Synthesis of glycodendrimers containing both fucoside and galactoside residues and their binding properties to Pa-IL and PA-IIL lectins from *Pseudomonas aeruginosa*†‡

Isabelle Deguise, David Lagnoux and René Roy*

Received (in Montpellier, France) 26th January 2007, Accepted 7th March 2007
First published as an Advance Article on the web 21st March 2007
DOI: 10.1039/b701237c

Homo- and hetero-bifunctional glycodendrimers ending with up to 16 fucoside and/or galactoside residues were synthesized in good yields using a convergent approach. The biologically active surface carbohydrate moieties were assembled in a single and efficient step using "click chemistry". The relative binding and cross-linking abilities of these glycodendrimers were evaluated by turbidimetric analyses using both PA-IL and PA-IIL lectins from *Pseudomonas aeruginosa*. Insoluble complexes were rapidly observed from the first and second generations as well as from the mixed glycodendrimer **32**. This hetero-bifunctional glycodendrimer was also evaluated with PA-IL alone and showed potent cross-linking properties. These novel heterobifunctional glycodendrimers may therefore constitute strong antiadhesin properties.

Introduction

Pseudomonas aeruginosa is a gram-negative bacterium found in various environments in nature including earth, water, and plants. It is also an opportunistic pathogen that can infect almost every human tissues when immunity barriers are lowered. Chronic lung colonization by this bacterium is the major cause of morbidity and mortality in cystic fibrosis (CF) patients.[1] CF patients show modifications in their respiratory and salivary mucins with a higher percentage of heavily fucosylated oligosaccharides,[2] which constitute active bindings sites for *P. aeruginosa*. For this reason, the different carbohydrate-binding proteins of these bacteria (pilin, flagellin and non-pili lectins) are of high therapeutic interest for their role in cell–cell recognition and specific cellular adhesion and uptake. *P. aeruginosa* expresses two intracellular and outer membrane lectins, PA-IL (LecA) and PA-IIL (LecB),[3] which are specific for D-galactose and L-fucose residues, respectively. These two lectins are therefore interesting targets for the prevention of bacterial colonization and potentially biofilm formation.[3]

The PA-IL lectin (51 kDa) is composed of four subunits of 121 amino acid residues and binds preferentially to D-galactose and its derivatives[4] with an association constant (K_a) of 3.4×10^4 M^{-1}.[5] The PA-IIL lectin (47 kDa) is also composed of four identical subunits of 114 amino acids and binds L-fucose and related monosaccharides[6] with a K_a of 1.6×10^6 M^{-1}.[7] Both lectins behave as classical Ca^{2+}-dependent tetrameric plant lectins, displaying agglutination activity.

The relatively weak binding affinities of single monosaccharides for these two lectins impede on the possibility for their use in blocking bacterial adhesive events in low, therapeutically realistic concentrations (IC_{50} ~mM). When more than one saccharide are clustered, there is usually an increase in affinity (avidity) and often specificity toward their corresponding carbohydrate binding proteins.[8] Glycodendrimers represent an interesting class of discrete small macromolecules mimicking multiantennary glycans that are widely used to emphasize multivalent binding interactions. Therefore, chemists and biochemists have thought that glycodendrimers could be used as molecular tools for the investigation and possibly manipulation of carbohydrate–protein interactions.[9] For instance, Roy and co-workers have demonstrated that dendrons having eight sialoside residues on the surface were a thousand-fold more effective than monomeric sialic acid for the inhibition of binding of Influenza virus to human erythrocytes.[10] Liskamp and co-workers have recently shown that a glycocluster containing four lactoside residues reached an inhibitory potency of 1667-fold relative to free lactose against the homodimeric galectin-1.[11] Several other examples[12] have demonstrated that multivalent inhibitors can increase these generally weak carbohydrate–protein binding interactions, an outcome originally referred to as the "glycoside cluster effect".[13]

Glycodendrimers are monodispersed relatively low molecular weight macromolecules. They represent chemically well-defined polymers when compared to glycopolymers. Thus, their chemically well defined structures represent potentially useful therapeutic agents in the prevention of bacterial and viral infections.

We present herein the design, synthesis, and biological properties of a new family of glycodendrimers with valencies between two and sixteen, which should be able to simultaneously inhibit either PA-IL and/or PA-IIL lectins. The synthesis of the first heterobifunctional glycodendrimers containing both L-fucoside and D-galactoside moieties on their

Department of Chemistry, Université du Québec à Montréal, P.O. Box 8888, Succ. Centre-Ville Montreal, Que, Canada H3C 3P8. E-mail: roy.rene@uqam.ca; Fax: +1 514 987 4054; Tel: +514 987 3000x2546

† This paper was published as part of the special issue on Dendrimers and Dendritic Polymers: Design, Properties and Applications.

‡ The HTML version of this article has been enhanced with colour images.

surface are thus reported herein. These glycodendrimers should have the property to bind both lectins PA-IL and PA-IIL and increase their biological activities for the preparation of new therapeutic antiadhesin agents against *P. aeruginosa*.

Results and discussion

Strategy

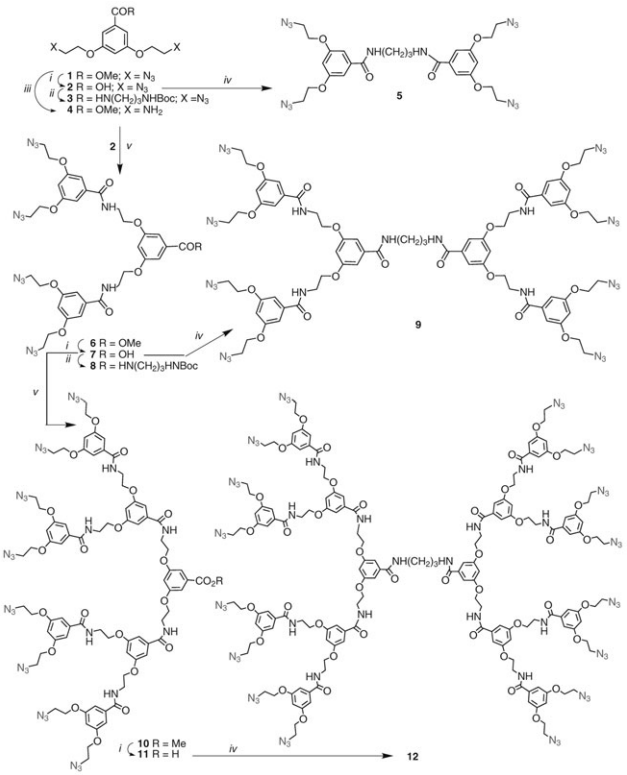
Dendrimers are usually synthesized either by a divergent or a convergent strategy. The strategy has been developed by Vögtle *et al.* in 1978.[14] According to this strategy, the dendrimers are built outward from the core, layer by layer. Each layer is often referred to as a generation growth. Alternatively, the convergent approach was first reported by Fréchet and Hawker in 1990.[15] This principle is based on the synthesis of each branched dendritic subunit (dendron) that are then assembled in one operation onto a preformed polyfunctional core. The main advantage of a convergent approach is the small number of reaction steps carried out at each generation. Only two reactions are performed at any given time. Moreover the difference in mass between any by-products and the desired product is usually considerable, thus the purification is easier compared to the divergent procedure.

We decided to use a convergent procedure known as the "outside in strategy". The synthesis strategy was based on the preparation of triazole-bearing dendrimer library *via* the copper(I)-catalyzed modern version of the classical Huisgen 1,3-dipolar cycloaddition of dendritic azides and carbohydrate terminal alkynes.[16] Copper(I) species were found to mediate the regioselective formation of 1,4-disubstituted 1,2,3-triazoles efficiently and in generally high yields.[17]

Synthesis

The repeating unit used for the dendrimer synthesis was the known[18] aromatic diazido ester **1** (Scheme 1), prepared by a slight modification of the published procedure. Thus, core structure **1** was obtained from 2-bromoethanol by reaction with sodium azide (H_2O, reflux) and then by treatment with *p*-toluenesufonyl chloride and Et_3N in CH_2Cl_2 to provide 2-azidoethyl benzenesulfonate. The later reacted with the two hydroxyl functions of methyl 3,5-dihydroxybenzoate using Cs_2CO_3 in DMF to afford **1** in a total yield of 60%.

The dendrimer synthesis was based on the formation of an amide linkage between an acid and a branching unit containing a bis-amine function. Dendron of generation one, bearing four azide end groups (**6**) was obtained from acid **2** and the branching unit **4** through an amide linkage. The acid **2** was previously synthesized by saponification of ester **1** using LiOH in THF in quantitative yield and diamine **4** was obtained by hydrogenation of the terminal azides in **1** using a catalytic amount of Pd/C 10% in MeOH. Diamine **4** was directly used without purification after filtration and evaporation for the dendrimer growth (Scheme 1). The total conversion of the azides to amines was confirmed by the disappearance of the intense azide signal at 2100 cm^{-1} in the IR of the crude reaction mixture. The amide synthesis was performed in DMF and (benzotriazol-1-yloxy)tris(dimethylamino)phosphonium hexafluorophosphate (BOP) was used as coupling reagent. Different washes were made in order to remove the remaining HMPA formed during the reaction which was otherwise difficult to remove by column chromatography. The first-generation dendron **6** was obtained as a white solid in a yield of 75% after column chromatography.

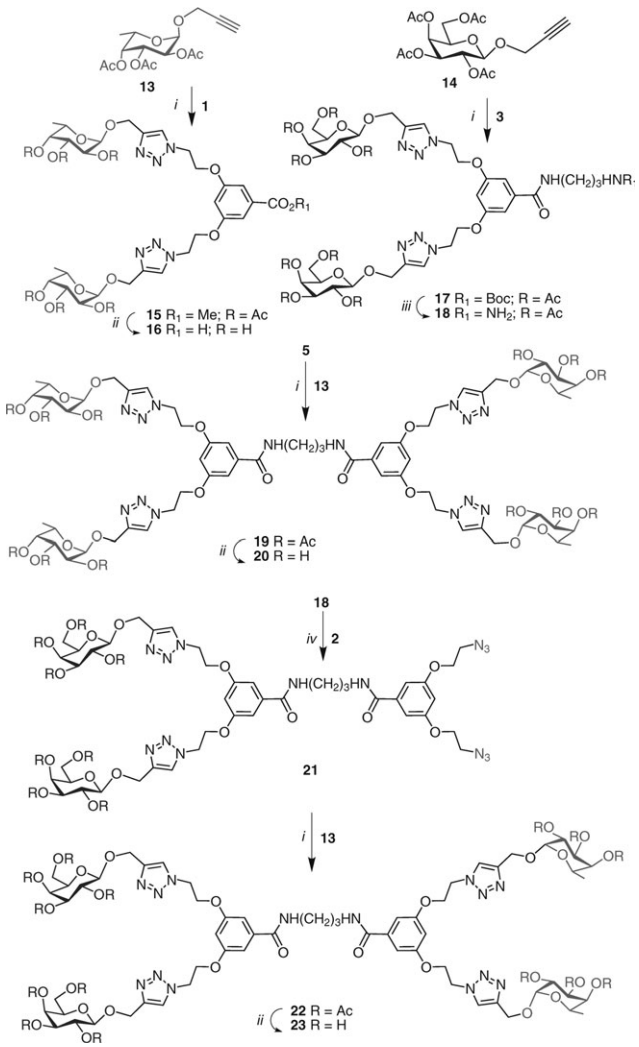


Scheme 1 *Reagents and conditions*: (i) LiOH, THF–H_2O; (ii) $BocHN(CH_2)_3NH_2$, BOP, DIPEA, DMF; (iii) Pd/C 10% H_2, MeOH; (iv) BOP, DIPEA, DMF, $H_2N(CH_2)_3NH_2$; (v) **4**, BOP, DIPEA, DMF.

By repetition of the same saponification–amide formation sequence with the diamine **4** and ester **6**, the second-generation dendron **10** (Scheme 1) was obtained in a yield of 67%. Dendrons **6** and **10** were characterized by NMR and ESI-MS. The generation growth in the synthesis of these two molecules and the completion of the substitutions were easily followed by ^1H NMR due to the characteristic signals of the methylene protons adjacent to the azide functionality (δ 3.5–3.6 ppm) and the methyl protons of the ester function (δ 3.8–3.9 ppm).

The well-characterized azido-terminated dendrons were then used for the click chemistry with prop-2-ynyl α-L-fucoside **13**. Fucoside **13** was obtained from L-(+)-fucose by treatment with acetic anhydride and pyridine, and the resulting per acetylated derivative was then treated with propargyl alcohol using a catalytic amount of $BF_3 \cdot EtO_2$ in a 45% yield.

When dendrons **1**, **6** and **10** were treated with fucoside **13** in the presence of $CuSO_4$ and sodium ascorbate in *t*-BuOH–H_2O (1 : 1), monofunctional glycodendrons **15** (Scheme 2), **24** (Scheme 3) and **33** (Scheme 5) with, respectively, 2, 4, 8 fucoside residues were obtained in 96, 80 and 77% yield, respectively after column chromatography. The complete conversion of the azides was again established by the

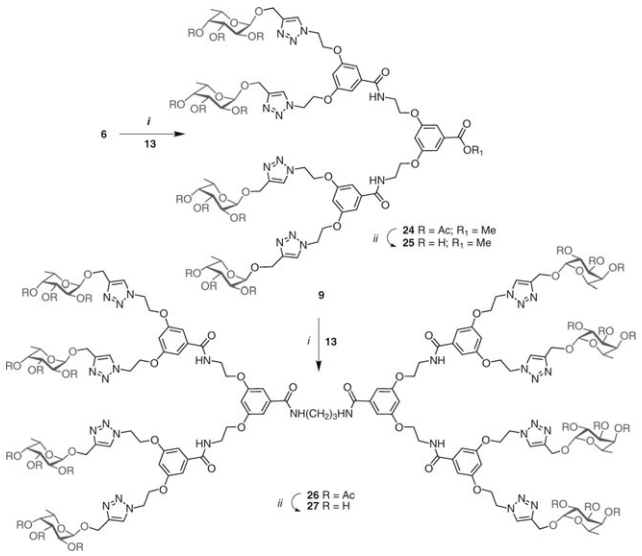


Scheme 2 *Reagents and conditions*: (i) $CuSO_4$, Na ascorbate, THF or *t*-BuOH, H_2O; (ii) MeONa, MeOH; (iii) TFA, CH_2Cl_2; (iv) BOP, DIPEA, DMF.

disappearance of the intense signal at 2100 cm^{-1} in the IR spectra. ^1H NMR showed the disappearance of the signal characteristic of the proton of the methylene adjacent to the azides at δ 3.5–3.6 ppm and the presence of singlet at δ 7.7 ppm characteristic of triazoles formed during the reaction. The completion of the multivalent glycodendrons were also confirmed by ESI-MS.

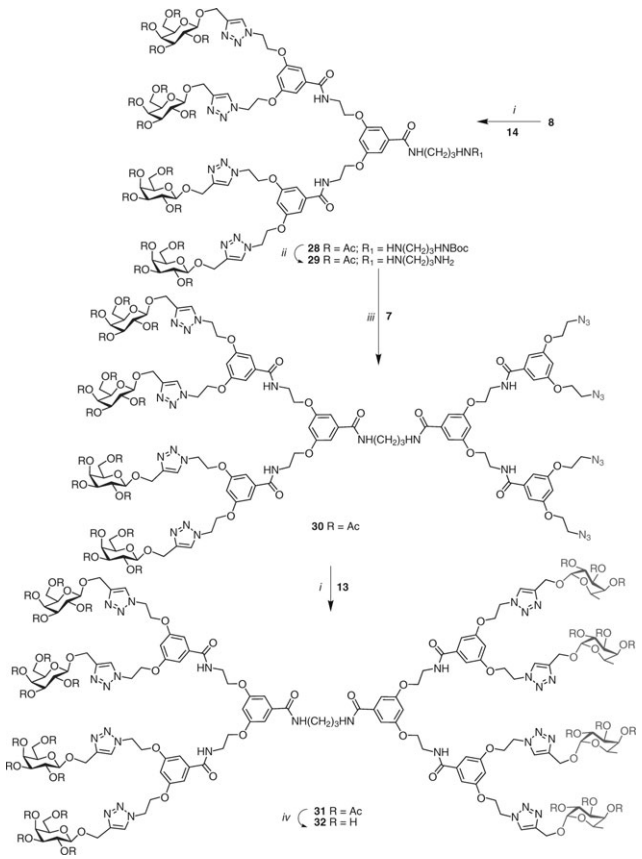
Three azido-ending dendrimers **5**, **9**, and **12** were further obtained from dendrons **2**, **7** or **11** and BOP as coupling reagent in yields of approximately 80% (Scheme 1) after column chromatography. The structures of these resulting dendrimers of generation zero, one, and two were confirmed by ESI-MS and ^1H NMR with the presence of characteristic signals at near δ 3.3 and at δ 1.8 ppm of the dendrimer core. The presence of the protons of the dendrimer core in the ^1H and ^{13}C NMR spectra were however not readily determined with increasing generation due to the size of the molecules.

These three dendrimers were then coated with fucoside **13** in the presence of $CuSO_4$ and sodium ascorbate. For **5** and **9** the solvent used for the reaction was *t*-BuOH at room temperature

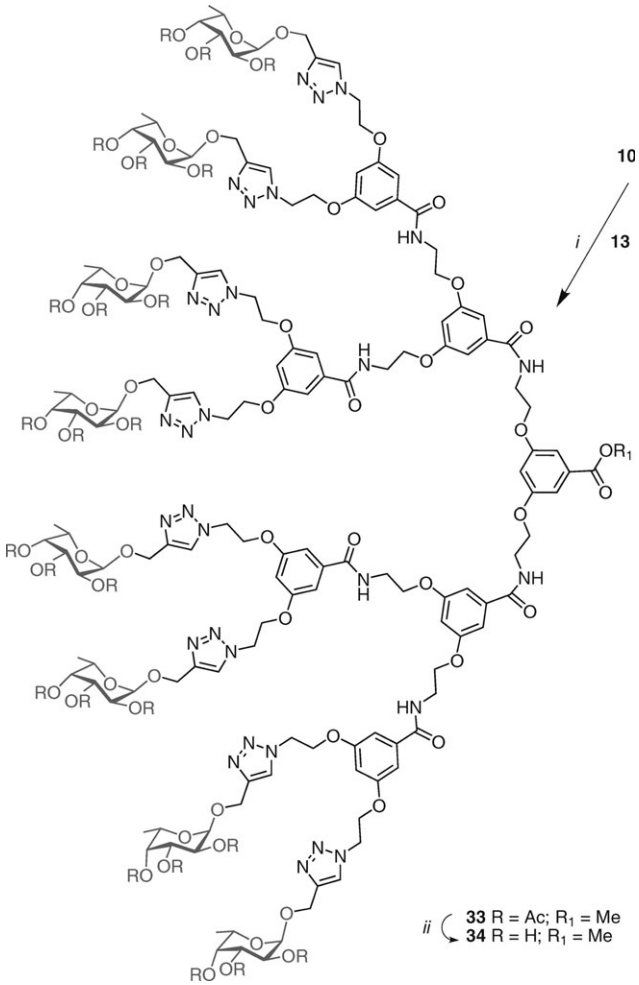


Scheme 3 *Reagents and conditions*: (i) $CuSO_4$, sodium ascorbate, *t*-BuOH, H_2O; (ii) MeONa, MeOH.

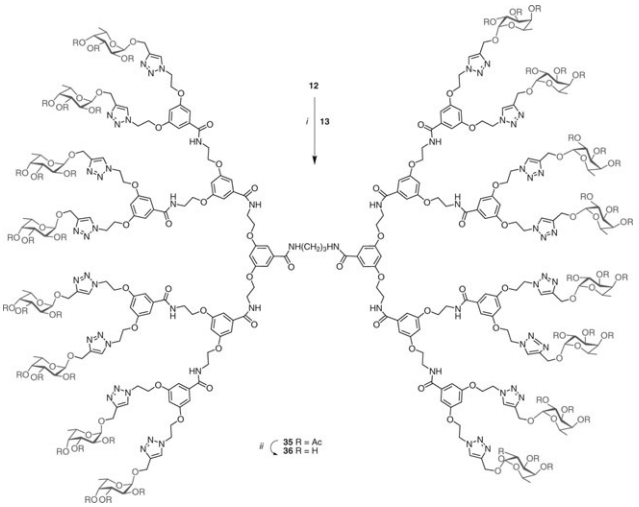
and the respective glycodendrimers **19** and **26** were obtained in 96 and 82% yields (Scheme 2 and Scheme 3). Due to solubility problems, the reaction between **12** and **13** was carried out in THF–H_2O at 50 °C. After 24 h, glycodendrimer **35** was finally obtained in 49% yield (Scheme 6).



Scheme 4 *Reagents and conditions*: (i) $CuSO_4$, sodium ascorbate, *t*-BuOH, H_2O; (ii) MeONa, MeOH; (iii) BOP, DIPEA, DMF.



Scheme 5 *Reagents and conditions*: (i) $CuSO_4$, sodium ascorbate, THF, H_2O; (ii) MeONa, MeOH.



Scheme 6 *Reagents and conditions*: (i) $CuSO_4$, sodium ascorbate, THF, H_2O; (ii) TFA, CH_2Cl_2; (iii) BOP, DIPEA, DMF; (iv) MeONa, MeOH.

At this point of the synthesis, homo and hetero-bifunctional glycodendrimers were synthesized. The homodendrimers were totally decorated with L-fucoside residues while heterodendrimers possessed half D-galactoside and half L-fucoside residues to provide them with the possibility of binding to either PA-IL and PA-IIL, respectively. The synthesis of the homodendrimers was based on the formation of two amide linkages between the acid function of the different dendrons to the 1,3-diaminopropane to offer 4, 8 or 16 azido functions.

The hetero-bifunctional glycodendrimers were synthesized in two steps. The first step was the formation of an amide linkage between the acid function of one of the dendrons and *tert*-butyl 3-aminopropylcarbamate followed by connection of galactoside derivatives **14** using click chemistry again. The second step was the connection of the second dendron after Boc-group removal and finally the linking of **13** to furnish a dendrimer containing both galactoside and fucoside residues on its surface. Toward this goal, known galactoside **14** was obtained in good yield (71%) from D-(+)-galactose, by treatment with acetic anhydride and pyridine, followed by treatment with propargyl alcohol using a catalytic amount of $BF_3 \cdot EtO_2$ in CH_2Cl_2 as for the propargyl fucoside **13** above. Dendron **1** and **6** were first hydrolyzed using LiOH to give **2** and **7** in quantitative yields. These acid-bearing dendrons were then coupled to *tert*-butyl 3-aminopropylcarbamate using BOP in 85% yield each (Scheme 1). The surface of these half dendrimers **3** and **8** were then covered with galactoside residues using alkyne **14** and $CuSO_4$ in THF to afford **17** and **28** in 92 and 77% yield (Scheme 2 and Scheme 4) after column chromatography. These molecules were fully characterized using ^1H and ^{13}C NMR spectroscopy and ESI-MS.

The Boc-protecting group present on the amine function at the focal point of dendrimers **17** and **28** was removed using TFA in CH_2Cl_2. The resulting amines **18** and **29** were purified using a short column chromatography and obtained in yields of 86 and 74%, respectively. The ^1H NMR showed the disappearance of the signal at δ 1.4 ppm characteristic of the Boc group. The second part of the dendrimer was attached using the BOP reagent and the corresponding azido dendrons **2** or **7**. Dendrimer **21** containing two galactoside residues and two azide functions on the surface (Scheme 2) was obtained in 71% yield as well as dendrimer **30** containing four galactoside residues and azide functions in 69% yield (Scheme 4). Finally, fucoside **13** was used with $CuSO_4$ in THF in order to introduce the second saccharide at the surface of the dendrimer. The hetero-glycodendrimers **22** and **31** were obtained in 66 and 68% yields, respectively. The introduction of fucoside **13** at the surface of these two dendrimers was clearly established from their ^1H NMR spectra based on the presence of signals at δ 4.6 ppm and at δ 1.1 ppm characteristic of the anomeric signal (H-1) of the galactoside and the C-6 methyl of the fucoside moiety. ESI-MS successfully confirmed the synthesis of these two molecules (Fig. 1).

All glycodendimers synthesized were de-*O*-acetylated using standard Zemplén conditions (NaOMe, MeOH) to afford one dendrimer with two fucose residues **16**, two dendrimers with four fucose residues **20** and **25**, two with eight fucose residues **27** and **34**, one with sixteen fucose residues **36**, one with two fucose and two galactose residues **23** and finally one with four fucose and four galactose residues **32**. All these glycodendrimers were characterized by NMR and ESI-MS.

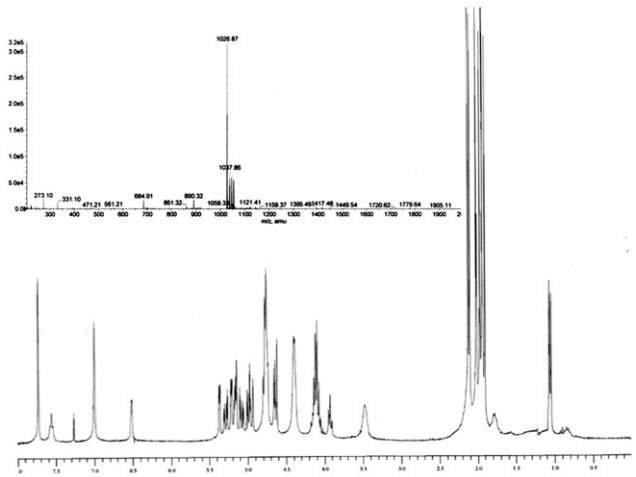


Fig. 1 ESI-MS and ^{1}H NMR spectra of heterodendrimer **22**.

Turbidimetric assays

The relative affinity and cross-linking ability of all glycodendrimers toward the fucose specific tetrameric PA-IIL lectin was first established by turbidimetric measurements as described in Fig. 2. When glycodendrimers **25**, **27**, **32**, **34** and **36** were mixed with PA-IIL (at concentrations equal to 1 mg mL^{-1}), insoluble complexes rapidly formed after only a few minutes. These results clearly demonstrated the necessity for a minimum of four L-fucoside residues on the same side of the dendrimers in order to form stable cross-linked lattices. Increasing the dendrimer generation did not cause further increase in the kinetic of precipitation with the lectin. This effect was shown when tetramer **25** was compared to octamer **34** and octamer **27** to 16-mer **36**. This can be explained by an unfavorable steric crowding with the lectin amino acids. The heterodendrimer **32**, having four galactosides and four fucosides showed an almost equipotent cross-linking ability with PA-IIL (O.D. ~0.2).

The reactivity of mixed octamer **32** was then tested against PA-IL in parallel to that of PA-IIL. The results are shown in Fig. 3. This glycodendrimer formed insoluble complexes with

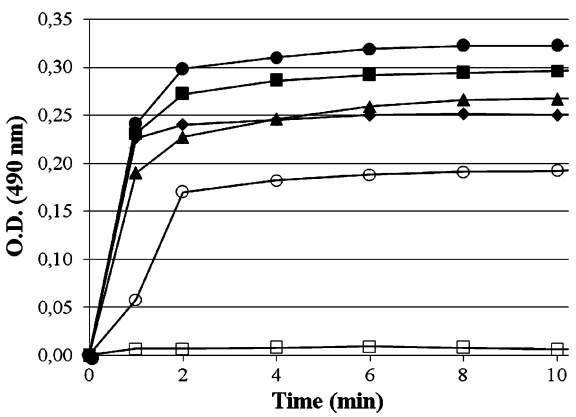


Fig. 2 Time course for the turbidimetric analyses of PA-IIL with glycodendrimers at concentration of 1 mg mL^{-1}: **23** (□), **25** (▲), **27** (●), **32** (○), **34** (◆), **36** (■).

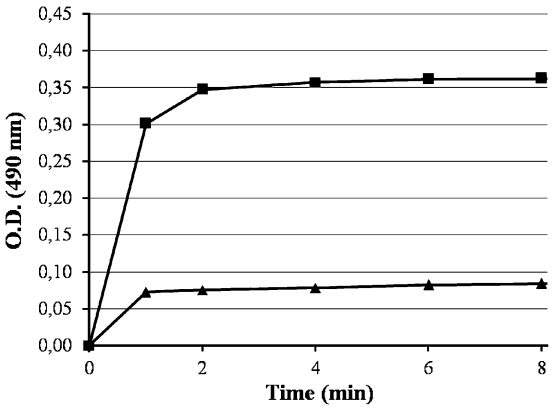


Fig. 3 Time course for the turbidimetric analyses of PA-IL and PA-IIL with heteroglycodendrimer **32** at concentration of 1 mg mL^{-1}: **32** with PA-IL (▲); **32** with PA-IIL (■).

both lectins, as planned. The heterodendrimer **32** was thus able to link both PA-IL and PA-IIL simultaneously, albeit with less intensity. Hence, it appeared that the complex formation between PA-IIL and **32** was more complete than the one formed with PA-IL. This was likely due to a higher affinity of the fucoside residues towards PA-IIL ($K_a = 1.6 \times 10^6$ M^{-1}) in comparison to that of the galactoside residues towards PA-IL ($K_a = 3.4 \times 10^4$ M^{-1}).[19] The specificity of each glycodendrimer towards its respective lectin was demonstrated by their inability to form insoluble complex with the other lectin (results not shown).

Conclusions

The syntheses of first- and second-generation glycodendrimers containing galactoside and/or fucoside moieties have been accomplished in good to excellent yields. The key step was the incorporation of the carbohydrate residues using a regioselective 1,3-dipolar cycloaddition catalyzed by copper(I) species generated *in situ* from copper sulfate and sodium ascorbate ("click chemistry"). Glycodendrimers **25**, **27**, **32**, **34** and **36** possessing a minimum of four fucoside residues on the same side showed fast cross-linking abilities with tetrameric *P. aeruginosa* PA-IIL lectin by forming insoluble complexes when mixed together. Heterodendrimer **32** containing four fucosides and four galactosides had the ability to recognize both binding site domains of PA-IL and PA-IIL. Future work is in progress to test the capacity of these novel glycodendrimers to inhibit the adhesion of *P. aeruginosa* to human respiratory tissues.

Experimental

General

Lectins PA-IL from *Pseudomonas aeruginosa* was purchased from Sigma while PA-IIL was a generous gift from Dr A. Imberty, CERMAV, Genoble (France). DMF was distilled from ninhydrin. MeOH was dried over 4 Å molecular sieves. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Gemini 300 MHz and Varian 500 MHz instruments with signals referenced to internal $CDCl_3$ (^{1}H, δ 7.27 ppm; ^{13}C, δ 77.0

ppm), D_2O (^1H, δ 4.79 ppm), DMSO-d_6 (^1H, δ 2.50 ppm; ^{13}C, δ 39.5 ppm). Turbidimetric analysis were measured with a microtiter plate reader Thermo Max. Mass spectral data were obtained by Dr Alexandra Furtos and Karine Venne (Mass Spectrometry Laboratory, Université de Montréal, Québec, Canada).

Turbidimetric analysis

Turbidimetric experiments were performed in Sarstedt round bottom plates of 96-wells in which 50 μL well^{-1} of a stock lectin solution prepared from PA-IIL or PA-IL (1 mg mL^{-1} in PBS with Ca^{2+}) were mixed with 50 μL of glycodendrimers (stock solutions of 1 mg mL^{-1} PBS with Ca^{2+}). The turbidimetric experiment for **32** was performed by adding to a 100 μL well^{-1} stock lectin solution prepared from PA-IL or PA-IIL (1 mg mL^{-1} PBS with Ca^{2+}) 100 μL of **32** (stock solutions of 1 mg mL^{-1} PBS with Ca^{2+}). The turbidity of the solutions was monitored by reading the optical density (O.D.) at 490 nm at regular time intervals until no noticeable changes could be observed. Each test was done in triplicate and the average is shown in Fig. 2 and 3.

Syntheses

Procedure 1: peptidic coupling. Methyl 3,5-bis(2-azidoethoxy)-benzoate **1** (1 eq.) and Pd/C 10% in MeOH were stirred under hydrogen for 6 h. Pd/C was removed by filtration and the filtrate containing the free amine **4** was evaporated and taken up with DMF. To the solution was added the required carboxylic acids (2.1 eq.), BOP (2.2 eq.) and DIPEA (12 eq.). The mixture was stirred 4 h at room temperature, then extracted with AcOEt and a solution of saturated $NaHCO_3$, $KHSO_4$ (0.5 M), H_2O and brine. The organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and chromatographed on a silica gel column.

Procedure 2: saponification. The esters were dissolved in THF and LiOH (2.2 eq./acid) in water was added. The solution was stirred 4 h then acidified with HCl (5 M) and extracted with AcOEt and HCl 1 M. The organic layers were dried on Na_2SO_4, filtered, concentrated under reduced pressure, and the residues were purified by silica gel column chromatography.

Procedure 3: peptide coupling of the core. To a solution of the carboxylic acids (1.2 or 2.2 eq.) was added the free amines (1 eq.), BOP (1.2 or 2.2 eq.) and DIPEA (6 or 12 eq.). The reaction mixture was stirred for 4 h at room temperature, then extracted with AcOEt and a solution of saturated $NaHCO_3$, $KHSO_4$ (0.5 M), H_2O and brine. The organic layers were dried on Na_2SO_4, filtered, concentrated under reduced pressure and chromatographed on a silica gel column.

Procedure 4: triazole synthesis. The azido dendrimers were dissolved on ^{t}BuOH or THF then the propargyl glycosides **13** or **14** (1.1 eq./azide function) were added to the solution. $CuSO_4$ (0.4 eq./azide function), sodium ascorbate (0.7 eq./azide function) and H_2O were then added and the solutions were stirred overnight at room temperature or heated at 50 °C, then extracted with AcOEt and a solution of saturated NH_4Cl and brine. The organic layers were dried on Na_2SO_4, filtered, concentrated under reduced pressure, and chromatographed on a silica gel column.

Procedure 5: Zemplén de-*O*-acetylation. Peracetylated glycodendrimers were dissolved in dry MeOH and MeONa was added until the pH reached a value of 9. The reactions were stirred until complete disappearance of the starting materials. Amberlite resin (H^+) was added in order to obtain a neutral pH and filtered. The filtrates were concentrated, dried under reduced pressure, and lyophilised.

Compound 2: procedure 2. Ester **1**[18] (310 mg, 1.01 mmol), LiOH (93 mg, 2.22 mmol), THF (5 mL) and H_2O (5 mL) were used. Pure acid **2** (283.6 mg, 0.36 mmol, 96%) was obtained after column chromatography (5% MeOH–DCM); ^1H NMR (300 MHz, $CDCl_3$): δ 7.30 (d, 2H, J = 2.20 Hz, H_3), 6.77 (t, 1H, J = 2.34 Hz, H_4), 4.20 (t, 4H, J = 4.94 Hz, H_2), 3.64 (t, 4H, J = 4.95 Hz, H_1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8, 159.5, 133.8, 107.9, 106.5, 67.8, 51.2.

Compound 3: procedure 3. Azido acid **2** (51.2 mg, 0.18 mmol, 1.2 eq.), *tert*-butyl 3-aminopropylcarbamate (25.4 mg, 0.15 mmol), BOP (77 mg, 0.18 mmol, 1.2 eq.), DIPEA (0.15 mL, 0.88 mmol, 6 eq.), DMF (3 mL) were used. Compound **3** was obtained after column chromatography (2% MeOH–DCM) (60 mg, 0.13 mmol, 85%); ^1H NMR (300 MHz, $CDCl_3$): δ 7.54 (br t, 1H, NH), 7.07 (d, 2H, J = 1.65 Hz, H_3), 6.61 (t, 1H, J = 2.20 Hz, H_4), 5.03 (br t, 1H, NH), 4.16 (t, 4H, J = 4.95 Hz, H_2), 3.58 (t, 4H, J = 4.95 Hz, H_1), 3.47 (q, 2H, J = 6.32, 12.22 Hz, H_5), 3.23 (q, 2H, J = 6.14, 12.09 Hz, H_7), 1.72–1.64 (m, 2H, H_6), 1.43 (s, 9H, H_9); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7, 159.3, 157.0, 136.8, 105.8, 105.2, 79.5, 67.1, 50.0, 36.9, 35.9, 29.9, 28.3; MS (ESI): m/z calc. $C_{19}H_{28}N_8O_5$: 448.22; found: 471.21 $[M + Na]^+$.

Compound 5: procedure 3. Acid **2** (173.2 mg, 0.59 mmol, 2.1 eq.), 1,3-diaminopropane (24 μL, 0.28 mmol), BOP (275 mg, 0.62 mmol, 2.2 eq.), DIPEA (0.59 mL 3.39 mmol, 12 eq.) and DMF (6 mL) were used. Tetraazide **5** (140 mg, 0.22 mmol, 80%) was obtained after column chromatography (2% MeOH–DCM); ^1H NMR (300 MHz, $CDCl_3$): δ 7.14 (br t, 2H, NH), 7.05 (d, 4H, J = 1.65 Hz, H_3), 6.64 (s, 2H, H_4), 4.20 (t, J = 4.67 Hz, 8H, H_2), 3,62 (t, 8H, J = 4.81 Hz, H_1), 3.55 (br d, 4H, H_5), 1.84 (br s, 2H, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.5, 159.5, 136.7, 106.0, 105.0, 67.3, 50.1, 36.3, 29.7; MS (ESI): m/z calc. $C_{25}H_{30}N_{14}O_6$: 622.25; found: 623.25 $[M + H]^+$.

Compound 6: procedure 1. Compound **2** (2.03 g, 6.94 mmol), 1 (840 mg, 3.30 mmol), BOP (3.21 g, 7.27 mmol), DIPEA (6.6 mL, 39.6 mmol) and DMF (30 mL) were used. Tetraazide ester **6** (2.0 g, 2.49 mmol, 75%) was obtained after column chromatography (1% MeOH–DCM); ^1H NMR (300 MHz, $CDCl_3$): δ 7.17 (d, 2H, J = 2.20 Hz, H_7), 6.96 (d, 4H, J = 2.20 Hz, H_3), 6.71 (br t, 2H, NH), 6.64 (t, 1H, J = 2.20 Hz, H_4), 6.61 (t, 2H, J = 2.20 Hz, H_8), 4.15 (br t, 12H, H_6 and H_2), 3.90 (s, 3H, H_9), 3.87–3.84 (m, 4H, H_5), 3.60 (t, 8H, J = 4.94 Hz, H_1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 166.4, 159,5, 136.6, 132.2, 108.2, 106.3, 106.1, 104.8, 67.2, 66.9, 52.3, 50.0, 39.5; MS (ESI): m/z calc. $C_{34}H_{38}N_{14}O_{10}$: 802.29; found: 803.30 $[M + H]^+$.

Compound 7: procedure 2. Ester **6** (300 mg, 0.37 mmol), LiOH (34 mg, 0.82 mmol), THF (2 mL) and H_2O (2 mL) were used. Acid **7** (283.6 mg, 0.36 mmol, 96%) was obtained after column chromatography (5% MeOH–DCM); ^{1}H NMR (300 MHz, MeOH): δ 7.15 (d, 2H, J = 2.47 Hz, H_7), 7.02 (d, 4H, J = 2.20 Hz, H_3), 6.68–6.64 (m, 3H, H_8 and H_4), 4.18–4.15 (m, 12H, H_6 and H_2), 3.73 (br t, 4H, H_5), 3.59 (t, 8H, J = 4.94 Hz, H_1); ^{13}C NMR (75 MHz, MeOH): δ 168.0, 165.9, 160,5, 137.2, 133.2, 107.7, 106.1, 105.8, 104.6, 66.2, 66.0, 51.9, 39.5; MS (ESI): m/z calc. $C_{33}H_{36}N_{14}O_{10}$: 788.27; found: 789.28 $[M + H]^+$.

Compound 8: procedure 3. Acid **7** (93.5 mg, 0.12 mmol, 1.2 eq.), *tert*-butyl 3-aminopropylcarbamate (17.2 mg, 0.10 mmol), BOP (52.4 mg, 0.12 mmol, 1.2 eq.), DIPEA (103 mg, 0.59 mmol, 6 eq.) and DMF (2 mL) were used. Boc-amide **8** (79 mg, 0.08 mmol, 85%) was obtained after column chromatography (3% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.60 (m, 3H, NH), 7.06 (d, 4H, J = 2.20, H_3), 6.79 (br s, 2H, H_4), 6.60 (t, 2H, J = 2.28 Hz, H_7), 6.26 (br s, 1H, H_8), 5.15 (br t, 1H, NH), 4.11 (t, 8H, J = 4.81 Hz, H_2), 3.94 (br s, 4H, H_6), 3.72 (br d, 4H, H_5), 3.55 (t, 8H, J = 4.95 Hz, H_1), 3.49–3.43 (m, 2H, H_9), 3.21–3.19 (m, 2H, H_{11}), 1.60–1.80 (m, 2H, H_{10}), 1,41 (s, 9H, H_{12}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.4, 159.4, 156.8, 136.5, 106.2, 105.5, 105.1, 104.0, 79.5, 67.1, 66.5, 50.0, 39.6, 37.2, 36.3, 29.6, 28.3.

Compound 9: procedure 3. Acid **7** (153.3 mg, 0.19 mmol, 2.1 eq.), 1,3-diaminopropane (9 μL, 0.07 mmol), BOP (90 mg, 0.20 mmol, 2.2 eq.), DIPEA (0.19 mL, 1.11 mmol, 12 eq.) and DMF (1 mL) were used. Octaazide dendrimer **9** (264 mg, 0.16 mmol, 84%) was obtained after column chromatography (2% MeOH–DCM); ^{1}H NMR (300 MHz, DMSO): δ 8.70 (br t, 4H, NH), 8.46 (br t, 2H, NH), 7.06 (d, 8H, J = 2.20 Hz, H_3), 7.02 (d, 4H, J = 1.92 Hz, H_7), 6.68 (d, 6H, J = 1.92 Hz, H_8 and H_4), 4.19 (t, 16H, J = 4.65 Hz, H_2), 4.13 (t, 8H, J = 5.63 Hz, H_6), 3.64 (t, 24H, J = 4.67 Hz, H_5 and H_1), 3.27–3.25 (m, 4H, H_9), 1.70–1.75 (m, 2H, H_{10}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.7, 167.6, 159.5, 159.4, 136.4, 136.2, 106.2, 105.5, 105.1, 104.2, 67.2, 66.5, 50.0, 39.7, 36.8, 29.2; MS (ESI): m/z calc. $C_{69}H_{78}N_{30}O_{18}$: 1614.61; found: 1615.62 $[M + H]^+$.

Compound 10: procedure 1. Acid **7** (362 mg, 0.46 mmol), **1** (55.6 mg, 0.22 mmol), BOP (213 mg, 0.48 mmol), DIPEA (0.46 mL, 2.62 mmol) and DMF (4 mL) were used. Octaazide dendron **10** (264 mg, 0.15 mmol, 67%) was obtained after column chromatography (4% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.56 (br t, 4H, NH), 7.42 (br t, 2H, NH), 7.02 (d, 10H, J = 2.20 Hz, H_{11} and H_3), 6.76 (br s, 4H, H_7), 6.56 (br s, 5H, H_{12} and H_4), 6.26 (br s, 2H, H_8), 4.05 (t, 20H, J = 4.67 Hz, H_{10} and H_2), 3.88 (br s, 8H, H_6), 3.82 (s, 3H, H_{13}), 3.68 (br s, 12H, H_9 and H_5), 3.51 (t, 16H, J = 4.67 Hz, H_1); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 167.4, 166.6, 159.5, 159.4, 159.3, 136.4, 136.2, 131.9, 108.1, 106.2, 105.7, 105.0, 104.1, 67.1, 66.7, 66.4, 52.3, 50.0, 39.5; MS (ESI): m/z calc. $C_{78}H_{86}N_{30}O_{22}$: 1794.65; found: 1795.66 $[M + H]^+$.

Compound 11: procedure 2. Ester **10** (242.8 mg, 0.14 mmol), LiOH (12 mg, 0.30 mmol), THF (1 mL) and H_2O (1 mL) were used. Acid **11** (202 mg, 0.11 mmol, 84%) was obtained after column chromatography (4% MeOH–$CHCL_3$); ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 8.08 (br s, 4H, NH), 7.97 (br s, 2H, NH), 7.03 (s, 10H, H_{11} and H_3), 6.92 (s, 4H, H_7), 6.54 (s, 5H, H_{12} and H_4), 6.41 (s, 2H, H_8), 4.06 (t, 20H, J = 4.53 Hz, H_{10} and H_2), 4.00 (br s, 8H, H_6), 3.67 (br s, 12H, H_9 and H_5), 3.50 (t, 16H, J = 4.53 Hz, H_1); ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 167.1, 166.9, 159.4, 159.2, 136.4, 105.9, 105.7, 104.5, 66.9, 66.1, 49.7, 39.1; MS (ESI): m/z calc. $C_{77}H_{84}N_{30}O_{22}$: 1780.64; found: 1781.64 $[M + H]^+$.

Compound 12: procedure 3. Acid **11** (90 mg, 0.05 mmol, 2.1 eq.), 1,3-diaminopropane (2 μL, 0.02 mmol), BOP (23.4 mg, 0.05 mmol, 2.2 eq.), DIPEA (50 mL, 0.29 mmol, 12 eq.) and DMF (1 mL) were used. 16-Mer azido dendrimer **12** (66 mg, 0.02 mmol, 76%) was obtained after column chromatography (4% MeOH–$CHCl_3$); ^{1}H NMR (300 MHz, $(CD_3)_2CO$): δ 8.40–8.18 (m, 14H, NH), 7.13 (d, 16H, J = 2.20 Hz, H_3), 7.01 (br s, 12H, H_{11} and H_7), 6.64 (br s, 8H, H_4), 6.50–6.43 (m, 6H, H_{12} and H_8), 4.14 (t, 32H, J = 4.67 Hz, H_2), 4.06 (br s, 24H, H_{10} and H_6), 3.69 (br s, 24H, H_9 and H_5), 3.58 (t, 16H, J = 4.67 Hz, H_1), 3.43 (br s, 4H, H_{13}), 1.79 (br s, 2H, H_{14}); ^{13}C NMR (75 MHz, $(CD_3)_2CO$): δ 167.6, 167.2, 160.2, 160.0, 137.3, 136.9, 106.6, 106.4, 104.9, 67.7, 66.8, 50.4, 39.7, 31.5; MS (ESI): m/z calc. $C_{158}H_{175}N_{61}O_{42}$: 3598.34; found: 1801.17 $[M + 2H]^{2+}$.

Compound 15: procedure 4. Ester **1** (51 mg, 0.17 mmol), fucoside **13** (120 mg, 0.37 mmol), $CuSO_4$ (33 mg, 0.13 mmol), sodium ascorbate (46 mg, 0.23 mmol), ^{t}BuOH (1 mL) and H_2O (1 mL) were used. Dendron **15** (153 mg, 0.16 mmol, 96%) was obtained after column chromatography (25% EtOAc–hexane); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (s, 2H, H_8), 7.18 (d, 2H, J = 2.20 Hz, H_{11}), 6.61 (t, 1H, J = 2.34 Hz, H_{12}), 5.34 (dd, 2H, J = 3.30, 10.71 Hz, H_3), 5.27 (dd, 2H, J = 1.10, 3.57 Hz, H_4), 5.19 (d, 2H, J = 3.85 Hz, H_1), 5.12 (dd, 2H, J = 3.57, 10.71 Hz, H_2) 4.83 (d, 2H, J = 12.64 Hz, H_{7a}), 4.78 (t, 4H, J = 4.95 Hz, H_9), 4.67 (d, 2H, J = 12.64 Hz, H_{7b}), 4.40 (t, 4H, J = 4.67 Hz, H_{10}), 4.18 (br q, 2H, H_5), 3.90 (s, 6H, H_{13}), 2.16 (s, 6H, Ac), 2.01 (s, 6H, Ac), 1.97 (s, 6H, Ac), 1.10 (d, 6H, J = 6.59 Hz, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.2, 169.9, 166.0, 158.7, 144.0, 132.3, 123.6, 108.3, 106.4, 95.6, 70.9, 67.8, 67.7, 66.5, 64.6, 61.1, 52.3, 49.5, 20.6, 20.5, 20.5, 15.7; MS (ESI): m/z calc. $C_{42}H_{54}N_6O_{20}$: 962.34; found: 963.35 $[M + H]^+$.

Compound 16: procedure 5. Ester **15** (38 mg, 0.04 mmol) in MeOH (1 mL) were used. Compound **16** (26 mg, 0.04 mmol, 96%) was obtained an amorphous solid; ^{1}H NMR (300 MHz, D_2O): δ 7.99 (s, 2H, H_8), 6.83 (d, 2H, J = 2.20 Hz, H_{11}), 6.23 (br t, 1H, H_{12}), 4.83–4.65 (m, 4H, H_3 and H_2), 4.57 (dd, 4H, J = 13.05, 25.41 Hz, H_7), 4.29–4.20 (m, 4H, H_{10}), 3.59–3.41 (m, 10H, J = 1.37, 2.47 Hz, H_9, H_5, H_4 and H_1), 0.73 (d, 6H, J = 6.59 Hz, H_6); ^{13}C NMR (75 MHz, DMSO): δ 175.2, 160.1, 146.0, 140.8, 127.1, 109.9, 105.8, 100.5, 73.2, 71.0, 69.5, 68.2, 62.6, 51.5, 16.6; MS (ESI): m/z calc. $C_{29}H_{40}N_6O_{14}$: 696.26; found: 697.27 $[M + H]^+$.

Compound 17: procedure 4. Azido dendron **3** (54.9 mg, 0.12 mmol), galactoside **14** (104 mg, 0.27 mmol, 2.2 eq.), $CuSO_4$

(24.5 mg, 0.10 mmol), sodium ascorbate (34 mg, 0.17 mmol), ^{t}BuOH (1 mL) and H_2O (1 mL) were used. Dimer **17** (137 mg, 0.11 mmol, 92%) was obtained after column chromatography (3% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.71 (s, 2H, H_8), 7.51 (br t, 1H, NH), 7.04 (br s, 2H, H_{11}), 6.53 (t, 1H, J = 2.20, 4.12 Hz, H_{12}), 5.38 (d, 2H, J = 3.30 Hz, H_4), 5.20 (dd, 2H, J = 7.97, 10.44 Hz, H_2), 5.02–4.95 (m, 5H, H_{7a}, H_3 and NH), 4.81–4.70 (m, 6H, H_{10} and H_{7b}), 4.64 (d, 2H, J = 7.69 Hz, H_1), 4.39 (t, 4H, J = 4.67 Hz, H_9), 4.20–4.07 (m, 4H, H_{6a} and H_5), 3.94 (t, 2H, J = 6.59 Hz, H_{6b}), 3.46 (br q, 2H, H_{13}), 3.22 (br q, 2H, H_{15}), 2.13 (s, 6H, Ac), 2.04 (s, 6H, Ac), 1.97 (s, 6H, Ac), 1.93 (s, 6H, Ac), 1.71–1.67 (m, 2H, H_{14}), 1.43 (s, 9H, H_{16}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 170.1, 170.0, 169.6, 168.1, 158.9, 144.3, 137.1, 123.7, 106.2, 104.8, 100.4, 79.5, 70.8, 70.7, 68.8, 67.0, 66.5, 62.9, 61.2, 49.6, 36.9, 35.9, 28.3, 20.6, 20.5; MS (ESI): m/z calc. $C_{53}H_{72}N_8O_{25}$: 1220.46; found: 1221.47 $[M + H]^+$.

Compound 18. Boc-dendrimer **17** (67 mg, 0.05 mmol) was treated with TFA (0.26 mL, 3.57 mmol) and CH_2Cl_2 (1 mL) for 4 h at 25 °C. Pure fucosylated tetramer **18** (53 mg, 0.05 mmol, 86%) was obtained after column chromatography (7% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.07–7.90 (m, 3H, NH), 7.77 (s, 2H, H_8), 6.89 (br s, 2H, H_{11}), 6.40 (br s, 1H, H_{12}), 5.39 (d, 2H, J = 3.30 Hz, H_4), 5.21–5.11 (m, 2H, H_2), 5.02 (dd, 2H, J = 3.28, 10.44 Hz, H_3), 4.95 (d, 2H, J = 12.35 Hz, H_{7a}), 4.82–4.62 (m, 8H, H_{10}, H_{7b} and H_1), 4.30 (br s, 4H, H_9), 4.21–4.05 (m, 4H, H_{6a} and H_5), 3.96 (t, 2H, J = 6.32 Hz, H_{6b}), 3.47 (br s, 2H, H_{13}), 3.22 (br s, 2H, H_{15}), 3.01 (br s, 2H, H_{14}), 2.13 (s, 6H, Ac), 2.03 (s, 6H, Ac), 1.99 (s, 6H, Ac), 1.92 (s, 6H, H_{CH_3CO}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.1, 170.0, 169.8, 168.3, 159.2, 144.3, 136.1, 124.1, 106.6, 105.6, 100.6, 71.0, 70.9, 69.1, 67.3, 66.7, 62.8, 61.3, 49.7, 37.1, 36.3, 27.2, 20.5, 20.4, 20.4; MS (ESI): m/z calc. $C_{48}H_{64}N_8O_{23}$: 1120.41; found: 1121.42 $[M + H]^+$.

Compound 19: procedure 4. Tetraazide **5** (50 mg, 0.08 mmol), fucoside **13** (16 mg, 0.35 mmol), $CuSO_4$ (32 mg, 0.13 mmol), sodium ascorbate (45 mg mmol), t-BuOH (1 mL) and H_2O (1 mL) were used. Fucosylated tetramer **19** (124 mg, 0.06 mmol, 80%) was obtained after column chromatography (4% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.76 (s, 4H, H_8), 7.54 (br s, 2H, NH), 7.00 (br s, 4H, H_{11}), 6.52 (br s, 2H, H_{12}), 5.30 (dd, 4H, J = 3.30, 10.71 Hz, H_3), 5.23 (d, 4H, J = 2.75 Hz, H_4), 5.17 (d, 4H, J = 3.57 Hz, H_1) 5.10 (dd, 4H, J = 3.57, 10.99 Hz, H_2), 4.82–4.64 (m, 64H, H_9 and H_7), 4.42 (br s, 8H, H_{10}), 4.12 (br q, 4H, H_5), 3.51 (br s, 4H, H_{13}), 2.14 (s, 12H, Ac), 1.99 (s, 12H, Ac), 1.95 (s, 12H, Ac), 1.82 (br s, 2H, H_{14}), 1.08 (d, J = 6.32 Hz, 12H, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 170.1, 167.0, 159.0, 144.1, 136.8, 123.9, 106.0, 105.1, 95.7, 71.0, 67.9, 67.8, 66.6, 64.6, 61.1, 49.7, 36.1, 29.1, 20.7, 20.6, 20.6, 15.7; MS (ESI): m/z calc. $C_{85}H_{110}N_{14}O_{38}$: 1934.71; found: 1935.71 $[M + H]^+$.

Compound 20: procedure 5. Peracetylated dendrimer **19** (36 mg, 0.02 mmol) and MeOH (1 mL) were used. Compound **20** (26 mg, 0.02 mmol, 98%) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, D_2O): δ 7.93 (s, 4H, H_8), 6.47 (s, 4H, H_{11}), 6.11 (s, 2H, H_{12}), 4.81 (s, 4H, H_1), 4.59–4.53 (m, 12H, H_7 and H_4), 4.04 (br s, 8H, H_{10}), 3.63–3.21 (m, 24H, H_{13}, H_9, H_5, H_3 and H_2), 1.74 (br s, 2H, H_{14}), 0.82 (d, 12H, J = 5.49 Hz, H_6); ^{13}C NMR (75 MHz, D_2O + $(CD_3)_2CO$): δ 168.0, 158.2, 143.9, 135.2, 124.9, 105.6, 104.2, 98.3, 71.3, 69.1, 67.5, 66.2, 66.0, 60.3, 49.3, 37.8, 27.1, 14.7; MS (ESI): m/z calc. $C_{61}H_{86}N_{14}O_{28}$: 1430.58; found: 1431.59 $[M + H]^+$.

Compound 21: procedure 3. Acid **2** (17 mg, 0.05 mmol, 1.2 eq.), amine **18** (54.3 mg, 0.05 mmol), BOP (26 mg, 0.06 mmol, 1.2 eq.), DIPEA (51 µl, 0.29 mmol, 6 eq.) and DMF (1 mL) were used. Azido dendrimer **21** (48.1 mg, 0.03 mmol, 71%) was obtained after column chromatography (6% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (s, 2H, H_8), 7.52 (br t, 1H, NH), 7.40 (br t, 1H, NH), 7.05 (d, 2H, J = 2.20 Hz, H_{11}), 7.02 (d, 2H, J = 2.20 Hz, H_{16}), 6.62 (t, 1H, J = 2.20 Hz, H_{12}), 6.53 (br t, 1H, H_{17}), 5.39 (d, 2H, J = 2.47 Hz, H_4), 5.19 (dd, 2H, J = 7.97, 10.43 Hz, H_2), 4.94–5.04 (m, 4H, H_{7a} and H_3), 4.73–4.83 (m, 6H, H_{10} and H_{7b}), 4.64 (d, 2H, J = 7.97 Hz, H_1), 4.40 (br t, 4H, H_9), 4.06–4.22 (m, 8H, H_{18}, H_{6a} and H_5), 3.93 (br t, 2H, H_{6b}), 3.60 (t, 4H, J = 4.67 Hz, H_{19}), 3.50 (br q, 2H, H_{15} and H_{13}), 2.13 (s, 6H, Ac), 2.04 (s, 6H, Ac), 1.97 (s, 6H, Ac), 1.94 (s, 6H, Ac), 1.84 (br s, 2H, H_{14}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 170.1, 170.0, 169.7, 167.3, 167.0, 159.5, 159.0, 144.3, 136.9, 136.7, 123.8, 106.4, 106.0, 104.8, 104.7, 100.4, 70.8, 70.7, 68.8, 67.2, 67.0, 66.5, 62.9, 61.2, 50.0, 49.6, 36.3, 29.4, 20.7, 20.6, 20.6, 20.5; MS (ESI): m/z calc. $C_{59}H_{74}N_{14}O_{26}$: 1394.49; found: 1395.50 $[M + H]^+$.

Compound 22: procedure 4. Azide **21** (38 mg, 0.03 mmol), fucoside **13** (20 mg, 0.06 mmol, 2.2 eq.), $CuSO_4$ (6 mg, 0.02 mmol), sodium ascorbate (8 mg, 0.04 mmol), t-BuOH (1 mL) and H_2O (1 mL) were used. Heterobifunctional dendrimer **22** (37 mg, 0.02 mmol, 66%) was obtained after column chromatography (2% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (s, 4H, H_8), 7.56 (br t, 2H, NH), 7.01 (s, 4H, H_{11} and $H_{11'}$), 6.51 (s, 2H, H_{12} and $H_{12'}$), 5.37 (d, 2H, J = 3.30 Hz, H_4), 5.29 (dd, 2H, J = 3.43, 10.85 Hz, $H_{3'}$), 5.21 (d, 2H, J = 3.85 Hz, $H_{4'}$), 5.18–5.15 (m, 4H, H_2 and $H_{1'}$), 5.08 (dd, 2H, J = 3.57, 10.99 Hz, $H_{2'}$), 5.01–4.94 (m, 4H, H_{7a} and H_3), 4.80–4.74 (m, 12H, H_{10}, H_9, $H_{7a'}$ and H_{7b}), 4.66–4.62 (m, 4H, $H_{7b'}$ and H_1), 4.39 (br d, 8H, $H_{10'}$ and H_9), 4.16–4.05 (m, 6H, H_{6a}, H_5 and $H_{5'}$), 3.93 (br t, 2H, H_{6b}), 3.48 (br q, 4H, H_{13} and $H_{13'}$), 2.13 (s, 6H, Ac), 2.11 (s, 6H, Ac), 2.02 (s, 6H, Ac), 1.98 (s, 6H, Ac), 1.95 (s, 6H, Ac), 1.94 (s, 6H, Ac), 1.91 (s, 6H, Ac), 1.80–1.78 (br m, 2H, H_{14}), 1.06 (d, 6H, J = 6.59 Hz, $H_{6'}$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.3, 170.3, 170.1, 170.0, 169.9, 169.6, 167.0, 166.8, 159.0, 158.9, 144.2, 144.1, 136.8, 136.7, 123.8, 106.2, 106.0, 105.0, 104.8, 100.3, 95.6, 70.9, 70.7, 70.6, 68.7, 67.9, 67.8, 66.9, 66.6, 64.6, 62.9, 61.1, 49.6, 36.1, 29.1, 20.7, 20.6, 20.5, 20.4, 15.7; MS (ESI): m/z calc. $C_{89}H_{114}N_{14}O_{42}$: 2050.72; found: 2051.73 $[M + H]^+$.

Compound 23: procedure 5. Peracetylated mixed glycodendrimer **22** (34.2 mg, 0.02 mmol) and MeOH (1 mL) were used. Unprotected **23** (24 mg, 0.02 mmol, quant.) was obtained as an amorphous solid; ^{1}H NMR (500 MHz, D_2O + $(CD_3)_2CO$): δ 8.04 (s, 2H, H_8), 8.01 (s, 2H, $H_{8'}$), 6.60 (s, 2H, H_{11}), 6.57 (s, 2H, $H_{11'}$), 6.31 (s, 1H, H_{12}), 6.25 (s, 1H, $H_{12'}$), 4.90–4.61 (m, 20H, H_9, H_7, $H_{9'}$, $H_{7'}$, $H_{4'}$ and $H_{1'}$), 4.35 (d, 2H, J = 7.63 Hz, H_1), 4.15–4.13 (m, 8H, H_{10} and $H_{10'}$), 3.82 (br d, 2H, H_3), 3.72–3.45 (m, 16H, H_6, H_5, H_4, H_2, $H_{5'}$, $H_{3'}$ and $H_{2'}$), 3.37

(br t, 4H, H_{13}), 1.39 (br s, 2H, H_{14}), 0.89 (d, 6H, J = 6.72 Hz, $H_{6'}$); ^{13}C NMR (75 MHz, D_2O + $(CD_3)_2CO$): δ 168.1, 158.3, 143.8, 143.3, 135.3, 125.4, 125.0, 105.7, 104.5, 104.3, 101.5, 98.3, 74.8, 72.4, 71.3, 70.2, 69.1, 68.1, 67.5, 66.2, 66.0, 61.2, 60.5, 60.3, 49.3, 38.0, 26.9, 14.7, MS (ESI): m/z calc. $C_{61}H_{86}N_{14}O_{28}$: 1462.57; found: 1463.58 $[M + H]^+$.

Compound 24: procedure 4. Azido ester **6** (94.2 mg, 0.12 mmol), fucoside **13** (158 mg, 0.48 mmol), $CuSO_4$ (47 mg, 0.19 mmol), sodium ascorbate (65 mg, 0.33 mmol), *t*-BuOH (1 mL) and H_2O (1 mL) were used. Tetrafucoside dendron **24** (198 mg, 0.09 mmol, 80%) was obtained after column chromatography (5% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.74 (s, 4H, H_8), 7.18 (d, 2H, J = 1.92 Hz, H_{15}), 6.97–7.07 (m, 2H, NH), 6.92 (br s, 4H, H_{11}), 6.68 (br s, 1H, H_{16}), 6.50 (br s, 2H, H_{12}), 5.33 (dd, 4H, J = 3.44, 10.85 Hz, H_3), 5.26 (d, 4H, J = 2.47 Hz, H_4), 5.18 (d, 4H, J = 3.85 Hz, H_1), 5.12 (dd, 4H, J = 3.57, 10.71 Hz, H_2), 4.85–4.65 (m, 16H, H_9 and H_7) 4.38 (br s, 8H, H_{10}), 4.23–4.11 (m, 8H, H_{14} and H_5), 3.88 (s, 3H, H_{17}), 3.87–3.78 (m, 4H, H_{13}), 2.16 (s, 12H, Ac), 2.00 (s, 12H, Ac), 1.97 (s, 12H, Ac), 1.10 (d, 12H, J = 6.31 Hz, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.5, 170.1, 166.8, 159.6, 159.0, 144.1, 136.9, 132.25, 123.8, 108.1, 106.3, 104.7, 95.6, 71.0, 68.0, 67.9, 67.0, 66.6, 64.7, 61.1, 52.3, 49.7, 39.5, 20.8, 20.7, 20.6, 15.8; MS (ESI): m/z calc. $C_{94}H_{118}N_{14}O_{42}$: 2114.75; found: 2115.75 $[M + H]^+$.

Compound 25: procedure 5. Peracetylated tetrafucoside **24** (150 mg, 0.07 mmol) and MeOH (1 mL) were used. Dendrimer **25** (112 mg, 0.07 mmol, quant.) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, DMSO): δ 8.66 (br t, 2H, NH), 8.18 (s, 4H, H_8), 7.07 (br s, 2H, H_{15}), 7.02 (s, 4H, H_{11}), 6.82 (s, 1H, H_{16}), 6.66 (s, 2H, H_{12}), 4.75–4.73 (m, 12H, H_{10} and H_1), 4.63 (d, 4H, J = 12.37 Hz, H_{7a}), 4.51–4.42 (m, 26H, H_9, H_{7b} and H_4), 4.12 (br t, 4H, H_{14}), 3.81–3.75 (m, 7H, H_{17} and H_5), 3.59-3.46 (m, 12H, H_{13}, H_3 and H_2), 1.05 (d, 12H, J = 6.32 Hz, H_6); ^{13}C NMR (75 MHz, DMSO): δ 165.8, 159.6, 158.9, 144.1, 136.3, 131.6, 124.4, 107.6, 106.4, 104.1, 98.6, 71.6, 69.6, 68.0, 66.4, 66.1, 60.1, 52.3, 48.9, 16.4; MS (ESI): m/z calc. $C_{70}H_{94}N_{14}O_{30}$: 1610.63; found: 1611.63 $[M + H]^+$.

Compound 26: procedure 4. Octaazide **9** (49.7 mg, 0.03 mmol), fucoside **13** (89 mg, 0.27 mmol), $CuSO_4$ (25 mg, 0.10 mmol), sodium ascorbate (34 mg, 0.17 mmol), *t*-BuOH (1 mL) and H_2O (1 mL) were used. Octafucoside dendrimer **26** (107 mg, 0.03 mmol, 82%) was obtained after column chromatography (6% MeOH–DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.78 (s, 8H, H_8), 7.76–7.60 (m, 6H, NH), 6.92 (s, 12H, H_{15} and H_{11}), 6.41–6.38 (m, 6H, H_{16} and H_{12}), 5.29 (dd, 8H, J = 3.30, 10.86 Hz, H_3), 5.22 (d, 8H, J = 2.93 Hz, H_4), 5.17 (d, 8H, J = 3.66 Hz, H_1), 5.09 (dd, 8H, J = 3.66, 10.75 Hz, H_2), 4.79 (d, 8H, J = 12.46 Hz, H_{7a}), 4.71 (s, 16H, H_{10}), 4.63 (d, 8H, J = 12.46 Hz, H_{7b}), 4.28 (s, 16H, H_9), 4.13 (q, 8H, J = 6.11 Hz, H_5), 4.02 (br s, 8H, H_{14}), 3.70 (br s, 8H, H_{13}), 3.52–3.42 (m, 4H, H_{17}), 2.14 (s, 24H, Ac), 1.97 (s, 24H, Ac), 1.95 (s, 24H, Ac), 1.89–1.77 (m, 2H, H_{18}), 1.06 (d, 24H, J = 6.35 Hz, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 170.1, 167.4, 167.2, 159.5, 158.9, 144.0, 136.7, 136.3, 124.0, 106.1, 105.8, 104.9, 104.8, 95.7, 71.0, 68.0, 67.8, 66.4, 64.7, 61.0, 49.6, 39.4, 37.1, 29.6, 20.7, 20.6, 20.5 15.7; MS (ESI): m/z calc. $C_{189}H_{238}N_{30}O_{82}$: 4241.54; found: 2121.78 $[M + 2H]^{2+}$; IR (cm^{-1}): ν = 1744.

Compound 27: procedure 5. Peracetylated fucoside **26** (48.3 mg, 0.01 mmol) and MeOH (1 mL) were used. Fucosylated dendrimer **27** (30 mg, 0.009 mmol, 82%) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, DMSO): δ 8.69 (br t, 4H, NH), 8.17 (s, 8H, H_8), 7.02 (br s, 12H, H_{15} and H_{11}), 6.65 (br s, 6H, H_{16} and H_{12}), 4.74–4.42 (m, 64H, H_{10}, H_9, H_7, H_4 and H_1), 4.11 (br s, 8H, H_{14}), 3.78 (br q, 8H, H_5), 3.58–3.14 (m, 28H, H_{17}, H_{13}, H_3 and H_2), 1.74 (br s, 2H, H_{18}), 1.04 (d, 24H, J = 6.04 Hz, H_6); ^{13}C NMR (75 MHz, DMSO): δ 165.7, 165.5, 159.4, 158.8, 144.1, 136.6, 136.3, 124.4, 106.3, 105.9, 104.1, 98.6, 71.6, 69.6, 68.0, 66.4, 66.1, 60.1, 48.9, 37.2, 29.2, 16.4; MS (ESI): m/z calc. $C_{61}H_{86}N_{14}O_{28}$: 3231.28; found: 1078.11 $[M + 3H]^{3+}$.

Compound 28: procedure 4. Boc-azide **8** (69 mg, 0.07 mmol), galactoside **14** (124 mg, 0.32 mmol, 4.4 eq.), $CuSO_4$ (29 mg, 0.12 mmol), sodium ascorbate (41 mg, 0.20 mmol), *t*-BuOH (1 mL) and H_2O (1 mL) were used. Tetragalactosylated dendron **28** (139.5 mg, 0.06 mmol, 77%) was obtained after column chromatography (4% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (s, 4H, H_8), 7.28 (br t, 2H, NH), 7.00 (br s, 2H, H_{15}), 6.93 (d, 4H, J = 1.10 Hz, H_{11}), 6.52 (br t, 1H, H_{16}), 6.49 (t, 2H, J = 2.20 Hz, H_{12}), 5.38 (d, 4H, J = 2.75 Hz, H_4), 5.22–5.16 (m, 5H, H_2 and NH), 5.12–4.94 (m, 8H, H_{7a} and H_3), 4.79–4.72 (m, 12H, H_{10} and H_{7b}), 4.65 (d, 4H, J = 7.69 Hz, H_1), 4.35 (t, 8H, J = 4.95 Hz, H_9), 4.03–4.08 (m, 12H, H_{14}, H_{6a} and H_5), 3.94 (br t, 4H, H_{6b}), 3.79–3.73 (m, 4H, H_{13}), 3.46–3.44 (m, 2H, H_{17}), 3.20–3.18 (m, 2H, H_{19}), 2.12 (s, 12H, Ac), 2.04 (s, 12H, Ac), 1.95 (s, 12H, Ac), 1.92 (s, 12H, Ac), 1.71–1.67 (m, 2H, H_{18}), 1.41 (s, 9H, H_{12}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.4, 170.2, 170.1, 169.8, 166.8, 159.6, 159.0, 144.3, 137.0, 136.8, 123.8, 106.5, 105.7, 104.8, 104.6, 100.4, 79.5, 70.8, 70.7, 68.8, 67.0, 66.5, 63.0, 61.2, 49.6, 39.4, 37.1, 36.0, 29.7, 28.4, 20.7, 20.6, 20.4, 20.5; MS (ESI): m/z calc. $C_{109}H_{140}N_{16}O_{51}$: 2488.89; found: 2489.89 $[M + H]^+$; IR (cm^{-1}): ν = 1750.

Compound 29. Boc derivative **28** (45 mg, 0.02 mmol) was treated with TFA (87 µl, 1.17 mmol) and CH_2Cl_2 (1 mL) for 4 h at 25 °C Amine **29** (31.9 mg, 0.01 mmol, 74%) was obtained after column chromatography (8% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.18–8.11 (m, 3H, NH), 7.86 (br s, 1H, NH), 7.74 (s, 4H, H_8), 7.69 (br s, 4H, H_{11}), 6.96 (br s, 2H, H_{15}), 6.45 (br s, 2H, H_{12}), 6.36 (br s, 1H, H_{16}), 5.38 (d, 4H, J = 3.30 Hz, H_4), 5.17 (dd, 4H, J = 7.97, 10.44 Hz, H_2), 5.02 (dd, 4H, J = 3.30, 10.44 Hz H_3), 4.93 (d, 4H, J = 12.64 Hz, H_{7a}), 4.77–4.64 (m, 16H, H_{10}, H_{7b} and H_1), 4.30 (br s, 8H, H_9), 4.19–4.06 (m, 12H, H_{14}, H_{6a} and H_5), 3.98–3.93 (m, 4H, H_{6b}), 3.67 (br s, 4H, H_{13}), 3.46 (br s, 2H, H_{17}), 2.95–2.87 (m, 4H, H_{19} and H_{18}), 2.11 (s, 12H, Ac), 2.02 (s, 12H, Ac), 1.95 (s, 12H, Ac), 1.92 (s, 12H, Ac); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.5, 170.2, 170.1, 169.8, 167.3, 159.5, 158.9, 144.1, 136.5, 135.4, 124.1, 106.3, 105.7, 105.1, 100.4, 70.8, 70.7, 68.8, 67.0, 66.4, 62.7, 61.2, 49.6, 39.4, 37.1, 36.0, 29.7, 20.6, 20.5, 20.4; MS (ESI): m/z calc. $C_{104}H_{132}N_{16}O_{49}$: 2388.83; found: 2389.84 $[M + H]^+$.

Compound 30: procedure 3. Acid **7** (13.6 mg, 0.02 mmol, 1.2 eq.), amine **29** (34 mg, 0.01 mmol), BOP (7.6 mg, 0.02 mmol, 1.2 eq.), DIPEA (15 μl, 0.09 mmol, 6 eq.) and DMF (2 mL) were used. Tetragalactosylated azide **30** (31 mg, 0.10 mmol, 69%) was obtained after column chromatography (6% MeOH–DCM); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.72 (s, 8H, H_8), 7.65 (br t, 4H, NH), 7.06 (d, 4H, J = 2.20 Hz, $H_{11'}$), 6.97 (br t, 1H, NH), 6.93 (br d, 6H, H_{15} and H_{11}), 6.76 (br s, 2H, $H_{15'}$), 6.58 (t, 2H, J = 2.20 Hz, $H_{12'}$), 6.44 (br s, 3H, H_{16} and H_{12}), 6.27 (br s, 1H, $H_{16'}$), 5.38 (d, 4H, J = 3.30 Hz, H_4), 5.18 (dd, J = 7.97, 10.44 Hz, 4H, H_2), 5.01 (dd, J = 3.30, 10.44 Hz 4H, H_3), 4.95 (d, 4H, J = 12.36 Hz, H_{7a}), 4.75 (d, 4H, J = 12.36 Hz, H_{7b}), 4.69–4.63 (m, 12H, H_{10} and H_1), 4.28 (br t, 8H, H_9), 4.19–4.07 (m, 20H, H_{14}, $H_{10'}$, H_{6a} and H_5), 3.96–3.92 (m, 8H, $H_{14'}$ and H_{6b}), 3.73 (br s, 8H, H_{13} and $H_{13'}$), 3.56–3.48 (m, 12H, H_{17}, $H_{17'}$ and $H_{9'}$), 2.12 (s, 12H, Ac), 2.03 (s, 12H, Ac), 1.95 (s, 12H, Ac), 1.92 (s, 12H, Ac), 1.80–1.82 (br qt, 2H, H_{18}); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.9, 170.6, 170.5, 170.1, 167.8, 167.6, 160.0, 159.9, 159.8, 159.3, 144.6, 137.1, 136.9, 136.8, 136.5 124.4, 106.7, 106.2, 105.4, 105.2, 100.9, 71.2, 71.1, 69.2, 67.6, 67.4, 66.8, 63.3, 61.6, 50.4, 50.0, 39.9, 37.5, 36.5, 21.7, 21.0, 20.9; MS (ESI): m/z calc. $C_{137}H_{166}N_{30}O_{58}$: 3159.10; found: 1580.55 $[M + 2H]^{2+}$.

Compound 31: procedure 4. Intermediate **30** (31 mg, 0.001 mmol), fucoside **13** (14.1 mg, 0.04 mmol, 4.4 eq.), $CuSO_4$ (3.9 mg, 0.02 mmol), sodium ascorbate (5.44 mg, 0.03 mmol), t-BuOH (1 mL) and H_2O (1 mL) were used. Mixed dendrimer **31** (30 mg, 0.007 mmol, 68%) was obtained after column chromatography (5% MeOH–DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.76 (s, 4H, H_8), 7.74 (s, 4H, $H_{8'}$), 7.72–7.55 (m, 4H, NH), 6.9 (s, 4H, $H_{15'}$ and H_{15}), 6.90 (s, 8H, $H_{11'}$ and H_{11}), 6.42 (s, 4H, $H_{12'}$ and H_{12}), 6.39 (s, 2H, $H_{16'}$ and H_{16}), 5.38 (s, 4H, H_4), 5.31–5.28 (m, 4H, $H_{3'}$), 5.22–5.16 (m, 12H, $H_{4'}$, H_2 and $H_{1'}$), 5.11–5.08 (m, 4H, $H_{2'}$), 5.03–4.94 (m, 8H, H_{7a} and H_3), 4.80–4.62 (m, 32H, H_{10}, $H_{9'}$, H_{7b}, $H_{7'}$ and H_1), 4.28 (br s, 16H, $H_{10'}$, and H_9) 4.17–3.94 (m, 20H, H_{13}, H_6, $H_{5'}$ and H_5), 3.73 (br s, 8H, H_{14}), 3.49 (br s, 4H, H_{17}), 2.13 (s, 12H, Ac), 2.11 (s, 12H, Ac), 2.02 (s, 12H, Ac), 1.97 (s, 12H, Ac), 1.95 (s, 12H, Ac), 1.92 (s, 12H, Ac), 1.91 (s, 12H, Ac), 1.82 (br s, 2, H_{18}), 1.07 (d, 12H, J = 6.35 Hz, H_6); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.6, 170.4 ,170.2, 170.3, 170.1, 170.0, 169.7, 167.1, 159.5, 158.9, 158.8, 144.1, 144.0, 136.7, 136.3, 124.0, 106.2, 106.1, 105.7, 104.8, 104.7, 103.6, 100.4, 95.6, 70.9, 70.7, 70.6, 68.7, 67.9, 67.8, 67.1, 66.9, 66.4, 65.7, 64.6, 62.8, 61.1, 61.0, 49.5, 39.3, 36.6, 24.6, 20.7, 20.6, 20.5, 15.7; MS (ESI): m/z calc. $C_{197}H_{246}N_{30}O_{90}$: 4471.56; found: 2236.78 $[M + 2H]^{2+}$. IR (cm^{-1}); ν = 1747.

Compound 32: procedure 5. Peracetylated dendrimer **31** (22.2 mg, 0.005 mmol) and MeOH (1 mL) were used. Unprotected mixed dendrimer **32** (16.4 mg, 0.005 mmol, quant.) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, DMSO): δ 8.67 (br s, 2H, NH), 8.46 (br s, 1H, NH), 8.17 (s, 4H, H_8), 8.16 (s, 4H, $H_{8'}$), 7.02 (br s, 12H, H_{15}, $H_{15'}$, H_{11} and $H_{11'}$), 6.67 (br s, 6H, H_{16}, $H_{16'}$, H_{12} and $H_{12'}$), 4.91–4.40 (m, 56H, H_{10}, $H_{10'}$, H_9, $H_{9'}$, H_7, $H_{7'}$, $H_{4'}$ and $H_{1'}$), 4.19 (d, 4H, J = 6.53 Hz, H_1), 4.11 (br s, 8H, H_{13} and $H_{13'}$), 3.78 (br q, 4H, $H_{5'}$), 3.61–3.26 (m, 44H, H_{17}, $H_{17'}$, H_{14}, $H_{14'}$, H_6, H_5, H_4, H_3, $H_{3'}$, H_2, and $H_{2'}$), 1.74 (br s, 2H, H_{18}), 1.04 (d, 12H, J = 6.59 Hz, $H_{6'}$); ^{13}C NMR (75 MHz, DMSO): δ 165.8, 159.4, 158.8, 144.1, 143.9, 136.6, 136.3, 124.7, 124.4, 106.3, 102.7, 98.6, 75.3, 73.4, 71.6, 70.5, 69.6, 68.2, 68.0, 66.4, 66.1, 61.3, 60.5, 60.1, 48.9, 37.3, 29.0; (MS (ESI): m/z calc. $C_{141}H_{190}N_{30}O_{62}$: 3295.26; found: 1099.42 $[M + 3H]^{3+}$.

Compound 33: procedure 4. Azido ester **10** (20.2 mg, 0.01 mmol), fucoside **13** (32.5 mg, 0.09 mmol, 8.8 eq.), $CuSO_4$ (9 mg, 0.04 mmol), sodium ascorbate (12 mg, 0.06 mmol), THF (1 mL) and H_2O (1 mL) were used. Octamer **33** (40 mg, 0.009 mmol, 77%) was obtained after column chromatography (3% MeOH–DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.77 (s, 8H, H_8), 7.54 (br t, 4H, NH), 7.36 (br s, 2H, NH), 7.10 (br s, 2H, H_{19}), 6.92 (br s, 8H, H_{11}), 6.82 (br s, 4H, H_{15}), 6.70 (br s, 1H, H_{20}) 6.42 (br s, 4H, H_{12}), 6.37 (br s, 2H, H_{16}), 5.30 (dd, 8H, J = 3.42, 10.74 Hz, H_3), 5.23 (d, 8H, J = 2.93 Hz, H_4), 5.17 (d, 8H, J = 3.42 Hz, H_1), 5.11 (dd, 8H, J = 3.42, 10.74 Hz, H_2), 4.79 (d, 8H, J = 12.70 Hz, H_{7a}), 4.72 (s, 16H, H_9), 4.64 (d, 8H, J = 12.70 Hz, H_{7b}), 4.29 (br s, 16H, H_{10}), 4.16–4.12 (m, 12H, H_{18} and H_5), 3.97 (br s, 8H, H_{14}), 3.85 (s, 3H, H_{21}), 3.73–3.70 (m, 12H, H_{17} and H_{13}), 2.15 (s, 24H, Ac), 1.98 (s, 24H, Ac), 1.96 (s, 24H, Ac), 1.08 (d, 24H, J = 6.34 Hz, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 170.1, 167.1, 158.6, 158.9, 144.1, 136.7, 136.4, 123.9, 106.2, 104.9, 95.7, 71.0, 68.0, 67.9, 66.5, 64.7, 61.1, 54.8, 49.6, 39.5, 20.7, 20.6, 15.8.

Compound 34: procedure 5. Peracetylated **33** (10.8 mg, 0.002 mmol) and MeOH (1 mL) were used. Octa-fucosylated dendron **34** (8 mg, 0.002 mmol, quant.) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, DMSO): δ 8.69 (s, 6H, NH), 8.17 (s, 8H, H_8), 7.03 (s, 14H, H_{19}, H_{15} and H_{11}). 6.65 (s, 7H, H_{20}, H_{16} and H_{12}), 4.74–4.43 (m, 64H, H_{10}, H_9, H_7, H_4 and H_1), 4.11 (s, 8H, H_{14}), 3.78 (s, 8H, H_5), 3.76–3.28 (m, 35H, H_{21}, H_{18}, H_{17}, H_{13}, H_3 and H_2), 1.03 (d, 24H, J = 6.32 Hz, H_6); ^{13}C NMR (75 MHz, DMSO): δ 165.9, 165.7, 159.7, 159.4, 158.9, 158.8, 144.1, 144.0, 136.4, 136.1, 124.4, 124.2, 106.4, 105.8, 98.6, 98.5, 71.6, 69.6, 68.0, 66.4, 66.1, 63.1, 60.1, 31.3, 16.4; MS (ESI): m/z calc. $C_{150}H_{198}N_{30}O_{62}$: 3411.33; found: 1706.67 $[M + 2H]^{2+}$.

Compound 35: procedure 4. 16-Mer **12** (66 mg, 0.02 mmol), fucoside **13** (106 mg, 0.32 mmol, 17.6 eq.), $CuSO_4$ (29 mg, 0.12 mmol), sodium ascorbate (41 mg, 0.2 mmol), t-BuOH (1 mL) and H_2O (1 mL) were used. Fucosylated dendrimer **35** (78.7 mg, 0.009 mmol, 49%) was obtained after column chromatography (7% MeOH–DCM); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.81 (br s, 12H, NH), 7.77 (s, 16H, H_8), 6.97 (br s, 16H, H_{11}), 6.85 (br s, 4H, H_{19}), 6.76 (br s, 8H, H_{15}), 6.42 (br s, 8H, H_{10}), 6.26 (br s, 6H, H_{20} and H_{16}), 5.28 (dd, 16H, J = 3.42, 10.74 Hz, H_3), 5.21 (d, 16H, J = 2.93 Hz, H_4), 5.16 (d, 16H, J = 3.91 Hz, H_1), 5.09 (dd, 16H, J = 3.91, 10.74 Hz, H_2), 4.77 (d, 16H, J = 12.70 Hz, H_{7a}), 4.69 (br s, 32H, H_9), 4.61 (d, 16H, J = 12.70 Hz, H_{7b}), 4.26 (br s, 32H, H_{10}), 4.12 (br q, 16H, H_5), 3.93 (br s, 24H, H_{18} and H_{14}), 3.64 (br s, 24H, H_{17} and H_{13}), 3.49 (br s, 4H, H_{21}), 2.50 (br s, 2H, H_{22}), 2.13 (s, 48H, H_{CH_3CO}), 1.96 (s, 48H, H_{CH_3CO}), 1.94 (s, 48H,

H_{CH_3CO}), 1.05 (d, 48H, J = 6.35 Hz, H_6); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 170.1, 167.1, 159.5, 159.4, 158.9, 144.0, 136.6, 136.2, 124.0, 106.1, 105.0, 95.6, 71.0, 67.9, 67.8, 66.4, 64.6, 61.0, 49.5, 39.5, 29.6, 20.7, 20.6, 20.5, 15.7; MS (ESI): m/z calc. $C_{397}H_{494}N_{62}O_{170}$: 8854.48; found: 1771.81 $[M + 5H]^{5+}$; IR (cm^{-1}): ν = 1751.

Compound 36: procedure 5. Peracetylated 16-mer fucosylated dendrimer **35** (77 mg, 0.009 mmol) and MeOH (1 mL) were used. Dendrimer **36** (57 mg, 0.008 mmol, 97%) was obtained as an amorphous solid; ^{1}H NMR (300 MHz, D_2O, HT): δ 8.32 (s, 16H, H_8), 7.13 (br s, 28H, H_{19}, H_{15} and H_{11}), 6.77 (br d, 14H, H_{20}, H_{16} and H_{12}), 5.28 (d, 16H, J = 3.22 Hz, H_4), 4.99 (br s, 64H, H_9, H_{7a} and H_1), 4.63 (br s, 32H, H_{10} and H_{7b}), 4.31–3.92 (m, 112H, H_{18}, H_{17}, H_{14}, H_{13}, H_5, H_3 and H_2), 3.65 (br s, 4H, H_{21}), 2.07 (br s, 2H, H_{22}), 1.35 (d, 48H, J = 6.45 Hz, H_6); ^{13}C NMR (75 MHz, DMSO): δ 169.0, 160.2, 159.7, 145.2, 136.8, 125.8, 107.5, 107.3, 106.0, 99.5, 72.6, 70.7, 69.0, 67.4, 61.6, 50.4, 40.2, 16.0; MS (ESI): m/z calc. $C_{301}H_{398}N_{62}O_{122}$: 6832.69; found: 1709.17 $[M + 4H]^{4+}$.

Acknowledgements

We are thankful to Natural Science and Engineering Research Council of Canada (NSERC) for a Canadian Research Chair in Therapeutic Chemistry (to R. R.). We are also thankful to Doctor Anne Imberty of the University of Grenoble (France) for kindly providing PA-IIL.

References

1 P. Rousel and G. Lamblin, *Adv. Exp. Med. Biol.*, 2003, **535**, 17.
2 A. Scharfman, S. Degroote, J. Beau, G. Lamblin, P. Roussel and J. Mazurier, *Glycobiology*, 1999, **9**, 757.
3 (*a*) N. Gilboa-Garber, *Lectins Biol., Biochem., Clin. Biochem.*, 1983, **3**, 495; (*b*) D. Tielker, S. Hacker, R. Loris, M. Strathmann, J. Wingender, S. Wilhelm, F. Rosenau and K.-E. Jaeger, *Microbiology*, 2005, **151**, 1313.
4 N. Gilboa-Garber, *FEBS Lett.*, 1972, **28**, 93.
5 N. Garber, U. Guempel, A. Belz, N. Gilboa-Garber and R. J. Doyle, *Biochim. Biophys. Acta*, 1992, **1116**, 331.
6 N. Gilboa-Garber, D. J. Katcoff and N. C. Garber, *FEMS Immunol. Med. Microbiol.*, 2000, **29**, 53.
7 N. Garber, U. Guempel, N. Gilboa-Garber and R. J. Doyle, *FEMS Microbiol. Lett.*, 1987, **48**, 331.
8 (*a*) M. Haraldsson and H. Lönn, *J. Biol. Chem.*, 1983, **258**, 199; (*b*) J. J. Lundquist and E. J. Toone, *Chem. Rev.*, 2002, **102**, 555.
9 L. L. Kiessling, J. E. Gestwicki and L. E. Strong, *Angew. Chem., Int. Ed.*, 2006, **45**, 2348.
10 J. D. Reuter, A. Myc, M. M. Hayes, Z. Gan, R. Roy, D. Q. R. Yin, L. T. Piehler, R. Esfand, D. A. Tomalia and J. R. Baker, *Bioconjugate Chem.*, 1999, **10**, 271.
11 S. André, R. J. Pieters, I. Vrasidas, H. Kaltner, I. Kuwabara, F.-T. Liu, R. M. J. Liskamp and H.-J. Gabius, *ChemBioChem*, 2001, **2**, 822.
12 (*a*) R. Roy, *Trends Glycosci. Glycotechnol.*, 2003, **15**, 291; (*b*) R. J. Pieters, *Trends Glycosci. Glycotechnol.*, 2004, **16**, 243; (*c*) D. Pagé and R. Roy, *J. Am. Chem. Soc.*, 1997, **119**, 2088; (*d*) E. K. Woller, E. D. Walter, J. R. Morgan, D. J. Singel and M. J. Cloninger, *J. Am. Chem. Soc.*, 2003, **125**, 8820; (*e*) M. Kôhn, J. M. Benito, C. Ortiz Mellet, T. K. Lindhorst and J. M. Garcia Fernandez, *ChemBioChem*, 2004, **5**, 771.
13 Y. C. Lee and R. T. Lee, *Acc. Chem. Res.*, 1995, **28**, 321.
14 E. Buhleier, W. Wehner and F. Vögtle, *Synthesis*, 1978, 155.
15 C. J. Hawker and J. M. J. Fréchet, *J. Am. Chem. Soc.*, 1990, **112**, 7638.
16 R. Huisgen, *Pure Appl. Chem.*, 1989, **61**, 613.
17 H. C. Kolb, M. G. Finn and K. B. Sharpless, *Angew. Chem., Int. Ed.*, 2001, **40**, 2004.
18 A. Sarkar, P. Ilankumaran, P. Kisanga and J. G. Verkade, *Adv. Synth. Catal.*, 2004, **346**, 1093.
19 A. Imberty, M. Wimmerova, E. P. Mitchell and N. Gilboa-Garber, *Microbes Infect.*, 2004, **6**, 221.