# Glycodendrimers based on cellobiosyl-derived monomers[1]

**Stacey A. Kalovidouris, W. Bruce Turnbull, and J. Fraser Stoddart**

**Abstract**: Reductive amination of suitably functionalized trisaccharide monomers, based on cellobiosylgalacto residues, has made it possible to construct high-molecular-weight glycodendrons and glycodendrimers for the display of large bioactive oligosaccharides and proteins in a well-defined manner.

*Key words*: cellobiose, glycodendrimers, reductive amination, trisaccharide monomers.

**Résumé** : L'amination réductrice de trisaccharides monomères fonctionnalisés de façon appropriée et attachés à de résidus cellobiosylgalactose permet de construire des glycodendrons et des glycodendrimères de masses moléculaires élevées grâce auxquels on peut présenter de grosses molécules d'oligosaccharides et de protéines bioréactifs d'une façon bien définie.

*Mots clés* : cellobiose, glycodendrimères, amination réductrice, trisaccharides monomères.

## Introduction

The incorporation of carbohydrates into dendritic structures continues to be pursued vigorously by a growing number of research groups (1). The driving force behind glycodendrimer research has been the desire to mimic Nature's use of multivalency (2) to enhance both the avidity and selectivity of interactions between oligosaccharide ligands and their corresponding protein receptors. There is a growing appreciation (3) that the structure of the underlying dendritic scaffold is as important to achieving efficient multivalent interactions as presenting multiple copies of the ligand. Thus, developing novel dendritic structures for this purpose may be considered to be a worthy pursuit. We (4, 5) and others (6) have identified that, in addition to the bioactive ligands, oligosaccharides show great potential as building blocks for multivalent and dendritic scaffolds. In this sense, carbohydrates can provide (7) vast diversity in constitution, configuration and conformation in addition to lending themselves well as multifunctional building blocks for constructing branched structures. Small changes in constitution can provide large differences in biological activities, e.g., in the highly selective recognition (8) of α-2,3- and α-2,6-linked sialosides by Siglecs 1 and 2, respectively. But perhaps the most subtle, yet profound, of possible structural changes results from the inversion of configuration at a single carbon atom such as in the repeating unit of the common (1→4)-linked polymers of glucose — i.e., amylose and cellulose (9). The α(1→4)-linkages in amylose promote the adoption of a helical structure by the polymer, in which intramolecular hydrogen bonding between primary and secondary hydroxy groups on adjacent turns of the helix, leads to the formation of channels capable of supramolecular complexation. In contrast, the β(1→4)-linkages of cellulose lead to a more extended structure promoting intermolecular hydrogen bonding between polymer strands and insoluble crystalline fibers. In addition to the changes in overall shape, the spacial distributions of substituent groups (e.g., C-6 hydroxymethyl groups) on the polymers are also different. Whereas, in amylose, all of the primary hydroxy functions point away from the same side of the polymer chain — reminiscent of the primary face of cyclodextrins — the same groups in cellulose are directed in opposing directions from adjacent sugar residues. The graphical representations of maltosyl and cellobiosyl residues shown in Fig. 1 illustrate the background behind our motivation to be able to compare

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*It was Ray Lemieux who provided intellectual leadership in the field of carbohydrate chemistry during the second half of the 20th century. His contribution to our fundamental knowledge of the nature of the carbohydrates was profound, all-encompassing, and far-reaching. During the last decade or so, our basic understanding of the mechanisms by which carbohydrates are bound by proteins has advanced enormously. These advances were only possible because of the seminal work done by Lemieux in the 1980s. We dedicate this paper to the memory of Ray.*

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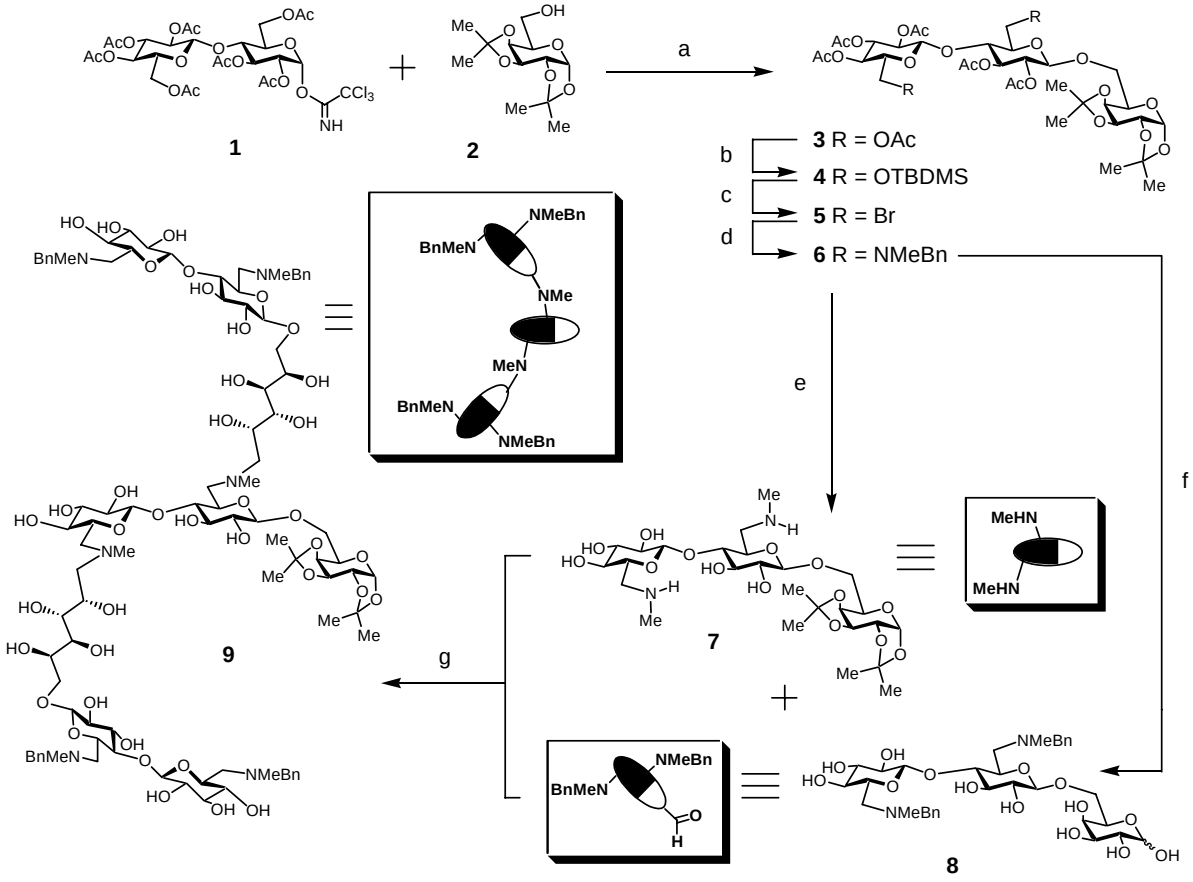
**Scheme 1.** (*a*) TMSOTf, $CH_2Cl_2$, 4 Å MS (75%); (*b*) NaOMe, MeOH; TBDMSCl, $C_5H_5N$; $Ac_2O$, $C_5H_5N$ (50% over three steps); (*c*) $Br_2$, $PPh_3$, $CH_2Cl_2$ (96%); (*d*) NHMeBn (57%); (*e*) NaOMe, MeOH (90%); $H_2$, $Pd(OH)_2$ on C, MeOH (quant.); (*f*) NaOMe, MeOH (90%); TFA, $H_2O$ (9:1) (80%); (*g*) $NaCNBH_3$, MeOH, AcOH (94%).




and contrast glycodendrons and glycodendrimers incorporating these two diastereoisomerically related residues.

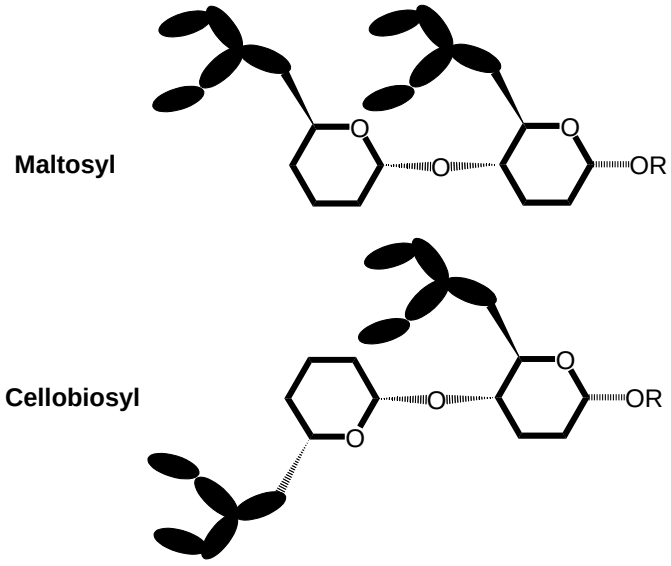
Recently, we have outlined (5) an approach for the synthesis of dendritic oligosaccharides via reductive amination of a reducing sugar, using a trisaccharide bearing two methylamino groups. Our first choice was to use a maltosylgalactose repeating unit that incorporates the α(1→4)-linkage (associated with amylose) between the branching points of resulting dendrons. Here, we describe the synthesis of analogous compounds that incorporate the corresponding β(1→4)-linkage of cellobiose in a first step toward the general development of oligosaccharide-based dendrimers that exhibit broad structural diversity derived from their constituent building blocks.

## Results and discussion

### Synthesis of the $AB_2$ monomers and the dendron

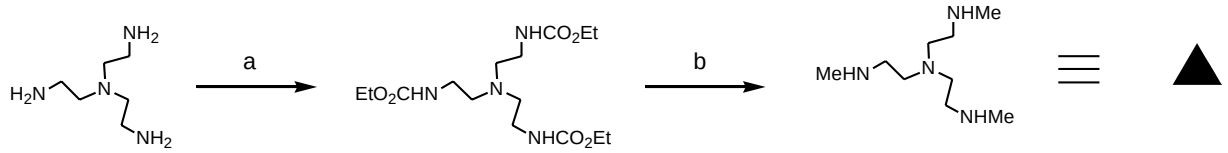
The synthesis of the first-generation cellobiosylgalacto-based dendron **9** is outlined in Scheme 1. Starting from the known (10) peracetylated α-cellobiosyl-trichloroacetimidate **1** as the glycosyl donor and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**2**) as the glycosyl acceptor, the protected trisaccharide **3** was obtained in 75% yield using TMSOTf as the promoter. With the ultimate objective being that of introducing protected secondary amino functions at the primary

**Fig. 1.** A graphical representation of maltosyl and cellobiosyl residues.




positions of the two glucopyranosyl residues, the *O*-acetyl protecting groups were removed using Zemplén conditions. Thereafter, the two primary hydroxyl groups were protected

**Scheme 2.** (*a*) $ClCO_2Et$, $C_6H_6$, $H_2O$, KOH (40%); (*b*) $LiAlH_4$, THF (56%).




**11** **12** **13**

**Fig. 2.** DEPT 135 spectrum ($CD_3OD$, 125 MHz) of dendron **9**.

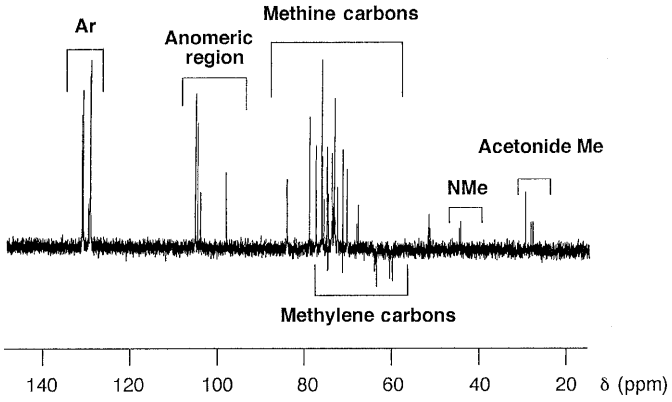
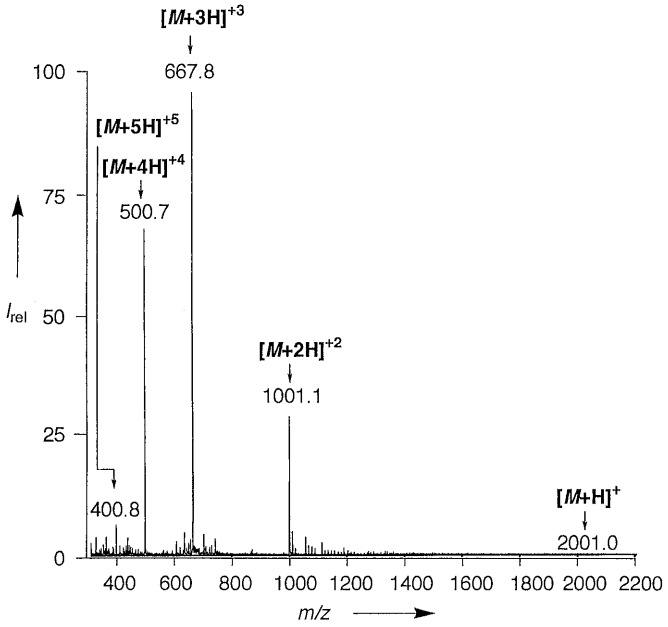



**Fig. 3.** ES-MS spectrum of dendron **9**.




as their TBDMS ethers before the secondary ones were reacetylated to afford the fully protected trisaccharide **4**. The last three steps were performed in an overall yield of 50%. The bis-silyl ether was then converted directly into the dibromide **5** in 96% yield with triphenylphosphine and bromine. When **5** was heated with neat benzylmethylamine, the fully protected trisaccharide (**6**) was obtained in 57% yield. One of the required $AB_2$ monomers, namely the trisaccharide (**7**), carrying two secondary amino functions, was isolated quantitatively following hydrogenolysis of **6** in the presence of Pearlman's catalyst. The other $AB_2$ monomer (**8**) was obtained in 80% yield following removal of the cyclic acetals in **6** by TFA-catalyzed hydrolysis. The two $AB_2$ monomers (**7** and **8**) were coupled by reductive amination to give the first-generation dendron (**9**) in 94% yield. DEPT-135 $^{13}C$ NMR and ES-MS spectra are presented in Figs. 2 and 3, respectively. Of the 11 different methylene carbon atoms present in the dendron, seven can be identified as negative peaks in the $^{13}C$ NMR spectrum. The ES-MS reveals peaks at 2001.0, 1001.1, 667.8, 500.7, and 400.8 for the $[M + H]^+$, $[M + 2H]^{2+}$, $[M + 3H]^{3+}$, $[M + 4H]^{4+}$, and $[M + 5H]^{5+}$ ions obtained from the dendron (**9**).

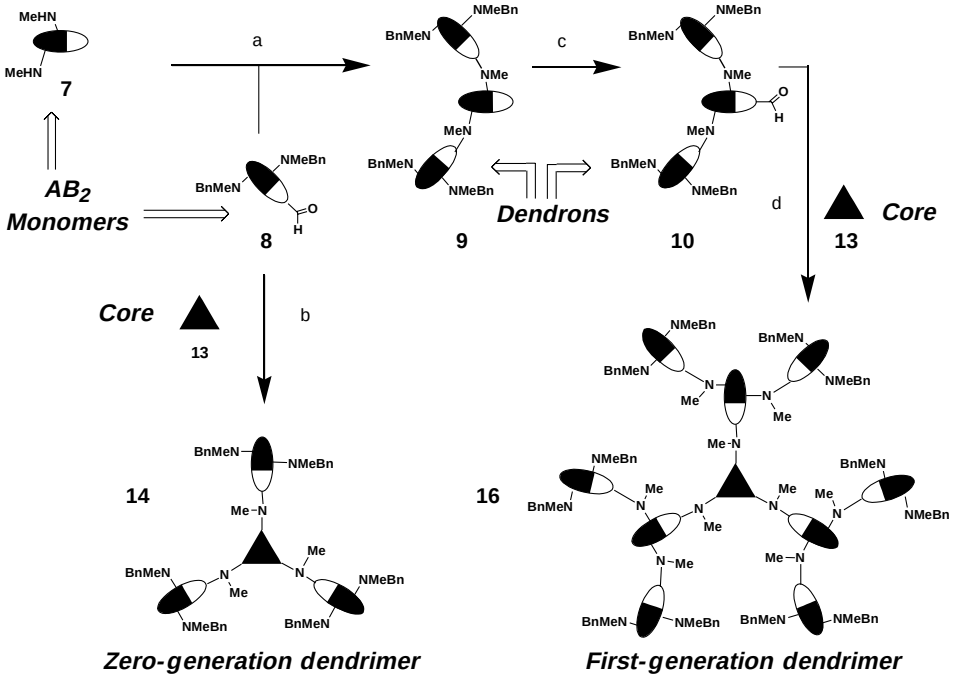
## Synthesis of the core

The synthesis of the tris[2-(methylamino)ethyl]amine-based core (**13**) is depicted in Scheme 2. A published procedure (11) was followed to obtain **13** in two steps, starting from tris(2-aminoethyl)amine (**11**). In the first step, the triscarbamate (**12**) was prepared by reacting **11** with ethylchloroformate under basic conditions. In the second step, **12** was reduced with lithium aluminum hydride to afford the tris[2-(methylamino)ethyl]amine core (**13**).

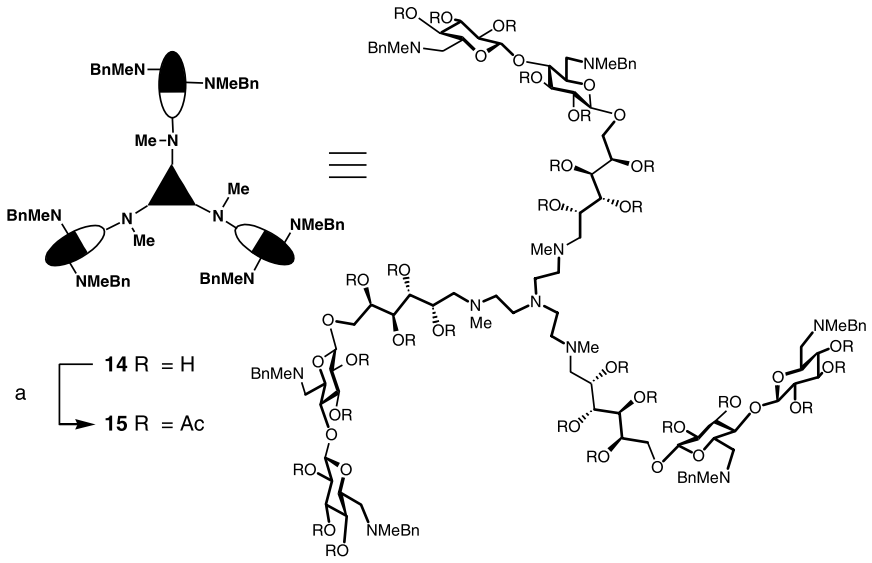
## Synthesis of the glycodendrimers

The syntheses of the zero-generation glycodendrimer (**14**) and the first-generation glycodendrimer (**16**) are summarized in Scheme 3. The graphical representations of molecular structures employed in this scheme are defined in Schemes 1 and 2. The zero-generation glycodendrimer (**14**) was isolated in 69% yield following coupling by reductive amination of the $AB_2$ monomer (**8**) with the tris[2-(methylamino)ethyl]amine core (**13**). This glycodendrimer was easily soluble in water. However, upon its acetylation (Scheme 4), the resulting peracetylated derivative (**15**) was soluble in polar organic solvents, e.g., methanol and dimethylformamide, but not in chlorinated solvents, e.g., dichloromethane and chloroform. The MALDI-TOF mass spectrum (Fig. 4) of **15** exhibited an $[M + H]^+$ peak at *m*/*z* 3407 with an isotope distribution that matches well with that of the calculated one. Employing reductive amination once again to couple the dendron (**10**) with the tris[2-(methylamino)ethyl]amine core (**13**) results in the formation of the first-generation glycodendrimer (**16**) in 56% yield. This glycodendrimer (**16**) and its peracetylated derivative (**17**) (see Scheme 5) exhibit solubility characteristics similar to those already described for the zero-generation counterparts **14** and **15**. The MALDI-TOF mass spectrum (Fig. 5) of **17** exhibited an $[M + H]^+$ peak at *m*/*z* 9078 along with fragmentation peaks at *m*/*z* 8062, 7159, 6227, 5153, 4305, 3017, and 1987. These fragmentations

**Scheme 3.** (*a*) $NaCNBH_3$, AcOH, MeOH (94%); (*b*) $NaCNBH_3$, AcOH, MeOH (69%); (*c*) TFA, $H_2O$ (9:1) (80%); (*d*) $NaCNBH_3$, AcOH, MeOH (56%).




**Scheme 4.** (*a*) $Ac_2O$, $C_5H_5N$, DMAP (45%).




result from cleavages of glycosyl linkages and β-elimination on the amine linkages at the positions indicated by open arrows in Fig. 5. These types of cleavages in oligosaccharide derivatives are well precedented in the literature (12).

## Experimental section

### General methods

Chemicals were purchased from Aldrich and were used as received except for sodium cyanoborohydride (Aldrich), which was purified by the published procedure (13). Reactions were carried out under a dry argon atmosphere and the solvents were dried prior to use according to literature procedures (14). Thin-layer chromatography (TLC) was carried out on aluminum sheets precoated with silica gel 60F (Merck 5554). The plates were inspected by UV light and developed either with iodine vapor or by treatment with 5% $H_2SO_4$ in EtOH, followed by heating. Column chromatography was carried out using silica gel 60F (Silicycle). Preparative reversed phase chromatography was performed on fully endcapped C-18, or on C-8 silica gel 100 (230–400 mesh, Fluka), and gel permeation chromatography (GPC) was performed using a 25 × 900 mm column of Sephadex LH20 resin (Sigma), eluting with MeOH. Analytical reversed

**Scheme 5.** (*a*) $Ac_2O$, $C_5H_5N$, DMAP (33%).

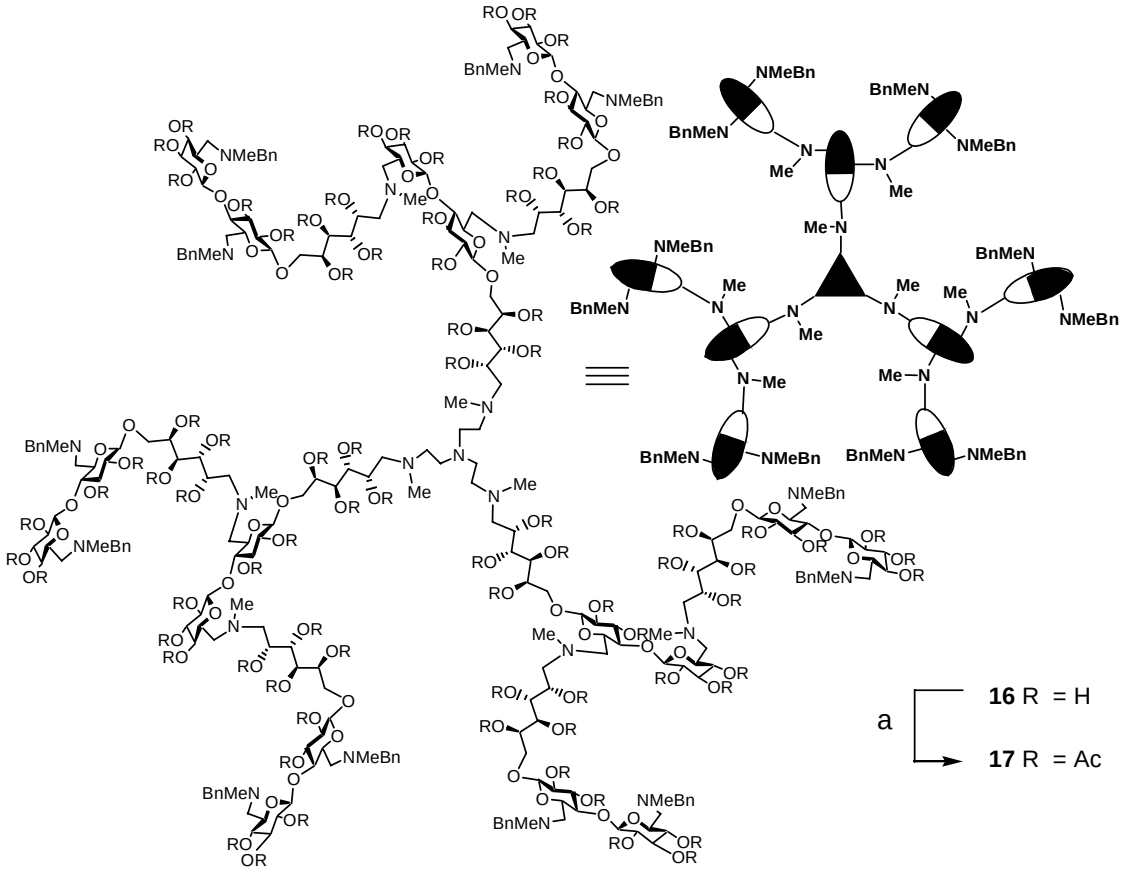
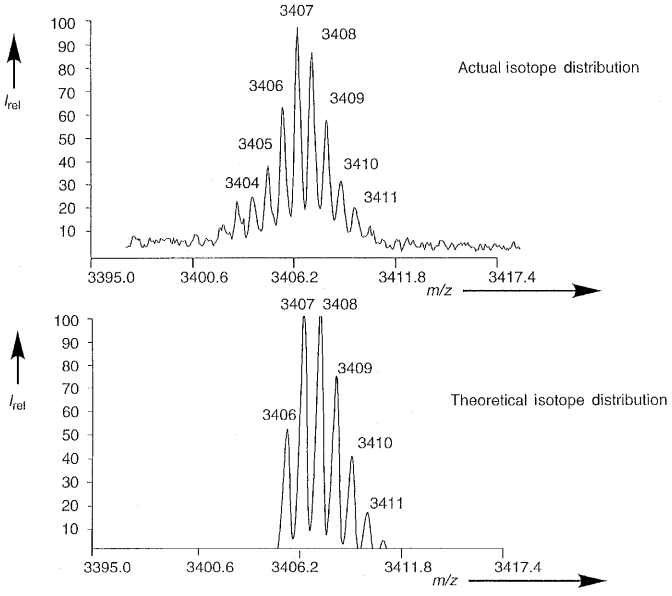



**Fig. 4**. MALDI-TOF mass spectrum of a zero-generation dendrimer **15**.

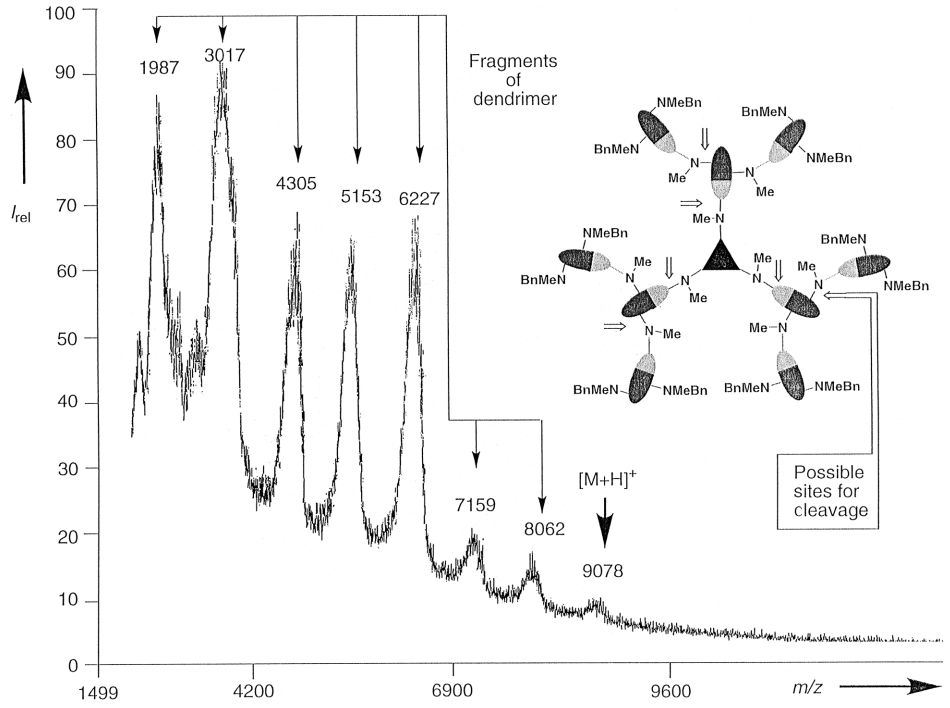



phase HPLC was conducted using a Hypersil 5 μm BDS C-18 silica column (ThermoQuest, 4.6 × 250 mm) under isocratic elution (MeOH–$H_2O$–TFA, 65:35:0.0001) with UV detection using a Dynamax PDA-2 diode array detector. Matrix-assisted laser desorption ionization time-of-flight mass spectra (MALDI-TOF-MS) and fast atom bombardment mass spectra (FAB-MS) were performed on either Perceptive Biosystems Voyager RP (MALDI) or VG SAB-SE (FAB) mass spectrometers. Electrospray mass spectrometry (ES-MS) was recorded on a Sciex API IIIR triple quadrupole electrospray mass spectrometer using $H_2O$–MeCN–HCOOH (50:50:0.1) as the mobile phase. $^1H$ and $^{13}C$ NMR spectra were recorded using Bruker ARX400, ARX500, and Advance 500 spectrometers with the residual solvent or TMS as the internal standard. The chemical shifts are expressed on the δ scale in parts per million (ppm). The following abbreviations are used to explain the observed multiplicities: s (singlet), d (doublet), dd (doublet of doublets), t (triplet), m (multiplet), br (broad).

### *2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl-(1→4)-2,3,6-tri-*O*-acetyl-*β*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (3)*

The glycosyl donor **1** (13.4 g, 17 mmol) and the glycosyl acceptor **2** (6.7 g, 26 mmol) were stirred with powdered 4 Å molecular sieves (13.0 g) in $CH_2Cl_2$ (250 mL) for 2 h under an argon atmosphere. The mixture was then cooled to 0°C and trimethylsilyl trifluoromethanesulfonate (610 μL, 3.4 mmol) was added and stirring was continued at 0°C for 30 min. The reaction was then quenched by the addition of $Et_3N$ (0.47 mL, 3.4 mmol). The solution was filtered through Celite and the filtrate was concentrated. Column chromatography ($SiO_2$, $CH_2Cl_2$:EtOAc (8:2)) gave **3** (11 g, 75%) as a solid foam. $[\alpha]_D^{20}$ –11.6 (*c* = 1 in $CHCl_3$). HR-MS (FAB)

**Fig. 5.** MALDI-TOF mass spectrum of a first-generation dendrimer **17**.




calcd. for $C_{38}H_{54}O_{23}Na$ (M + Na): 901.2954; found: 901.2976. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 1.36, 1.42, 1.43, 1.53 (4 × s, 12H, 2 × $CMe_2$), 1.91, 1.94, 1.96, 1.98, 2.02, 2.06 (7 × s, 21H, 7 × Ac), 3.57–3.59 (m, 1H, H-5b), 3.59–3.61 (m, 2H, H-6a, H-5c), 3.68 (t, $J$ = 9.3 Hz, 1H, H-4b), 3.80–3.85 (m, 1H, H-5a), 3.91 (dd, $J_{5,6}$ = 3.8 Hz, $J_{6,6'}$ = 11.4 Hz, 1H, H-6a′), 3.98 (br d, $J_{6,6'}$ = 12.5 Hz, 1H, H-6c), 4.04 (dd, $J_{5,6}$ = 5.0 Hz, $J_{6,6'}$ = 12.1 Hz, 1H, H-6b), 4.10 (d, $J$ = 7.84 Hz, 1H, H-4a), 4.22 (m, 1H, H-2a), 4.28 (dd, $J_{5,6}$ = 4.6 Hz, $J_{6,6'}$ = 12.5 Hz, 1H, H-6c′), 4.42–4.47 (m, 2H, H-1c, H-6b′), 4.55 (m, 2H, H-1b, H-3a), 4.82–4.87 (m, 2H, H-2c, H-2b), 4.99–5.14 (m, 3H, H-4c, H-3c, H-3b), 5.42 (d, $J_{1,2}$ = 4.9 Hz, 1H, H-1a). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: 20.6 (3C), 20.7, 20.8, 20.9, 21.0, 24.4, 25.0, 25.9, 26.0, 59.1, 59.2, 60.0, 60.3, 68.4, 68.5, 68.6, 68.7, 69.0, 69.3, 69.5, 69.8 (2C), 70.0 (2C), 72.0 (2C), 75.0, 95.0, 101.0 (2C), 169.4, 169.8, 169.9, 170.1, 170.4, 170.5, 170.6.

### *2,3,4-Tri-*O*-acetyl-6-*O*-tert-butyldimethylsilyl-*β*-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*O*-tert-butyldimethylsilyl-*β*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (4)*

The acetyl protecting groups in **3** were removed under standard Zemplén conditions (NaOMe–MeOH) and then *tert*-butyldimethylsilyl chloride (3 g, 20 mmol) was added to a stirred solution of the deacetylated trisaccharide **3** (3 g, 5.1 mmol) in $C_5H_5N$ (15 mL) at 0°C. After 1 h, additional *tert*-butyldimethylsilyl chloride (1 g, 6.6 mmol) was added, and stirring was continued at room temperature overnight before quenching the reaction with MeOH. The mixture was concentrated and redissolved in $CH_2Cl_2$ and washed with 1 M HCl, sat. $NaHCO_3$, and $H_2O$, before drying over anhyd $Na_2SO_4$, and concentrating to an oil. This oil was treated with $Ac_2O$ (20 mL) and $C_5H_5N$ (20 mL) and the solution was left to stir at room temperature overnight. Following concentration and coevaporation with PhMe, the mixture was dissolved in EtOAc (500 mL) and washed consecutively with 1 M HCl, sat. $NaHCO_3$, and sat. NaCl solutions, before drying ($Na_2SO_4$), and concentrating to a foam. Column chromatography ($SiO_2$, $CH_2Cl_2$:EtOAc (9:1)) gave **4** (2.69 g, 50%) as a foamy semisolid. $[\alpha]_D^{20}$ –17.9 ($c$ = 1 in $CHCl_3$). HR-MS (FAB) calcd. for $C_{46}H_{78}O_{21}Si_2Na$ (M + Na): 1045.4472; found: 1045.4501. $^1$H NMR ($CDCl_3$, 400 MHz) δ: 0.00, 0.01, 0.08, 0.09 (4 × s, 12H, 4 × SiMe), 0.80, 0.91 (2 × s, 18H, 2 × $SiCMe_3$), 1.30 (s, 6H, $CMe_2$), 1.40, 1.49 (2 × s, 6H, $CMe_2$), 1.96, 1.99, 2.03, 2.04, 2.07 (5 × s, 15H, 5 × Ac), 3.28 (m, 1H, H-5b), 3.43–3.44 (m, 1H, H-5c), 3.61 (m, 1H, H-6a′), 3.67–3.73 (m, 2H, H-6c, H-6c′), 3.87 (m, 4H, H-4b, H-5a, H-6b, H-6b′), 3.96 (dd, $J_{5,6}$ = 4.1 Hz, $J_{6,6'}$ = 11.2 Hz, 1H, H-6a), 4.16 (br d, $J$ = 7.9 Hz, 1H, H-4a), 4.27 (m, 1H, H-2a), 4.49 (d, $J$ = 8.0 Hz, 1H, H-1b), 4.56 (dd, $J_{2,3}$ = 2.0 Hz, $J_{3,4}$ = 7.9 Hz, 1H, H-3a), 4.66 (d, $J_{1,2}$ = 8.0 Hz, 1H, H-1c), 4.80–4.85 (m, 2H, H-2b, H-2c), 4.98 (t, $J_{3,4} \approx J_{4,5}$ = 9.5 Hz, 1H, H-4c), 5.02–5.15 (m, 2H, H-3b, H-3c), 5.50 (d, $J_{1,2}$ = 4.9 Hz, 1H, H-1a). $^{13}$C NMR ($CDCl_3$, 100 MHz) δ: –5.5, –5.4, –5.3, –4.9, 18.4, 18.6, 20.6, 20.7, 20.8, 20.9, 21.0, 24.4, 25.0, 25.8 26.9, 26.0 (3C), 26.1 (3C), 60.4, 63.0, 67.5, 68.3, 68.5, 70.1, 70.4, 70.5, 70.6, 70.7, 71.0, 71.1, 72.1, 75.1, 75.3, 94.9, 100.2, 100.6, 108.6, 109.3, 169.2, 169.9, 170.2, 170.3, 170.4.

### *2,3,4-Tri-*O*-acetyl-6-bromo-6-deoxy-*β*-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-bromo-6-deoxy-*β*-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose (5)*

Bromine (0.234 mL, 4.6 mmol) was added with stirring at 0°C to a solution of bis-silylether **4** (1.9 g, 1.9 mmol), $PPh_3$ (1.25 g, 25.5 mmol), and $CH_2Cl_2$ (15 mL). The orange precipitate, which formed immediately, dissolved after stirring for 19 h at room temperature, to give a clear brown solution.

This solution was diluted with $CH_2Cl_2$ (100 mL) and was washed with sat. $NaHCO_3$ followed by $H_2O$, before drying ($Na_2SO_4$), filtering, and concentrating. Column chromatography ($SiO_2$, $CH_2Cl_2$:EtOAc (9:1)) gave **5** (1.6 g, 96%) as a foamy semisolid. $[\alpha]_D^{20}$ –22.9 ($c$ = 1 in $CHCl_3$). HR-MS (FAB) calcd. for $C_{34}H_{48}Br_2O_{19}Na$ (M + Na): 943.1038; found: 943.1036. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 1.32, 1.43, 1.49, 1.59 (4 × s, 12H, 2 × $CMe_2$), 1.99, 2.04, 2.05, 2.06, 2.08 (5 × s, 15H, 5 × Ac), 3.32–3.36 (m, 1H, H-5b), 3.48 (dd, $J_{5,6}$ = 2.6 Hz, $J_{6,6'}$ = 8.8 Hz, 1H, H-6b), 3.56–3.60 (m, 1H, H-5c), 3.66–3.76 (m, 1H, H-6c), 3.85 (t, $J$ = 9.2 Hz, 1H, H-4b), 3.91–3.93 (m, 1H, H-5a), 4.00 (dd, $J_{5,6}$ = 3.5 Hz, $J_{6,6}$ = 7.8 Hz, 1H, H-6a), 4.18 (dd, $J_{3,4}$ = 6.27 Hz, $J_{4,5}$ = 1.63 Hz, 1H, H-4a), 4.27–4.29 (m, 1H, H-2a), 4.57 (d, $J$ = 7.9 Hz, 1H, H-3a), 4.58 (d, $J$ = 7.9 Hz, 1H, H-3c), 4.9–5.3 (m, 4H, H-3b, H-3c, H-4c, H-2c), 5.48 (d, $J$ = 4.9 Hz, 1H, H-1a). $^{13}$C NMR ($CDCl_3$, 125 MHz) δ: 20.7, 20.8 (3C), 21.1, 24.5, 25.2, 26.1 (2C), 30.4, 31.7, 67.9, 69.4, 70.5, 70.7, 70.8, 71.4, 71.6, 71.8, 71.9, 72.9, 73.4 (2C), 76.9, 96.3, 99.9, 101.1, 108.8, 109.5, 169.0, 169.4, 169.9, 170.0, 170.4.

### *2,3,4-Tri*-O-*acetyl-6*-N-*benzyl-6-deoxy-6-methylamino*-β-D-*glucopyranosyl-(1→4)-2,3-di*-O-*acetyl-6*-N-*benzyl-6-deoxy-6-methylamino*-β-D-*glucopyranosyl-(1→6)-1,2:3,4-di*-O-*isopropylidene*-α-D-*galactopyranose (6)*

The dibromide **5** (0.4 g, 0.4 mmol) and *N*-benzylmethylamine (0.28 mL) were stirred together at 80°C overnight. The next day, the reaction mixture was concentrated, redissolved in $C_5H_5N$ (2 mL) and $Ac_2O$ (2 mL), and left to stir at room temperature overnight. The brown solution was coevaporated with PhMe before the resulting oily liquid was diluted in $CH_2Cl_2$ and washed consecutively with 1 M HCl, sat. $NaHCO_3$ and $H_2O$, dried ($Na_2SO_4$), filtered, and concentrated to an oil. Column chromatography ($SiO_2$, hexanes–EtOAc (6:4 to 1:1)) gave **6** (0.2 g, 57%) as an amorphous tan foam. $[\alpha]_D^{20}$ –15.8 ($c$ = 1 in $CHCl_3$). HR-MS (MALDI-TOF) calcd. for $C_{50}H_{68}N_2O_{19}$ (M + H): 1001.4494; found: 1001.4480. $^1$H NMR ($CDCl_3$, 500 MHz) δ: 1.29, 1.31, 1.40, 1.49 (4 × s, 12H, 2 × $CMe_2$), 1.80, 1.94, 1.97, 1.99, 2.01 (5 × s, 15H, 5 × Ac), 2.23, 2.36 (2 × br s, 6H, 2 × NMe), 2.42–2.58 (m, 2H, H-6c, H-6c′), 2.75–2.85 (m, 2H, H-6b, H-6b′), 3.40–3.68 (m, 6H, H-5b, H-5c, H-6a′, 3 × PhC*H*), 3.86–4.00 (m, 4H, H-4b, H-5a, H-6a, PhC*H*), 4.15 (dd, $J_{3,4}$ = 6.5 Hz, $J_{4,5}$ = 1.4 Hz, 1H; H-4a), 4.28 (m, 1H, H-2a), 4.50 (d, $J$ = 7.65 Hz, 1H, H-1b), 4.56 (dd, $J_{3,4}$ = 2.25 Hz, $J_{3,2}$ = 5.6 Hz, 1H, H-3a), 4.79–4.90 (m, 4H, H-2b, H-2c, H-4c, H-1c), 5.01 (t, $J_{2,3} \approx J_{3,4}$ = 8.9 Hz, 1H, H-3c), 5.16 (t, $J_{2,3} \approx J_{3,4}$ = 9.5 Hz, 1H, H-3b), 5.48 (d, $J_{1,2}$ = 4.9 Hz, 1H, H-1a), 7.25–7.36 (m, 10H, Ar-H). $^{13}$C NMR ($CDCl_3$, 125 MHz) δ: 20.4, 20.5, 20.6, 20.7, 21.0, 24.2, 24.9, 25.5, 25.9, 42.8, 43.5, 56.5, 57.3, 62.3, 62.8, 67.5, 68.7, 70.3, 70.5, 71.4, 71.8, 72.3, 73.2 (3C), 75.6, 76.7, 76.9, 96.1, 99.3, 101.2, 108.5, 109.2, 125.0 (2C), 126.9 (4C), 128.3 (4C), 128.9 (2C), 169.5, 169.8, 169.9, 170.1, 170.4.

### *6-Deoxy-6-methylamino*-β-D-*glucopyranosyl-(1→4)-6-deoxy-6-methylamino*-β-D-*glucopyranosyl-(1→6)-1,2:3,4-di*-O-*isopropylidene*-α-D-*galactopyranose (7)*

To a methanolic (5 mL of MeOH) solution of the pentaacetate **6** (1 g, 1 mmol), NaOMe (1mL, 0.5 M in MeOH, 0.5 mmol) was added and the mixture was left to stir at room temperature overnight. The solution was then neutralized with Amberlite IR-120 ($H^+$ form) ion exchange resin, filtered, and concentrated. A solution of this deacetylated product (0.6 g, 0.76 mmol) in MeOH (50 mL) was treated with 10% $Pd(OH)_2$/C (300 mg) under $H_2$ for 2 h. The solution was filtered through a bed of Celite and the filtrate was concentrated to give **7** (460 mg, 90%) as an amorphous solid upon freeze-drying from $H_2O$. $[\alpha]_D^{20}$ –17.9 ($c$ = 1 in $CHCl_3$). ES-MS (M + H): 611.4. $^1$H NMR ($CD_3OD$, 500 MHz) δ: 1.33, 1.34, 1.40, 1.52 (4 × s, 12H, 2 × $CMe_2$), 2.44, 2.46 (2 × br s, 6H, 2 × NMe), 2.61 (dd, $J_{5,6}$ = 8.3 Hz, $J_{6,6'}$ = 12.7 Hz, 1H, H-6c), 2.65 (dd, $J_{5,6}$ = 7.8 Hz, $J_{6,6'}$ = 12.6 Hz, 1H, H-6b), 2.95 (dd, $J_{5,6}$ = 2.8 Hz, $J_{6,6'}$ = 12.7 Hz, 1H, H-6c′), 3.13 (dd, $J_{5,6}$ = 2.8 Hz, $J_{6,6'}$ = 12.6 Hz, 1H, H-6b′), 3.15 (t, $J_{3,4} \approx J_{4,5}$ = 9.2 Hz, 1H, H-4c), 3.18–3.26 (m, 2H, H-2b, H-2c), 3.31–3.42 (m, 3H, H-3c, H-4b, H-5c), 3.44–3.54 (m, 2H, H-3b, H-5b), 3.65 (dd, $J_{5,6}$ = 8.2 Hz, $J_{6,6'}$ = 11.4 Hz, 1H, H-6a), 4.01–4.05 (m, 2H, H-5a, H-6a), 4.28 (dd $J_{3,4}$ = 8.0 Hz, $J_{4,5}$ = 1.5 Hz, H-4a), 4.30 (d, $J_{1,2}$ = 7.8 Hz, 1H, H-1b), 4.34 (d, $J_{1,2}$ = 7.9 Hz, 1H, H-1c), 4.36 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, H-2a), 4.62 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 8.0 Hz, 1H, H-3a), 5.51 (d, $J_{1,2}$ = 4.9 Hz, 1H, H-1a). $^{13}$C NMR ($CD_3OD$, 125 MHz) δ: 24.6, 25.1, 26.3 (2C), 36.1 (2C), 53.1, 53.5, 66.8, 68.9, 69.8, 71.9, 72.4, 73.5, 74.4, 74.7, 74.8, 75.0, 75.5, 77.8, 82.9, 97.7, 104.4, 104.8, 110.0, 110.4.

### *6*-N-*Benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→4)-6*-N-*benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→6)-D-galactose (8)*

The diacetonide **6** (620 mg, 785 μmol) was dissolved in 90% aq TFA (5 mL) and was allowed to stir at room temperature for 10 min before coevaporation with MeOH three times. Column chromatography (C-8 reversed phase silica, $H_2O$ to MeOH) gave **8** (445 mg, 80%) as an amorphous solid after freeze-drying from $H_2O$. $[\alpha]_D^{20}$ 0 ($c$ = 1 in $H_2O$). ES-MS ($m/z$): 711.5 $[M + H]^+$. Selected $^1$H NMR data ($CD_3OD$, 500 MHz) δ: 2.26 (2 × s, 6H, 2 × NMe), 2.61 (dd, $J_{5,6}$ = 7.9 Hz, $J_{6,6'}$ = 13.0 Hz, 1H, H-6c), 2.73 (dd, $J_{5,6}$ = 7.5 Hz, $J_{6,6'}$ = 13.5 Hz, 1H, H-6b), 2.78 (dd, $J_{5,6}$ = 3.5 Hz, $J_{6,6'}$ = 13.0 Hz, 1H, H-6c′), 3.10 (br d, $J_{6,6'}$ = 13.5 Hz, 1H, H-6b′), 3.14 (t, $J_{3,4} \approx J_{4,5}$ = 9.2 Hz, 1H, H-4c), 3.21 (t, $J_{1,2} \approx J_{2,3}$ = 8.0 Hz, 1H, H-2c), 3.26 (dd, $J_{1,2}$ = 8.0 Hz, $J_{2,3}$ = 9.0 Hz, 1H, H-2b), 3.34 (t, $J_{3,4} \approx J_{4,5}$ = 9.0 Hz, 1H, H-3c), 4.32–4.45 (m, ca. 2.5H, β-anomerics), 5.14 (d, $J_{1,2}$ = 3.4 Hz, ca. 0.5H, H-1a (α)), 7.25–7.39 (m, 10H, 2 × $C_6H_5$).

### *6,6′*-N,N′-*bis[6,6′-bis*-N-*benzylmethylamino-6,6′-dideoxy*-β-*cellobiosyl-(1→6)-D-galactit-1-yl]-6,6′-dideoxy-6,6′-dimethylamino*-β-*cellobiosyl-(1→6)-1,2:3,4-di*-O-*isopropylidene*-α-D-*galactopyranose (9)*

Acetic acid (10 μL, 200 μmol) was added to a solution of the reducing sugar **8** (211 mg, 300 μmol), the bismethylamine **7** (70 mg, 114 μmol), and sodium cyanoborohydride (49 mg, 740 μmol) in MeOH (1 mL). The reaction mixture was stirred and heated under reflux for 8 h. Since HPLC analysis indicated that the reaction had gone to completion, the mixture was allowed to cool to room temperature, diluted with $H_2O$ (3 mL), and purified by preparative reversed phase chromatography (15 g C-18 reversed phase, MeOH–$H_2O$–TFA (0:100:0.0001 to 100:0:0.0001)) to afford

pure **9** (216 mg, 94%). $[\alpha]_D^{20}$ –6.7 (*c* = 1 in $H_2O$). ES-MS (*m*/*z*): 2001.0 $[M + H]^+$, 1001.1 $[M + 2H]^{+2}$, 667.8 $[M + 3H]^{+2}$, 500.7 $[M + 4H]^{+4}$, 400.8 $[M + 5H]^{+5}$. Selected $^1$H NMR data ($CD_3OD$, 500 MHz) δ: 1.30, 1.33, 1.38, 1.50 (4 × s, 12H, 2 × $CMe_2$), 2.70 (br s, 12H, 4 × N*Me*Bn), 2.88 (br s, 3H, NMe), 2.98 (br s, 3H, NMe), 3.13 (t, $J_{3,4} \approx J_{4,5}$ = 9.1 Hz, 2H, H-4f, H-4i), 3.17 (t, $J_{3,4} \approx J_{4,5}$ = 9.0 Hz, 1H, H-4c), 3.37 (t, $J_{2,3} \approx J_{3,4}$ = 9.1 Hz, 3H, H-3c, H-3f, H-3i), 3.44 (t, $J_{3,4} \approx J_{4,5}$ = 9.0 Hz, 3H, H-4b, H-4e, H-4f), 4.36 (m, 1H, H-2a), 4.40–4.49 (m, 6H, H-1b, H-1c, H-1e, H-1f, H-1h, H-1i), 4.62 (dd, $J_{2,3}$ = 2.2 Hz, $J_{3,4}$ = 7.9 Hz, 1H, H-3a), 5.51 (d, $J_{1,2}$ = 4.9 Hz, 1H, H-1a), 7.42–7.50 (m, 20H, 4 × $C_6H_5$). Selected $^{13}$C/DEPT135/HMQC NMR data ($CD_3OD$, 125 MHz) δ: 24.6 (C*Me*$_2$), 25.1 (C*Me*$_2$), 26.4 (2C, C*Me*$_2$), 41.8 (2C, N*Me*Bn), 42.1 (2C, N*Me*Bn), 42.8 (NMe), 43.4 (NMe), 58.1, 58.8 (2 × 3C, C-6b, C-6c, C-6e, C-6f, C-6h, C-6i), 61.9 (2C, 2 × *C*$H_2$Ph), 62.2 (2C, C-1d, C-1g), 62.4 (2C, 2 × *C*$H_2$Ph), 69.9 (C-6a), 73.3, 73.4 (C-6d, C-6g), 76.1 (C-3b), 76.3 (C-3e, C-3h), 77.8 (3C, C-3c, C-3f, C-3i), 83.0, 83.1, 83.2 (C-4b, C-4e, C-4h), 97.7 (C-1a), 103.8, 104.5 (2C), 105.0 (2C), 105.1 (C-1b, C-1c, C-1e, C-1f, C-1h, C-1i), 110.1, 110.5 (2 × *C*$Me_2$), 130.1 (4 × C-Ar), 130.2 (2 × C-Ar), 130.3 (2 × C-Ar), 130.4 (2 × C-Ar), 130.6 (2 × C-Ar), 131.8 (4 × C-Ar), 132.1 (2 × C-Ar), 132.2 (2 × C-Ar) 162.9 (2 × C-Ar), 163.2 (2 × C-Ar).

***6,6′*-N,N′-*bis*[*6,6′-bis*-N-*benzylmethylamino-6,6′-dideoxy*-β-*cellobiosyl-(1→6)-D-galactit-1-yl*]-*6,6′-dideoxy-6,6′-dimethylamino*-β-*cellobiosyl-(1→6)-D-galactose (10)***

The diacetonide **9** (120 mg, 60 μmol) was dissolved in 90% aq TFA (5 mL) and was allowed to stir at room temperature for 10 min before coevaporation with MeOH three times. Column chromatography (C-8 reversed phase silica, $H_2O$ to MeOH) gave **10** (90 mg, 80%) as an amorphous solid after freeze-drying from $H_2O$. $[\alpha]_D^{20}$ –1 (*c* = 1 in $H_2O$). ES-MS (*m*/*z*): 1920.3 $[M + H]^+$, 961.2 $[M + 2H]^{+2}$, 641.1 $[M + 3H]^{+3}$, 480.9 $[M + 4H]^{+4}$. Selected $^1$H NMR data ($CD_3OD$, 500 MHz) δ: 4.37–4.39 (br m, ca. 6.5H, anomerics), 5.06 (br s, ca. 0.5 H, H-1a (α)), 7.36–7.46 (m, 20H, $C_6H_5$).

***Tris(2-{*N*-[*6*-N-*benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→4)-6*-N-*benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→6)-D-galactit-1-yl*]*methylamino*}*ethyl*)*amine (14)***

Acetic acid (2.28 μL, 45 μmol) was added to a solution of the reducing sugar **8** (50 mg, 70 μmol), tris[2-(methylamino)ethyl]amine (**13**) (11) (3 mg, 19 μmol), and sodium cyanoborohydride (43 mg, 682 μmol) in MeOH (1000 μL). The reaction mixture was stirred and heated under reflux for 6 h. When HPLC analysis indicated that the reaction had gone to completion, the mixture was allowed to cool to room temperature, diluted with $H_2O$ (2 mL), and purified by preparative reversed phase chromatography (15 g C-18 reversed phase, MeOH–$H_2O$–TFA (0:100:0.0001 to 100:0:0.0001)) to afford **14** (30 mg, 69%). $[\alpha]_D^{20}$ –48 (*c* = 1 in $H_2O$). LR-FAB (*m*/*z*): 2288.4 $[M + H]^+$. Selected $^1$H NMR ($CD_3OD$, 500 MHz) δ: 2.77, 2.90 (2 × 3C, N*Me*Bn), 4.36–4.40 (m, 6H, anomerics), 7.39–7.46 (m, 30H, $C_6H_5$). Selected $^{13}$C NMR data ($CD_3OD$, 125 MHz) δ: 64.9 (C-6a), 104.5, 105.1 (C-1b, C-1c).

***Tris(2-{*N*-*methyl*[*2,3,4-tri*-O-*acetyl-6*-N-*benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→4)-2,3-di*-O-*acetyl-6*-N-*benzylmethylamino-6-deoxy*-β-D-*glucopyranosyl-(1→6)-2,3,4,5-tetra*-O-*acetyl*-D-*galactit-1-yl*]*amino*}*ethyl*)*amine (15)***

The zero-generation dendrimer **14** (30 mg) was dissolved in a solution of DMAP (2 mg) in $Ac_2O$ (4 mL) and $C_5H_5N$ (4 mL) and the mixture was left to stir at room temperature for 36 h and then concentrated by coevaporation with PhMe before diluting with EtOAc and washing with 1 M HCl, sat. $NaHCO_3$ and sat. NaCl solutions, drying ($Na_2SO_4$), and concentrating to an oil. GPC ($CHCl_3$:MeOH, 3:1) gave **15** (20 mg, 45%) as an oil. $[\alpha]_D^{20}$ –40 (*c* = 1 in MeOH). MALDI-TOF (*m*/*z*): 3407 $[M + H]^+$, 3429 $[M + Na]^+$, 3446 $[M + K]^+$. $^1$H NMR (DMF-$d_7$, 500 MHz) δ: 1.92, 1.96, 2.02, 2.05, 2.06, 2.07, 2.11, 2.12, 2.27 (9 × s, 81H, 27 × COMe), 2.4–2.6 (m, 18H, H-6), 2.74 (br s, 9H, 3 × NMe), 2.74 (br s, 9H, 3 × NMe), 2.92 (br s, 18 H, 6 × NMe), 3.91–3.96 (m, 18H, NC$H_2$Ph), 4.28 (dd, 3H, *J* = 4.4 Hz, *J* = 7.41 Hz, H-4), 4.78 (dd, 3H, *J* = 7.8 Hz, *J* = 9.4 Hz, H-3), 4.86–4.90 (m, 3H, H-5), 5.06 (d, 3H, *J* = 7.9 Hz, H-1), 5.16 (t, 3H, *J* = 9.0 Hz, H-2), 5.22 (d, 3H, 9.0 Hz, H-1), 5.27–5.45 (m, 24H), 7.27–7.43 (m, 30H, $C_6H_5$). DEPT-135 $^{13}$C NMR (DMF-$d_7$, 125 MHz) δ: 20.2, 20.4, 20.5, 20.6, 20.7, 21.0, 42.4, 42.9, (57.2), (58.2), (62.3), (67.8), 68.3, 68.7, 69.4, 71.1, 71.8, 72.2, 72.5, 73.1, 73.5, 74.7, 77.2, 100.0, 100.5, 127.3, 128.7, 129.2, 129.3.

***Tris[2-(*N*-{*6,6′*-N,N′-*bis*[*6,6′-bis*-N-*benzylmethylamino-6,6′-dideoxy*-β-*cellobiosyl-(1→6)-D-galactit-1-yl*]-*6,6′-dideoxy-6,6′-dimethylamino*-β-*cellobiosyl-(1→6)-D-galactit-1-yl*}*methylamino*)*ethyl*]*amine (16)***

Acetic acid (2.28 μL, 45 μmol) was added to a solution of the reducing sugar **10** (90 mg, 47 μmol), tris[2-(methylamino)ethyl]amine **13** (2 mg, 12 μmol), and sodium cyanoborohydride (10 mg, 121 μmol) in MeOH (1 mL). The reaction mixture was stirred and heated under reflux for 6 h. When HPLC analysis indicated that the reaction had gone to completion, the mixture was allowed to cool to room temperature, diluted with $H_2O$ (2 mL), and purified by preparative reversed phase chromatography (15 g C-18 reversed phase, MeOH–$H_2O$–TFA (0:100:0.0001 to 100:0:0.0001)) to afford **16** (60 mg, 56%). $[\alpha]_D^{20}$ –27 (*c* = 1 in $H_2O$). MALDI-TOF (*m*/*z*): 5926.1 $[M + Na]^+$. Selected $^1$H NMR ($CD_3OD$, 500 MHz): δ: 4.32–4.43 (m, 18H, anomerics), 7.40–7.50 (m, 60H, $C_6H_5$).

***Tris[2-(*N*-*methyl*{*2,2′,3,3′,4′-penta*-O-*acetyl-6,6′-dideoxy-6,6′-di*-N-*methyl-6,6′-bis*[*2,2′,3,3′,4′-penta*-O-*acetyl-6,6′-bis*-N-*benzylmethylamino-6,6′-dideoxy*-β-*cellobiosyl-(1→6)-2,3,4,5-tetra*-O-*acetyl*-D-*galactit-1-yl*]*amino*-β-*cellobiosyl-(1→6)-2,3,4,5-tetra*-O-*acetyl*-D-*galactit-1-yl*}*amino*)*ethyl*]*amine (17)***

The first-generation dendrimer **16** (35 mg, 15 μmol) was dissolved in a solution of DMAP (2 mg) in $Ac_2O$ (4 mL) and $C_5H_5N$ (4 mL) and was left to stir at room temperature for 36 h and then concentrated by coevaporation with PhMe before diluting with EtOAc and washing with 1 M HCl, sat. $NaHCO_3$ and sat. NaCl solutions, drying ($Na_2SO_4$), and concentrating to an oil. GPC ($CHCl_3$:MeOH, 3:1) gave **17** (18 mg, 33%) as an oil. $[\alpha]_D^{20}$ –19 (*c* = 1 in $H_2O$). MALDI-TOF (*m*/*z*): 9078 $[M + H]^+$. $^1$H NMR (DMF-$d_7$, 500 MHz,

350 K) δ: 1.34, 1.41, 1.96, 1.99, 2.02, 2.03, 2.06, 2.07, 2.09, 2.14, 2.16, 2.19, 2.21 (13 × s, 243H, 81 × COMe), 2.4–2.6 (m, 18H, H-6), 2.74 (br s, 9H, 3 × NMe), 2.77–2.81 (br s, 27H, 9 × NMe), 2.87–2.93 (br s, 36H, 12 × NMe), 3.91 (m, 36H, NC$H_2$Ph), 4.51–4.85 (m, 41H), 5.12–5.38 (m, 41H), 5.51–5.70 (m, 41H), 7.51–7.59 and 7.89 (m, 60H, $C_6H_5$). DEPT-135 $^{13}$C NMR (DMF-$d_7$, 125 MHz, 300 K) δ: 20.3, 20.4, 20.5, 20.6, 20.8, 21.1, 47.5, 47.8, (57.0), (57.3), 64.6, (62.0), (67.7), 68.2, 68.3, 68.6, 70.1, 71.7, 73.1, 73.4, 74.5, 76.0, 81.1, 97.2, 102.8, 103.4, 128.9, 128.9, 129.7, 129.8, 130.9, 131.2.

## Conclusion

The research we have reported in this short paper has established that we can not only synthesize glycodendrons containing cellobiosylgalacto residues but we can also attach these glycodendrons to a trivalent core. These glycodendrons and glycodendrimers add further diversity to the carbohydrate scaffolds we are currently constructing to display large bioactive oligosaccharides (15) and proteins (16) in a predetermined and reasonably precise way on the peripheries of such glycodendrons and glycodendrimers.

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## References

1. (*a*) T. Lindhorst. Top. Curr. Chem. **218**, 201 (2002); (*b*) W.B. Turnbull and J.F. Stoddart. Rev. Mol. Biotechnol. **90**, 231 (2002).
2. R.T. Lee and Y.C. Lee (*Editors*). *In* Neoglycoconjugates: Preparation and applications. Academic Press, San Diego. 1994.
3. I. Vrasidas, N.J. de Mol, R.M.J. Liskamp, and R.J. Pieters. Eur. J. Org. Chem. 4685 (2001).
4. (*a*) B. Colonna, V.R. Harding, S.A. Nepogodiev, F.M. Raymo, N. Spencer, and J.F. Stoddart. Chem. Eur. J. **4**, 1244 (1998); (*b*) P.R. Ashton, S.E. Boyd, C.L. Brown, N. Jayaraman, S.A. Nepogodiev, and J.F. Stoddart. Chem. Eur. J. **2**, 1115 (1997).
5. (*a*) W.B. Turnbull, S.A. Kalovidouris, and J.F. Stoddart. Chem. Eur. J. **8**, 2988 (2002); (*b*) W.B. Turnbull, A.R. Pease, and J.F. Stoddart. ChemBioChem. **1**, 70 (2000).
6. (*a*) K. Sadalapure and T.K. Lindhorst. Angew. Chem. Int. Ed. **39**, 2010 (2000); (*b*) H. Sashiwa, Y. Makimura, Y. Shigemasa, and R. Roy. J. Chem. Soc. Chem. Commun. 909 (2000); (*c*) S. Sabesan, J.O. Duus, S. Neira, P. Domaille, S. Kelm, J.C. Paulson, and K. Bock. J. Am. Chem. Soc. **114**, 8363 (1992).
7. R.A. Laine. Glycobiology, **4**, 759 (1994).
8. G. Reuter and H.-J. Gabius. Biol. Chem. Hoppe–Seyler, **377**, 325 (1996).
9. (*a*) P.M. Collins and R.J. Ferrier. *In* Monosaccharides. John Wiley and Sons, New York. 1995; (*b*) B. Bernet and A. Vasella. Helv. Chim. Acta, **83**, 2055 (2000).
10. F.J. Urban, B.S. Moore, and R. Breitenbach. Tetrahedron Lett. **31**, 4421 (1990).
11. H. Schmidt, C. Lensink, S.K. Xi, and J.G. Verkade. Z. Anorg. Allg. Chem. 75 (1989).
12. (*a*) T. Yamagaki and H. Nakanishi. Anal. Sci. **17**, 83 (2001); (*b*) D.J. Harvey, A.P. Hunter, R.H. Bateman, J. Brown, and G. Critchley. Int. J. Mass Spectrom. 131 (1999); (*c*) T. Yamagaki. Trends Glycosci. Glycotechnol. **11**, 227 (1999); (*d*) Y. Liu and D.E. Clemmer. Anal. Chem. **69**, 2504 (1997); (*e*) K.K. Mock, M. Davey, and J.S. Cottrell. Biochem. Biophys. Res. Commun. **177**, 644 (1991); (*f*) B. Domon and C.E. Costello. Glycoconjugate J. **5**, 397 (1988).
13. C.F. Lane. Synthesis, 135 (1975).
14. D.D. Perrin and W.L.F. Armarego. *In* Purification of laboratory chemicals. 3rd ed. Pergamon Press, Oxford. 1988.
15. (*a*) J.R. Allen and S.J. Danishefsky. J. Am. Chem. Soc. **121**, 10 875 (1999); (*b*) E.C. Rodriguez, L.A. Marcaurelle, and C.R. Bertozzi. J. Org. Chem. **63**, 7134 (1998). (*c*) P.P. Deshpande and S.J. Danishefsky. Nature (London), **387**, 164 (1997).
16. R.C. Werlen, M. Lankinen, R.E. Offord, P.A. Schubiger, A. Smith, and K. Rose. Cancer Res. **56**, 809 (1996).