Synthesis of Fragments of the Glycocalyx Glycan of the Parasite *Schistosoma mansoni*

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Abstract: The chemical synthesis of α-L-Fuc*p*-(1 → 3)-β-D-Gal*p*NAc-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-α-D-Gal*p*O$(CH_2)_5NH_2$, β-D-Gal*p*NAc-(1 → 4)-[α-L-Fuc*p*-(1 → 3)-]β-D-Glc*p*NAc-(1 → 3)-α-D-Gal*p*O$(CH_2)_5NH_2$, and α-L-Fuc*p*-(1 → 3)-β-D-Gal*p*NAc-(1 → 4)-[α-L-Fuc*p*-(1 → 3)-]β-D-Glc*p*NAc-(1 → 3)-α-D-Gal*p*O$(CH_2)_5NH_2$ is described. These structures represent fucosylated oligosaccharide fragments of the glycocalyx glycan of the cercarial stage of the parasite *Schistosoma mansoni*, and in protein-conjugated form they are potential diagnostics in the search for antibodies raised against the glycan in the serum of infected humans.

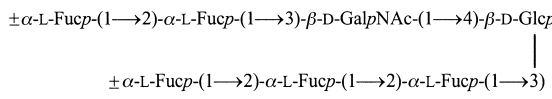
Keywords: carbohydrates · glycocalyx · glycosylation · oligosaccharides · *Schistosoma mansoni*

Introduction

Schistosomiasis, a parasitic infection affecting more than 200 million people in tropical and subtropical regions, is caused by blood-dwelling flukes of the genus *Schistosoma*. The most important species of this genus are *S. mansoni*, *S. haematobium*, and *S. japonicum*.[1] The infective parasitic stage, the cercaria, enters the host through the skin, evoking an inflammatory response. From this stage, until approximately three weeks after infection, the parasite, present as a young schistosomulum, is most susceptible to immune damage.[2] In the cercarial stage of the life cycle of the parasite, the entire surface of the parasite is covered by a 1 μm thick, highly immunogenic, fucose-rich glycocalyx. Recently, the nonreducing terminal sequences of the O-linked carbohydrate chain as part of the glycocalyx (GCX) were elucidated as follows:[3]

An important feature of the *Schistosoma* infection is that, after the cercarial stage, the developing worm becomes resistant to, or even invisible to, certain parts of the host's defence system by several evasion mechanisms.[4–8] The severest pathology of the infection is caused by the eggs of the parasite that get stuck in the human body.[9] In order to be able to treat the infection with chemotherapeutics before the onset of egg production, an early diagnostic method for schistosomiasis is required. Serological detection of antibodies, raised against the glycocalyx of the cercarial stage of the parasite *S. mansoni*, could certainly be such an early diagnostic method.

It is speculated that both the fucosyl appendages and the α-linked galactose residue are likely to be involved in GCX's action as a potent immunological modulator.[3] The exact role of the various domains of the GCX in immunological stimulation can only be assessed with neoglycoconjugates prepared from fragments of the GCX. However, the availability of well-defined oligosaccharides of the GCX from biological sources in sufficient amounts is limited. To replace isolated material in both immunological studies and for diagnostic purposes, a synthetic program for the preparation of several oligosaccharide fragments present in the GCX was initiated. In the first part of this project the chemical synthesis of the nonfucosylated backbone trisaccharide β-D-Gal*p*NAc-(1 → 4)-β-D-Glc*p*NAc-(1 → 3)-α-D-Gal*p*O$(CH_2)_5NH_2$ has been undertaken.[10] Here, we report the synthesis of fucosy-



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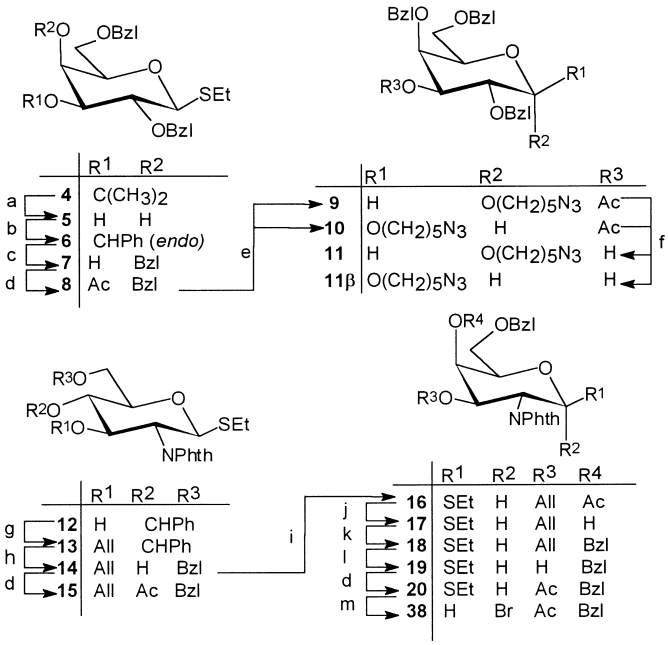
lated oligosaccharide fragments α-L-Fuc*p*-(1→3)-β-D-Gal*p*NAc-(1→4)-β-D-Glc*p*NAc-(1→3)-α-D-Gal*p* (**1**), β-D-Gal*p*NAc-(1→4)-[α-L-Fuc*p*-(1→3)]-β-D-Glc*p*NAc-(1→3)-α-D-Gal*p* (**2**) and α-L-Fuc*p*-(1→3)-β-D-Gal*p*NAc-(1→4)-[α-L-Fuc*p*-(1→3)]-β-D-Glc*p*NAc-(1→3)-α-D-Gal*p* (**3**) of the GCX glycan of the cercarial stage of the parasite *S. mansoni* bearing an aminopentyl spacer for conjugation to carrier molecules (Figure 1).

Results and Discussion

Our initial synthetic strategy was based on the preparation of a suitably protected backbone trisaccharide β-D-Gal*p*NPhth-(1→4)-β-D-Glc*p*NPhth-(1→3)-α-D-Gal*p* (**23**) carrying an azidopentyl spacer. Temporary protection of the positions to be fucosylated with an *O*-acetyl group for the Gal*p*NPhth residue and an *O*-allyl group for the Glc*p*NPhth moiety provides a possibility to prepare both tetrasaccharides **1** and **2** as well as the pentasaccharide **3**. The remaining hydroxyl groups are protected with benzyl groups. Relevant monosaccharide building blocks for the stepwise synthesis of **23** are 5-azidopentyl 2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (**11**), ethyl 4-*O*-acetyl-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**15**), and ethyl 3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (**20**) (Scheme 1).



Scheme 1. a) 60% aq HOAc, 60°C; b) α,α-dimethoxytoluene, *p*TsOH; c) $LiAlH_4$, $AlCl_3$, DCM, Et_2O; d) pyridine, Ac_2O; e) 5-azidopentanol, MeOTf, Et_2O, 0°C; f) NaOMe, MeOH, DCM; then $TiCl_4$, 4 Å, DCM; g) AllBr, NaH, THF; h) Me_3NBH_3, $AlCl_3$, 4 Å, THF; i) Tf_2O, pyridine, DCM, 0°C, then TBAA, DMF; j) K_2CO_3, MeOH, THF; k) BzlBr, Ag_2O, KI, 4 Å, DMF; l) $(Ph_3P)_3RhCl$, EtOH, HCl, acetone; m) Br_2, DCM, 0°C.

For the synthesis of acceptor **11** the isopropylidene group of ethyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-1-thio-β-D-galactopyranoside[10] (**4**) was removed (→**5**, quantitative), and a dioxolane-type *endo*-3,4-*O*-benzylidene acetal was stereoselectively introduced by a kinetically controlled reaction (→**6**, 76%).[11] The reductive opening of the benzylidene ring with lithium aluminium hydride/aluminium(III) chloride[12] resulted in derivative **7** (77%). Conventional acetylation of **7** afforded thioglycoside **8** (96%). Condensation of **8** with 5-azidopentanol[13] in diethyl ether in the presence of methyl triflate[14] as a promoter gave an inseparable mixture of the 1,2-*cis*- (**9**) and 1,2-*trans*-glycosides (**10**) in approximately a 1:1 molar ratio (^{1}H NMR data) in a yield of 89%. After removal of the acetyl function, the anomeric mixture could be separated by means of column chromatography to give pure **11** (32%) and a mixture of the α- (**11**) and β- (**11*β***) anomers (59%). The rapid anomerization of the anomeric mixture (α:β-ratio 3:7; ^{1}H NMR data) with titanium tetrachloride[15] resulted in a mixture of **11** and **11*β*** in a 9:1 molar ratio (^{1}H NMR data). Separation of the mixture by column chromatography afforded pure **11** in 30% yield (total yield 62%). The presence of the azido group in **11** was established by IR analysis (ν_{max} 2098 cm^{-1}), and the 1,2-*cis* glycosidic linkage by ^{1}H NMR analysis (J(H1,H2) = 4.1 Hz).

Ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[14] (**12**) (Scheme 1) was the starting compound for both the glucosamine donor **15** and the galactosamine donor **20**. For the synthesis of **15**, compound **12** was treated with allyl bromide in the presence of sodium hydride to give crystalline **13** in a yield of 80%. Regioselective opening of the 4,6-*O*-benzylidene ring in **13** with borane-trimethylamine complex and aluminium(III) chloride[16] in tetrahydrofuran yielded **14** (85%). Conventional acetylation of **14** resulted in the desired glucosamine donor **15**. For the preparation of the galactosamine donor **20**, glucosamine derivative **14** was converted into the corresponding galactosamine derivative **16** (epimerization at C-4) by an S_N2 displacement reaction of *O*-triflate by *O*-acetate. For this, **14** was treated with triflic anhydride in dichloromethane in the presence of pyridine, and then the 4-*O*-triflated intermediate was treated with tetrabutylammoni-

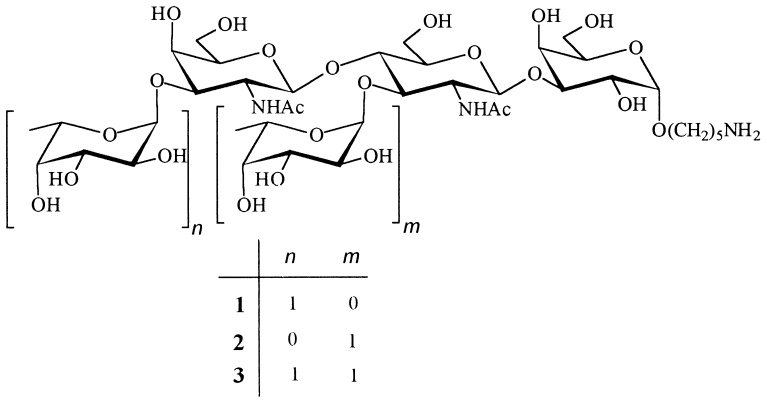


Figure 1. Synthesized oligosaccharide fragments of the glycocalyx glycan.

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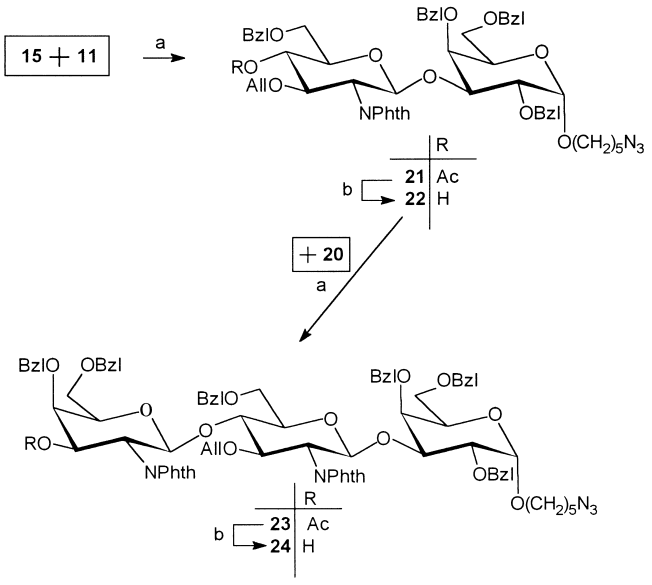
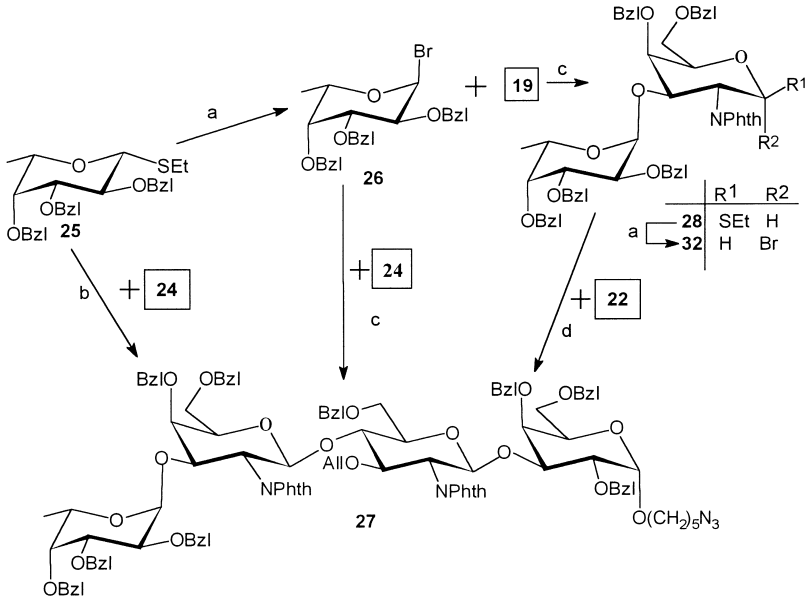
um acetate[17] in *N*,*N*-dimethylformamide to produce **16** (78%). The removal of the acetyl function with potassium carbonate in tetrahydrofuran/methanol 1:1 (→**17**, 73%), followed by benzylation using benzyl bromide in the presence of potassium iodide and silver(I) oxide in *N*,*N*-dimethylformamide afforded derivative **18** (82%). Compound **18** was *O*-deallylated with tris(triphenylphosphine)rhodium(I) chloride[18] as catalyst in ethanol to yield **19** (72%). Conventional acetylation of **19** resulted in the desired galactosamine donor **20**.

Condensation of **15** with **11** in diethyl ether in the presence of methyl triflate as a promoter afforded disaccharide **21** in a yield of 78% (Scheme 2). After removal of the acetyl group with potassium carbonate in tetrahydrofuran/methanol 1:1 (→**22**, 89%), acceptor **22** was coupled with galactosamine donor **20** in diethyl ether in the presence of methyl triflate as a promoter to furnish the aimed backbone trisaccharide **23** (82%), carrying *O*-benzyl-persistent, and *O*-allyl and *O*-acetyl temporary protecting groups. *O*-Deacetylation of **23** with potassium carbonate in tetrahydrofuran/methanol 1:1 gave the trisaccharide acceptor **24** (85%).



Scheme 2. a) MeOTf, Et_2O, 0 °C; b) K_2CO_3, MeOH, THF.

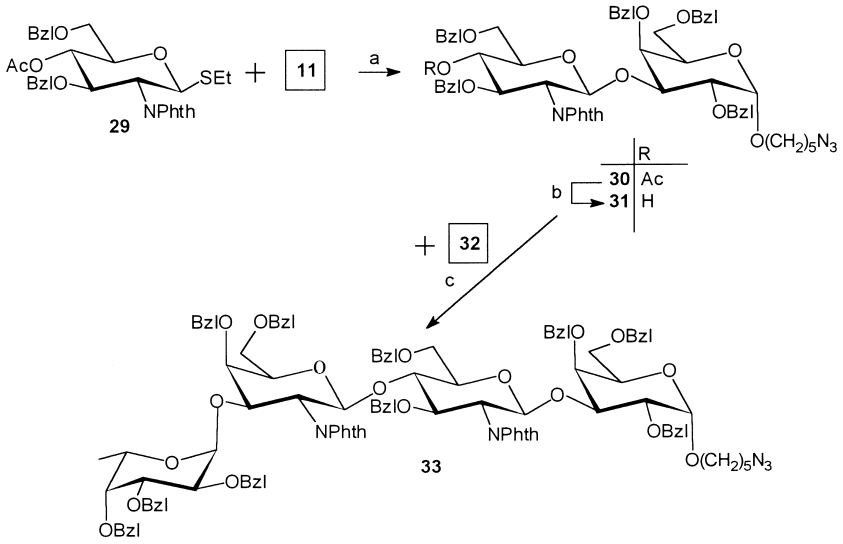
For the fucosylation of the backbone trisaccharide at the 3-position of the galactosamine residue, both ethyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (**25**)[14] and the corresponding bromo sugar **26** were used (Scheme 3). The reaction of acceptor **24** with **25** was promoted by copper(II) bromide/



Scheme 3. a) Br_2, DCM, 0 °C; b) $CuBr_2$, TBABr, 4 Å, DCM, DMF; c) TBABr, 4 Å, DCM, DMF; d) MeOTf, 4 Å, Et_2O, 0 °C.

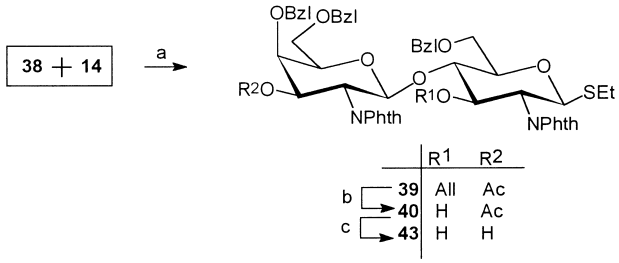
tetrabutylammonium bromide[19] to give tetrasaccharide **27** in a yield of 32%. Condensation of **24** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide (**26**) under Lemieux conditions[20] yielded tetrasaccharide **27** in a yield of 42%. Because fucosylations of **24** could only be achieved with moderate yields, the introduction of the α-fucosyl linkage at an earlier stage of the synthesis was also investigated. Thus, tetrasaccharide **27** was prepared by a 2+2 block synthesis as follows: Galactosamine derivative **19** was fucosylated with donor **26** under Lemieux conditions to yield disaccharide donor **28** (35%). Condensation of thioglycoside **28** with disaccharide acceptor **22** in the presence of methyl triflate resulted in tetrasaccharide **27** in a yield of 65%. For the deprotection of tetrasaccharide **27** as well as for the preparation of oligosaccharides bearing a fucose residue attached to the 3-position of the glucosamine moiety of the backbone trisaccharide, the removal of the allyl group in the presence of an azido function was required. However, under the tested conditions (tris(triphenylphosphine)rhodium(I) chloride in ethanol, palladium(II) chloride/copper(I) chloride, sodium borohydride/iodine, palladium on carbon/acetic acid), complex reaction mixtures and low yields were obtained. To overcome this difficulty, our preliminary synthetic strategy had to be modified. For the preparation of the tetrasaccharide α-L-Fuc*p*-(1→3)-β-D-Gal*p*NAc-(1→4)-β-D-Glc*p*NAc-(1→3)-α-D-Gal*p*O$(CH_2)_5NH_2$ (**1**), ethyl 4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**29**)[21] was used, bearing a 3-*O*-benzyl instead of a 3-*O*-allyl group (Scheme 4). Condensation of **29** with acceptor **11** in the presence of *N*-iodosuccinimide/silver triflate[22] afforded disaccharide **30** (83%), which was *O*-deacetyled to give **31** (81%). Glycosylation of **31** with bromosugar **32**, obtained from thioglycoside **28**, in the presence of silver triflate afforded tetrasaccharide **33** in 84% yield.

For the preparation of the tetrasaccharide β-D-Gal*p*NAc-1→4)-[α-L-Fuc*p*-(1→3)-]β-D-Glc*p*NAc-(1→3)-α-D-Gal*p*O-



Scheme 4. a) NIS, AgOTf, 4 Å, DCM, acetonitrile, −15 °C; b) K_2CO_3, MeOH, THF; c) AgOTf, 4 Å, DCM, toluene, −50 °C.

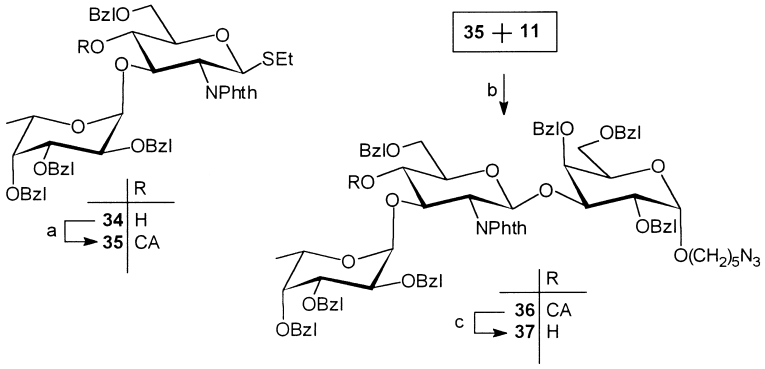
$(CH_2)_5NH_2$ (**2**), disaccharide **34**[23] was applied as a fucosylated glucosamine building block (Scheme 5). Chloroacetylation[24] of disaccharide **34** gave glycosyl donor **35** in 85% yield. Condensation of **35** with acceptor **11** in diethyl ether in the presence of methyl triflate as a promoter yielded trisaccharide **36** (65%). Surprisingly, the removal of the chloroacetyl group with thiourea failed. However, the chloroacetyl function of **36** could be removed by treatment with potassium carbonate in tetrahydrofuran/methanol 1:1 to furnish trisaccharide acceptor **37** in 90% yield. Attempted glycosylation of **37** by using galactosamine donor **20** with various promoters (methyl triflate, *N*-iodosuccinimide–silver triflate) failed. Condensation of **37** with the corresponding bromosugar and trichloroacetimidate galactosamine donors (both prepared from **20**) promoted by silver triflate and trimethylsilyl triflate, respectively, also failed (data not shown). The low reactivity of HO-4′ in **37** may be due to its sterically hindered position; this might explain both the unsuccessful removal of the chloroacetyl group of **36** with thiourea and results of attempted glycosylations under various conditions. To overcome this difficulty, the order of glycosylation reactions had to be changed. Condensation of bromosugar **38** (prepared from **20**, Scheme 1) with glucosamine derivative **14** in the presence of silver triflate afforded **39** (Scheme 6). Disaccharide **39** turned out to be a suitably protected key intermediate for both the preparation of tetrasaccharide **2** and pentasaccharide **3**. *O*-Deallylation of compound **39** using tris(triphenylphosphine)rhodium(I) chloride as catalyst gave disaccharide acceptor **40** in 71% yield. Attempted fucosylation of acceptor **40** with donor **26** in the presence of tetrabutylammonium bromide failed to give acceptable yields. However, condensation of disaccharide **40** with **26** in the presence of silver triflate resulted in trisaccharide **41** in a yield of 48% (Scheme 7). Coupling of thioglycoside **41** with acceptor **11** in diethyl ether in the presence of methyl triflate as a promoter yielded tetrasaccharide **42** (64%).



Scheme 6. a) AgOTf, 4 Å, DCM, toluene, −40 °C; b) $[Rh(Ph_3P)_3Cl]$, EtOH, HCl, acetone; c) AcCl, MeOH, DCM, 0 °C/RT.

For the preparation of pentasaccharide **3**, disaccharide **40** was *O*-deacetylated with acetyl chloride[25] in methanol/dichloromethane (3:1) to give disaccharide **43** (Scheme 6). Condensation of acceptor **43** with fucosyl donor **26** in the presence of silver triflate afforded tetrasaccharide **44** in a yield of 75% (Scheme 8). Finally, coupling of tetrasaccharide thioglycoside **44** with acceptor **11** afforded pentasaccharide **45** in 54% yield.

To furnish target compounds **1**, **2**, and **3**, the phthalimido functions of tetrasaccharides **33** and **42**, and pentasaccharide **45**, respectively, were removed by treatment with ethylenediamine in 1-butanol,[26] and the resulting products *N*-acetylated, then hydrogenolyzed in or-



Scheme 5. a) Chloroacetylchloride, DCM, pyridine, −40 °C/−20 °C; b) MeOTf, 4 Å, Et_2O, 0 °C; c) K_2CO_3, MeOH, THF.

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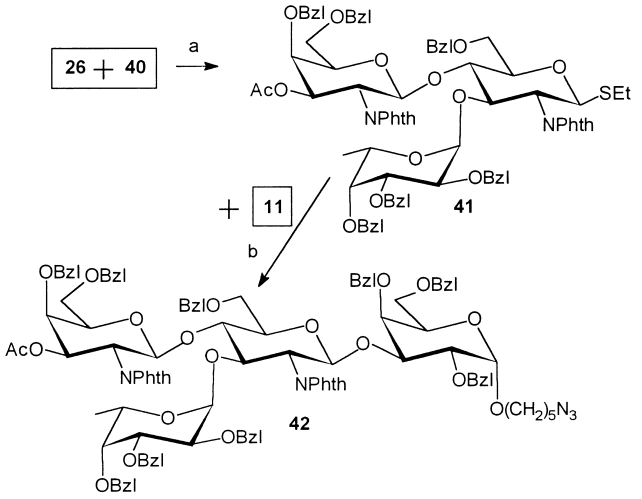
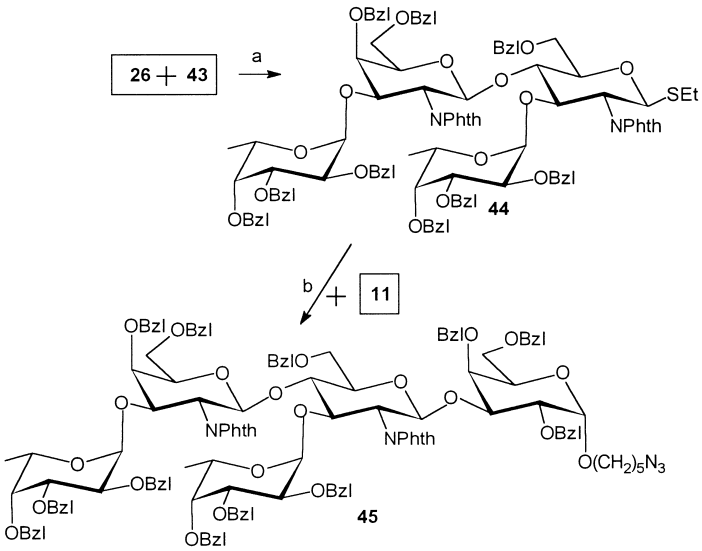


Scheme 7. a) AgOTf, 4 Å, DCM, *sym*-collidine, toluene, −30 °C; b) MeOTf, 4 Å, Et_2O, 0 °C.



Scheme 8. a) AgOTf, 4 Å, DCM, *sym*-collidine, toluene, −30 °C; b) MeOTf, 4 Å, Et_2O, 0 °C.

der to convert the azido function into an amino group and to remove the benzyl functions. The identity of the deprotected oligosaccharides was established by ^{1}H NMR spectroscopy. The synthesized compounds in protein-conjugated form are potential diagnostics in the search for antibodies raised against the glycan in the serum of infected humans. Results of interaction studies using surface plasmon resonance between panels of GCX-specific monoclonal antibodies and protein-conjugated **1**, **2**, and **3** will be published elsewhere.

Experimental Section

General methods: Optical rotations were measured at room temperature with a Perkin–Elmer 241 automatic polarimeter. Melting points were determined on a Kofler apparatus and are uncorrected. TLC was performed on Kieselgel 60 F_{254} (Merck) with detection by charring with 50% aqueous sulfuric acid. Column chromatography was performed on Silica gel 60 (Merck 63–200 mesh). ^{1}H (200, 300, and 500 MHz) and ^{13}C (50.3 and 125.76 MHz) NMR spectra were recorded with Bruker WP-200 SY (300 K), Bruker AM-300 (300 K), Bruker DRX-500, and Bruker AMX-500 spectrometers. Internal references: TMS ($\delta = 0.00$ for ^{1}H in $CDCl_3$), $CDCl_3$ ($\delta = 77.00$ for ^{13}C in $CDCl_3$), and acetone ($\delta = 2.225$ for ^{1}H in D_2O). Matrix-assisted laser desorption ionisation time-of-flight (MALDI-TOF) spectra were obtained on a Voyager-DE™ mass spectrometer. Samples were dissolved in doubly distilled water (2 mg mL^{-1}) and mixed on the sample plate with the matrix 2,4-dihydroxybenzoic acid (DHB) in doubly distilled water (10 mg mL^{-1}) in a ratio of 1:1.

Ethyl 2,6-di-*O*-benzyl-1-thio-*β*-D-galactopyranoside (5): A solution of **4**[10] (11.3 g, 25.4 mmol) in acetic acid/water 6:4 (200 mL) was kept for 1 h at 60 °C, and was then concentrated and co-concentrated with toluene (3 × 15 mL). Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 95:5) gave **5** (9.87 g, 96%), isolated as a syrup. $[\alpha]_D^{20} = -6.1$ ($c = 0.8$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.32$ (t, 3H; SCH_2CH_3), 2.18 and 2.34 (2 brs, 2H; 2OH, can be deuterated), 2.68–2.83 (m, 2H; SCH_2CH_3), 4.02 (dd, ^3J(H3,H4) = 3.3 Hz, ^3J(H4,H5) < 1 Hz, 1H; H4), 4.42 (d, ^3J(H1,H2) = 9.4 Hz, 1H; H1), 4.70 and 4.83 (2 ABq, each 2H; 2PhCH_2), 7.11–7.39 (m, 10H; aromatic); elemental analysis calcd (%) for $C_{22}H_{28}O_5S$ (404.16): C 65.32, H 6.98; found: C 65.36, H 6.97.

Ethyl 2,6-di-*O*-benzyl-*endo*-3,4-*O*-benzylidene-1-thio-*β*-D-galactopyranoside (6): *p*-Toluenesulfonic acid monohydrate (50 mg) was added to a stirred solution of **5** (1.00 g, 2.47 mmol) in *α*,*α*-dimethoxytoluene (8 mL). After 6 min, $NaHCO_3$ (100 mg) was added, and the mixture diluted with CH_2Cl_2 (200 mL). The organic layer was then washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 8:2) gave **6** (925 mg, 76%), isolated as a syrup. $[\alpha]_D^{20} = -18.4$ ($c = 1.3$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.29$ (t, 3H; SCH_2CH_3), 2.62–2.85 (m, 2H; SCH_2CH_3), 4.52 (d, ^3J(H1,H2) = 9.4 Hz, 1H; H1), 4.55–4.80 (m, 4H; 2PhCH_2), 5.91 (s, 1H; PhC*H*), 7.23–7.37 (m, 15H; aromatic); elemental analysis calcd (%) for $C_{29}H_{32}O_5S$ (492.10): C 70.70, H 6.55; found: C 70.65, H 6.58.

Ethyl 2,4,6-tri-*O*-benzyl-1-thio-*β*-D-galactopyranoside (7): A mixture of $LiAlH_4$ (250 mg) and $AlCl_3$ (250 mg) in Et_2O (6 mL) was added to a solution of **6** (750 mg, 1.52 mmol) in CH_2Cl_2 (6 mL). After 20 min, the excess of reagent was decomposed with EtOAc (5 mL), and $Al(OH)_3$ was precipitated with water. The organic layer was decanted, and the residue washed with EtOAc (2 × 50 mL). The combined organic solutions were washed with water (3 × 50 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 7:3) gave **7** (580 mg, 77%), isolated as a syrup. $[\alpha]_D^{20} = -2.2$ ($c = 0.7$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25$ (t, 3H; SCH_2CH_3), 2.19 (brs, 1H; OH, can be deuterated), 2.68–2.85 (m, 2H; SCH_2CH_3), 4.41 (d, ^3J(H1,H2) = 9.5 Hz, 1H; H1), 4.45–4.90 (m, 6H; 3 PhCH_2), 7.25–7.38 (m, 15H; aromatic); elemental analysis calcd (%) for $C_{29}H_{34}O_5S$ (494.21): C 70.42, H 6.93; found: C 70.37, H 6.90.

Ethyl 3-*O*-acetyl-2,4,6-tri-*O*-benzyl-1-thio-*β*-D-galactopyranoside (8): Compound **7** (450 mg, 0.91 mmol) was treated with pyridine/acetic anhydride 1:1 (20 mL) for 2 h. The mixture was concentrated, and toluene (3 × 15 mL) was evaporated from the residue. Purification of the residue by column chromatography (hexane/EtOAc 8:2) gave **8** (468 mg, 96%), isolated as a syrup. $[\alpha]_D^{20} = -28.4$ ($c = 0.7$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (t, 3H; SCH_2CH_3), 1.88 (s, 3H; OAc), 2.75–2.85 (m, 2H; SCH_2CH_3), 3.81 (dd, ^3J(H2,H3) = 9.8 Hz, 1H; H2), 4.01 (dd, ^3J(H4,H5) < 1 Hz, 1H; H4), 4.40–4.88 (m, 6H; 3 PhCH_2), 4.48 (d, ^3J(H1,H2) = 9.8 Hz, 1H; H1), 4.93 (dd, ^3J(H3,H4) = 3.1 Hz, 1H; H3), 7.20–7.40 (m, 15H; aromatic); elemental analysis calcd (%) for $C_{31}H_{36}O_6S$ (536.22): C 69.37, H 6.77; found: C 69.29, H 6.70.

5-Azidopentyl 2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (11): MeOTf (310 μL, 2.75 mmol) was added to a mixture of **8** (590 mg, 1.1 mmol), 5-azidopentanol[13] (213 mg, 1.65 mmol), and 4 Å molecular sieves in Et_2O (15 mL) at 0 °C. After stirring for 5 h, TLC (hexane/EtOAc 8:2) showed the formation of a new spot ($R_f = 0.23$). Et_3N was added, and the mixture diluted with CH_2Cl_2 (100 mL), washed with water, dried, filtered, and concentrated. Column chromatography of the residue gave an inseparable mixture of the 1,2-*cis*- (**9**) and 1,2-*trans*-glycosides (**10**) (590 mg, 89%) in approximately a 1:1 molar ratio (^{1}H NMR data). The mixture of **9** and **10** (560 mg, 0.93 mmol) was dissolved in MeOH/CH_2Cl_2 9:1 (15 mL), and NaOMe was added. After 1 h, the solution was neutralised with DOWEX-50 (H^+) resin, filtered, and concentrated. Purification of the residue by

column chromatography (CH_2Cl_2/EtOAc 97:3) gave a mixture of the α,β-anomers **11**/**11**$\boldsymbol{\beta}$ (308 mg, 59%) and pure **11** (179 mg, 32%). A solution of the mixture of **11** and **11**$\boldsymbol{\beta}$ (308 mg, 0.55 mmol) in CH_2Cl_2 (5 mL) containing molecular sieves (4 Å) was stirred for 30 min under Ar. Then, a solution of $TiCl_4$ (64 μL, 0.58 mmol) in CH_2Cl_2 (2 mL) was added, and after 10 min solid $NaHCO_3$ (50 mg) was also added. The mixture was diluted with CH_2Cl_2 (100 mL), washed with water (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 95:5) gave **11** (168 mg, 30%; total yield 62%), isolated as a syrup. $[\alpha]_D^{20} = +46.0$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.37-1.72$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 2.29 (br s, 1H; OH, can be deuterated), 3.21 (t, 2H; CH_2N_3), 3.81 (dd, ^3J(H2,H3) = 10.0 Hz, 1H; H2), 4.40–4.85 (m, 6H; 3 PhCH_2), 4.81 (d, ^3J(H1,H2) = 4.1 Hz, 1H; H1), 7.25–7.40 (m, 15H; aromatic); IR (KBr): $\tilde{\nu}_{max} = 2098\ cm^{-1}$ (N_3); elemental analysis calcd (%) for $C_{32}H_{39}N_3O_6$ (561.28): C 69.41, H 7.00; found: C 69.44, H 7.05.

For analytical purposes 15 mg of **11**$\boldsymbol{\beta}$ was also collected. $[\alpha]_D^{20} = +2.3$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.35-1.75$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 2.29 (br s, 1H; OH, can be deuterated), 3.20 (t, 2H; CH_2N_3), 4.33 (d, ^3J(H1,H2) = 7.1 Hz, 1H; H1), 4.48, 4.69, and 4.82 (3 ABq, each 2H; 3 PhCH_2), 7.20–7.40 (m, 15H; aromatic).

Ethyl 3-*O*-allyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (13): A solution of **12**[14] (3.74 g, 8.47 mmol) and allyl bromide (3.58 mL, 41.3 mmol) in THF (30 mL) was added dropwise to sodium hydride (634 mg, 26.41 mmol), and the mixture stirred overnight. When TLC (hexane/EtOAc 7:3) indicated the reaction was complete, the mixture was diluted with EtOAc, filtered through Celite, and washed with water (3 × 25 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography ($CH_2Cl_2 \rightarrow CH_2Cl_2$/EtOAc 97:3) gave crystalline **13** (3.26 g, 80%). M.p. 130–132 °C (from EtOH); $[\alpha]_D^{20} = +9.6$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.21$ (t, 3H; SCH_2CH_3), 2.62–2.78 (m, 2H; SCH_2CH_3), 4.38 (dd, ^3J(H2,H3) = 10.0 Hz, 1H; H2), 4.83–5.06 (m, 2H; H_2C=CHCH$_2$O), 5.41 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 5.45–5.65 (m, 1H; H$_2$C=CHCH$_2$O), 5.59 (s, 1H; PhCH), 7.35–7.85 (m, 9H; aromatic); elemental analysis calcd (%) for $C_{26}H_{27}NO_6S$ (481.16): C 64.84, H 5.66; found: C 64.87, H 5.61.

Ethyl 3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (14): A mixture of borane-trimethylamine complex (2.78 g, 38.1 mmol), powdered 4 Å molecular sieves (3 g), **13** (2.50 g, 5.20 mmol), and THF (50 mL) was stirred for 1 h at room temperature. Then, $AlCl_3$ (5.12 g, 38.4 mmol) was added, and the mixture stirred for 5 h in the dark, when TLC (CH_2Cl_2/EtOAc 95:5) showed the conversion of **13** into **14**. The mixture was diluted with CH_2Cl_2 (250 mL), filtered through Celite, washed with cold 0.5 M H_2SO_4, water, 5% aq $NaHCO_3$, and water, dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 95:5) gave **14** (2.13 g, 85%), isolated as a syrup. $[\alpha]_D^{20} = +5.5$ ($c = 1.2$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.19$ (t, 3H; SCH_2CH_3), 2.53–2.78 (m, 2H; SCH_2CH_3), 2.94 (br s, 1H; OH, can be deuterated), 4.27 (dd, ^3J(H2,H3) = 9.0 Hz, 1H; H2), 4.61 (ABq, 2H; PhCH_2), 4.85–5.10 (m, 2H; H_2C=CHCH$_2$O), 5.32 (d, ^3J(H1,H2) = 9.1 Hz, 1H; H1), 5.50–5.70 (m, 1H; H$_2$C=CHCH$_2$O), 7.26–7.91 (m, 9H; aromatic); elemental analysis calcd (%) for $C_{26}H_{29}NO_6S$ (483.17): C 64.57, H 6.05; found: C 64.61, H 6.08.

Ethyl 4-*O*-acetyl-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (15): Compound **14** (1.5 g, 3.1 mmol) was treated with pyridine/acetic anhydride 1:1 (10 mL), as described for **8**. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 98:2) gave **15** (1.55 g, 95%), isolated as a syrup. $[\alpha]_D^{20} = +61.4$ ($c = 0.7$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.25$ (t, 3H; SCH_2CH_3), 2.05 (s, 3H; OAc), 2.62–2.78 (m, 2H; SCH_2CH_3), 4.39 (dd, ^3J(H2,H3) = 9.0 Hz, 1H; H2), 4.58 (br s, 2H; PhCH_2), 4.82–5.15 (m, 2H; H_2C=CHCH$_2$O), 5.10 (dd, ^3J(H3,H4) = 8.7 Hz, ^3J(H4,H5) = 9.9 Hz, 1H; H4), 5.32 (d, ^3J(H1,H2) = 9.2 Hz, 1H; H1), 5.44–5.63 (m, 1H; H$_2$C=CHCH$_2$O), 7.28–7.81 (m, 9H; aromatic); elemental analysis calcd (%) for $C_{28}H_{31}NO_7S$ (525.18): C 63.98, H 5.95; found: C 63.94, H 5.89.

Ethyl 4-*O*-acetyl-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (16): A solution of trifluoromethanesulfonic anhydride (654 μL, 3.89 mmol) in CH_2Cl_2 (4 mL) was added to a solution of **14** (1.27 g, 2.63 mmol) in CH_2Cl_2 (10 mL) and pyridine (485 μL, 6.0 mmol) at 0 °C. After stirring for 2 h, TLC (CH_2Cl_2/EtOAc 95:5) showed the formation of a new spot. Then, tetrabutylammonium acetate (1.95 g, 6.48 mmol) and DMF (5 mL) were added at 0 °C. After 5 h, an additional amount of tetrabutylammonium acetate (1.95 g, 6.48 mmol) was added, and the reaction was stirred overnight at room temperature. Then, the mixture was diluted with EtOAc (200 mL), washed with 10% aq NaCl (3 × 30 mL), dried ($MgSO_4$), filtered, concentrated, and co-concentrated with toluene. Purification of the residue by column chromatography (hexane/EtOAc 7:3) afforded **16** (1.08 g, 78%), isolated as a syrup. $[\alpha]_D^{20} = +24.1$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.22$ (t, 3H; SCH_2CH_3), 2.14 (s, 3H; OAc), 2.60–2.79 (m, 2H; SCH_2CH_3), 4.39 (dd, ^3J(H3,H4) = 3.0 Hz, 1H; H3), 4.51 (dd, ^3J(H2,H3) = 10.0 Hz, 1H; H2), 4.55 (ABq, 2H; PhCH_2), 4.94–5.12 (m, 2H; H_2C=CHCH$_2$O), 5.34 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 5.45–5.61 (m, 1H; H$_2$C=CHCH$_2$O), 5.61 (dd, ^3J(H4,H5) < 1 Hz, 1H; H4), 7.29–7.48 and 7.73–7.91 (m, 9H; aromatic); elemental analysis calcd (%) for $C_{28}H_{31}NO_7S$ (525.18): C 63.98, H 5.94; found: C 63.96, H 5.92.

Ethyl 3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (17): Potassium carbonate (521 mg, 3.77 mmol) was added to a solution of **16** (990 mg, 1.88 mmol) in MeOH/THF 1:1 (10 mL). After stirring for 4 h, the mixture was diluted with CH_2Cl_2 (100 mL), washed with 10% aq NaCl (3 × 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 95:5) gave **17** (664 mg, 73%), isolated as a syrup. $[\alpha]_D^{20} = +26.5$ ($c = 0.4$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.19$ (t, 3H; SCH_2CH_3), 2.55–2.81 (m, 3H; SCH_2CH_3 and OH, the OH can be deuterated), 4.21 (dd, ^3J(H4,H5) < 1 Hz, 1H; H4), 4.32 (dd, ^3J(H3,H4) = 3.0 Hz, 1H; H3), 4.59 (dd, ^3J(H2,H3) = 10.0 Hz, 1H; H2), 4.95–5.14 (m, 2H; H_2C=CHCH$_2$O), 5.27 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 5.53–5.73 (m, 1H; H$_2$C=CHCH$_2$O), 7.26–7.95 (m, 9H; aromatic); elemental analysis calcd (%) for $C_{26}H_{29}NO_6S$ (483.17): C 64.57, H 6.05; found: C 64.61, H 6.01.

Ethyl 3-*O*-allyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (18): Ag_2O (786 mg, 3.39 mmol) and benzyl bromide (300 μL, 2.52 mmol) were added to a mixture of **17** (410 mg, 0.85 mmol), potassium iodide (307 mg, 1.85 mmol), and 4 Å molecular sieves in DMF (5 mL) at 0 °C. The mixture was stirred for 5 h, then diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with 10% aq $Na_2S_2O_3$ (3 × 25 mL) and water (2 × 25 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography ($CH_2Cl_2 \rightarrow CH_2Cl_2$/EtOAc 98:2) gave **18** (400 mg, 82%), isolated as a syrup. $[\alpha]_D^{20} = +29.8$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.17$ (t, 3H; SCH_2CH_3), 2.58–2.80 (m, 2H; SCH_2CH_3), 3.77–3.86 and 4.00–4.06 (m, 2H; H$_2$C=CHCH$_2$O), 4.04 (dd, ^3J(H4,H5) < 1 Hz, 1H; H4), 4.33 (dd, ^3J(H3,H4) = 2.6 Hz, 1H; H3), 4.47 (ABq, 2H; PhCH_2), 4.76 (ABq, 2H; PhCH_2), 4.79 (dd, ^3J(H2,H3) = 10.4 Hz, 1H; H2), 4.92–5.14 (m, 2H; H_2C=CHCH$_2$O), 5.26 (d, ^3J(H1,H2) = 10.4 Hz, 1H; H1), 5.55–5.68 (m, 1H; H$_2$C=CHCH$_2$O), 7.25–7.35 (m, 10H; 2 Ph), 7.60–7.85 (m, 4H; Phth); elemental analysis calcd (%) for $C_{33}H_{35}NO_6S$ (573.22): C 69.08, H 6.15; found: C 69.12, H 6.09.

Ethyl 4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (19): A solution of **18** (384 mg, 0.67 mmol) in EtOH (30 mL) containing tris(triphenylphosphine)rhodium(I) chloride (284 mg, 307 μmol) was boiled under reflux for 3 h, then cooled, and concentrated. A solution of the residue in acetone/1 M hydrochloric acid 9:1 (20 mL) was boiled for 1 h, when TLC (CH_2Cl_2/EtOAc 95:5) showed the complete conversion of the prop-1-enyl ether into **19** ($R_f = 0.46$). The mixture was concentrated, and purification of the residue by column chromatography (CH_2Cl_2/EtOAc 95:5) gave **19** (257 mg, 72%), isolated as a syrup. $[\alpha]_D^{20} = +20.2$ ($c = 0.8$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.22$ (t, 3H; SCH_2CH_3), 1.77 (br s, 1H; OH, can be deuterated), 2.57–2.77 (m, 2H; SCH_2CH_3), 4.03 (dd, ^3J(H3,H4) = 2.5 Hz, ^3J(H4,H5) < 1 Hz, 1H; H4), 5.31 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 7.19–7.38 and 7.58–7.80 (m, 14H; aromatic); elemental analysis calcd (%) for $C_{30}H_{31}NO_6S$ (533.19): C 67.52, H 5.86; found: C 67.47, H 5.91.

Ethyl 3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (20): Compound **19** (200 mg, 0.37 mmol) was treated with pyridine/acetic anhydride 1:1 (10 mL), as described for **8**, to give **20** (210 mg, 97%), isolated as a syrup. $[\alpha]_D^{20} = +25.4$ ($c = 0.4$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.18$ (t, 3H; SCH_2CH_3), 1.79 (s, 3H; OAc), 2.59–2.78 (m, 2H; SCH_2CH_3), 4.12 (dd, ^3J(H4,H5) < 1 Hz, 1H; H4), 4.48 (ABq, 2H; PhCH_2), 4.64 (ABq, 2H; PhCH_2), 4.81 (dd, ^3J(H2,H3) = 10.7 Hz, 1H; H2), 5.41 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 5.73 (dd,

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^3J(H3,H4) = 3.1 Hz, 1H; H3), 7.20–7.40 and 7.60–7.90 (m, 14H; aromatic); elemental analysis calcd (%) for $C_{32}H_{33}NO_7S$ (575.20): C 66.77, H 5.78; found: C 66.71, H 5.79.

5-Azidopentyl (4-*O*-acetyl-3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (21): A solution of **11** (320 mg, 0.57 mmol) and **15** (390 mg, 0.74 mmol) in Et_2O (15 mL) containing 4 Å molecular sieves was stirred for 30 min under Ar, then methyl triflate (500 μL, 4.44 mmol) was added at 0 °C. After stirring for 12 h, Et_3N was added, and the mixture diluted with CH_2Cl_2 (100 mL), washed with water, dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 97:3) gave **21** (456 mg, 78%), isolated as a glass. $[\alpha]_D^{20} = +7.1$ ($c = 2.5$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.27–1.59$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 1.99 (s, 3H; OAc), 3.14 (t, 2H; CH_2N_3), 4.78–5.15 (m, 2H; H_2C=CHCH$_2$O), 5.05 (dd, ^3J(H4′,H5′) = 10.5 Hz, 1H; H4′), 5.46 (d, ^3J(H1′,H2′) = 8.1 Hz, 1H; H1′), 5.45–5.67 (m, 1H; H_2C=C*H*CH$_2$O), 7.14–7.95 (m, 24H; aromatic); elemental analysis calcd (%) for $C_{58}H_{64}N_4O_{13}$ (1024.45): C 67.94, H 6.30; found: C 67.97, H 6.35.

5-Azidopentyl (3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (22): Compound **21** (500 mg, 0.49 mmol) was treated with potassium carbonate (140 mg, 1.01 mmol) in MeOH/THF 1:1 (8 mL), as described for **17**, to afford **22** (425 mg, 89%), isolated as a syrup. $[\alpha]_D^{20} = -10.9$ ($c = 0.9$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25–1.59$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 2.90 (br s, 1H; OH, can be deuterated), 3.14 (t, 2H; CH_2N_3), 4.81–5.12 (m, 2H; H_2C=CHCH$_2$O), 5.47 (d, ^3J(H1′,H2′) = 8.1 Hz, 1H; H1′), 5.52–5.78 (m, 1H; H_2C=C*H*CH$_2$O), 7.15–7.94 (m, 24H; aromatic); elemental analysis calcd (%) for $C_{56}H_{62}N_4O_{12}$ (982.44): C 68.40, H 6.36; found: C 68.37, H 6.34.

5-Azidopentyl (3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-(3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (23): A solution of **22** (580 mg, 0.59 mmol) and **20** (466 mg, 0.81 mmol) in Et_2O (20 mL) was stirred in the presence of 4 Å molecular sieves for 20 min under Ar, then methyl triflate (550 μL, 4.86 mmol) was added at 0 °C. After stirring for 12 h, pyridine (1 mL) was added, and the mixture was concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 96:4) gave **23** (724 mg, 82%), isolated as a syrup. $[\alpha]_D^{20} = -18.6$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25–1.59$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 1.77 (s, 3H; OAc), 3.06 (t, 2H; CH_2N_3), 4.56–5.05 (m, 2H; H_2C=CHCH$_2$O), 5.28 (d, ^3J(H1″,H2″) = 7.7 Hz, 1H; H1″), 5.47 (d, ^3J(H1′,H2′) = 8.1 Hz, 1H; H1′), 5.41–5.61 (m, 1H; H_2C=C*H*CH$_2$O), 5.67 (dd, ^3J(H2″,H3″) = 11.4 Hz, ^3J(H3″,H4″) = 3.1 Hz, 1H; H3″), 7.01–7.95 (m, 38H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 20.56$ (CO*C*H$_3$), 23.24, 28.47, and 28.74 ($OCH_2(CH_2)_3CH_2N_3$), 51.17 (CH_2N_3), 52.57 and 56.49 (C2′, C2″), 97.39, 97.14, and 99.66 (C1, C1′, C1″), 115.84 (H_2C=), 135.00 (−CH=), 167.52, 168.48, and 169.96 (C=O); elemental analysis calcd (%) for $C_{86}H_{89}N_5O_{19}$ (1495.62): C 69.00, H 6.00; found: C 69.08, H 5.97.

Ethyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-*β*-D-galactopyranoside (28): Bromine (40 μL, 0.79 mmol) was added to a solution of **25** (250 mg, 0.52 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound, a few drops of cyclohexene followed by 4 Å molecular sieves were added. After stirring the mixture for 30 min under Ar, a solution of **19** (140 mg, 0.26 mmol) in DMF (3 mL) and tetrabutylammonium bromide (250 mg, 0.79 mmol) were added. The reaction mixture was stirred for 3 d, diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with 5% aq $NaHCO_3$ (3 × 20 mL) and water (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 8:2→7:3) afforded **28** (87 mg, 35%), isolated as a syrup. $[\alpha]_D^{20} = +22.5$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 0.86$ (d, 3H; CMe), 1.22 (t, 3H; SCH$_2$C*H*$_3$), 2.55–2.85 (m, 2H; SC*H*$_2$CH$_3$), 4.66 (d, ^3J(H1′,H2′) = 3.1 Hz, 1H; H1′), 4.85 (dd, ^3J(H2,H3) = 10.5 Hz, 1H; H2), 5.50 (d, ^3J(H1,H2) = 10.5 Hz, 1H; H1), 7.13–7.85 (m, 29H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 14.96$ (C*Me*), 16.33 (SCH$_2$CH$_3$), 23.72 (SCH$_2$CH$_3$), 51.27 (C2), 67.77 (C5′), 72.81, 72.99, 73.41, 74.17, and 74.59 (OCH$_2$Ph), 80.99 (C1), 99.46 (C1′), 168.76 (C=O); elemental analysis calcd (%) for $C_{57}H_{59}NO_{10}S$ (949.39): C 72.05, H 6.26; found: C 72.02, H 6.29.

5-Azidopentyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-(4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-(3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (27)

Procedure A: Compound **23** (120 mg, 79 μmol) was treated with potassium carbonate (11 mg, 79 μmol) in MeOH/THF 1:1 (6 mL), as described for **17**, to afford **24** (100 mg, 85%; $[\alpha]_D^{20} = -13.2$ ($c = 0.61$ in $CHCl_3$)). Bromine (10 μL, 0.19 mmol) was added to a solution of **25** (60 mg, 125 μmol) in dry CH_2Cl_2 (3 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound, the mixture was concentrated and co-concentrated with dry CH_2Cl_2 (2 × 3 mL). A solution of the residue (**26**) in dry CH_2Cl_2 (2 mL) was added to a stirred mixture of **24** (88 mg, 59 μmol), tetrabutylammonium bromide (60 mg, 188 μmol), and 4 Å molecular sieves in DMF (2 mL). After stirring for 24 h, the mixture was diluted with CH_2Cl_2 (50 mL), filtered through Celite, washed with water (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 7:3) gave **27** (47 mg, 42%), isolated as a syrup.

Procedure B: A mixture of **24** (70 mg, 47 μmol), **25** (60 mg, 124 μmol), $CuBr_2$ (63 mg, 284 μmol), tetrabutylammonium bromide (68 mg, 213 μmol), and 4 Å molecular sieves was stirred in CH_2Cl_2/DMF 3:1 (4 mL) for 24 h under Ar. Then, the mixture was diluted with CH_2Cl_2 (50 mL), filtered through Celite, washed with water (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 7:3) gave **27** (29 mg, 32%), isolated as a syrup.

Procedure C: A solution of **22** (44 mg, 44 μmol) and **28** (62 mg, 65 μmol) in Et_2O (2 mL) containing 4 Å molecular sieves was stirred for 30 min under Ar, then methyl triflate (44 μL, 0.39 mmol) was added at 0 °C. After 12 h, pyridine (0.2 mL) was injected and the mixture filtered through Celite, concentrated, and co-concentrated with toluene. Purification of the residue by gel filtration over LH-20 (CH_2Cl_2/MeOH 1:1), followed by column chromatography (hexane/EtOAc 7:3) yielded **27** (50 mg, 65%), isolated as a syrup. $[\alpha]_D^{20} = -6.6$ ($c = 0.1$ in $CHCl_3$). For ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; elemental analysis calcd (%) for $C_{111}H_{115}N_5O_{22}$ (1869.80): C 71.24, H 6.20; found: C 71.20, H 6.21.

5-Azidopentyl (4-*O*-acetyl-3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (30): A mixture of AgOTf (20 mg, 80 μmol) and *N*-iodosuccinimide (180 mg, 798 μmol) in acetonitrile (2 mL) was added to a solution of **11** (100 mg, 177 μmol) and **29**[21] (153 mg, 266 μmol) in dry CH_2Cl_2 (3 mL) containing 4 Å molecular sieves at −15 °C. When TLC showed the disappearance of **11** and the formation of a new spot ($R_f = 0.45$ hexane/EtOAc 6:4), pyridine (0.1 mL) was added. The mixture was diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with 10% aq $Na_2S_2O_3$ (3 × 20 mL), 10% aq $NaHCO_3$ (3 × 20 mL), and water (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/CH_2Cl_2/EtOAc 6:3:1) gave **30** (160 mg, 83%), isolated as a glass. $[\alpha]_D^{20} = +16.5$ ($c = 0.6$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25–1.54$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 1.94 (s, 3H; OAc), 3.14 (t, 2H; CH_2N_3), 5.16 (dd, ^3J(H3′,H4′) = 9.1 Hz, 1H; H4′), 5.42 (d, ^3J(H1′,H2′) = 8.2 Hz, 1H; H1′), 6.87–7.74 (m, 29H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 20.91$ (CO*C*H$_3$), 23.24, 28.47, and 28.74 ($OCH_2(CH_2)_3CH_2N_3$), 51.21 (CH_2N_3), 56.14 (C2′), 97.38 (C1), 99.67 (C1′), 169.77 (C=O); elemental analysis calcd (%) for $C_{62}H_{66}N_4O_{13}$ (1074.46): C 69.24, H 6.19; found: C 69.20, H 6.22.

5-Azidopentyl (3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (31): Compound **30** (140 mg, 0.13 mmol) was treated with potassium carbonate (36 mg, 0.26 mmol) in MeOH/THF 1:1 (4 mL) as described for **17**, to afford **31** (110 mg, 81%), isolated as a syrup. $[\alpha]_D^{20} = -5.1$ ($c = 0.2$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.25–1.57$ (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 3.07–3.17 (m, 3H; CH_2N_3 and OH, can be deuterated), 5.44 (d, ^3J(H1′,H2′) = 8.1 Hz, 1H; H1′), 6.95–7.77 (m, 29H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta = 23.24$, 28.47, and 28.74 ($OCH_2(CH_2)_3CH_2N_3$), 51.17 (CH_2N_3), 55.91 (C2′), 67.57 (O*C*H$_2$(CH$_2$)$_4$N$_3$), 72.91, 73.24, 73.56, 74.33, and 74.71 (O*C*H$_2$Ph), 97.30 (C1), 99.57 (C1′), 167.57 and 167.79 (C=O); elemental analysis calcd (%) for $C_{60}H_{64}N_4O_{12}$ (1032.45): C 69.75, H 6.24; found: C 69.68, H 6.28.

Table 1. 500 MHz ^{1}H NMR data (300 K) of the oligosaccharides **27**, **33**, **36**, **42**, and **45**. For the assignments, two-dimensional COSY, HSQC, TOCSY, HMBC, and ROESY experiments were applied.

	GalNPhth	GlcNPhth	Gal	Fuc (GalNPhth)	Fuc (GlcNPhth)
27					
H1 (*J*(H1,H2) [Hz])	5.58 (8.4)	5.33 (8.1)	4.37 (~5.0)	4.66 (3.6)	
H2	4.72	4.28	3.62	3.75	
H3	4.40	4.36	3.95	3.57	
H4	3.96	4.12	3.94	3.41	
H5	3.72	3.50	3.81	3.93	
H6	3.61, 3.61	3.57, 3.55	3.42, 3.32	0.89	
33					
H1 (*J*(H1,H2) [Hz])	5.58 (8.4)	5.31 (8.1)	4.36 (3.6)	4.66 (3.6)	
H2	4.82	4.29	3.59	3.75	
H3	4.43	4.43	3.93	3.58	
H4	3.94	4.25	3.94	3.41	
H5	n.d.[a]	3.50	3.79	3.90	
H6	3.61, 3.59	3.55, 3.47	3.41, 3.33	0.86	
36					
H1 (*J*(H1,H2) [Hz])		5.70 (8.4)	4.46 (5.3)		4.52 (3.3)
H2		4.44	3.74		3.61
H3		4.56	4.15		3.73
H4		5.14	4.06		3.44
H5		3.85	3.93		3.92
H6		3.64, 3.64	3.48, 3.42		0.99
42					
H1 (*J*(H1,H2) [Hz])	5.52 (8.5)	5.23 (8.7)	4.32 (3.5)		4.79 (2.9)
H2	4.69	4.56	3.58		3.70
H3	5.78	4.27	3.88		3.30
H4	4.13	n.d.[a]	3.95		n.d.[a]
H5	3.70	3.43	3.77		3.66
H6	3.68, 3.76	3.08, 3.40	3.28, 3.46		1.36
45					
H1 (*J*(H1,H2) [Hz])	5.58 (8.4)	5.24 (7.9)	4.32 (4.2)	4.67 (3.2)	4.80 (3.7)
H2	4.72	4.55	3.58	3.78	3.69
H3	4.42	4.27	3.92	3.58	3.31
H4	n.d.[a]	4.38	n.d.[a]	3.42	n.d.[a]
H5	3.62	n.d.[a]	3.79	3.94	3.70
H6	n.d.[a]	3.09, 3.40	3.29, 3.41	0.69	1.38

[a] n.d.: not determined.

5-Azidopentyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-(4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-(3,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (33): Bromine (8 μL, 0.15 mmol) was added to a solution of **28** (114 mg, 120 μmol) in dry CH_2Cl_2 (4 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound and the formation of a new spot (**32**), the mixture was concentrated and co-concentrated with dry CH_2Cl_2 (2 × 3 mL). A solution of the residue (**32**) in dry CH_2Cl_2 (2 mL) was added to a stirred mixture of **31** (77 mg, 75 μmol) and 4 Å molecular sieves in dry CH_2Cl_2 (2 mL). The mixture was stirred for 30 min under Ar, and then a solution of AgOTf (54 mg, 215 μmol) in toluene (2 mL) was added at −50 °C. After 1 h, pyridine (0.1 mL) was added and the mixture diluted with CH_2Cl_2 (50 mL), filtered through Celite, washed with 10% aq $Na_2S_2O_3$ (3 × 10 mL), 5% aq $NaHCO_3$ (3 × 10 mL), and water (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/CH_2Cl_2/EtOAc 6:3:1) gave **33** (113 mg, 84%), isolated as a glass. $[\alpha]_D^{20} = +7.6$ (c = 0.3 in $CHCl_3$). For ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; elemental analysis calcd (%) for $C_{115}H_{117}N_5O_{22}$ (1919.82): C 71.88, H 6.14; found: C 71.92, H 6.11.

Ethyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-6-*O*-benzyl-4-*O*-chloroacetyl-2-deoxy-2-phthalimido-1-thio-*β*-D-glucopyranoside (35): Chloroacetylchloride (50 μL, 0.63 mmol) in CH_2Cl_2 (1 mL) was added to a solution of **34**[23] (270 mg, 314 μmol) and pyridine (0.25 mL) in CH_2Cl_2 (2.5 mL) at −40 °C, and the mixture was kept for 24 h at −20 °C. Then, the mixture was diluted with CH_2Cl_2 (50 mL), washed with 5% aq $NaHCO_3$ (3 × 10 mL) and water (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2 → CH_2Cl_2/EtOAc 98:2) gave **35** (250 mg, 85%), isolated as a pale yellow syrup. $[\alpha]_D^{20} = +38.0$ (c = 0.3 in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.95 (d, 3H; CMe), 1.24 (t, 3H; SCH_2CH_3), 2.61–2.81 (m, 2H; SCH_2CH_3), 4.51 (d, ^3J(H1′,H2′) = 2.0 Hz, 1H; H1′), 5.08 (dd, ^3J(H3,H4) = ^3J(H4,H5) = 9.7 Hz, 1H; H4), 5.51 (d, ^3J(H1,H2) = 10.0 Hz, 1H; H1), 6.99–7.85 (m, 24H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): δ = 14.98 (SCH_2CH_3), 16.04 (C*Me*), 24.03 (SCH_2CH_3), 41.18 ($ClCH_2$–), 54.17 (C2), 68.37 (C5′), 69.85 (C6), 72.55, 73.12, 73.47, and 73.68 (OCH_2Ph), 80.97 (C1), 101.96 (C1′), 166.71, 167.80, and 168.69 (C=O); elemental analysis calcd (%) for $C_{52}H_{54}ClNO_{11}S$ (935.31): C 66.72, H 5.82; found: C 66.75, H 5.78.

5-Azidopentyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-(6-*O*-benzyl-4-*O*-chloroacetyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (36): Methyl triflate (180 μL, 1.6 mmol) was added to a mixture of **11** (100 mg, 177 μmol), **35** (236 mg, 248 μmol) and 4 Å molecular sieves in Et_2O (7 mL) at 0 °C. After stirring for 24 h, Et_3N (0.2 mL) was added, and the mixture diluted with CH_2Cl_2 (50 mL), washed with 5% aq $NaHCO_3$ (2 × 10 mL) and water (2 × 10 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2 → CH_2Cl_2/EtOAc 98:2) gave **36** (166 mg, 65%), isolated as a syrup. $[\alpha]_D^{20} = +27.5$ (c = 0.3 in $CHCl_3$). For ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; elemental analysis calcd (%) for $C_{82}H_{87}ClN_4O_{17}$ (1434.58): C 68.59, H 6.11; found: C 68.62, H 6.13.

5-Azidopentyl (2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)-(6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (37): Potassium carbonate (20 mg, 146 μmol) was added to a solution of **36** (140 mg, 97 μmol) in MeOH/THF 1:1 (4 mL), and the mixture stirred for 2 h. The mixture was then diluted with CH_2Cl_2 (50 mL), washed with water (3 × 10 mL), and the combined washings were

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Table 2. 125.76 MHz ^{13}C NMR data (300 K) of the oligosaccharides **27**, **33**, **36**, **42**, and **45**. For the assignments, HSQC and HMBC experiments were applied.

	GalNPhth	GlcNPhth	Gal	Fuc (GalNPhth)	Fuc (GlcNPhth)
27					
C1	97.68	100.13	97.80	99.88	
C2	53.83	56.90	76.23	75.45	
C3	78.28	77.71	78.91	80.00	
C4	74.51	76.32	77.79	78.18	
C5	73.39	74.64	69.63	68.00	
C6	68.44	68.86	69.95	16.77	
33					
C1	97.51	100.06	97.70	99.92	
C2	53.86	56.90	76.18	75.48	
C3	78.09	77.39	79.05	80.12	
C4	74.66	76.45	77.80	78.15	
C5	73.39	74.70	69.64	68.06	
C6	68.90	68.35	69.94	16.73	
36					
C1		99.90	97.84		102.29
C2		56.19	76.11		75.16
C3		79.16	79.47		79.90
C4		74.93	77.75		78.94
C5		72.59	68.65		69.55
C6		70.21	69.79		16.36
42					
C1	97.28	100.01	97.74		97.20
C2	52.87	57.79	76.66		74.50
C3	71.54	73.69	78.57		79.01
C4	74.39	n.d.[a]	77.54		n.d.[a]
C5	74.43	74.70	69.65		68.77
C6	67.69	67.98	70.06		16.98
45					
C1	97.70	100.01	97.80	99.88	97.00
C2	53.91	57.90	76.61	75.54	74.80
C3	72.31	73.12	78.80	80.05	79.24
C4	n.d.[a]	73.45	n.d.[a]	78.35	n.d.[a]
C5	73.39	n.d.[a]	69.70	68.42	68.82
C6	n.d.[a]	68.05	70.10	16.62	17.45

[a] n.d.: not determined.

extracted with CH_2Cl_2 (3×10 mL). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/CH_2Cl_2/EtOAc 6:3:1) gave **37** (120 mg, 90%), isolated as a syrup. $[\alpha]_D^{20}=+4.9$ ($c=0.6$ in $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): $\delta=1.06$ (d, 3H; CMe), 1.35–1.62 (m, 6H; $OCH_2(CH_2)_3CH_2N_3$), 3.21 (brs, 1H; OH, can be deuterated), 3.13 (t, 2H; CH_2N_3), 4.52 (d, ^3J(H1″,H2″) = 2.7 Hz, 1H; H1″), 5.59 (d, ^3J(H1′,H2′) = 7.8 Hz, 1H; H1′), 6.93–7.82 (m, 39H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=16.41$ (C*Me*), 23.30, 28.53, and 28.80 ($OCH_2(CH_2)_3CH_2N_3$), 51.64 (CH_2N_3), 60.36 (C2′), 67.71 ($OCH_2(CH_2)_4N_3$), 97.56 (C1), 99.82 (C1′), 100.79 (C1″), 168.08 and 168.36 (C=O); elemental analysis calcd (%) for $C_{80}H_{86}N_4O_{16}$ (1358.60): C 70.66, H 6.38; found: C 70.62, H 6.41.

Ethyl (3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-(3-*O*-allyl-6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-*β*-D-glucopyranoside (39): Bromine (55 μL, 1.0 mmol) was added to a solution of **20** (470 mg, 0.82 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound and the formation of a new spot (**38**), the mixture was concentrated and co-concentrated with dry CH_2Cl_2 (2×5 mL). A solution of **14** (352 mg, 0.73 mmol) in CH_2Cl_2 (4 mL) and 4 Å molecular sieves were added to the residue (**38**). After stirring the mixture for 20 min under Ar, a solution of AgOTf (320 mg, 1.25 mmol) in toluene (7 mL) was added at −40 °C. After 1.5 h, pyridine (0.5 mL) was added, and the mixture diluted with CH_2Cl_2 (200 mL), filtered through Celite, washed with 10% aq $Na_2S_2O_3$ (3×50 mL), 5% aq $NaHCO_3$ (3×50 mL), and water (2×50 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 98:2→96:4) gave **39** (330 mg, 45%), isolated as a syrup. $[\alpha]_D^{20}=+10.9$ ($c=1.8$ in $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): $\delta=1.11$ (t, 3H; SCH_2CH_3), 1.77 (s, 3H; OAc), 2.47–2.66 (m, 2H; SCH_2CH_3), 4.85–5.19 (m, 2H; H_2C=$CHCH_2O$), 5.12 (d, ^3J(H1,H2) = 10.5 Hz, 1H; H1), 5.49 (d, ^3J(H1′,H2′) = 8.3 Hz, 1H; H1′), 5.38–5.58 (m, 1H; H_2C=$CHCH_2O$), 5.65 (dd, ^3J(H2′,H3′) = 11.5 Hz, ^3J(H3′,H4′) = 3.0 Hz, 1H; H3′), 7.19–7.89 (m, 23H; aromatic); ^{13}C NMR (50.3 MHz, $CDCl_3$): $\delta=14.90$ (SCH_2CH_3), 20.62 ($COCH_3$), 23.66 (SCH_2CH_3), 52.61 and 54.94 (C2, C2′), 80.91 (C1), 97.26 (C1′), 116.11 (H_2C=), 134.04 (−CH=), 167.63, 168.47, and 170.02 (C=O); elemental analysis calcd (%) for $C_{56}H_{56}N_2O_{13}S$ (996.35): C 67.45, H 5.66; found: C 67.51, H 5.64.

Ethyl (3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-(6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-*β*-D-glucopyranoside (40): A solution of **39** (610 mg, 0.61 mmol) and tris(triphenylphosphine)rhodium(I) chloride (276 mg, 299 μmol) in EtOH (40 mL) was boiled under reflux for 5 h, then cooled and concentrated. A solution of the residue in acetone/1M hydrochloric acid 9:1 (20 mL) was boiled for 30 min, when TLC (CH_2Cl_2/EtOAc 98:2) showed a complete conversion of the prop-1-enyl ether into **40** ($R_f=0.43$). Then, the mixture was concentrated, and a solution of the residue in CH_2Cl_2 (100 mL) was washed with 10% aq NaCl (3×20 mL) and water (2×20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (CH_2Cl_2/EtOAc 98:2) gave **40** (415 mg, 71%), isolated as a syrup. $[\alpha]_D^{20}=+24.3$ ($c=0.6$ in $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$): $\delta=1.13$ (t, 3H; SCH_2CH_3), 1.58 (brs, 1H; OH, can be deuterated), 1.81 (s, 3H; OAc), 2.51–2.65 (m, 2H; SCH_2CH_3), 5.20 (d, ^3J(H1,H2) = 10.5 Hz, 1H; H1), 5.45 (d, ^3J(H1′,H2′) = 8.4 Hz, 1H; H1′), 5.68 (dd, ^3J(H2′,H3′) = 11.5 Hz, ^3J(H3′,H4′) = 3.0 Hz, 1H; H3′), 7.00–7.88 (m, 23H; aromatic); elemental analysis calcd (%) for $C_{53}H_{52}N_2O_{13}S$ (956.32): C 66.51, H 5.48; found: C 66.61, H 5.50.

Ethyl (3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)]-(6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-*β*-D-glucopyranoside (41): Bromine (46 μL, 0.89 mmol) was added to a solution of **25** (610 mg, 1.27 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound, the mixture was concentrated and co-concentrated with dry CH_2Cl_2 (2×5 mL). Then, a solution of **40** (344 mg, 0.36 mmol) and *sym*-collidine (300 μL) in dry CH_2Cl_2 (10 mL) and 4 Å molecular sieves were added to the residue. The mixture was stirred for 30 min under Ar, then AgOTf (514 mg, 2.0 mmol) in toluene (10 mL) was added at −30 °C. After 2 h, pyridine (0.5 mL) was added, and the mixture diluted with CH_2Cl_2 (200 mL), filtered through Celite, washed with 10% aq $Na_2S_2O_3$ (3×20 mL), 5% aq $NaHCO_3$ (3×20 mL), and water (2×20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/CH_2Cl_2/EtOAc 4:2:1) gave **41** (237 mg, 48%), isolated as a glass. $[\alpha]_D^{20}=-44.5$ ($c=0.2$ in $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$, 300 K) (for the assignments, two-dimensional COSY and HSQC experiments were applied): $\delta=1.09$ (t, 3H; SCH_2CH_3), 1.32 (d, 3H; CMe), 1.84 (s, 3H; OAc), 2.50–2.64 (m, 2H; SCH_2CH_3), 5.01 (d, ^3J(H1,H2) = 10.5 Hz, 1H; H1), 5.47 (d, ^3J(H1′,H2′) = 8.5 Hz, 1H; H1′), 5.72 (dd, ^3J(H2′,H3′) = 11.5 Hz, ^3J(H3′,H4′) = 3.0 Hz, 1H; H3′), 7.00–7.91 (m, 38H; aromatic); ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta=14.75$ (SCH_2CH_3), 16.56 (C*Me*), 20.59 ($COCH_3$), 29.65 (SCH_2CH_3), 52.37 and 55.56 (C2, C2′), 80.86 (C1), 96.84 and 96.99 (C1′, C1″), 167.41, 168.61, and 169.91 (C=O); elemental analysis calcd (%) for $C_{80}H_{80}N_2O_{17}S$ (1372.52): C 69.94, H 5.87; found: C 69.90, H 5.89.

5-Azidopentyl (3-*O*-acetyl-4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-*α*-L-fucopyranosyl)-(1→3)]-(6-*O*-benzyl-2-deoxy-2-phthalimido-*β*-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-*α*-D-galactopyranoside (42): A solution of **11** (22 mg, 40 μmol) and **41** (55 mg, 39 μmol) in dry Et_2O (2 mL) containing 4 Å molecular sieves was stirred for 30 min under Ar, then methyl triflate (45 μL, 0.4 mmol) was added at 0 °C. After 20 h, pyridine was injected, and the mixture diluted with CH_2Cl_2 (50 mL), washed with water (2×10 mL), dried ($MgSO_4$), filtered, and concentrated. Gel filtration of the residue over LH-20 (CH_2Cl_2/MeOH 1:1), followed by purification by silica column chromatography (hexane/EtOAc 7:3) afforded **42** (46 mg, 64%), isolated as a syrup. $[\alpha]_D^{20}=-35.5$ ($c=2.1$ in $CHCl_3$). For ^1H and ^{13}C NMR data, see Tables 1 and 2, respectively; elemental analysis calcd (%) for $C_{110}H_{113}N_5O_{23}$ (1871.78): C 70.52, H 6.08; found: C 70.49, H 6.12.

Ethyl (4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-(1→4)-(6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (43): Acetyl chloride (300 μL) was added to a solution of **40** (287 mg, 100 μmol) in MeOH/CH_2Cl_2 3:1 (15 mL) at 0 °C, and the mixture stirred for 3 d at room temperature, then concentrated. Purification of the residue by column chromatography (hexane/EtOAc 6:4) gave **43** (184 mg, 67 %), isolated as a syrup. $[\alpha]_D^{20} = +11.9$ ($c = 0.3$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.13$ (t, 3H; SCH_2CH_3), 1.43 and 2.03 (2 br s, 2H; 2 OH, can be deuterated), 2.50–2.70 (m, 2H; SCH_2CH_3), 5.20 (d, ^3J(H1,H2) = 10.5 Hz, 1H; H1), 5.33 (d, ^3J(H1′,H2′) = 8.0 Hz, 1H; H1′), 7.22–7.41 and 7.65–7.90 (m, 23H; aromatic); elemental analysis calcd (%) for $C_{51}H_{50}N_2O_{12}S$ (914.31): C 66.94, H 5.51; found: C 66.88, H 5.53.

Ethyl (2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-(4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)]-(6-*O*-benzyl-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (44): Bromine (110 μL, 2.0 mmol) was added to a solution of **25** (747 mg, 1.56 mmol) in dry CH_2Cl_2 (10 mL) at 0 °C. After 20 min, when TLC showed the disappearance of the starting compound, the mixture was concentrated and co-concentrated with dry CH_2Cl_2 (2 × 5 mL). Then, a solution of **43** (155 mg, 170 μmol) and *sym*-collidine (316 μL) in CH_2Cl_2 (10 mL) and 4 Å molecular sieves were added to the residue. The mixture was stirred for 30 min under Ar, then a solution of AgOTf (616 mg, 2.4 mmol) in toluene (10 mL) was added at −30 °C. After 2 h, pyridine (0.5 mL) was added, and the mixture diluted with CH_2Cl_2 (100 mL), filtered through Celite, washed with 10 % aq $Na_2S_2O_3$ (3 × 20 mL), 5 % aq $NaHCO_3$ (3 × 20 mL), and water (2 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. Purification of the residue by column chromatography (hexane/EtOAc 7:3) yielded **44** (224 mg, 75 %), isolated as a glass. $[\alpha]_D^{20} = -20.5$ ($c = 1.1$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$, 300 K) (for the assignments two-dimensional COSY and HSQC experiments were applied): $\delta = 0.72$ (d, 3H; CMe), 1.15 (t, 3H; SCH_2CH_3), 1.40 (d, 3H; CMe), 2.55–2.75 (m, 2H; SCH_2CH_3), 4.63 (d, ^3J(H1″,H2″) = 3.6 Hz, 1H; H1″), 4.79 (d, ^3J(H1‴,H2‴) = 3.6 Hz, 1H; H1‴), 5.07 (d, ^3J(H1,H2) = 8.1 Hz, 1H; H1), 5.58 (d, ^3J(H1′,H2′) = 8.5 Hz, 1H; H1′), 7.08–7.90 (m, 53H; aromatic); ^{13}C NMR (125.76 MHz, $CDCl_3$): $\delta = 16.49$ (C*Me*), 17.17 (C*Me*), 53.53 and 56.13 (C2, C2″), 81.35 (C1), 97.20 (C1‴), 97.30 (C1′), 99.61 (C1″); elemental analysis calcd (%) for $C_{105}H_{106}N_2O_{20}S$ (1746.71): C 72.14, H 6.12; found: C 72.21, H 6.15.

5-Azidopentyl (2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-(4,6-di-*O*-benzyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl)-(1→4)-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)]-(6-*O*-benzyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-α-D-galactopyranoside (45): A solution of **11** (19 mg, 34 μmol) and **44** (51 mg, 29 μmol) in Et_2O (2 mL), containing 4 Å molecular sieves was stirred for 30 min under Ar, then methyl triflate (24 μL, 214 μmol) was added at 0 °C. After 20 h, pyridine (0.2 mL) was injected, and the mixture filtered through Celite, concentrated and co-concentrated with toluene. Gel filtration of the residue over LH-20 (CH_2Cl_2/MeOH 1:1), followed by purification by silica column chromatography (hexane/EtOAc 8:2) afforded **45** (41 mg, 54 %), isolated as a syrup. $[\alpha]_D^{20} = -22.8$ ($c = 1.2$ in $CHCl_3$); for ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; elemental analysis calcd (%) for $C_{135}H_{139}N_5O_{26}$ (2245.97): C 72.13, H 6.24; found: C 72.21, H 6.20.

5-Aminopentyl (α-L-fucopyranosyl)-(1→3)-(2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1→4)-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-α-D-galactopyranoside (1): Ethylenediamine (1 mL) was added to a solution of **33** (18.7 mg, 9.8 μmol) in 1-butanol (1 mL). The mixture was stirred overnight under Ar at 90 °C, then co-concentrated with toluene and dried under high vacuum. The residue was dissolved in MeOH (1 mL), and Ac_2O (1 mL) added at 0 °C. The mixture was kept for 1 h at 0 °C, then concentrated and co-concentrated with toluene. A solution of the residue in 1-butanol (1.6 mL) and water (0.6 mL), containing 10 % Pd–C (10 mg) and a few drops of 25 % aq NH_3 (pH 9), was hydrogenated for 1 h. By flushing with Ar for 1 h, the pH of the solution decreased to 7, then HOAc was added (pH 5), and the mixture hydrogenated for another two days. After filtration and concentration, the crude product was purified by HiTrap gel filtration (aq 5 mM NH_4HCO_3) to give **1** (5.3 mg, 61 %). $[\alpha]_D^{20} = -1.6$ ($c = 1$ in water); for ^{1}H NMR data, see Table 3; MS (MALDI-TOF): *m*/*z* calcd for $C_{33}H_{59}N_3O_{20}$ (817.37); found: 840.36 $[M+Na]^+$.

5-Aminopentyl (2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1→4)-[(α-L-fucopyranosyl)-(1→3)]-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-α-D-galactopyranoside (2): Compound **42** (18.2 mg, 9.6 μmol) was converted into **2**, as described for **1**, to afford **2** (5.1 mg, 57 %). $[\alpha]_D^{20} = -2.1$ ($c = 0.7$ in water); for ^{1}H NMR data, see Table 3; MS (MALDI-TOF): *m*/*z* calcd for $C_{33}H_{59}N_3O_{20}$ (817.37); found: 840.32 $[M+Na]^+$.

Table 3. 500 MHz ^{1}H NMR data of the oligosaccharides **1** (295 K), **2** (280 K), and **3** (300 K). For the assignments, two-dimensional TOCSY experiments with short and long mixing times were applied.

	GalNAc	GlcNAc	Gal	Fuc (GalNAc)	Fuc (GlcNAc)
1					
H1 (J(H1,H2) [Hz])	4.59 (8.4)	4.70 (7.3)	4.90 (2.0)	5.00 (3.4)	
H2	4.06	3.77	3.87	3.70	
H3	3.79	3.74	3.88	3.89	
H4	3.98	n.d.[a]	4.17	3.81	
H5	n.d.[a]	n.d.[a]	n.d.[a]	4.12	
H6 (J(H5,H6) [Hz])	n.d.[a]	n.d.[a]	n.d.[a]	1.20 (6.8)	
NC(O)CH_3	2.05, 2.03				
2					
H1 (J(H1,H2) [Hz])	4.46 (8.4)	4.67 (7.8)	4.89 (∼1)		5.13 (br s)
H2	3.99	3.97	3.83		3.69
H3	3.72	3.86	3.88		3.96
H4	3.90	3.90	4.18		3.84
H5	n.d.[a]	3.51	n.d.[a]		4.89
H6 (J(H5,H6) [Hz])	n.d.[a]	n.d.[a]	n.d.[a]		1.27 (5.9)
NC(O)CH_3	2.04, 2.02				
3					
H1 (J(H1,H2) [Hz])	4.51 (7.9)	4.70 (7.9)	4.90 (∼1)	4.98 (4.3)	5.13 (3.7)
H2	4.08	3.95	3.86	3.69	3.69
H3	3.73	3.87	3.86	3.92	3.96
H4	3.95	3.90	4.17	3.82	3.83
H5	n.d.[a]	n.d.[a]	n.d.[a]	4.11	4.85
H6 (J(H5,H6) [Hz])	n.d.[a]	n.d.[a]	n.d.[a]	1.20 (6.7)	1.27 (6.7)
NC(O)CH_3	2.03, 2.02				

[a] n.d.: not determined.

5-Aminopentyl (α-L-fucopyranosyl)-(1→3)-(2-deoxy-2-acetamido-β-D-galactopyranosyl)-(1→4)-[(α-L-fucopyranosyl)-(1→3)]-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-(1→3)-α-D-galactopyranoside (3): Compound **45** (7.2 mg, 3.17 μmol) was converted into **3**, as described for **1**, to give **3** (1.8 mg, 54 %). $[\alpha]_D^{20} = -34.7$ ($c = 0.1$ in water); for ^{1}H NMR data, see Table 3; MS (MALDI-TOF): *m*/*z* calcd for $C_{39}H_{69}N_3O_{24}$ (963.43); found: 986.37 $[M+Na]^+$.

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