Synthesis and Characterization of a Chiral Dendrimer Derived from Pentaerythritol

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The synthesis and characterization of chiral dendrimer **1** in its racemic form is reported. The chirality of this macromolecule, with a molecular weight of 2831, is based on a pentaerythritol core, acting as a stereocenter with four dendritic substituents of different generation. The synthesis is making use of a newly developed, general route to a multisubstituted pentaerythritol derivative. Resolution of **1** is hampered by conformational flexibility. The latter, however, allows detailed ^{1}H-NMR characterization indicating the stratified structure of the dendrimer. Considerable resolution of the ^{1}H-NMR signals of the inner protons in C_6D_6 and C_6D_5N suggests that **1** adopts an overall chiral shape in solution.

Introduction

Recently, dendritic macromolecules have received considerable interest due to their unique hyperbranched polymeric structure and their well-defined three-dimensional architecture.[1] Dendrimers emanate from a central core and have a well-defined number of generations and end groups. They are synthesized in a stepwise way via a repetitive reaction sequence. The syntheses described so far are either convergent or divergent of character.[2] Polyamineamide dendrimers as introduced by Tomalia et al., using the divergent method, represent the first reported class and well-defined spherical shapes have been synthesized up to molecular weights of 700.000.[1a] The convergent route of Fréchet et al. is based on the synthesis of aromatic-ether dendritic wedges that are joined together in the last step of the dendrimer synthesis.[2f] Various other dendrimers based on one of these approaches have been disclosed, including a large scale synthesis[3] and dendrimers using chiral building blocks.[4]

In almost all examples presented today, the overall shape of the dendrimer is symmetrical of nature, i.e., the dendritic wedges attached to the core are of the same generation. In this paper we present the synthesis and characterization of chiral dendrimer **1** in its racemic form. The chirality is based on a pentaerythritol core with four dendrimer substituents of different generation (Figure 1). Dendrimer **1**, with a molecular weight of 2831, should offer us detailed insight into the conformational flexibility of this new type of molecules.

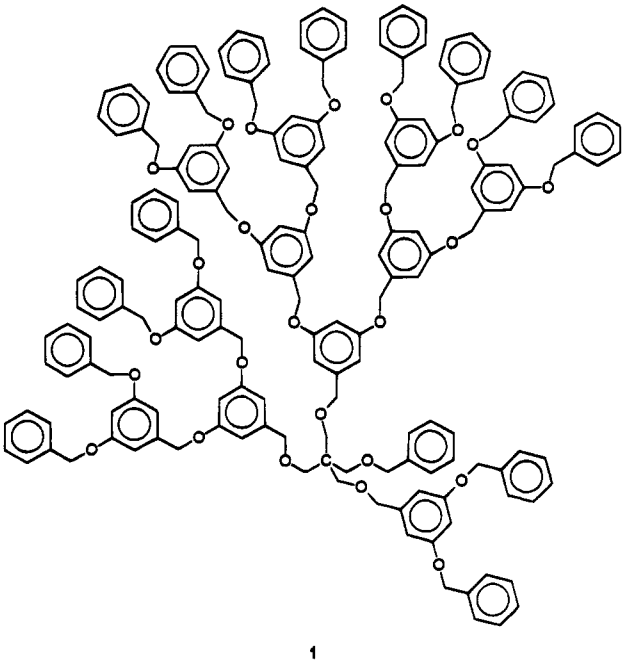

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Figure 1.

Results and Discussion

A global synthetic scheme is given in Scheme 1. The aromatic-ether dendritic wedges [G-1]-Br, [G-2]-Br, and [G-3]-Br have been synthesized using the Hawker–Fréchet convergent approach[2f,i,5] and the step-by-step introduction of these dendritic wedges is performed by a newly developed method for the selective deprotection of a multisubstituted pentaerythritol derivative.

The multisubstituted pentaerythritol derivative **10** (see Scheme 2) was synthesized from commercially available

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(5) For the dendritic wedges, the nomenclature used by Hawker and Fréchet is adopted here.

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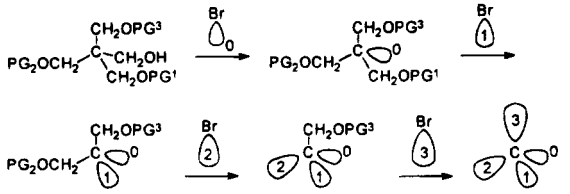
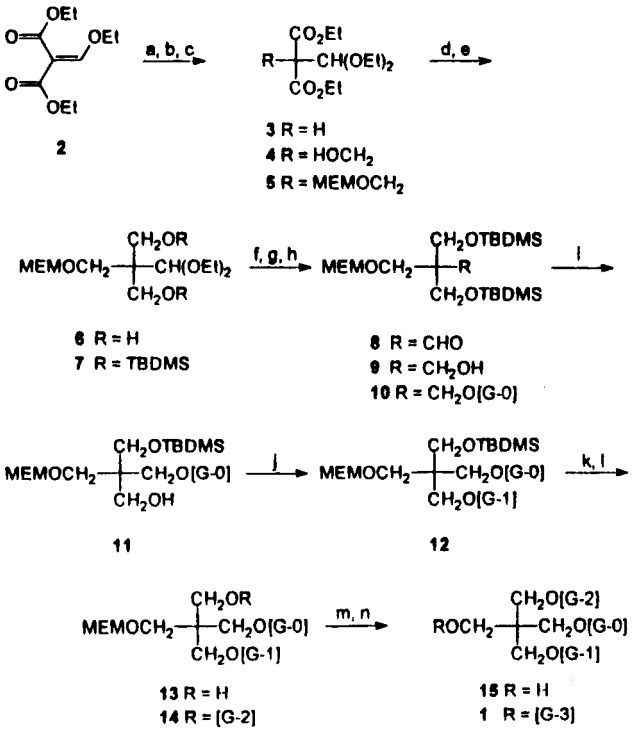
Scheme 1. Global Synthetic Scheme for Chiral Dendrimer 1; PG^n Stands for Protecting Group Number *n*



Scheme 2. Synthesis of 1[a]



[a] (a) EtOH, Na, 50 °C; 87%; (b) K_2CO_3, paraformaldehyde, DMF; 82%; (c) MEMCl, $(i\text{-Pr})_2EtN$, CH_2Cl_2; 81%; (d) $LiAlH_4$, Et_2O; 86%; (e) TBDMSCl, imidazole, DMF, 87%; (f) *p*-TsOH, Me_2CO, reflux, 15 min.; 62%; (g) $NaBH_4$, 1,4-dioxane; 82%; (h) NaH, $PhCH_2Br$ (=[G-0]-Br), THF, reflux; 70%; (i) $ZnBr_2$, CH_2Cl_2; 77%; (j) NaH, [G-1]-Br, THF, reflux; 78%; (k) Bu_4NF, THF; 92%; (l) NaH, [G-2]-Br, THF, reflux, 96%; (m) *B*-chlorocatecholborane, CH_2Cl_2; 76%; (n) NaH, [G-3]-Br, THF, reflux; 74%.

diethyl (ethoxymethylene)malonate (**2**) in eight steps, of which the first two steps were described previously,[6] yielding diethyl (diethoxymethyl)(hydroxymethyl)malonate (**4**). The alcohol moiety of **4** was converted into the corresponding MEM ether **5** using a standard procedure.[7] Lithium aluminum hydride reduction of the malonate diester then produced diol **6**. This diol was protected as the bis TBDMS-ether[8] and subsequent reaction of the acetal functionality by treatment with a catalytic amount of *p*-toluenesulfonic acid in boiling acetone for 15 min gave aldehyde **8**. Sodium borohydride reduction of **8** afforded the corresponding alcohol **9**, which was subsequently coupled to the first dendritic wedge ([G-0]) in a Williamson synthesis, using sodium hydride and benzyl bromide ([G-0]-Br), to give the desired achiral **10**.

In order to synthesize a dendrimer with four different generations attached to the core, it was necessary to deprotect only one of the two equivalent TBDMS groups. In this reaction the stereocenter was introduced and a method accomplishing this, using anhydrous $ZnBr_2$ in dichloromethane, was found by accident in our attempts to remove the MEM protecting-group.[7] Spectral elucidation of the product by ^1H- and ^{13}C-NMR spectroscopy unambiguously revealed that chiral alcohol **11** was formed. The introduction of enantioselectivity in this reaction using a variety of chiral auxiliaries failed so far, as was demonstrated by ^1H-NMR experiments with a chiral shift reagent (europium(III) tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]).

The remaining part of the synthesis of the chiral dendrimer was realized by alkylating the alcohol moiety of **11** in a Williamson synthesis with sodium hydride and the bromide of the second dendritic wedge ([G-1]-Br), thus providing **12**. In the next step the remaining TBDMS-groups was smoothly removed using tetrabutylammonium fluoride in THF,[8] after which a next coupling step, using sodium hydride and the bromide of the third dendritic wedge ([G-2]-Br) in another Williamson synthesis, produced **14**.

The cleavage of the MEM ether of **14** was not as straightforward as we anticipated. Using a host of various cleavage reagents (e.g., $ZnBr_2$,[7] $TiCl_4$,[7] butyllithium/hexane at −78 °C followed by $Hg(OAc)_2$[9] and $(i\text{-PrS})_3B$[10]), either no reaction took place or substantial degradation of the substrate occurred. Eventually deprotection, furnishing **15**, was accomplished in good yield (76%) with *B*-chlorocatecholborane in anhydrous CH_2Cl_2.[11] The last step in our synthesis consisted again of a Williamson coupling, this time using sodium hydride and the bromide of the fourth dendritic wedge ([G-3]-Br), yielding racemic chiral dendrimer **1** in a yield of 74%. After chromatographic purification the dendrimer was obtained in a purity of >99% as determined by means of HPLC with silica Lichrosorb 60 as stationary phase. Solvent-free samples of **1**, as determined by NMR spectroscopy, could be obtained after extended drying under reduced pressure. Dendrimer **1** proved to be very susceptible to Claisen rearrangements, yielding polar (phenolic) impurities; storage at temperatures as low as −40 °C was necessary to prevent degradation. Hence, HPLC in combination with ^1H-NMR spectroscopy should be regarded as optimal techniques to determine the purity of this type of dendrimers. Elemental analysis and mass spectroscopy were not suitable techniques in this case. An overall yield of 4.6% is obtained in the 13-step synthesis of **1** from diethyl (ethoxymethylene)malonate (**2**).

Dendrimer **1** as well as all the intermediates are fully characterized. The ^1H-NMR spectrum of **1** in $CDCl_3$ shows an interesting feature for the resonances of the benzylic protons, revealing the stratified structure of the dendrimer. As can be seen in Figure 2, these resonances consist of a set of six singlets, centered around $\delta = 4.9$ ppm, with an intensity ratio of 16:8:8:4:4:4 and of a set of four partially overlapping singlets near $\delta = 4.4$ ppm with an intensity ratio of 2:2:2:2. The strongest signal (a) arises from the outermost benzylic protons of the largest dendritic wedge ([G-3]), being the only signal with

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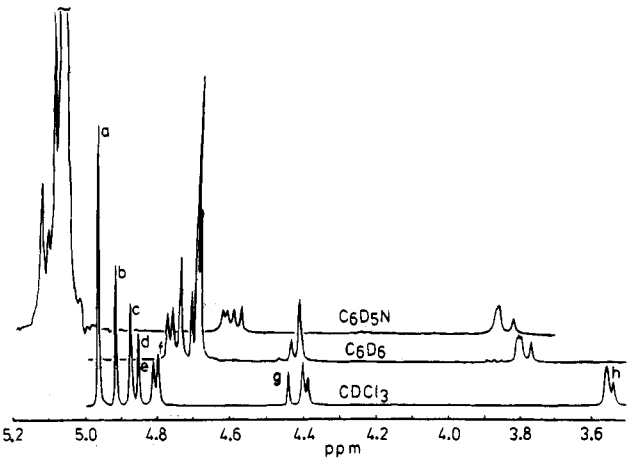

Figure 2. The ether region of the 400.13 MHz ^{1}H-NMR spectrum of **1** in $CDCl_3$, C_6D_6, and C_6D_5N, respectively.

an intensity of sixteen protons. The two singlets with an intensity of eight (b, c) are interpreted as originating from the outermost benzylic protons of the one but largest dendritic wedge ([G-2]) and the one but outermost benzylic protons of the largest dendritic wedge ([G-3]). Furthermore, the three singlets with an intensity of four (d, e, f) are ascribed to the benzylic protons in the next, more inwardly positioned, layer of the dendritic wedges [G-3], [G-2], and [G-1]. Finally, the benzylic protons directly attached to the pentaerythritol core appear as the four partially overlapping singlets near $\delta = 4.4$ ppm (g). Moreover, the pentaerythrityl protons appear as an ill-resolved resonance at $\delta = 3.5-3.6$ ppm (h). By recording the ^{1}H-NMR spectrum in C_6D_6 and C_6D_5N, respectively, a remarkable difference in chemical shift for the pentaerythrityl protons (C_6D_6) or for the most inner benzylic protons (C_5D_5N) is observed (see Figure 2); both signals appear as four resolved singlets in a 2:2:2:2 ratio in the abovementioned solvents. The difference in structure of the two largest substituents in **1**, i.e., [G-2] and [G-3], is 17 σ-bonds apart from the pentaerythrityl protons and 15 σ-bonds apart from the most inner benzylic protons, being too far from the core to differentiate between the CH_2-groups in electronic properties. Therefore, we propose that dendrimer **1** can adopt an overall chiral shape in solution, which structure strongly depends on the solvent and/or complexation of **1** with solvent.

Another interesting feature of the ^{1}H-NMR spectrum is the sharpness of the peaks, compared to the size of the molecule. The reason for this is found in the substantial conformational freedom present in the molecule; considerable peak broadening appears only at temperatures below 230 K. However, no evidence has been found for the existence of a preferred conformational rotamer, and no diastereotopic protons could be detected.

The significant flexibility of the molecule at room temperature is also demonstrated in our attempts to resolve **1** in its enantiomers by means of HPLC with chiral stationary phases. In all cases we have observed a single Gaussian peak for racemic **1**, while no resolution was obtained.

It is foreseen that reduction of the conformational freedom may facilitate the resolution of a chiral dendrimer. This decrease in flexibility can be obtained by increasing the crowding of the different groups in the molecule. In order to realize this, the possibility of synthesizing a chiral dendrimer with higher generations attached to the core is available. At the moment the synthesis of these compounds is an important goal in our further research on chiral dendrimers. Moreover, in this paper we have presented a new method for the selective deprotection of a multisubstituted pentaerythritol core, which, more generally, can find use in the synthesis of quaternary compounds containing four different substituents.

Experimental Section

Anhydrous dichloromethane was prepared by distillation from K_2CO_3, anhydrous DMF by vacuum distillation after standing on BaO for 72 h, and anhydrous THF by distillation from lithium aluminum hydride. Dry diethyl ether was prepared by standing on $CaCl_2$ and subsequent drying with sodium wire. ^{1}H-NMR spectra were measured on a Bruker AM 400 spectrometer at 400.13 MHz. ^{13}C-NMR spectra were run at the same apparatus at 100.62 MHz with proton noise decoupling. All NMR samples were routinely dissolved in $CDCl_3$ and all δ values are given in ppm downfield from tetramethylsilane. The dendritic wedges used in the synthesis of the dendrimer were prepared according to the literature procedure of Hawker and Fréchet.[2f]

Diethyl (Diethoxymethyl)malonate (3). To a stirred solution of diethyl (ethoxymethylene)malonate (**2**) (129.5 g; 0.60 mol) in absolute ethanol (1 L) was added sodium metal (2.0 g; 88 mmol) in small pieces. The sodium was allowed to react completely, after which the mixture was brought to 45 °C and stirred at that temperature for 3 h. The mixture was neutralized with glacial acetic acid and the ethanol was evaporated in vacuo, after which the residue was taken up in dichloromethane (500 mL). Washing of the organic phase with water (3 × 250 mL), drying ($MgSO_4$), and evaporation of the solvent gave crude **3**, which was purified by distillation in vacuo: $bp_{0.09}$ 79–81 °C. Yield: 136.5 g (87%). ^{1}H NMR: δ 1.19 (t, 6H), 1.27 (t, 6H), 3.58–3.78 (m, 5H), 4.21 (q, 4H), 5.11 (d, 1H). ^{13}C NMR: δ 13.9, 15.2, 57.1, 61.4, 63.2, 100.9, 166.0.

Diethyl (Diethoxymethyl)(hydroxymethyl)malonate (4). A solution of **3** (122.1 g; 0.47 mol), paraformaldehyde (23.9 g; 0.79 mol), and potassium carbonate (7.2 g; 0.072 mol) in anhydrous DMF (400 mL) was stirred for 48 h, after which water was added (1 L). Extraction with dichloromethane (3 × 500 mL), washing of the organic phase with water (5 × 500 mL), drying ($MgSO_4$), and evaporation of the solvent gave crude **4**. Purification was accomplished by distillation in vacuo: $bp_{0.07}$ 107–109 °C. Yield: 111.1 g (82%). ^{1}H NMR: δ 1.21 (t, 6H), 1.26 (t, 6H), 3.21 (t, 1H), 3.70–3.92 (m, 4H), 4.17–4.25 (m, 6H), 5.19 (s, 1H). ^{13}C NMR: δ 13.9, 15.2, 61.3, 61.5, 63.4, 66.9, 105.2, 167.3.

Diethyl (Diethoxymethyl)[[(2-methoxyethoxy)methoxy]-methyl]malonate (5). A solution of MEM chloride (47.1 g; 0.38 mol), compound **4** (98.2 g; 0.34 mol), and diisopropylamine (70 mL) in anhydrous dichloromethane (500 mL) was stirred until TLC analysis showed complete conversion (ca. 6 h, eluent hexane/ethyl acetate 2:1 v/v). Washing of the reaction mixture with aqueous, saturated sodium bicarbonate (3 × 300 mL), drying of the organic phase over $MgSO_4$ and evaporation of the solvent gave the crude product. Purification was accomplished by vacuum distillation: $bp_{0.04}$ 136–138 °C. Yield: 98.3 g (77%). ^{1}H NMR: δ 1.20 (t, 6H), 1.26 (t, 6H), 3.40 (s, 3H), 3.54–3.84 (m, 8H), 4.11 (s, 2H), 4.18–4.26 (m, 4H), 4.71 (s, 2H), 5.04 (s, 1H). ^{13}C NMR: δ 13.9, 15.1, 58.9, 61.1, 63.7, 66.0, 66.6, 67.2, 71.6, 95.8, 103.0, 167.6.

2-(Diethoxymethyl)-2-[[(2-methoxyethoxy)methoxy]-methyl]-1,3-propanediol (6). To a suspension of lithium aluminum hydride (15.6 g; 0.41 mol) in anhydrous diethyl ether (500 mL) was added dropwise compound **5** (95.4 g; 0.25 mol) at such a rate that gentle reflux of the diethyl ether was maintained during the reaction. The mixture was allowed to stir at room temperature for another 1 h, after which water (15.5 mL), aqueous sodium hydroxide (2.3 g of sodium hydroxide in 15.5 mL of water) and, again, water (46.5 mL) were

added carefully. Filtration and evaporation of the solvent yielded 61.4 g of the pure product (83%) as a colorless liquid. ^{1}H NMR: δ 1.23 (t, 6H), 3.16 (t, 2H), 3.40 (s, 3H), 3.53–3.92 (m, 14H), 4.62 (s, 1H), 4.70 (s, 2H). ^{13}C NMR: δ 15.2, 48.2, 58.7, 61.9, 66.2, 66.8, 67.2, 71.5, 95.4, 105.8.

1,1-Diethoxy-2,2-bis[[(*tert*-butyldimethylsilyl)oxy]-methyl]-3-[(2-methoxyethoxy)methoxy]propane (7). A solution of **6** (45.6 g; 0.154 mol), imidazole (63.2 g; 0.93 mol), and TBDMS chloride (67.2 g; 0.45 mol) in anhydrous DMF (150 mL) was stirred for 24 h and subsequently the reaction mixture was taken up in water (400 mL). Extraction with diethyl ether (3 × 200 mL), washing of the organic phase with water (5 × 150 mL), drying ($MgSO_4$), and evaporation of the solvent yielded the bis-silyl derivative **7** as an oil (contaminated with *tert*-butyldimethylsilanol), which was used in the next reaction without further purification. Yield (for the crude product): 70.2 g (87%).

2,2-Bis[[(*tert*-butyldimethylsilyl)oxy]methyl]-3-[(2-methoxyethoxy)methoxy]propanal (8). A solution of *p*-toluenesulfonic acid monohydrate (9.0 g; 47 mmol) and crude **7** (69.4 g; 0.132 mol) in acetone (900 mL) was boiled under reflux for 15 min. After cooling down of the reaction mixture to room temperature, aqueous sodium bicarbonate (5% w/v; 150 mL) was added and the acetone was evaporated in vacuo. Addition of diethyl ether (500 mL), washing of the organic layer with water (3 × 200 mL), drying ($MgSO_4$), and evaporation of the solvent yielded the crude aldehyde, which was purified by column chromatography with hexane/ethyl acetate 6:1 v/v as eluent (R_f = 0.31), giving pure **8** as a colorless liquid in a yield of 37.0 g (62%). ^{1}H NMR: δ 0.05 (s, 12H), 0.87 (s, 18H), 3.39 (s, 3H), 3.53–3.66 (m, 4H), 3.73 (s, 2H), 3.83 (m, 4H), 4.68 (s, 2H), 9.69 (s, 1H). ^{13}C NMR: δ −5.7, 18.2, 25.8, 57.6, 59.0, 60.3, 65.3, 66.7, 71.6, 95.9, 204.7.

2,2-Bis[[(*tert*-butyldimethylsilyl)oxy]methyl]-3-[(2-methoxyethoxy)methoxy]-1-propanol (9). To a solution of aldehyde **8** (15.4 g; 34.2 mmol) in 1,4-dioxane (150 mL) was added sodium borohydride (1.0 g; 26.4 mmol) in small portions, after which the mixture was stirred for 1 h. Addition of water (600 mL), extraction with dichloromethane (3 × 200 mL), drying ($MgSO_4$), and evaporation of the solvent yielded the crude alcohol. Purification was accomplished by means of column chromatography (eluent hexane/ethyl acetate 3:1 v/v; R_f = 0.29). Yield: 15.2 g (85%). ^{1}H NMR: δ 0.04 (s, 12H), 0.88 (s, 18H), 3.01 (t, 1H), 3.39 (s, 3H), 3.52 (s, 2H), 3.54–3.58 (m, 2H), 3.62 (s, 4H), 3.66–3.70 (m, 4H), 4.68 (s, 2H). ^{13}C NMR: δ −5.7, 18.1, 25.8, 45.4, 59.0, 63.0, 65.5, 66.7, 67.5, 71.7, 95.8.

1-(Benzyloxy)-2,2-bis[[(*tert*-butyldimethylsilyl)oxy]-methyl]-3-[(2-methoxyethoxy)methoxy]propane (10). To a solution of alcohol **9** (5.0 g; 11.1 mmol) in anhydrous THF (40 mL) was added pentane-washed sodium hydride (0.42 g; 17.5 mmol). After stirring for 1 h, benzyl bromide (2.69 g; 15.7 mmol) was added and the reaction mixture was boiled under reflux until TLC showed complete conversion (eluent hexane/ethyl acetate 3:1 v/v; ca. 20 h). Addition of water (250 mL), extraction with dichloromethane (3 × 100 mL), drying ($MgSO_4$), and evaporation of the solvent yielded the crude product, which was purified with column chromatography (eluent hexane/ethyl acetate 10:1 v/v; R_f = 0.28). Yield: 4.2 g (70%). ^{1}H NMR: δ 0.01 (s, 12H), 0.87 (s, 18H), 3.37 (s, 3H), 3.40 (s, 2H), 3.48–3.53 (m, 4H), 3.55 (s, 4H), 3.62–3.66 (m, 2H), 4.46 (s, 2H), 4.68 (s, 2H), 7.25–7.35 (m, 5H). ^{13}C NMR: δ −5.6, 18.2, 25.9, 46.4, 59.0, 60.9, 66.3, 66.4, 68.6, 71.7, 73.3, 95.9, 127.2, 127.3, 128.2, 138.9.

***rac*-3-(Benzyloxy)-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-[[(2-methoxyethoxy)methoxy]methyl]-1-propanol (11).** To a solution of **10** (3.3 g; 6.0 mmol) in anhydrous dichloromethane (30 mL) was added hourly dry, powdered zinc bromide in portions of 1 g. This was continued until TLC showed complete conversion (eluent hexane/ethyl acetate 2:1 v/v; ca. 7 h, a total of 6.95 g (31 mmol) was consumed). Addition of diisopropyl ether (150 mL), extraction of the organic phase with aqueous sodium bicarbonate (2 × 100 mL) and brine (2 × 100 mL), respectively, and drying ($MgSO_4$) and evaporation of the solvent gave the crude alcohol. Column chromatography (eluent hexane/ethyl acetate 2:1 v/v; R_f = 0.28) yielded the pure compound as the racemic mixture in a yield of 2.0 g (77%). ^{1}H NMR: δ 0.04 (s, 6H), 0.88 (s, 9H), 2.94 (t, 1H), 3.38 (s, 3H), 3.50 (s, 2H), 3.51–3.54 (m, 2H), 3.57 (s, 2H), 3.64–3.67 (m, 4H), 3.72 (d, 2H), 4.49 (s, 2H), 4.68 (s, 2H), 7.27–7.38 (m, 5H). ^{13}C NMR: δ −5.7, 18.2, 25.8, 45.1, 59.0, 63.4, 65.5, 66.7, 67.6, 70.5, 71.7, 73.6, 95.8, 127.4, 127.5, 128.3, 128.3.

***rac*-3-(Benzyloxy)-1-[[3,5-bis(benzyloxy)benzyl]oxy]-2-[[(*tert*-butyldimethylsilyl)oxy]methyl]-2-[[(2-methoxyethoxy)methoxy]methyl]propane (12).** This substance was prepared from **11** (1.9 g; 4.5 mmol) and [G-1]-Br (2.1 g; 5.4 mmol) as described for **10** in a yield of 2.5 g (78%). Purification was effected by means of column chromatography (eluent hexane/ethyl acetate 5:1 v/v; R_f = 0.26). ^{1}H NMR: δ 0.02 (s, 6H), 0.88 (s, 9H), 3.29 (s, 3H), 3.43–3.45 (m, 2H), 3.48 (ds, 4H), 3.59 (s, 2H), 3.60–3.63 (s, 4H), 3.64 (s, 2H), 4.40 (s, 2H), 4.46 (s, 2H), 4.67 (s, 2H), 4.96 (s, 4H), 6.51 (t, 1H), 6.57 (d, 2H), 7.18–7.39 (m, 15H). ^{13}C NMR: δ −5.7, 18.1, 25.7, 45.7, 58.7, 61.3, 66.2, 66.4, 68.8, 68.9, 69.8, 71.6, 73.1, 95.7, 100.7, 106.1, 127.1, 127.3, 127.8, 128.1, 128.4, 136.7, 138.7, 141.2, 159.8.

***rac*-2-[(Benzyloxy)methyl]-3-[[3,5-bis(benzyloxy)benzyl]oxy]-2-[[(2-methoxyethoxy)methoxy]methyl]-1-propanol (13).** Compound **12** (2.5 g; 3.4 mmol) was desilylated with 3 equiv of tetrabutylammonium fluoride (10 mL of a 1 M solution in THF). After completion of the reaction (ca. 48 h), water (200 mL) was added. Extraction of the aqueous phase with diisopropyl ether (3 × 75 mL), drying ($MgSO_4$), and evaporation of the organic solvent produced the crude product. Column chromatography (eluent hexane/ethyl acetate 1:1 v/v; R_f = 0.26) gave the pure compound in a yield of 2.0 g (92%). ^{1}H NMR: δ 2.84 (t, 1H), 3.34 (s, 3H), 3.48–3.66 (m, 10H), 3.72 (d, 2H), 4.42 (s, 2H), 4.48 (s, 2H), 4.67 (s, 2H), 5.00 (s, 4H), 6.51–6.56 (m, 3H), 7.27–7.43 (m, 15H). ^{13}C NMR: δ 44.8, 59.0, 65.2, 66.7, 67.7, 70.0, 70.6, 70.7, 71.7, 73.4, 73.5, 95.7, 101.0, 106.3, 127.4, 127.5, 128.0, 128.3, 128.5, 136.8, 138.2, 140.8, 160.0.

***rac*-2-[(Benzyloxy)methyl]-3-[[3,5-bis(benzyloxy)benzyl]oxy]-1-[[3,5-bis[[3,5-bis(benzyloxy)benzyl]oxy]benzyl]oxy]-2-[[(2-methoxyethoxy)methoxy]methyl]propane (14).** This compound was prepared from **13** (1.9 g; 3.0 mmol) and [G-2]-Br (3.2 g; 4.0 mmol) as described for **10** in a yield of 4.0 g (96%). Purification was accomplished by means of column chromatography (eluent hexane/ethyl acetate 3:2 v/v; R_f = 0.28). ^{1}H NMR: δ 3.40 (s, 3H), 3.42–3.46 (m, 2H), 3.55, 3.56 and 3.57 (ts, 6H), 3.61–3.64 (m, 2H), 4.44 (s, 2H), 4.46 (s, 2H), 4.50 (s, 2H), 4.70 (s, 2H), 4.92 (s, 4H), 4.96 (s, 4H), 5.01 (s, 8H), 6.49–6.58 (m, 8H), 6.67 (d, 4H), 7.21–7.45 (m, 35H). ^{13}C NMR: δ 45.4, 58.9, 66.7, 67.0, 69.6, 69.7, 69.9, 70.0, 70.1, 71.7, 73.4, 73.5, 95.8, 100.9, 101.5, 106.1, 106.4, 127.1, 127.2, 127.6, 127.8, 127.9, 128.2, 128.6, 136.6, 136.7, 138.8, 139.4, 141.4, 141.5, 159.7, 159.8, 160.0.

***rac*-2-[(Benzyloxy)methyl]-2-[[[3,5-bis(benzyloxy)benzyl]oxy]methyl]-3-[[3,5-bis[[3,5-bis(benzyloxy)benzyl]oxy]-benzyl]oxy]-1-propanol (15).** Removal of the MEM group was accomplished by treating compound **14** (1.2 g; 0.92 mmol) with an equimolar amount of *B*-chlorocatecholborane (142 mg; 0.92 mmol) in anhydrous dichloromethane (10 mL) during 30 min, after which water (4 mL) was added and the reaction mixture was stirred for another 20 min. Addition of dichloromethane (75 mL), washing of the organic phase with 10% (w/v) aqueous sodium hydroxide (2 × 40 mL) and brine (2 × 40 mL), respectively, and drying ($MgSO_4$) and evaporation of the organic solvent gave crude **15**, which was purified with column chromatography (eluent dichloromethane/diethyl ether 50:1 v/v; R_f = 0.25) in a yield of 0.87 g (76%). ^{1}H NMR: δ 2.80 (br s, 1H), 3.54, 3.55, and 3.56 (ts, 6H), 3.76 (br s, 2H), 4.40 (s, 2H), 4.42 (s, 2H), 4.46 (s, 2H), 4.91 (s, 4H), 4.94 (s, 4H), 5.00 (s, 8H), 6.47–6.54 (m, 6H), 6.55 (t, 2H), 6.65 (d, 4H), 7.20–7.42 (m, 35H). ^{13}C NMR: δ 45.1, 65.9, 69.9, 70.0, 70.1, 70.7, 70.9, 73.4, 73.5, 101.1, 101.5, 106.2, 106.3, 127.3, 127.5, 127.9, 128.0, 128.3, 128.5, 128.6, 136.7, 136.8, 138.2, 139.3, 140.8, 140.9, 159.9, 160.0, 160.1.

***rac*-2-[(Benzyloxy)methyl]-2-[[[3,5-bis(benzyloxy)benzyl]oxy]methyl]-3-[[3,5-bis[[3,5-bis(benzyloxy)benzyl]oxy]-benzyl]oxy]-1-[[3,5-bis[[3,5-bis[[(3,5-bis(benzyloxy)benzyl]-**

oxy]benzyl]oxy]benzyl]oxy]propane (1). Chiral dendrimer **1** was obtained in the racemic form by reaction of **15** (0.48 g; 0.38 mmol) with [G-3]-Br (0.75 g; 0.45 mmol) as described for **11** in a yield of 0.80 g (74%). Purification was accomplished by means of preparative HPLC (eluent dichloromethane/acetonitrile 99:1 v/v) with Silica Lichrosorb SI-60 5 μm (column dimensions 100 × 16 mm i.d.); detection with UV light at λ = 254 nm) as stationary phase. ^{1}H NMR: δ 3.54 (s, 2H), 3.56 (br s, 6H), 4.39 (s, 2H), 4.40 (s, 4H), 4.44 (s, 2H), 4.80 (s, 4H), 4.82 (s, 4H), 4.85 (s, 4H), 4.87 (s, 8H), 4.91 (s, 8H), 4.96 (s, 16H), 6.41–6.61 (m, 25H), 6.63 (d, 8H), 7.18–7.40 (m, 75H). ^{13}C NMR: δ 45.7, 69.3, 69.4, 69.7, 69.8, 69.9, 70.0, 73.1, 73.2, 100.8, 101.4, 101.5, 106.0, 106.3, 106.4, 127.1, 127.2, 127.5, 127.8, 127.9, 128.2, 128.5, 136.7, 136.8, 138.8, 139.1, 139.3, 141.3, 141.4, 141.4, 159.7, 159.8, 159.9, 160.0, 160.1.

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Supplementary Material Available: ^{1}H- and ^{13}C-NMR spectra of **1**, **6**, and **8–15** (20 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.