Dendrimers with Alternating Amine and Ether Generations

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Dendrimers having alternating aryl benzyl ether and tertiary amine generations and up to 16 bis-(2-methoxyethyl)amine end groups and four internal tertiary amines were synthesized by sequential etherification, amidation of secondary amines, and $LiAlH_4$ reduction to tertiary amines. The bis-(2-methoxyethyl)amine dendrimers are soluble in common organic solvents and in aqueous buffer solutions at pH < 4.7. At 2.8 mM, the dendrimer increases the solubility of pyrene in water 30-fold, and the solvated pyrene is not aggregated.

Since the pioneering divergent syntheses of Tomalia[1] and Newkome[2] and the convergent synthesis of Hawker and Frechet,[3] many different types of dendritic macromolecules have been synthesized.[4] Much emphasis now is on functional dendrimers.[4c,e] We have been intrigued by poly(propylene imine) (PPI) dendrimers that can trap and release smaller molecules.[5] The polar ends of amphiphilic dendrimers make them water-soluble, and their less polar cores and branching units solvate hydrophobic molecules.[2,6] Carboxylic acid terminated dendrimers serve as micelle substitutes in electrokinetic capillary chromatography.[7] The internal volume of poly(amidoamine) (PAMAM) dendrimers terminated with eight carboxylic acids provided confined sites for the polymerization of lipophilic monomers in aqueous solution.[8] Dendrimers with terminal ammonium salts and long all-hydrocarbon core and branching units trap lipophilic guest molecules such as diphenylhexatriene, naphthalene, and dyes in aqueous solutions.[6d] Carboxylic acid terminated PAMAM dendrimers having a long aliphatic chain in the core host hydrophobic dyes in aqueous solution.[9] Dendritic unimolecular micelles, unlike dynamically aggregated surfactant micelles, retain their colloid structure no matter how dilute the solution. These unique properties of dendrimers may enable applications in medicine[10] and catalysis.[11]

The cores and branch points as well as the end groups can be reactive functional groups. The commercial PPI and PAMAM dendrimers have tertiary amines at the branch points. The PPI and PAMAM dendrimers are prepared by repetitive conjugate addition of primary amines to acrylonitrile or methyl acrylate, followed by conversion to primary amines via hydrogenation of the resulting nitriles[12] or by amidation of the methyl esters with excess ethylenediamine.[1] Amidation also is the key chain extending step in the synthesis of dendrimers with three new branches at each branch point.[13] The preparation of wholly polyamine dendrimers by the reduction of amides is rare,[14] although the amide connectivity is highly useful in dendrimer synthesis because of its chemical stability[1,15] and because many high yield amidation methods are available from synthesis of polyamides and polypeptides.

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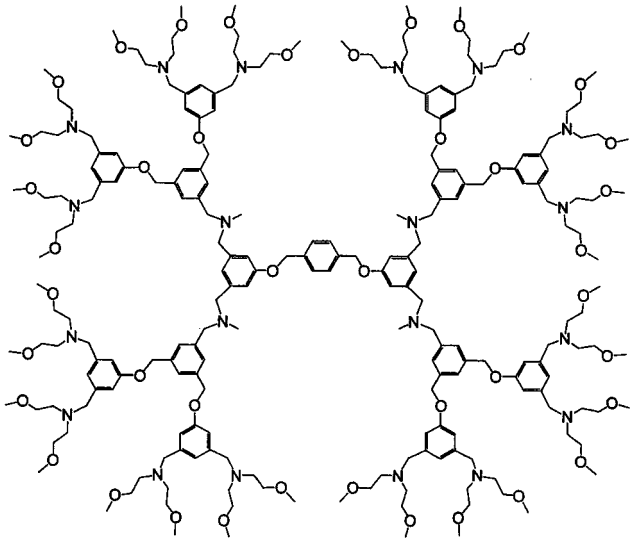
Our aim with amine dendrimers is to evaluate their potential as catalysts of reactions in aqueous solutions. Nonpolar organic compounds will partition into the less polar interiors of the dendrimers. Primary and tertiary amine end groups and tertiary amine branch points can serve as ligands for metal ion complexes. Conversion of the tertiary amines to quaternary ammonium ions gives compact polyelectrolyte structures that attract counterions as reagents or catalysts. In our first study of dendrimer catalysis, the activity of a terminal quaternary ammonium dendrimer with no internal active sites and little free volume was much less than that of a quaternary ammonium ion latex for decarboxylation of 6-nitrobenzisoxazole-3-carboxylate and for *o*-iodosobenzoate-catalyzed hydrolysis of *p*-nitrophenyl diphenyl phosphate.[11c]

With catalysis as the application goal, we have synthesized dendrimers with both terminal and internal tertiary amines. An example is dendrimer **1**, which has 16 bis(2-methoxyethyl)amine end groups, four internal tertiary amine groups, a hydrophobic core, and alternating ether and amine layers. The structures are analogues of layer block copolymers[16] and may solvate large lipophilic molecules in the multiple hydrophobic layers. Such structures cannot be obtained from dynamically aggregated surfactants.



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Results and Discussion

The strategy for the syntheses of **1** and related amine–ether dendrimers is to form alternating layers by Williamson ether syntheses and amidations of secondary amines, and to form tertiary amines by reduction of amides. Polyamides frequently are insoluble in most common organic solvents, and so highly solubilizing bis(2-methoxyethyl)amine and -amide end groups were used throughout. The outer layer of end groups and terminal branches of a dendrimer count for at least half of the mass and are the interface between dendrimer and medium that mainly determines its solubility.

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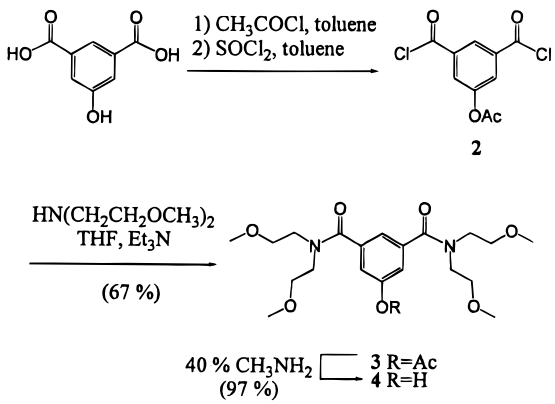
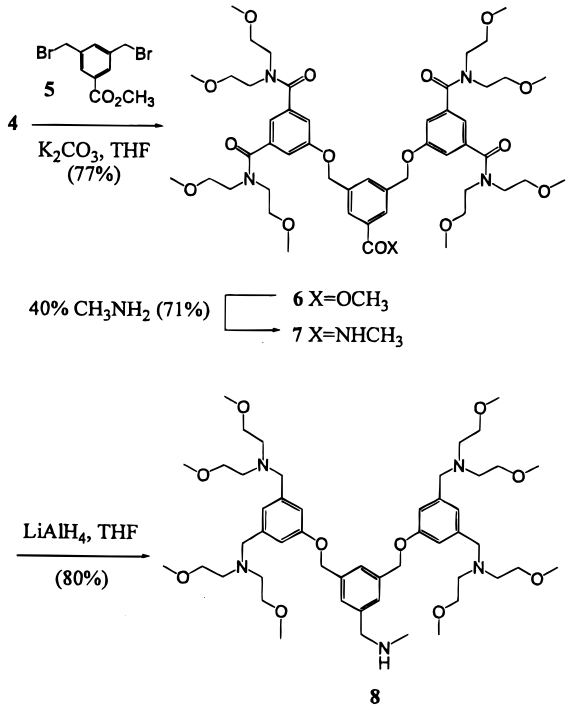
Scheme 1



Scheme 2



Bis(2-methoxyethyl)amine Terminated Dendron. The amide-terminated dendron **4** was synthesized by the method of Scheme 1. The hydroxyl group of 5-hydroxyisophthalic acid was protected using acetyl chloride, and the two carboxylic acid groups were converted to acid-chloride using thionyl chloride to give **2**. The crude product **2** was treated with bis(2-methoxyethyl)amine to form dendron **3,** and the protecting group of **3** was subsequently removed by aqueous methylamine to give corresponding phenol **4**.

Branching monomer **5** was prepared by NBS bromination of methyl 3,5-dimethylbenzoate in 60% yield.[17] The syntheses of the amide terminated amide dendron **7** and the amine terminated amine dendron **8** are shown in Scheme 2. Ester **6** was synthesized by etherification of 2 equiv of phenol **4** with 1 equiv of dibromide **5** and was converted to amide **7** using 40% aqueous $MeNH_2$. Both the terminal and the focal amide groups of **7** were converted to amine groups by $LiAlH_4$ in THF to give amine **8** in 91% yield. The secondary amine formed at the focal point of **8** becomes the site for subsequent

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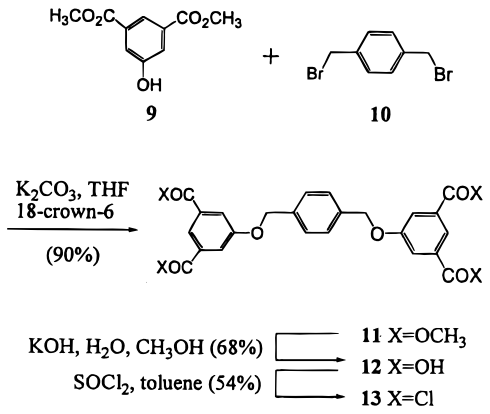
Scheme 3



coupling reactions. The bis(2-methoxyethyl)amine groups were stable to the conditions of both amidation and $LiAlH_4$ reduction, and they may even serve as proton acceptors in the coupling of polyamine dendrons with the core units.

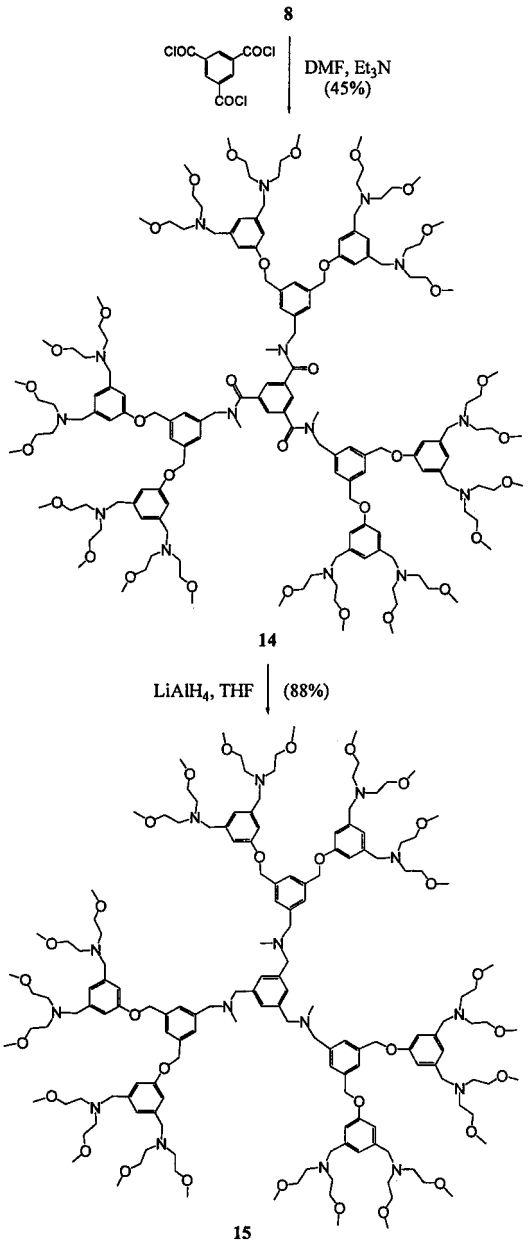
Tetraacid chloride **13** was synthesized as shown in Scheme 3. Two equivalents of dimethyl 5-hydroxyisophthalate (**9**) and 1 equiv of α,α′-dibromo-*p*-xylene (**10**) gave tetraester **11**, which was hydrolyzed to tetraacid **12** and then converted to the acid chloride **13** by reaction with thionyl chloride in toluene.[18]

Coupling of the Dendrons to the Cores. Internal amide groups in the layer block dendrimers were formed by amidation of carboxylic acid chloride cores and were reduced to tertiary amines. The terminal amides were directly converted to tertiary amines in the dendron *prior to* the formation of the dendrimers. Thus, amine **8** reacted with benzene-1,3,5-tricarbonyl trichloride in DMF to give dendrimer **14** in 45% isolated yield as shown in Scheme4. The relatively low yield resulted from the difficulty of separating **14** from starting material **8**. Since the two compounds tailed badly during chromatography on untreated silica gel, dendrimer **14** was purified using preparative silica gel plates pretreated with trimethylamine. Purity was confirmed by NMR, ESI-MS, TLC and HPLC analysis. The reduction of **14** by $LiAlH_4$ in THF gave the polyamine dendrimer **15** in 88% yield (Scheme 4).

The amide−amine dendrimer **16** with 16 terminal tertiary amine and four internal amide groups was prepared by the same method as **14** using excess amine **8** with the core unit **13** in DMF and purified using preparative silica gel plates pretreated with trimethylamine. The interior amide groups of **16** were reduced to the interior tertiary amine groups by $LiAlH_4$ to afford the dendrimer **1** (Scheme 5).

Other Approaches to Alternating Amide−Ether Dendrimers. Some other approaches to terminal amide functionality gave low yields or separation difficulties. A dendrimer was synthesized having structure identical with that of **16** except for methyl carboxylate instead of bis(2-methoxyethyl)carboxamide end groups. Treatments of the dendrimer with sixteen methyl esters with methylamine, dimethylamine, and benzylamine gave dendrimers with sixteen secondary terminal amides in good yield, but the compounds were soluble only in DMF and DMSO. Attempts to reduce the polyamides to polyamines with borane and $LiAlH_4$ were not successful due to their low solubility in THF and in dioxane and to the formation of gels. Amidations of terminal esters with secondary amines suffered from incomplete conversions even at elevated temperature and with NaCN as a catalyst.

Scheme 4



Characterization. The polyamine dendron **8** and dendrimers **14**−**16** and **1** were characterized by IR, ^1H and ^{13}C NMR, and ESI-MS. LSIMS mass analyses were used for amide dendrons and monomers. Purities were analyzed by TLC and HPLC.

FT-IR was very useful for determining the completeness of the amidations from the disappearance of the carbonyl chloride band of the core units at 1760−1770 cm^{-1} and for determining the completeness of $LiAlH_4$ reduction from the disappearance of amide band at 1650−1640 cm^{-1} (Figure 1).

NMR analysis was not very useful for the characterization of the aromatic tertiary amide dendrimers because each amide group exists in two conformations due

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Scheme 5

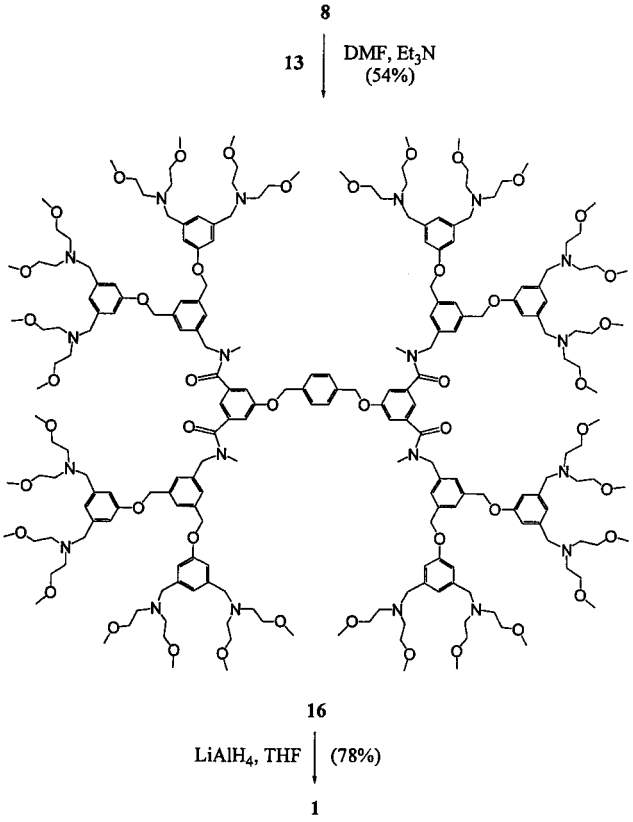

Figure 1. FTIR spectra of polyamine dendron **8** (top), internal polyamide/terminal polyamine dendrimer **16** (middle), and polyamine dendrimer **1** (bottom).

to slow rotation about the carbonyl C−N bond and each conformation gives its own spectrum. However, the NMR spectra of the polyamine dendrimers were much sharper. The ^{1}H NMR spectra of the interior amide dendrimer **16** and the wholly polyamine dendrimer **1** are compared in Figure 2. The proton NMR spectrum of dendrimer **16** containing interior amides shows the NCH_3 signal spread over 2.7−3.2 ppm and the broad NC$\mathbf{H}_2$ signal spread over 4.4−4.9 ppm. The signals in the aromatic region are also complicated. The proton NMR spectrum of the corresponding polyamine dendrimer **1**, on the other hand, has an extremely clean NMR spectrum, and the coupling between the terminal ethylene groups could be identified

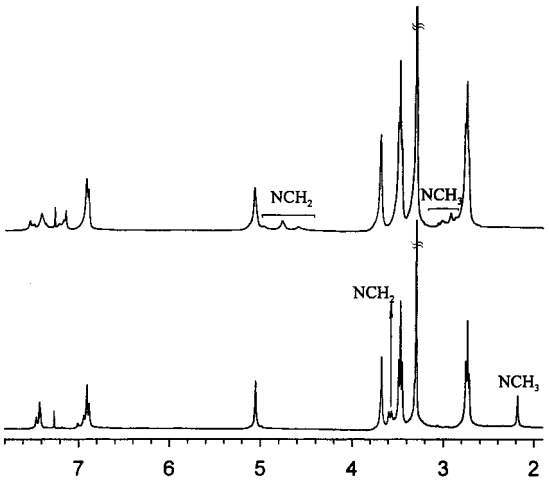

Figure 2. 400 MHz ^{1}H NMR spectra of internal polyamide/terminal polyamine dendrimer **16** (top) and polyamine dendrimer **1** (bottom).

(Figure 2). The carbon NMR spectrum of amine dendrimer **1** was also much better resolved than that of amide−amine dendrimer **16**.

The ESI-MS spectrum of dendron **8** from water/acetonitrile/acetic acid (50:50:0.5) predominantly contained $[M + H]^+$ and $[M + 2H]^{2+}$ ions, while the spectra of dendrimers **14**−**16** and **1** mainly contained ions with 2+ to 7+ charge in which one charge was due to sodium or potassium and the rest were due to protons. These data indicate that the desired dendron and dendrimers are the predominant species in the samples. The ESI-MS spectra of dendrimers **14** and **16** showed no peaks from the starting material **8**.

Solubility and Molecular Inclusion. The bis(2-methoxyethyl)amine terminated polyamide and polyamine dendrimers are readily soluble in toluene, ether, THF, chloroform, acetone, methanol, and DMF. Solubility in organic solvents is essential for synthesis and purification. Polyamine dendrimers **1** and **15** are also soluble in aqueous acetic acid/sodium acetate buffer solutions at pH 4.74, but the solubility decreases dramtically above pH 4.74. The lipophilic compatability and the solubility in aqueous solution are desired properties for the catalytic application of the polyamine dendrimers as unimolecular micelles.

The microenvironment of the hydrophobic interior of the bis(2-methoxyethyl)amine terminated dendrimers was probed by solubilizing pyrene in aqueous solution at pH 3.0. The limiting solubility of pyrene in a 2.8×10^{-3} M solution of dendrimer **1** measured by UV−vis absorption spectrophotometry is $\sim 2.5 \times 10^{-5}$ M, more than 30 times higher than in pure water (8×10^{-7} M). Pyrene has been dissolved into poly(propylene imine) dendrimer solutions at similar concentrations.[19] Pyrene aggregates in water as shown by concentration-dependent λ_{max}. The UV−vis spectra of pyrene in dendrimer **1** obey Beer's law up to 2.31×10^{-5} M, and λ_{max} does not change with concentration as shown in Figure 3. This proves that the pyrene dissolves into the dendrimer unimolecularly.

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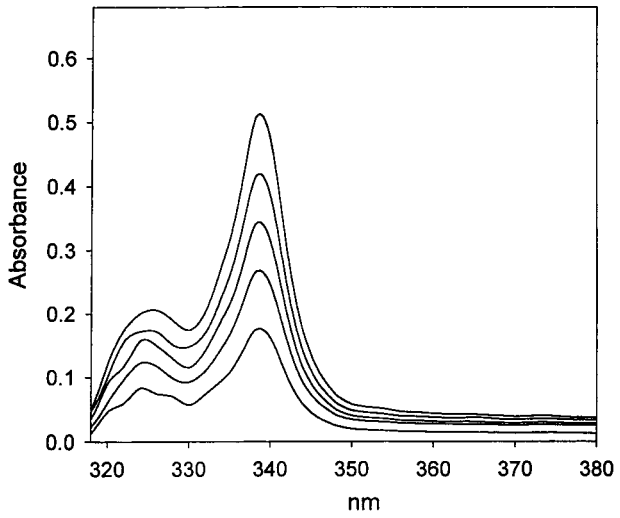

Figure 3. UV−vis absorption spectra of pyrene at concentrations of 0.77, 1.16, 1.54, 1.92, and 2.31 × 10^{-5} M in 2.80 × 10^{-3} M aqueous dendrimer **1** at pH 3.0.

Experimental Section

All starting materials were from Aldrich and were used as received unless otherwise stated. THF was freshly distilled from sodium. Pyridine and triethylamine were dried over 3 Å molecular sieves and freshly distilled. All glassware was dried at 170 °C before use. ^{1}H NMR spectra at 400 or 300 MHz NMR spectra and ^{13}C NMR spectra at 100.6 or 75.4 MHz were recorded with the solvent proton signal as the reference. Liquid secondary ion mass spectra (LSIMS) were obtained using a 25 keV primary Cs^+ ion beam and 3-nitrobenzyl alcohol as the matrix. Electrospray mass spectra were acquired by infusing the samples in water:acetonitrile:acetic acid (50:50:0.5) at a flow rate of 1 μL min^{-1}. Calculated *m*/*z* values for all mass spectra are for the lowest mass isotopomer. Analytical TLC was performed on Kodak thin-layer chromatography plates with silica gel GF_{254}. Preparative TLC was performed on Aldrich silica gel GF plates (1000 μm thick), and the plates were pre-developed with 2% trimethylamine in CH_2Cl_2 and activated at 60 °C for 6 h. Baker silica gel (40 μm) was used for flash chromatography. HPLC was carried out with a reversed-phase C_{18} column, 50/50 methanol/chloroform as solvent, and UV detection at 350 nm.

5-Acetoxy-1,3-bis[*N*,*N*-bis(2-methoxyethyl)]benzenedicarboxamide (3). A mixture of 6.01 g (33.0 mmol) of 5-hydroxyisophthalic acid, 10.80 g (138.0 mmol) of acetyl chloride, and 10 mL of toluene was stirred under reflux for 6 h. Thionyl chloride (11.02 g, 92.0 mmol) was added, and the mixture was stirred for 7 h under reflu, and concentrated under reduced pressure. The oily residue **2** was dissolved in 10 mL of THF. A solution of 9.06 g (68.0 mmol) of bis(2-methoxyethyl)amine in 15 mL of THF and triethylamine (8.10 g, 80.0 mmol) was added slowly with stirring at 0 °C, and the mixture was stirred for 30 min at 0 °C and 4 h at room temperature, added to 30 mL of water, extracted with $CHCl_3$ (2 × 50 mL), washed with water, dried over $MgSO_4$, and evaporated to a light yellow oil, which was eluted through a short column chromatography (SiO_2, MeOH/$CHCl_3$ 2:98) to give 10.11 g (67%) of **3** as a thick oil: IR (film on NaCl) ν_{max} 1738, 1638, 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 2.36 (s, 3H), 3.3−3.4 (2 br s, 6H each), 3.4−3.8 (4 br s, 4H each), 7.22 (s, 2H), 7.40 (s, 1H); ^{13}C NMR ($CDCl_3$, δ) 20.47, 44.70, 49.09, 58.22, 69.65, 70.14, 120.75, 122.46, 137.48, 149.58, 168.09, 169.76; LSIMS (*m*/*z*) calcd for $C_{22}H_{34}N_2O_8$ 454.2, found 455 $[M + H]^+$.

5-Hydroxy-1,3-bis[*N*,*N*-bis(2-methoxyethyl)]benzenedicarboxamide (4). Acetate **3** (10.00 g, 22.0 mmol), 10 mL of methanol, and 20 mL of 40% aqueous $MeNH_2$ were stirred for 8 h at room temperature. The mixture was concentrated on a rotary evaporator, acidified to pH 4−5 using 2% aqueous HCl, and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4, and evaporated to give 9.70 g (97%) of **4** as a light yellow thick oil: IR (film on NaCl) ν_{max} 3195, 1638, 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 3.3−3.4 (2 br s, 6H each), 3.4−3.8 (4 br s, 4H each), 6.82 (s, 2 H), 6.85 (s, 1H), 8.58 (br, 1H); ^{13}C NMR ($CDCl_3$, δ) 44.63, 49.40, 58.00, 69.73, 70.33, 120.80, 122.25, 137.80, 149.75, 168.01; LSIMS (*m*/*z*) calcd for $C_{20}H_{32}N_2O_7$ 412.2, found 413 $[M + H]^+$.

Methyl 3,5-Bis(bromomethyl)benzoate (5).[17] A mixture of 1.97 g (12.0 mmol) of **4**, 4.38 g (24.6 mmol) of NBS, 34 mg of dibenzoyl peroxide, and 36 mL of carbon tetrachloride in a 50 mL round-bottom flask fitted with a condenser was stirred, heated to reflux with an IR lamp, and irradiated with a medium-pressure 450 W Hg lamp for 60 min. After cooling, the mixture was filtered, and the solid was washed with dichloromethane. The combined organic solution was washed with 1% aqueous sodium carbonate and with water, dried, and evaporated to a gummy residue that was crystallized from hexane at −20 °C and recrystallized from hexane at room temperature to give 58% of white solid **5**: mp 91−93 °C (lit.[17] mp 92−93 °C); IR (film on NaCl) ν_{max} 1730, 1438, 1317, 1231, 776, 705, 698 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 3.92 (s, 3H), 4.50 (s, 4H), 7.59 (s, 1H), 7.93 (t, 2H); ^{13}C NMR ($CDCl_3$, δ) 52.10, 81.74, 129.82, 133.27, 133.40, 138.70, 164.50; LSIMS (*m*/*z*) calcd for $C_{10}H_{10}Br_2O_2$ 319.9, found 321, 323, 325 $[M + H]^+$.

Ester 6. A solution of 3.34 g (8.1 mmol) of phenol **4**, 1.30 g (4.04 mmol) of bromide **5**, and 1.66 g (12.0 mmol) of K_2CO_3 in 38 mL of THF was stirred under nitrogen at 65 °C for 24 h. The mixture was concentrated, and 20 mL of water (20 mL) was added. The mixture was extracted with chloroform, washed with 1% aqueous Na_2CO_3 and water, and dried over $MgSO_4$. Flash chromatography (MeOH/$CHCl_3$, 2:98) afforded 3.03 g (77%) of **6** as a colorless thick oil: IR (film on NaCl) ν_{max} 1730, 1638, 1596 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 3.3−3.4 (2 br s, 6H each), 3.4−3.8 (4 br s, 4H each), 3.95 (s, 3H), 5.18 (s, 4H), 7.08 (s, 2H), 7.12 (s, 4H), 7.72 (s, 1H), 8.08 (s, 2H); ^{13}C NMR ($CDCl_3$, δ) 45.37, 49.86, 52.49, 59.02, 69.61, 70.54, 70.94, 114.60, 118.49, 128.40, 130.76, 131.21, 137.62, 138.52, 158.38, 166.59, 171.22; LSIMS (*m*/*z*) calcd for $C_{50}H_{72}N_4O_{16}$ 984.5, found 984 $[M]^+$.

Amide 7. A solution of 3.20 g (3.25 mmol) of ester **6** in 6 mL of methanol and 18 mL of 40% aqueous $MeNH_2$ was stirred at room temperature for 24 h. The mixture was concentrated, acidified to pH 4 using 2% aqueous HCl, and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried over Na_2SO_4, concentrated, and flash chromatographed (MeOH/$CHCl_3$, 2:98) to give 2.12 g (71%) of **7** as a colorless thick oil: IR (film on NaCl) ν_{max} 3359, 1637, 1595 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 2.96 (d, 3H), 3.3−3.4 (2 br s, 6H each), 3.4−3.8 (4 br s, 4H each), 5.18 (s, 4H), 7.18 (6H), 7.59 (s, 1H), 7.82 (s, 2H); ^{13}C NMR ($CDCl_3$, δ) 26.51, 44.93, 49.39, 58.56, 69.32, 70.07, 70.45, 114.31, 118.01, 125.63, 128.70, 135.40, 137.09, 138.05, 157.94, 167.22, 170.77; LSIMS (*m*/*z*) calcd for $C_{50}H_{73}N_5O_{15}$ 983.5, found 983 $[M^+]$, 984 $[M + H]^+$.

Amine 8. A suspension of 98 mg (2.58 mmol) of $LiAlH_4$ and 16 mL of THF under nitrogen was cooled to 0 °C, and 998 mg (1.01 mmol**)** of **7** in 4 mL of THF was added slowly with stirring at 0 °C. The mixture was stirred at 70 °C for 24 h, cooled, and slowly poured into 20 mL of saturated aqueous Na_2SO_4 solution at 0 °C. The mixture was acidified to pH 1 using 6 M aqueous HCl, washed with Et_2O (2 × 5 mL), added to 10 M aqueous NaOH to pH 12, and extracted with Et_2O (3 × 15 mL). The organic solution was washed with water, dried over K_2CO_3, evaporated, and dried under vacuum to give 722 mg (80%) of **8** as a thick oil: IR (film on NaCl) ν_{max} 1593 cm^{-1}; ^{1}H NMR ($CDCl_3$, δ) 2.49 (s, 3H), 2.76 (t, 16H), 3.34 (s, 24H), 3.48 (t, 16H), 3.68 (s, 8H), 5.18 (s, 4H), 6.87 (s, 2H), 6.92 (s, 4H), 7.36−7.46 (m, 3H); ^{13}C NMR ($CDCl_3$, δ) 36.01, 53.60, 55.79, 58.61, 59.48, 69.63, 71.15, 113.51, 121.74, 125.25, 126.73, 137.55, 140.81, 140.85, 158.77; ESIMS (*m*/*z*) calcd for $C_{50}H_{83}N_5O_{10}$ 913.6, found 914.8 $[M + H]^+$, 457.9 $[M + 2H]^{2+}$.

Tetraester 11. A mixture of 2.10 g (10.0 mmol) of dimethyl 5-hydroxyisophthalate (**9**), 1.29 g (4.90 mmol) of α,α′-dibromo-*p*-xylene (**10**), 2.21 g (16.0 mmol) of K_2CO_3, 0.10 g of 18-crown-6 ether, and 38 mL of THF was stirred under nitrogen at 65 °C for 24 h. The mixture was concentrated, and 20 mL of 1%

aqueous Na_2CO_3 was added at 0 °C. The solid was collected, washed with water and ether, and dried under vacuum at 50 °C to give 2.31 g (90%) of **11** as a white powder: mp 186−188 °C; IR (KBr) ν_{max} 1730, 1602, 1459, 1346, 1246, 1040, 755 cm^{-1}; ^1H NMR ($CDCl_3$, δ) 3.96 (s, 12H), 5.19 (s, 4H), 7.50 (s, 4H), 7.84 (d, 4H), 8.32 (t, 2H); ^{13}C NMR ($CDCl_3$, δ) 52.40, 70.08, 120.22, 123.38, 127.95, 131.94, 136.25, 158.83, 166.23; LSIMS (*m*/*z*) calcd for $C_{28}H_{26}O_{10}$ 522.2, found 523 $[M + H]^+$.

Tetracarboxylic Acid 12. A solution of 1.02 g (1.95 mmol) of ester **11**, 10 mL of methanol, 450 mg (8.02 mmol) of KOH, and 10 mL of water was stirred under nitrogen at 50−60 °C for 48 h. The mixture was concentrated, and 6 M aqueous HCl was added slowly at 0 °C. The precipitate was collected, washed with water, and dried under vacuum to give 0.62 g (68%) of acid **12** as a white solid: IR (KBr) ν_{max} 3500−2500, 1708, 1602 cm^{-1}; ^1H NMR (DMSO-d_6, δ) 5.29 (s, 4H, CH_2O), 7.58 (s, 4H), 7.81 (s, 4 H), 8.18 (s, 2H), 13.40 (br, 4H); ^{13}C NMR (DMSO-d_6, δ) 69.7, 119.8, 122.8, 128.2, 133.0, 136.7, 158.9, 166.8.

Tetracarboxylic Acid Chloride 13. A mixture of 400 mg (0.850 mmol) of acid **12**, 4 mL of toluene, and 4 mL of $SOCl_2$ was stirred under nitrogen at 70−75 °C for 48 h. The precipitate was collected, washed with ether (2 × 3 mL), and dried under vacuum to give 250 mg (54%) of **13** as a light yellow solid: mp 189−192 °C; IR (KBr) ν_{max} 1765, 1597, 1304, 681 cm^{-1}; ^1H NMR (DMSO-d_6, δ) 5.25 (s, 4H, CH_2O), 7.58 (s, 4H), 7.78 (s, 4H), 8.10 (s, 2H); ^{13}C NMR (DMSO-d_6, δ) 69.49, 119.64, 122.60, 127.97, 132.74, 136.46, 159 (br), 166.49.

Dendrimer 14. To a solution of 645 mg (0.706 mmol) of amine **8** in 4.0 mL of DMF were added 60 mg (0.23 mmol) of 1,3,5-benzenetricarboxylic acid chloride and 63 mg (0.80 mmol) of pyridine, and the mixture was stirred under nitrogen at 60 °C for 24 h. DMF was removed under reduced pressure. The residue was dissolved in 1.5 M aqueous HCl and washed with ether (2 × 5 mL). Aqueous 5 M NaOH was added to pH 11 at 0 °C. The aqueous mixture was extracted with ether (3 × 10 mL), and the combined organic solution was washed with water, dried over potassium carbonate, and concentrated to an oil. The crude product was purified on trimethylamine-pretreated preparative silica gel plates (trimethylamine/methanol/chloroform, 0.5:2.5:97) to give 300 mg (45%) of **14** as a light yellow thick oil: IR (film on NaCl) ν_{max} 1641, 1590 cm^{-1}; ^1H NMR ($CDCl_3$, δ): 2.78 (m, 48H), 2.81−3.14 (m, 9H), 3.31 (s, 72H), 3.50 (m, 48H), 3.70 (s, 24H), 4.5−4.84 (br, 6H), 5.06 (s, 12H), 6.91 (br s, 18H), 7.2−7.7 (m, 9H); ^{13}C NMR ($CDCl_3$, δ): 45.31, 53.57, 58.64, 59.47, 64.07, 69.46, 69.66, 71.14, 113.56, 113.63, 121.89, 125.58, 126.35, 127.81, 137.55, 138.26, 139.66, 140.95, 141.06, 158.96; ESIMS (*m*/*z*) calcd for $C_{159}H_{249}N_{15}O_{33}$ 2896.8, found 1450.4 $[M + 2H]^{2+}$, 967.2 $[M + 3H]^{3+}$, 725.6 $[M + 4H]^{4+}$, 580.4 $[M + 5H]^{5+}$.

Dendrimer 15. By the procedure for amine **8**, 38 mg (1.0 mmol) of $LiAlH_4$, 17 mL of THF, and 250 mg (0.0862 mmol) of **14** gave 216 mg (88%) of **15** as a thick oil: IR (film on NaCl) ν_{max} 1590 cm^{-1}; ^1H NMR ($CDCl_3$, δ) 2.18 (s, 9H), 2.76 (t, 48H), 3.34 (s, 72H), 3.46 (t, 48H), 3.58 (m, 12H), 3.68 (s, 24H), 5.18 (s, 12H), 6.84 (m, 18H), 7.2−7.5 (m, 9H); ^{13}C NMR ($CDCl_3$, δ) 44.98, 53.58, 58.70, 59.50, 69.63, 69.78, 71.10, 113.80, 113.94, 122.10, 125.64, 125.71, 127.90, 128.07, 137.52, 137.78, 140.81, 158.99; ESIMS (*m*/*z*) calcd for $C_{159}H_{255}N_{15}O_{30}$ 2854.9, found 1429.2 $[(M + 2H)]^{2+}$.

Dendrimer 16. By the method for dendrimer **14**, 548 mg (0.600 mmol) of amine **8**, 4.0 mL of DMF, 70 mg (0.13 mmol) of **13**, and 60 mg (0.59 mmol) of triethylamine gave 280 mg (54%) of **16** as a light yellow thick oil: IR (film on NaCl) ν_{max} 1648, 1597 cm^{-1}; ^1H NMR ($CDCl_3$, δ) 2.76 (m, 64H), 2.8−3.1 (br, 12H), 3.34 (m, 96H), 3.50 (m, 64H), 3.78 (s, 32H), 4.4−4.9 (br, 8 H), 5.06 (m, 16H), 6.90 (m, 24H), 7.12−7.25 (m, 6H), 7.35−7.6 (m, 12H); ^{13}C NMR ($CDCl_3$, δ) 53.55, 58.70, 59.47, 69.58, 71.02, 113.82, 122.24, 126.32, 127.26, 127.95, 138.20, 140.83, 158.95; ESIMS (*m*/*z*:) calcd for $C_{224}H_{342}N_{20}O_{46}$ 4048.5, found 2026.4 $[M + 2H]^{2+}$, 1351.2 $[M + 3H]^{3+}$, 1014.0 $[M + 4H]^{4+}$, 811.2 $[M + 5H]^{5+}$, 676.0 $[M + 6H]^{6+}$.

Dendrimer 1. By the method for amine **8**, 38 mg (1.00 mmol) of $LiAlH_4$, 17 mL of THF, and 220 mg (0.0543 mmol) of **16** gave 169 mg (78%) of **1** as a thick oil: IR (film on NaCl) ν_{max} 1591 cm^{-1}; ^1H NMR ($CDCl_3$, δ) 2.19 (s, 12H), 2.76 (t, 64H), 3.34 (s, 96H), 3.46 (t, 64H), 3.53−3.62 (m, 16H), 3.67 (s, 32H), 5.08 (s, 16H), 6.85−7.05 (m, 32H), 7.40−7.48 (m, 14H); ^{13}C NMR ($CDCl_3$, δ) 41.93, 53.60, 58.70, 59.52, 61.81, 62.19, 69.81, 71.10, 113.83, 122.07, 125.77, 127.88, 136.81, 137.58, 140.84, 159.07; ESIMS (*m*/*z*) calcd for $C_{224}H_{350}N_{20}O_{42}$ 3992.6, found 1998.8 $[M + 2H]^{2+}$, 1332.8 $[M + 3H]^{3+}$, 1000.0 $[M + 4H]^{4+}$, 800.0 $[M + 5H]^{5+}$, 666.8 $[M + 6H]^{6+}$, 571.6 $[M + 7H]^{7+}$.

Solubility Measurements. Solubilities of the dendrimers, and of pyrene in dendrimer solutions, were tested by adding 4−5 mg of the sample into 1.0 mL of the solvent or aqueous solution in a 4 mL vial and stirring magnetically for 15 min. The sample was judged soluble if a clear solution formed, slightly soluble if a cloudy solution formed, and insoluble if the oil or solid remained unchanged.

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Supporting Information Available: ^1H and ^{13}C NMR spectra and mass spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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