Toward Chiral Polyhydroxylated Dendrimers. Preparation and Chiroptical Properties

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Four dendrimers (**1b**−**4b**) containing chiral vicinal diol-based subunits were prepared from their acetonide-protected precursors (**1a**−**4a**). The optical activity of these chiral dendritic structures was successfully modeled using structurally similar, low molecular weight model compounds. Using the $[\Phi]_d$ values of the low molecular weight model compounds **5b**−**7b**, we calculated $[\Phi]_d$ values for dendrimers **1b**−**4b** that agree to within 4.5% of the observed values. Agreement between the optical activity of the model compounds and that of the dendrimers leads to the conclusion that the conformational equilibria of the dendrimer subunits are not perturbed relative to those of the model compounds.

Introduction

The structural diversity of dendritic macromolecules, accompanied by the search for new properties and applications, has increased dramatically over the past decade.[1] Chiral dendrimers have attracted attention largely because of their potential for enantioselective clathration of guest molecules.[2] Such behavior could lead to applications in sensor technology, chemical separations, and asymmetric catalysis. We have previously reported efforts toward the synthesis of chiral dendrimers and the analysis of their conformations in solution.[3] However, those structures were in protected form and, therefore, were devoid of the desired hydrogen-bond donors in the interior cavities of the dendrimers that would be useful not only for enthalpic interactions with clathrated guests but also as anchoring points for metals. We present here the synthesis and characterization of several prototypical polyhydroxylated dendrimers. In addition, our newly demonstrated approach[3d,e] to modeling the optical activity of chiral dendritic systems by using structurally similar low molecular weight model compounds is shown to be successful in the analysis of the chiroptical properties of these more flexible structures.

Results and Discussion

Preparation of Polyhydroxylated Dendrimers. Protected dendrimers **1a**−**4a** were constructed from chiral, nonracemic subunits in a convergent fashion.[3c,d] The design criterion for these chiral subunits was that they contain functionality appropriate for hydrogen bonding within the interior cavities of dendrimers.[3b] To this end, we chose chiral vicinal diols, which have been successfully utilized in such applications as molecular recognition[4] and asymmetric catalysis,[5] but which are acetonide-protected here for synthetic purposes. To investigate the effectiveness of these and other similar dendrimers in such applications, it was necessary to identify methods for successfully deprotecting the acetonide moieties within these structures.

Although many methods exist for acetonide deprotection,[6] we found that several of them, including those using Dowex resin and various acid/solvent combinations, led to limited or extensive decomposition of the dendritic material. However, treatment of **1a** and **2a** with 3 N HCl in acetonitrile at ambient temperature[7] provides polyhydroxylated zeroth-generation[8] dendrimers **1b** and **2b** in 53 and 67% yields, respectively (Chart 1). Deprotected zeroth-generation dendrimer **3b** was obtained in 41% yield, although solubility problems necessitated an increase in reaction temperature to 55 °C to dissolve the

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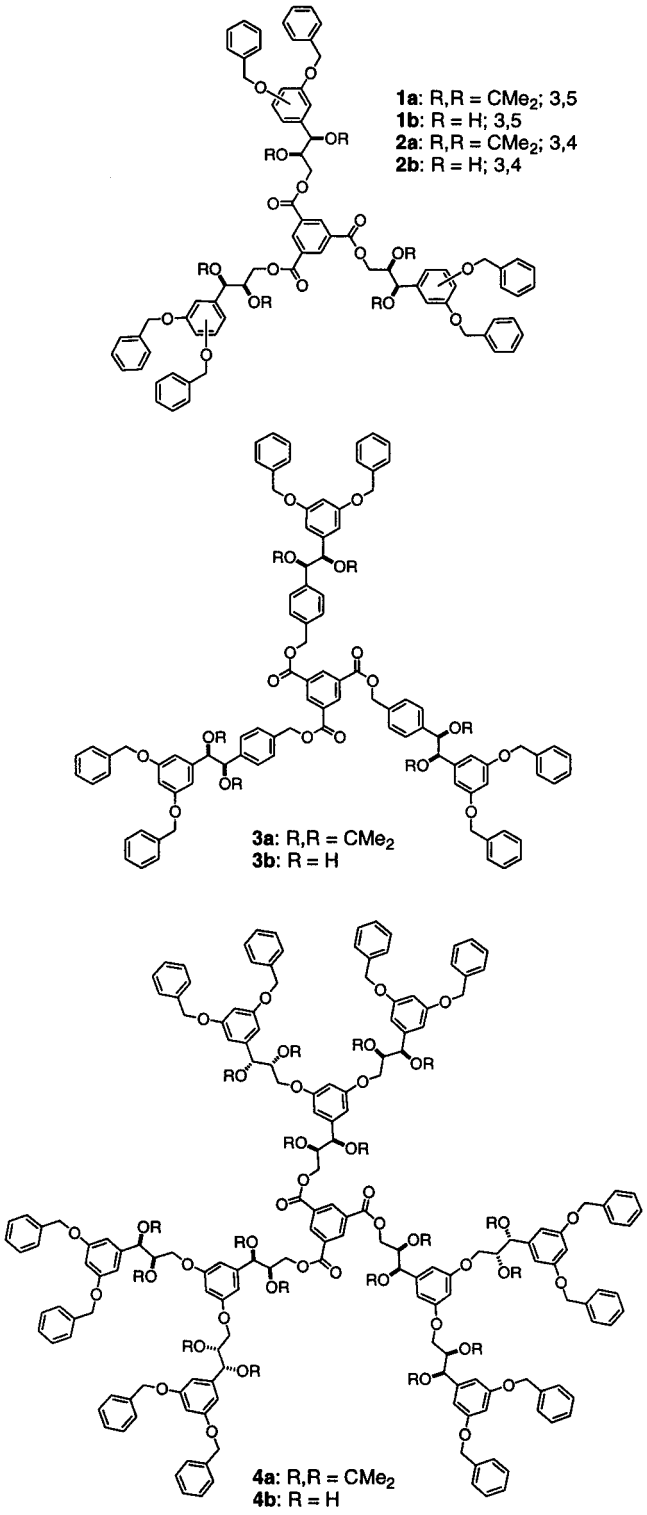
Chart 1



protected precursor **3a**. Deprotected first-generation[8] dendrimer **4b** was obtained in 29% yield after trituration and precipitation from methanol. Deprotected zeroth-generation dendrimers **1b**−**3b** were obtained as glassy solids, whereas first-generation **4b** was obtained as a colorless solid. Dendrimer **4b**, containing 18 hydroxy groups, precipitated out of solution during the course of the reaction. This suggests that the benzyloxy groups on the dendrimer periphery do not provide a sufficient nonpolar shell and/or that these lower-generation dendrimers do not yet possess a dense shell exterior. Deprotection of higher-generation dendrimers may be complicated by this solubility factor. Dendrimers **1b**−**4b** have been characterized by ^{1}H and ^{13}C NMR and MALDI MS. In general, the absence of any ^{1}H and ^{13}C NMR resonances for the methyl groups of the dioxolane ring confirms that dendrimers **1b**−**4b** have been fully deprotected. For example, specific analysis of the ^{13}C NMR spectrum of deprotected dendrimer **3b** (Figure 1) illustrates characteristic differences from that of its protected precursor. The absence of signals corresponding to the diastereotopic methyl carbons (27 ppm) and the acetal carbon (109.5 ppm) of **3a** in the spectrum of **3b** confirms successful deprotection of the dendrimer. In addition, the stereogenic carbinol carbons at 85 ppm in protected **3a** have shifted upfield to 78 ppm in deprotected **3b**, in accord with literature values.[3b]

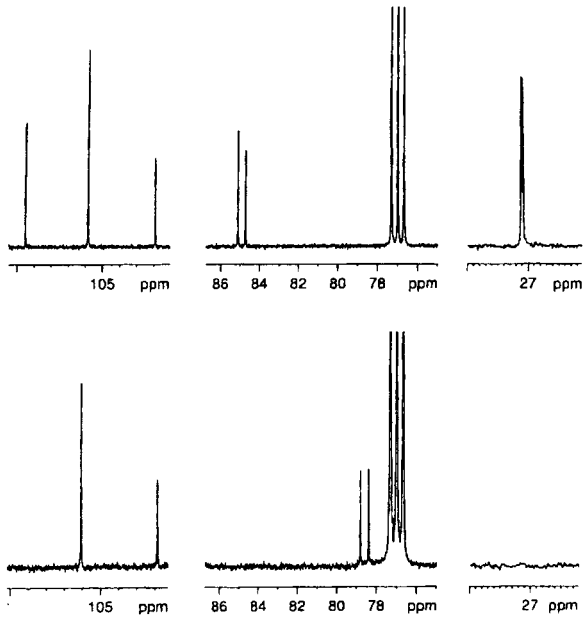


Figure 1. Selected regions of the ^{13}C NMR spectra of dendrimer **3b** (bottom) and its acetonide-protected precursor **3a** (top).

The ^{1}H NMR spectrum of deprotected first-generation **4b** not only clearly supports the removal of the acetonide groups from this larger dendrimer but also provides more direct confirmation of structural integrity during the deprotection process (Figure 2). As expected, prior to deprotection, the two pairs of diastereotopic acetonide methyl resonances are evident at approximately 1.5 ppm (Figure 2a), yet they are absent after deprotection (Figure 2b). Also appearing in the spectrum of **4b** are four doublet resonances for the OH protons between 4.6 and 4.2 ppm (Figure 2b, ○ peaks). That all of the hydroxyl protons appear as doublets precludes the occurrence of transesterifications of the hydroxyester functionalities of the zeroth-generation shell. Acyl transfer at these sites would generate $-CH_2OH$ residues, the hydroxyl protons of which would appear as triplets. Additional structural confirmation includes the 1:1:2:2 integration ratio of the hydroxyl peaks, which is an accurate reflection of the number of hydroxyl protons in the first- and second-generational shells of **4b**. Three-bond coupling of the hydroxyl protons to adjacent methine protons can also be observed. For example, the benzylic methine protons in **4a** appear as doublets (Figure 2a, Δ peaks), yet with

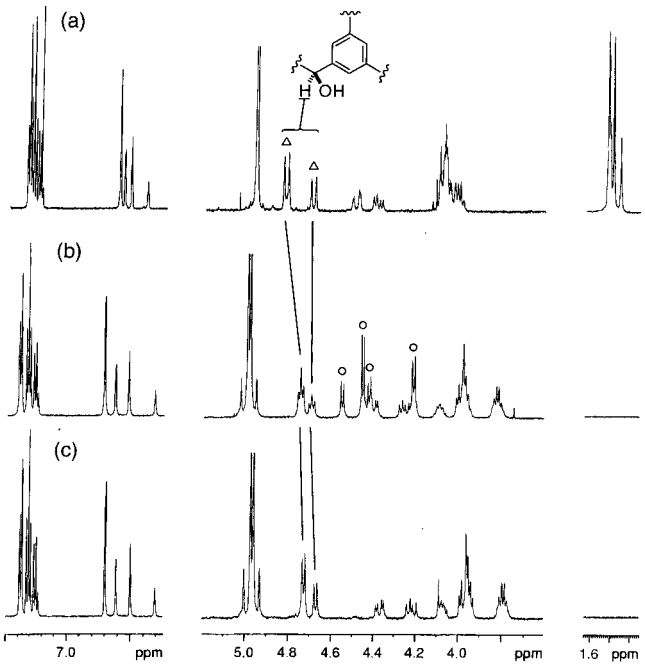


Figure 2. Regions of the ^{1}H NMR spectra of (a) acetonide-protected dendrimer **4a**, (b) deprotected dendrimer **4b**, and (c) dendrimer **4b** + D_2O. For explanation of symbols see text.

the introduction of adjacent hydroxyl protons in **4b**, they appear as apparent triplets (Figure 2b). Upon addition of D_2O to the sample, the resonances of the hydroxyl protons disappear, along with the observed couplings to the methine protons (Figure 2c).

Chiroptical Studies. We have demonstrated in previous reports[3c−e] that, in analogy to work with linear polymer systems,[9] it is possible to gain information about the conformation of chiral dendrimers by comparing the chiroptical properties of a dendrimer with those of structurally similar, low molecular weight model compounds. Agreement between the molar optical rotation ($[\Phi]_D$) value of the dendrimer and the sum of the $[\Phi]_D$ values of the appropriate model compounds indicates that the conformational equilibria for the model compounds and the monomeric units of the dendrimer are similar, i.e., conformational order has not developed in the larger molecule. In one of these reports,[3d] we showed that we could accurately calculate the optical activities of dendrimers **1a**−**4a** using the optical activities of one or two low molecular weight model compounds. However, the acetonide-protecting groups in **1a**−**4a** restrict rotation about the bond between the stereogenic centers and render the conformation of the subunits relatively invariable. This makes perturbation of the conformation of the subunits relative to the model compounds unlikely. However, the increased flexibility of the subunits in the corresponding deprotected dendrimers (e.g., **1b**−**4b**) might increase the likelihood of conformational perturbation.

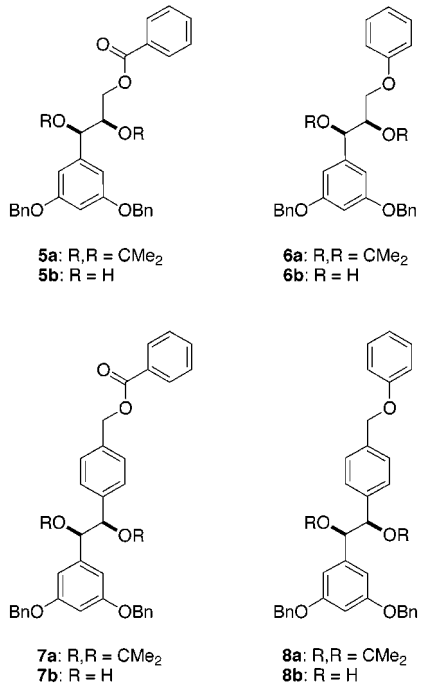
Specific and molar rotations for compounds **1b**−**4b** are reported in Table 1 (columns 3 and 4). Note that **1b** and **4b** are zeroth- and first-generation dendrimers, respectively, constructed from the same AB_2 monomer and that **1b** and **2b** each consist of three identical chiral subunits. These zeroth-generation dendrimers differ from each other only in the position of attachment of the peripheral benzyl groups.[10] Compound **3b** is the only structure reported here from subunits of its type. Inspection of the molar optical rotation per chiral unit (Table 1, column 5) for **1b**, **2b**, and **4b** reveals a constant value for the former two compounds but a significant increase as dendrimer generation increases from **1b** to **4b**.

Table 1. Chiroptical Data[a] for Polyhydroxy Dendrimers 1b−4b

compound	FW	$[\alpha]_D$[b]	$[\Phi]_D$[c]	$[\Phi]_D/n$[d]
1b	1297.42	+28.2	+366	+122
2b	1297.42	+27.6	+358	+119
3b	1525.71	+85.0	+1297	+432
4b	2931.22	+48.2	+1413	+157

[a] All rotations measured in acetone. [b] Specific rotation (10^{-1} deg cm^2 g^{-1}). [c] Molar rotation (10 deg cm^2 mol^{-1}). [d] Number of chiral subunits = n.

Chart 2



To interpret the chiroptical data in Table 1, model compounds **5b**−**7b** (Chart 2) were prepared from the corresponding acetonide-protected precursors **5a**−**7a**.[3d] Compound **5b** models subunits directly attached to the central linker in **1b**, **2b**, and **4b**, and compound **6b**, in turn, models subunits in the outer (first) generational shell of **4b**. Compound **7b** is the model subunit for **3b**. In addition to these model compounds, **8b** was prepared for comparison purposes with **7b**, as well as for modeling outer-shell subunits in higher-generation dendrimers not reported here. As can be seen from the polarimetry data listed in Table 2, there is a general trend of an increase in the molar optical rotation ($[\Phi]_D$) value on going from esters to ethers (e.g., **5b** → **6b** and **7b** → **8b**). This trend was observed before in the acetonide-protected subunits.[3d] Hence, the contribution of the subunits to the overall optical activity of the dendrimers should vary with their relative placement in the larger structure. For example, a higher overall molar optical rotation per chiral unit

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(10) We have previously shown that the change in constitution from 3,5- to 3,4-linkages does not significantly affect the optical activity of subunits in these systems. See ref 3d.

Table 2. Chiroptical Data[a] for Model Compounds 5−8

compound	FW	$[\alpha]_D$[b]	$[\Phi]_D$[c]
5b	484.55	+24.4	+118
6b	456.54	+37.0	+169
7b	560.65	+73.6	+413
8b	532.64	+88.9	+474

[a] All rotations measured in acetone. [b] Specific rotation (10^{-1} deg cm^2 g^{-1}). [c] Molar rotation (10 deg cm^2 mol^{-1}).

Table 3. Calculated Chiroptical Values for Compounds 1b−4b

	compound	formula	$[\Phi]_D$ (% error)[a]
1	**1b**	3 × **5b**	+354 (3.3)
2	**2b**	3 × **5b**	+354 (1.1)
3	**3b**	3 × **7b**	+1239 (4.5)
4	**4b**	(3 × **5b**) + (6 × **6b**)	+1368 (3.2)

[a] % error calculated as [|(calculated − observed)|/observed] × 100.

($[\Phi]_D/n$) value is expected with increasing generation (i.e., with a greater percentage of ether subunits).

Using the data in Table 2, we can now calculate expected optical activities for **1b**−**4b**. The $[\Phi]_D$ value of **5b** matches quite closely the $[\Phi]_D/n$ values for both zeroth-generation dendrimers **1b** and **2b**. Indeed, using the $[\Phi]_D$ value of **5** to calculate molar rotations for **1b** and **2b** gives values that agree to within 3.3% of the observed values (Table 3, entries 1 and 2). Similarly, using **7b** as the model compound for **3b** results in a calculated $[\Phi]_D$ value within 4.5% of the observed value (Table 3, entry 3). Both compounds **5b** and **6b** are necessary for modeling the structure of first-generation **4b**, and the result is a calculated $[\Phi]_D$ value within 3.2% of the observed value (Table 3, entry 4).

This close agreement between the optical activity of dendrimers **1b**−**4b** and that of the model compounds **5b**−**7b** indicates that the conformational equilibria of the dendrimer subunits are not perturbed relative to those of the model compounds.[3c,d] Therefore, chiral conformational order is not evident in **1b**−**4b** under these solvent and temperature conditions. However, future analysis of higher-generation deprotected dendrimers containing free hydroxy groups may exhibit conformational order through intramolecular communication between subunits.

Summary

We have prepared and characterized several prototypical polyhydroxylated dendritic compounds. Analysis of the chiroptical properties of these structures reveals that changes in optical activity with increasing generation are a result of constitutional effects rather than chiral conformational order. The preparation of higher-generation dendrimers and the analysis of interactions of these structures with small guest molecules are ongoing efforts in our laboratory.

Experimental Section

Materials and Methods. NMR spectra were acquired on commercial instruments. All chemicals were purchased from commercial suppliers and used as received, unless otherwise specified. All reactions were conducted in oven-dried glassware under an inert atmosphere (N_2). Acetonitrile was distilled from CaH_2 under dry nitrogen. Other solvents, such as ethyl acetate, dichloromethane, and hexane, were used as received. Flash chromatography using silica (Natland International Corp., silica gel 200−400 mesh) was performed by the method of Still et al.[11] Thin-layer chromatography (TLC) was performed on precoated TLC plates (silica gel HLO, F-254, Scientific Adsorbants, Inc. or Merck). Compounds **1a**−**4a** and **5a**−**8a** were prepared according to literature procedures.[3d]

Tris[(2*R*,3*R*)-3-[3,5-bis(benzyloxy)phenyl]-2,3-dihydroxypropyl] Trimesate (1b). A solution of **1a** (246 mg, 0.173 mmol), CH_3CN (18 mL), and 3 N HCl (6 mL) was stirred at room temperature. After 14 h, TLC (SiO_2, 3:2 ethyl acetate−petroleum ether) indicated consumption of starting material. The reaction mixture was diluted with ethyl acetate (100 mL) and H_2O (50 mL), the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with brine (1 × 100 mL), dried (Na_2SO_4), and concentrated. The residue was purified by flash chromatography (SiO_2, 3:2 ethyl acetate−petroleum ether) to provide dendrimer **1b** (118 mg, 53%) as a colorless, glassy solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 3H), 7.36−7.25 (m, 30H), 6.60 (d, J = 2.0 Hz, 6H), 6.47 (t, J = 2.0 Hz, 3H), 4.95 (s, 12H), 4.63 (d, J = 6.5 Hz, 3H), 4.40 (dd, J = 3.5, 11.5 Hz, 3H), 4.18 (dd, J = 6.0, 12.0 Hz, 3H), 4.02 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 160.1, 142.6, 136.6, 134.6, 130.8, 128.5, 128.0, 127.5, 105.8, 101.8, 74.6, 73.7, 70.1, 66.2; MS (MALDI) m/z 1321.0 (M + Na), 1337.2 (M + K); $[\alpha]_D$ = +28.2 (c 0.84, acetone). Anal. Calcd for $C_{78}H_{72}O_{18}$: C, 72.20; H, 5.59. Found: C, 71.72; H, 5.81.

Tris[(2*R*,3*R*)-3-[3,4-bis(benzyloxy)phenyl]-2,3-dihydroxypropyl] Trimesate (2b). Following the procedure for **1b**, dendrimer **2a** (493 mg, 0.348 mmol), CH_3CN (36 mL), and 3 N HCL (12 mL) yielded dendrimer **2b** (300 mg, 67%) as a colorless, glassy solid after purification by flash chromatography (SiO_2, 7:3 ethyl acetate−petroleum ether): ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 3H), 7.35−7.15 (m, 30H), 6.95 (br s, 3H), 6.82 (br m, 6H), 5.06 (s, 6H), 5.02 (s, 6H), 4.55 (br t, 3H), 4.3−3.7 (m, 12H), 3.3 (br m, 3H); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 164.3, 136.74, 136.68, 134.2, 132.9, 130.4, 128.1, 128.0, 127.5, 127.2, 127.0, 119.7, 114.1, 113.4, 74.1, 73.6, 70.9, 70.7, 66.1; MS (MALDI) m/z 1319.5 (M + Na); $[\alpha]_D$ = +27.6 (c 1.16, acetone).

Tris{4-[(1*R*,2*R*)-2-[3,5-bis(benzyloxy)phenyl]-1,2-dihydroxyethyl]benzyl} Trimesate (3b). A solution of dendrimer **3a** (201 mg, 0.122 mmol), CH_3CN (20 mL), and 3 N HCL (3 mL) was stirred at 55 °C. After 12 h, TLC (SiO_2, 7:3 ethyl acetate−petroleum ether) indicated consumption of starting material. The reaction mixture was diluted with ethyl acetate (30 mL) and H_2O (25 mL), the organic layer was separated, and the aqueous layer was extracted with ethyl acetate (3 × 30 mL). The combined organic layers were concentrated, and the residue was purified by flash chromatography (SiO_2, 7:3 ethyl acetate−petroleum ether) to provide dendrimer **3b** (194 mg, 25%) as a colorless, glassy solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 3H), 7.36−7.23 (m, 36H), 7.14 (d, J = 8.2 Hz, 6H), 6.45 (t, J = 2.2 Hz, 3H), 6.36 (d, J = 2.2 Hz, 6H), 5.29 (s, 6H), 4.87 and 4.83 (AB pattern, J = 11.5 Hz, 12H), 4.67 (br dd, 3H), 4.58 (br dd, 3H), 3.07 (br d, 3H), 2.90 (br d, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5, 159.7, 142.3, 140.4, 136.7, 134.9, 134.7, 131.0, 128.5, 128.0, 127.9, 127.5, 127.3, 106.0, 101.9, 78.8, 78.4, 70.0, 67.0; MS (MALDI) m/z 1548.3 (M + Na); $[\alpha]_D$ = +85.0 (c 1.36, acetone). Anal. Calcd for $C_{96}H_{84}O_{18}$: C, 75.58; H, 5.55. Found: C, 74.92; H, 5.76.

Tris{(*R*,*R*,*R*,*R*,*R*,*R*)-3-[3,5-bis{3-[3,5-bis(benzyloxy)phenyl]-2,3-dihydroxypropyl}phenyl]-2,3-dihydroxypropyl} Trimesate (4b). Following the procedure for **1b**, dendrimer **4a** (695 mg, 0.211 mmol), CH_3CN (73 mL), and 3 N HCl (12 mL) yielded a white solid that precipitated out of the reaction mixture. After filtration and precipitation from MeOH, dendrimer **4b** (179 mg, 29%) was obtained as a colorless solid: ^{1}H NMR (400 MHz, acetone-d_6) δ 8.73 (s, 3H), 7.40−7.24 (m, 60H), 6.71 (d, J = 2.2 Hz, 12H), 6.63 (d, J = 2.1 Hz, 6H), 6.52 (t, J = 2.3 Hz, 6H), 6.31 (t, J = 2.2 Hz, 3H), 5.01 (AB pattern, J = 12 Hz, 12H), 4.97 (AB pattern, J = 12.0 Hz, 12H), 4.75 (t, J = 4.4 Hz, 6H), 4.74 (t, J = 4.3 Hz, 3H), 4.57

(11) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(d, J = 4.4 Hz, 3H), 4.46 (d, J = 4.6 Hz, 6H), 4.45 (d, J = 4.4 Hz, 3H), 4.40 (dd, J = 8.0, 3.6 Hz, 3H), 4.27−4.22 (m, 9H), 4.13−4.05 (m, 3H), 4.01−3.94 (m, 12H), 3.83−3.80 (m, 6H); ^{13}C NMR (100 MHz, acetone-d_6) δ 165.3, 160.9, 160.7, 145.9, 145.3, 138.3, 135.0, 132.2, 129.2, 128.5, 128.4, 126.8, 106.7, 106.5, 101.9, 101.4, 75.2, 75.1, 74.6, 74.3, 70.5, 70.2, 67.5; MS (MALDI) m/z 2954.4 (M + Na), 2971.0 (M + K); $[\alpha]_D$ = +48.2 (c 0.78, acetone). Anal. Calcd for $C_{174}H_{168}O_{42}$: C, 71.30; H, 5.78. Found: C, 70.38; H, 6.01.

(2*R*,3*R*)-3-[3,5-Bis(benzyloxy)phenyl]-2,3-dihydroxypropyl Benzoate (5b). Following the procedure for **1b**, ester **5a** (57 mg, 0.11 mmol), CH_3CN (4 mL), and 3 N HCl (1 mL) yielded ester **5b** (52 mg, 98%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−7.99 (m, 2H), 7.56 (tt, J = 7.4, 1.4 Hz, 1H), 7.44−7.28 (m, 12H), 6.62 (d, J = 2.2 Hz, 2H), 6.54 (t, J = 2.3 Hz, 1H), 4.98 (s, 4H), 4.65 (d, J = 6.4 Hz, 1H), 4.38 (dd, J = 7.9, 3.9 Hz, 1H), 4.21 (dd, J = 11.8, 6.0 Hz, 1H), 4.03 (ddd, J = 6.0, 4.1, 4.0 Hz, 1H), 2.85 (br s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 160.2, 142.4, 136.6, 133.2, 129.7, 128.5, 128.4, 128.0, 127.5, 125.8, 105.8, 101.9, 74.6, 74.2, 70.1, 65.5; $[\alpha]_D$ = +24.4 (c 2.60, acetone). Anal. Calcd for $C_{30}H_{28}O_6$: C, 74.36; H, 5.82. Found: C, 74.06; H, 5.51.

(1*R*,2*R*)-1-[3,5-Bis(benzyloxy)phenyl]-3-phenoxy-1,2-propanediol (6b). Following the procedure for **1b**, ether **6a** (63 mg, 0.13 mmol), CH_3CN (4 mL), and 3 N HCl (1 mL) yielded diol **6b** (55 mg, 95%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.25 (m, 12H), 6.95 (tt, J = 7.3, 1.0 Hz, 1H), 6.84 (m, 2H), 6.62 (d, J = 2.2 Hz, 2H), 6.54 (t, J = 2.3 Hz, 1H), 4.96 and 4.91 (AB pattern, J = 11.6 Hz, 4H), 4.77 (dd, J = 3.6, 2.6 Hz, 1H), 4.02−3.95 (m, 2H), 3.83 (dd, J = 5.1, 4.4 Hz, 1H), 2.80 (d, J = 3.2 Hz, 1H), 2.69 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.12, 158.3, 142.6, 136.7, 129.5, 128.6, 128.0, 127.5, 121.3, 114.6, 105.7, 102.0, 74.6, 70.1, 68.4; $[\alpha]_D$ = +37.0 (c 1.60, acetone). Anal. Calcd for $C_{29}H_{28}O_5$: C, 76.30; H, 6.18. Found: C, 76.40; H, 5.57.

4-[(1R,2R)-2-[3,5-Bis(benzyloxy)phenyl]-1,2-dihydroxyethyl]benzyl Benzoate (7b). Following the procedure for **1b**, ester **7a** (74 mg, 0.12 mmol), CH_3CN (4 mL), and 3 N HCl (1 mL) yielded ester **7b** (60 mg, 88%) as a colorless oil after purification by flash column chromatography [SiO_2, CH_2Cl_2 (200 mL), gradient to ethyl acetate]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02−8.00 (m, 2H), 7.52 (tt, J = 7.4, 1.3 Hz, 1H), 7.40−7.26 (m, 14H), 7.15−7.13 (m, 2H), 6.48 (t, J = 2.3 Hz, 1H), 6.38 (d, J = 2.3 Hz, 2H), 5.30 (s, 2H), 4.91 and 4.88 (AB pattern, J = 11.6 Hz, 4H), 4.67 (dd, J = 4.5, 2.3 Hz, 1H), 4.60 (dd, J = 4.2, 2.7 Hz, 1H), 2.82 (d, J = 2.7 Hz, 1H), 2.78 (d, J = 3.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 159.7, 142.3, 140.0, 136.8, 135.7, 133.0, 130.0, 129.6, 128.5, 128.4, 128.0, 127.9, 127.4, 127.2, 106.1, 102.0, 78.9, 78.5, 70.0, 66.3; $[\alpha]_D$ = +73.6 (c 3.02, acetone). Anal. Calcd for $C_{36}H_{32}O_6$: C, 77.12; H, 5.75. Found: C, 76.44; H, 5.40.

(1R,2R)-1-[3,5-Bis(benzyloxy)phenyl]-2-(4-phenoxymethylphenyl)-1,2-ethanediol (8b). Following the procedure for **1b**, ether **8a** (51 mg, 89 mmol), CH_3CN (4 mL), and 3 N HCl (1 mL) yielded diol **8b** (46 mg, 98%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35−7.22 (m, 14H), 7.14 (d, J = 8.1 Hz, 2H), 6.91−6.89 (m, 3H), 6.48 (t, J = 2.3 Hz, 1H), 6.38 (d, J = 2.3 Hz, 2H), 5.00 (s, 2H), 4.92 and 4.87 (AB pattern, J = 11.6 Hz, 4H), 4.67 (dd, J = 6.5, 2.1 Hz, 1H), 4.61 (dd, J = 7.0, 2.3 Hz, 1H), 2.75 (d, J = 2.5 Hz, 1H), 2.72 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 158.7, 142.2, 139.6, 136.8, 129.4, 128.5, 127.9, 127.4, 127.2, 127.1, 120.9, 114.8, 106.0, 101.9, 78.9, 78.5, 70.0, 69.6; $[\alpha]_D$ = +88.9 (c 0.76, acetone). Anal. Calcd for $C_{35}H_{32}O_5$: C, 78.92; H, 6.05. Found: C, 78.72; H, 5.94.

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