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Syntheses of New 1 → (2 + 1) *C*-Branched Monomers for the Construction of Multifunctional Dendrimers

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ABSTRACT: For the purpose of providing a route to multifunctionalized dendrimers, new types of 1 → (2 + 1) *C*-branched monomers, possessing either ester and protected hydroxy groups or mixed esters, were designed and synthesized. Thus, di-*tert*-butyl 4-(3-[X]oxypropyl)-4-aminoheptanedioate (X = MeCO, **4**; X = CH_2CH_2CN, **6**; X = $CH_2C_6H_5$, **7**) was prepared in high yields via the protection of the nitro precursor **2** (X = H), which was readily accessible from the Michael addition of 4-nitrobutanol with *tert*-butyl acrylate, followed by catalytic reduction. These monomers were readily attached to an appropriate four-directional core to produce the first-generation dendrimers (e.g., **9**−**11**). The related second-generation dendrimer (**15**), possessing two different functional groups on both the surface and interior, was convergently synthesized from monomer **3**. Alternatively, the mixed ester **17** was prepared starting with benzyl 4-nitrobutanoate (**16**); selective deprotection offered access to the representative 1 → (2 + 1) *C*-branched monomer **20**, which was converted to dendrimers **29** and **30** with a single novel terminus per dendron. These 1 → (2 + 1) *C*-branched monomers offer synthetic versatility to place different functionality at different levels within or on the surface of the dendritic construct.

Introduction

Since their inception,[1,2] dendrimers as well as their less-than-perfect, hyperbranched analogues have received considerable attention due, in part, to their unique globular structures, physical properties,[3−12] and catalytic activity.[13−16] In general, synthetic methodologies for dendritic construction are categorized into either a divergent[1,2] or convergent[17] mode, which consists of the stepwise, iterative reaction processes based on branched[18] or traditional commercial linear monomers. Appropriate selection of monomer, multidirectional core, and/or mode of assembly thus ultimately defines the supramacromolecular properties of dendrimers, such as size, shape, solubility, viscosity, and thermal behaviors, internal and surface functionality, aptitude for catalysis, and unimolecular micelle properties.[19,20]

With respect to dendritic construction, a variety of branched monomers have been developed over the past decade. In general, they can be classified as 1 → 2 (**A**) and 1 → 3 branching monomers (**B**, Figure 1), which generally lead to uniform fractal patterns.[3] Although a combinatorial approach has been presented[21−24] to instill random multifunctionalization, to enhance functional diversity into dendritic materials, we herein report the simple synthesis of 1 → (2 + 1) *C*-branching monomers (**C**) and demonstrate their utility for the assembly of new dendritic families possessing tailored protected moieties for subsequent activation after completion of the construct. Other monomers specifically crafted for the purpose of multifunctional group introduction include the *P*-based building blocks of Majoral and co-workers[25] and others.[26−32]

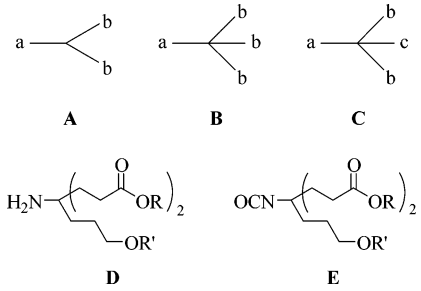

Figure 1. Simple monomer branching patterns with 1 → (2+1) branched amine and isocyanate examples.

Experimental Section

General Section. The melting points were determined in capillary tubes with an Electrothermal 9100 apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 300 and 71 MHz, respectively, on a Varian GEMINI 300 MHz spectrometer and were obtained in $CDCl_3$, unless otherwise stated. Mass spectral data were obtained on either a Bruker Esquire electrospray ion trap mass spectrometer (ESI-MS) or a Bruker Reflex-III MALDI−TOF mass spectrometer. All reagents were obtained from Aldrich Chemical Co. and used without further purification. THF was distilled under nitrogen with $LiAlH_4$ as drying agent and triphenylmethane as indicator.

4-Nitrobutanol (1). To a stirred solution of *tert*-butyl acrylate (14 g, 109 mmol) in $MeNO_2$ (300 mL) was added Triton-B (1 mL, 40 wt % solution in MeOH) at 25 °C, stirred for 12 h, and then concentrated in vacuo to ca. 50 mL. Et_2O (50 mL) was added, and the mixture was washed with water (50 mL × 2) and saturated aqueous NaCl solution (50 mL) and then dried ($MgSO_4$). The mixture was concentrated in vacuo to give crude *tert*-butyl 4-nitrobutanoate as a light yellowish liquid (11.6 g), which was dissolved in formic acid (95%, 40 mL) and stirred for 4 h at 25 °C. The mixture was concentrated to dryness in vacuo to afford the crude 4-nitrobutanoic acid.

A solution of this crude acid intermediate (11 g, 82.64 mmol) in THF (20 mL) was slowly added into a BH_3·THF solution

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(248 mL, 1 M, 248 mmol) at 0 °C, and then the mixture was refluxed for 6 h. After cooling to 0 °C, water (20 mL) was added cautiously to hydrolyze an excess BH_3 and alkoxy−boron complex. After removal of the solvent in vacuo, the residue was treated with saturated aqueous $NaHCO_3$ (50 mL) and extracted with Et_2O (100 mL × 2). The combined extract was washed with a saturated aqueous NaCl solution (50 mL), dried ($MgSO_4$), and concentrated to dryness in vacuo to afford (90%) **1** as a colorless liquid[33] (8.9 g). ^{1}H NMR: δ 1.47 (m, 2H, CH_2-CH_2OH), 1.94 (m, 2H, C$H_2CH_2CH_2OH$), 3.26 (br s, 1H, OH), 3.49 (t, J = 6.2 Hz, 2H, CH_2OH), 4.31 (t, J = 7.0 Hz, 2H, O_2-NCH_2). ^{13}C NMR: δ 23.6 (*C*$H_2CH_2CH_2OH$), 28.6 (*C*H_2CH_2OH), 61.0 (*C*H_2OH), 75.2 (O_2N*C*).

Di-*tert*-butyl 4-(3-Hydroxypropyl)-4-nitroheptanedioate (2). To a stirred mixture of 4-nitrobutanol (**1**; 2.43 g, 20.4 mmol) and *tert*-butyl acrylate (10.45 g, 81.6 mmol) was added Triton-B (2 mL, 40 wt % solution in MeOH) at 25 °C; the mixture was maintained for 36 h at 25 °C. The excess *tert*-butyl acrylate was removed in vacuo to give a yellowish residue, which was dissolved in ether, washed sequentially with 5% aqueous HCl (25 mL), 10% aqueous $NaHCO_3$ (25 mL), and saturated aqueous NaCl, and then dried ($MgSO_4$). The organic mixture was concentrated in vacuo to give a residue, which was column chromatographed (SiO_2) eluting with a 2:1 mixture of *n*-hexane/EtOAc to afford (75%) ester **2** as a colorless liquid (5.74 g). ^{1}H NMR: δ 1.42 [s, 18H, C(CH_3)$_3$], 1.49 (m, 2H, CH_2CH_2OH), 1.87 (br s, 1H, OH), 1.99 (m, 2H, C$H_2CH_2CH_2OH$), 2.19 (m, 8H, C$H_2CH_2CO_2$), 3.64 (t, J = 6.1 Hz, 2H, CH_2OH). ^{13}C NMR: δ 26.5 (*C*H_2CH_2OH), 27.8 [C(*C*H_3)$_3$], 29.6 (*C*H_2CO_2), 30.2 (*C*$H_2CH_2CO_2$), 31.6 (*C*$H_2CH_2CH_2OH$), 61.4 (*C*H_2OH), 80.8 (*C*Me$_3$), 92.6 (O_2N*C*), 171.2 (*C*O_2). ESI-MS: found 397.9 (M + Na)$^+$ (calcd 398.2).

Di-*tert*-butyl 4-(3-Acetoxypropyl)-4-nitroheptanedioate (3). To a stirred mixture of **2** (1.85 g, 4.927 mmol) and pyridine (468 mg, 5.912 mmol) in $CHCl_3$ (20 mL) was added Ac_2O (603 mg, 5.912 mmol) at 0 °C. After stirring for 6 h at 25 °C, the mixture was washed with water (20 mL), dried ($MgSO_4$), and concentrated in vacuo to dryness. The crude product was column chromatographed (SiO_2) eluting with a mixture of *n*-hexane/EtOAc (1:1) to afford (94%) acetate **3** as a white solid (1.93 g); mp 69.5−70 °C. ^{1}H NMR: δ 1.41 [s, 3H, C(CH_3)$_3$], 1.56 (m, 2H, CH_2CH_2O), 1.94 (m, 2H, C$H_2CH_2CH_2O$), 2.04 (s, 3H, CH_3), 2.18 (m, 8H, C$H_2CH_2CO_2$), 4.04 (t, J = 6.0 Hz, 2H, CH_2O). ^{13}C NMR: δ 20.8 (CO*C*H_3), 22.9 (*C*H_2CH_2O), 27.9 (*C*H_3), 29.7 (*C*H_2CO_2), 30.3 (*C*$H_2CH_2CO_2$), 31.7 (*C*H_2CH_2-CH_2O), 63.4 (*C*H_2O), 81.0 (*C*Me$_3$), 92.4 (O_2N*C*), 170.8 (CH_3*C*O_2), 171.0 (*C*O_2-*tert*-Bu). ESI-MS: found 439.9 (M + Na)$^+$ (calcd 440.2).

Di-*tert*-butyl 4-(3-Acetoxypropyl)-4-aminoheptanedioate (4). To a solution of acetate **3** (1.87 g, 4.479 mmol) in absolute EtOH (50 mL) was added Raney-Ni[34] (5 g); then the mixture was stirred under 60 psi of H_2 for 12 h at 25 °C. The catalyst was carefully filtered (*pyrophoric*), and the filtrate was concentrated in vacuo to afford (87%) amine **4** as a colorless oil (1.51 g). ^{1}H NMR: δ 1.36 [s, 3H, C(CH_3)$_3$], 1.44 (m, 2H, C$H_2CH_2CH_2O$), 1.60 (m, 2H, CH_2CH_2O), 1.72 (t, J = 7.9 Hz, 4H, C$H_2CH_2CO_2$), 1.98 (s, 3H, CH_3), 2.25 (t, J = 7.9 Hz, 4H, CH_2CO_2), 4.00 (t, J = 6.1 Hz, 2H, CH_2O), 4.30 (br s, 2H, NH_2). ^{13}C NMR: δ 21.0 (CO*C*H_3), 22.7 (*C*H_2CH_2O), 28.1 (*C*H_3), 29.7 (*C*H_2CO_2), 33.0 (*C*$H_2CH_2CO_2$), 34.3 (*C*$H_2CH_2CH_2O$), 55.1 (H_2N*C*), 64.3 (*C*H_2O), 80.7 (*C*Me$_3$), 171.1 (Me*C*O_2), 172.6 (*C*O_2-*tert*-Bu). ESI-MS: found 387.9 (M + H)$^+$ (calcd 388.3).

Di-*tert*-butyl 4-Amino-4-(3-hydroxypropyl)heptanedioate (5). To a solution of alcohol **2** (3.50 g, 9.32 mmol) in absolute EtOH (50 mL) was added Raney-Ni (12 g); then the mixture was stirred under 60 psi of H_2 for 12 h at 25 °C. The catalyst was filtered, and the filtrate was concentrated in vacuo to afford (81%) amine **5** as a white solid (2.6 g); mp 89−90 °C. ^{1}H NMR: δ 1.40 [s, 18H, C(CH_3)$_3$], 1.42 (m, 2H, CH_2CH_2OH), 1.56 (m, 2H, C$H_2CH_2CH_2OH$), 1.65 (t, J = 7.8 Hz, 4H, CH_2-CH_2CO_2), 2.19 (t, J = 7.8 Hz, 4H, CH_2CH_2CO_2), 2.59 (br s, 3H, NH_2 and OH), 3.56 (t, J = 5.6 Hz, 2H, CH_2OH). ^{13}C NMR: δ 26.8 (*C*H_2CH_2O), 27.9 (*C*H_3), 29.9 (*C*H_2CO_2), 34.0 (*C*H_2CH_2-CO_2), 36.9 (*C*$H_2CH_2CH_2OH$), 52.6 (H_2N*C*), 62.8 (*C*H_2OH), 80.4 (*C*Me$_3$), 172.9 (*C*O_2-*tert*-Bu). ESI-MS: found 346.0 (M + H)$^+$ (calcd 346.3).

Di-*tert*-butyl 4-Amino-4-[3-(2-cyanoethoxy)propyl]heptanedioate (6). To a solution of amine **5** (2.49 mg, 7.21 mmol) in THF (20 mL) was added powdered KOH (81 mg, 1.44 mmol). The mixture was stirred 30 min at 25 °C, and then acrylonitrile (765 mg, 14.42 mmol) was added; the mixture was stirred for 12 h at 25 °C. Et_2O (50 mL) was added to the mixture with rapid stirring, and the resulting yellow solid was filtered, then the filtrate was washed with water and saturated aqueous NaCl, and dried ($MgSO_4$). The solvent was removed in vacuo to give (98%) nitrile **6** as a colorless liquid (2.81 g). ^{1}H NMR: δ 1.38 (m, 2H, CH_2CH_2O), 1.43 [s, 18H, C(CH_3)$_3$], 1.58 (m, 2H, C$H_2CH_2CH_2O$), 1.64 (t, J = 8.1 Hz, 4H, C$H_2CH_2CO_2$), 1.98 (br s, 2H, NH_2), 2.25 (t, J = 8.1 Hz, 4H, CH_2CO_2), 2.58 (t, J = 6.3 Hz, 2H, CH_2CN), 3.47 (t, J = 6.3 Hz, 2H, CH_2O), 3.63 (t, J = 6.3 Hz, 2H, OCH_2CH_2CN). ^{13}C NMR: δ 18.5 (*C*H_2CN), 23.2 (*C*H_2CH_2O), 27.7 (*C*H_3), 29.7 (*C*H_2CO_2), 34.1 (*C*$H_2CH_2CO_2$), 35.5 (*C*$H_2CH_2CH_2O$), 52.2 (H_2N*C*), 65.0 (O*C*H_2*C*H_2CN), 71.2 (*C*H_2O), 79.8 (*C*Me$_3$), 117.6 (*C*N), 172.8 (*C*O_2-*tert*-Bu). ESI-MS: found 398.9 (M + H)$^+$ (calcd 399.3).

Di-*tert*-butyl 4-Amino-4-(3-benzyloxy)propylheptanedioate (7). 1. Benzylation. To a stirred suspension of NaH (60% in oil; 106 mg, 2.66 mmol) in THF (10 mL) was slowly added a solution of alcohol **2** (1 g, 2.66 mmol) in THF (5 mL). After 30 min, benzyl bromide (682 mg, 3.99 mmol) and a catalytic amount of 15-crown-5 were added. The mixture was stirred at 25 °C for 12 h and then extracted with Et_2O (25 mL). The organic layer was washed with water (5 mL, 2X) and then saturated NaCl solution (5 mL) and dried (Na_2SO_4). After concentration in vacuo, the crude product was column chromatographed (SiO_2) eluting with a solution of *n*-hexane/EtOAc (2:1) to afford (72%) the desired benzyl protected ether as a colorless oil (891 mg). ^{1}H NMR: δ 1.43 (s, [C(CH_3)$_3$], 18 H), 1.56, 1.98, 2.21 (m, 12H), 3.47 (t, CH_2OCH_2Ph, 2H, J = 6.1 Hz), 4.49 (s, CH_2Ph, 2H), 7.29 (m, Ar*H*, 5H). ^{13}C NMR: δ 23.98 (*C*H_2CH_2O), 27.92 (*C*H_3), 29.73 (*C*H_2CO_2), 30.39 (*C*$H_2CH_2CO_2$), 32.06 (*C*$H_2CH_2CH_2O$), 69.25 (*C*H_2O), 72.84 (*C*H_2Ph), 80.88 (*C*Me$_3$), 92.68 (*C*NO_2), 127.47, 127.53, 128.3, 138.1 (Ar*C*), 171.1 (*C*O_2). ESI-MS: found 488.3 (M + Na)$^+$ (calcd 488.3).

2. Reduction. To a sonicated solution of $NiCl_2$·$6H_2O$ (357 mg, 1.503 mmol) in MeOH (10 mL) was added $NaBH_4$ (170 mg, 4.509 mmol) in small portions to prevent excess heating. The in situ generated Ni_2B catalyst was sonicated for an additional 30 min, and then the above benzyl ether (700 mg, 1.505 mmol) in EtOH/toluene (10:1, 11 mL) was added. The suspension was stirred at 25 °C with the slow addition of $NaBH_4$ (341 mg, 9.018 mmol) over 2 h. After the final aliquot, the stirred mixture was maintained for an additional 30 min, and then the mixture was filtered through a Celite pad; the pad was washed with MeOH. The combined filtrate was concentrated in vacuo to generate a pale green solid, which was dissolved into CH_2Cl_2 and sequentially washed with aqueous NH_4OH (2%, 2 × 5 mL) and water (2 × 5 mL) and then dried ($MgSO_4$). The solvent was removed in vacuo to afford (65%) the desired amine **7** as a colorless oil (425 mg). ^{1}H NMR: δ 1.43 [s, C(CH_3)$_3$, 18H], 1.58, 1.84, 2.21, 2.34 (m, 12H), 3.48 (br t, CH_2OCH_2Ph, 2H), 4.49 (s, CH_2Ph), 6.2 (br, NH_2), 7.28 (m, Ar*H*, 5H). ^{13}C NMR: δ 24.9 (*C*H_2CH_2O), 27.85 (*C*H_3), 29.82 (*C*H_2CO_2), 30.11 (*C*$H_2CH_2CO_2$), 34.35 (*C*H_2CH_2-CH_2O), 60.9 (*C*NH_2), 69.96 (*C*H_2O), 72.78 (*C*H_2Ph), 80.09 (*C*Me$_3$), 127.45, 128.21, 138.1 (Ar*C*), 172.4 (*C*O_2). ESI-MS: found 436.3 (M + H)$^+$ (calcd 436.3).

Dendrimer 9. To a stirred mixture of monomer **4** (997 mg, 2.572 mmol) and diisopropylethylamine (DIEA; 332 mg, 2.572 mmol) in THF (15 mL) was slowly added a solution of the tetraacyl chloride[35] **8**, prepared from the corresponding acid[36] (291 mg, 584 μmol) dissolved in THF (5 mL) at 0 °C; then the mixture was maintained for 12 h at 25 °C. After filtration, the filtrate was concentrated in vacuo to give a residue, which was column chromatographed (SiO_2) eluting with a 1:2 mixture of *n*-hexane/EtOAc to afford (61%) tetraacetate **9** as a white solid (680 mg); mp 82−84 °C. ^{1}H NMR: δ 1.43 [s, 72H, C(CH_3)$_3$], 1.59 (m, 8H, CH_2CH_2O), 1.78 (m, 8H, C$H_2CH_2CH_2O$), 1.97 (m, 16H, C$H_2CH_2CO_2$), 2.05 (s, 12H, COCH_3), 2.21 (t, J

= 8.4 Hz, 16H, CH_2CO_2), 2.37 (t, J = 5.7 Hz, CH_2CONH), 3.33 (s, 8H, C$^{4°}CH_2O$), 3.65 (t, J = 5.7 Hz, 8H, OCH_2CH_2CONH), 4.03 (t, J = 6.4 Hz, 8H, CH_2OAc), 6.26 (s, 1H, N*H*). ^{13}C NMR: δ 20.8 (CO*C*H$_3$), 22.6 (CH$_2$*C*H$_2$CH$_2$O), 28.0 [C(*C*H$_3$)$_3$], 29.6 (*C*H$_2$CO$_2$), 29.7 (*C*H$_2$CH$_2$CO$_2$), 30.9 (*C*H$_2$CH$_2$CH$_2$O), 37.3 (*C*H$_2$-CONH), 45.3 (*C*$^{4°}$), 57.3 (CONH*C*), 64.4 (*C*H$_2$OAc), 67.6 (O*C*H$_2$-CH$_2$CONH), 68.9 (C$^{4°}$*C*H$_2$O), 80.3 (*C*Me$_3$), 170.6 (CONH), 170.8 (CH$_3$*C*O$_2$), 172.5 (*C*O$_2$-*tert*-Bu). MALDI−TOF MS: found 1924.153 (M + Na)$^+$ (calcd 1924.154).

Dendrimer 10. To a solution of **9** (400 mg, 210 μmol) dissolved in MeOH (10 mL) was added powdered K_2CO_3 (145 mg, 1.05 mmol); the mixture was stirred for 1 h at 25 °C, then CH_2Cl_2 (10 mL) was added, and the mixture was filtered. The filtrate was concentrated in vacuo to dryness and column chromatographed (SiO_2) eluting with EtOAc to afford (82%) the tetraol **10** as a colorless liquid (300 mg). ^{1}H NMR: δ 1.43 [s, 72H, C(C*H*$_3$)$_3$], 1.52 (m, 8H, C*H*$_2$CH$_2$OH), 1.72 (m, 8H, C*H*$_2$-CH$_2$CH$_2$OH), 1.99 (m, 16H, C*H*$_2$CH$_2$CO$_2$), 2.21 (t, J = 7.8 Hz, 16H, CH$_2$C*H*$_2$CO$_2$), 2.36 (t, J = 5.7 Hz, C*H*$_2$CONH), 3.38 (s, 8H, C$^{4°}$C*H*$_2$O), 3.40 (br s, 4H, OH), 3.61 (t, J = 5.9 Hz, 8H, C*H*$_2$OH), 3.67 (t, J = 5.7 Hz, 8H, OC*H*$_2$CH$_2$CONH), 6.50 (s, 1H, NH). ^{13}C NMR: δ 26.5 (*C*H$_2$CH$_2$OH), 28.3 [C(*C*H$_3$)$_3$], 30.1 (*C*H$_2$CO$_2$), 30.2 (*C*H$_2$CH$_2$CO$_2$), 31.5 (*C*H$_2$CH$_2$CH$_2$OH), 37.9 (*C*H$_2$CONH), 45.6 (C$^{4°}$), 57.7 (CONH*C*), 62.4 (*C*H$_2$OH), 67.9 (O*C*H$_2$CH$_2$CONH), 69.6 (C$^{4°}$*C*H$_2$O), 80.7 (*C*Me$_3$), 171.3 (CONH), 173.2 (*C*O$_2$-*tert*-Bu). MALDI−TOF MS: found 1756.037 (M + Na)$^+$ (calcd 1756.112).

Dendrimer 11. To a stirred mixture of monomer **6** (649 mg, 1.628 mmol) and DIEA (210 mg, 1.628 mmol) in THF (15 mL) was slowly added a solution of the tetraacyl chloride[35] (230 mg, 1.628 mmol) in THF (5 mL) at 0 °C, and then the mixture was stirred for 12 h at 25 °C. The mixture was filtered, and the filtrate was concentrated in vacuo to give a residue, which was column chromatographed (SiO_2) eluting with a mixture of *n*-hexane/EtOAc (1:4) to afford (65%) the tetraamide **11** as a clear liquid (515 mg). ^{1}H NMR: δ 1.43 [s, 72H, C(C*H*$_3$)$_3$], 1.55 (m, 8H, C*H*$_2$CH$_2$O), 1.75 (m, 8H, C*H*$_2$CH$_2$CH$_2$O), 1.95 (m, 16H, C*H*$_2$CH$_2$CO$_2$), 2.21 (m, 16H, CH$_2$C*H*$_2$CO$_2$), 2.37 (t, J = 5.7 Hz, C*H*$_2$CONH), 2.60 (t, J = 6.4 Hz, 8H, C*H*$_2$CN), 3.33 (s, 8H, C$^{4°}$C*H*$_2$O), 3.46 (t, J = 6.2 Hz, 8H, C*H*$_2$O), 3.63 (t, J = 5.7 Hz, 8H, OC*H*$_2$CH$_2$CONH), 3.65 (t, J = 6.4 Hz, 8H, OC*H*$_2$CH$_2$CN), 6.23 (s, 1H, N*H*). ^{13}C NMR: δ 18.8 (*C*H$_2$CN), 23.4 (*C*H$_2$CH$_2$O), 28.0 [C(*C*H$_3$)$_3$], 29.8 (*C*H$_2$CO$_2$), 29.9 (*C*H$_2$CH$_2$-CO$_2$), 31.0 (*C*H$_2$CH$_2$CH$_2$O), 37.4 (*C*H$_2$CONH), 45.3 (*C*$^{4°}$), 57.5 (CONH*C*), 65.2 (*C*H$_2$O), 67.6 (O*C*H$_2$CH$_2$CONH), 68.9 (C$^{4°}$*C*H$_2$O), 71.2 (O*C*H$_2$CH$_2$CN), 80.4 (*C*Me$_3$), 118.0 (*C*N), 170.7 (*C*ONH), 172.7 (*C*O$_2$-*tert*-Bu). ESI-MS: found 1969.4 (M + Na)$^+$ (calcd 1968.2).

To a solution of **11** dissolved in MeOH was added powdered K_2CO_3; the mixture was stirred for 4 h at 25 °C, then CH_2Cl_2 was added, and the mixture was filtered. The filtrate was concentrated in vacuo to dryness and column chromatographed (SiO_2) eluting with EtOAc to afford (80+%) the tetraol **10**, identical to that derived from the acetate.

4-(3-Acetoxypropyl)-4-nitroheptanedioic Acid (12). The mixture of ester **3** (1.89 g, 4.526 mmol) dissolved in HCO_2H (20 mL) was stirred for 4 h at 25 °C. The mixture was concentrated in vacuo to afford (100%) acid **12** as a bright yellow liquid (1.38 g). ^{1}H NMR: δ 1.58 (m, 2H, CH$_2$C*H*$_2$CH$_2$O), 1.99 (m, 2H, C*H*$_2$CH$_2$CH$_2$O), 2.07 (s, 3H, C*H*$_3$), 2.30 (m, 4H, C*H*$_2$CH$_2$CO$_2$), 2.39 (m, 4H, CH$_2$C*H*$_2$CO$_2$), 4.07 (t, J = 6.0 Hz, 2H, C*H*$_2$O), 11.1 (br s, 2H, CO$_2$*H*). ^{13}C NMR: δ 20.9 (CO*C*H$_3$), 23.0 (CH$_2$*C*H$_2$CH$_2$O), 28.5 (*C*H$_2$CO$_2$), 29.9 (*C*H$_2$CH$_2$CO$_2$), 32.0 (*C*H$_2$CH$_2$CH$_2$O), 63.8(CH$_2$CH$_2$*C*H$_2$O), 92.3 (O$_2$N*C*), 171.9 (CH$_3$*C*O$_2$), 177.8 (*C*O$_2$H). ESI-MS: found 305.4 (M + H)$^+$ (calcd 306.1).

Dendron 13. To a solution of **12** (710 mg, 2.325 mmol) in DMF (10 mL) was added DCC (959 mg, 4.65 mmol) and 1-HOBT (628 mg, 4.65 mmol) at 25 °C. After the mixture was stirred for 30 min, monomer **4** (1.982 g, 5.115 mmol) was added and then maintained for 24 h at 25 °C. After filtration, the filtrate was concentrated in vacuo to give a crude product, which was column chromatographed (SiO_2) eluting with a mixture of *n*-hexane/EtOAc (3:2) to afford (76%) dendron **13** as a colorless liquid (1.84 g). ^{1}H NMR: δ1.44 [s, 36H, C(C*H*$_3$)$_3$], 1.53−2.14 (m, 24H, C*H*$_2$), 2.06 (s, 9H, COC*H*$_3$), 2.21 (br t, J = 7.5 Hz, 12H, C*H*$_2$CO$_2$), 4.04 (m, 6H, C*H*$_2$COCH$_3$), 6.18 (br s, 2H, NH). ^{13}C NMR: δ 20.6 & 20.7 (CO*C*H$_3$), 22.4 and 22.7 (CH$_2$*C*H$_2$CH$_2$O), 27.8 (*C*H$_3$), 29.4 (*C*H$_2$CO$_2$), 29.6 (*C*H$_2$CH$_2$CO$_2$), 30.6 (*C*H$_2$CONH), 30.8 (*C*H$_2$CH$_2$CH$_2$O), 31.0 (*C*H$_2$CH$_2$CONH), 31.5 (CH$_2$CH$_2$CH$_2$O), 57.4 (CONH*C*), 63.4 and 64.1 (*C*H$_2$O), 80.2 (*C*Me$_3$), 92.7 (O$_2$N*C*), 170.2 (*C*ONH), 170.5 and 170.7 (*C*OCH$_3$), 172.4 (*C*O$_2$-*tert*-Bu). ESI-MS: found 1066.8 (M + Na)$^+$ (calcd 1066.6).

Amine Dendron 14. To a solution of **13** (1.03 g, 986 μmol) in absolute EtOH (30 mL) was added Raney-Ni (2 g), and then the mixture was stirred under 90 psi of H_2 for 12 h at 40 °C. The catalyst was filtered (*pyrophoric*), and the filtrate was concentrated in vacuo to give a crude product, which was column chromatographed (SiO_2) eluting with a mixture of EtOAc/MeOH (5:1) to afford (75%) amine **14** as a colorless oil (750 mg). ^{1}H NMR: δ 1.43 [s, 36H, C(C*H*$_3$)$_3$], 1.55−2.00 (m, 24H, C*H*$_2$), 2.05 (s, 9H, COC*H*$_3$), 2.19−2.38 (m, 12H, C*H*$_2$CO$_2$), 4.04 (m, 6H, C*H*$_2$COCH$_3$), 6.18 (br s, 2H, NH). ^{13}C NMR: δ 20.99 & 21.04 (CO*C*H$_3$), 22.5 and 22.7 (CH$_2$*C*H$_2$CH$_2$O), 28.1 [C(*C*H$_3$)$_3$], 29.8 (*C*H$_2$CO$_2$), 29.9 (*C*H$_2$CH$_2$CO$_2$), 30.9 (*C*H$_2$CH$_2$-CONH), 31.3 (*C*H$_2$CONH), 33.7 and 33.8 (*C*H$_2$CH$_2$CH$_2$O), 57.7 (H$_2$N*C*), 64.2 & 64.5 (*C*H$_2$O), 80.7 (*C*Me$_3$), 171.08 and 171.17 (*C*OCH$_3$), 172.3 (*C*ONH), 173.0 (*C*O$_2$-*tert*-Bu). ESI-MS: found 1014.9 (M + H)$^+$ (calcd 1014.7) and 1036.7 (M + Na)$^+$.

Second-Generation Dendrimer 15. To a cooled mixture of amine **14** (730 mg, 720 μmol) and DIEA (93 mg, 720 μmol) in CH_2Cl_2 (10 mL) at 0 °C was slowly added a solution of the tetraacyl chloride **8** (82 mg, 164 μmol) dissolved in CH_2Cl_2 (5 mL), and then the mixture was stirred for 24 h at 25 °C. After filtration, the filtrate was concentrated in vacuo to give a crude product, which was column chromatographed (SiO_2) eluting with a *n*-hexane/EtOAc mixture (9:1) to afford (35%) **15** as a white powder (250 mg). ^{1}H NMR: δ 1.30 [s, 144H, C(C*H*$_3$)$_3$], 1.40−1.82 (m, 48H, C*H*$_2$C*H*$_2$CH$_2$O), 1.91 and 1.92 (s, 36H, COC*H*$_3$), 2.03−2.06 (m, 96H, C*H*$_2$C*H*$_2$CO$_2$), 2.25 (br t, 8H, OCH$_2$C*H*$_2$CONH), 3.19 (br s, 8H, C$^{4°}$C*H*$_2$O), 3.49 (br t, 8H, OC*H*$_2$CH$_2$CONH), 3.90 (m, 24H, C*H*$_2$COCH$_3$), 6.38 and 6.73 (br s, 12H, NH). ^{13}C NMR: δ 21.1 (CO*C*H$_3$), 22.7 (*C*H$_2$CH$_2$O), 28.2 [C(*C*H$_3$)$_3$], 29.9 (*C*H$_2$CO$_2$), 30.0 (*C*H$_2$CH$_2$CO$_2$), 31.0 (*C*H$_2$-CH$_2$CH$_2$O), 31.7 (*C*H$_2$CH$_2$CO$_2$), 34.1 (*C*H$_2$CH$_2$CH$_2$O), 37.6 (*C*H$_2$CONH), 45.5 (*C*$^{4°}$), 57.6 and 58.1 (CONH*C*), 64.6 and 64.8 (*C*H$_2$OAc), 67.9 (O*C*H$_2$CH$_2$CONH), 69.6 (C$^{4°}$*C*H$_2$O), 80.6 (*C*Me$_3$), 171.05 and 171.21 (*C*OCH$_3$), 171.25 and 172.9 (*C*ONH), 172.8 (*C*O$_2$-*tert*-Bu). MALDI−TOF MS: found 4430.100 (M + Na)$^+$ (calcd 4429.665).

Benzyl 4-Nitrobutanoate (16). To a solution of benzyl acrylate (3 mL, 20 mmol) in $MeNO_2$ (100 mL) was added DIEA (500 μL), and then the mixture was stirred for 16 h at 25 °C. The mixture was reduced in vacuo, and the residue was column chromatographed (SiO_2) eluting with 25% EtOAc in hexane to afford (84%) ester **16** as a clear oil (2.4 g). ^{1}H NMR: δ 2.34 (quintet, CH$_2$C*H*$_2$CH$_2$, 2H), 2.54 (t, C*H*$_2$CO$_2$, 2H, J = 7.5 Hz), 4.48 (t, O$_2$NC*H*$_2$, 2H, J = 6.7 Hz), 5.18 (s, C*H*$_2$Ph, 2H), 7.40 (s, Ph*H*, 5H). ^{13}C NMR: δ 22.4 (CH$_2$*C*H$_2$CH$_2$), 30.5 (*C*H$_2$CO$_2$), 66.7 (*C*H$_2$Ph), 74.3 (O$_2$N*C*H$_2$), 128.3 (4-Ar*C*), 128.5 (3-Ar*C*), 128.7 (2-Ar*C*), 135.6 (1-Ar*C*), 171.8 (*C*O$_2$). ESI-MS: found 224.19 (M + H)$^+$ (calcd 224.24).

Di-*tert*-butyl 4-(2-*tert*-Benzyloxycarbonylethyl)-4-nitroheptanedioate (17). To a solution of ester **16** (3.26 g, 14.6 mmol) in dried THF (100 mL) was added *tert*-butyl acrylate (4.28 mL, 29.2 mmol) and Triton-B (250 μL of a 40% in MeOH), and then the mixture was stirred for 16 h at 25 °C. The mixture was concentrated in vacuo to give a residue, which was column chromatographed (SiO_2) eluting with 25% EtOAc in hexane to give (86%) triester **17** as a white solid (6.01 g). ^{1}H NMR: δ 1.39 [s, C(C*H*$_3$)$_3$, 18H], 2.16 (s, C*H*$_2$C*H*$_2$CO$_2$CH$_2$, CH$_2$C*H*$_2$CO$_2$, 8H), 2.30 (dd, C*H*$_2$CO$_2$, 4H, J = 10.5 Hz), 5.07 (s, C*H*$_2$Ph, 2H), 7.31 (s, Ph*H*, 5H). ^{13}C NMR: δ 27.9 [C(*C*H$_3$)$_3$], 28.5 (*C*H$_2$CH$_2$CO$_2$CH$_2$), 29.6 (*C*H$_2$CH$_2$CO$_2$), 30.0 (*C*H$_2$CO$_2$CH$_2$), 30.2 (*C*H$_2$CO$_2$), 66.6 (*C*H$_2$Ph), 81.0 (*C*Me$_3$), 91.9 (O$_2$N*C*), 128.2 (4-Ar*C*), 128.3 (3-Ar*C*), 128.5 (2-Ar*C*), 135.3 (1-Ar*C*), 171.5 (*C*O$_2$), 170.9 (*C*O$_2$CH$_2$). ESI-MS: found 480.43 (M + H)$^+$ (calcd 480.58).

4-Nitro-4-di(2-*tert*-butoxycarbonylethyl)butanoic Acid (18). A suspension of benzyl ester **16** (2.0 g, 12.1 mmol) and 10% Pd on activated carbon (600 mg) in MeOH (50 mL) was hydrogenated at 60 psi at 25 °C for 12 h. The solution was then cautiously filtered through Celite (*pyrophoric*), and the solvent was concentrated to afford (94%) acid **18**, as a clear oil (1.7 g). ^{1}H NMR: δ 2.16 (s, CH_2CH$_2$CO$_2$, 8H), 2.30 (dd, CH_2-CO$_2$, 4H, J = 10.5 Hz). ^{13}C NMR: δ 27.9 [C(CH_3)$_3$], 28.5, 29.6 (CH_2CH$_2$CO$_2$), 30.2 (CH_2CO$_2$), 81.0 (*C*Me$_3$), 91.9 (O$_2$N*C*), 171.5 (*C*O$_2$R), 174.0 (*C*O$_2$H). ESI-MS: found 390.44 (M + H)$^+$ (calcd 390.20).

Di-*tert*-butyl 4-{2-[5-(4′-Terpyridinyloxy)pentylcarbamoyl]ethyl}-4-nitroheptanedioate (19). To a solution of acid **18** (1.06 g, 2.72 mmol) in dried DMF were added DCC (1.24 g, 5.97 mmol) and 1-HOBT (920 mg, 5.97 mmol) at 25 °C. The mixture was stirred for 2 h; then 1-amino-(4′-terpyridinyloxy)pentane[37,38] (2.48 g, 5.97 mmol) was added, and the solution was agitated for 24 h. The white precipitate was filtered, and the filtrate was concentrated in vacuo to give a crude oil, which was column chromatographed eluting with 20% EtOAc in hexane to give (93%) amide **19** as a colorless solid (2.7 g). ^{1}H NMR: δ 1.26 (s, CH_3, 18H), 1.39 (m, NHCH$_2$CH_2CH_2, 4H), 1.70 (q, CH_2CH$_2$O, 2H), 2.05 (m, CH_2CH_2-CONH, CH_2CH_2CO$_2$, 12H), 3.09 (m, NHCH_2, 2H), 4.05 (t, CH_2O, 2H), 5.76 (t, CON*H*, 1H), 7.16 (dd, 5,5″-tpy*H*, 2H), 7.67 (dd, 4,4″-tpy*H*, 2H), 7.82 (s, 3′,5′-tpy*H*, 2H), 8.44 (d, 3,3″-tpy*H*, 2H), 8.51 (d, 6,6″-tpy*H*, 2H). ^{13}C NMR: δ 23.1 (NHCH$_2$-CH$_2$*C*H$_2$), 27.7 (*C*H$_3$), 28.3 (*C*H$_2$CH$_2$O), 28.9 (NHCH$_2$*C*H$_2$), 29.5 (*C*H$_2$CH$_2$CO$_2$), 29.9 (*C*H$_2$CO$_2$), 30.2 (*C*H$_2$CH$_2$CONH), 30.9 (*C*H$_2$CONH), 39.3 (CONH*C*H$_2$), 67.6 (*C*H$_2$O), 80.7 (*C*Me$_3$), 92.3 (O$_2$N*C*), 107.0 (5,5″-tpy*C*), 121.1 (4,4″-tpy*C*), 123.6 (3,3″-tpy*C*), 136.5 (3′,5′-tpy*C*), 148.7 (6,6″-tpy*C*), 155.7 (2,2″-tpy*C*), 156.7 (2′,6′-tpy*C*), 166.8 (4′-tpy*C*), 170.6 (*C*ONH), 170.9 (*C*O$_2$); IR 3312, 1730, 1651 cm^{-1}. ESI-MS: found 706.3 (M + H)$^+$ (calcd 706.4).

Di-*tert*-butyl 4-{2-[5-(4′-Terpyridinyloxy)pentylcarbamoyl]ethyl}-4-aminoheptanedioate (20). An absolute EtOH (100 mL) suspension of **19** (1 g, 1.59 mmol) and T-1 Raney-Ni (7 g) was hydrogenated at 120 psi at 40 °C for 20 h. The solution was cautiously filtered (*pyrophoric*) through Celite, after which the solvent was concentrated in vacuo. The residue was dissolved in EtOAc and then sequentially washed with dilute aqueous NaOH, water, and brine. The solution was dried (Na$_2$SO$_4$), filtered, and concentrated in vacuo to give (91%) amine **20** as a yellow oil (860 mg). ^{1}H NMR: δ 1.33 (s, CH_3, 18H), 1.48 (m, NHCH$_2$CH_2CH_2, 4H), 1.76 (q, CH_2CH$_2$O, 2H, J = 6.1 Hz), 2.15 (m, CH_2CH_2CONH, CH_2CH_2CO$_2$, 12H), 3.15 (m, NHCH_2, 2H), 4.10 (t, CH_2O, 2H, J = 6.1 Hz), 6.13 (s, CON*H*, 1H), 7.23 (dd, 5,5″-tpy*H*, 2H), 7.75 (dd, 4,4″-tpy*H*, 2H), 7.89 (s, 3′,5′-tpy*H*, 2H), 8.53 (d, 3,3″-tpy*H*, 2H), 8.51 (d, 6,6″-tpy*H*, 2H). ^{13}C NMR: δ 23.3 (NHCH$_2$CH$_2$*C*H$_2$), 27.7 (*C*H$_3$), 28.4 (*C*H$_2$CH$_2$O), 29.1 (NHCH$_2$*C*H$_2$), 29.7 (*C*H$_2$CH$_2$CO$_2$), 30.7 (*C*H$_2$-CH$_2$CONH), 34.1 (*C*H$_2$CO$_2$), 34.9 (*C*H$_2$CONH), 39.2 (CON-HCH$_2$), 52.3 (H$_2$N*C*), 67.7 (*C*H$_2$O), 80.1 (*C*Me$_3$), 107.1 (5,5″-tpy*C*), 121.1 (4,4″-tpy*C*), 123.6 (3,3″-tpy*C*), 136.6 (3′,5′-tpy*C*), 148.8 (6,6″-tpy*C*), 155.8 (2,2″-tpy*C*), 156.8 (2′,6′-tpy*C*), 166.9 (4′-tpy*C*), 172.8 (*C*ONH), 172.9 (*C*O$_2$). IR: 3299, 1727, 1648 cm^{-1}. ESI-MS: found 677.8 (M + H)$^+$ (calcd 677.8).

4-(2-Benzyloxycarbonylethyl)-4-nitroheptanedioic Acid (21). A solution of triester **17** (4.57 g, 9.53 mmol) in HCO$_2$H (100 mL, 95%) was stirred at 25 °C for 16 h. After concentration in vacuo, toluene (50 mL) was added, and the solution was again evaporated in vacuo to azeotropically remove residual formic acid. The resultant solid was recrystallized from water to give (96%) monoester **21** as a white solid (3.6 g). ^{1}H NMR: δ 2.13 (s, CH_2CH$_2$CO$_2$, CH_2CH_2CO$_2$H, 10H), 2.34 (d, CH$_2$CH_2CO$_2$, 4H, J = 7.8 Hz), 5.04 (s, CH_2Ph, 2H), 7.32 (s, Ph, 5H). ^{13}C NMR: δ 28.2 (*C*H$_2$CH$_2$CO$_2$), 29.5 (*C*H$_2$CH$_2$CO$_2$H), 29.8 (*C*H$_2$CO$_2$), 30.7 (*C*H$_2$CO$_2$H), 65.9 (*C*H$_2$Ph), 92.8 (O$_2$N*C*), 128.1 (4-Ph*C*), 128.2 (3-Ph*C*), 128.5 (2-Ph*C*), 136.1 (1-Ph*C*), 171.7 (*C*O$_2$CH$_2$), 173.3 (*C*O$_2$H). ESI-MS: found 389.97 (M + H)$^+$ (calcd 390.34).

Heptaester 23. To a stirred solution of acid **21** (1.06 g, 2.72 mmol) in dry DMF were added DCC (1.24 g, 5.97 mmol) and 1-HOBT (920 mg, 5.97 mmol) at 25 °C; after 2 h, Behera's amine[39] (**22**; 2.48 g, 5.97 mmol) was added. The mixture was stirred for 24 h, after which the white precipitate was filtered. The filtrate was concentrated in vacuo to give a crude oil, which was column chromatographed eluting with 20% EtOAc in hexane to (93%) **23** as a colorless solid (2.7 g). ^{1}H NMR: δ 1.29 [s, C(CH_3)$_3$, 54H], 1.83 (m, CH_2CH$_2$CO$_2$, 12H), 2.08 (m, CH_2CO$_2$, CH_2CH_2CONH, CH_2CH$_2$CO$_2$CH$_2$, 20H), 2.26 (m, CH_2-CO$_2$CH$_2$, 2H), 4.98 (s, CH_2Ph, 2H), 6.21 (CON*H*, 2H), 7.21 (s, Ph, 5H). ^{13}C NMR: δ 27.6 [C(*C*H$_3$)$_3$], 28.1 (*C*H$_2$CH$_2$CO$_2$CH$_2$), 29.2 (*C*H$_2$CH$_2$CONH, *C*H$_2$CH$_2$CO$_2$), 30.6 (*C*H$_2$CO$_2$CH$_2$), 30.8 (*C*H$_2$CONH), 57.1 (CONH*C*), 66.2 (*C*H$_2$Ph), 80.0 (*C*Me$_3$), 92.1 (O$_2$N*C*), 127.8 (4-Ph*C*), 128.0 (3-Ph*C*), 128.1 (2-Ph*C*), 135.1 (1-Ph*C*), 169.8 (*C*ONH), 171.4 (*C*O$_2$CH$_2$), 172.2 (*C*O$_2$). This was directly debenzylated to the corresponding free acid **24**.

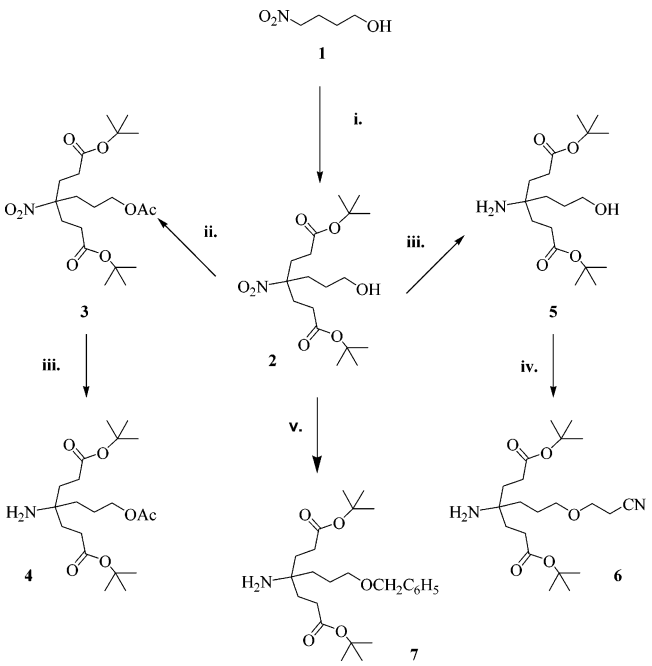
Bis(amido)acid 24. An absolute EtOH (100 mL) solution of heptaester **23** (2.4 g, 2.27 mmol) in the presence of 10% Pd on activated carbon (400 mg) was hydrogenated at 60 psi at 25 °C for 12 h. The solution was cautiously filtered through Celite, and the solvent was reduced in vacuo to give (100%) monoacid **24** as a white solid (2.2 g). ^{1}H NMR: δ 1.36 [s, C(CH_3)$_3$, 54H], 1.89 (m, CH_2CH$_2$CO$_2$, 12H), 2.12 (m, CH_2CO$_2$, CH_2CH_2CONH, CH_2CH$_2$CO$_2$CH$_2$, 20H), 2.26 (m, CH_2CO$_2$CH$_2$, 2H), 6.34 (CON*H*, 2H), 9.14 (CO$_2$*H*). ^{13}C NMR: δ 27.6 [C(*C*H$_3$)$_3$], 29.4 (*C*H$_2$CH$_2$CO$_2$H, *C*H$_2$CH$_2$CONH, *C*H$_2$CH$_2$CO$_2$), 30.8 (*C*H$_2$CO$_2$H, *C*H$_2$CONH), 57.2 (CONH*C*), 80.3 (*C*Me$_3$), 92.3 (O$_2$N*C*), 170.8 (*C*ONH), 172.6 (*C*O$_2$R), 174.0 (*C*O$_2$H). ESI-MS: found 1073.35 (M + H)$^+$ (calcd 1073.33).

Second-Generation Amide 25. To a stirred solution of acid **24** (2.8 mg, 2.8 mmol) in dry DMF were added DCC (598 mg, 2.8 mmol) and 1-HOBT (391 mg, 2.8 mmol) at 25 °C; after 2 h, amine **20** (1.9 g, 2.8 mmol) was added. The mixture was stirred for 24 h, after which the white precipitate was filtered. The filtrate was concentrated in vacuo to give a crude oil, which was column chromatographed eluting with 20% EtOAc in hexane to give (80%) **25** as a white solid (3.6 g). ^{1}H NMR: δ 1.21 [s, C(CH_3)$_3$, 72H], 1.37 (m, NHCH$_2$CH_2CH_2, 4H), 1.76 (m, CH_2CH$_2$O, CH_2CH$_2$CO$_2$, CH_2CH$_2$CONH, 20H), 2.01 (CH_2CH_2CONH, CH_2CO$_2$, CH_2CONH, 30H), 3.04 (m, NHCH_2, 2H), 4.01 (t, CH_2O, 2H, J = 5.8 Hz), 6.28 (CON*H*, 3H), 6.64 (CON*H*, 1H), 7.11 (dd, 5,5″-tpy*H*, 2H), 7.62 (dd, 4,4″-tpy*H*, 2H), 7.78 (s, 3′,5′-tpy*H*, 2H), 8.39 (d, 3,3″-tpy*H*, 2H), 8.45 (d, 6,6″-tpy*H*, 2H). ^{13}C NMR: δ 23.0 (NHCH$_2$CH$_2$*C*H$_2$), 27.6 (*C*H$_3$), 28.2 (*C*H$_2$CH$_2$O), 28.8 (NHCH$_2$*C*H$_2$), 29.3 (1st-*C*H$_2$*C*H$_2$CONH, 2nd-*C*H$_2$*C*H$_2$CO$_2$), 30.1 (2nd-*C*H$_2$CH$_2$CONH), 30.8 (2nd-*C*H$_2$*C*H$_2$-CO$_2$), 33.4 (2nd-*C*H$_2$CONH), 39.1 (NH*C*H$_2$), 57.0 (2nd-CN-HCO), 57.1 (2nd-CNHCO), 67.5 (*C*H$_2$O), 79.9 (*C*Me$_3$), 80.0 (*C*Me$_3$), 92.5 (O$_2$N*C*), 106.9 (5,5″-tpy*C*), 120.0 (4,4″-tpy*C*), 123.4 (3,3″-tpy*C*), 136.3 (3′,5′-tpy*C*), 148.5 (6,6″-tpy*C*), 155.6 (2,2″-tpy*C*), 156.5 (2′,6′-tpy*C*), 166.7 (4′-tpy*C*), 170.3 (*C*ONH), 170.7 (*C*ONH), 172.3 (*C*O$_2$). IR: 3332, 2978, 2934, 1730, 1679, 1653, 1154 cm^{-1}; this *tert*-butyl ester was directly transformed to the corresponding methyl ester for mass spectral analysis.

Methyl Ester 26. A stirred solution of ester **25** (3 g, 1.84 mmol) in MeOH (100 ML) and a trace of concentrated H$_2$SO$_4$ (200 μL) was refluxed for 24 h, after which the mixture was reduced in volume in vacuo to give residue, which was dissolved in CH$_2$Cl$_2$ and then sequentially washed with dilute aqueous NaOH, water, and brine. The solution was dried (Na$_2$SO$_4$), filtered, and reduced in vacuo to give an oil, which was column chromatographed (Al$_2$O$_3$) eluting with 5% MeOH in EtOAc to afforded (66%) methyl ester **26** as white solid (1.6 g). ^{13}C NMR: δ 23.2 (NHCH$_2$CH$_2$*C*H$_2$), 27.9 (*C*H$_2$CH$_2$-CONH, *C*H$_2$CH$_2$CO$_2$), 28.3 (*C*H$_2$CH$_2$O), 28.9 (NHCH$_2$*C*H$_2$), 29.1 (*C*H$_2$CO$_2$), 30.6 (*C*H$_2$CONH), 39.3 (CONH*C*H$_2$), 51.5 (CO$_2$*C*H$_3$), 57.0 (2nd-*C*CONH), 57.2 (2nd-*C*CONH), 67.7 (*C*H$_2$O), 92.9 (O$_2$N*C*), 107.0 (5,5″-tpy*C*), 121.0 (4,4″-tpy*C*), 123.6 (3,3″-tpy*C*), 136.5 (3′,5′-tpy*C*), 148.7 (6,6″-tpy*C*), 155.7 (2,2″-tpy*C*), 156.7 (2′,6′-tpy*C*), 166.9 (4′-tpy*C*), 170.7 (*C*ONH), 173.4 (*C*O$_2$). MALDI−TOF MS: found 1394.19 (M + H)$^+$ (calcd 1394.53).

Second-Generation Dendron 27. A suspension of methyl ester **26** (1.2 g, 930 μmol), T-1 Raney-Ni (10 g), and absolute EtOH (100 mL) was hydrogenated at 120 psi at 40 °C for 48 h. The solution was cautiously filtered (*pyrophoric*) through Celite, after which the solvent was removed in vacuo to give a

Scheme 1. Synthesis of the Initial Monomers[a]

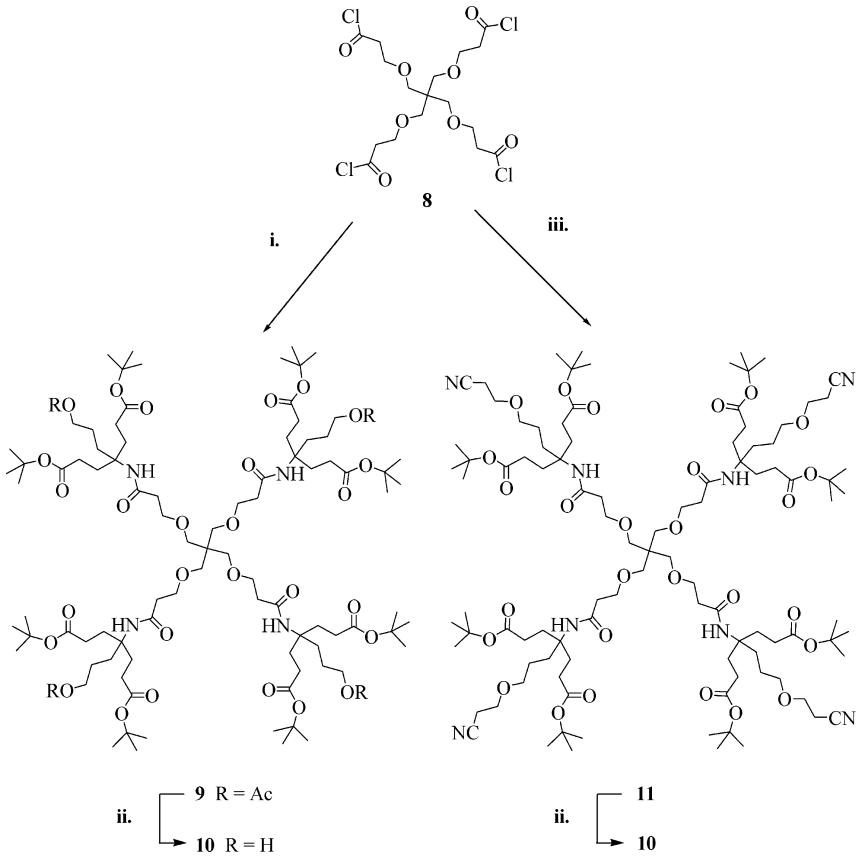


[a] (i) CH_2=$CHCO_2$-*t*-Bu (xs), Triton-B, 25 °C; (ii) Ac_2O, pyr, $CHCl_3$, 0 °C, then 25 °C, 6 h; (iii) Raney-Ni, EtOH, 60 psi of H_2, 25 °C, 12 h; (iv) CH_2=CHCN, KOH, *p*-dioxane, 25 °C, 12 h; (v) $C_6H_5CH_2Br$, NaH, 15-crown-5, THF 25 °C, 12 h; Ni_2B, $NaBH_4$, EtOH, 25 °C, 2 h.

residue that was dissolved in EtOAc and sequentially washed with dilute aqueous NaOH, water, and brine. The solution was dried (Na_2SO_4), filtered, and concentrated in vacuo to give a crude solid, which was column chromatographed (Al_2O_3) eluting with 66% MeOH in EtOAc to give (76%) amine **27** as a clear solid (900 mg). ^{1}H NMR: δ 1.37 (m, NHCH$_2$C*H*$_2$C*H*$_2$, 4H), 1.76 (m, C*H*$_2$CH$_2$O, C*H*$_2$CH$_2$CO$_2$, C*H*$_2$CH$_2$CONH, 20H), 2.01 (C*H*$_2$C*H*$_2$CONH, C*H*$_2$CO$_2$, C*H*$_2$CONH, 30H), 3.04 (m, NHC*H*$_2$, 2H), 3.50 (s, C*H*$_3$, 24H), 4.01 (t, C*H*$_2$O, 2H, J = 5.8 Hz), 6.28 (CON*H*, 3H), 6.64 (CON*H*, 1H), 7.11 (dd, 5,5″-tpy*H*, 2H), 7.62 (dd, 4,4″-tpy*H*, 2H,), 7.78 (s, 3′,5′-tpy*H*, 2H), 8.39 (d, 3,3″-tpy*H*, 2H), 8.45 (d, 6,6″-tpy*H*, 2H). ^{13}C NMR: δ 23.2 (NHCH$_2$CH$_2$*C*H$_2$), 28.1 (*C*H$_2$CH$_2$CONH, *C*H$_2$CH$_2$CO$_2$), 28.4 (*C*H$_2$CH$_2$O), 29.2 (*C*H$_2$CO$_2$), 29.6 (NHCH$_2$*C*H$_2$), 31.1 (*C*H$_2$-CONH), 34.6 (*C*H$_2$CONH), 39.3 (CONH*C*H$_2$), 51.6 (CO$_2$*C*H$_3$), 53.6 (H$_2$N*C*), 56.7 (2nd-CNHCO), 57.1 (2nd-*C*NHCO), 67.8 (*C*H$_2$O), 107.1 (5,5″-tpy*C*), 121.1 (4,4″-tpy*C*), 123.7 (3,3″-tpy*C*), 136.6 (3′,5′-tpy*C*), 148.8 (6,6″-tpy*C*), 155.8 (2,2″-tpy*C*), 156.8 (2′,6′-tpy*C*), 166.9 (4′-tpy*C*), 172.8 (*C*ONH), 173.5 (*C*O$_2$). MALDI−TOF MS: found 1386.27 (M + Na)$^+$ (calcd 1386.54).

First-Generation Dendrimer 29. A mixture of tetraacid **28**[36] (97 mg, 230 μmol), 1-HOBT (136 mg, 1.01 mmol), and DCC (208 mg, 1.01 mmol) in DMF (20 mL) was stirred at 25 °C for 2 h, and then amine **20** (683 mg, 1.01 mmol) in DMF (10 mL) was added, followed by stirring for 3 days. After filtration, the solvent was removed in vacuo to give a residue, which was dissolved in EtOAc (500 mL) and washed with water (3×) and then saturated brine. The organic phase was dried (Na_2SO_4), concentrated in vacuo, and chromatographed (Al_2O_3) eluting with EtOAc to give (67%) **29** as a spongy white solid (469 mg). ^{1}H NMR: δ 1.33 (s, C*H*$_3$, 18H), 1.48 (m, NHCH$_2$C*H*$_2$C*H*$_2$, 4H), 1.76 (q, C*H*$_2$CH$_2$O, 2H, J = 6.2 Hz), 2.15 (m, C*H*$_2$C*H*$_2$CONH, C*H*$_2$C*H*$_2$CO$_2$, 12H), 3.15 (m, NHC*H*$_2$, 2H), 4.10 (t, C*H*$_2$O, 2H, J = 6.1 Hz), 6.13 (s, CON*H*, 1H), 7.23 (dd, 5,5″-tpy*H*, 2H), 7.75 (dd, 4,4″-tpy*H*, 2H), 7.89 (s, 3′,5′-tpy*H*, 2H), 8.53 (d, 3,3″-tpy*H*, 2H, J = 7.9 Hz), 8.51 (d, 6,6″-tpy*H*, 2H, J = 4.2 Hz). ^{13}C NMR: δ 23.0 (NHCH$_2$CH$_2$*C*H$_2$), 27.6 (*C*H$_3$), 28.3 (*C*H$_2$-CH$_2$O), 28.8 (NHCH$_2$*C*H$_2$), 29.3 (*C*H$_2$CH$_2$CO$_2$), 29.8 (*C*H$_2$CO$_2$), 30.1 (*C*H$_2$CH$_2$CONH), 30.4 (*C*H$_2$CONH), 36.9 (OCH*C*H$_2$), (39.1

Scheme 2. Synthesis of First-Tier Dendrimers[a]



[a] (i) **4** (4 equiv), DIEA, THF, 0 °C, then 25 °C, 12 h; (ii) K_2CO_3, MeOH, 1 h, 25 °C; (iii) **6** (4 equiv), DIEA, THF, 0 °C, then 25 °C.

(CONH*C*H$_2$), 44.9 (*C*CH$_2$O), 57.0 (*C*NHCO), 67.2 (C*C*H$_2$O), 67.4 (*C*H$_2$Otpy), 68.6 (OC*H*$_2$CH$_2$CONH), 106.8 (5,5″-tpy*C*), 120.8 (4,4″-tpy*C*), 123.4 (3,3″-tpy*C*), 136.3 (3′,5′-tpy*C*), 148.5 (6,6″-tpy*C*), 155.5 (2,2″-tpy*C*), 156.5 (2′,6′-tpy*C*), 166.6 (4′-tpy*C*), 170.6 (*C*ONH), 172.3 (*C*O$_2$). MALDI−TOF MS: found 3077.14 (M + Na)$^+$ (calcd 3077.72).

Second-Generation Dendrimer 30 was prepared in an identical manner to that of **27** from the tetraacid **28** (230 μmol), except using amine **27** (1.01 mmol) to give (67%) **30** as a spongy white solid (469 mg). ^{1}H NMR: δ 1.37 (m, NHCH$_2$C*H*$_2$C*H*$_2$, 4H), 1.76 (m, C*H*$_2$CH$_2$O, C*H*$_2$CH$_2$CO$_2$, C*H*$_2$CH$_2$CONH, 20H), 2.01 (C*H*$_2$C*H*$_2$CONH, C*H*$_2$CO$_2$, C*H*$_2$CONH, 30H), 3.04 (m, NHC*H*$_2$, 2H), 3.50 (s, C*H*$_3$, 24H), 4.01 (t, C*H*$_2$O, 2H, J = 5.8 Hz), 6.28 (CON*H*, 3H), 6.64 (CON*H*, 1H), 7.11 (dd, 5,5″-tpy*H*, 2H), 7.62 (dd, 4,4″-tpy*H*, 2H), 7.78 (s, 3′,5′-tpy*H*, 2H), 8.39 (d, 3,3″-tpy*H*, 2H, J = 7.9 Hz), 8.45 (d, 6,6″-tpy*H*, 2H, J = 4.4 Hz). ^{13}C NMR: δ 23.3 (NHCH$_2$CH$_2$*C*H$_2$), 28.2 (*C*H$_2$CH$_2$-CONH, *C*H$_2$CH$_2$CO$_2$), 28.4(*C*H$_2$CH$_2$O), 29.2 (*C*H$_2$CO$_2$), 29.6 (NHCH$_2$*C*H$_2$), 31.1 (*C*H$_2$CONH), 34.8 (*C*H$_2$CONH-tpy), 37.4 (OCH*C*H$_2$CONH), 39.4 (CONH*C*H$_2$), 45.3 (*C*CH$_2$O), 51.6 (CO$_2$*C*H$_3$), 56.9 (2nd-*C*CONH), 57.1 (2nd-*C*CONH), 66.7 (C*C*H$_2$O), 67.9 (*C*H$_2$Otpy), 69.2 (O*C*H$_2$CH$_2$CONH), 107.2 (5,5″-tpy*C*), 121.1 (4,4″-tpy*C*), 123.7 (3,3″-tpy*C*), 136.7 (3′,5′-tpy*C*), 148.9 (6,6″-tpy*C*), 155.9 (2,2″-tpy*C*), 156.9 (2′,6′-tpy*C*), 167.1 (4′-tpy*C*), 171.0, 173.6 (*C*ONH, *C*O$_2$). MALDI−TOF: found 5829.27 (M + Na)$^+$ (calcd 5829.21).

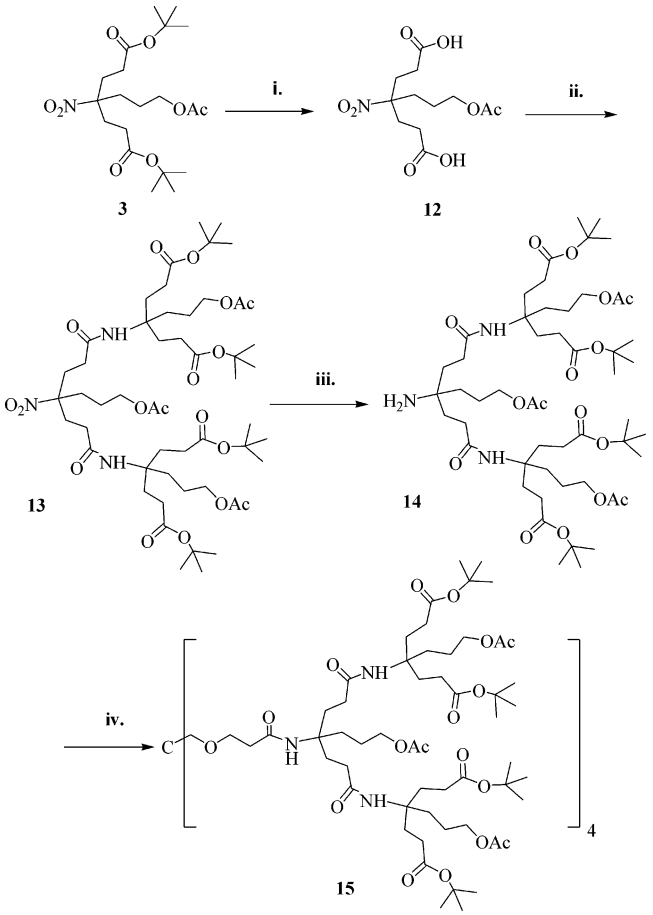
Results and Discussion

Syntheses of Ester and Alcohol Building Blocks. Considering complementary selective protection or deprotection for monomeric functional groups, amine **D** or its related isocyanate **E**, both possessing ester and a protected hydroxyl groups, was initially chosen as a key target, although numerous alternative modifications can be envisioned. Hence, to obtain the desired monomers, nitrobutanol **1** was initially prepared by the modified procedure of Wehrli[33] by reacting an excess of *tert*-butyl acrylate with MeNO$_2$ in the presence of a catalytic amount of Triton-B to afford the *tert*-butyl 4-nitrobutanoate that was subsequently treated with formic acid and then reduced with BH$_3$·THF to afford (90% overall yield) the desired 4-nitrobutanol (**1**).

Diester **2** was then prepared by treatment of butanol **1** with excess *tert*-butyl acrylate and added Triton-B, as catalyst (Scheme 1). Michael addition proceeded smoothly at 25 °C and afforded (75%), after column chromatography, the diadduct **2**; its formation was supported by a chemical shift (^{13}C NMR) from 75.2 to 92.6 ppm, assigned to the *C*NO$_2$ moiety, along with the molecular ion peak (ESI-MS) at m/z 397.9 [M + Na]$^+$. Notably, there were isolatable yields of the monoadduct, *tert*-butyl 4-nitro-7-hydroxyheptanoate, which offers entrance to a 1 → (1 + 1 + 1) *C*-branched monomer series.

To introduce a selective, removable protecting group for the hydroxyl moiety, alcohol **2** was treated with Ac$_2$O in pyridine to give (94%) the corresponding acetate **3**; the acetate moiety is well-known to be stable under both mildly acidic conditions (HCO$_2$H) used for hydrolysis of the *tert*-butyl ester groups and Raney-Ni-catalyzed reduction of the focal nitro group.[40] Therefore, as expected, acetate **3** was successfully reduced (87%) to amine **4** by means of Raney-Ni catalyst under 60 psi of hydrogen in EtOH at 25 °C. Structural confirmation of amine **4** included (^{13}C NMR) the appropriate shift for the *C*$^{4°}$ center from 92.4 (O$_2$N*C*) to 55.1 ppm (H$_2$N*C*) as well as the peak for the molecular ion (ESI-MS) at m/z 439.9 [M + Na]$^+$. Alternatively, alcohol **2** was directly subjected to a catalytic hydrogenation (Raney-Ni) at 25 °C affording (81%) amine **5**, showing an identical shift

Scheme 3. Convergent Synthesis of Second-Tier Dendrimer[a]

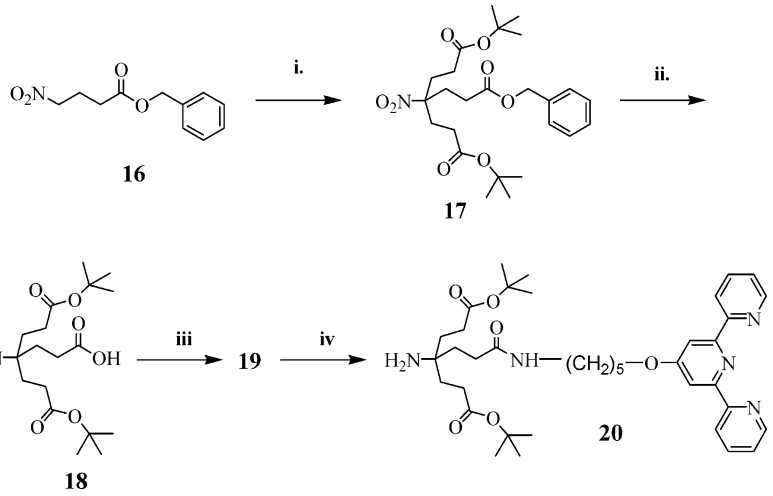


[a] (i) HCO$_2$H, 4 h, 25 °C; (ii) **4** (2 equiv), 1-HOBT, DCC, DMF, 24 h, 25 °C; (iii) Raney-Ni, EtOH, 90 psi of H$_2$, 12 h, 40 °C; (iv) C(CH$_2$OCH$_2$CH$_2$COCl)$_4$ (**8**), DIEA, CH$_2$Cl$_2$, 24 h, 25 °C.

(^{13}C NMR) for the *C*$^{4°}$ center and the expected peak (ESI-MS) at m/z 346.0 [M + H]$^+$. During these reductions, lactonization products were not detected; however, it is crucial to maintain strict adherence to a 25 °C temperature limit; increased temperatures can result in intramolecular cyclization.[36] Employing Bruson's method,[35,41] reaction of amino alcohol **5** with acrylonitrile in the presence of powdered KOH in *p*-dioxane furnished (98%) nitrile **6**, which was characterized (^{13}C NMR) by the signals at 65.0 and 71.2 ppm indicative of ethereal bond (*C*−O−*C*) formation and a signal at 117.6 ppm corresponding to the newly attached cyano moiety. A molecular ion peak (ESI-MS) for **6** was detected at 398.9 [M + H]$^+$. Acrylonitrile is herein used as a *protecting group*[42−45] that either can be subsequently removed under basic conditions or can be reduced to the terminal amine.[46] The O-benzylated counterpart to **6** was readily prepared in two steps from alcohol **2** by initial O-protection (72%) via treatment with benzyl bromide and then selective reduction of the nitro group with NaBH$_4$ in the presence of the in situ generated Ni$_2$B to give (65%) ether **7**.

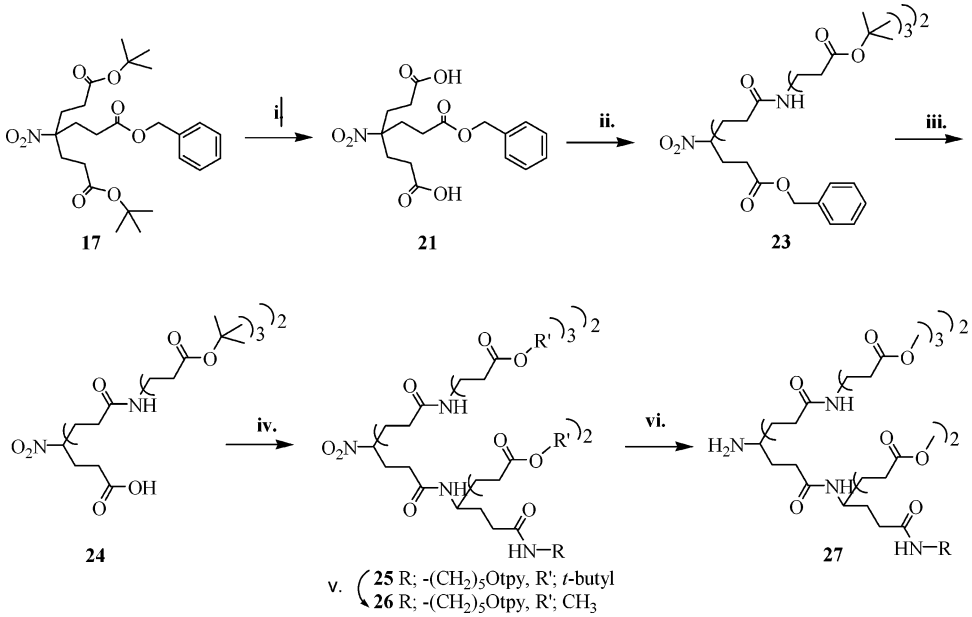
Synthesis of Dendrimers Utilizing the Ester and Protected Alcohol Monomers. Initially, the first-generation dendrimer **9** was synthesized (61%) by amidation with tetraacid chloride[35] **8** with 4 equiv of monomer **4** (Scheme 2). ^{13}C NMR spectra of tetraacetate **9** revealed the expected downfield shift of the *C*$^{4°}$ signal from 55.1 (H$_2$N*C*) to 57.3 ppm (CONH*C*) as well as a

Scheme 4. Synthesis of Monofunctionalized Dendron 20[a]



[a] (i) $CH_2{=}CHCO_2$-*t*-Bu (xs), Triton-B, 16 h, 25 °C; (ii) Pd−C, MeOH, 60 psi of H_2, 12 h, 25 °C; (iii) $H_2N(CH_2)_5O$-4′-tpy, DCC, 1-HOBT, DMF, 25 °C, 24 h; (iv) Raney-Ni, EtOH, 120 psi H_2, 20 h, 40 °C.

Scheme 5. Synthesis of Tier Functionalized Dendrons[a]

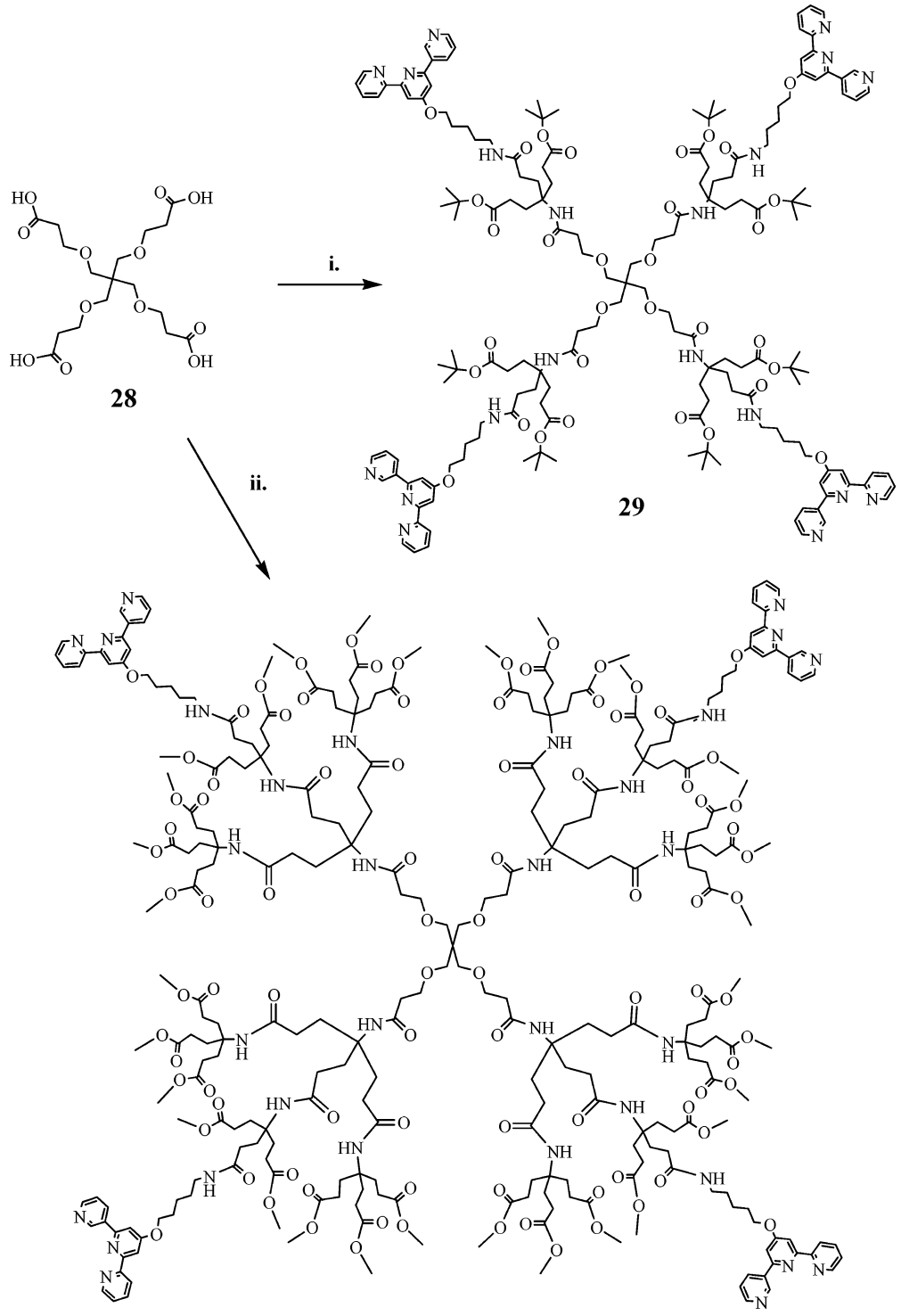


[a] (i) HCO_2H, 16 h, 25 °C; (ii) $H_2NC(CH_2CH_2CO_2$-*t*-$Bu)_3$, DCC, 1-HOBT, DMF, 24 h, 25 °C; (iii) Pd−C, EtOH, 60 psi of H_2, 12 h, 25 °C; (iv) amine **20**, DCC, 1-HOBT, DMF, 25 °C, 24 h; (v) MeOH, H_2SO_4 (traces), 24 h; (vi) Raney-Ni, EtOH, 120 psi of H_2, 48 h, 40 °C.

peak at 170.6 ppm (*C*ONHC), confirming the conversion; an indicative molecular ion peak (MALDI−TOF MS) at *m*/*z* 1924.153 $[M + Na]^+$ was also observed. Deacetylation of dendrimer **9** via transesterification (K_2CO_3, MeOH) generated the corresponding tetraol **10**, as confirmed (^{13}C NMR) by the absence of the acetyl group resonances (170.8 and 20.8 ppm), the presence of *tert*-butyl group signals [80.3 and 28.3 ppm corresponding to the *C*Me_3 and *C*H_3 groups, respectively], and the appearance of a new resonance at 62.4 ppm assigned to the *C*H_2OH termini. Dendrimer **11**, possessing cyano terminal moieties, was analogously synthesized (65%) employing amine monomer **6**. Identical shifts (^{13}C NMR) associated with the $C^{4°}$ and amide carbonyl moieties (57.5 and 170.7 ppm, respectively) as well as the ESI-MS molecular ion peak (*m*/*z* 1969.4 $[M + Na]^+$) validated its structure. Treatment **11** with base in methanol generated the free tetraol, as formed by deprotection of the above acetate.

Preparation of a second-generation dendrimer **15** was achieved convergently (Scheme 3). Diester **3** was converted (100%) with formic acid to the corresponding diacid **12**, as confirmed by the absence of the relevant ^{13}C NMR absorptions. Using standard amidation conditions[47] to couple diacid **12** to amine **4** afforded (76%) the nitrodiamide **13** as shown by the appearance (^{13}C NMR) of four different carbonyl peaks corresponding to the two different acetate moieties (171.08 and 171.17 ppm), the amide carbonyls (172.3 ppm), and the terminal esters (173.0 ppm). The ESI-MS spectrum of trisacetate **13** revealed the expected molecular ion at 1066.8 amu $[M + Na]^+$. Catalytic reduction of the nitro moiety of dendron **13** with Raney-Ni yielded (75%) the second-generation aminotriacetate dendron **14** as confirmed by the appearance (^{13}C NMR) of a new peak at 56.0 ppm for the *C*NH_2 group. Subsequently, the second-generation dendrimer **15** was accessed (35%) by amidation of the known tetraacid chloride[35] **8** using diiso-

Scheme 6. Synthesis of Functionalized Dendrimers[a]



[a] (i) Dendron **20** (4 equiv), DCC, 1-HOBT, DMF, 25 °C, 3 days; (ii) dendron **27** (4 equiv), DCC, 1-HOBT, DMF, 25 °C, 3 days.

propylethylamine (DIEA) with dendron **14** and confirmed (^{13}C NMR) by the observation of the shift of the dendron focal quaternary carbon absorption to the corresponding C^4°NHCO group position in the dendrimer (56.0−58.1 ppm), the appearance of two different amide carbonyl signals (171.25 and 172.9 ppm), and the molecular ion peak (MALDI−TOF MS) at *m*/*z* 4430.10 $[M + Na]^+$.

Synthesis of Dendrimers Utilizing Branched Polyester Monomers. As an alternative approach, 1 → (2 + 1) branched monomers possessing different ester groups were prepared in which a controlled or selective hydrolysis will free either one or two ester moieties. The approach (Scheme 4) utilizes the Michael addition of $MeNO_2$ to commercially available benzyl acrylate in the presence of diisopropylethylamine to afford (84%) benzyl 4-nitrobutyrate (**16**), which was characterized (^{13}C NMR) by the appearance of a new resonance at 74.3 ppm (CNO_2) and the disappearance of the acrylate double-bond absorptions. Triester **17**, possessing a single benzyl ester, was then synthesized (86%) by treatment of nitroester **16** with *tert*-butyl acrylate (Triton B, THF) under typical Michael reaction conditions and shown to

exhibit (^{13}C NMR) the expected chemical shift for the $C^{4^\circ}NO_2$ moiety at 91.9 ppm and the molecular ion signal (ESI-MS) at *m*/*z* 480.43 $[M + H]^+$.

Deprotection with catalytic hydrogenation of the benzyl ester group gave (94%) the corresponding monoacid diester **18** whose structure was supported by the disappearance (^{13}C NMR) of absorptions due to the benzyl group, a new peak at 174.0 ppm (CO_2H), and a molecular ion peak (ESI-MS) at *m*/*z* 390.44 $[M + H]^+$. Monoacid **18** was subsequently coupled with 1-amino-5-[4′-(terpyridinyloxy)]pentane[37,38] using traditional peptide coupling conditions[47] to afford (93%) nitroamide **19** which was characterized (^{13}C NMR) by the observation a new peak at 170.6 ppm (*C*ONH) and the disappearance of the acid carbonyl peak (174.0 ppm) as well as a molecular ion peak (ESI-MS) at *m*/*z* 706.3 $[M + H]^+$. Reduction of the nitro moiety with Raney-Ni catalyst in absolute EtOH at 40 °C afforded (87%) the corresponding amine **20**, whose structure was identified (^{13}C NMR) by the anticipated upfield chemical shift of the resonance assigned to the C^{4° from 92.3 to 52.3 ppm. A molecular ion peak (ESI-MS) at *m*/*z* 677.8 $[M + H]^+$ further confirmed the desired NO_2 to NH_2 transformation. Amine **20** can also be prepared in three steps by amidation of 4-nitrobutanoic acid with 1-amino-5-[4′-(terpyridinyloxy)]pentane, subsequent treatment with a slight excess of *tert*-butyl acrylate, and reduction catalyzed with Raney-nickel.

Focusing on the *tert*-butyl ester groups of monomer **17**, treatment with formic acid at 25 °C for 24 h afforded (ca. 100%) the corresponding diacid **21** (Scheme 5). Characterization (^{13}C NMR) included the disappearance of the peaks attributed to the *tert*-butyl ester groups and appearance of the acid carbonyl peak at 173.3 ppm. Treatment of diacid **21** with an aminotriester building block **22**[39] under DCC amidation conditions gave the bis(amide) **23** as indicated by the expected downfield shift (^{13}C NMR) of the C^{4°NH signal at 52.9 (for **22**) to 57.1 ppm (C^{4°NHCO) and by the disappearance of the acid carbonyl resonance. Catalytic deprotection with Pd/C of the benzyl-modified acid moiety of monomer **23** afforded the monoacid **24**, as shown by the disappearance (^{13}C NMR) of benzyl group absorptions, the observation of a new peak at 174.0 ppm (CO_2H), and the molecular ion peak (ESI-MS) at *m*/*z* 1073.35 $[M + H^+]$.

The second-generation, terpyridinyl-modified monomer **25** was then prepared by treatment of monoacid **24** with amine **20** using DCC with 1-HOBT in DMF. Key assignments (^{13}C NMR) characterizing the transformation included the disappearance of the acid carbonyl resonance, the observation of a signal at 170.3 ppm assigned to the newly formed amide carbonyl moiety, and a downfield shift (Δ 5 ppm) of the C^{4° signal analogous to that observed in monomer **23**. Reduction of the nitro moiety **25** with Raney-Ni in absolute EtOH at various temperatures, hydrogen pressures, and reaction times failed to afford the desired focal amine; thus to circumvent this problem, the *tert*-butyl ester groups were transesterified, thereby reducing the inherent steric hindrance.

Transesterification of dendron **25** with MeOH and a trace of H_2SO_4 afforded the corresponding octa(methyl ester) dendron **26**, which was confirmed (^{13}C NMR) by the presence of a new methyl ester absorption (51.5 ppm) coupled with the complete absence of resonances typically associated with *tert*-butyl groups as well as the MALDI−TOF MS data with the peak at *m*/*z* 1394.19 $[M + H]^+$. Nitro group reduction of methyl ester **26** with Raney-Ni afforded the desired amine **27**, which was analogously identified (^{13}C NMR) by the chemical shift change for C^{4° moiety from 92.9 to 53.6 ppm, confirming the desired $C^{4^\circ}NO_2$ to $C^{4^\circ}NH_2$ transformation and the peak (MALDI−TOF MS) at *m*/*z* 1386.27 $[M + Na]^+$.

The versatility of the modular protocol is represented by attachment of these dendrons to generate the first-generation dendrimer **29** possessing four terpyridine functional groups (one in each quadrant) via peptide coupling of known tetraacid core[36] **28** with 4 equiv of building block **20** (Scheme 6). The conversion was demonstrated (^{13}C NMR) by the disappearance of the signal at 52.3 ppm $C^{4^\circ}NH_2$ moiety of the dendron and the appearance of a peak at 57.0 ppm corresponding to the new C^{4°NHCO group as well as the correct molecular ion peak at *m*/*z* 3077.14 $[M + Na]^+$. Analogously, a second-generation dendrimer **30** was prepared by DCC amidation of 1 equiv of tetraacid **28** and 4 equiv of the larger, terpyridinyl-modified dendron **27**. Nearly identical ^{13}C NMR absorptions were observed for the second-generation construct, when compared to its smaller counterpart; the correct molecular ion peak (MALDI−TOF MS) at *m*/*z* 5829.27 $[M + Na]^+$ affirmed the assembly. These dendrimers possessing one unique functional group per dendron have been shown[48] to form (ca. 90%) of spirometallodendrimers by treatment with $FeCl_2$, supporting the facile intramolecular interactions in these hyperbranched constructs.

Conclusion

New 1 → (2 + 1) *C*-branching building blocks were synthesized from the key intermediate **2**, which was readily prepared from Michael addition reaction of 4-nitrobutanol (**1**) and *tert*-butyl acrylate in the presence of Triton-B, as a catalyst. A series of simple monomers building blocks **4**, **6**, and **7** can be readily used to prepare the first-generation dendrimers (**9**−**11**) based on the tetraacid chloride as a core. The second-generation dendrimer **15** was synthesized by means of a convergent method in which each tier possesses the common 1 → (2 + 1) functional groups. Deprotection of **15** with formic acid can then generate the free octaacid, which has been demonstrated on a related dendrimer series[49,50] to afford the higher level tiers with (1 → 3) Behera's amine[39] or deprotection with base will free the acetate moieties leaving the *tert*-butyl ester intact. Using the same thought process with minor modification, the 1 → (2 + 1) tris(ester) **17** was synthesized and then debenzylated, amidated, and catalytically reduced to give **20**, which with formic acid to remove the ester groups gave the diacid that can be divergently treated with Behera's amine and reduced to give dendron **27**. Combination of these 1 → (2 + 1) monomers permits the selective placement of a single unique moiety either at an internal level or on the surface per dendron depending of the order of construction. Therefore, controlled modifications of appropriately placed functional groups can lead to new types of dendrimers with specifically located utilitarian moieties.

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