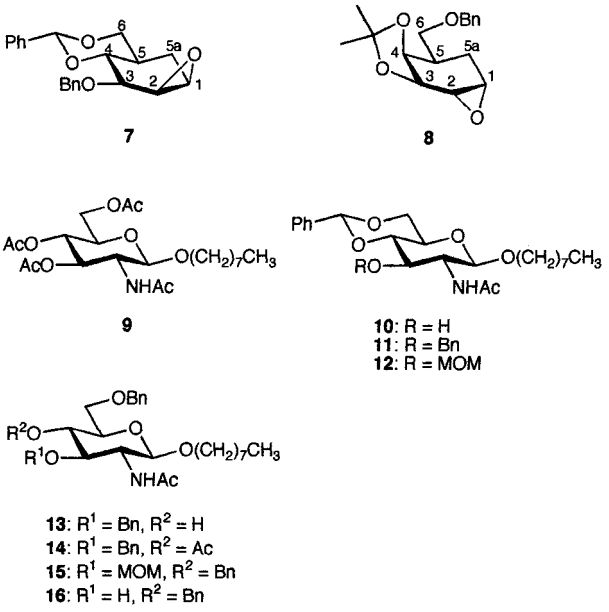




Scheme 1. The hydroxy groups of *N*-acetyl-β-lactosaminide and -isolactosaminide, on which α-(1→3/4)-fucosyl transferase transfers an α-Fuc residue: two types of pseudo-*N*-acetyllactosaminides and -isolactosaminides, designed as potential acceptor substrates and/or inhibitors of the transferase

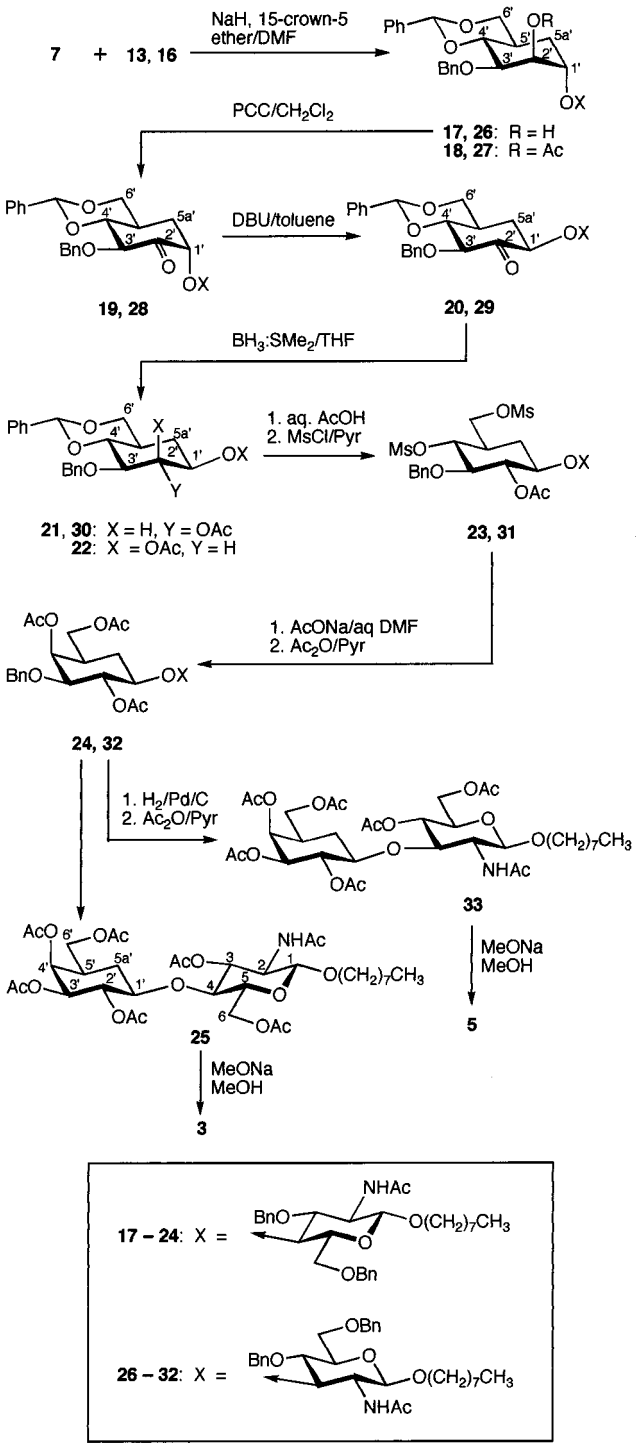


Scheme 2. Synthesis of the building blocks **13** and **16**

talyst and then totally benzylated to the 4,6-di-*O*-benzyl derivative **15** (66%). Removal of the methoxymethyl group with conc. hydrochloric acid in THF gave the 3-OH unprotected derivative **16** (94%).

Coupling of 1,2-anhydro-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-D-mannopyranose[10] **7** and an oxide anion generated from the 4-OH-unprotected derivative **13** (1.2 molar equiv.) by treatment with sodium hydride in DMF was carried out in the presence of 15-crown-5 ether for 26 h at 70°C, affording a 66% yield of a single diaxially opened product **17**. Its α-D-*manno* configuration was established by the ^{1}H-NMR spectra of **17** and its 2′-acetate **18**. The ^{1}H-NMR spectrum ($CDCl_3$) of the latter revealed a doublet of doublets (δ = 5.59, $J_{1',2'}$ = 1.6, $J_{2',3'}$ = 2.3 Hz) due to 2′-H. Transformation of the α-D-*manno* to the β-D-*gluco* configuration was effected by basic epimerization[11][12] at C-1′ and -2′ through the 5a′-carbahex-2′-ulo-1′,5′-pyranose derivative **19**. Thus, oxidation of **17** with PCC in dichloromethane in the presence of molecular sieves (4 Å) gave the crystalline ketone **19** in 75% yield. Treatment of **19** with DBU in toluene for 2.5 h at 60°C produced the desired anomer **20** in 79% yield. The structure was confirmed ^{1}H-NMR-spectroscopically by the appearance of the signal [δ = 4.27, dd, $J_{1',5a'(ax)}$ = 11.7, $J_{1',5a'(eq)}$ = 5.9 Hz] due to 1′-H. Selective reduction of the carbonyl function was successfully carried out by use of borane−dimethyl sulfide in THF to give, after acetylation and separation by silica-gel column chromatography, the 5a′-carbadisaccharide **21** with β-D-*gluco* (69%), together with **22** with β-D-*manno* configuration (15%). The structures were established on the basis of ^{1}H-NMR signals due to the C-2′ protons. In the spectra of **21** and **22**, the signals due to 2′-H appear as doublets of doublets (δ = 4.97, $J_{1',2'} = J_{2',3'}$ = 9.2 Hz) and (δ = 5.63, $J_{1',2'} = J_{2',3'}$ = 2.9 Hz), respectively, supporting the assigned structures. Attempted inversion[12] of the configuration at C-4′of **21** to β-D-*galacto* configuration was made through S_N2 reaction of the sulfonate ester. Thus, de-*O*-benzylidenation of **21** with aqueous acetic acid followed by conventional mesylation gave the 4′,6′-dimesylate **23** (72%). Treatment of **23** with excess of sodium acetate in aqueous DMF for 2 days at 120°C, followed by acetylation, afforded the 4′-epimeric diacetate **24** in 85% yield. The ^{1}H-NMR spectrum of **24** contained a broad singlet (δ = 5.52) ascribable to equatorial 4′-H. Hydrogenolysis of **24** in the presence of 10% Pd/C in methanol for 2 h at room temperature, followed by acetylation, gave the hexaacetyl derivative **25** (93%) of octyl 2-acetamido-4-*O*-(5a-carba-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**3**). De-*O*-acetylation[8] of **25** and purification by silica-gel column chromatography with chloroform/methanol (3:1) afforded **3** (91%).

Similar reaction of the epoxide **7** with an oxide anion from the 3-unprotected derivative **16** was carried out at



Scheme 3. Synthesis of ether-linked octyl *N*-acetyl-5a′-carba-β-lactosaminide (**3**) and -isolactosaminide (**5**)

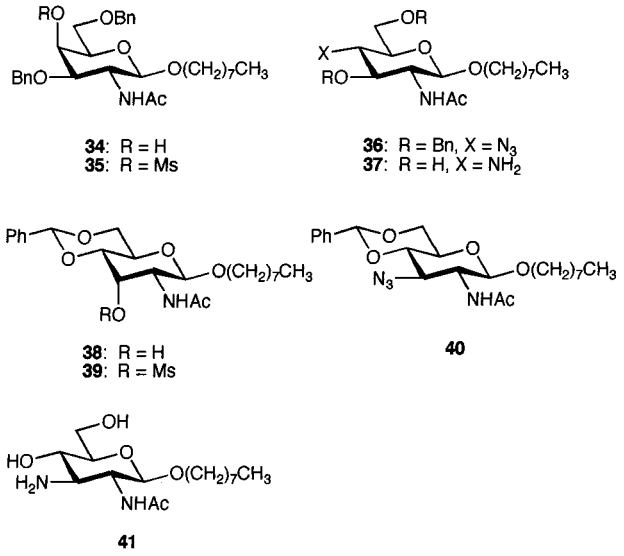
80°C for 4 days to give a single coupling product **26** in rather low yield (48%). The reactivity of **16** has been shown to be considerably decreased compared to that of **13**, seemingly due to the steric effects and/or the presence of the acetamido group adjacent to the oxide anion. The α-D-*manno* configuration of **26** was firmly confirmed by the ^{1}H-NMR spectrum of its 2′-acetate **27**. Transformation of **26** into the β-D-*gluco* structure was similarly conducted by the sequence of reaction: oxidation with PCC [→ **28** (71%)], epimerization with DBU [→ **29** (81%)], and selective reduction with borane–dimethyl sulfide [→ **30** (61%)]. Epimerization at C-4′ was also carried out by S_N2 reaction of the 4′,6′-dimesylate **31** with an acetate ion, giving the triacetate **32** (82%) having a 5a′-carba-β-D-galactopyranose residue. Hydrogenolysis of **32** followed by acetylation gave the hexaacetyl derivative **33** of octyl 2-acetamido-3-*O*-(5a-carba-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**5**). De-*O*-acetylation[8] gave the free carbadisaccharide **5**.

Synthesis of Imino-Linked Octyl 5a′-Carbalactosaminide (4) and -isolactosaminide (6)

Since 1,2-anhydro-6-*O*-benzyl-3,4-*O*-isopropylidene-5a-carba-α-D-galactopyranose[13] (**8**) had been successfully used to prepare *N*-alkyl-5a-carba-β-D-galactopyranosylamines,[13] where the epoxide ring was readily cleaved by alkylamines, giving selectively the diequatorially opening products, the epoxide **8** was therefore expected to be usable and applicable as the carba-sugar donor for direct incorporation of an imino-linked 5a-carba-β-D-galactopyranose residue into oligosaccharide chain.

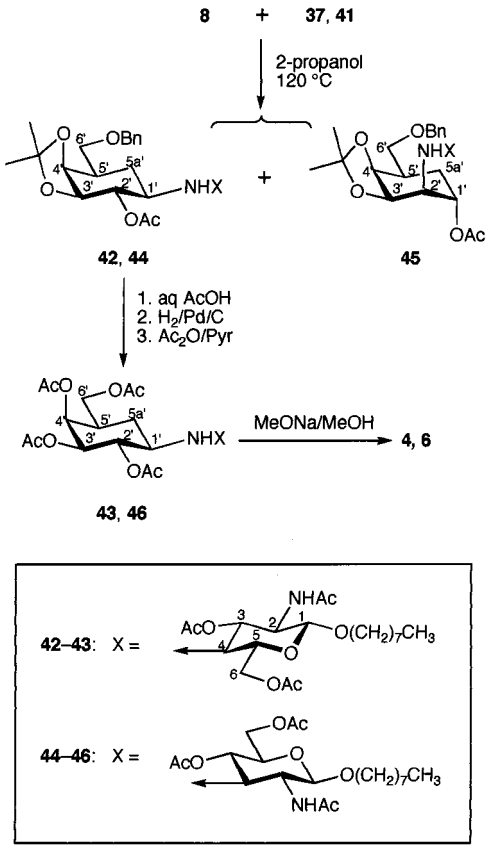
Octyl 2-acetamido-4-amino-2,4-dideoxy-β-D-glucopyranoside (**37**) was first prepared from **13**. Oxidation of **13** with acetic anhydride in DMSO gave the ketone, which without purification was subsequently reduced with L-selectride in THF at −15°C gave selectively crystalline epimeric alcohol **34** in 58% yield. Mesylation of **34** gave the mesylate **35** (87%), treatment of which with excess sodium azide in aqueous DMF at 120°C for 2 days afforded the azide **36** in 96% yield. Hydrogenolysis of both the azido and benzyl groups in the presence of 10% Pd/C afforded after purification by ion exchange on Dowex 50W-X2 (H^+) resin with aqueous ammoniacal methanol the free base **37** in 80% yield. On the other hand, compound **10** was similarly oxidized with acetic anhydride in DMSO followed by selective reduction of the ketone, giving the epimeric alcohol [→ **38** (76%)]. The alcohol **38** was converted into the mesylate **39** (65%), which was subjected to azidolysis in aqueous DMF to afford the azide **40** (92%). Hydrogenolysis of **40** with 10% Pd/C afforded after purification by the resin column octyl 2-acetamido-3-amino-2,3-dideoxy-β-D-glucopyranoside (**41**) in 90% yield.

Coupling of an equal molar amount of the epoxide **8** and the amine **37** in 2-propanol in a sealed tube for 3 weeks at 120°C gave, after acetylation and purification by silica-gel column chromatography, a single carbadisaccharide derivative **42** as the triacetate in 37% yield. The reactivity of the bulky amine **37** toward **8** was shown to be very slow, thereby producing selectively a desired positional isomer which was derived through unfavorable diequatorial attack at C-1 of the epoxide ring. Large steric hindrance between the 5-hydroxymethyl group of **37** and the ketal group of **8** seemed to hamper the nucleophilic attack at C-2. The ^{1}H-NMR spectrum revealed a doublet of doublets of doublets ($\delta = 1.05$, $J \approx 11.7$ Hz) due to the axial proton of C-5a. De-



Scheme 4. Synthesis of the building block **41**

O-isopropylidenation with aq. acetic acid and subsequent hydrogenolysis with 10% Pd/C followed by acetylation afforded the hepta-*N*,*O*-acetyl derivative **43** of octyl 5a′-carba-β-lactosaminide **4** in 83% yield. The ^{1}H-NMR spectrum showed two coupled doublets of doublets (δ = 4.99, $J_{1',2'} = J_{2',3'} = 10.3$ Hz) and (δ = 4.80, $J_{2',3'} = 10.3$, $J_{3',4'} = 2.9$ Hz) ascribed to 2′-H and 3′-H, supporting the assigned structure. De-*O*-acetylation[8] and purification on Dowex 50W-X2 (H^+) resin gave the free carbadisaccharide **4** in a quantitative yield.

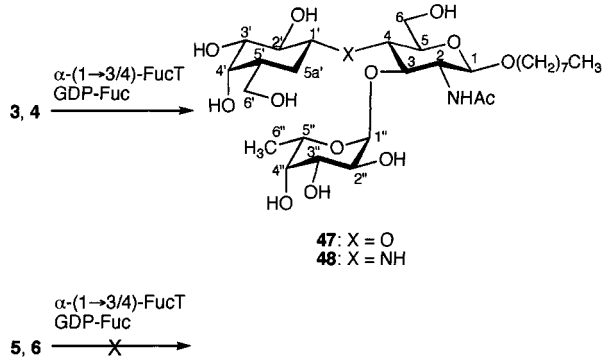


Scheme 5. Synthesis of imino-linked octyl *N*-acetyl-5a′-carba-β-lactosaminide (**4**) and -isolactosaminide (**6**)

Similar coupling of **8** and **41** followed by acetylation afforded after chromatography on silica gel with acetone/toluene (1:5) two positional isomers **44** and **45** in 38 and 24% yield, respectively. The ^{1}H-NMR spectrum of the diequatorially opening product **44** revealed two coupled doublets of doublets (δ = 4.82, $J_{1',2'} = 8.4$, $J_{2',3'} = 7.3$ Hz) and (δ = 3.96, $J_{2',3'} = 7.3$, $J_{3',4'} = 5.5$ Hz) due to 2′-H and 3′-H, respectively. Whereas, the spectrum of **45** showed a narrow doublet of doublets of doublets (δ = 4.89, J = 1.8, 1.8 and 5.9 Hz) due to 1′-H, indicating the α-D-*manno* configuration of the carba-sugar residue. The nucleophilicity of the amino group of **41**, compared with that of **37**, seemed to be essentially improved by sterically releasing from the influence of the bulky 5-hydroxymethyl function. The hepta-*N*,*O*-acetyl derivative **46** obtained from **44** showed a doublet of doublet (δ = 5.00, $J \approx 8.2$ Hz) due to 2′-H in the ^{1}H-NMR spectrum, supporting the assigned structure. De-*O*-acetylation of **46** gave the free carbadisaccharide **6**.

Evaluation of the 5a′-Carbadisaccharides 3, 4, 5, and 6 as an Acceptor for α-(1→3/4)-Fucosyltransferase

Compounds **3** and **4** were found to be acceptor substrates for human-milk α-(1→3/4)-fucosyltransferase[5] with kinetic parameters comparable to those for standard β-D-Gal*p*-(1→4)-β-D-Glc*p*NAc−O(CH$_2$)$_8$COOCH$_3$. The K_m values are 1.9 ± 0.2 mM for **3** and 1.6 ± 0.1 mM for **4** both somewhat higher than the K_m value of 0.6 mM for the standard acceptor. The *V*m(ax) values were 66% (**3**) and 100% (**4**) relative to the standard acceptors. Small-scale reaction of **3** and **4** with GDP-fucose and milk fucosyltransferase resulted in conversion to trisaccharides **47** and **48**, respectively. Surprisingly, compounds **5** and **6** were neither acceptors nor inhibitors for milk fucosyltransferase suggesting that α-(1→4) transfer is not possible. The milk preparation contains a mixture of two different fucosyltransferase enzymes, a dual specificity α-(1→3/4)-fucosyltransferase and an α-(1→3)-fucosyltransferase. These enzymes were separated by gel-permeation chromatogra-



Scheme 6. Enzymatic synthesis of the 5a′-carbatrisaccharides **47** and **48**

phy[14] to see if the panel of substrates could distinguish between the two enzyme forms. Both forms utilized compounds **3** and **4** as acceptor substrates while **5** and **6** were neither substrates nor inhibitors for the enzyme. To our knowledge, this is the first demonstration of a specific substrate for an α-1,3-fucosyltransferase.

Experimental Section

Melting points: Mel-Temp capillary melting-point apparatus, uncorrected values. − Specific rotations: Jasco DIP-370 polarimeter, 1-dm cells. − IR spectra: Jasco IR-810. − ^{1}H-NMR spectra: Jeol JNM GSX-270 FT (270 MHz), Jeol Lambda-300 (300 MHz), and Varian Unity 500 (500 MHz); solvent $CDCl_3$ with internal standard tetramethylsilane (TMS), CD_3OD with external standard acetone, D_2O with external standard acetone. − Mass spectra: positive-ion electrospray ionization with a Micromass Zab Hybrid Spec Sector-TOF. − TLC: Silica Gel 60 GF (E. Merck, Darmstadt); detection by charring with concd. H_2SO_4. − Column chromatography: Wakogel C-300 (silica gel, 300 Mesh, Wako Chemical, Osaka). − Organic solutions, after drying with anhydrous Na_2SO_4, were concentrated at < 50°C at diminished pressure. − All free carbadisaccharides **3**, **4**, **5**, and **6** were homogeneous on TLC and ^{1}H-NMR-spectroscopic analyses, and directly used for biological assay and enzymatic synthesis.

Octyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (9): 2-Amino-2-deoxy-D-glucopyranose hydrochloride (2.0 g, 9.3 mmol) was dissolved in methanolic 1 M sodium methoxide (9.3 mL), and the mixture was stirred for 40 min at room temperature. A white crystalline product was collected by filtration, which was treated with acetic anhydride (11 mL) in pyridine (23 mL) overnight at room temperature. After addition of methanol (6 mL), the mixture was concentrated to dryness. The residue was dissolved in dichloromethane (25 mL) and the solution was treated with *n*-octanol (10 mL, 63 mmol), potassium sulfate (2.5 g, 18 mmol), and ferric chloride (2.44 g) for 16 h at room temperature. Then the mixture was diluted with chloroform (300 mL), washed with satd. aqueous sodium hydrogen carbonate and water thoroughly, dried, and concentrated. The residue was chromatographed on silica gel (135 g, ethyl acetate/toluene, 1:1) to give **9** (1.83 g, 44%) as crystals, m.p. 120−122°C (from EtOH). − $[\alpha]_D^{28}$ = +15 (*c* = 0.96, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.56 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 5.32 (dd, $J_{2,3}$ = 10.6, $J_{3,4}$ = 9.3 Hz, 1 H, 3-H), 5.06 (dd, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 4.69 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.27 (dd, $J_{5,6a}$ = 4.8, J_{6gem} = 12.3 Hz, 1 H, 6a-H), 4.13 (dd, $J_{5,6b}$ = 2.6 Hz, 1 H, 6b-H), 3.86 [ddd, *J* = 6.0, 6.0, and 9.5 Hz, 1 H, OC*H*$_2$(CH$_2$)$_6$Me], 3.79 (ddd, 1 H, 2-H), 3.70 (ddd, 1 H, 5-H), 3.47 [ddd, *J* = 7.0, 7.0, and 9.5 Hz, 1 H, OC*H*$_2$(CH$_2$)$_6$Me], 2.08, 2.03, 2.02, and 1.95 (4 s, each 3 H, 4 × Ac), 1.26 [br. s, 12 H, OCH$_2$(C*H*$_2$)$_6$Me]. − $C_{22}H_{37}NO_9$ (459.6): calcd. C 57.50, H 8.12, N 3.05; found C 57.18, H 8.42, N 3.10.

Octyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (10): Compound **9** (6.53 g, 14.2 mmol) was dissolved in methanol (100 mL) and the solution was treated with methanolic 1 M sodium methoxide (1.5 mL) for 1 h at room temperature. After neutralization with Amberlite IR 120B (H^+) resin, the mixture was concentrated to dryness. The residue was then treated with benzaldehyde (220 mL) and zinc chloride (9.14 g, 67 mmol) for 3 h at room temperature. The reaction mixture was poured into a mixture of hexane (1 L) and water (500 mL), and precipitates were collected by filtration, giving **10**[9] (5.27 g, 88%) as crystals, m.p. 115−118°C (from EtOH). − $[\alpha]_D^{28}$ = +51 (*c* = 0.8, CH_3Cl).− $C_{23}H_{35}NO_6$ (421.5): calcd. C 65.53, H 8.37, N 3.32; found C 65.40, H 8.59, N 3.32.

Octyl 2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (11): A solution of **10** (4.64 g, 11 mmol) in DMF (185 mL) was treated with 60% sodium hydride (0.88 g, 22 mmol) for 30 min at room temperature, and, after addition of benzyl bromide (1.57 mL, 13.2 mmol), it was further stirred for 6 h at room temperature. After the reaction was quenched with methanol, the mixture was diluted with ethyl acetate (1 L) , washed with water, dried, and concentrated. The crystalline residue was recrystallized from ethanol to give the benzyl ether[9] **11** (4.62 g, 82%), m.p. 220−223°C (from EtOH). − $[\alpha]_D^{28}$ = +13 (*c* = 0.8, $CHCl_3$). − $C_{30}H_{41}NO_6$ (511.7): calcd. C 70.42, H 8.08, N 2.74; found C 70.33, H 8.20, N 3.08.

Octyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methoxymethyl-β-D-glucopyranoside (12): To a solution of **11** (511 mg, 1.21 mmol) in dichloromethane (15 mL) was added *N*,*N*-diisopropylethylamine (1.27 mL, 7.28 mmol) and it was stirred for 30 min at room temperature. After addition of chloromethyl methyl ether (0.28 mL, 3.64 mmol), it was stirred for 4 h at 40°C. The mixture was diluted with ethyl acetate (3 L), washed with 0.5 M hydrochloric acid, saturated sodium hydrogen carbonate, and water, dried, and concentrated. The residue was chromatographed on a silica-gel column (30 g, acetone/toluene, 1:6) to give **12** (510 mg, 90%) as crystals, m.p. 208−210°C (from EtOH), R_f = 0.60 (ethanol/toluene 1:5). − $[\alpha]_D^{28}$ = +4.5 (*c* = 1.04, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$) (inter alia): δ = 5.79 (d, $J_{2,NH}$ = 8.1 Hz, 1 H, NH), 5.52 (s, 1 H, PhC*H*), 4.85 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.34 (dd, $J_{5,6a}$ = 4.9, J_{6gem} = 10.4 Hz, 1 H, 6a-H), 4.23 (dd, $J_{2,3}$ = 9.9, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 3.77 (dd, $J_{5,6b}$ = 9.9 Hz, 1 H, 6b-H), 3.60 (dd, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 2.01 (s, 3 H, Ac). − $C_{25}H_{39}NO_7$ (465.6): calcd. C 64.49, H 8.44, N 3.01; found C 64.30, H 8.71, N 3.20.

Octyl 2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (13): To a solution of **11** (1.21 g, 2.64 mmol) in THF (60 mL) were added molecular sieves (4 Å) (1.8 g), a trace of methyl orange, sodium cyanoborohydride (1.78 g, 28.3 mmol), and it was stirred for 30 min at room temperature. Satd. hydrochloric acid/diethyl ether was added to acidify the mixture until it turned pink. After stirring for 30 min, the mixture was filtered through a Celite bed and the filtrate was washed with satd. sodium hydrogen carbonate and water, dried, and concentrated. The residue was chromatographed on silica gel (120 g, acetone/toluene, 1:6) to give **13** (0.82 g, 68%) as crystals, m.p. 116−118°C (from EtOH). − $[\alpha]_D^{24}$ = +8 (*c* = 1.6, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$) (inter alia): δ = 5.60 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 4.87 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.04 (dd, $J_{2,3}$ 9.5, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 3.64 (dd, $J_{4,5}$ = 8.4 Hz, 1 H, 4-H), 3.53 (dd, $J_{5,6b}$ = 4.8, J_{6gem} = 9.5 Hz, 1 H, 6b-H), 3.23 (ddd, 1 H, 2-H), 1.89 (s, 3 H, Ac) − $C_{30}H_{43}NO_6$ (513.7): calcd. C 70.14, H 8.43, N 2.73; found C 69.90, H 8.74, N 2.90.

Octyl 2-Acetamido-4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (14): Compound **13** (20 mg, 0.039 mol) was treated with acetic anhydride (1 mL) and pyridine (2 mL) overnight at room temperature. After addition of small methanol, the mixture was concentrated to dryness. The residue was chromatographed on silica gel (2 g, ethyl acetate/toluene, 1:8) to give **14** (20 mg) as a hygroscopic syrup. − $[\alpha]_D^{20}$ = +16 (*c* = 0.26, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.34−7.19 (m, 10 H, 2 × Ph), 5.63 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 5.02 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.97 (dd, $J_{3,4}$ = 9.3, $J_{4,5}$ = 9.6 Hz, 1 H, 4-H), 4.60−4.53 (m, 4 H, 2 × C*H*$_2$Ph), 4.37 (dd, $J_{2,3}$ = 9.9 Hz, 1 H, 3-H), 3.86 [ddd, *J* = 6.6, 6.6, and 9.7 Hz, 1 H, OC*H*$_2$(CH$_2$)$_6$Me], 3.66 (ddd, $J_{5,6a}$ = 4.0, $J_{5,6b}$ 5.5 Hz, 1 H, 5-H), 3.56−3.54 (m, 2 H, 6,6-H), 3.46 [ddd, *J* = 6.6,

7.0, and 9.7 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.16 (ddd, 1 H, 2-H), 1.89 and 1.86 (2 s, each 3 H, 2 Ac), 1.58−1.27 [m, 12 H, $OCH_2(CH_2)_6Me$], 0.87 [t, 3 H, J = 7.0 Hz, 1 H, $OCH_2(CH_2)_6CH_3$]. − $C_{32}H_{45}NO_7$ (555.7): calcd. C 69.16, H 8.16, N 2.52; found C 68.97, H 8.45, N 2.67.

Octyl 2-Acetamido-4,6-di-*O*-benzyl-2-deoxy-3-*O*-methoxymethyl-β-D-glucopyranoside (15): A solution of **12** (2.54 g, 5.46 mmol) in ethanol/ethyl acetate (1:1, 30 mL) was hydrogenolyzed in the presence of 10% Pd/C for 1.5 h at room temperature. The catalyst was removed by filtration and the filtrate was concentrated. The residue was dissolved in dry DMF (32 mL) and the solution was treated with sodium hydride (0.89 g, 22 mmol) for 30 min at room temperature. To the mixture was added benzyl bromide (1.46 mL,. 12 mmol), and it was stirred for 2 h at room temperature. After addition of a small amount of methanol, the mixture was diluted with ethyl acetate (300 mL), washed with water, dried, and concentrated. The residue was crystallized from ethanol to give **15** (2.0 g, 66%) as crystals, m.p. 124−125°C (from EtOH). − $[\alpha]_D^{25}$ = +35 (c = 0.95, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.35−7.17 (m, 10 H, 2 × Ph), 5.68 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 4.82 and 4.64 (ABq, J_{gem} = 6.6 Hz, each 1 H, CH_2OMe), 4.69 and 4.56 (ABq, J_{gem} = 11.0 Hz, each 1 H, CH_2Ph), 4.61 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.59 and 4.55 (ABq, J_{gem} = 11.2 Hz, each 1 H, CH_2Ph), 3.90 (dd, $J_{5,6a}$ = 5.9, J_{6gem} = 9.9 Hz, 1 H, 6a-H), 3.86 (dd, $J_{5,6b}$ = 3.3, Hz, 1 H, 6b-H), 3.73−3.51 [m, 5 H, 2-H, 3-H, 4-H, $OCH_2(CH_2)_6Me$], 3.45 [ddd, J = 7.0, 7.0, and 9.9 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.35 (s, 3 H, CH_2OCH_3), 1.99 (s, 3 H, Ac), 1.56−1.27 [m, 12 H, $OCH_2(CH_2)_6Me$], 0.87 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{32}H_{47}NO_7$ (557.7): calcd. C 68.91, H 8.49, N 2.51; found C 68.68, H 8.68, N 2.79.

Octyl 2-Acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (16): A mixture of **12** (165 mg, 0.295 mmol), THF (4 mL), and conc. hydrochloric acid (180 mL) was stirred for 4 h at room temperature. After neutralization with sodium hydrogen carbonate, the mixture was concentrated. The residue was chromatographed on a silica-gel column (8 g, acetone/toluene, 1:5) to give **16** (142 mg, 94%) as crystals, m.p. 111−112°C (from EtOH). − $[\alpha]_D^{23}$ = −19 (c = 0.9, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.34−7.21 (m, 10 H, Ph), 5.80 (br. s, 1 H, NH), 4.93 and 4.59 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.61 and 4.54 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.43 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 3.93−3.85 [m, 2 H, 4-H, $OCH_2(CH_2)_6Me$], 3.75 (dd, $J_{5,6a}$ = 1.1, J_{6gem} 11.1 Hz, 1 H, 6a-H), 3.69 (ddd, $J_{4,5}$ = 10.6, $J_{5,6b}$ = 3.3 Hz, 1 H, 5-H), 3.54−3.41 [m, 4 H, H-2, H-3, H-6b, $OCH_2(CH_2)_6Me$], 2.03 (s, 3 H, Ac), 1.59−1.27 [m, 12 H, $OCH_2(CH_2)_6Me$], 0.88 [t, 3 H, J = 7.0 Hz, 1 H, $OCH_2(CH_2)_6CH_3$]. − $C_{30}H_{43}NO_6$ (513.7): calcd. C 70.15, H 8.44, N 2.73; found C 70.14, H 8.44, N 2.94.

Octyl (4,6-*O*-Benzylidene-3-*O*-benzyl-5a-carba-α-D-mannopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (17): To a solution of **13** (780 mg, 1.47 mmol) in DMF (12 mL) were added sodium hydride (110 mg, 4.4 mmol) and 15-crown-5 ether (0.88 mL, 4.1 mmol), and the mixture was stirred for 30 min at room temperature. A solution of 1,2-anhydro-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-D-mannopyranose (**7**, 428 mg, 1.26 mmol) in DMF (6.5 mL) was added to the mixture, and it was stirred for 26 h at 70°C. After treatment with methanol, the mixture was diluted with ethyl acetate (200 mL), washed thoroughly with water, dried, and concentrated. The residue was chromatographed on a silica-gel column (110 g, ethyl acetate/toluene, 1:3) to give **17** (512 mg, 66%) as a colorless syrup. − $[\alpha]_D^{20}$ = −23 (c = 0.9, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.36−7.26 (m, 20 H, Ph), 5.62 (d, $J_{2,NH}$ = 7.6 Hz, 1 H, NH), 5.60 (s, 1 H, $CHPh$), 4.86 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.75 and 4.49 (ABq, J_{gem} = 11.5 Hz, each 1 H, CH_2Ph), 4.74 and 4.63 (ABq, J_{gem} = 11.7 Hz, each 1 H), and 4.61 and 4.57 (ABq, J_{gem} = 12.5 Hz, each 1 H) (2 × CH_2Ph), 4.16−4.12 (m, 2 H, 1′-H, 2′-H), 4.11 (dd, $J_{2,3}$ = 9.2, $J_{3,4}$ = 8.8 Hz, 1 H, 3-H), 4.00 (dd, $J_{5',6'a}$ = 4.4, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.93 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.9 Hz, 1 H, 4′-H), 3.83 [ddd, J = 6.6, 6.6, and 9.9 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.77−3.72 (m, 3 H, 6,6-H, 3′-H), 3.62 (dd, $J_{3,4}$ = 8.8, $J_{4,5}$ = 8.4 Hz, 1 H, 4-H), 3.57 (dd, $J_{5',6'b}$ = 11.0 Hz, 1 H, 6′b-H), 3.51−3.48 (m, 1 H, 5-H), 3.44 [ddd, 1 H, $OCH_2(CH_2)_6Me$], 3.31 (ddd, $J_{2,3}$ = 9.2, 1 H, 2-H), 2.10−2.07 (m, 1 H, 5′-H), 1.86 (s, 3 H, Ac), 1.57−1.26 [m, 14 H, 5a′,5a′-H, $OCH_2(CH_2)_6Me$], 0.87 [t, J = 6.6 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{51}H_{65}NO_{10}$ (852.1): calcd. C 71.89, H 7.69, N 1.64; found C 71.81, H 7.66, N 1.81.

Octyl (2-*O*-Acetyl-4,6-*O*-benzylidene-3-*O*-benzyl-5a-carba-α-D-mannopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (18): Compound **17** (21 mg, 25 μmol) was treated with acetic anhydride (1 mL) in pyridine (2 mL) overnight at room temperature. After addition of methanol, the mixture was diluted with ethyl acetate (30 mL), washed with water, dried, and concentrated. The residue was chromatographed on a silica-gel column (2 g, ethyl acetate/toluene, 1:4) to give **18** (17 mg, 77%) as a syrup. − $[\alpha]_D^{28}$ = −17 (c = 0.39, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.63−7.19 (m, 20 H, Ph), 5.60 (s, 1 H, $CHPh$), 5.59 (dd, $J_{1',2'}$ = 1.6, $J_{2',3'}$ = 2.3 Hz, 1 H, 2′-H), 5.49 (d, $J_{2,NH}$ = 7.8 Hz, 1 H, NH), 4.86 and 4.55 (ABq, J_{gem} = 11.7 Hz, each 1 H, CH_2Ph), 4.86 (d, $J_{1,2}$ = 6.8 Hz, 1 H, 1-H), 4.63 and 4.59, and 4.62 and 4.53 (2 ABq, J_{gem} = 12.2 Hz, each 1 H, CH_2Ph), 4.12 (dd, $J_{2,3}$ = 9.3, $J_{3,4}$ = 8.3 Hz, 1 H, 3-H), 4.08 (m, 1 H, 1′-H), 4.00 (dd, $J_{5',6'a}$ = 4.4, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.87 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.8 Hz, 1 H, 4′-H), 3.84 (m, 1 H, 3′-H), 3.81 [ddd, J = 6.4, 6.4, and 9.3 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.71 (m, 2 H, 6,6-H), 3.69 (dd, $J_{4,5}$ = 8.3 Hz, 1 H, 4-H), 3.58 (dd, $J_{5',6'b}$ = 11.0 Hz, 1 H, 6′b-H), 3.50−3.41 [m, 2 H, 5-H, $OCH_2(CH_2)_6Me$], 3.36 (ddd, $J_{2,3}$ = 9.3 Hz, 1 H, 2-H), 2.15 (m, 1 H, 5′-H), 2.00 (s, 3 H, OAc), 1.79 (s, 3 H, NAc), 1.73−1.18 [m, 14 H, H-5a′,5a′, $OCH_2(CH_2)_6Me$]. − $C_{53}H_{67}NO_{11}$ (894.1): calcd. C 71.20, H 7.55, N 1.57; found C 71.16, H 7.66, N 1.75.

Octyl (3-*O*-Benzyl-4,6-*O*-benzylidene-5a-carba-α-D-*arabino*-hex-2-ulopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (19): To a solution of **17** (790 mg, 0.927 mmol) in dichloromethane (16 mL) were added PCC (1.0 g, 4.64 mmol) and molecular sieves (4 Å) (1.0 g), and the suspension was stirred for 1 h at room temperature. After addition of Celite (2.5 g), the reaction mixture was filtered through a silica-gel column (15 g), which was washed thoroughly with diethyl ether. The filtrate and washings were combined and concentrated to give the residue, which was chromatographed on a silica-gel column (70 g, ethyl acetate/toluene, 1:5) to give **19** (596 mg, 75%) as crystals, m.p. 138−140°C (from EtOH). − $[\alpha]_D^{26}$ = −44 (c = 0.46, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.51−7.23 (m, 20 H, 4 × Ph), 5.54 (s, 1 H, $CHPh$), 5.52 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 4.87 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.77 and 4.49 (ABq, J_{gem} = 11.5 Hz, each 1 H, CH_2Ph), 4.68 (d, $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 4.67 and 4.40 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.65 and 4.55 (ABq, J_{gem} = 12.5 Hz, each 1 H, CH_2Ph), 4.30 (m, 1 H, 1′-H), 4.16 (dd, $J_{2,3}$ = $J_{3,4}$ = 8.4 Hz, 1 H, 3-H), 4.10 (dd, $J_{5',6'a}$ = 4.4, $J_{6'gem}$ = 11.4 Hz, 1 H, 6′a-H), 3.86−3.39 [m, 8 H, 4-H, 5-H, 6,6-H, 4′-H, 6′b-H, $OCH_2(CH_2)_6Me$], 3.23 (ddd, $J_{2,3}$ = 8.4 Hz, 1 H, 2-H), 2.52 (m, 1 H, 5′-H), 2.01−1.86 [m, 1 H, 5a′(eq)-H], 1.83 (s, 3 H, Ac), 1.56−1.25 [m, 12 H, $OCH_2(CH_2)_6Me$], 1.05 [m, 1 H, 5a′(ax)-H], 0.87 [t, J = 6.6 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{51}H_{63}NO_{10}$ (850.1): calcd. C 72.06, H 7.47, N 1.65; found C 72.22, H 7.64, N 1.75.

Octyl (3-*O*-Benzyl-4,6-*O*-benzylidene-5a-carba-β-D-*arabino*-hex-2-ulopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (20): To a solution of **19** (84 mg, 98 μmol) in toluene (3.3 mL) was added DBU (22 mL, 0.15 mmol), and the mixture was stirred for 2.5 h at 60°C, and then concentrated. The residue was dissolved in ethyl acetate (30 mL) and the solution was washed with water, dried, and concentrated. The product was purified by a silica-gel column (8 g, ethyl acetate/toluene, 1:3) to give **20** (66 mg, 79%) as crystals, m.p. 215−218°C (from EtOH). − $[\alpha]_D^{27}$ = −22 (*c* = 0.27, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.52−7.21 (m, 20 H, 4 × Ph), 5.76 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.47 (s, 1 H, C*H*Ph), 4.82 and 4.57 (ABq, J_{gem} = 12.3 Hz, each 1 H) and 4.76 and 4.61 (ABq, J_{gem} = 11.7 Hz, each 1 H) (2 × CH_2Ph), 4.75 (d, $J_{1,2}$ = 6.9 Hz, 1 H, 1-H), 4.62 and 4.46 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.27 [dd, $J_{1',5a'(ax)}$ = 11.7, $J_{1',5a'(eq)}$ = 5.9 Hz, 1 H, 1′-H], 4.10 (dd, $J_{5',6'a}$ = 6.9, $J_{6'gem}$ = 9.2 Hz, 1 H, 6′a-H), 4.00−3.38 [m, 11 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 3′-H, 4′-H, 6′b-H, OCH_2(CH$_2$)$_6$Me], 1.92 (s, 3 H, Ac), 1.86 [m, 1 H, 5a′(eq)-H], 1.69 (m, 1 H, 5′-H), 1.58−1.27 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 1.01 [m, 1 H, 5a′(ax)-H], 0.88 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{51}H_{63}NO_{10}$ (850.1): calcd. C 72.06, H 7.47, N 1.65; found C 72.06: H, 7.54, N 1.95.

Octyl [2-*O*-Acetyl-4,6-*O*-benzylidene-3-*O*-benzyl-5a-carba-β-D-gluco- and -mannopyranosyl]-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (21 and 22): To a solution of **20** (40 mg, 47 μmol) in THF (2.5 mL) was added 2 M borane−dimethyl sulfide (in THF, 70 μL, 0.14 mmol), and it was stirred for 3.5 h at room temperature. After addition of methanol (0.1 mL), the mixture was diluted with ethyl acetate (30 mL), washed with water thoroughly, dried, and concentrated. The residue (ca. 40 mg) was treated with acetic anhydride (1 mL) in pyridine (2 mL) overnight at room temperature. The mixture was processed in the usual manner to give a mixture of the acetates, which was chromatographed on a silica-gel column (4 g, ethyl acetate/toluene, 1:4) to give **21** (29 mg, 69%) and **22** (6 mg, 15%) as a syrup. − **21**: $[\alpha]_D^{29}$ = −25 (*c* = 0.91, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.49−7.23 (m, 20 H, 4 × Ph), 5.92 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.51 (s, 1 H, C*H*Ph), 4.97 (dd, $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 9.2 Hz, 1 H, 2′-H), 4.88 and 4.58 (ABq, J_{gem} = 11.7 Hz, each 1 H, CH_2Ph), 4.76−4.64 (m, 3 H, H-1, CH_2Ph), 4.61 and 4.46 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.02 (dd, $J_{5',6'a}$ = 4.4, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.84−3.36 (m, 10 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 4′-H, OCH_2(CH$_2$)$_6$Me], 3.47 (dd, $J_{3',4'}$ = 9.2 Hz, 1 H, 3′-H), 3.42 (dd, $J_{5',6'b}$ = 11.0 Hz, 1 H, 6′b-H), 1.97 and 1.93 (2 s, each 3 H, 2 × Ac), 1.87−1.21 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.86 [t, *J* = 6.8 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{53}H_{67}NO_{11}$ (894.1): calcd. C 71.20, H 7.55, N 1.57; found C 71.04, H 7.67, N 1.69. − **22**: $[\alpha]_D^{29}$ = −12 (*c* = 0.56, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.48−7.15 (m, 20 H, 4 × Ph), 5.63 (dd, $J_{1',2'}$ = $J_{2',3'}$ = 2.9 Hz, 1 H, 2′-H), 5.55 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.51 (s, 1 H, C*H*Ph), 4.79 (dd, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.68 (s, 2 H, CH_2Ph), 4.65 and 4.47 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.64 and 4.49 (ABq, J_{gem} = 12.5 Hz, each 1 H, CH_2Ph), 3.99−3.31 [m, 12 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 4′-H, 6′,6′-H, OCH_2(CH$_2$)$_6$Me], 3.26 (dd, $J_{3',4'}$ = 9.5 Hz, 1 H, 3′-H), 2.11 and 1.86 (2 s, each 3 H, 2 × Ac), 1.84−1.25 [m, 15 H, 5′-H, 5a′,5a′-H. OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 6.6 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{53}H_{67}NO_{11}$ (894.1): calcd. C 71.20, H 7.55, N 1.57; found C 71.04; H, 7.67, N 1.69.

Octyl (2-*O*-Acetyl-3-*O*-benzyl-4,6-di-*O*-methanesulfonyl-5a-carba-β-D-glucopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (23): A mixture of **21** (66 mg, 74 μmol) and 60% aqueous acetic acid (4 mL) was stirred for 5 h at 70°C, and then concentrated. The residue was dissolved in pyridine (1.3 mL) and the solution was treated with methanesulfonyl chloride (34 mL, 0.45 mmol) for 3 h at room temperature. The mixture was diluted with ethyl acetate (30 mL), washed with water, dried, and concentrated. The residue was chromatographed on silica gel (4 g, ethyl acetate/toluene, 1:3) to give **23** (52 mg, 72%) as a syrup. − IR (film, cm^{-1}): $\tilde{\nu}$ = 3280 (NH), 1750 (ester), 1650, 1560 (amide), 1180 (mesyl). − $[\alpha]_D^{24}$ = −13 (*c* = 0.32, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.39−7.20 (m, 15 H, 3 × Ph), 5.95 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.03 (dd, $J_{1',2'}$ = $J_{2',3'}$ = 9.5 Hz, 1 H, 2′-H), 4.73−4.42 (m, 7 H, 1-H, 3 × CH_2Ph), 4.45 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.9 Hz, 1 H, 4′-H), 4.16 (m, 2 H, 6′,6′-H), 3.91−3.36 (m, 10 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 3′-H, OCH_2(CH$_2$)$_6$Me], 3.00 and 2.80 (2 s, each 3 H, 2 × Ms), 2.13 (m, 1 H, 5′-H), 1.96 and 1.93 (2 s, each 3 H, 2 × Ac), 1.75−1.25 [m, 14 H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 6.6 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{48}H_{67}NO_{15}S_2$ (962.2): calcd. C 59.92, H 7.02, N 1.46; found C 59.69, H 7.22, N 1.58.

Octyl (2,4,6-Tri-*O*-acetyl-3-*O*-benzyl-5a-carba-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (24): A mixture of **23** (22 mg, 23 μmol), anhydrous sodium acetate (38 mg, 0.46 mmol), and aqueous 80% DMF (1.3 mL) was stirred for 2 d at 120°C, and, after cooling, diluted with ethyl acetate (30 mL). The solution was washed with water, dried, and concentrated. The residue was acetylated in the usual manner, and the product was chromatographed on silica gel (2 g) with acetone/hexane (1:3) to give **24** (17 mg, 85%) as a syrup. − IR (film, cm^{-1}): $\tilde{\nu}$ = 3280 (NH), 1750 (ester), 1660 (amide). − $[\alpha]_D^{23}$ = −18 (*c* = 0.89, $CHCl_3$): − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.37−7.20 (m, 15 H, 3 × Ph), 5.93 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 5.52 (br. s, 1 H, 4′-H), 5.10 (dd, $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 9.9 Hz, 1 H, 2′-H), 4.74 and 4.61 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.68 and 4.38 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.63 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.59 and 4.43 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 3.87−3.54 [m, 9 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 6′,6′-H, OCH_2(CH$_2$)$_6$Me], 3.42−3.33 [m, 2 H, 1′-H, OCH_2(CH$_2$)$_6$Me], 3.20 (dd, $J_{3',4'}$ = 2.9 Hz, 1 H, 3′-H), 2.09, 2.05, 2.01, and 1.93 (4 s, each 3 H, 4 × Ac), 1.72−1.24 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{50}H_{67}NO_{13}$ (890.1): calcd. C 67.47, H 7.59, N 1.57; found C 67.40, H 7.77, N 1.80.

Octyl (2,3,4,6-Tetra-*O*-acetyl-5a-carba-β-D-galactopyranosyl)-(1→4)-2-acetamido-3,6-di-*O*-acetyl-2-deoxy β-D-glucopyranoside (25): A solution of **24** (16.7 mg, 19 mmol) in ethanol (0.5 mL) was hydrogenolyzed in the presence of 10% Pd/C (5 mg) under atmospheric pressure of hydrogen for 2 h at room temperature. The catalyst was removed by filtration and the filtrate was concentrated. The residue was acetylated in the usual manner and the product was purified by chromatography on silica gel (1 g, acetone/toluene, 1:3) to give **25** (13 mg, 93%) as a syrup. − $[\alpha]_D^{26}$ = −16 (*c* = 0.3, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.64 (d, $J_{2,NH}$ = 9.5 Hz, 1 H, NH), 5.43 (br. s, 1 H, 4′-H), 5.22 (dd, $J_{1',2'}$ = 9.5, $J_{2',3'}$ = 10.3 Hz, 1 H, 2′-H), 4.92 (dd, $J_{2,3}$ = 9.2, $J_{3,4}$ = 7.7 Hz, 1 H, 3-H), 4.78 (dd, $J_{3',4'}$ = 2.9 Hz, 1 H, 3′-H), 4.52 (dd, $J_{5,6a}$ = 2.8, J_{6gem} = 11.5 Hz, 1 H, 6a-H), 4.41 (d, $J_{1,2}$ = 7.0 Hz, 1 H, 1-H), 4.20 (dd, $J_{5,6b}$ = 4.9 Hz, 1 H, 6b-H), 4.04 (ddd, 1 H, 2-H), 3.98 (dd, $J_{5',6'a}$ = 8.4, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.88 (dd, $J_{5',6'b}$ = 6.2 Hz, 1 H, 6′b-H), 3.79 [ddd, *J* = 6.2, 6.2, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.57−3.47 (m, 3 H, 4-H, 5-H, 1′-H), 3.41 [ddd, *J* = 7.0, 7.0, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 2.13, 2.10, 2.08, 2.06, 2.05, 1.97, and 1.96 (7 s, each 3 H, 7 × Ac), 1.56−1.25 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 6.8 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{35}H_{55}NO_{16}$ (745.8): calcd. C 56.36, H 7.43, N 1.88; found C 56.07, H 7.70, N 1.87.

Octyl (5a-Carba-β-D-galactopyranosyl)-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (3): A solution of **25** (9.0 mg, 12 μmol) in methanol (1 mL) was treated with methanolic 1 M sodium methoxide (0.1 mL) for 3.5 h at room temperature. After neutralization with Amberlite IR-120B (H^+) resin, the mixture was concentrated and the residue was chromatographed on silica gel (0.6 g) with chloroform/methanol (3:1) to give **3** (5.8 mg, 91%) as a white powder. − IR (film, cm^{-1}): $\tilde{\nu}$ = 3440 (NH, OH), 1640 (amide). − $[\alpha]_D^{22}$ = +11 (*c* = 0.2, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 4.37 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 3.99−3.22 [m, 14 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 2′-H, 3′-H, 4′-H, 6′,6′-H, OCH_2(CH$_2$)$_6$Me], 1.96 (s, 3 H, Ac), 1.56−1.29 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.90 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3].

Octyl (4,6-*O*-Benzylidene-3-*O*-benzyl-5a-carba-α-D-mannopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (26): To a solution of **16** (935 mg, 1.82 mmol) in DMF (6 mL) were added sodium hydride (218 mg, 5.46 mmol) and 15-crown-5 ether (1.1 mL, 5.46 mmol), and the mixture was stirred for 1 h at room temperature. A solution of **7** (3.08 g, 9.10 mmol) in DMF (8 mL) was then added to it, and the mixture was heated for 4 d at 80°C. After treatment with methanol, the mixture was diluted with ethyl acetate (350 mL), washed with water, dried, and concentrated. The residue was chromatographed on silica gel (200 g) with acetone/toluene (1:7) to give **26** (744 mg, 48%) as a colorless syrup. − $[\alpha]_D^{28}$ = −27 (*c* = 0.59, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.60−7.19 (m, 20 H, 4 × Ph), 5.79 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.61 (s, 1 H, C*H*Ph), 4.88 (d, $J_{1,2}$ = 7.3 Hz, 1 H, 1-H), 4.76 and 4.50 (ABq, J_{gem} = 11.5 Hz, each 1 H, CH_2Ph), 4.65 and 4.54 (ABq, J_{gem} = 11.9 Hz, each 1 H, CH_2Ph), 4.63 and 4.56 (ABq, J_{gem} = 10.8 Hz, each 1 H, CH_2Ph), 4.19−4.12 (m, 2 H, 3-H, 1′-H), 4.07 (dd, $J_{5',6'a}$ = 4.4, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.95 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.9 Hz, 1 H, H-4′), 3.88−3.54 [m, 8 H, 5-H, 6,6-H, 2′-H, 3′-H, 6′b-H, OCH_2(CH$_2$)$_6$Me], 3.44 [ddd, *J* = 6.6, 6.6, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.12 (ddd, $J_{2,3}$ = 7.0 Hz, 1 H, 2-H), 2.16 (m, 1 H, 5′-H), 1.98 (s, 3 H, Ac), 1.64−1.26 [m, 14 H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{51}H_{65}NO_{10}$ (852.1): calcd. C 71.89, H 7.69, N 1.64; found C 71.63, H 7.67, N 1.81.

Octyl (4-*O*-Acetyl-4,6-*O*-benzylidene-3-*O*-benzyl-5a-carba-α-D-mannopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (27): Compound **26** (46 mg, 54 mmol) was acetylated in the usual manner. The product was purified on a silica-gel column (5 g, ethyl acetate/toluene, 1:4) to give **27** (44 mg, 92%) as a syrup. − $[\alpha]_D^{20}$ = −29 (*c* = 1.04, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.52−7.15 (m, 20 H, 4 × Ph), 5.84 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.62 (s, 1 H, C*H*Ph), 5.55 (dd, $J_{1',2'}$ = $J_{2',3'}$ = 2.6 Hz, 1 H, 2′-H), 4.84 (d, $J_{1,2}$ = 7.0 Hz, 1 H, 1-H), 4.72 and 4.51 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.63−4.53 (m, 4 H, 2 × CH_2Ph), 4.17 (dd, $J_{2,3}$ = 7.3, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 4.13 (m, 1 H, 1′-H), 4.08 (dd, $J_{5',6'a}$ = 4.0, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.89 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 9.9 Hz, 1 H, 4′-H), 3.86 (dd, 1 H, 3′-H), 3.83 [ddd, *J* = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.73−3.55 (m, 5 H, 4-H, 5-H, 6,6-H, 6′b-H), 3.42 (ddd, 1 H, 2-H), 2.17 (m, 1 H, 5′-H), 2.02 and 1.96 (2 s, each 3 H, 2 × Ac), 1.87−1.26 [m, 14 H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{53}H_{67}NO_{11}$ (894.1): calcd. C 71.20, H 7.55, N 1.57; found C 71.12, H 7.93, N 1.76.

Octyl (3-*O*-Benzyl-4,6-*O*-benzylidene-5a-carba-α-D-*arabino*-hex-2-ulopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (28): Compound **26** (541 mg, 0.634 mmol) was oxidized with PCC (684 mg, 3.17 mmol) in dichloromethane (11 mL) as described in the preparation of **19**. The reaction mixture was passed through a silica-gel column (15 g) and washed with diethyl ether thoroughly. The filtrate and washings were combined and concentrated to give, after recrystallization from ethanol, **28** (384 mg, 71%) as crystals, m.p. 176−178°C. − IR (film, cm^{-1}): $\tilde{\nu}$ = 3440 (NH), 1740 (C=O), 1650 (amide). − $[\alpha]_D^{25}$ = −21 (*c* = 0.9, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.51−7.14 (m, 20 H, 4 × Ph), 5.73 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 5.56 (s, 1 H, C*H*Ph), 4.70 and 4.52 (ABq, J_{gem} = 10.4 Hz, each 1 H, CH_2Ph), 4.64 (d, $J_{1,2}$ = 7.0 Hz, 1 H, 1-H), 4.63 (d, $J_{3',4'}$ = 10.3 Hz, 1 H, 3′-H), 4.62 and 4.54 (ABq, J_{gem} = 11.9 Hz, each 1 H, CH_2Ph), 4.57 and 4.39 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.43 [dd, $J_{1',5a'(ax)}$ = $J_{1',5a'(eq)}$ = 2.6 Hz, 1 H, 1′-H], 4.22 (dd, $J_{5',6'a}$ = 4.2, $J_{6'gem}$ = 11.4 Hz, 1 H, 6′a-H), 3.91 (dd, $J_{3,4}$ = 8.4 Hz, 1 H, 3-H), 3.83 [ddd, *J* = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.75 (m, 2 H, 6,6-H), 3.68−3.60 (m, 2 H,. 4′-H, 6′b-H), 3.57 (dd, $J_{4,5}$ = 7.7 Hz, 1 H, 4-H), 3.52−3.38 [m, 3 H, 2-H, 5-H, OCH_2(CH$_2$)$_6$Me], 2.64 (m, 1 H, 5′-H), 2.01 (s, 3 H, Ac), 1.56−1.19 [m, 14 H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.88 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{51}H_{63}NO_{10}$ (850.1): calcd. C 72.06, H 7.47, N 1.65; found C 71.78, H 7.49, N 1.95.

Octyl (3-*O*-Benzyl-4,6-*O*-benzylidene-5a-carba-β-D-*arabino*-hex-2-ulopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (29): A solution of **28** (329 mg, 0.387 mmol) in toluene (13 mL) was treated with DBU (87 mL, 0.58 mmol) for 2.5 h at 60°C, and then concentrated. The residue was dissolved in ethyl acetate (60 mL) and the solution was washed with water, dried, and concentrated. The product was purified by a silica-gel column (16 g, ethyl acetate/toluene, 1:3) to give **29** (265 mg, 81%) as crystals, m.p. 195−198°C (from EtOH). − $[\alpha]_D^{26}$ −39 (*c* = 0.89, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.49−7.17 (m, 20 H, 4 × Ph), 5.49 (s, 1 H, C*H*Ph), 5.49 (br. s, 1 H, NH), 4.84 and 4.65 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.71 and 4.53 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.70 and 4.58 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.68 (d, $J_{1,2}$ = 7.0 Hz, 1 H, 1-H), 4.45 (m, 1 H, 1′-H), 4.04 (dd, $J_{5',6'a}$ = 4.2, $J_{6'gem}$ = 10.6 Hz, 1 H, 6′a-H), 4.04 (d, $J_{3',4'}$ = 10.3 Hz, 1 H, 3′-H), 3.89 [ddd, *J* = 6.6, 6.6, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.78 (m, 2 H, 6,6-H), 3.75−3.67 (m, 2 H, 3-H, 4-H), 3.59 (dd, $J_{4',5'}$ = 10.3 Hz, 1 H, 4′-H), 3.52 (dd, $J_{5',6'b}$ = 10.6 Hz, 1 H, 6′b-H), 3.51−3.39 [m, 3 H, 2-H, 5-H, OCH_2(CH$_2$)$_6$Me], 2.02 (s, 3 H, Ac), 1.74 (m, 1 H, 5′-H), 1.65−1.28 [m, 13 H, 5a′(eq)-H, OCH$_2$(CH_2)$_6$Me], 1.11 [ddd, $J_{1',5a'(ax)}$ = $J_{5',5a'(eq)}$ = $J_{5a'gem}$ = 12.8 Hz, 1 H, 5a′(ax)-H], 0.88 [t, *J* = 6.6 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{51}H_{63}NO_{10}$ (894.1): calcd. C 72.02, H 7.47, N 1.65; found C 72.26, H 7.60, N 1.85.

Octyl (2-*O*-Acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-5a-carba-β-D-glucopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (30): Compound **29** (233 mg, 0.274 mmol) was reduced with 2 M borane−dimethyl sulfide (THF solution, 0.41 mL, 0.82 mmol) in THF (14 mL) for 13 h at room temperature. The reaction mixture was processed as described in the preparation of **21** and **22**. After conventional acetylation, the product was purified by a silica-gel column (19 g, ethyl acetate/toluene, 1:5) to give **30** (149 mg, 61%) as a syrup. − $[\alpha]_D^{20}$ = −5.5 (*c* = 0.45, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.47−7.16 (m, 20 H, 4 × Ph), 5.67 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 5.48 (s, 1 H, C*H*Ph), 5.00 (dd, $J_{1',2'}$ = $J_{2',3'}$ = 9.2 Hz, 1 H, 2′-H), 4.88 and 4.53 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.87 (d, $J_{1,2}$ = 7.3 Hz, 1 H, 1-H), 4.66−4.58 (m, 4 H, 2 × CH_2Ph), 4.04 (dd, $J_{2,3}$ = $J_{3,4}$ = 8.4 Hz, 1 H, 3-H), 3.95 (dd, $J_{5',6'a}$ = 4.0, $J_{6'gem}$ = 11.0 Hz, 1 H, 6′a-H), 3.83 [ddd, *J* = 6.6, 6.6, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.75−3.40 [m, 8 H, 4-H, 5-H, 6,6-H, 1′-H, 2′-H, 3′-H, 4′-H, OCH_2(CH$_2$)$_6$Me], 3.31 (dd, $J_{5',6'b}$ = 10.6, $J_{6'gem}$ = 11.0 Hz, 1 H,

6′b-H), 3.13 (ddd, 1 H, 2-H), 2.01 and 1.93 (2 s, each 3 H, 2 × Ac), 1.91−1.26 [m, 14 H, 5′-H, 5a′eq-H, $OCH_2(CH_2)_6Me$], 0.88 [t, J = 6.6 Hz, 3 H, $OCH_2(CH_2)_6CH_3$], 0.76 [m, 1 H, 5a′(ax)-H]. − $C_{53}H_{67}NO_{11}$ (894.1): calcd. C 71.20, H 7.55, N 1.57; found C 71.05, H 7.70, N 1.82.

Octyl (2-*O*-Acetyl-3-*O*-benzyl-4,6-di-*O*-methanesulfonyl-5a-carba-β-D-glucopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (31): Compound **30** (131 mg, 0.146 mmol) was treated with 60% aqueous acetic acid (8 mL) for 1 h at 70°C, and the resulting diol was mesylated as described in the preparation of **23** to give, after silica-gel chromatography (15 g, ethyl acetate/toluene, 1:2), **31** (114 mg, 81%) as a colorless syrup. − $[\alpha]_D^{21}$ = −12 (c = 1.0, $CHCl_3$). − IR (film, cm^{-1}): $\tilde{\nu}$ = 3300 (NH), 1740 (ester), 1660 (amide), 1180 (mesyl). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.39−7.22 (m, 15 H, 3 × Ph), 5.68 (d, $J_{2,NH}$ = 8.1 Hz, 1 H, NH), 5.05 (dd, $J_{1',2'} = J_{2',3'}$ = 9.7 Hz, 1 H, 2′-H), 4.76−4.55 (m, 7 H, 1-H, 3 × CH_2Ph), 4.48 (dd, $J_{3',4'} = J_{4',5'}$ = 10.1 Hz, 1 H, 4′-H), 4.21 (dd, $J_{5',6'a}$ = 3.7, $J_{6'gem}$ = 10.3 Hz, 1 H, 6′a-H), 4.12 (dd, $J_{5',6'b}$ = 4.4 Hz, 1 H, 6′b-H), 3.85−3.48 [m, 9 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 3′-H, $OCH_2(CH_2)_6Me$], 3.41 [ddd, J = 6.6, 7.0, and 9.5 Hz, 1 H, $OCH_2(CH_2)_6Me$], 2.97 and 2.80 (2 s, each 3 H, 2 × Ms), 2.19 (m, 1 H, 5′-H), 2.03 and 1.97 (2 s, each 3 H, 2 × Ac), 1.70−1.26 [m, 14 H, 5a′,5a′-H, $OCH_2(CH_2)_6Me$], 0.88 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{48}H_{67}NO_{15}S_2$ (962.2): calcd. C 59.92, H 7.02, N 1.46; found C 59.98, H 7.19, N 1.58.

Octyl (2,4,6-Tri-*O*-acetyl-3-*O*-benzyl-5a-carba-β-D-galactopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (32): A mixture of **31** (105 mg, 0.109 mmol), anhydrous sodium acetate (178 mg, 2.17 mmol), and 80% aqueous DMF (6.3 mL) was stirred for 2 d at 120°C. The reaction mixture was processed as described in the preparation of **24**, and the product was acetylated conventionally. Silica-gel chromatography (8 g, acetone/hexane, 1:3) gave **32** (79 mg, 82%) as a colorless syrup. − $[\alpha]_D^{21}$ = +18 (c = 0.9, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.35−7.16 (m, 15 H, 3 × Ph), 5.65 (d, $J_{2,NH}$ = 7.0 Hz, 1 H, NH), 5.53 (br. s, 1 H, 4′-H), 5.16 (dd, $J_{1',2'} = J_{2',3'}$ = 10.1 Hz, 1 H, 2′-H), 4.88 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.69 and 4.34 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.62−4.51 (m, 4 H, 2 × CH_2Ph), 4.04 (dd, $J_{2,3}$ = 8.1, $J_{3,4}$ = 8.4 Hz, 1 H, 3-H), 3.89−3.40 [m, 9 H, 4-H, 5-H, 6,6-H, 1′-H, 6′,6′-H, $OCH_2(CH_2)_6Me$], 3.24 (dd, $J_{3',4'}$ = 2.9 Hz, 1 H, 3′-H), 3.13 (ddd, 1 H, 2-H), 2.09, 2.05, 2.01, and 1.88 (4 s, each 3 H, 4 × Ac), 1.77−1.27 [m, 15 H, 5′-H, 5a′,5a′-H, $OCH_2(CH_2)_6Me$], 0.88 [t, J = 6.6 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{50}H_{67}NO_{13}$ (890.1): calcd. C 67.47, H 7.59, N 1.57; found C 67.26, H 7.87, N 1.82.

Octyl (2,3,4,6-Tetra-*O*-acetyl-5a-carba-β-D-galactopyranosyl)-(1→3)-2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranoside (33): A solution of **32** (35 mg, 39 mmol) in ethanol (1 mL) was hydrogenolyzed in the presence of 10% Pd/C catalyst as described in the preparation of **25**, and the product was acetylated conventionally. Silica-gel chromatography (3 g, acetone/hexane, 1:3) gave **33** (20 mg, 70%) as a colorless syrup. − $[\alpha]_D^{24}$ = −24 (c = 0.65, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.70 (d, $J_{2,NH}$ = 7.0 Hz, 1 H, NH), 5.41 (br. s, 1 H, 4′-H), 5.20 (dd, $J_{1',2'} = J_{2',3'}$ = 10.1 Hz, 1 H, 2′-H), 5.05 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.87 (dd, $J_{3,4}$ = 8.8, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 4.74 (dd, $J_{3',4'}$ = 2.9 Hz, 1 H, 3′-H), 4.33 (dd, $J_{2,3}$ = 9.2 Hz, 1 H, 3-H), 4.14 (dd, $J_{5,6a}$ = 5.1, J_{6gem} = 12.3 Hz, 1 H, 6a-H), 4.07 (dd, $J_{5,6b}$ = 2.9 Hz, 1 H, 6b-H), 3.97 (dd, $J_{5',6'a}$ = 8.6, $J_{6'gem}$ = 11.2 Hz, 1 H, 6′a-H), 3.88−3.80 [m, 2 H, 6′b-H, $OCH_2(CH_2)_6Me$], 3.67−3.43 [m, 3 H, 5-H, 1′-H, $OCH_2(CH_2)_6Me$], 2.97 (ddd, 1 H, 2-H), 2.13, 2.08, 2.07, 2.06, 2.05, 2.01, and 1.96 (7 s, each 3 H, 7 × Ac), 1.72−1.27 [m, 15 H, 5′-H, 5a′,5a′-H, $OCH_2(CH_2)_6Me$], 0.88 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{35}H_{55}NO_{16}$ (745.8): calcd. C 56.36, H 7.43, N 1.88; found C 56.26, H 7.69, N 2.11.

Octyl (5a-Carba-β-D-galactopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-glucopyranoside (5): Compound **33** (12 mg, 15 μmol) was treated with methanolic sodium methoxide as described in the preparation of **3**, and the product was purified by a silica-gel column (0.7 g) with methanol/chloroform (1:3) as an eluent to give **5** (7.3 mg, 96%) as a white powder. − $[\alpha]_D^{20}$ = −42 (c = 0.37, MeOH). − ^{1}H NMR (270 MHz, CD_3OD): δ = 4.35 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 3.94−3.17 [m, 14 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, 1′-H, 2′-H, 3′-H, 4′-H, 6′,6′-H, $OCH_2(CH_2)_6Me$], 1.97 (s, 3 H, Ac), 1.86−1.30 [m, 15 H, 5′-H, 5a′,5a′-H, $OCH_2(CH_2)_6Me$], 0.90 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$].

Octyl 2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-galactopyranoside (34): To a solution of **13** (256 mg, 0.498 mmol) in dry DMSO (7.7 mL) was added acetic anhydride (1.4 mL), and it was stirred overnight at room temperature. The reaction mixture was diluted with ethyl acetate (50 mL) and washed with water thoroughly, dried, and concentrated. The residue (ca. 290 mg) was dissolved in THF (5.8 mL) and the solution was treated with L-Selectride (2.5 mL, 2.5 mmol) for 7 h at −15°C. The mixture was diluted with diethyl ether (50 mL), washed with aqueous satd. ammonium chloride and water, dried, and concentrated. The residue was chromatographed on silica gel (25 g) with ethyl acetate/toluene (1:3) to give **34** (149 mg, 58%) as crystals, m.p. 114−116°C (from EtOH). − $[\alpha]_D^{28}$ = +17 (c = 1.0, MeOH). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.38−7.24 (m, 10 H, 2 × Ph), 5.63 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 4.93 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.70−4.49 (m, 4 H, 2 × CH_2Ph), 4.25 (dd, $J_{2,3}$ = 10.6, $J_{3,4}$ = 3.3 Hz, 1 H, 3-H), 4.07 (dd, $J_{4,5}$ = 3.3 Hz, 1 H, 4-H), 3.84 [ddd, J = 6.6, 6.6, and 9.9 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.81 (m, 1 H, 5-H), 3.76 (dd, $J_{5,6a}$ = 5.9, J_{6gem} = 13.2 Hz, 1 H, 6a-H), 3.66 (m, 1 H, 6b-H), 3.47 [ddd, J = 7.0, 7.0, and 9.9 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.47 (ddd, 1 H, 2-H), 1.91 (s, 3 H, Ac), 1.57−1.25 [m, 12 H, $OCH_2(CH_2)_6Me$], 0.87 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{30}H_{43}NO_6$ (513.7): calcd. C 70.15, H 8.44, N 2.73; found C 69.89, H 8.74, N 3.03.

Octyl 2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-4-*O*-methanesulfonyl-β-D-galactopyranoside (35): To a solution of **34** (131 mg, 0.255 mmol) in pyridine (2.6 mL) was added methanesulfonyl chloride (59 mL, 0.77 mmol), and it was stirred for 2.5 h at room temperature. The mixture was diluted with ethyl acetate (30 mL), washed with water thoroughly, dried, and concentrated. Silica-gel chromatography (15 g, ethyl acetate/toluene, 1:4) gave **35** (131 mg, 87%) as a syrup. − $[\alpha]_D^{27}$ = +31 (c = 0.3, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.40−7.24 (m, 10 H, 2 × Ph), 5.56 (d, $J_{2,NH}$ = 7.0 Hz, 1 H, NH), 5.36 (dd, $J_{3,4}$ = 2.8 Hz, 1 H, 4-H), 4.95 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.82 and 4.42 (ABq, J_{gem} = 11.0 Hz, each 1 H, CH_2Ph), 4.66 and 4.50 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.37 (dd, $J_{2,3}$ = 11.0 Hz, 1 H, 3-H), 3.86−3.78 [m, 2 H, 5-H, $OCH_2(CH_2)_6Me$], 3.71 (m, 2 H, 6,6-H), 3.45 [ddd, J = 7.0, 7.0, and 9.5 Hz, 1 H, $OCH_2(CH_2)_6Me$], 3.31 (ddd, 1 H, 2-H), 3.04 (s, 3 H, Ms), 1.92 (s, 3 H, Ac), 1.54−1.25 [m, 12 H, $OCH_2(CH_2)_6Me$], 0.87 [t, J = 7.0 Hz, 3 H, $OCH_2(CH_2)_6CH_3$]. − $C_{31}H_{45}NO_8S$ (591.8): calcd. C 62.92, H 7.67, N 2.37; found C 62.69, H 7.87, N 2.46.

Octyl 2-Acetamido-4-azido-3,6-di-*O*-benzyl-2,4-dideoxy-β-D-glucopyranoside (36): A mixture of **35** (125 mg, 0.211 mmol), sodium azide (548 mg, 8.44 mmol), and aqueous 80% DMF (2.5 mL) was stirred for 2 d at 120°C, and, after cooling, the mixture was diluted with ethyl acetate (30 mL) and washed with water, dried, and concentrated. The residue was chromatographed on silica gel (10 g, acetone/toluene, 1:19) to give **36** (101 mg, 96%) as crystals, m.p.

117−119°C (from EtOH). − $[\alpha]_D^{27}$ = +83 (*c* = 0.44, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.36−7.24 (m, 10 H, 2 × Ph), 5.64 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 4.91 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.86 and 4.63 (ABq, J_{gem} = 11.4 Hz, each 1 H, CH_2Ph), 4.65 and 4.55 (ABq, J_{gem} = 12.1 Hz, each 1 H, CH_2Ph), 4.21 (dd, $J_{2,3}$ = $J_{3,4}$ = 9.9 Hz, 1 H, 3-H), 3.83 (ddd, *J* = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.75 (dd, $J_{5,6a}$ = 2.6, J_{6gem} = 11.2 Hz, 1 H, 6a-H), 3.70 (dd, $J_{5,6b}$ = 4.0 Hz, 1 H, 6b-H), 3.60 (dd, $J_{3,4}$ = 9.9, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.44 [ddd, *J* = 7.0, 7.0, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.38 (ddd, 1 H, 5-H), 3.10 (ddd, 1 H, 2-H), 1.87 (s, 3 H, Ac), 1.54−1.26 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 0.87 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{30}H_{42}N_4O_5$ (538.7): calcd. C 66.89, H 7.86, N 10.40; found C 66.42, H 7.83, N 10.47.

Octyl 2-Acetamido-4-amino-2,4-dideoxy-β-D-glucopyranoside (37): A solution of **36** (99 mg, 0.200 mmol) in ethanol/ethyl acetate (1:1) (4 mL) containing 1 M hydrochloric acid (0.4 mL) was hydrogenolyzed in the presence of 10% Pd/C (10 mg) for overnight at room temperature. The solution was filtered and the filtrate was concentrated to give **37** (53 mg, 80%) as a white powder. − $[\alpha]_D^{27}$ = −37 (*c* = 0.13, MeOH). − ^{1}H NMR (270 MHz, CD_3OD): δ = 4.55 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 3.87−3.09 [m, 8 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, OCH_2(CH$_2$)$_6$Me], 2.02 (s, 3 H, Ac), 1.54−1.20 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 0.90 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − This compound was without further purification used in the next reaction.

Octyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-allopyranoside (38): To a solution of **10** (482 mg, 1.14 mmol) in DMSO (14 mL) was added acetic anhydride (3.2 mL), and it was stirred overnight at room temperature. The mixture was diluted with ethyl acetate (100 mL), washed with water, dried, and concentrated. The residue (ca. 507 mg) was treated with L-Selectride (11.4 mL, 11.4 mmol) in THF (30 mL) for 2 h at −10°C. The reaction mixture was processed as described for the preparation of **34** to give after chromatography on silica gel (50 g, acetone/toluene, 1:5) compound **38** (365 mg, 76%) as white crystals, m.p. 220−222°C (from EtOH). − $[\alpha]_D^{26}$ = −58 (*c* = 0.78, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.90−7.23 (m, 5 H, Ph), 5.99 (d, $J_{2,NH}$ = 9.2 Hz, 1 H, NH), 5.59 (s, 1 H, C*H*Ph), 4.66 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 4.38 (dd, $J_{5,6a}$ = 4.8, J_{6gem} = 10.3 Hz, 1 H, 6a-H), 4.27 (dd, $J_{2,3}$ = 2.8, $J_{3,4}$ = 2.6 Hz, 1 H, 3-H), 4.15 (ddd, 1 H, 2-H), 3.97 (ddd, $J_{4,5}$ = 9.2, $J_{5,6b}$ = 10.3 Hz, 1 H, 5-H), 3.86 [ddd, *J* = 6.2, 6.2, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.79 (dd, 1 H, 6b-H), 3.65 (dd, 1 H, 4-H), 3.44 [ddd, *J* = 7.0, 7.0, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 2.02 (s, 3 H, Ac), 1.55−1.27 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 0.88 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{23}H_{35}NO_6$ (421.5): calcd. C 65.53, H 8.37, N 3.32; found C 65.25, H 8.61, N 3.40.

Octyl 2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-methanesulfonyl-β-D-altropyranoside (39): Compound **38** (151 mg, 0.359 mmol) was treated with methanesulfonyl chloride (83 mL, 1.08 mmol) in pyridine (3 mL) as described for preparation of **35** to give **39** (117 mg, 65%) as white crystals, m.p. 181−183°C (from EtOH). − $[\alpha]_D^{26}$ = −70 (*c* = 0.4, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.44−7.23 (m, 5 H, Ph), 5.74 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 5.57 (s, 1 H, C*H*Ph), 5.27 (dd, $J_{2,3}$ = $J_{3,4}$ = 2.6 Hz, 1 H, 3-H), 4.66 (d, $J_{1,2}$ = 8.8 Hz, 1 H, 1-H), 4.41 (dd, $J_{5,6a}$ = 4.4, J_{6gem} = 9.9 Hz, 1 H, 6a-H), 4.27 (ddd, 1 H, 2-H), 3.93−3.84 [m, 2 H, 5-H, OCH_2(CH$_2$)$_6$Me], 3.81 (dd, $J_{4,5}$ = 9.5 Hz, 1 H, 4-H), 3.79 (dd, $J_{5,6b}$ = 9.9 Hz, 1 H, 6b-H), 3.46 [ddd, *J* = 7.0, 7.0, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 2.96 (s, 3 H, Ms), 2.03 (s, 3 H, Ac), 1.66−1.28 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 3.97 (ddd, $J_{4,5}$ = 9.2, $J_{5,6b}$ = 10.3 Hz, 1 H, 5-H), 0.88 [t, 3 H, *J* = 7.0 Hz, 1 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{24}H_{37}NO_8S$ (499.6): calcd. C 57.70, H 7.46, N 2.80; found C 57.43, H 7.68, N 2.96.

Octyl 2-Acetamido-3-azido-4,6-*O*-benzylidene-2,3-dideoxy-β-D-glucopyranoside (40): A mixture of **39** (91 mg, 0.183 mmol), sodium azide (300 mg, 4.58 mmol), and aqueous 80% DMF (2 mL) was stirred for 24 h at 120°C. After cooling, the reaction mixture was diluted with ethyl acetate (30 mL), washed with water, dried, and concentrated. The residue was chromatographed on silica gel (8 g) with acetone/toluene (1:13) to give **40** (75 mg, 92%) as white crystals, m.p. 235−237°C (from EtOH). − $[\alpha]_D^{26}$ = −9 (*c* = 0.13, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.48−7.27 (m, 5 H, Ph), 5.86 (d, $J_{2,NH}$ = 7.7 Hz, 1 H, NH), 5.56 (s, 1 H, C*H*Ph), 5.02 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 4.49 (dd, $J_{2,3}$ = 8.8, $J_{3,4}$ = 9.2 Hz, 1 H, 3-H), 4.35 (dd, $J_{5,6a}$ = 4.4, J_{6gem} = 10.3 Hz, 1 H, 6a-H), 3.84 [ddd, *J* = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.77 (dd, $J_{5,6b}$ = 9.5 Hz, 1 H, 6b-H), 3.58 (ddd, $J_{4,5}$ = 8.8, $J_{5,6b}$ = 10.3 Hz, 1 H, 5-H), 3.51 (dd, 1 H, 4-H), 3.49 [ddd, *J* = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.08 (ddd, 1 H, 2-H), 2.03 (s, 3 H, Ac), 1.56−1.27 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 0.88 [t, *J* = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{23}H_{34}N_4O_5$ (446.6): calcd. C 61.86, H 7.68, N 12.55; found C 61.59, H 7.68, N 12.34.

Octyl 2-Acetamido-3-amino-2,3-dideoxy-β-D-glucopyranoside (41): A solution of **40** (69 mg, 0.154 mmol) in ethanol/ethyl acetate (1:1.) (4.1 mL) was hydrogenolyzed in the presence of 10% Pd/C catalyst (10 mg) and 1 M hydrochloric acid (0.3 mL) overnight at room temperature. The mixture was filtered and the filtrate was concentrated and the residue was chromatographed on a column of Dowex 50W-X2 (H^+) resin (10 mL) with aqueous conc. ammonia/methanol (1:8) to give **41** (46 mg, 90%) as a white powder. − $[\alpha]_D^{27}$ = −12 (*c* = 0.2, MeOH). − ^{1}H NMR (270 MHz, CD_3OD): δ = 4.57 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 3.90−3.21 [m, 8 H, 2-H, 3-H, 4-H, 5-H, 6,6-H, OCH_2(CH$_2$)$_6$Me], 2.03 (m, 3 H, Ac), 1.56−1.18 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 0.90 [br. s, 3 H, OCH$_2$(CH$_2$)$_6$CH_3].

Octyl 3,6-Di-*O*-acetyl-2-acetamido-4-(2-*O*-acetyl-6-*O*-benzyl-1-deoxy-3,4-*O*-isopropylidene-5a-carba-β-D-glucopyranos-1-yl)amino-2,4-dideoxy-β-D-glucopyranoside (42): A mixture of **8** (183 mg, 0.632 mmol) and **37** (21 mg, 63 μmol) in 2-propanol (1.5 mL) was heated in a sealed tube for 3 weeks at 120°C, and then concentrated. The residue was acetylated conventionally, and the products were chromatographed on a silica-gel column (5 g) with acetone/toluene (1:5) to give **42** (18 mg, 38%) as a white powder. − $[\alpha]_D^{27}$ = +18 (*c* = 0.8, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.39−7.27 (m, 5 H, Ph), 5.55 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 4.80−4.73 (m, 2 H, 3-H, 2′-H), 4.58−4.48 (m, 3 H, 6a-H, CH_2Ph), 4.39 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.26 (dd, $J_{3',4'}$ = 4.8, $J_{4',5'}$ = 3.7 Hz, 1 H, 4′-H), 4.17 (dd, $J_{5,6b}$ = 5.5, J_{6gem} = 11.4 Hz, 1 H, 6b-H), 3.95 (dd, $J_{2',3'}$ = 7.7 Hz, 1 H, 3′-H), 3.92 (m, 1 H, 2-H), 3.80 [ddd, *J* = 6.2, 6.2, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.61 (dd, $J_{5',6'a}$ = 6.6, $J_{6'gem}$ = 9.2 Hz, 1 H, 6′a-H), 3.44 (dd, $J_{5',6'b}$ = 8.8 Hz, 1 H, 6′b-H), 3.41 [ddd, *J* = 6.6, 6.6, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.33 (m, 1 H, 5-H), 2.67 (dd, $J_{3,4}$ = 9.5, $J_{4,5}$ = 9.9 Hz, 1 H, 4-H), 2.28 (m, 1 H, H-1′), 2.09, 2.07, 2.04, and 1.93 (4 s, each 3 H, 4 × Ac), 2.00−1.97 [m, 2 H, 5′-H, 5a′(eq)-H], 1.72−1.26 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 1.49 and 1.32 (2 s, each 3 H, CMe$_2$), 1.05 [ddd, $J_{1',5a'(ax)}$ = $J_{5',5a'(ax)}$ = $J_{5a'gem}$ = 11.7 Hz, 1 H, 5a′(ax)-H], 0.87 [t. 3 H, *J* = 7.0 Hz, 1 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{39}H_{60}N_2O_{12}$ (748.9): calcd. C 62.55, H 8.08, N 3.74; found C 62.55, H 8.31, N 3.78.

Octyl 3,6-Di-*O*-acetyl-2-acetamido-2,4-dideoxy-4-(2,3,4,6-tetra-*O*-acetyl-1-deoxy-5a-carba-β-D-glucopyranos-1-yl)amino-β-D-glucopyranoside (43): A mixture of **42** (29 mg, 38 μmol) and 80% aqueous acetic acid (0.6 mL) was stirred for 2 h at 60°C, and then concentrated. The residue (ca. 26 mg) was dissolved in ethanol (2 mL), and the solution was acidified with aqueous 1 M hydrochloric

acid and hydrogenolyzed in the presence of 10% Pd/C under atmospheric pressure of hydrogen for 2 h. The solution was filtered and concentrated. The residue was acetylated conventionally and the product was purified by a silica-gel chromatography (2.5 g, acetone/toluene, 1:5) to give **43** (24 mg, 83%) as a colorless syrup. − $[\alpha]_D^{27} = -21$ (c = 0.2, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.60 (d, $J_{2,NH}$ = 8.4 Hz, 1 H, NH), 5.45 (br. s, 1 H, 4′-H), 4.99 (dd, $J_{1',2'} = J_{2',3'}$ = 10.3 Hz, 1 H, 2′-H), 4.81 (dd, $J_{2,3}$ = 11.0, $J_{3,4}$ = 9.9 Hz, 1 H, 3-H), 4.80 (dd, $J_{3',4'}$ = 2.9 Hz, 1 H, 3′-H), 4.55 (dd, $J_{5,6a}$ = 1.8, J_{6gem} = 11.7 Hz, 1 H, 6a-H), 4.43 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 4.15 (dd, $J_{5,6b}$ = 5.9 Hz, 1 H, 6b-H), 4.18−3.86 (m, 3 H, 2-H, 6′,6′-H), 3.80 (ddd, J 6.6, 6.6, and 9.9 Hz, 1 H) and 3.42 (ddd, J 7.0, 7.0, and 9.9 Hz, 1 H) [OCH_2(CH$_2$)$_6$Me], 3.34 (m, 1 H, H-5), 2.69 (dd, $J_{3,4}$ 9.9, $J_{4,5}$ 9.5 Hz, 1 H, H-4), 2.52 (m, 1 H, H-1′), 2.18−1.98 [m, 2 H, H-5′, H-5a′(eq)], 2.10, 2.09, 2.08, 2.06, 2.05, 1.95, and 1.94 (7 s, each 3 H, 7 × Ac), 1.59−1.26 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 1.17 [m, 1 H, H-5a′(ax)], 0.87 [t, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{35}H_{56}N_2O_{15}$ (744.9): calcd. C 56.44, H 7.58, N 3.76; found C 56.18, H 7.86, N 3.65.

Octyl 2-Acetamido-4-(1-deoxy-5a-carba-β-D-glucopyranos-1-yl)amino-2,4-dideoxy-β-D-glucopyranoside (4): Compound **43** (4.4 mg, 5.9 μmol) was treated with methanolic sodium methoxide conventionally. The product was purified by a column of Dowex 50W-X2 (H^+) resin (1 mL) with satd. aqueous ammonia/methanol (1:8) as an eluent to give **4** (2.9 mg, ca. 100%) as a white powder. − $[\alpha]_D^{19} = -36$ (c = 0.5, MeOH). − ^{1}H NMR (270 MHz, CD_3OD): δ = 4.36 (d, $J_{1,2}$ 8.4 Hz, 1 H, H-1), 3.97 (br. s, 1 H, H-4′), 3.88−3.83 (m, 2 H, H-6,6), 3.62 (dd, $J_{2,3}$ 9.9 Hz, 1 H, H-2), 3.62−3.34 [m, 7 H, H-3, H-2′, H-3′, H-6′,6′, OCH_2(CH$_2$)$_6$Me], 3.19 (m, 1 H, H-5), 2.67 (dd, $J_{3,4}$ 9.9, $J_{4,5}$ 9.5 Hz, 1 H, H-4), 2.60 (m, 1 H, H-1′), 1.96 (s, 3 H, Ac), 1.82 [m, 1 H, H-5a′(eq)], 1.64−1.30 [m, 13 H, H-5′, OCH$_2$(CH_2)$_6$Me], 1.26 [m, 1 H, H-5a′(ax)], 0.90 [t, 3 H, OCH$_2$(CH$_2$)$_6$CH_3].

Octyl 2-Acetamido-4,6-di-*O*-acetyl-3-(2-*O*-acetyl-6-*O*-benzyl-1-deoxy-3,4-*O*-isopropylidene-5a-carba-β-D-glucopyranos-1-yl)amino-2,3-dideoxy-β-D-glucopyranoside (44) and 1-*O*-Acetyl-6-*O*-benzyl-3,4-*O*-isopropylidene-2-(octyl 4,6-*O*-acetyl-2-acetamido-2,3-dideoxy-β-D-glucopyranosid-3-yl)amino-5a-carba-α-D-talopyranoside (45): A mixture of **8** (129 mg, 0.443 mmol) and **41** (74 mg, 0.22 mmol) in 2-propanol (1.5 mL) was heated in a sealed tube for 3 weeks at 120°C, and then concentrated. The residue was acetylated conventionally, and the products were chromatographed on a silica-gel column (15 g) with acetone/toluene (1:5) to give **44** (63 mg, 38%) and **45** (39 mg, 24%) as a white powder. − **44**: R_f = 0.60 (ethanol/toluene 1:5). − $[\alpha]_D^{27} = +10$ (c = 0.7, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.38−7.23 (m, 5 H, Ph), 5.69 (br. s, 1 H, NH), 4.82 (dd, $J_{1',2'}$ = 8.4, $J_{2',3'}$ = 7.3 Hz, 1 H, 2′-H), 4.79 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.73 (dd, $J_{3,4} = J_{4,5}$ = 9.2 Hz, 1 H, 4-H), 4.52 (m, 2 H, CH_2Ph), 4.27 (m, 1 H, 4′-H), 4.23 (dd, $J_{5,6a}$ = 5.1, J_{6gem} = 12.1 Hz, 1 H, 6a-H), 4.09 (dd, $J_{5,6b}$ = 2.6 Hz, 1 H, 6b-H), 3.96 (dd, $J_{3',4'}$ = 5.5 Hz, 1 H, 3′-H), 3.82 [ddd, J = 6.2, 6.2, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.65 (m, 1 H, 5-H), 3.60 (dd, $J_{5',6'a}$ = 7.0, $J_{6'gem}$ = 8.8 Hz, 1 H, 6′a-H), 3.45 [ddd, J = 7.0, 7.0, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.42 (dd, $J_{5',6'b}$ = 7.3 Hz, 1 H, 6′b-H), 3.30 (m, 1 H, 2-H), 3.18 (m, 1 H, 3-H), 2.50 (m, 1 H, 1′-H), 2.13, 2.07, 2.03, and 1.99 (4 s, each 3 H, 4 × Ac), 1.96−1.89 [m, 2 H, H-5′, H-5a′(eq)], 1.58−1.27 [m, 12 H, OCH$_2$(CH_2)$_6$Me], 1.50 and 1.31 (2 s, each 3 H, CMe$_2$), 1.13 [ddd, $J_{1',5a'(ax)} = J_{5',5a'(ax)} = J_{5a'gem}$ = 11.7 Hz, 1 H, 5a′(ax)-H], 0.88 [t, J = 7.0 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{39}H_{60}N_2O_{12}$ (748.9): calcd. C 62.55, H 8.08, N 3.74; found C 62.25, H 8.35, N 4.04. − **45**: R_f = 0.56 (ethanol/toluene, 1:5). − $[\alpha]_D^{27} = -13$ (c = 0.6, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 7.36−7.25 (m, 5 H, Ph), 5.54 (d, $J_{2,NH}$ = 7.3 Hz, 1 H, NH), 4.89 [dd, $J_{1',2'} = J_{1',5a'(eq)}$ = 1.8, $J_{1',5a'(ax)}$ 5.9 Hz, 1 H, 1′-H], 4.79 (dd, $J_{3,4} = J_{4,5}$ = 9.2 Hz, 1 H, 4-H), 4.53 (m, 2 H, CH_2Ph), 4.31 (m, 1 H, 4′-H), 4.30 (dd, $J_{5,6a}$ = 4.4, J_{6gem} = 12.1 Hz, 1 H, 6a-H), 4.21 (d, $J_{1,2}$ = 7.7 Hz, 1 H, 1-H), 4.07 (dd, $J_{5,6b}$ = 2.2 Hz, 1 H, 6b-H), 4.04−3.97 (m, 2 H, 3-H, 3′-H), 3.86 [ddd, J = 6.6, 6.6, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.66 (m, 1 H, 5-H), 3.59 (dd, $J_{5',6'a}$ = 7.7, $J_{6'gem}$ = 9.0 Hz, 1 H, 6′a-H), 3.46 [ddd, J = 7.0, 7.0, and 9.5 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.41 (dd, $J_{5',6'b}$ = 6.6 Hz, 1 H, 6′b-H), 2.87 (m, 1 H, 2′-H), 2.59 (m, 1 H, 2-H), 2.13, 2.07, 2.03, and 1.96 (4 s, each 3 H, 4 × Ac), 1.67−1.26 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 1.49 and 1.31 (2 s, each 3 H, CMe$_2$), 0.88 [t, 3 H, J = 7.0 Hz, 1 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{39}H_{60}N_2O_{12}$ (748.9): calcd. C 62.55, H 8.08, N 3.74; found C 62.31, H 8.33, N 3.63.

Octyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-dideoxy-3-(2,3,4,6-tetra-*O*-acetyl-1-deoxy-5a-carba-β-D-glucopyranos-1-yl)amino-β-D-glucopyranoside (46): Compound **44** (57 mg, 76 μmol) was treated with 80% aqueous acetic acid (1 mL) and then hydrogenolyzed as in the preparation of **43**. After conventional acetylation, the product was purified by a silica-gel chromatography (5 g, acetone/toluene, 1:8) to give **46** (35 mg, 62%) as a colorless syrup. − $[\alpha]_D^{24} = -16$ (c = 1.1, $CHCl_3$). − ^{1}H NMR (270 MHz, $CDCl_3$): δ = 5.58 (br. s, 1 H, NH), 5.43 (br. s, 1 H, 4′-H), 5.00 (dd, $J_{1',2'} = J_{2',3'}$ = 8.2 Hz, 1 H, 2′-H), 4.80−4.70 (m, 3 H, 1-H, 4-H, 3′-H), 4.26 (dd, $J_{5,6a}$ = 5.1, J_{6gem} = 11.9 Hz, 1 H, 6a-H), 4.10 (dd, $J_{5,6b}$ = 1.1 Hz, 1 H, 6b-H), 3.93−3.85 (m, 2 H, 6′,6′-H), 3.82 [ddd, J = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.67 (m, 1 H, 5-H), 3.45 [ddd, J = 6.6, 6.6, and 9.9 Hz, 1 H, OCH_2(CH$_2$)$_6$Me], 3.25−3.19 (m, 2 H, 2-H, 3-H), 2.79−2.65 (m, 1 H, 1′-H), 2.12, 2.09, 2.08, 2.07, 2.04, 2.02, and 1.96 (7 s, each 3 H, 7 × Ac), 1.87−1.27 [m, 15 H, 5′-H, 5a′,5a′-H, OCH$_2$(CH_2)$_6$Me], 0.88 [t, 3 H, OCH$_2$(CH$_2$)$_6$CH_3]. − $C_{35}H_{56}N_2O_{15}$ (744.9): calcd. C 56.44, H 7.58, N 3.76; found C 56.24, H 7.85, N 3.79.

Octyl 2-Acetamido-3-(1-deoxy-5a-carba-β-D-glucopyranos-1-yl)-amino-2,3-dideoxy-β-D-glucopyranoside (6): Compound **46** (29 mg, 39 μmol) was treated in methanol with methanolic sodium methoxide and the product was purified similarly in the preparation of **4** to give **6** (17 mg, 91%) as a white powder. − $[\alpha]_D^{24} = -45$ (c = 0.9, MeOH). − ^{1}H NMR (270 MHz, CD_3OD): δ = 4.36 (d, $J_{1,2}$ = 8.1 Hz, 1 H, 1-H), 3.97 (br. s, 1 H, 4′-H), 3.89−3.24 [m, 11 H, 2-H, 4-H, 5-H, 6,6-H, 2′-H, 3′-H, 6′,6′-H, OCH_2(CH$_2$)$_6$Me], 2.66 (dd, $J_{2,3} = J_{3,4}$ = 9.5 Hz, 1 H, 3-H), 2.53 [ddd, $J_{1',2'}$ = 8.4, $J_{1',5a'(eq)}$ = 11.4, $J_{1,5a'(eq)}$ = 3.3 Hz, 1 H, 1′-H], 1.97 (s, 3 H, NAc), 1.75 [m, 1 H, 5a′(eq)-H], 1.53−1.30 [m, 13 H, 5′-H, OCH$_2$(CH_2)$_6$Me], 1.22 [m, 1 H, 5a′(ax)-H], 0.90 [t, J = 6.6 Hz, 3 H, OCH$_2$(CH$_2$)$_6$CH_3].

Evaluation of the 5a′-Carbadisaccharides 3, 4, 5, and 6 as Acceptor Substrates for α-(1→3/4)-Fucosyltransferase, and Enzymatic Synthesis of 5a′-Carbatrisaccharides 47 and 48: Human-milk α-(1→3/4)-fucosyltransferase was isolated by ion-exchange chromatography on SP-Sephadex C-50 and affinity chromatography on a GDP-hexanolamine Sepharose column.[14] Standard assays with 0.5 mM of the test compounds were utilized to screen for potential substrates and inhibitions of fucosyltransferase.[14] For kinetic characterizations, radiochemical assays were carried out at 37°C employing six concentrations of acceptors **3** or **4**, 50 μM GDP-Fuc donor (including 100000 dpm GDP-[^{3}H]Fuc), 20 mM Hepes buffer, pH = 7.0, 20 mM $MnCl_2$, 0.2% bovine serum albumin and enzyme in 20 mL final volume. To confirm that substrates were converted to products small-scale enzymatic synthesis was carried out. Fucosyltransferase (14 milliunits in 350 mL of 20 mM Hepes buffer, pH = 7.0, 20 mM $MnCl_2$, 0.2% bovine serum albumin) was added to 0.25

mg of **3**, **4**, or **6**. Reaction was initiated by the addition of 0.5 mg of GDP-Fuc. After incubation at ambient temperature for three weeks with addition of 20 μg of GDP-Fuc every 2 d, reaction products were isolated by loading the reaction mixtures onto Waters C_{18} reverse-phase cartridges. The cartridges were washed with 40 mL of water, then the products eluted with 20 mL of 60% MeOH/H_2O. The MeOH/H_2O eluate was concentrated under diminished pressure, the residue was dissolved in water (10 mL), passed through a Millex-GV filter (0.22 μM) and the filtrate was lyophilized. Under these conditions, no reaction was observed for compound **6** while **3** and **4** were converted to **47** and **48**, respectively. − **47**: ^{1}H NMR (500 MHz, D_2O) (inter alia): δ = 5.19 (d, $J_{1'',2''}$ = 4.0 Hz, 1 H, 1′′-H), 4.51 (d, $J_{1,2}$ = 8.2 Hz, 1 H, 1-H), 4.43 (br. q, J = 6.8 Hz, 1 H, 5′′-H), 2.02 (s, 3 H, Ac), 1.21 (d, 3 H, J = 6.8 Hz, 1 H, 6′′-H). − HRMS: $C_{29}H_{53}NO_{14}Na$ (662.3364): found 662.3366. − **48**: ^{1}H NMR (500 MHz, D_2O) (inter alia): δ = 5.15 (d, $J_{1'',2''}$ = 4.0 Hz, 1 H, 1′′-H), 4.48 (br. q, J = 6.7 Hz, 1 H, 5′′-H), 4.47 (d, $J_{1,2}$ = 8.4 Hz, 1 H, 1-H), 2.90 (t, $J_{3,4}$ = $J_{4,5}$ = 9.7 Hz, 1 H, 4-H), 2.02 (s, 3 H, Ac), 1.21 (d, 3 H, J = 6.7 Hz, 1 H, 6′′-H). − HRMS: $C_{29}H_{54}N_2O_{13}Na$ (661.3524): found 661.3521.

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[1] A part of this work has previously been reported: S. Ogawa, N. Matsunaga, M. M. Palcic, *Carbohydr. Lett*. **1997**, *2*, 299−306.
[2] S. Ogawa, K. Hirai, T. Odagiri, N. Matsunaga, T. Yamazaki, and A. Nakajima, *Eur. J. Org. Chem*. **1998**, 1099−1109.
[3] J. P. Prieels, D. Monnom, M. Dolmans, T. A. Beyer, R. L. Hill, *J. Biol. Chem.* **1981**, *256*, 10456−10463; B. A. Macher, E. H. Holmes, S. J. Swiedler, C. L. M. Stults, C. A. Srnka, *Glycobiology* **1991**, *1*, 577−584.
[4] S. I. Hakomori, *Adv. Cancer Res.*, **1989**, *52*, 257−331; H. Schachter, in *Molecular Glycobiology* (Eds.: M. Fukuda, O. Hindsgaul), IRL Press, Oxford, New York, Tokyo, **1994**, pp. 88−162.
[5] M. M. Palcic, A. P. Venot, R. M. Ratcliffe, O. Hindsgaul, *Carbohydr. Res.* **1989**, *190*, 1−11; Y. Ichikawa, Y.-C. Lin, D. P. Dumas, G.-J. Shen, E. Garcia-Junceda, M. A. Williams, R. Bayer, C. Ketcham, L. E. Walker, J. C. Paulson, C.-H. Wong, *J. Am. Chem. Soc*. **1992**, *114*, 9283−9298; M. Du, O. Hindsgaul, *Carbohydr. Res.* **1995**, *286*, 87−105.
[6] S. Ogawa, T. Furuya, H. Tsunoda, O. Hindsgaul, K. Stangier, M. M. Palcic, *Carbohydr. Res.* **1995**, *271*, 197−205.
[7] I. Takai, Y. Ishido, S. Adachi, *Jpn. Pat. Appl.* JP 72491, **1991** (*Chem. Abstr*. **1991**, *115*, 72149).
[8] G. Zemplén, E. Pacus, *Ber. Dtsch. Chem. Ges.* **1929**, *62*, 1613−1614.
[9] C. Malet, O. Hindsgaul, *Carbohydr. Res.* **1997**, *303*, 51−65.
[10] S. Ogawa, T. Tonegawa, K. Nishi, *Carbohydr. Res.* **1992**, *229*, 173−182.
[11] S. Ogawa, K. Hirai, M. Ohno, T. Furuya, S. Sasaki, H. Tsunoda, *Liebigs Ann*. **1996**, 673−677.
[12] S. Ogawa, K. Hirai, T. Yamazaki, A. Nakajima, N. Matsunaga, *Carbohydr. Lett*. **1996**, *2*, 183−188.
[13] H. Tsunoda, S. Ogawa, *Liebigs Ann. Chem*. **1994**, 103−107.
[14] S. Gosselin, M. M. Palcic, *Bioorg. Med. Chem*. **1996**, *4*, 2023−2028.

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