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An Expedient Approach to Internally Functionalized Chiral Dendrimers: Synthesis of a Dendritic Molecule Incorporating Furanoside Skeleton

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Abstract: In an approach to chiral dendritic molecules, a dendrimer incorporating pentose units in the interior and hexose units in the periphery is built up on a 1, 3, 5-trisubstituted aromatic core by using 1,2:5,6-diisopropylidene glucose as the carbohydrate precursor and a 3, 5-disubstituted aromatic unit as the branching block. The carbohydrate moiety also provides internal functionalities in the form of hemiacetal moiety of the furanoside ring.

Dendrimers are hyperbranched polymers of unique architecture, and their well-defined structure coupled with globular shape imparts some interesting biological and structural properties, which are useful for the development of new materials.[1] Dendrimers are expected to find important applications in catalysis,[2] encapsulation,[3] light-harvesting systems,[4] sequestering,[5] generation of materials of biochemical interest, and in other areas. So development of useful synthetic strategies for different dendritic skeletons remains an ever-important task.[6] In this context much attention has been focused on carbohydrate dendrimers due to their profound importance in biological recognition processes. This includes the well-known carbohydrate recognizing proteins such as lectins.[7] To modify the functional behavior of a dendrimer, it is necessary to make structural changes in a dendrimer by incorporating useful "internal" functionalities, which can affect the microenvironment of the dendrimer.[8] Presence of functionalities in the interior of the dendritic framework may pave the way for conjugation of other molecules such as peptides, thus leading to molecules with interesting and more specific biological properties.[7c,9] This makes the synthesis of dendrimers incorporating carbohydrate skeletons in the interior as well as in the periphery a worthwhile task, because apart from providing a chiral internal environment, introduction of other functional entities in the dendrimer skeleton will also be possible via conjugation through glycosidation or other methods. We report herein an expedient synthesis of dendritic species, which incorporate carbohydrate derived units as internal as well as the peripheral functionalities. Recently we demonstrated that 1,2:5,6-diisopropylideneglucofuranose is a particularly useful scaffold for carrying out different reactions leading to a variety of chiral products, which can again be transformed to a second generation of molecules of diverse skeletal frameworks.[10] The easy functionalization and defunctionalization of the diisopropylideneglucose moiety induced us to incorporate this unit in a dendritic structure, and a recent report[11] on its use for a similar purpose has prompted us to describe below the convergent synthesis of dendritic molecules from the aforementioned scaffold using a 1, 3, 5-trisubstituted aromatic core and a 3, 5-disubstituted aromatic branching block. The substitution pattern of the aromatic units proved to be beneficial to the characterization of the resulting dendrimers by NMR spectral analysis.

The synthesis of the core involved the alkylation of 1,2:5,6-diisopropylidene glucose (**2**) with 1,3,5-tris-bromomethylbenzene (**1**)[12a] in the presence of NaH in THF leading to the formation of **3**[12b,c] in 60% yield (Scheme 1). The ^{1}H NMR spectrum of **3** exhibited the three aromatic protons as a singlet at δ 7.24. A sequence of reactions involving removal of 5, 6-isopropylidene groups giving **4** followed by vicinal diol cleavage by $NaIO_4$ and subsequent oxidation of the resulting trialdehyde using silver oxide furnished the tricarboxylic acid derivative **5** in 50% overall yield from **3** (Scheme 1).

The present approach was based on the formation of amide bonds as the growth generating method. It appeared to be advantageous to use an aromatic amine **9** as the branching unit (Scheme 2), because the presence

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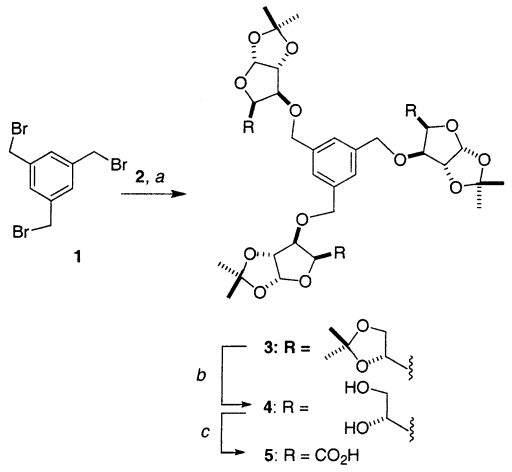
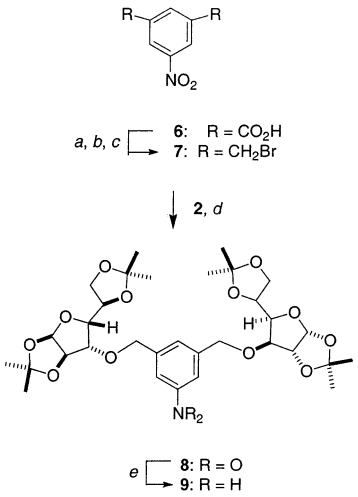
SCHEME 1[a]



[a] Reagents and conditions: (a) NaH, THF, reflux, 24 h, 60%. (b) 75% aq. AcOH, 12 h, 94%. (c) i. $NaIO_4$, MeOH−H_2O, 0−25 °C, 1 h, 90% ii. $AgNO_3$, KOH, EtOH−H_2O, 0−25 °C, 5 h, 60%.

SCHEME 2[a]



[a] Reagents and condition: (a) PCl_5, 120 °C, 1.5 h, 90%. (b) $NaBH_4$, diglyme, 6 h, 0−25 °C, 70%. (c) PBr_3, diethyl ether, 0 °C, 6 h, 97%. (d) NaH, THF, reflux, 6 h, 60%. (e) $FeSO_4$, NH_4OH, EtOH−H_2O, reflux, 3−4 h, 86%.

of the 1, 3, 5-trisubstituted aromatic moiety would considerably facilitate the characterization of the dendritic compounds by ^{1}H NMR spectroscopy. The synthesis of **9** started with the nitrocarboxylic acid **6**, which was converted to the known bis-bromomethyl derivative **7**[12d] in 61% overall yield via an alternative sequence of reactions involving formation of the corresponding acid chloride, $NaBH_4$ reduction, and treatment of the resulting diol with phosphorus tribromide. Alkylation of **2** with **7** in the presence of NaH gave rise to the nitro derivative **8**. The facility of the hydrolytic cleavage of the acetal functions of **9** in acidic medium called for reduction of the nitro group under a nonacidic condition. Consequently **8** was reduced by ferrous sulfate and ammonia in ethanol−water giving **9** in 86% yield.[13] The ^{1}H NMR spectrum of **9** revealed one-proton and two-proton singlets due to the aromatic protons at δ 6.64 and 6.62, respectively.

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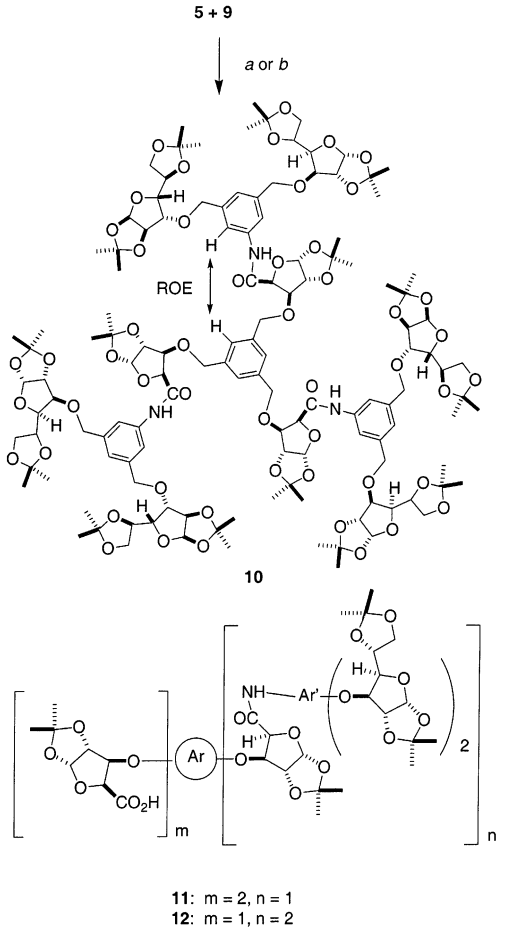
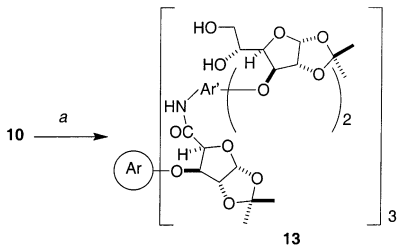
SCHEME 3[a]



[a] Reagents: (a) DCC, CH_2Cl_2, 25 °C, 48 h, **10** (20%), **11** (15%), **12** (40%). (b) HOBT, DCC, CH_2Cl_2, 25 °C, 72 h, **10** (65%), **11**/**12** (0%).

The coupling of the tricarboxylic acid **5** and the amine **9** was first attempted by using DCC. The reaction was found to be sluggish, because after 48 h the desired dendritic molecule **10** was formed in only 20% yield, whereas the incomplete dendrimers **11** and **12** were obtained in 15% and 40% yields, respectively (Scheme 3). The stepwise formation of the three species was evident from the TLC monitoring of the reaction. However, the yield of **10** was enhanced to 65% by using 1-hydroxybenzotriazole (HOBT) along with DCC in the reaction. More importantly, the formation of **11** or **12** was not observed in this reaction. The dendrimer **10** was characterized by ^{1}H and ^{13}C NMR spectral data including HSQC, ROESY, HMBC and HSQMBC. The symmetrical nature of **10** was evident from the ^{1}H and ^{13}C NMR spectra. The ^{1}H NMR spectrum revealed the numbers of the anomeric protons of the internal and the peripheral furanoside moieties in the ratio of 1:2 as expected of the symmetrical structure of **10**. The singlet at δ 7.13 due to the protons of the core aromatic ring provided the reference for the number of other equivalent protons in the ^{1}H NMR spectrum. The presence of three types of aromatic protons indicated the occurrence of the core as well as the three branching units. The ROESY spectrum of **10** exhibited a strong ROE between the aromatic protons of the core and the branch aromatic rings

SCHEME 4[a]



[a] Reagents: (a) 75% aq AcOH, 25 °C, 12 h, 95%.

(Scheme 3). This suggested that the peripheral units folds back on to the core in the NMR solvent (CD_3OD). The MALDI-TOF mass spectral data were also consistent with the molecular weight of **10**.

The occurrence of the protected furanoside rings in **10** is useful for the generation of other dendritic species. As an example, **10** could be easily converted to a dendritic compound **13** (Scheme 4) in 95% yield by treatment with 75% aqueous acetic acid, which selectively removes the 5,6-isopropylidene group, thereby generating four hydroxyl functions per branching unit. The importance of dendrimers with peripheral hydroxyl groups is well-known in dendrimer chemistry.[6a] The ^{1}H NMR spectrum of **13** exhibited the characteristic peaks having the required integration values due to the amide, aromatic, and anomeric protons. Additionally the two sets of methyl of the peripheral furanoside rings and the two sets of methyl of the internal furanoside rings appeared in the ratio of 2:1 as required by the structure of **13**. The ^{13}C NMR spectrum of **13** exhibited only two peaks due to the quaternary carbon atoms of the isopropylidene groups of the peripheral and the internal furanoside rings at δ 111.7 and δ 113.0, respectively, as expected for the structure. Also the four different sets of methyl carbon atoms in **13** were distinctly visible in the ^{13}C NMR spectrum. The molecular weight of **13** was consistent with the MALDI-TOF mass spectral data. An important feature of **13** is that it represents a potentially important precursor, which can give rise to a variety of other dendritic molecules by way of oxidation or functionalization of the vicinal OH groups.

In conclusion, the work described above provided an approach which will be useful for constructing chiral dendrimers containing hexose units in the periphery and pentose-derived linking units in the interior.[14] The anomeric carbon atoms of the carbohydrate residues provide sites for future conjugation with other useful units such as peptides. Additionally, the peripheral carbohydrate units can give rise to other functionalities through deprotection and/or derivatization.

Experimental Section

General. Melting points are uncorrected. NMR spectra are recorded on 300 and 600 MHz NMR spectrometers. FAB mass spectra are obtained in 3-nitrobenzyl alcohol matrix. MALDI-TOF mass spectral analysis was performed on CHCA matrix on a reflector mode. Solutions were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. Petroleum ether refers to fraction boiling at 60−80 °C. Unless otherwise mentioned silica gel of 60−120 mesh size was used for column chromatography. Elemental analyses were performed at the Indian Association for the Cultivation of Science, Kolkata.

Tris-1,2:5,6-diisopropylideneglucofuranose Derivative 3. 1,2:5,6-Diisopropylidene glucose (**2**) (2.40 g, 9.23 mmol) was added in portions to a stirred suspension of NaH (0.244 g, 10.17 mmol) in THF (60 mL) at 0 °C. After the addition was over, the mixture was stirred at 25 °C for 1 h. To this mixture was added dropwise with stirring a solution of 1, 3, 5-tris-bromomethyl benzene **1** (1.10 g, 3.08 mmol) in THF (40 mL) at 0 °C and stirring was continued for 30 min. The mixture was heated at reflux for 24 h. It was then cooled to 0 °C and few drops of water were added to destroy excess NaH. After concentration of the mixture, the residue was extracted with CH_2Cl_2. The combined organic layers were washed with water, dried, and concentrated. The residue was chromatographed over silica gel (EtOAc: petroleum ether, 1:4) to give **3** (1.65 g, 60%) as a colorless syrup, $[\alpha]^{25}_D$ −37.2 (*c* 0.42, $CHCl_3$). IR (Neat, cm^{-1}): 2986, 2935, 1614. MS (FAB): *m*/*z* 917 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24 (s, 3H), 5.90 (d, 3H, J = 3.6 Hz), 4.66 (s, 6H), 4.58 (d, 3H, J = 3.6 Hz), 4.36 (dd, 3H, J = 5.8, 6.0 Hz), 4.15−4.08 (m, 6H), 4.04−3.99 (m, 6H), 1.49 (s, 9H), 1.43 (s, 9H), 1.37 (s, 9H), 1.31 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.3 (q), 125.9 (CH), 111.8 (q), 109.0 (q), 105.2 (CH), 82.7 (CH), 81.9 (CH), 81.2 (CH), 72.5 (CH), 72.1 (CH_2), 67.4 (CH_2), 26.8 (2 × CH_3), 26.2 (CH_3), 25.5 (CH_3). Anal. Calcd for $C_{45}H_{66}O_{18}$: C, 60.39; H, 7.43. Found: C, 60.12; H, 7.42.

Tris-1,2-isopropylideneglucofuranose Derivative 4: A solution of **3** (1.5 g, 1.68 mmol) in 75% aq AcOH (50 mL) was stirred for 12 h at 25 °C. The mixture was then concentrated and the residue was coevaporated with toluene (3 × 40 mL) yielding the diol **4** (1.22 g, 94%) as a white foam, $[\alpha]^{25}_D$ −64.9 (*c* 0.36, $CHCl_3$). IR (KBr, cm^{-1}): 3421, 2940. MS (FAB). *m*/*z* 775 (M + H), 797 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32 (s, 3H), 5.94 (d, 3H, J = 3.5 Hz), 4.76 (d, 3H, J = 11.7 Hz), 4.66 (d, 3H, J = 3.6 Hz), 4.51 (d, 3H, J = 11.7 Hz), 4.07−4.01 (m, 9H), 3.82−3.79 (m, 3H), 3.63−3.61 (m,3H), 1.48 (s, 9H), 1.33 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1 (q), 127.3 (CH), 111.8 (q), 105.1 (CH), 81.8 (CH), 81.6 (CH), 79.9 (CH), 71.5 (CH_2), 69.1 (CH), 64.6 (CH_2), 26.6 (CH_3), 26.2 (CH_3). Anal. Calcd for $C_{36}H_{54}O_{18}$: C, 55.81; H, 7.02. Found: C, 55.65; H, 6.88.

Triacid 5. To a solution of the diol **4** (1.15 g, 1.48 mmol) in MeOH (40 mL) was added with stirring a solution of $NaIO_4$ (1.14 g, 5.33 mmol) in water (10 mL) dropwise at 0 °C. Stirring was continued at 0 °C for 1 h. The mixture was filtered and the filtrate was concentrated under reduced pressure. The residue was extracted with CH_2Cl_2, dried, and removal of solvent afforded a syrupy material. To a solution of $AgNO_3$ (2.05 g, 12.06 mmol) in water (5 mL) was added a solution of the above material in EtOH (2 mL) followed by a solution of KOH (1.37 g, 24.4 mmol) in H_2O (5 mL) dropwise at 0 °C with vigorous stirring. The mixture was stirred for an additional 5 h at 25 °C. It was then filtered and washed with water, and the filtrate was concentrated. The residue was cooled and acidified with 2 N HCl. The mixture was extracted with CH_2Cl_2, and the organic layer was washed with water, dried, and removal of solvent afforded the tricarboxylic acid **5** (0.58 g, 54%) as a white foam, $[\alpha]^{25}_D$ −43.3 (*c* 1.98, $CHCl_3$). IR (KBr, cm^{-1}): 3531, 1743, 1632. MS (FAB): *m*/*z* 727 (M +H), 749 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.62 (br s, 3H), 7.06 (s, 3H), 6.08 (d, 3H, J = 3.2 Hz), 4.94 (d, 3H, J = 3.6 Hz), 4.69 (d, 3H, J = 3.2 Hz), 4.64 (d, 3H, J = 11.2 Hz), 4.47 (d, 3H, J = 11.1 Hz), 4.32 (d, 3H, J = 3.5 Hz), 1.51 (s, 9H), 1.35 (s, 9H). ^{13}C NMR (75 Hz, $CDCl_3$): δ 173.1 (q), 137.3 (q), 126.0 (CH), 112.9 (q), 106.1 (CH), 83.5 (CH), 81.6 (CH), 79.5 (CH), 72.5 (CH_2), 27.0 (CH_3), 26.4 (CH_3). Anal. Calcd for $C_{33}H_{42}O_{18}$: C, 54.54; H, 5.83. Found: C, 54.18; H, 5.52.

Bis-1,2:5,6-Diisopropylideneglucofuranose Derivative 8. 1,2:5,6-Diisopropylidene-α-D-glucofuranose (**2**) (2.5 g, 9.72 mmol) was added in portions to a stirred suspension of NaH (0.26 g, 10.7 mmol) in THF (60 mL) at 0 °C. After the addition was over, the mixture was stirred at 25 °C for 1 h. A solution of **7** (vide

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Supporting Information for procedure) (1.5 g, 4.86 mmol) in THF (40 mL) was added dropwise to the mixture at 0 °C, and the stirring was continued for 30 min. The mixture was then heated under reflux for 6 h. Water was added to the mixture at 0 °C to destroy excess NaH, and after concentration of the mixture, the residue was extracted with CH_2Cl_2. The organic layer was washed with water and dried. Removal of solvent gave a syrupy liquid, which was chromatographed over silica gel (EtOAc: petroleum ether, 1:5) giving **8** (1.9 g, 60%) as a colorless foam, $[\alpha]^{25}_D$ −63.8 (*c* 0.22, $CHCl_3$). IR (KBr, cm $^{-1}$): 1537. MS (FAB): *m/z* 690 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.19 (s, 2H), 7.60 (s, 1H), 5.92 (d, 2H, J = 3.6 Hz), 4.80 (d, 2H, J = 12.6 Hz), 4.73 (d, 2H, J = 12.6 Hz), 4.62 (d, 2H, J = 3.7 Hz), 4.36 (dt, 2H, J = 8.4, 5.7 Hz), 4.16−4.01 (m, 8H), 1.50 (s, 6H), 1.43 (s, 6H), 1.38 (s, 6H), 1.33 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 148.7 (q), 140.0 (q), 131.6 (CH), 121.5 (CH), 111.9 (q), 109.3 (q), 105.3 (CH), 82.6 (CH), 82.2 (CH), 81.3 (CH), 72.3 (CH), 70.9 (CH_2), 67.6 (CH_2), 26.8 (CH_3), 26.7 (CH_3), 26.2 (CH_3), 25.3 (CH_3). Anal. Calcd for $C_{32}H_{45}NO_{14}$: C, 57.56; H, 6.79; N, 2.10. Found: C, 57.90; H, 6.51; N, 2.42.

Amine 9. Aqueous NH_4OH (30%, 31 mL) was added dropwise with stirring to a solution of $FeSO_4$ (22.4 g) in water (84 mL). After the addition was over, a solution of **8** (1.8 g, 2.7 mmol) in EtOH (5 mL) was slowly added to the previous mixture of ferrous hydroxide formed, and the mixture was heated under reflux for 4 h in an atmosphere of N_2. After it was cooled to 25 °C, the mixture was diluted with CH_2Cl_2 (50 mL) and filtered. The residue was washed repeatedly with CH_2Cl_2, and the filtrate was placed in a separatory funnel. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (2 × 30 mL). The combined organic layer was washed with water and dried. Removal of solvent afforded a syrupy residue, which on chromatography over silica gel (100−200 mesh size; EtOAc:petroleum ether, 1:4) gave **9** (1.48 g, 86%) as a pale yellow foam, $[\alpha]^{25}_D$ −31.7 (*c* 2.54, $CHCl_3$). IR (KBr, cm $^{-1}$): 3462, 3372, 1610; MS (FAB): *m/z* 638 (M + H), 660 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.64 (s, 1H), 6.62 (s, 2H), 5.89 (d, 2H, J = 3.7 Hz), 4.61−4.57 (m, 6H), 4.38−4.32 (m, 2H), 4.15−4.00 (m, 8H), 1.49 (s, 6H), 1.43 (s, 6H), 1.38 (s, 6H), 1.31 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 146.8 (q), 139.2 (q), 116.7 (CH), 113.5 (CH), 111.8 (q), 109.0 (q), 105.3 (CH), 82.7 (CH), 81.7 (CH), 81.3 (CH), 72.5 (CH), 72.2 (CH_2), 67.4 (CH_2), 26.9 (CH_3), 26.8 (CH_3), 26.3 (CH_3), 25.5 (CH_3). Anal. Calcd for $C_{32}H_{47}NO_{12}$: C, 60.27; H, 7.43; N, 2.20. Found: C, 60.26; H, 7.12; N, 2.46.

Dendritic Compound 10: **Method A.** To a solution of **5** (0.2 g, 0.275 mmol) and **9** (0.53 g, 0.832 mmol) in CH_2Cl_2 (2.5 mL), DCC (0.2 g, 0.970 mmol) was added at 0 °C with stirring, and the stirring was continued at 25 °C for 48 h. The mixture was then filtered and washed with CH_2Cl_2. The organic layer was washed with water, dried, and removal of solvent gave a syrupy liquid, which was chromatographed over basic alumina (EtOAc: petroleum ether, 1:2) affording **10** (0.142 g, 20%). Further elution afforded **12** (0.216 g, 40%) and **11** (0.056 g, 15%). **10**: $[\alpha]^{25}_D$ −66.1 (*c* 1.09, $CHCl_3$). IR (KBr, cm^{-1}): 1693, 1610. MS (MALDI-TOF): *m/z* 2585.6 (M + H). ^{1}H NMR (600 MHz, CD_3OD): δ 7.60 (s, 6H), 7.13 (s, 3H), 6.83 (s, 3H), 6.09 (d, 3H, J = 3.5 Hz), 5.88 (d, 6H, J = 3.7 Hz), 4.77 (d, 3H, J = 3.5 Hz), 4.68 (d, 6H, J = 11.8 Hz), 4.67 (m, 6H), 4.61 (m, 3H), 4.59 (d, 6H, J = 11.8 Hz), 4.34 (ddd, 6H, J = 7.3, 6.3, 5.5 Hz), 4.14 (m, 3H), 4.12 (m, 6H), 4.12 (d, 3H, J = 12.4 Hz), 4.06 (d, 3H, J = 12.4 Hz), 4.02 (dd, 6H, J = 8.5, 5.5 Hz), 3.98 (d, 6H, J = 3.2 Hz), 3.91 (dd, 6H, J = 8.5, 5.5 Hz), 1.52 (s, 9H), 1.45 (s, 18H), 1.41 (s, 9H), 1.38 (s, 18H), 1.31(s, 18H), 1.27 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8 (q), 139.1 (q), 137.7 (q), 137.5 (q), 126.0 (CH), 122.3 (CH), 118.0 (CH), 112.9 (q), 111.8 (q), 109.0 (q), 105.6 (CH), 105.2 (CH), 82.6 (CH), 82.3 (CH), 82.0 (CH), 81.2 (CH), 77.2 (CH), 72.4 (CH), 72.1 (CH_2), 71.9 (CH_2), 67.3 (CH_2), 27.0 (CH_3), 26.8 (2 x CH_3), 26.5 (CH_3), 26.2 (CH_3), 25.4 (CH_3). Anal. Calcd for $C_{129}H_{177}N_3O_{51}$: C, 59.92; H, 6.90; N, 1.63. Found: C, 59.63; H, 6.63; N, 1.54.

11. MS (MALDI-TOF): *m/z* 1345.4 (M + H). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.34 (s, 1H), 7.56 (s, 2H), 7.13−7.11 (m, 4H), 6.08−6.04 (m, 3H), 5.89 (d, 2H, J = 3.6 Hz), 5.03 (br, 2H), 4.82 (d, 1H, J = 3.1 Hz), 4.47−4.46 (m, 12H), 4.40−4.28 (m, 4H), 4.15−3.99 (m, 12H), 1.49 (s, 9H), 1.47 (s, 6H), 1.42 (s, 6H), 1.37 (9H), 1.34 (s, 6H), 1.30 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.8 (q), 152.8 (q), 139.2 (q), 137.7 (q), 126.3 (CH), 122.4 (CH), 117.9 (CH), 112.8 (q), 111.8 (q), 109.0 (q), 105.7 (CH), 105.3 (CH), 84.5 (CH), 82.7 (CH), 82.5 (CH), 82.1 (CH), 81.3 (CH), 80.7 (CH), 72.5 (CH), 72.2 (CH_2), 72.0 (CH_2), 67.4 (CH_2), 27.2 (CH_3), 26.8 (CH_3), 26.7 (2 x CH_3), 26.3 (CH_3), 25.5 (CH_3).

12. $[\alpha]^{25}_D$ −54.1 (*c* 1.19, $CHCl_3$). IR (KBr, cm^{-1}): 3403, 1696, 1614. MS (MALDI-TOF): *m/z* 1966 (M), 1989 (M + Na). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.36 (s, 2H), 7.55 (s, 4H), 7.10 (s, 2H), 7.07 (s, 3H), 6.06 (d, 2H, J = 3.1 Hz), 6.01 (d, 1H, J = 3.6 Hz), 5.89 (d, 4H, J = 3.5 Hz), 5.01 (d, 1H, J = 4.3 Hz), 4.81 (d, 2H, J = 3.0 Hz), 4.66 (s, 8H), 4.60−4.59 (m, 6H), 4.55−4.45 (m, 4H), 4.44−4.23 (m, 10H), 4.14−4.07 (m, 8H), 4.03−3.98 (m, 8H), 1.48 (21H), 1.42 (12H), 1.36 (12H), 1.35 (s, 9H), 1.30 (s,12H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.0 (q), 165.8 (q), 152.8 (q), 139.1 (q), 137.8 (q), 137.5 (q), 126.2 (CH), 122.3 (CH), 117.9 (CH), 113.0 (q), 112.7 (q), 111.7 (q), 109.0 (q), 105.6 (CH), 105.2 (CH), 84.4 (CH), 82.6 (CH), 82.5 (CH), 82.4 (CH), 82.2 (CH), 82.0 (CH), 81.25 (CH), 81.19 (CH), 80.6 (CH), 77.2 (CH), 72.4 (CH), 72.3 (CH_2), 72.1 (CH_2), 71.9 (CH_2), 67.3 (CH_2), 27.2 (CH_3), 27.0 (CH_3), 26.8 (2 x CH_3), 26.4 (CH_3), 26.2 (CH_3), 25.9 (CH_3), 25.4 (CH_3). Anal. Calcd for $C_{97}H_{132}N_2O_{40}$: C, 59.26; H, 6.77; N, 1.42. Found: C, 59.54; H, 6.97; N, 1.71.

Method B. A solution of **5** (0.2 g, 0.275 mmol), HOBT (0.23 g, 1.70 mmol), and DCC (0.21 g, 1.0 mmol) in CH_2Cl_2 (5 mL) was stirred at 0 °C for 1 h and then the mixture was stirred for another 1 h at 25 °C. It was then cooled to 0 °C and **9** (0.53 g, 0.832 mmol) was added to the mixture and stirred at 25 °C for 72 h. The mixture was then filtered and washed with CH_2Cl_2. The organic layer was washed with water, dried and removal of solvent gave a syrupy liquid, which was chromatographed over basic alumina (EtOAc:petroleum ether, 1:2) affording **10** (0.46 g, 65%) as a foam.

Hydroxy Compound 13. A solution of **10** (70 mg, 0.027 mmol) in 75% aq. AcOH (5 mL) was stirred for 12 h at 25 °C. The mixture was then concentrated and the residue was coevaporated with toluene yielding the diol **13** (60 mg, 95%) as a white foam, IR (KBr, cm^{-1}): 3397, 1677, 1614. MS (MALDI-TOF): *m/z* 2346 (M + H). ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.59 (s, 3H), 7.38 (s, 6H), 7.09 (s, 3H), 6.82 (s, 3H), 6.08 (d, 3H, J = 3.3 Hz), 5.91 (d, 6H, J = 3.3 Hz), 4.81 (d, 3H, J = 2.7 Hz), 4.66−4.57 (m, 18H), 4.49−4.45 (m, 6H), 4.24−4.21 (m, 6H), 4.03 (m, 18H), 3.79−3.76 (m, 6H), 3.58−3.56 (m, 6H), 1.53 (s, 9H), 1.48 (s, 18H), 1.38 (s, 9H), 1.32 (s, 18H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.7 (q), 138.9 (q), 137.5 (q), 137.0 (q), 124.7 (CH), 123.0 (CH), 118.8 (CH), 113.0 (q), 111.7 (q), 105.7 (CH), 105.0 (CH), 82.3 (CH), 82.0 (CH), 81.9 (CH), 81.8 (CH), 81.3 (CH), 80.0 (CH), 71.9 (CH_2), 71.3 (CH_2), 68.8 (CH), 64.7 (CH_2), 27.0 (CH_3), 26.6 (CH_3), 26.5 (CH_3), 26.2 (CH_3). Anal. Calcd for $C_{111}H_{153}N_3O_{51}$: C, 56.84; H, 6.58; N, 1.79. Found: C, 56.56; H, 6.84; N, 2.07.

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Supporting Information Available: Preparative procedure for **7**. ^{1}H and ^{13} C NMR spectra of **3**−**5** and **7**−**13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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