Large Oligosaccharide-Based Glycodendrimers**

W. Bruce Turnbull,[a, b] Stacey A. Kalovidouris,[a] and J. Fraser Stoddart*[a]

Abstract: Carbohydrate-based dendritic structures composed of 21 and 27 monosaccharide residues have been synthesized in a convergent manner from trisaccharide building blocks. The oligosaccharide AB_2 monomers are based on a maltosyl$\beta(1\rightarrow6)$galactose structure, which has been modified to include two methylamino groups at the primary positions of the glucosyl residues. Reductive alkylation of the secondary amino groups, with the innate formyl function of a second oligosaccharide monomer, allows for the chemoselective construction of dendritic wedges, while employing a minimal number of protecting groups. The first-generation dendron can be coupled either to another AB_2 monomer, to give a second-generation dendron, or to a tris[2-(methylamino)-ethyl]amine-based core moiety, to provide a carbohydrate-based dendrimer. Alternating α- and β-glucosyl residues in the monomers and dendrons, simplifies ^{1}H NMR spectra as a consequence of spreading out the anomeric proton signals. Monomers and dendrons were characterized by extensive one- and two-dimensional NMR spectroscopy in addition to FAB, electrospray, and MALDI-TOF mass spectrometry. Molecular dynamics simulations revealed similar conformations in the dendrons as in the isolated trisaccharide repeating units.

Keywords: carbohydrates · dendrimers · glycodendrimers · oligosaccharides · reductive amination

Introduction

Nature uses carbohydrates for a variety of functions, ranging from energy storage, through structural materials, to information transfer through a complex sugar code[1] or "glycocode" based on stereochemistry and conformation. This glycocode is usually read through molecular recognition of the oligosaccharide by proteins called lectins,[2] although sometimes by other oligosaccharides.[3] Although *individual* interactions between lectins and their carbohydrate ligands are relatively weak,[4] the multivalent presentation[5] of both ligands and receptors at a cell surface remarkably enhances both the affinity[6] and selectivity[7] of the interactions. Chemists who have committed themselves to intervening in these binding processes,[8] starting with Lee's[9] glycoclusters[10] (Figure 1a) and proceeding through glycopolymers[11] (Figure 1b) with many pendant saccharides to the structurally well defined, highly branched polymers called glycodendrimers (Figure 1c and d),[12] have most successfully adopted Nature's multivalent approach to their work. These studies have not only provided potent inhibitors of protein-carbohydrate interactions,[9, 13] but they have also led to an increased understanding of multivalent processes.[6, 7, 14]

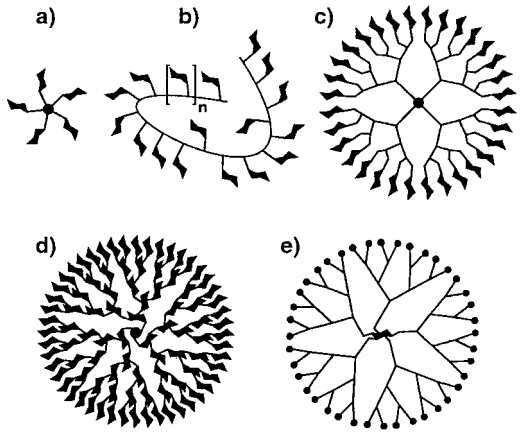

Figure 1. Graphical representation of multivalent neoglycoconjugates: a) glycocluster, b) glycopolymer, c) carbohydrate-coated dendrimer, d) carbohydrate-based dendrimer, and e) carbohydrate-centered dendrimer.

In synthetic chemistry, by comparison, monosaccharides have long been employed as sources of chirality[15] for the synthesis of even more elaborate chiral compounds, and additionally, in recent times, as scaffolds[16] for constructing

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[**] Synthetic Carbohydrate Dendrimers, Part 9: for Part 8, see: W. B. Turnbull, A. R. Pease, J. F. Stoddart, *ChemBioChem* **2000**, *1*, 70–74.

  0947-6539/02/0813-2988 $ 20.00+.50/0

peptidomimetics.[17] Oligosaccharides have been used[18] to arrange guanidinium groups in arrays suitable for binding to DNA, and various functionalities, including metal complexes and coenzymes, have been appended onto cyclodextrins to provide enzyme-like catalysts.[19] Carbohydrates, with their multiple functional groups and structural diversity have also been employed as scaffolds for the multivalent display of other, biologically important, saccharides. While mono- and disaccharides have been used as cores for glycoclusters,[13a, 20] and for arranging sialyllactosamines[21] in varying orientations for binding to influenza hemagglutinin, cyclodextrins have been employed extensively for clustering mono- and oligosaccharides,[22] and glycodendrons.[23] Finally, the polysaccharide, chitosan, has also been used recently as a scaffold for attaching both monosaccharides and glycodendrons.[24]

It has been noted that, conceptually, there are several limiting designs for molecules described as glycodendrimers (Figure 1c, d, and e).[25] Firstly, there are carbohydrate-coated dendrimers in which the saccharides are present only around the periphery of a non-carbohydrate dendritic scaffold, secondly, at the other end of the spectrum, there are fully carbohydrate dendrimers, in which saccharides form the branching units of the dendrimer, and thirdly, there are carbohydrate-centered dendrimers. Although considerable interest has been shown in dendrimers constructed from chiral building blocks,[26] only a few examples of glycodendrimers and glycodendrons that incorporate saccharides into their branched skeletons have been described to date.[27–29]

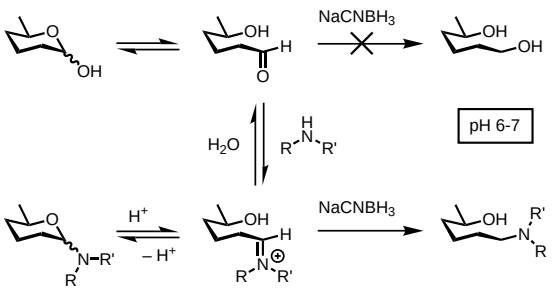
Here we present an approach that we have been developing for the synthesis of carbohydrate-based dendritic skeletons,[29] which could be further elaborated with biologically important oligosaccharides or proteins around their peripheries.

Results and Discussion

Concept and synthetic design: Several important lessons for designing glycodendrimers have emerged from literature studies. Firstly, optimal biological activities are usually attained[30] with glycodendrimers of moderate valency rather than with high-generation dendrimers that have reached their "starburst limit".[31] Secondly, small changes in the structure of the underlying scaffold can have considerable effects on binding affinities.[30b] Thirdly, the distances which must be spanned in order to cross-link lectin binding sites can be on the order of several nanometres, especially in systems involving monovalent lectins arranged in multivalent arrays at a cell surface.[32] Although glycopolymers[11d] and other polyvalent glycoconjugates[33] may perform well in such situations, they cannot readily provide information regarding the optimal arrangement of both the ligands and lectins that is required for efficient recognition at the cell surface—information that well-defined, nanometer-scale, low valency dendrimers may be able to provide.

We chose to use oligosaccharides as the building blocks for the structures of our dendrimers[29] on account of 1) their low toxicity and immunogenicity, 2) the size advantage that they offer over monosaccharide building blocks when it comes to constructing large dendrons, and 3) their fairly well defined and predictable conformations[34] that would provide the dendrons and dendrimers with shapes which could be controlled by the appropriate selection of their constituent oligosaccharides.

One of our original aims in designing the synthesis of these molecules was to try to minimize our use of protecting groups during the coupling reactions, as we had previously found[27] that the extra steric bulk associated with protecting groups limits the yields of branched products and increases the number of synthetic steps that need to be performed on the growing dendrons. Thus, we decided to focus on using reductive amination[35, 36] (Scheme 1) as a suitable chemoselective means of coupling the oligosaccharides together in



Scheme 1. Reductive amination. The aldehyde function of a reducing sugar reacts with a secondary amine to provide an iminium ion which is selectively reduced by $NaCNBH_3$, under neutral conditions to give a tertiary amine. The aldehyde group is not susceptible to reduction by $NaCNBH_3$ under these conditions.

the presence of many unprotected hydroxyl groups in these molecules. To make branched products employing this reaction, we required an AB_2 monomer that possesses either 1) one aldehyde and two amino groups or 2) two aldehydes and one amine. As a reducing sugar already contains an aldehyde function, we chose to introduce two complementary amino groups into an existing oligosaccharide (Figure 2). Although this approach would require several synthetic steps in order to introduce, into the AB_2 monomers, all of the necessary functionality for chemoselective coupling, we anticipated that these monomers could then be built into large dendrons in only a few more additional steps.

Two important issues that also had to be addressed were 1) how to purify the dendrons and dendrimers and 2) how to simplify the NMR spectroscopic characterization of these structurally complex molecules.

Although Nature constructs branched oligosaccharides in a divergent fashion,[37] mediated by glycosyl transferases, this process typically provides glycans exhibiting microheterogeneity,[37] that is, small "defects" through incomplete glycosylations. Similar problems that are associated[38] with the divergent construction of dendrimers may be circumvented by adopting a convergent synthesis,[39] that is, starting at the dendrimer's periphery and proceeding towards its core. Here, typically only two or three reactions need to be performed at a time on each molecule, allowing easier purification of the reaction products. Unprotected oligosaccharides, especially those containing amino functions, do not lend themselves well to silica gel chromatography. However, hydrophobic glyco-

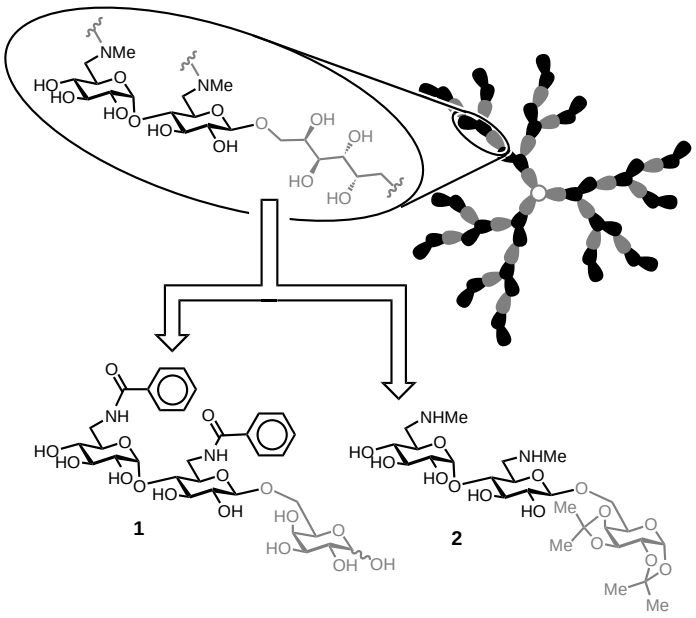
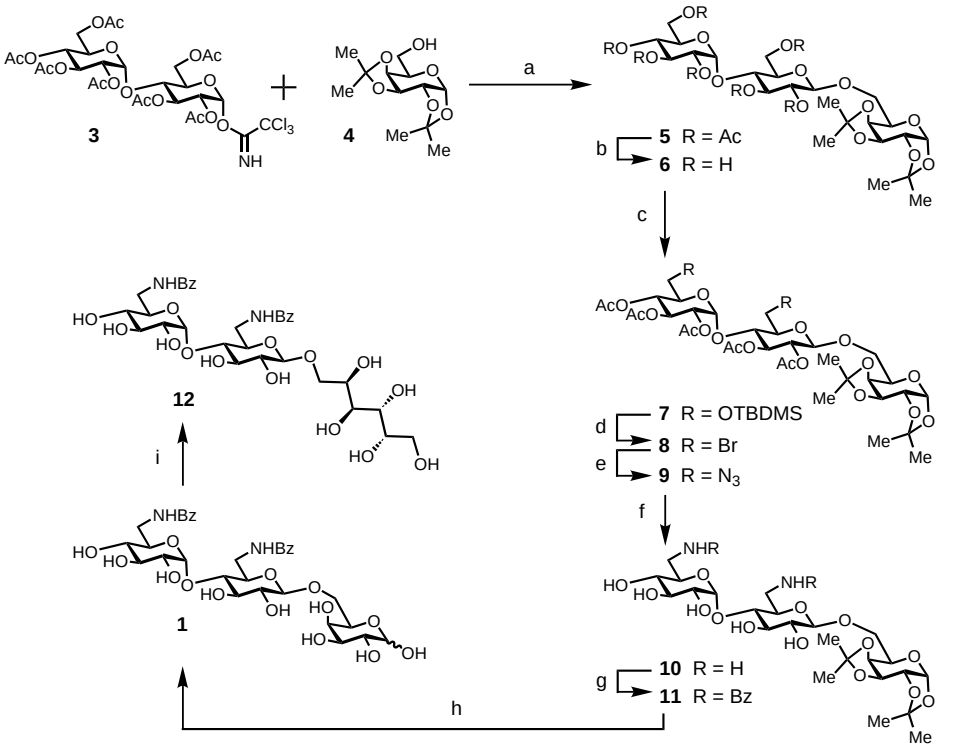


Figure 2. Retrosynthetic analysis of an oligosaccharide-based glycodendrimer with a maltosylgalactityl trisaccharide repeating unit. The outer portion of the dendrimer is derived from the benzamide-protected reducing sugar **1**, following reductive amination with the diamine **2**, which forms the internal branching units of the dendrimer.

sides can be handled easily on reversed-phase silica,[40] and so we chose to use benzamide groups (Figure 2) at the periphery of the dendrons to provide both 1) a degree of hydrophobicity to the dendrons and also 2) a UV-active probe for following the progress of reactions by reversed-phase HPLC. We addressed the issue of NMR characterization by choosing a linear β-maltosyl-(1 $\rightarrow$ 6)-galactose trisaccharide scaffold, in the first instance, for developing the coupling chemistry. A combination of both α- and β-linkages in the monomer trisaccharides helps to disperse the anomeric signals, which allows for easier identification of individual spin systems in the ^{1}H NMR spectra.

Synthesis of AB_2 monomers: The key trisaccharide scaffold was readily synthesized (Scheme 2) from maltose and galactose through the coupling of maltosyl trichloroacetimidate **3**[41] and the diacetone galactose derivative **4** to give the protected trisaccharide **5** in over 80% yield. Following deacetylation under Zemplén conditions, the amino functions were introduced into the primary positions of the glucosyl residues by a standard protecting-group approach. The primary hydroxy groups of the trisaccharide **6** were converted to *tert*-butyldimethylsilyl (TBDMS) ethers, before acetylating the secondary positions to give compound **7**. This bis-silyl ether was converted directly into the dibromide **8** by using triphenylphosphine and bromine, and then sodium azide was used to introduce nitrogen into the primary positions. It was found to be preferable to remove the acetyl groups from the diazide **9** prior to reduction, otherwise the 4-*O*-acetyl group on the terminal glucosyl residue migrates rapidly to give the 6-acetamido derivative. Following deprotection and azide reduction by transfer hydrogenation with hydrazine and Pearlman's catalyst, the diamine **10** was treated with benzoyl chloride in pyridine. The *O*-benzoates were removed under Zemplén conditions to provide the *N*-protected trisaccharide **11**. This approach was found to give better reproducibility than acylation using the Schotten–Baumann procedure. The isopropylidene acetals were hydrolyzed selectively with 90% trifluoroacetic acid (TFA) to give the hemiacetal **1** in good yield. Compound **1** provided very complex NMR spectra on account of the mixture of isomers that a reducing galactose residue can adopt. Consequently, the hemiacetal was reduced with sodium borohydride to give a single alditol derivative **12**, allowing easier characterization of this compound.

Since preliminary reductive amination experiments[29] using this masked aldehyde and primary diamine gave complex product mixtures of secondary and tertiary amines that proved tedious to separate, the bis-secondary amine AB_2



Scheme 2. Reagents: a) TMSOTf/CH_2Cl_2/4 Å MS (81%); b) NaOMe/MeOH (97%) c) 1. TBDMSCl/C_5H_5N, 2. Ac_2O/C_5H_5N (75% over two steps); d) $Br_2/PPh_3/CH_2Cl_2$ (95%); e) NaN_3/DMF (95%); f) 1. NaOMe/MeOH, 2. N_2H_4/Pd(OH)$_2$ on C/MeOH (93% over two steps); g) 1. BzCl/C_5H_5N, 2. NaOMe/MeOH (80% over two steps); h) TFA/H_2O (9:1) (80%); i) $NaBH_4$/MeOH (87%).

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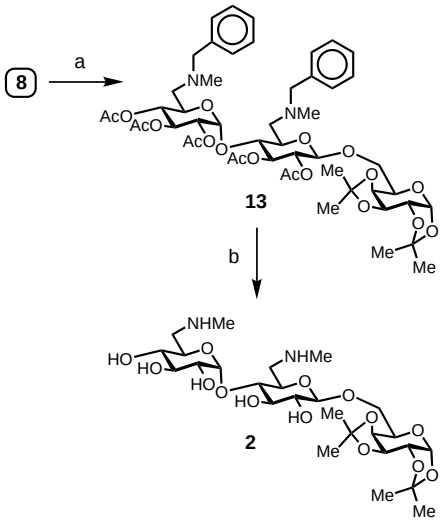
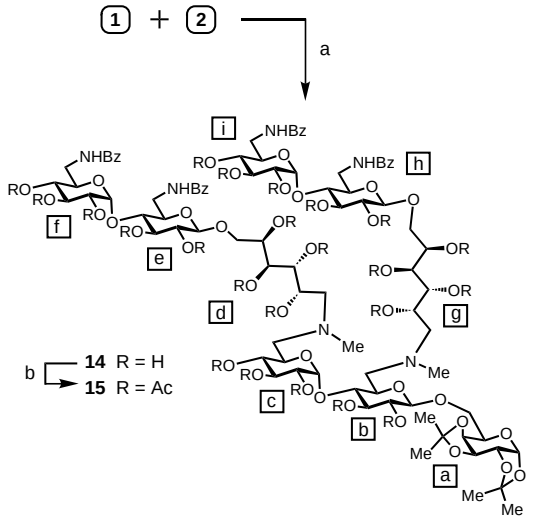
monomer **2** was also prepared (Scheme 3). The dibromide **8** was heated in *N*-benzylmethylamine to give, after replacing any acetates that were lost in the aminolysis side reaction, the bis-tertiary amine **13** in moderate yield. Again, it proved advantageous to remove the acetates prior to hydrogenolytic deprotection of the amino groups with hydrogen over Pearlman's catalyst.



Scheme 3. Reagents: a) 1. MeNHBn/Δ, 2. Ac_2O/C_5H_5N (42% over two steps); b) 1. NaOMe/MeOH, 2. $H_2/Pd(OH)_2$ on C/MeOH (92% over two steps).

Synthesis and characterization of a first-generation dendron: Reductive amination (Scheme 4) of the reducing sugar **1** with the diamine **2** was conducted with $NaCNBH_3$ at approximately pH 6–7. Under these conditions,[42] $NaCNBH_3$ reduces selectively iminium ions yet does not reduce aldehydes to alcohols. However, as $NaCNBH_3$ may also contain traces of $NaBH_4$, which does readily reduce aldehydes, it is preferable to purify the $NaCNBH_3$ according to a literature procedure[42] prior to use. Although reductive aminations can be conducted



Scheme 4. Reagents: a) $NaCNBH_3$/AcOH/MeOH (78%); b) Ac_2O/C_5H_5N (86%). Monosaccharide residue labels (in squares) for compound **14** relate to ^{1}H NMR spectra assignments given in Figures 3, 4, and 5 and in the Experimental Section.

in aqueous solution, the reaction proceeds more rapidly in MeOH, to give, almost exclusively,[29] the bis-tertiary amine dendron **14**. Reactions were followed by analytical HPLC as all of the amino compounds streaked badly on TLC. Following completion of the reaction, the product was isolated by reversed-phase chromatography with a solvent gradient from 100% H_2O to 100% MeOH (0.01% TFA throughout). The product eluted with approximately 70% MeOH, but curiously, beyond this solvent composition, any product still to be eluted was retained on the column. Further elution with approximately 70% MeOH allowed the remaining product to be recovered from the column. The first-generation dendron was found to be soluble in both H_2O and MeOH.

Although this first-generation dendron is already quite a complex molecule, a number of features may be easily identified in its NMR spectra (Figure 3). In addition to signals corresponding to the acetonide and benzamide protecting groups, the portion of the ^{1}H NMR spectrum from $\delta = 4.0$–5.5 ppm shows the expected five anomeric signals, indicating a degree of "pseudo-symmetry" in the molecule. The three α-anomeric signals are well dispersed from the two β-anomeric signals that overlap, in part, with two ring protons from the reducing-terminal galactose residue. Broadening of the signals relating to the protons around the branching point of the dendron is reflected in the DEPT-135 spectrum, in which low intensity peaks are observed for the corresponding ^{13}C nuclei, suggesting some restricted motion around the branching α-glycosidic linkage. Beyond these observations, severe overlap of resonances prevented easy assignment of the rest of the signals. The dendron was acetylated (Scheme 4) to try to improve the dispersion of the ring proton signals, and aid in their assignment. A combination of DEPT-135 and HMQC spectra of the peracetate **15** (Figure 4) allowed the identification of the anomeric signals and also the methylene signals, which conveniently fall into three groups—those attached to 1) *O*-glucosyl residues, 2) *N*-methyl groups, and 3) *N*-benzamide groups. With these introductions into each monosaccharide spin system, a combination of COSY and TOCSY 2D spectra allowed full assignment of all of the pyranose ring protons. Although the protons attached to C6 of the two galactityl residues appear as essentially equivalent in the ^{1}H NMR spectrum,[43] those attached to C1 of these residues do not share this "pseudo-symmetry". We hoped that we could distinguish these positions directly using through-space couplings across the amino linkages using a T-ROESY[44] experiment, but all such correlations were too close to the diagonal for clear identification. However, off diagonal correlations (Figure 5) between the H5s of the glucopyranosyl residues and the *N*-methyl groups and between the *N*-methyls and H2s of the galactityl residues allowed unambiguous identification of all carbohydrate proton signals, with the exception of H3 and H4 in each of the two galactityl units. Although no unambiguous correlations to these protons were observed in the homonuclear experiments conducted, the remaining four signals could be identified, by elimination, in the HMQC spectrum (Figure 4).

Synthesis and characterization of a second-generation dendron: With a first-generation dendron in hand, it was then

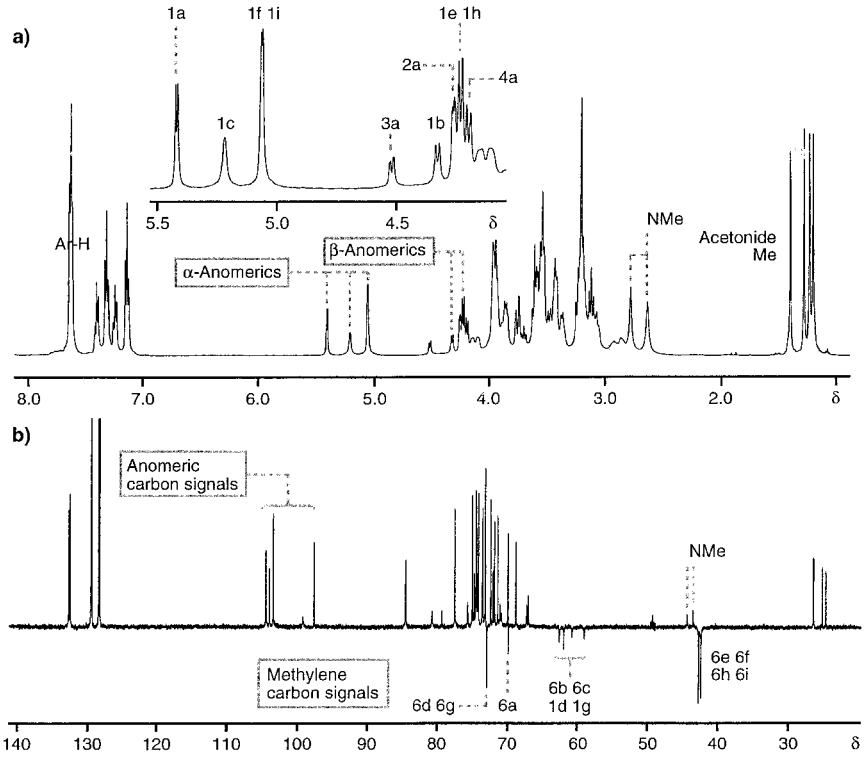


Figure 3. a) ^{1}H NMR spectrum (500 MHz, CD_3OD) of dendron **14** with an expansion of the anomeric region inset. b) DEPT-135 spectrum (125 MHz, CD_3OD) of the same compound, showing low intensity signals for nuclei around the branching point of the dendron.

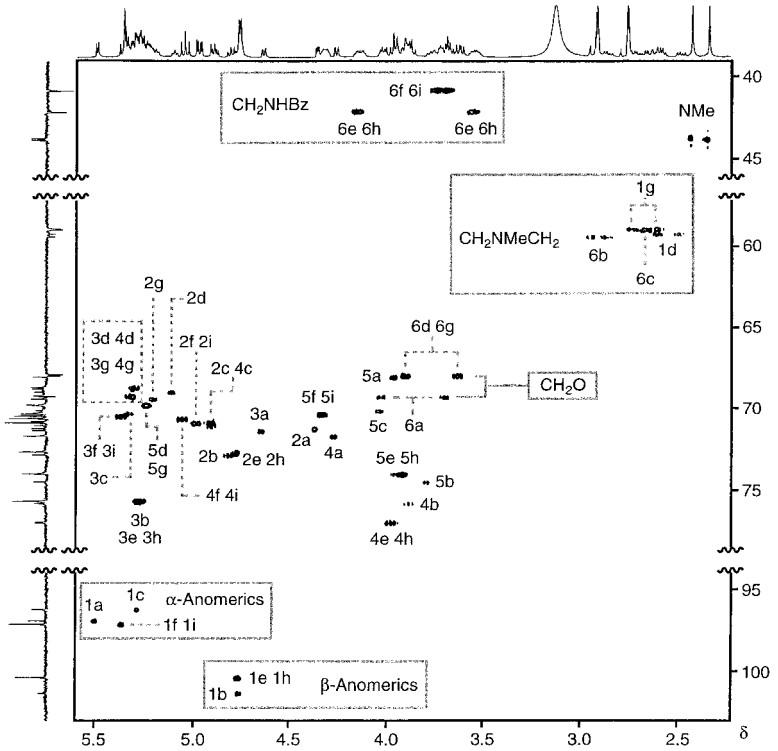


Figure 4. HMQC and DEPT-135 spectra of acetylated dendron **15** (500 MHz, $[D_7]$DMF), indicating the locations of the anomeric and methylene signals.

possible to synthesize a second-generation dendron. The isopropylidene acetals in the dendron **14** were hydrolyzed with TFA, as before, and both HPLC and electrospray mass spectroscopy indicated that the product (**16**) was homogeneous, albeit a mixture of anomers. Reductive amination of this reducing sugar with the bis-methylamino monomer **2**, under similar conditions to those used previously, gave the second-generation dendron **17** (Scheme 5), composed of 21 monosaccharide residues. On this occasion, since the product streaked quite badly on C-18 reversed-phase silica (Figure 6), it was separated from excess of starting material and under-substituted products by gel-permeation chromatography on Sephadex LH20 resin. The electrospray mass spectrum (Figure 7a) showed signals for $[M+6H]^{6+}$, $[M+5H]^{5+}$, $[M+4H]^{4+}$, and $[M+3H]^{3+}$, in accord with the six tertiary amino groups in the structure. The ^{1}H NMR spectrum gave good agreement between the integrals for the acetonide and benzamide protecting groups with the expected ratio of 40:12 protons. The anomeric region of this spectrum (Figure 7b) had seven anomeric signals—three in the "β-region" with integration ratios of approximately 4:2:1 and four signals in the "α-region" with ratios 4:2:1:1. A full assignment of the signals was not attempted as a consequence of the severe overlap of resonances.

Synthesis and characterization of a first-generation dendrimer: Continuing with the reductive amination theme, a trivalent amine was identified as a suitable core for the synthesis of a first-generation dendrimer. Reductive alkylation of tris-primary amine **18** has been reported[35c] for the synthesis of small glycoclusters, but, as with our[29] earlier experiments using reductive amination, mixtures of secondary and tertiary amines resulted. Therefore, we opted to use the known tris[2-(methylamino)ethyl]amine **20**,[45] which was prepared from commercially available tris(2-aminoethyl)amine **18** in two steps (Scheme 6). Tris-amine **18** was treated with ethylchloro-

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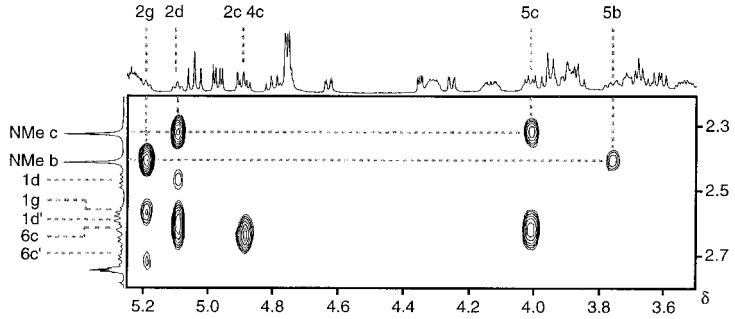


Figure 5. Section from the TROESY spectrum of acetylated dendron **15** (500 MHz, [D_7]DMF), showing crosspeaks to the NMe groups.

formate under basic conditions, and then the resulting tris-carbamate **19** was reduced with lithium aluminum hydride to afford **20**.

Reductive amination of the reducing sugar **16** with the trivalent core **20** was conducted at about pH 6–7 with $NaCNBH_3$, as in previous examples, to give the first-generation dendrimer **21** (Scheme 7). This water soluble dendrimer **21** was separated from excess of the starting material and under-substituted products by gel permeation chromatography on Sephadex G-50 resin (Figure 8). The MALDI-TOF mass spectrum showed the expected $[M+K]^+$ at $m/z = 5920.5$. The ^1H NMR spectrum of **21** displayed considerable line broadening in D_2O, even up to 85 °C, and coupling constants were found only to begin to resolve in [D_7]DMF around 100 °C. Therefore, **21** was acetylated to form **22** with the aim of obtaining a better resolved spectrum. The MALDI-TOF mass spectrum of **22** exhibited a molecular ion peak that was consistent with the acetylated dendrimer. The HMQC spectrum of **22** was also in good agreement with the proposed structure; however, signals for the core moiety could not be assigned unambiguously as a consequence of increased line broadening (especially associated with the tertiary amine groups), and many of the signals in the DEPT-135 spectrum were also found to be very weak.

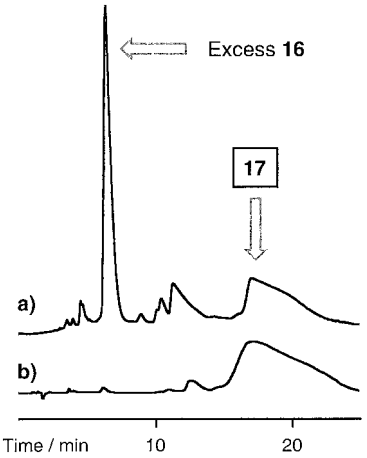
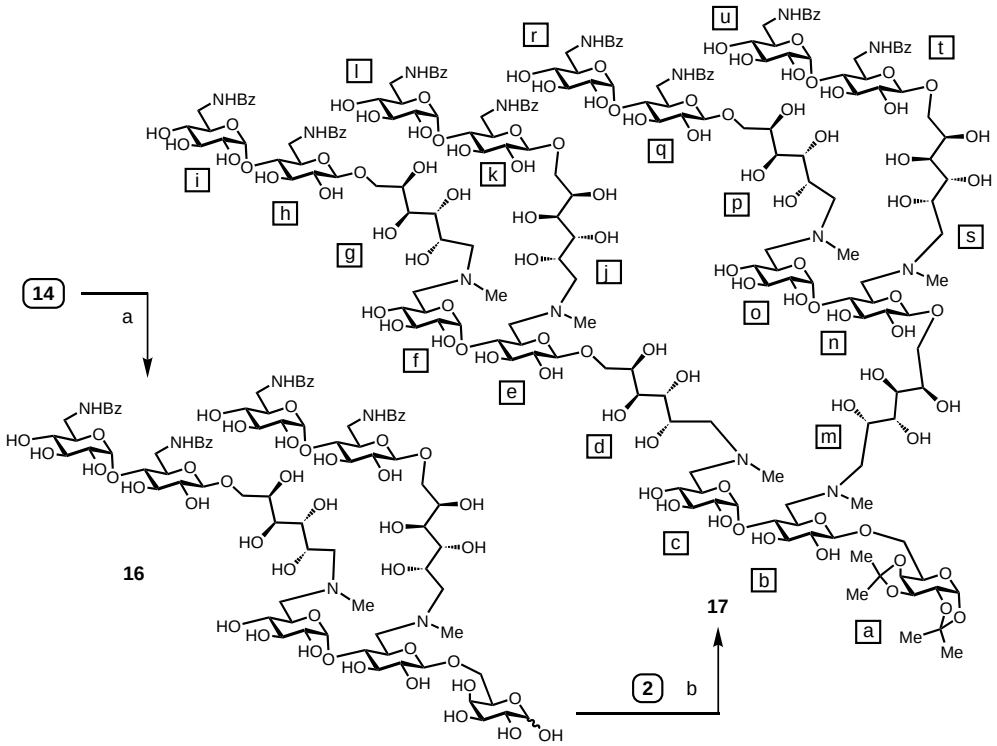


Figure 6. C-18 Reversed phase HPLC analysis (MeOH/H_2O/TFA, 65:35:0.0001 → 90:10:0.0001) of a) the reductive amination reaction mixture and b) the 21-mer dendron **17**, following isolation by gel permeation chromatography.



Scheme 5. Reagents: a) TFA/H_2O (9:1) (60%); b) $NaCNBH_3$/AcOH/MeOH (25%). Monosaccharide residue labels (in squares) for compound **17** relate to ^1H NMR spectra assignments given in Figure 7 and the Experimental Section

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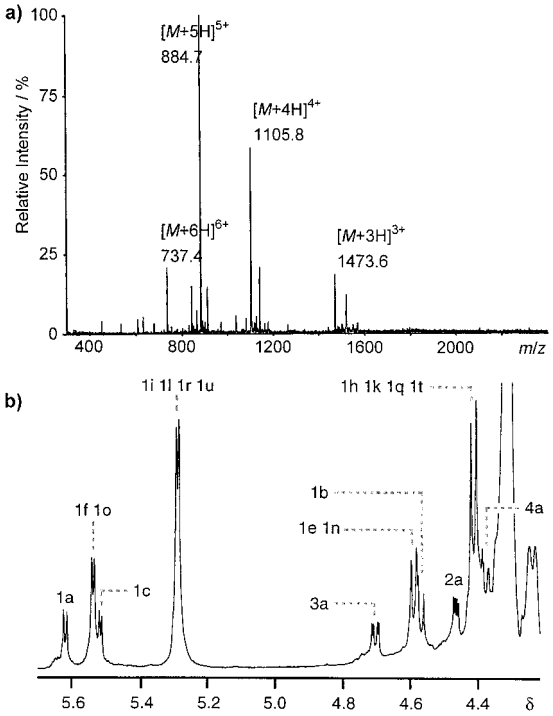
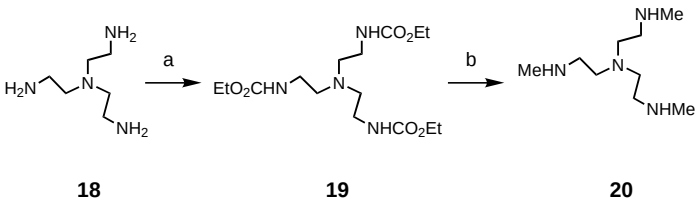
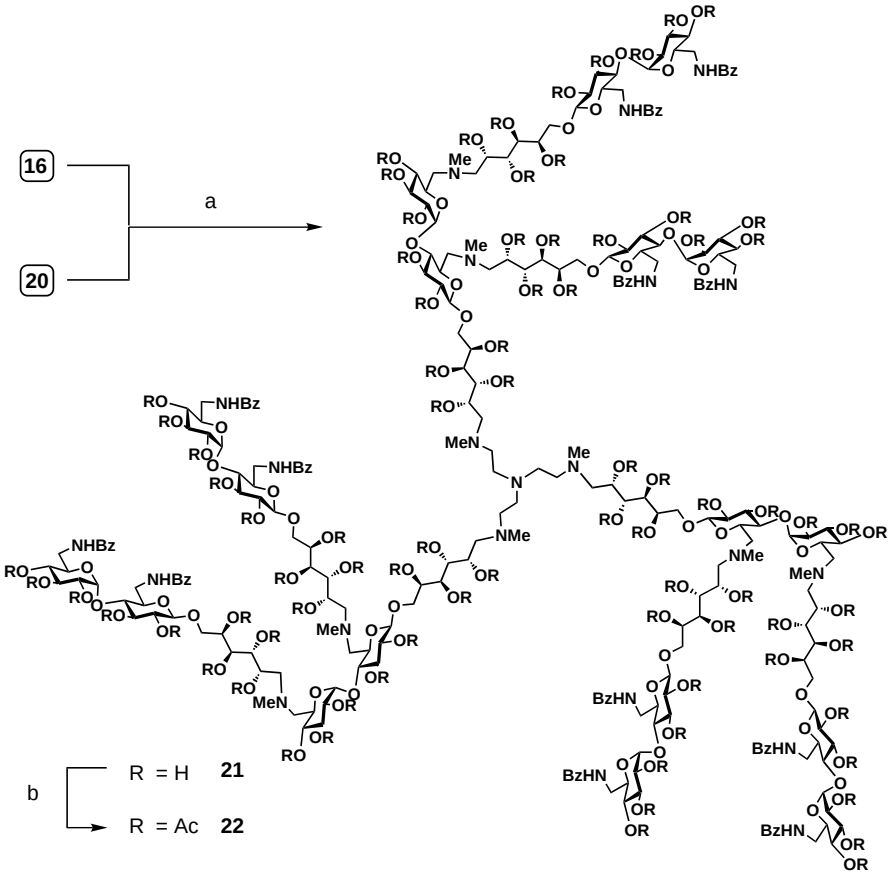


Figure 7. Characterization of the second-generation dendron **17**. a) Electrospray mass spectrum and b) partial ^{1}H NMR spectrum (500 MHz, D_2O) showing the anomeric region.



Scheme 6. Reagents: a) $ClCO_2Et/C_6H_6/H_2O/KOH$ (40%); b) $LiAlH_4$/THF (56%).

Molecular modeling of the second-generation dendron: Oligosaccharides, although flexible about their glycosidic linkages, are known[34] to adopt certain preferred conformations in solution. The solution conformations of alditols have been investigated, and it has been reported[46] that galactitol principally adopts an extended zig-zag conformation in which there are no unfavorable 1,3-*cis*-interactions between the hydroxyl substituents. Molecular dynamics (MD) simulations of the second-generation dendron **17** were used to assess the flexibility of the dendron and to search for low energy conformations. Plots of the ϕ versus ψ torsion angles for the Glc$\alpha(1\rightarrow4)$Glc linkages (Figure 9a and b) showed a single major conformation throughout all of the MD runs. However, the galactityl portion of the isolated trisaccharide repeat unit occupied several conformations (Figure 9a and b), under the conditions of the experiment, as evidenced from the plots of the C1–C4 versus C2–C5 and the C2–C5 versus C3–C6 torsion angles. The galactityl units in **17** (Figure 9b), by comparison, appeared to interconvert between these conformers only slowly (in a 4 ns MD run at 300 K), typically remaining close to their starting conformations. Therefore, to generate a large variety of structures in search of a global minimum conformation, a 4 ns MD run was conducted at 600 K, providing a full set of conformations similar to those shown in Figure 9a, for each trisaccharide repeat unit in the dendron. The lowest energy conformer obtained from minimization of 50 structures selected during the run is shown in Figure 9c. The average distance from the reducing terminal anomeric carbon to the peripheral benzamide nitrogen atoms was 17.5 Å during both the 600 K MD run and in the final minimized structure. Average distances between individual pairs of benzamide nitrogen atoms varied from 5 Å for those in the same maltosyl unit, to 18 Å separating N6q and N6l. The slow interconversions of the galactityl units and consistent conformations of the maltosyl branching points suggest that it should be possible to vary the shapes of these molecular



Scheme 7. Reagents: a) $NaCNBH_3$/AcOH/MeOH (54%); b) Ac_2O/C_5H_5N/DMAP (50%).

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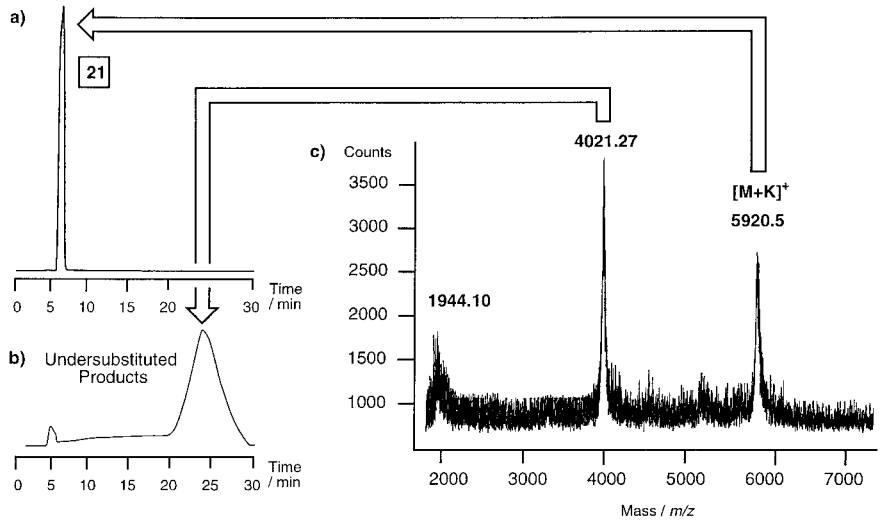

Figure 8. GPC traces of a) first-generation dendrimer **21**, b) undersubstituted products of the reductive amination reaction, and c) a MALDI-TOF mass spectrum of the product mixture isolated from the reaction.

scaffolds selectively, and thus influence the presentation of bioactive saccharides attached at the dendrons' peripheries by the appropriate selection of carbohydrate building blocks.

Conclusion

The synthesis of oligosaccharide-based dendrons and dendrimers by the reductive amination of suitable trisaccharide building blocks has been accomplished. The chemoselective coupling reaction allows dendron synthesis in the presence of only a few protecting groups, unlike earlier approaches to making carbohydrate-based dendrimers through chemical glycosylation. Furthermore, only a few synthetic steps are required to construct large dendrons, with the trisaccharide building blocks in hand. Interpretation of ^{1}H and ^{13}C NMR spectra is facilitated by including alternating α- and β-glycosidic linkages in both the monomers and dendrons, and acetylation of a first-generation dendron allowed for an almost complete assignment of its ^{1}H and ^{13}C NMR spectra through a combination of two-dimensional experiments. Molecular modeling reveals that the key maltose-based branching points on the dendrons retain the conformation of the parent compound and that the galactityl chains appear less flexible than in an isolated fragment of the dendron. Dendrons and dendrimers, such as these, should find useful application as scaffolds for the construction of large multivalent glycoconjugates. Studies to this effect will be reported in due course.

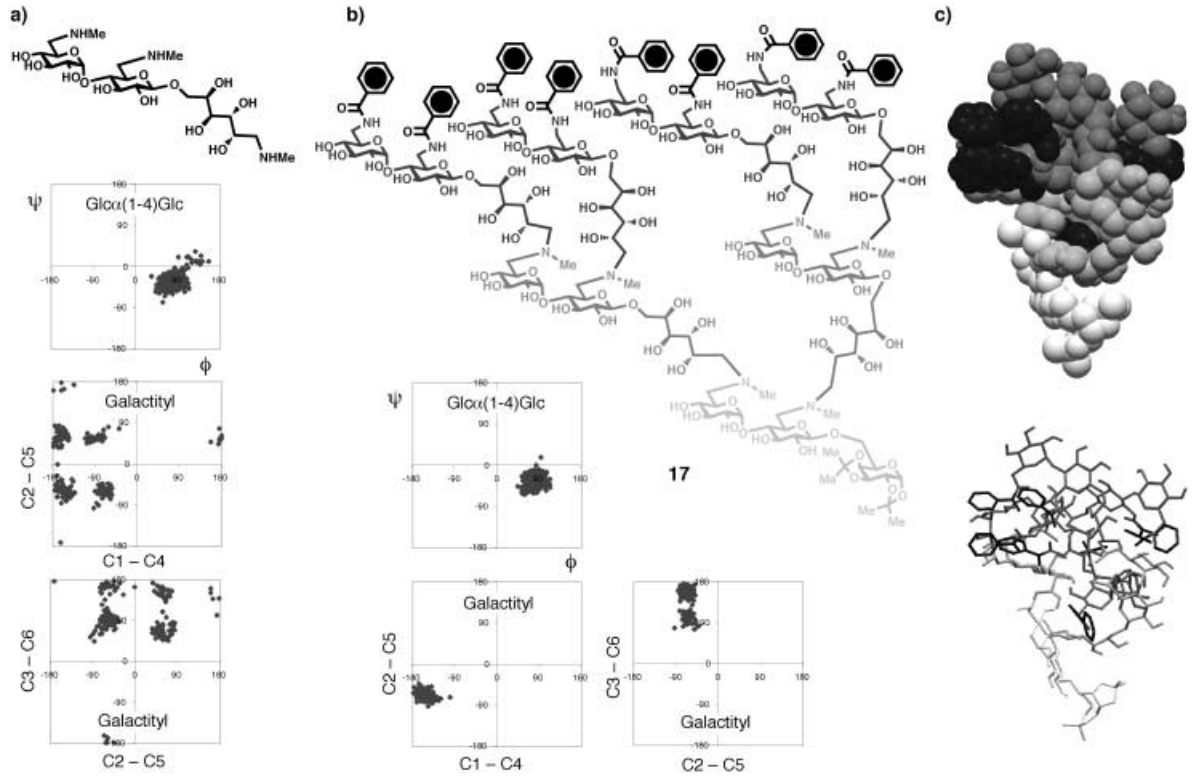

Figure 9. Plots of torsion angles, sampled during MD simulations, for the Glcα(1 $\rightarrow$ 4)Glc glycosidic linkage (ϕ vs. ψ) and the carbon backbone of the galactityl residue (C1-C4 vs. C2-C5 and C2-C5 vs. C3-C6) in a) an isolated trisaccharide repeat unit and b) representative examples from the second-generation dendron **17**. The MD simulations were conducted for a) 1 ns and b) 5 ns at 300 K as described in the Experimental section. c) Space-filling and polytube representations of the second-generation dendron **17**, highlighting the constituent trisaccharide residues in light grey through to dark grey and the peripheral benzamide groups in black.

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Experimental Section

General methods: All solvents were dried prior to use, according to standard methods. Sodium cyanoborohydride (Aldrich) was purified[42] as its dioxane complex prior to use. Otherwise, commercial reagents were used, without further purification. Analytical TLC was performed on silica gel 60-F_{254} (Merck) with detection by fluorescence and/or by charring following immersion in 5% H_2SO_4/EtOH. During workup, organic solutions were washed two or three times with equal volumes of each of the aqueous solutions listed. All concentrations were performed in vacuo. Flash chromatography was performed with silica gel 60 (Silicycle). Analytical reversed-phase HPLC was conducted by 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) and analytical GPC was performed by using a Ultrahydrogel 250 GPC column (7.8×250 mm) in water and UV detection with a Dynamax PDA-2 diode array detector. Preparative reversed-phase chromatography was conducted on fully endcapped C-18 or C-8 silica gel 100 (230–400 mesh, Fluka), and gel-permeation chromatography was performed using a 25×900 mm column of Sephadex LH20 resin (Sigma), eluting with MeOH. Optical rotations were measured at the sodium D-line with a Rudolph Research AUTOPOL IV automatic polarimeter. $[\alpha]_D$ values are given in units of 10^{-1} deg cm^2 g^{-1}. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker ARX400 spectrometer (at 400 MHz and 100 MHz, respectively) and on either Bruker ARX500 or Bruker Avance 500 spectrometers (at 500 MHz and 125 MHz, respectively) at ambient temperature unless stated otherwise. ^{1}H NMR and ^{13}C NMR spectra were referenced using their residual solvent signals as internal standards or to *t*BuOH for spectra run in D_2O. Signals were assigned using a combination of DEPT-135, dqf-COSY, and HMQC experiments, and where appropriate TOCSY and T-ROESY experiments. Gradient-selected versions of these 2D experiments were used on the Avance 500 spectrometer. All 2D experiments were acquired in phase sensitive mode. TOCSY and T-ROESY experiments used 70 ms and 500 ms mixing times, respectively. For trisaccharides, the monosaccharide residues are labeled a, b, c from the reducing terminus. For dendrons, the monosaccharide residues are labeled a to u as described in Schemes 4 and 5. The following abbreviations were used to explain the signal multiplicities or characteristics: s, singlet; d, doublet; dd, double doublet; pt, pseudo-triplet; pdt, pseudo-double-triplet; m, multiplet; br, broad. Fast atom bombardment (FAB) mass spectra were recorded on a VG ZAB-SE spectrometer using a 3-nitrobenzyl alcohol matrix. Fragment ions[47] resulting from loss of one or two monosaccharide residues from the reducing terminus are labeled as $[M-a]^+$ and $[M-(a+b)]^+$, respectively. For compounds that displayed only fragment ions in their FAB mass spectra, the samples were doped with sodium acetate to give strong $[M+Na]^+$, or they were studied by electrospray mass spectrometry (ES-MS) recorded on a Sciex API IIIR triple quadrupole electrospray mass spectrometer using H_2O/MeCN/HCOOH, 50:50:0.1 as the mobile phase. MALDI-TOF data were acquired with a DE-STR instrument and the matrix used was a methanolic solution containing cyano α-hydroxy cinnaminic acid and ammonium acetate. Elemental analyses were performed by Quantitative Technologies, NJ (USA).

2,3,4,6-Tetra-*O*-acetyl-α-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 (5): A solution of the trichloroacetimidate **3**[41] (15.0 g, 19.2 mmol) and the acceptor **4** (10.0 g, 38.4 mmol) in CH_2Cl_2 (275 mL) was stirred with powdered 4 Å molecular sieves (15.0 g) for 2 h under an argon atmosphere. After cooling the mixture to 0 °C, trimethylsilyl trifluoromethanesulfonate (695 μL, 3.8 mmol) was added dropwise over 5 min and stirring was continued at this temperature for 30 min. Triethylamine (0.7 mL, 5.0 mmol) was added to quench the reaction before filtering the solution through Celite and concentrating. Column chromatography (SiO_2, hexanes/EtOAc, 6:4 to 1:1) gave the trisaccharide **5** (13.6 g, 81%) as a solid foam. $[\alpha]_D^{20} = +9.2$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.32$, 1.33, 1.45, 1.50 (4s, 12H; $2CMe_2$), 2.00, 2.01, 2.02, 2.03, 2.04, 2.09, 2.14 (7s, 21H; 7COMe), 3.65–3.71 (m, 2H; H6a, H5b), 3.89–4.06 (m, 5H; H5a, H6a′, H4b, H5c, H6c), 4.18 (dd, $J_{3,4} = 7.9$ Hz, $J_{4,5} = 1.8$ Hz, 1H; H4a), 4.21–4.27 (m, 2H; H6b, H6c′), 4.29 (dd, $J_{1,2} = 4.9$ Hz, $J_{2,3} = 2.4$ Hz, 1H; H2a), 4.48 (dd, $J_{5,6} = 2.7$ Hz, $J_{6,6'} = 12.1$ Hz, 1H; H6b′), 4.58 (dd, $J_{2,3} = 2.4$ Hz, $J_{3,4} = 7.9$ Hz, 1H; H3a), 4.64 (d, $J_{1,2} = 7.9$ Hz, 1H; H1b), 4.81–4.88 (m, 2H; H2b, H2c), 5.05 (pt, $J_{3,4} \approx J_{4,5} = 9.7$ Hz, 1H; H4c), 5.26 (pt, $J_{2,3} \approx J_{3,4} = 9.0$ Hz, 1H; H3b), 5.36 (dd, $J_{2,3} = 10.4$ Hz, $J_{3,4} = 9.7$ Hz, 1H; H3c), 5.41 (d, $J_{1,2} = 4.0$ Hz, 1H; H1c), 5.49 (d, $J_{1,2} = 4.9$ Hz, 1H; H1a); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.6$ (3C), 20.7, 20.8, 20.9, 21.0, 24.4, 25.0, 25.9, 26.0, 61.5, 62.9, 67.7, 68.0, 68.5, 69.3, 69.4, 70.0, 70.4, 70.6, 71.2, 71.9, 72.1, 72.8, 75.2, 95.5, 96.2, 101.0, 108.6, 109.4, 169.4, 169.8, 169.9, 170.1, 170.4, 170.5, 170.6; FABMS: *m*/*z* (%): 901.29 (100) $[M+Na]^+$, 619.24 (20) $[M-a]^+$, 331.11 (20) $[M-(a+b)]^+$; elemental analysis calcd (%) for $C_{38}H_{54}O_{23}$ (878.8): C 51.93, H 6.19; found: C 51.84, H 6.13.

α-D-Glucopyranosyl-(1→4)-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (6): A solution of the heptaacetate **5** (13.6 g, 15.5 mmol) and NaOMe (3 mL, 0.5 M in MeOH, 1.5 mmol) in MeOH (250 mL) was kept overnight at RT. The solution was neutralized with Amberlite IR-120 (H^+ form) ion-exchange resin, filtered, and concentrated to afford **6** (8.8 g, 97%) as a white solid. $[\alpha]_D^{20} = +11.6$ ($c = 1$ in H_2O); ^{1}H NMR (500 MHz, CD_3OD): $\delta = 1.33$, 1.34, 1.40, 1.52 (4s, 12H; $2CMe_2$), 3.24–3.29 (m, 2H; H2b, H4c), 3.39 (m, 1H; 5b), 3.44 (dd, $J_{1,2} = 3.7$ Hz, $J_{2,3} = 9.7$ Hz, 1H; H2c), 3.54 (pt, $J_{3,4} \approx J_{4,5} = 9.1$ Hz, 1H; H4b), 3.59–3.71 (m, 5H, H6a, H3b, H3c, H5c, H6c), 3.79–3.85 (m, 2H; H6b, H6c′), 3.90 (dd, $J_{5,6} = 1.6$ Hz, $J_{6,6'} = 12.2$ Hz, 1H; H6b′), 4.02–4.08 (m, 2H; H5a, H6a′), 4.28–4.33 (m, 2H; H4a, H1b), 4.38 (dd, $J_{1,2} = 4.9$ Hz, $J_{2,3} = 2.4$ Hz, 1H; H2a), 4.63 (dd, $J_{2,3} = 2.4$ Hz, $J_{3,4} = 7.9$ Hz, 1H; H3a), 5.16 (d, $J_{1,2} = 3.7$ Hz, 1H; H1c), 5.52 (d, $J_{1,2} = 4.9$ Hz, 1H; H1a); ^{13}C NMR (125 MHz, CD_3OD): $\delta = 24.5$, 25.1, 26.3 (2C), 62.15, 62.7, 68.8, 69.9, 71.4, 71.8, 71.9, 72.4, 74.1, 74.6, 74.7, 75.0, 76.6, 77.5, 81.2, 97.7, 102.9, 104.6, 110.1, 110.4; FABMS: *m*/*z* (%): 717.5 (100) $[M+Cs]^+$, 607.5 (96) $[M+Na]^+$; HRFABMS: calcd for $C_{24}H_{40}O_{16}Na$ $[M+Na]^+$: 607.2214; found: *m*/*z*: 607.2203.

2,3,4-Tri-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-α-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 (7): *tert*-Butyldimethylsilyl chloride (5.16 g, 34.2 mmol) was added to a stirred solution of the trisaccharide **6** (8.0 g, 13.7 mmol) in C_5H_5N (80 mL) at 0 °C. After 1 h, more *tert*-butyldimethylsilyl chloride (5.16 g, 34.2 mmol) was added and stirring was continued at this temperature for a further 1 h and then at RT for 1 h before quenching the reaction by adding MeOH. The mixture was concentrated and then treated with Ac_2O (40 mL) and C_5H_5N (40 mL) at 60 °C overnight. Following concentration and co-evaporation with toluene, the mixture was dissolved in EtOAc (500 mL) and washed consecutively with 1M HCl, saturated $NaHCO_3$, and saturated NaCl solutions, before drying over anhydrous Na_2SO_4 and concentrating to a foam. Column chromatography (SiO_2, hexanes/EtOAc, 7:3 to 6:4) gave the bis-silylether **7** (10.4 g, 75%) as a solid foam. $[\alpha]_D^{20} = +15.0$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 0.02$, 0.03, 0.08, 0.09 (4s, 12H; 4SiMe), 0.88, 0.90 (2s, 18H; $2SiCMe_3$), 1.32 (s, 6H; CMe_2), 1.44, 1.49 (2s, 6H; CMe_2), 1.98, 1.99, 2.01, 2.02, 2.04 (5s, 15H; 5COMe), 3.35 (m, 1H; H5b), 3.59–3.65 (m, 2H; H6a, H6c), 3.71 (dd, $J_{5,6} = 1.5$ Hz, $J_{6,6'} = 11.5$ Hz, 1H; H6c′), 3.86–4.02 (m, 7H; H5a, H6a′, H4b, H6b, H6b′, H5c), 4.16 (dd, $J_{3,4} = 7.9$ Hz, $J_{4,5} = 1.7$ Hz, 1H; H4a), 4.27 (dd, $J_{1,2} = 4.9$ Hz, $J_{2,3} = 2.4$ Hz, 1H; H2a), 4.56 (m, 2H; H3a, H1b), 4.75–4.80 (m, 2H; H2b, H2c), 5.12 (pt, $J_{3,4} \approx J_{4,5} = 9.8$ Hz, 1H; H4c), 5.24 (pt, $J_{2,3} \approx J_{3,4} = 9.4$ Hz, 1H; H3b), 5.34 (pt, $J_{2,3} \approx J_{3,4} = 10.0$ Hz, 1H; H3c), 5.37 (d, $J_{1,2} = 3.7$ Hz, 1H; H1c), 5.48 (d, $J_{1,2} = 4.9$ Hz, 1H; H1a); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = -5.5$, −5.4, −5.1, −4.9, 18.4, 18.6, 20.6, 20.7, 20.8, 20.9, 21.0, 24.4, 25.0, 25.9 (2C), 26.0 (3C), 26.1 (3C), 61.5, 62.0, 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, 96.2, 100.8, 108.6, 109.3, 169.2, 169.9, 170.2, 170.3, 170.4 ; FABMS: *m*/*z* (%): 1045.23 (100) $[M+Na]^+$, 763.40 (10) $[M-a]^+$, 403.21 (80) $[M-(a+b)]^+$; elemental analysis calcd (%) for $C_{46}H_{78}O_{21}Si_2$ (1023.29): C 53.99, H 7.68; found: C 54.10, H 7.28.

2,3,4-Tri-*O*-acetyl-6-bromo-6-deoxy-α-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 (8): Bromine (1.25 mL, 24.4 mmol) was added dropwise to a stirred solution of the bis-silylether **7** (10.4 g, 10.2 mmol) and triphenylphosphine (6.7 g, 25.5 mmol) in CH_2Cl_2 at 0 °C, forming a precipitate. The mixture was allowed to warm to room temperature over 20 h, by which time, the precipitate had fully dissolved. The solution was diluted with CH_2Cl_2 (400 mL) and was washed consecutively with saturated $NaHCO_3$ solution and water, before drying over anhydrous Na_2SO_4 and concentrating. Column chromatography (SiO_2, CH_2Cl_2/EtOAc, 9:1 to 85:15) gave the dibromide **8** (8.9 g, 95%) as a solid foam. $[\alpha]_D^{20} = +8.0$ ($c = 1$ in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 1.32$, 1.33, 1.45, 1.50 (4s, 12H; $2CMe_2$), 2.01, 2.02, 2.05, 2.06, 2.07 (5s, 15H; 5COMe), 3.43 (dd, $J_{5,6} = 5.0$ Hz, $J_{6,6'} = 11.5$ Hz, 1H; H6c), 3.61 (dd, $J_{5,6'} =$

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2.7 Hz, $J_{6,6'}$ = 11.5 Hz, 1H; H6c′), 3.65–3.80 (m, 4H; H6a, H5b, H6b, H6b′), 3.93 (m, 1H; H5c), 4.00–4.08 (m, 3H; H5a, H6a′, H4b), 4.19 (dd, $J_{3,4}$ = 7.9 Hz, $J_{4,5}$ = 1.8 Hz, 1H; H4a), 4.29 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, 1H; H2a), 4.59 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, 1H; H3a), 4.68 (d, $J_{1,2}$ = 7.8 Hz, 1H; H1b), 4.83–4.88 (m, 2H; H2b, H2c), 5.04 (pt, $J_{3,4} \approx J_{4,5}$ = 9.6 Hz, 1H; H4c), 5.28 (pt, $J_{2,3} \approx J_{3,4}$ = 9.2 Hz, 1H; H3b), 5.37 (dd, $J_{2,3}$ = 10.5 Hz, $J_{3,4}$ = 9.5 Hz, 1H; H3c), 5.42 (d, $J_{1,2}$ = 3.9 Hz, 1H; H1c), 5.50 (d, $J_{1,2}$ = 5.0 Hz, 1H; H1a); ^{13}C NMR, (100 MHz, $CDCl_3$): δ = 20.5, 20.6, 20.7, 20.9, 21.0, 24.4, 25.0, 25.9, 26.0, 31.6, 32.9, 67.8, 69.0, 69.1, 69.4, 70.0, 70.4, 70.6, 70.7, 71.2, 71.9, 72.5, 73.8, 74.8, 95.1, 96.2, 100.9, 108.6, 109.4, 169.3, 169.7, 170.0, 170.2; FABMS: *m/z* (%): 943.32 (100) $[M+Na]^+$, 661.23 (35) $[M-a]^+$; elemental analysis calcd (%) for $C_{34}H_{48}Br_2O_{19}$ (920.55): C 44.36, H 5.26; found: C 44.60, H 5.22.

2,3,4-Tri-*O*-acetyl-6-azido-6-deoxy-α-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-azido-6-deoxy-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (9): A mixture of the dibromide **8** (7.00 g, 7.6 mmol), NaN_3 (4.90 g, 76 mmol) and DMF (60 mL) was stirred at 75 °C for 12 h, and then concentrated to about 25 mL. The mixture was diluted with EtOAc (500 mL) and washed with saturated NaCl solution, before drying over anhydrous Na_2SO_4, and concentrating to a syrup. Column chromatography (SiO_2, hexanes/EtOAc, 60:40 to 55:45) gave the diazide **9** (6.1 g, 95%) as white crystals. $[\alpha]_D^{20}$ = +23.2 (*c* = 0.5 in $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.32, 1.33, 1.45, 1.50 (4s, 12H; 2CMe_2), 2.00, 2.02, 2.03, 2.04, 2.05 (5s, 15H; 5COMe), 3.32 (dd, $J_{5,6}$ = 5.3 Hz, $J_{6,6'}$ = 13.4 Hz, 1H; H6c), 3.43 (dd, $J_{5,6'}$ = 2.7 Hz, $J_{6,6'}$ = 13.4 Hz, 1H; H6c′), 3.48 (dd, $J_{5,6}$ = 4.8 Hz, $J_{6,6'}$ = 13.5 Hz, 1H; H6b), 3.65–3.75 (m, 3H; H5a, H6a, H6b′), 3.85 (ddd, $J_{4,5}$ = 10.0 Hz, $J_{5,6}$ = 5.3 Hz, $J_{5,6'}$ = 2.7 Hz, 1H; H5c), 3.92 (m, 1H; H5b), 4.01–4.07 (m, 2H; H6a′, H4b), 4.18 (dd, $J_{3,4}$ = 7.9 Hz, $J_{4,5}$ = 1.9 Hz, 1H; H4a), 4.29 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, 1H; H2a), 4.58 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, 1H; H3a), 4.66 (d, $J_{1,2}$ = 7.9 Hz, 1H; H1b), 4.81 (dd, $J_{1,2}$ = 4.0 Hz, $J_{2,3}$ = 10.5 Hz, 1H; H2c), 4.88 (dd, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 9.6 Hz, 1H; H2b), 4.98 (pt, $J_{3,4} \approx J_{4,5}$ = 9.6, 1H; H4c), 5.27 (pt, $J_{2,3} \approx J_{3,4}$ = 9.2 Hz, 1H; H3b), 5.32 (dd, $J_{3,4}$ = 9.5 Hz, $J_{2,3}$ = 10.5 Hz, 1H; H3c), 5.41 (d, $J_{1,2}$ = 4.0 Hz, 1H; H1c), 5.50 (d, $J_{1,2}$ = 5.0 Hz, 1H; H1a); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.5, 20.6 (2C), 20.9, 21.0, 24.3, 25.0, 25.9, 26.0, 50.9, 51.0, 67.7, 69.0, 69.1, 69.2, 69.5, 70.0, 70.4, 70.6, 71.2, 71.9, 72.1, 73.7, 75.0, 95.1, 96.2, 100.9, 108.6, 109.4, 169.5, 169.8, 170.0, 170.2, 170.4; FABMS: *m/z* (%): 866.84 (100) $[M+Na]^+$, 585.33 (65) $[M-a]^+$; HRFABMS: calcd for $C_{34}H_{48}N_6O_{19}Na$ $[M+Na]^+$: 867.2872; found: *m/z*: 867.2878.

6-Amino-6-deoxy-α-D-glucopyranosyl-(1→4)-6-amino-6-deoxy-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (10): A solution of the the pentaacetate **9** (1.60 g, 1.89 mmol) and NaOMe (1 mL, 0.5 M in MeOH, 0.5 mmol) in MeOH (20 mL) was kept overnight at RT. The solution was neutralized with Amberlite IR-120 (H^+ form) ion-exchange resin, filtered, and concentrated. A solution of this residue and hydrazine hydrate (0.6 mL) in MeOH (50 mL) was heated under reflux for 4 h in the presence of 10% $Pd(OH)_2$/C (1.0 g). The solution was filtered through Celite and concentrated to give, after freeze-drying from H_2O, the diamine **10** (1.03 g, 93%) as an amorphous solid. $[\alpha]_D^{20}$ = +12.0 (*c* = 1 in H_2O); ^{1}H NMR (500 MHz, CD_3OD): δ = 1.33, 1.34, 1.39, 1.52 (4s, 12H; 2CMe_2), 2.76–2.83 (m, 2H, H6b, H6c), 3.04 (dd, $J_{5,6'}$ = 2.9 Hz, $J_{6,6'}$ = 13.4 Hz, 1H; H6c′), 3.12 (dd, $J_{5,6'}$ = 1.6 Hz, $J_{6,6'}$ = 13.8 Hz, 1H; H6b′), 3.17 (pt, $J_{3,4} \approx J_{4,5}$ = 9.5 Hz, 1H; H4c), 3.26 (dd, $J_{1,2}$ = 7.9 Hz, $J_{2,3}$ = 9.3 Hz, 1H; H2b), 3.35–3.42 (m, 2H; H4b, H5b), 3.45 (dd, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 9.5 Hz, 1H; H2c), 3.58–3.72 (m, 4H; H6a, H3b, H3c, H5c), 4.03–4.09 (m, 2H; H5a, H6a′), 4.32 (dd, $J_{3,4}$ = 7.9 Hz, $J_{4,5}$ = 1.1 Hz, 1H; H4a), 4.34 (d, $J_{1,2}$ = 7.9 Hz, 1H; H1b), 4.38 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, 1H; H2a), 4.64 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, 1H; H3a), 5.20 (d, $J_{1,2}$ = 3.7 Hz, 1H; H1c), 5.52 (d, $J_{1,2}$ = 5.0 Hz, 1H; H1a); ^{13}C NMR (100 MHz, CD_3OD): δ = 24.6, 25.1, 26.3 (2C), 43.6, 43.7, 68.8, 69.8, 71.9, 72.0, 72.4, 73.0, 74.0, 74.2, 74.6, 74.7, 76.0, 77.5, 82.9, 97.7, 102.8, 104.6, 110.0, 110.4; FABMS: *m/z* (%): 605.25 (100) $[M+Na]^+$, 583.27 (50) $[M+H]^+$; HRFABMS: calcd for $C_{24}H_{43}N_2O_{14}$ $[M+H]^+$: 583.2714; found: *m/z*: 583.2737.

6-Benzamido-6-deoxy-α-D-glucopyranosyl-(1→4)-6-benzamido-6-deoxy-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-O-isopropylidene-α-D-galactopyranose (11): Benzoyl chloride (2.77 mL, 24.0 mmol) was added dropwise to a solution of the diamine **10** (1.00 g, 1.72 mmol) in C_5H_5N at 0 °C. After stirring the mixture at RT for 24 h, the reaction was quenched by adding MeOH and concentrated. The resulting oil was dissolved in EtOAc and washed consecutively with 1 M HCl, saturated $NaHCO_3$, and saturated NaCl solutions, before drying over anhydrous Na_2SO_4 and concentrating to a foam. Benzoate esters were removed using NaOMe (1 mL, 0.5 M in MeOH, 0.5 mmol) in MeOH (50 mL), followed by neutralization with AcOH. Column chromatography (SiO_2, CH_2Cl_2/MeOH, 9:1 to 85:15) gave the bis-benzamide **11** (1.08 g, 80%) as an amorphous solid. $[\alpha]_D^{20}$ = −9.0 (c = 1 in MeOH); ^{1}H NMR (500 MHz, CD_3OD): δ = 1.26, 1.31, 1.32, 1.49 (4s, 12H; 2CMe_2), 3.20 (pt, $J_{3,4} \approx J_{4,5}$ = 9.5 Hz, 1H; H4c), 3.25–3.30 (m, 2H; H2b, H6b), 3.33 (pt, $J_{3,4} \approx J_{4,5}$ = 9.2 Hz, 1H; H4b), 3.49–3.54 (m, 2H; H5b, H2c), 3.61–3.73 (m, 4H; H6a, H3b, H3c, H6c), 3.88 (dd, $J_{5,6'}$ = 2.5 Hz, $J_{6,6'}$ = 14.0 Hz, 1H; H6c′), 3.97–4.07 (m, 4H; H5a, H6a′, H6b′, H5c), 4.18 (dd, $J_{3,4}$ = 8.0 Hz, $J_{4,5}$ = 1.4 Hz, 1H; H4a), 4.30 (d, $J_{1,2}$ = 7.9 Hz, 1H; H1b), 4.33 (dd, $J_{1,2}$ = 5.0 Hz, $J_{2,3}$ = 2.4 Hz, 1H; H2a), 4.55 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, 1H; H3a), 5.16 (d, $J_{1,2}$ = 3.8 Hz, 1H; H1c), 5.47 (d, $J_{1,2}$ = 5.0 Hz, 1H; H1a), 7.26 (m, 2H; 2Ar-H), 7.35 (m, 1H; Ar-H), 7.43 (m, 2H; 2Ar-H), 7.52 (m, 1H; Ar-H), 7.72–7.77 (m, 4H; 4Ar-H); ^{13}C NMR (125 MHz, CD_3OD): δ = 24.6, 25.1, 26.3 (2C), 42.4, 42.5, 68.9, 69.7, 71.8, 71.9, 72.5, 73.2, 73.6, 74.2, 74.4, 74.6, 74.8, 77.4, 84.5, 97.7, 103.4, 104.2, 110.0, 110.4, 128.3 (2C), 128.5 (2C), 129.4 (2C), 129.5 (2C), 132.5, 132.6, 135.4, 135.6, 170.2, 170.8; FABMS: *m/z* (%): 813.30 (10) $[M+Na]^+$, 791.31 (100) $[M+H]^+$, 775.30 (5) $[M-15]^+$, 531.20 (20) $[M-a]^+$; HRFABMS: calcd for $C_{38}H_{51}N_2O_{16}$ $[M+H]^+$: 791.3238; found: *m/z*: 791.3246.

6-Benzamido-6-deoxy-α-D-glucopyranosyl-(1→4)-6-benzamido-6-deoxy-β-D-glucopyranosyl-(1→6)-D-galactose (1): The diacetonide **11** (620 mg, 785 μmol) was treated with 90% aqueous TFA (5 mL) at RT for 15 min before concentration and co-evaporation with MeOH. Column chromatography (C-8 reversed-phase silica, H_2O to MeOH) gave the reducing sugar **1** (445 mg, 80%) as an amorphous solid after freeze drying from H_2O. $[\alpha]_D^{20}$ = +60.8 (*c* = 1 in H_2O); selected ^{1}H NMR data (400 MHz, CD_3OD): δ = 4.32–4.43 (β-anomers), 5.10–5.16 (α-anomers), 7.22 (m, 2H), 7.34 (m, 1H), 7.41 (m, 2H), 7.50 (m, 1H), 7.70 (m, 4H); ESMS: *m/z* (%): 711.2 (100) $[M+H]^+$, 733.1 (15) $[M+Na]^+$.

6-Benzamido-6-deoxy-α-D-glucopyranosyl-(1→4)-6-benzamido-6-deoxy-β-D-glucopyranosyl-(1→6)-D-galactitol (12): A portion of the hemiacetal **1** (40 mg, 56 μmol) was reduced with sodium borohydride (20 mg, 528 μmol) in MeOH (1 mL) at RT for 2 h. The reaction was quenched by adding Me_2CO, and concentrated. Column chromatography (C-8 reversed-phase silica, H_2O to MeOH) gave the alditol **12** (35 mg, 87%) as a glassy solid. $[\alpha]_D^{20}$ = +13 (*c* = 0.2 in H_2O); ^{1}H NMR (500 MHz, CD_3OD): δ = 3.18–3.23 (m, 2H; H6b, H4c), 3.27 (dd, $J_{1,2}$ = 7.8 Hz, $J_{2,3}$ = 9.5 Hz, 1H; H2b), 3.33 (pt, $J_{3,4} \approx J_{4,5}$ = 8.8 Hz, 1H; H4b), 3.48–3.56 (m, 2H; H5b, H2c), 3.60–3.72 (m, 8H; H1a, H1a′, H3a, H4a, H6a, H3b, H3c, H6c), 3.87 (dd, $J_{5,6}$ = 2.6 Hz, $J_{6,6'}$ = 14.0 Hz, 1H; H6c′), 3.90 (ptd, $J_{1,2} \approx J_{1',2}$ = 6.3 Hz, $J_{2,3}$ = 1.3 Hz, 1H; H2a), 3.98 (dd, $J_{5,6'}$ = 4.9 Hz, $J_{6,6'}$ = 9.8 Hz, 1H; H6a′), 4.06–4.10 (m, 2H; H5a, H5c), 4.12 (dd, $J_{5,6'}$ = 2.0 Hz, $J_{6,6'}$ = 14.0 Hz, 1H; H6b′), 4.30 (d, $J_{1,2}$ = 7.8 Hz, 1H; H1b), 5.15 (d, $J_{1,2}$ = 3.7 Hz, 1H; H1c), 7.25 (m, 2H; 2Ar-H), 7.37 (m, 1H; Ar-H), 7.44 (m, 2H; 2Ar-H), 7.52 (m, 1H; Ar-H), 7.74 (m, 4H; 4Ar-H); ^{13}C NMR (125 MHz, CD_3OD): δ = 42.4, 42.7, 65.0, 70.2, 71.2, 71.3, 71.7, 73.1, 73.2, 73.6, 74.3, 74.5, 74.6, 75.1, 77.5, 84.6, 103.5, 104.5, 128.3 (2C), 128.5 (2C), 129.4 (2C), 129.5 (2C), 132.5, 132.7, 135.5 (2C), 170.3, 170.9; ESMS: *m/z* (%): 713.3 (100) $[M+H]^+$, 735.2 (70) $[M+Na]^+$.

2,3,4-Tri-*O*-acetyl-6-*N*-benzylmethylamino-6-deoxy-α-D-glucopyranosyl-(1→4)-2,3-di-*O*-acetyl-6-*N*-benzylmethylamino-6-deoxy-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (13): A solution of the dibromide **8** (1.90 g, 2.1 mmol) in *N*-benzylmethylamine (5.7 mL) was stirred at 80 °C for 20 h. The reaction mixture was concentrated and the crude product mixture was re-acetylated with C_5H_5N (2 mL) and Ac_2O (2 mL) at RT overnight. The solution was concentrated, re-dissolved in EtOAc, and washed with saturated $NaHCO_3$ and saturated NaCl solutions, before drying over anhydrous Na_2SO_4 and concentrating to an oil. Column chromatography (SiO_2, hexanes/EtOAc, 6:4 to 1:1) gave the protected diamine **13** (0.87 g, 42%) as an amorphous solid. $[\alpha]_D^{20}$ = +12.0 (*c* = 1 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.34, 1.36, 1.43, 1.54 (4s, 12H; 2CMe_2), 1.88, 2.02, 2.04, 2.07, 2.10 (5s, 15H; 5COMe), 2.28, 2.35 (2brs, 6H; 2NMe), 2.46–2.53 (m, 2H; H6c, H6c′), 2.92 (dd, $J_{5,6}$ = 7.7 Hz, $J_{6,6'}$ = 13.5 Hz, 1H; H6b), 3.05 (bd, $J_{6,6'}$ = 13.5 Hz, 1H; H6b′), 3.52 (m, 2H; NCH_2Ph), 3.66 (d, $J_{A,B}$ = 13.4 Hz, 1H; NCH_2Ph), 3.74–3.81 (m, 3H; NCH_2Ph, H6a, H5b), 3.85 (pt, $J_{3,4} \approx J_{4,5}$ = 8.9 Hz, 1H; H4b), 3.96 (m, 1H; H5a), 4.01–4.06 (m, 2H; H6a′, H5c), 4.21 (dd, $J_{3,4}$ = 7.9 Hz, $J_{4,5}$ = 1.5 Hz, 1H; H4a), 4.33 (dd, $J_{1,2}$ = 4.9 Hz, $J_{2,3}$ = 2.4 Hz, 1H; H2a), 4.61 (dd, $J_{2,3}$ = 2.4 Hz, $J_{3,4}$ = 7.9 Hz, 1H; H3a), 4.67 (d, $J_{1,2}$ = 7.9 Hz, 1H; H1b), 4.85 (dd, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ = 10.6 Hz, 1H; H2c), 4.88 (pt, $J_{1,2} \approx J_{2,3}$ = 8.2 Hz, 1H; H2b), 4.96 (pt, $J_{3,4} \approx J_{4,5}$ = 9.7 Hz, 1H; H4c), 5.27–5.34 (m, 2H; H3b,

H3c), 5.43 (d, $J_{1,2}=3.9$ Hz, 1H; H1c), 5.54 (d, $J_{1,2}=5.0$ Hz, 1H; H1a), 7.25–7.36 (m, 10H; Ar-H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=20.5$, 20.6 (3C), 20.8, 24.3, 24.9, 25.8, 25.9, 42.6, 43.7, 57.2, 57.6, 62.2, 63.3, 67.6, 68.6, 69.6, 70.1, 70.2 (2C), 70.3, 70.5, 71.1, 72.1, 73.9, 74.7, 75.2, 95.1, 96.1, 100.6, 108.6, 109.3, 126.8, 126.9, 128.1 (2C), 128.2 (2C), 128.8 (2C), 128.9 (2C), 138.7, 138.8, 169.5, 169.8, 169.9, 170.1, 170.4; FABMS: m/z (%): 1001.45 (100) $[M+H]^+$, 985.10 (10) $[M-15]^+$, 741.20 (10) $[M-a]^+$, 392.17 (20) $[M-(a+b)]^+$; HRFABMS: calcd for $C_{50}H_{68}N_2O_{19}$ $[M+H]^+$: 1001.4494; found: m/z: 1001.4486.

6-Deoxy-6-methylamino-α-D-glucopyranosyl-(1→4)-6-deoxy-6-methylamino-β-D-glucopyranosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (2): A solution of the pentaacetate **13** (870 mg, 0.87 mmol) and NaOMe (0.5 mL, 0.5M in MeOH, 0.25 mmol) in MeOH (5 mL) was stirred at RT for 4 h. The solution was neutralized with Amberlite IR-120 (H^+ form) ion exchange resin, filtered and concentrated. A solution of the residue in MeOH (50 mL) was treated with 10% $Pd(OH)_2$/C (300 mg) under a hydrogen atmosphere for 2 h. The solution was filtered through Celite and concentrated to give the bismethylamine **2** (490 mg, 92%) as an amorphous solid after freeze-drying from H_2O. $[\alpha]_D^{20}=+15.6$ ($c=1$ in H_2O); ^{1}H NMR (500 MHz, CD_3OD): $\delta=1.33$, 1.34, 1.40, 1.52 (4s, 12H; $2CMe_2$), 2.44, 2.46 (2brs, 6H; 2NMe), 2.73–2.81 (m, 2H; H6b, H6c), 2.91–3.10 (m, 2H; H6b′, H6c′), 3.19 (pt, $J_{3,4}\approx J_{4,5}=9.4$ Hz, 1H; H4c), 3.25 (dd, $J_{1,2}=7.9$ Hz, $J_{2,3}=9.1$ Hz, 1H; H2b), 3.37 (pt, $J_{3,4}\approx J_{4,5}=9.1$ Hz, 1H; H4b), 3.44 (dd, $J_{1,2}=3.6$ Hz, $J_{2,3}=9.1$ Hz, 1H; H2c), 3.54 (m, 1H; H5b), 3.58–3.70 (m, 3H; H6a, H3b, H3c), 3.77 (m, 1H; H5c), 4.01–4.08 (m, 2H; H5a, H6a′), 4.30 (dd, $J_{3,4}=8.0$ Hz, $J_{4,5}=1.0$ Hz, 1H; H4a), 4.33 (d, $J_{1,2}=7.9$ Hz, 1H; H1b), 4.37 (dd, $J_{1,2}=4.9$ Hz, $J_{2,3}=2.4$ Hz, 1H; H2a), 4.63 (dd, $J_{2,3}=2.4$ Hz, $J_{3,4}=8.0$ Hz, 1H; H3a), 5.19 (d, $J_{1,2}=3.6$ Hz, 1H; H1c), 5.51 (d, $J_{1,2}=4.9$ Hz, 1H; H1a); ^{13}C NMR (125 MHz, CD_3OD): $\delta=24.6$, 25.1, 26.3, 26.4, 36.1, 36.4, 53.2, 53.9, 68.9, 69.8, 71.9, 72.0, 72.2, 72.5, 73.7, 74.0, 74.1, 74.7, 74.8, 77.4, 82.9, 97.8, 102.2, 104.4, 110.0, 110.5; FABMS: m/z (%): 611.50 (100) $[M+H]^+$, 351.33 (5) $[M-a]^+$; HRFABMS: calcd for $C_{26}H_{46}N_2O_{14}$ $[M+H]^+$: 611.3027; found: m/z: 611.3032.

6,6′-*N*,*N*′-Bis[6,6′-bis-benzamido-6,6′-dideoxy-β-maltosyl-(1→6)-D-galactit-1-yl]-6,6′-dideoxy-6,6′-dimethylamino-β-maltosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (14): A solution of the reducing sugar **1** (192 mg, 270 μmol), the diamine **2** (55 mg, 90 μmol), acetic acid (5 μL, 90 μmol) and sodium cyanoborohydride (34 mg, 540 μmol) in MeOH (4 mL) was heated under reflux for 8 h. The reaction mixture was cooled to RT, concentrated to approximately 1 mL and diluted with H_2O (8 mL), before being subjected to column chromatography (C-8 reversed-phase: MeOH/H_2O/TFA, 0:100:0.0001 to 100:0:0.0001) to afford the dendron **14** (140 mg, 70%) as its bis-TFA salt. $[\alpha]_D^{20}=+23.0$ ($c=1$ in H_2O); ^{1}H NMR (500 MHz, CD_3OD): $\delta=1.31$, 1.33, 1.38, 1.50 (4s, 12H; $2CMe_2$), 2.74 (brs, 3H; NMe), 2.88 (brs, 3H; NMe), 2.93–3.06 (brm, 2H), 3.15–3.36 (m, 15H), 3.45–3.74 (m, 22H), 3.81 (pt, $J=9.1$, 1H), 3.87 (brd, $J=13.9$, 2H), 3.93–4.10 (m, 11H), 4.18–4.28 (brm, 2H), 4.30 (dd, $J_{3,4}=7.9$ Hz, $J_{4,5}=1.3$ Hz, 1H; H4a), 4.33 (d, $J_{1,2}=7.7$ Hz, 2H; H1e, H1h), 4.36 (dd, $J_{1,2}=4.9$ Hz, $J_{2,3}=2.4$ Hz, 1H; H2a), 4.43 (d, $J_{1,2}=7.8$ Hz, 1H; H1b), 4.61 (dd, $J_{2,3}=2.3$ Hz, $J_{3,4}=7.9$ Hz, 1H; H3a), 5.16 (d, $J_{1,2}=3.6$ Hz, 1H; H1f, H1i), 5.32 (brd, $J_{1,2}\approx 3.0$ Hz, 1H; H1c), 5.52 (d, $J_{1,2}=4.9$ Hz, 1H; H1a), 7.25 (m, 4H; 4Ar-H), 7.35 (m, 2H; 2Ar-H), 7.43 (m, 4H; 4Ar-H), 7.52 (m, 2H; 2Ar-H), 7.74 (m, 8H; 8Ar-H); ^{13}C NMR (125 MHz, CD_3OD): $\delta=24.7$, 25.1, 26.4, 26.5, 42.2 (2C), 42.7 (2C), 43.6, 44.4, 59.1, 60.8, 62.0, 62.6, 67.1, 67.3, 68.9, 69.9, 70.0 (2C), 70.9, 71.1, 71.4 (2C), 71.8, 71.9, 72.1, 72.5, 73.0 (2C), 73.2 (3C), 73.6 (2C), 73.7, 74.2 (2C), 74.4, 74.5 (2C), 74.6 (2C), 74.8, 75.1 (2C), 75.7, 77.6 (2C), 79.4, 80.8, 84.5, 84.6, 97.7, 99.3, 103.5 (2C), 104.0, 104.5 (2C), 110.1, 110.5, 128.3 (4C), 128.5 (4C), 129.4 (4C), 129.5 (4C), 132.5 (2C), 132.7 (2C), 135.4 (2C), 135.5 (2C), 170.3 (2C), 170.8 (2C); ESMS: m/z (%): 1001.0 (100) $[M+2H]^{2+}$, 2001.2 (5) $[M+H]^+$; calcd for $C_{90}H_{130}N_6O_{44}$ $[M]$: 2000.0; average of observed m/z: 2000.1.

2,3,2′,3′,4′-Penta-*O*-acetyl-6,6′-dideoxy-6,6′-dimethylamino-6,6′-*N*,*N*′-bis[2,3,2′,3′,4′-penta-*O*-acetyl-6,6′-bisbenzamido-6,6′-dideoxy-β-maltosyl-(1→6)-2,3,4,5-tetra-*O*-acetyl-D-galactit-1-yl]-β-maltosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (15): A solution of the dendron **14** (35 mg, 17 μmol) and DMAP (2 mg) in Ac_2O (4 mL) and C_5H_5N (4 mL) was stirred at RT for 36 h, and then concentrated. The mixture was diluted with EtOAc (50 mL) and washed consecutively with 1M HCl, saturated $NaHCO_3$, and saturated NaCl solutions, before drying over anhydrous Na_2SO_4 and concentrating to a foam. Column chromatography (SiO_2, CH_2Cl_2/MeOH, 95:5, then Sephadex LH20, MeOH) gave the peracetate **15** (40 mg, 86%) as a solid foam. $[\alpha]_D^{20}=+24.8$ ($c=1$ in $CHCl_3$); ^{1}H NMR (500 MHz, $[D_7]$DMF, 350 K): $\delta=1.32$, 1.33, 1.40, 1.49 (4s, 12H; $2CMe_2$), 1.94–2.10 (m, 69H; 23COMe), 2.32, (s, 3H; NMe-c) 2.35 (s, 3H; NMe-b), 2.46 (dd, $J_{1,1'}=13.4$ Hz, $J_{1,2}=7.0$ Hz, 1H; H1d), 2.55–2.62 (m, 3H, H6c, H1d′, H1g), 2.66 (dd, $J_{5,6'}=6.0$ Hz, $J_{6,6'}=14.3$ Hz, 1H; H6c′), 2.71 (dd, $J_{1,1'}=13.6$ Hz, $J_{1,2}=5.4$ Hz, 1H; H1g′), 2.84 (dd, $J_{5,6}=7.2$ Hz, $J_{6,6'}=14.0$ Hz, 1H; H6b), 2.92 (dd, $J_{5,6'}=1.9$ Hz, $J_{6,6'}=14.0$ Hz, 1H; H6b′), 3.50–3.56 (m, 2H; H6e, H6h), 3.61 (dd, $J_{5,6}=7.6$ Hz, $J_{6,6'}=11.0$ Hz, 2H; H6d, H6g), 3.65–3.78 (m, 6H; H6a, H5b, H6f, H6f′, H6i, H6i′), 3.85–3.92 (m, 5H; H4b, H6d′, H5e, H6g′, H5h), 3.94–3.98 (m, 3H; H5a, H4e, H4h), 4.00–4.04 (m, 2H; H6a′, H5c), 4.10–4.16 (m, 2H; H6e′, H6h′), 4.25 (dd, $J_{3,4}=7.9$ Hz, $J_{4,5}=1.7$ Hz, 1H; H4a), 4.29–4.33 (m, 2H; H5f, H5i), 4.35 (dd, $J_{1,2}=4.9$ Hz, $J_{2,3}=2.4$ Hz, 1H; H2a), 4.63 (dd, $J_{2,3}=2.4$ Hz, $J_{3,4}=7.9$ Hz, 1H; H3a), 4.74–4.78 (m, 5H; H1b, H1e, H2e, H1h, H2h), 4.80 (pt, $J_{1,2}\approx J_{2,3}=8.0$ Hz, 1H; H2b), 4.87–4.91 (m, 2H; H2c, H4c), 4.97 (dd, $J_{1,2}=3.9$ Hz, $J_{2,3}=10.5$ Hz, 2H; H2f, H2i), 5.04 (pt, $J_{3,4}\approx J_{4,5}=9.6$, 2H; H4f, H4i), 5.09 (ptd, $J_{1,2}\approx J_{1',2}=7.0$ Hz, $J_{2,3}=1.8$ Hz, 1H; H2d), 5.18–5.37 (m, 16H; H3b, H1c, H3c, H3d, H4d, H5d, H3e, H1f, H3f, H2g, H3g, H4g, H5g, H3h, H1i, H3i), 5.49 (d, $J_{1,2}=5.0$ Hz, 1H; H1a), 7.39 (m, 4H; 4Ar-H), 7.46–7.50 (m, 6H; 6Ar-H), 7.53–7.56 (m, 2H; 2Ar-H), 7.90–7.94 (m, 8H; 8Ar-H), 8.11–8.17 (m, 4H; 4NH*Bz*); ^{13}C NMR (125 MHz, $[D_7]$DMF, 350 K): $\delta=20.3$–20.9 (m, 23C), 24.6, 25.1, 26.2, 26.3, 40.8 (2C), 42.2 (2C), 43.8, 43.9, 58.9, 59.0, 59.3, 59.4, 67.9, 68.0, 68.1, 68.8, 68.9, 69.1, 69.2, 69.3, 69.4, 69.5, 69.8, 69.9, 70.2, 70.3, 70.4 (2C), 70.5 (2C), 70.7 (2C), 70.8, 70.9 (2C), 71.1, 71.3, 71.4, 71.8, 72.7 (2C), 72.9, 74.0 (2C), 74.5, 75.7 (3C), 75.8, 76.9, 77.0, 96.2, 96.9, 97.1 (2C), 100.4 (2C), 101.3, 108.8, 109.5, 127.9 (4C), 128.0 (4C), 128.6 (4C), 128.8 (4C), 131.4 (2C), 131.7 (2C), 135.4 (2C), 135.7 (2C), 167.6 (2C), 167.9 (2C), 169.8–170.7 (m, 23C); MALDI-TOF: m/z: 2990 $[M+Na]^+$.

6,6′-*N*,*N*′-Bis[6,6′-bisbenzamido-6,6′-dideoxy-β-maltosyl-(1→6)-D-galactit-1-yl]-6,6′-dideoxy-6,6′-dimethylamino-β-maltosyl-(1→6)-D-galactose (16): The diacetonide **14** (104 mg, 47 μmol) was treated with 90% aqueous TFA (5 mL) at RT for 15 min before concentration and co-evaporation with MeOH. Column chromatography (C-18 reversed-phase silica, H_2O to MeOH) gave the reducing sugar **16** (60 mg, 60%) as an amorphous solid after freeze drying from H_2O. $[\alpha]_D^{20}=+37.6$ ($c=1$ in H_2O); ^{1}H NMR (500 MHz, D_2O, 323 K): $\delta=3.00$–3.06 (brm, 6H; 2NMe), 3.26–4.34 (m, 58H), 4.38–4.41 (2d, $J_{1,2}=8.0$ Hz, 2H; H1e, H1h), 4.56–4.63 (3d, $J_{1,2}=8.0$ Hz, ca. 2.5H; $H1a_\beta$, H1b), 5.25 (d, $J_{1,2}=3.6$ Hz, ca. 0.5H; $H1a_\alpha$), 5.27 (d, $J_{1,2}=3.8$ Hz, 2H; H1f, H1i), 5.59 (d, $J_{1,2}=3.7$ Hz, 1H; H1c), 7.25 (m, 4H; 4Ar-H), 7.34 (m, 2H; 2Ar-H), 7.47 (m, 4H; 4Ar-H), 7.52 (m, 4H; 4Ar-H), 7.59 (m, 2H; 2Ar-H), 7.66 (m, 4H; 4Ar-H); ESMS: m/z (%): 960.7 (100) $[M+2H]^{2+}$, 1921.0 (5) $[M+H]^+$; calcd for $C_{84}H_{122}N_6O_{44}$: $M=1919.9$; average of observed m/z: 1919.7.

6,6′-*N*,*N*′-Bis[6,6′-*N*,*N*′-bis[6,6′-bisbenzamido-6,6′-dideoxy-β-maltosyl-(1→6)-D-galactit-1-yl]-6,6′-dideoxy-6,6′-dimethylamino-β-maltosyl-(1→6)-D-galactit-1-yl}-6,6′-dideoxy-6,6′-dimethylamino-β-maltosyl-(1→6)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (17): Sodium cyanoborohydride (2.9 mg, 46.1 μmol) was added in three portions over the course of 3 h, to a solution of the reducing sugar **16** (60 mg, 27.9 μmol), the diamine **2** (5.7 mg, 9.3 μmol), and acetic acid (0.5 μL, 9.1 μmol) in MeOH (300 μL) heated under reflux. Heating was continued overnight. After cooling to room temperature, the reaction mixture was diluted with MeOH (2 mL), before being subjected to gel permeation chromatography (Sephadex LH20: MeOH) to afford **17** (10 mg, 25%) as an amorphous solid after freeze-drying from H_2O. Selected ^{1}H NMR data (500 MHz, D_2O, 343 K): $\delta=1.34$, 1.36, 1.45, 1.55 (4s, 12H; $2CMe_2$), 2.80–2.90 (m, 18H; 6NMe), 4.82 (d, $J_{1,2}=7.9$ Hz, 4H; H1h, H1k, H1q, H1t), 4.87 (dd, $J_{1,2}=4.9$ Hz, $J_{2,3}=2.4$ Hz, 1H; H2a), 4.97 (d, $J_{1,2}=8.0$ Hz, 1H; H1b), 5.00 (d, $J_{1,2}=8.1$ Hz, 2H; H1e, H1n), 5.11 (dd, $J_{2,3}=2.4$ Hz, $J_{3,4}=7.9$ Hz, 1H; H3a), 5.69 (d, $J_{1,2}=3.7$ Hz, 4H; H1i, H1l, H1r, H1u), 5.91 (d, $J_{1,2}=3.8$ Hz, 1H; H1c), 5.93 (d, $J_{1,2}=3.7$ Hz, 2H; H1f, H1o), 6.02 (d, $J_{1,2}=4.9$ Hz, 1H; H1a); ESMS: m/z (%): 737.4 (20) $[M+6H]^{6+}$, 884.7 (100) $[M+5H]^{5+}$, 1105.8 (55) $[M+4H]^{4+}$, 1473.6 (20) $[M+3H]^{3+}$; calcd for $C_{194}H_{290}N_{14}O_{100}$: $[M]$ 4418.5; average of observed m/z: 4418.4.

Tris[2-(*N*-{6,6′-*N*,*N*′-bis[6,6′-bisbenzamido-6,6′-dideoxy-β-maltosyl-(1→6)-D-galactit-1-yl]-6,6′-dideoxy-6,6′-dimethylamino-β-maltosyl-(1→6)-D-galactit-1-yl}methylamino)ethyl]amine (21): Acetic acid (2.28 μL, 45 μmol) was added to a solution of the reducing sugar **16** (90 mg, 47 μmol), tris[2-(methylamino)ethyl]amine **20**[45] (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. The mixture was allowed to cool to

  0947-6539/02/0813-2998 $ 20.00+.50/0 *Chem. Eur. J.* **2002**, *8*, No. 13

room temperature, diluted with H_2O (2 mL) and purified by preparative GPC Chromatography (Sephadex G-50, H_2O) to afford **21** (38 mg, 54%). $[\alpha]_D^{20} = +32$ ($c = 1$ in H_2O); selected ^{1}H NMR data (500 MHz, [D$_7$]DMF, 373 K): $\delta = 4.42$ (d, $J_{1,2} = 7.2$ Hz, 6H; H1e, H1h), 4.58 (d, $J_{1,2} = 7.5$ Hz, 3H; H1b), 5.20 (d, $J_{1,2} = 3.4$ Hz, 6H; H1f, H1i), 5.52 (br d, $J_{1,2} \approx 3.0$ Hz, 3H; H1c); MALDI-TOF: m/z: 5920.5 $[M+K]^+$.

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′-bisbenzamido-6,6′-dideoxy-*β*-maltosyl-(1 → 6)-2,3,4,5-tetra-*O*-acetyl-D-galactit-1-yl]amino-*β*-maltosyl-(1 → 6)-2,3,4,5-tetra-*O*-acetyl-D-galactit-1-yl}amino)ethyl]amine (22): The first-generation dendrimer **21** (38 mg, 6 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. The solution was concentrated by co-evaporation with PhMe, before diluting with EtOAc and washing with 1M HCl, saturated $NaHCO_3$, and saturated NaCl solutions, drying (Na_2SO_4), and concentrating to an oil. GPC chromatography (MeOH) gave **22** (27 mg, 50%) as an oil. $[\alpha]_D^{20} = +24$ ($c = 1$ in H_2O); selected ^{1}H NMR ([D$_7$]DMF, 500 MHz, 350 K): $\delta = 1.98$–2.17 (m, 243H; 81 COMe), 2.37 (s, 9H; 3 NMe), 2.43 (s, 9H; 3 NMe), 3.57 (m, 6H; H6e, H6h), 3.68 (m, 6H; H6f, H6i), 3.64 (m, 6H; H6f′, H6i′), 3.65 (m, 9H; H6a, H6d, H6g), 3.88 (m, 9H; H6a′, H6d′, H6g′), 3.93 (m, 6H; H5e, H5h), 3.99 (m, 6H; H4e, H4h), 4.02 (m, 3H; H5c), 4.13 (m, 6H; H6e′, H6h′), 4.33 (m, 6H; H5f, H5i), 4.72 (m, 3H; H1b), 4.77 (m, 9H; H2b, H2e, H2h), 4.78 (m, 6H; H1e, H1h), 4.90 (m, 6H; H2c, H4c), 4.97 (dd, $J_{1,2} = 3.9$ Hz, $J_{2,3} = 10.5$ Hz, 6H; H2f, H2i), 5.04 (pt, $J_{3,4} \approx J_{4,5} = 9.6$, 6H; H4f, H4i), 5.28 (m, 12H; H1c, H3b, H3e, H3h), 5.38 (m, 6H; H1f, H1i), 7.41 (m, 4H; 12 Ar-H), 7.50 (m, 6H; 18 Ar-H), 7.57 (m, 2H; 6 Ar-H), 7.94 (m, 8H; 24 Ar-H); selected DEPT-135 ^{13}C NMR ([D$_7$]DMF, 125 MHz): $\delta = 40.1$ (C6f, C6i), 42.0 (C6e, C6h), 72.4 (C2b, C2e, C2h), 73.4 (C5e, C5h), 75.5 (C3b, C3e, C3h), 76.6 (C4e, C4h), 96.0 (C1c), 96.9 (C1f, C1i), 99.9 (C1e, C1h), 100.0 (C1b), 127.9 (C-Ar), 128.0 (C-Ar), 128.6 (C-Ar), 128.8 (C-Ar), 131.5 (C-Ar), 131.7 (C-Ar); MALDI-TOF: m/z: 9222 $[M+H]^+$.

Molecular modeling: The molecular model of the second-generation dendron **17** was developed in a "convergent" fashion analogous to its chemical synthesis. Each of the distinct trisaccharide building blocks were constructed in the INPUT submode of Macromodel v5.0 and minimized by using the PRCG algorithm[48] with the Amber* forcefield[49] and the GB/SA solvation model for H_2O,[50] to a final energy gradient of < 0.05 kJ Å^{-1}. The molecules were subjected to a molecular dynamics (MD) run (1 ns, 300 K, 1.5 fs timestep) and structures, sampled at regular intervals, were each minimized as before, to select the conformer to be used in constructing the dendron. Appropriate trisaccharides were then linked together to form a first- and then a second-generation dendron. The process of minimization, MD, and minimization was repeated at each stage. The picture of **17** (Figure 9c) shows the lowest energy conformer obtained after minimization of 50 structures selected from a 4 ns MD run at 600 K. Conformational flexibility of the building blocks and dendrons were assessed by monitoring changes in selected torsion angels in both the maltosyl and galactityl units during MD runs.

Acknowledgement

This research was supported by the Wellcome Trust through the award of an International Prize Travelling Research Fellowship (054997/Z/98/Z) to WBT, and by the National Science Foundation (equipment grant CHE-9974928 and CHE-9808175). We thank Dr A. R. Pease for assistance with molecular modeling experiments.

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Received: January 30, 2002 [F3841]

  0947-6539/02/0813-3000 $ 20.00+.50/0