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Synthesis and Characterization of Poly(ether amide) Dendrimers Containing Different Core Molecules

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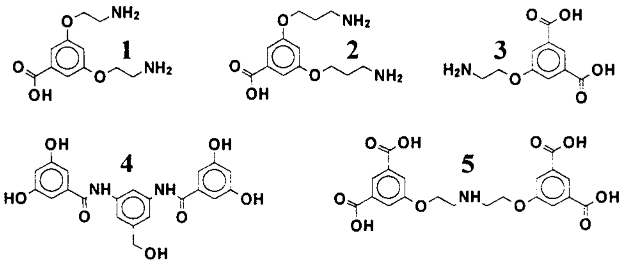
ABSTRACT: The synthesis of novel poly(ether amide) dendrimers containing different symmetrical benzenetriamides as core molecules is presented. The synthesis was carried out in a stepwise convergent manner to build up poly(ether amide) dendrons where 5-(2-aminoethoxy)isophthalic acid is the branching repeating unit. Three defined dendrons were subsequently attached to a central core. For this key reaction step *O*-(benzotriazol-1-yl)-*N*,*N*,*N*′,*N*′-tetramethyluronium tetrafluoroborate (TBTU) was preferably used as activating agent to form the desired amide groups. $^1H/^{13}C$ NMR spectroscopy, MALDI-TOF-MS, SEC, and DSC were used to characterize the obtained dendrimers. The incorporated central units had a remarkable influence on the glass transition temperatures (T_g) within the series of dendrimers.

Introduction

Synthesis and application of dendrimers are rapidly growing areas in polymer science.[1,2] Ideally, dendrimers are perfectly branched, monodisperse macromolecules that originate from a core molecule. Their highly branched structure and the large number of functional groups in the periphery as well as the internal cavities offer unique physical and chemical properties, resulting in remarkable potential applications such as photocatalysts,[3] novel amphiphiles,[4] complexing agents,[5] and MRI contrast agents.[6] Dendrimers are usually prepared in a stepwise synthesis based on divergent or convergent strategy which leads to high control over structure, size, and shape of the molecules.[1,2]

Originating from the work of Tomalia and Newkome, there is a particular interest in amidic dendritic macromolecules (e.g., poly(amido amine)s, poly(ester amide)s, poly(ether amide)s, and poly(aramide)s) to investigate structure−property relationships[7−11] and possible applications.[6,12−16] Commonly, these dendrimers possess an aliphatic backbone which guarantees good solubility in most conventional solvents and reduces synthetic problems, e.g., due to steric hindrance. However, there have been also several synthetic efforts to realize dendritic poly(ether amide)s containing aromatic units. Scheme 1 summarizes the branching units **1**,[17] **2**,[18] **3**,[19] **4**,[20] and **5**[21] used for the synthesis of aromatic−aliphatic dendritic macromolecules with amide linkages. The repeating units **1**−**4** were used to synthesize dendrons/wedges[17,19,20] or dendronized polymers.[18] Only **5** was successfully incorporated in different dendrimer generations.[21]

Scheme 1. Repeating Units 1−5 Used for the Synthesis of Aromatic−Aliphatic Dendritic Macromolecules with Amide Linkage[17−21]



Up to now the thermal behavior or dynamic processes of these dendritic molecules in correlation to structural differences are not studied in detail. To our knowledge, the dendrons of Voit et al.[19] and Fréchet et al.[20] exhibit glass transitions above room temperature. Broad-band dielectric spectroscopy was applied to monodendrons based on **3** (with ester end groups) to obtain deeper insight into the molecular dynamic processes in the solid state.[22] It was found that the dynamic glass transitions scaled well with calorimetric data, and different β-relaxation processes could be assigned to local fluctuations of the ester end groups, the amide linkages, and the Boc-protected focal amine groups. Therefore, interesting aspects arise concerning the structure−property relationships, e.g., T_g, when poly(ether amide) dendrons with aromatic branching units react with different core molecules to dendrimers.

We report now on the synthesis and characterization of different dendrimers up to generation 3 built by amide formation based on the convergent strategy and using different core molecules. The influence of the structural changes on the glass transition temperature will be discussed in detail.

Experimental Section

General. All substances were used as purchased from Aldrich, Acros, or Fluka without purification if not described otherwise. All reactions were carried out under nitrogen. The following abbreviations were used: DMF (dimethylformamide), CDI (*N*,*N*′-carbonyldiimide), TBTU (*O*-(benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate), DCC (dicyclohexylcarbodiimide), HOBT (1-hydroxybenzotriazole). Abbreviations for NMR spectroscopy are s (singlet), d (douplet), t (triplet), q (quartet), m (multiplet), and br s (broadened signal).

Measurements. The NMR spectroscopic experiments were performed in 5 mm o.d. sample tubes with a Bruker DRX 500 NMR spectrometer at 500.13 MHz for ^1H NMR spectra and at 125.75 MHz for ^{13}C NMR spectra. DMSO-d_6 was used as solvent for all NMR experiments. For internal calibration the solvent peaks of DMSO were used: δ (^{13}C) = 39.60 ppm; δ (^1H) = 2.50 ppm. The signal assignment was done by $^1H-^1H$

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COSY, ^{1}H−^{13}C HMQC, and ^{1}H−^{13}C HMBC 2D NMR experiments using the standard pulse sequences provided by Bruker. The SEC measurements were performed with a modular chromatographic equipment containing an HPLC pump, refractive index detector, and manual injection valve (KNAUER, Berlin, Germany) at ambient temperature. A column set containing two ZORBAX columns PSM 60 and PSM 300 (Rockland Technologies Inc./USA) was used. The injection volume was 20 μL. The sample concentration was $c = 2$ g/L. The flow rate was 0.5 mL/min. The experiments were carried out with a mixture of dimethylacetamide/water (98v/2v/LiCl 3 g/L) as eluent. The molar masses were calculated using a calibration obtained from MALDI-TOF-MS results on the identical samples. The MALDI-TOF-MS experiments were performed on a HP G2030A MALDI-TOF-MS system (Hewlett-Packard) with delayed extraction option. The desorption/ionization was performed by a pulsed N$_2$ laser. The mass spectra were obtained from 28 kV acceleration voltage. The matrix was 2,5-dihydroxybenzoic acid, sinapinic acid, or 1,4-di[2-(5-phenyloxazoyl)]benzene using Na$^+$, Li$^+$, or Cs$^+$ as modifier. The mixture of sample and matrix was dried on the sample holder in a vacuum. The measurements were carried out with positive polarity. The thermal behavior was investigated using a Perkin-Elmer DSC 7 with Pyris software 3.51. The samples were measured in the temperature range from − 60 to 180 °C at scan rate of 20 K/min. To eliminate the influence of residual solvent, the glass transition temperatures were determined from the second heating run by the Δc_p half-step method. The investigations for thermal stability were done by a Perkin-Elmer TGA 7 at a heating rate of 10 K/min in the temperature range from 50 to 700 °C in a nitrogen atmosphere.

Materials. 1,3,5-Tris[*N*-(3-methoxycarbonylpropyl)aminocarbonyl]benzene (7). Trimesic acid (**6**) (3.15 g, 15 mmol) was dissolved in dry DMF (140 mL), and then CDI (7.78 g, 48 mmol) was added to the reaction solution in which immediately CO$_2$ was formed and observed by a bubble counter. After stirring overnight at room temperature methyl 4-aminobutanoate hydrochloride (7.14 g, 46.5 mmol) was added to the reaction solution. Afterward, triethylamine (8.34 mL, 60 mmol, 6.06 g) was dropped into the mixture, which was stirred at room temperature for a further 24 h. After evaporation of the solvent under high-vacuum conditions at 40 °C the residue was taken up in ethyl acetate (120 mL). The organic phase was washed with 50 mL of diluted aqueous HCl, 2 × 50 mL of distilled water, and 50 mL of aqueous NaHCO$_3$ solution. After drying of the organic phase with anhydrous Na$_2$SO$_4$, the solvent was distilled under reduced pressure (1 × 10^{-2} mbar) at 30 °C. Crystallization of the crude product was carried out under stirring in 50 mL of diethyl ether and 20 mL of methanol under refluxing. After 20 min complete dissolution of the product was observed, and the hot mixture was filtered via a glass frit. To accelerate the precipitation of the ester **7**, the solution was stored at 5 °C overnight. Separation of **7** was achieved by filtration. The product was washed with 300 mL of *n*-hexane and dried in a vacuum at 30 °C to yield **7** (6.09 g, 80%) as a white solid.

^{1}H NMR: δ = 1.82 (m, 6H, C*H*$_2$−CH$_2$−CO−OCH$_3$); 2.41 (t, 6H, CH$_2$−C*H*$_2$−CO−OCH$_3$); 3.32 (q, 6H, R−CO−NH−C*H*$_2$−CH$_2$); 3.60 (s, 9H, CO−OCH$_3$); 8.39 (s, 3H, aromatic H); 8.73 ppm (t, 3H, R−CO−N*H*-CH$_2$). ^{13}C NMR: δ = 25.25 (*C*H$_2$−CH$_2$−CO−OCH$_3$); 31.61 (CH$_2$−*C*H$_2$−CO−OCH$_3$); 39.51 (R−CO−NH−*C*H$_2$); 52.12 (OCH$_3$); 129.28 (aromatic CH); 135.84 (quaternary aromatic C); 166.43 (R-*C*O−NH−CH$_2$); 173.99 ppm (*C*O−OCH$_3$). IR (solid, KBr): ν = 3070.7, 2987.4, 2951.2, 1724.4, 1631.3, 1556.9. MS (FAB; *M* = 507.54 g/mol): *m*/*z* (%) = 508 (38%) [M + H]$^+$. Elemental Analysis (C$_{24}$H$_{33}$N$_3$O$_9$): calcd C 56.8, H 6.6, N 8.3; found C 56.8, H 6.5, N 8.3.

1,3,5-Tris[*N*-(3-carboxypropyl)aminocarbonyl]benzene (8). The ester **7** (0.25 g, 0.49 mmol) was dissolved in methanol (15 mL) and cooled to 0 °C with an ice bath. Then 10 mL of 1 N NaOH was added to the solution, which was stirred at 0 °C for 4 h. After addition of 10 mL of distilled water the reaction solution was neutralized with 1 N HCl and acidified to pH 2−3. Slow precipitation of the desired product was observed, and the solution was stirred for an additional 2 h. After filtration the product was dried under vacuum at 80 °C to yield **8** (0.148 g, 65%) as a white solid.

^{1}H NMR: δ = 1.79 (m, 6H, C*H*$_2$−CH$_2$−CO−OH); 2.31 (t, 6H, CH$_2$−C*H*$_2$−CO−OH); 3.31 (q, 6H, R−CO−NH−C*H*$_2$−CH$_2$); 8.39 (s, 3H, aromatic H); 8.72 (t, 3H, R−CO−N*H*−CH$_2$); 12.10 ppm (br s, 3H, CH$_2$−CO−O*H*). ^{13}C NMR: δ = 25.31 (*C*H$_2$−CH$_2$−CO−OH); 31.96 (CH$_2$−*C*H$_2$−CO−OH); 39.64 (R−CO−NH−*C*H$_2$); 129.27 (aromatic CH); 135.88 (quaternary aromatic C); 166.43 (R-*C*O−NH−CH$_2$); 175.09 ppm (CO−OH). IR (solid; cm^{-1}): ν = 3367.6, 3071.2, 2968.2, 1722.1, 1707.01, 1635.2, 1593.6. MS (FAB; *M* = 465.46 g/mol): *m*/*z* (%) = 464 (26%) [M − H]$^+$. Elemental Analysis (C$_{21}$H$_{27}$N$_3$O$_9$·1H$_2$O): calcd C 52.17, H 6.05, N 8.69; found C 52.74, H 5.82, N 8.63.

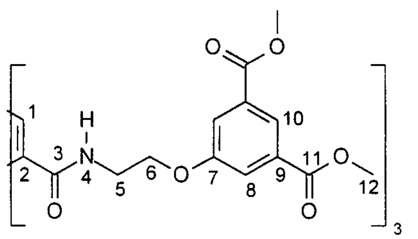
1,3,5-Tris[*N*-(10-methoxycarbonyldecyl)aminocarbonyl]benzene (9).[23] Trimesic acid (**6**) (0.798 g, 3.80 mmol) was dissolved in dry dichloromethane (80 mL), and then CDI (1.98 g, 12.2 mmol) was added to the reaction solution. Immediately CO$_2$ was formed and observed by a bubble counter. After stirring at room temperature for 3 h, methyl 10-aminoundecanoate hydrochloride (3.08 g, 11.6 mmol) was added to the reaction solution. Afterward, triethylamine (5.0 mL, 36.0 mmol, 3.64 g) was dropped into the mixture, which was stirred at room temperature for further 24 h. After evaporation of the solvent under high-vacuum conditions at 40 °C the residue was taken up in ethyl acetate (120 mL). The organic phase was washed with 50 mL of diluted aqueous HCl, 2 × 50 mL of distilled water, and 50 mL of aqueous NaHCO$_3$ solution. After drying of the organic phase with anhydrous Na$_2$SO$_4$ the solvent was distilled under reduced pressure (1 × 10^{-2} mbar) at 30 °C. Crystallization of the crude product was carried out by stirring in refluxing methanol and subsequent storage at 5 °C for 5 days. The precipitate was separated from methanol by filtration. Recrystallization was repeated twice using identical conditions. **9** was yielded as white solid (0.91 g, 30%).

^{1}H NMR: δ = 1.25 (br s, 30H, CH$_2$−(C*H*$_2$)$_5$−CH$_2$−CH$_2$−CO−OCH$_3$); 1.30 (m, 6H, R−CO−NH−CH$_2$−CH$_2$−C*H*$_2$−(CH$_2$)$_5$); 1.48 (m, 6H, (CH$_2$)$_5$−C*H*$_2$−CH$_2$−CO−OCH$_3$); 1.53 (m, 6H, R−CO−NH−CH$_2$−C*H*$_2$−CH$_2$); 2.18 (t, 6H, CH$_2$−C*H*$_2$−CO−OCH$_3$); 3.27 (q, 6H, R−CO−NH−C*H*$_2$−CH$_2$); 3.56 (s, 9H, CO−OCH$_3$), 8.35 (s, 3H, aromatic H); 8.60 ppm (t, 3H, R−CO−N*H*−CH$_2$). ^{13}C NMR (DMSO-*d*$_6$, 75 MHz): δ = 24.55 (*C*H$_2$−CH$_2$−CO−OCH$_3$); 26.56 (R−CO−NH−CH$_2$−CH$_2$−*C*H$_2$); 28.60, 28.80, 28.84, 28.95, 29.00, and 29.08 (R−CO−NH−CH$_2$−*C*H$_2$ and CH$_2$−(*C*H$_2$)$_5$−CH$_2$−CH$_2$−CO−OCH$_3$); 33.72 (*C*H$_2$−CO−OCH$_3$); 39.42 (R−CO−NH−*C*H$_2$); 52.43 (CO−O*C*H$_3$); 128.32 (aromatic CH); 135.20 (quaternary aromatic C); 165.49 (R−*C*O−NH−CH$_2$); 173.95 ppm (*C*O−OCH$_3$).

1,3,5-Tris[*N*-(10-carboxydecyl)aminocarbonyl]benzene (10).[23] Ester **9** (0.20 g, 0.25 mmol) was dissolved in methanol (40 mL). Then 10 mL of 1 N NaOH was added to the solution, which was stirred at room temperature overnight. After addition of 10 mL of distilled water, the reaction solution was neutralized with 1 N HCl and acidified to pH 2−3. Slow precipitation of the desired product was observed, and the solution was stirred for an additional 2 h. After filtration the product was dried under vacuum at 80 °C to yield **10** (0.142 g, 75%) as a white solid.

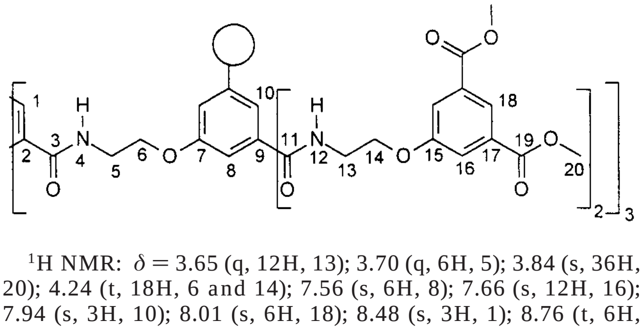
^{1}H NMR: δ = 1.25 (br s, 30H, CH$_2$−(C*H*$_2$)$_5$−CH$_2$−CH$_2$−CO−OH); 1.30 (m, 6H, R−CO−NH−CH$_2$−CH$_2$−C*H*$_2$−(CH$_2$)$_5$); 1.48 (m, 6H, (CH$_2$)$_5$−C*H*$_2$−CH$_2$−CO−OH); 1.53 (m, 6H, R−CO−NH−CH$_2$−C*H*$_2$−CH$_2$); 2.18 (t, 6H, CH$_2$−C*H*$_2$−CO−OH); 3.27 (q, 6H, R−CO−NH−C*H*$_2$−CH$_2$); 8.35 (s, 3H, aromatic H); 8.60 (t, 3H, R−CO−N*H*−CH$_2$); 11.96 ppm (br. s, 3H, R−CO−OH). ^{13}C NMR (DMSO-*d*$_6$, 75 MHz): δ = 24.55 (*C*H$_2$−CH$_2$−CO−OH); 26.56 (R−CO−NH−CH$_2$−CH$_2$−*C*H$_2$); 28.60, 28.80, 28.84, 28.95, 29.00, and 29.08 (R−CO−NH−CH$_2$−*C*H$_2$ and (*C*H$_2$)$_5$−CH$_2$−CH$_2$−CO−OH); 33.72 (*C*H$_2$−CO−OH); 39.42 (R−CO−NH−*C*H$_2$); 128.32 (aromatic CH); 135.20 (quaternary aromatic C); 165.49 (R−*C*O−NH−CH$_2$); 174.51 ppm (*C*O−OCH$_3$).

1,3,5-Tris{*N*-[2-(3,5-methoxycarbonylphenoxy)ethyl]aminocarbonyl}benzene (14). CDI (1.8 mmol, 292 mg) was added under stirring to a solution of trimesic acid (**6**) (0.5 mmol, 105 mg) in dry DMF (25 mL). The reaction solution was stirred at room temperature for a further 1.5 h. In another flask the dendron **11** (1.6 mmol, 464 mg) and triethylamine (400 μL, 2.88 mmol, 291 mg) were dissolved in dry DMF (40 mL), and the resulting mixture was stirred at room temperature for 1 h. Then, both solutions were combined and kept at room temperature for 1 day. The solvent was removed in a vacuum, and the residue was dropped under stirring into cold methanol (450 mL). After separation and drying of the precipitate in a vacuum the dendrimer **14** was received as a white solid (371 mg, 81%). A further purification step of **14** can be done using flash chromatography (dichloromethane as eluent) on octyl-modified silica gel to obtain the dendrimer in ≤30% for analytical purposes. However, this procedure has no significant influence on the purity as determined by SEC.



^{1}H NMR: $\delta = 3.70$ (q, 6H, 5); 3.87 (s, 18H, 12); 4.29 (t, 6H, 6); 7.71 (s, 6H, 8); 8.06 (s, 3H, 10); 8.43 (s, 3H, 1); 8.90 ppm (t, 3H, 4). ^{13}C NMR: $\delta = 38.99$ (5); 52.54 (12); 66.81 (6); 119.47 (8); 121.94 (10); 128.75 (1); 131.60 (9); 134.77 (2); 158.75 (7); 165.18 (11); 165.84 ppm (3). Elemental Analysis ($C_{57}H_{66}N_6O_{21}$): calcd C 59.00, H 5.00, N 4.60; found C 58.27, H 5.02, N 4.69.

1,3,5-Tris{*N*-[2-(3,5-(N-(2-(3,5-methoxycarbonylphenoxy)ethyl)aminocarbonyl)phenoxy)ethyl]aminocarbonyl}benzene (15). A solution of trimesic acid (**6**) (0.29 mmol, 61 mg) in anhydrous DMF (20 mL) was cooled to 0 °C. DCC (0.9 mmol, 186 mg) and HOBT (0.87 mmol, 118 mg) were added, and the reaction solution was stirred at 0 °C for 1 h. In another flask the dendron **12** (0.928 mmol, 679 mg) and triethylamine (300 μL, 2.16 mmol, 218 mg) were taken up in DMF (80 mL), and the resulting mixture was stirred at room temperature for 1 h. Then both solutions were combined at 0 °C and kept at room temperature for 4 days. The solvent was removed in a vacuum at 40 °C. The residue (4−6 mL) was dropped under stirring into ethyl acetate (450 mL) for 1 day and then cooled to 0 °C for a further 4 h. The obtained gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum at 40 °C dendrimer **15** was obtained as crude product (290 mg, 45%). A further purification step was applied on small amounts (7−10 mg) of **15** using flash chromatography on octyl-modified silica gel (dichloromethane as eluent) to separate the byproducts. The average yield of purified **15** via flash chromatography was between 25 and 35% as a white solid. An alternative method for the purification was the fractional precipitation using DMF/ethyl acetate where the yield of **15** was also ≤30%.



^{1}H NMR: $\delta = 3.65$ (q, 12H, 13); 3.70 (q, 6H, 5); 3.84 (s, 36H, 20); 4.24 (t, 18H, 6 and 14); 7.56 (s, 6H, 8); 7.66 (s, 12H, 16); 7.94 (s, 3H, 10); 8.01 (s, 6H, 18); 8.48 (s, 3H, 1); 8.76 (t, 6H, 12); 8.94 ppm (t, 3H, 4). ^{13}C NMR: $\delta = 38.92$ (13); 39.05 (5); 52.49 (20); 66.48 (6); 66.78 (14); 115.90 (8); 118.96 (10); 119.41 (16); 121.90 (18); 128.75 (1); 131.54 (17); 134.77 (2); 135.79 (9); 158.25 (7); 158.72 (15); 165.13 (19); 165.80 (3); 165.82 ppm (11).

1,3,5-Tris{*N*-[3-(*N*-(2-(3,5-Methoxycarbonylphenoxy)ethyl)aminocarbonyl)propyl]aminocarbonyl}benzene (16). TBTU (0.66 mmol, 212 mg) was added under stirring to a solution of the core molecule **8** (0.21 mmol, 98 mg) in dry DMF (20 mL), and the mixture was stirred for 1.5 h. In another flask the dendron **11** (0.65 mmol, 188.6 mg) and triethylamine (300 μL, 2.88 mmol, 218 mg) were dissolved in dry DMF (50 mL), and the resulting mixture was stirred at room temperature for 1 h. Then, both solutions were combined and kept at room temperature for 4 days. The volatile was removed in a vacuum, and the obtained residue was dropped under stirring into ethyl acetate (450 mL) and cooled to 0 °C for 4 h. The resulting gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum, **16** was received as a white solid (194 mg, 79%). In a further purification step small amounts (7−10 mg) of **16** were separated from the byproducts by flash chromatography (dichloromethane as eluent) on octyl-modified silica gel. The average yield of purified **16** via flash chromatography was between 20 and 30%.

^{1}H NMR: $\delta = 1.77$ (m, 6H, 6); 2.17 (t, 6H, 7); 3.27 (q, 6H, 5); 3.45 (q, 6H, 10); 3.87 (s, 24H, 17); 4.12 (t, 6H, 11); 7.67 (s, 6H, 13); 8.06 (s, 3H, 15); 8.07 (t, 3H, 9); 8.36 (s, 3H, 1); 8.62 ppm (t, 3H, 4). ^{13}C NMR: $\delta = 25.31$ (6); 32.91 (7); 38.08 (10); 39.17 (5); 52.61 (17); 67.23 (11); 119.48 (13); 121.94 (15); 128.41 (1); 131.59 (14); 135.09 (2); 158.79 (12); 165.23 (16); 165.53 (3); 172.23 ppm (8) (NMR assignment compare Figure 1).

1,3,5-Tris{*N*-[3-(*N*-(2-(3,5-(N-(2-(3,5-methoxycarbonylphenoxy)ethyl)aminocarbonyl)phenoxy)ethyl)aminocarbonyl)propyl]aminocarbonyl}benzene (17). TBTU (0.20 mmol, 64 mg) was added to a solution of the core molecule **8** (0.064 mmol, 30 mg) in dry DMF (10 mL), and the mixture was stirred for 1.5 h. In another flask the dendron **12** (0.20 mmol, 146 mg) and triethylamine (400 μL, 2.88 mmol, 291 mg) were taken up in dry DMF (30 mL), and the resulting mixture was stirred at room temperature for 1 h. Then the both solutions were combined and kept at room temperature for 4 days. The solvent was removed in a vacuum, and the obtained residue was dropped under stirring into ethyl acetate (450 mL) and cooled to 0 °C for 5 h. The resulting gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum **17** was received as brown solid (141 mg, 88%). Purification of **17** was carried out by flash chromatography (dichloromethane as eluent) on octyl-modified silica gel. The average yield of purified **17** using flash chromatography was ≤30%.

^{1}H NMR: $\delta = 1.77$ (m, 6H, 6); 2.17 (t, 6H, 7); 3.27 (q, 6H, 5); 3.45 (q, 6H, 10); 3.66 (q, 12H, 18); 3.86 (s, 36H, 25); 4.07 (t, 6H, 11); 4.25 (t, 12H, 19); 7.53 (s, 6H, 13); 7.68 (s, 12H, 21); 7.93 (s, 3H, 15); 8.04 (s, 6H, 23); 8.07 (t, 3H, 9); 8.35 (s, 3H, 1); 8.63 (t, 3H, 4); 8.76 ppm (t, 6H, 17). ^{13}C NMR: $\delta = 25.27$ (6); 32.86 (7); 38.19 (10); 38.92 (18); 39.16 (5); 52.53 (25); 66.81 (19); 66.90 (11); 115.90 (13); 118.93 (15); 119.45 (21); 121.92 (23); 128.38 (1); 131.56 (22); 135.05 (2); 135.78 (14); 158.26 (12); 158.77 (20); 165.16 (24); 165.52 (3); 165.85 (16); 172.19 ppm (8) (NMR assignment compare Figure 1).

1,3,5-Tris{*N*-[3-(*N*-(2-(3,5-(N-(2-(3,5-(*N*-(2-(3,5-methoxycarbonylphenoxy)ethyl)aminocarbonyl)phenoxy)ethyl)aminocarbonyl)phenoxy)ethyl)aminocarbonyl)propyl]aminocarbonyl}benzene (18). TBTU (0.20 mmol, 64 mg) was added to a solution of the core molecule **8** (0.064 mmol, 30 mg) in dry DMF (10 mL), and the mixture was stirred for 1.5 h. In another flask the dendron **13** (0.21 mmol, 340 mg) and triethylamine (400 μL, 2.88 mmol, 291 mg) were dissolved in dry DMF (20 mL), and the resulting mixture was stirred at room temperature for 1 h. Then, both solutions were combined and kept at room temperature for 4 days. The solvent was removed in a vacuum, and the obtained residue was dropped under stirring into ethyl acetate (400 mL). The solution was stirred at room temperature overnight. The resulting gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum, **18** was yielded as crude product (275 mg, 83%). Purification of **18** was carried out by the use of flash chromatography (dichloromethane as solvent) on octyl-modified silica gel. The average yield of purified **18** using flash chromatography was ≤30%.

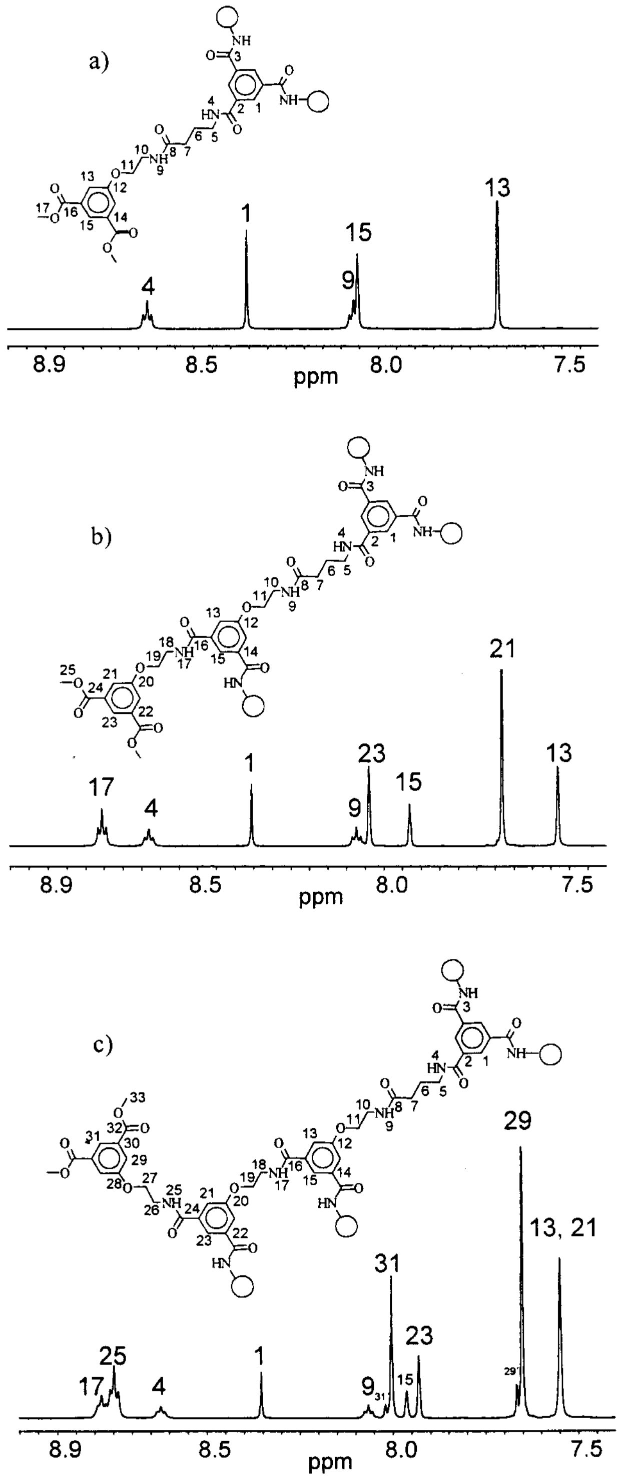
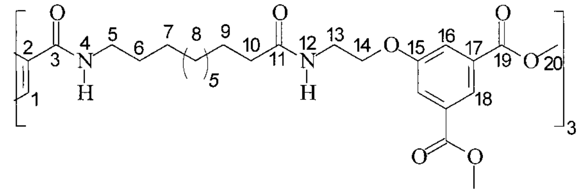


Figure 1. ^{1}H NMR spectra of (a) **16**, (b) **17**, and (c) **18** (aromatic and amide proton region). For full signal assignment (^{1}H and ^{13}C NMR), see Experimental Section.

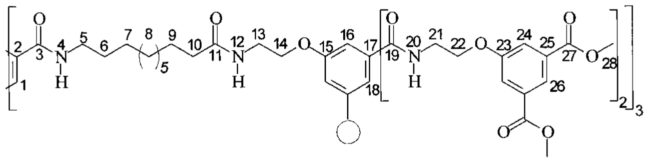
^{1}H NMR: δ = 1.76 (m, 6H, 6); 2.16 (t, 6H, 7); 3.26 (q, 6H, 5); 3.44 (q, 6H, 10); 3.65 (m, 36H, 18 and 26); 3.83 (s, 72H, 33); 4.06 (t, 6H, 11); 4.21 (t, 12H, 19); 4.23 (t, 24H, 27); 7.55 (s, 18H, 13 and 21); 7.65 (s, 24H, 29); 7.93 (s, 6H, 23); 7.96 (s, 3H, 15); 8.00 (s, 12H, 31); 8.07 (t, 3H, 9); 8.36 (s, 3H, 1); 8.62 (t, 3H, 4); 8.75 (t, 12H, 25); 8.78 ppm (t, 6H, 17). ^{13}C NMR: δ = 25.27 (6); 32.86 (7); 38.19 (10); 38.91 (18 and 26); 39.18 (5); 52.49 (33); 66.49 (19); 66.78 (27); 66.90 (11); 115.89 (13 and 21); 118.95 (15 and 23); 119.41 (29); 121.90 (31); 128.38 (1); 131.52 (30); 135.04 (2); 135.79 (14 and 22); 158.26 (20); 158.29 (12); 158.72 (28); 165.14 (32); 165.51 (3); 165.84 (16 and 24); 172.19 ppm (8) (NMR assignment compare Figure 1).

1,3,5-Tris{*N*-[10-(*N*-(2-(3,5-methoxycarbonylphenoxy)ethyl)aminocarbonyl)decyl]aminocarbonyl}benzene (19). TBTU (0.66 mmol, 212 mg) was added under stirring to a solution of the core molecule **10** (0.21 mmol, 159.6 mg) in dry DMF (10 mL), and the resulting mixture was stirred for 1.5 h. In another flask the dendron **11** (0.65 mmol, 188 mg) and triethylamine (300 μL, 2.16 mmol, 218 mg) were taken up in dry DMF (50 mL), and the resulting mixture was stirred at room temperature for 1 h. Then, both solutions were combined and kept at room temperature for 4 days. The solvent was removed in a vacuum, and the obtained residue was dropped under stirring into ethyl acetate (450 mL) and cooled to 0 °C for 4 h. The resulting gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum **19** was obtained as pure white solid (194 mg, 63%). Further purification of **19** was achieved by fractional precipitation using DMF/ethyl acetate. The average yield of **19** via fractional precipitation was ≤20%.



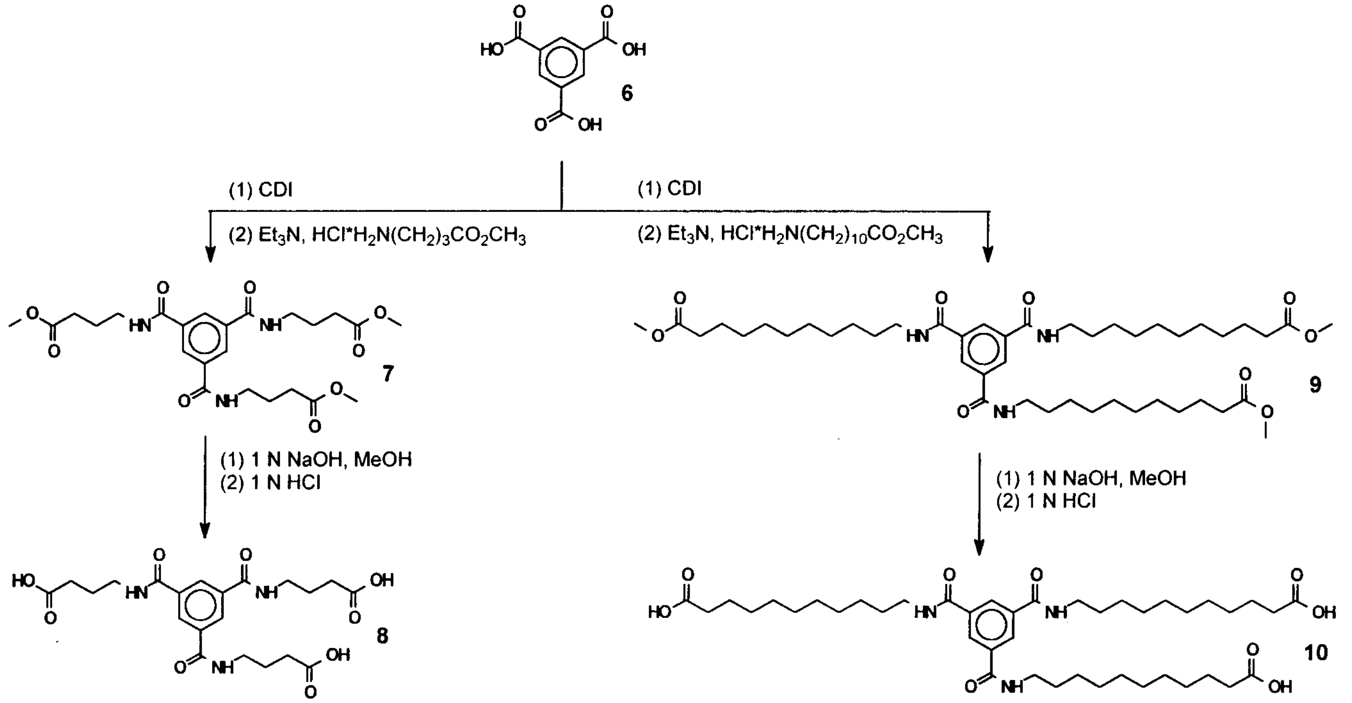
^{1}H NMR: δ = 1.18 (br s, 30H, 8); 1.25 (m, 6H, 7); 1.45 (m, 6H, 9); 1.51 (m, 6H, 6); 2.05 (t, 6H, 10); 3.25 (q, 6H, 5); 3.43 (q, 6H, 13); 3.88 (s, 12H, 20); 4.10 (t, 6H, 14); 7.67 (s, 6H, 16); 7.98 (t, 3H, 12); 8.07 (s, 3H, 18); 8.36 (s, 3H, 1); 8.61 ppm (t, 3H, 4). ^{13}C NMR: δ = 25.26 (9); 26.52 (7); 28.59, 28.79, 28.80, 28.93, 28.98, and 29.04 (6 and 8); 35.32 (10); 38.02 (13); 39.38 (5); 52.56 (20); 67.26 (14); 119.46 (16); 121.88 (18); 128.29 (1); 131.56 (17); 135.14 (2); 158.86 (15); 165.19 (19); 165.43 (3); 172.53 ppm (11).

1,3,5-Tris{*N*-[10-(*N*-(2-(3,5-(*N*-(2-(3,5-methoxycarbonylphenoxy)ethyl)aminocarbonyl)phenoxy)ethyl)aminocarbonyl)decyl]aminocarbonyl}benzene (20). TBTU (0.20 mmol, 64 mg) was added to a solution of the core molecule **10** (0.064 mmol, 48.6 mg) in anhydrous DMF (10 mL), and the mixture was stirred for 1.5 h. In another flask the dendron **12** (0.20 mmol, 146 mg) and triethylamine (300 μL, 2.16 mmol, 218 mg) were taken up in dry DMF (20 mL), and the resulting mixture was stirred at room temperature for 1 h. Then both solutions were combined and kept at room temperature for 4 days. The solvent was removed in a vacuum, and the obtained residue was dropped under stirring into ethyl acetate (450 mL) and cooled to 0 °C for 5 h. The resulting gel-like precipitate was separated from the solution via a glass frit. After drying of the precipitate in a vacuum **20** was received as pure white solid (141 mg, 78%). Further purification of **20** was achieved by flash chromatography (dichloromethane as eluent) on an octyl-modified silica gel. The average yield of purified **20** via flash chromatography was been ≤30%. However, no increased purity could be detected by SEC after this additional purification step.

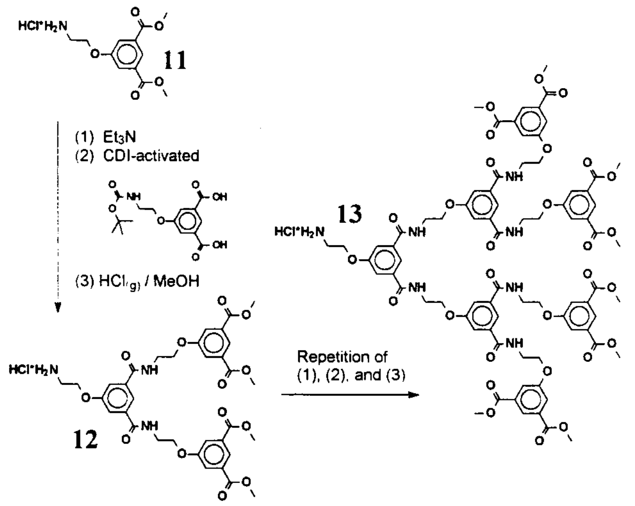


^{1}H NMR: δ = 1.17 (br s, 30H, 8); 1.23 (m, 6H, 7); 1.45 (m, 6H, 9); 1.49 (m, 6H, 6); 2.05 (t, 6H, 10); 3.24 (q, 6H, 5); 3.43 (q, 6H, 13); 3.67 (q, 12H, 21); 3.86 (s, 36H, 28); 4.06 (t, 6H, 14); 4.26 (t, 12H, 22); 7.53 (s, 6H, 16); 7.68 (s, 12H, 24); 7.94 (s, 3H, 18); 7.98 (t, 3H, 12); 8.04 (s, 6H, 26); 8.34 (s, 3H, 1); 8.56 (t, 3H, 4); 8.76 ppm (t, 6H, 20). ^{13}C NMR: δ = 25.26 (9); 26.52 (7); 28.67, 28.79, 28.82, 28.93, 28.99, and 29.05 (6 and 8); 35.34 (10); 38.14 (13); 38.93 (21); 39.40 (5); 52.52 (28); 66.83 (22); 66.94 (14); 115.91 (16); 118.92 (18); 119.44 (24); 121.92

Scheme 2. Synthetic Route for the Core Molecules 8 and 10



Scheme 3. Synthesis of the Dendrons 11−13



(26); 128.27 (1); 131.57 (25); 135.14 (2); 135.75 (17); 158.31 (15); 158.78 (23); 165.17 (27); 165.42 (3); 165.83 (19); 172.56 ppm (11).

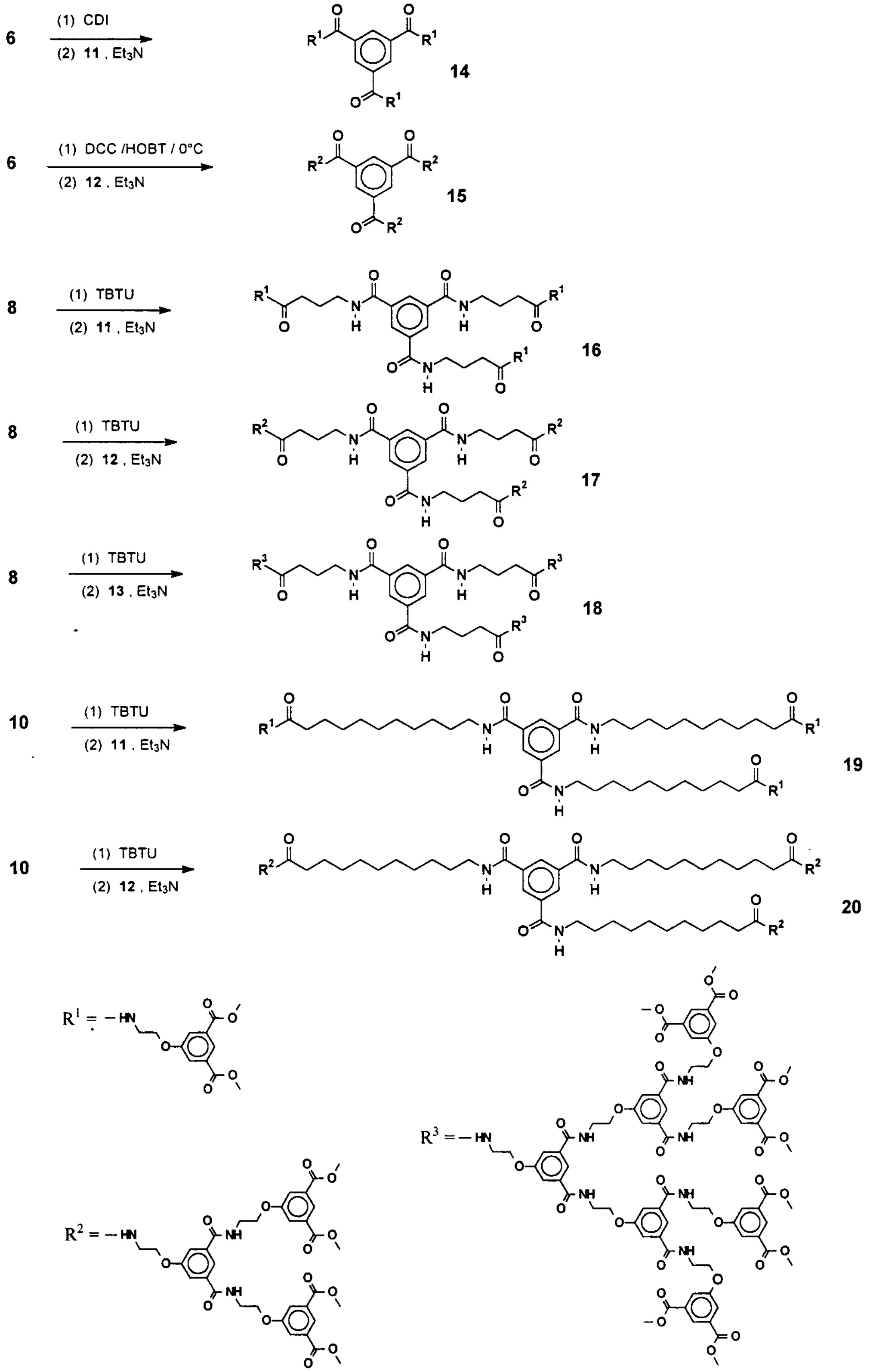
Results and Discussion

The intended amidic dendrimers based on the branching unit **3** have been realized up to generation 3 by preparing dendrons and subsequently attaching several of these to a core molecule. Schemes 2 and 3 show the core molecules **6**, **8**, and **10**, and the dendrons **11 12**, and **13** used for the synthesis of the poly(ether amide) dendrimers under discussion.

The dendrons **11, 12**, and **13** based on 5-(2-aminoethoxy)isophthalic acid (**3**) were synthesized by the convergent method using activation and protection methods from the peptide chemistry.[19] To obtain dendrimers with different core molecules, trimesic acid (**6**) and the acids **8** and **10** were selected as central units. The core molecule **6** is commercially available. 1,3,5-Tris{*N*-[(3-carboxy)propyl]aminocarbonyl}benzene (**8**) is realized as shown in Scheme 2. Reaction of CDI-activated core **6** with 3.1 equiv of deprotonated methyl 4-aminobutanoate hydrochloride gave the ester-terminated amide **7** in 80% yield after precipitation from methanol/diethyl ether. Finally, hydrolysis of the esters and the following acidification of the carboxylate groups into free acid groups **8** is obtained in 65% yield. The synthesis of **10** was carried out using the reaction of CDI-activated core **6** with 3.1 equiv of deprotonated methyl 11-aminoundecanoate hydrochloride in dichloromethane. After purification by precipitation, the yield of ester-terminated amide **9** was 30%. The subsequent conversion of the ester groups in **9** into acid groups has been achieved in 75% yield.

Synthesis of Dendrimers. a. Dendrimers Based on Core Molecule 6. The complete synthesis of dendrimers **14**−**20** is shown in Scheme 4. Coupling of 1 equiv of CDI-activated core **6** with 3.2 equiv of the dendron **11** and an excess of triethylamine in DMF gave dendrimer **14** in 81% yield after precipitation in cold methanol. The reaction of **11** with other core molecules such as 1,3,5-benzenetricarbonyl trichloride or core **6** activated with DCC/HOBT had no significant influence on the yield of **14**. Reaction of 1 equiv of DCC/HOBT-activated core **6** with 3.2 equiv of the dendron **12** and an excess of triethylamine in DMF gave dendrimer **15** as crude product in 45% yield after precipitation in ethyl acetate. A small amount of the crude product **15** was purified by repeated precipitation in ethyl acetate to separate the excess of dendron **12**. The use of TBTU to activate core **6** had no advantage compared to the coupling reagent DCC/HOBT in order to realize dendrimer **15** in higher yields. The coupling of dendron **12** with CDI-activated core **6** resulted in undesired substitution of core **6** with only one or two dendrons of **12**. This incomplete reaction was not observed using DCC/HOBT or TBTU as activating agent. In the synthesis of a third generation poly(ether amide) dendrimer, we observed nearly complete reaction of core **6** with dendron **13** after a long reaction time of about 4 days. But

Scheme 4. Synthetic Route for the Dendrimers 14–20



the complete separation of the excess of dendron **13** from the third generation dendrimer was not possible by flash chromatography or repeated precipitation.

b. Dendrimers Based on Core Molecule 8. The reaction of 3.1 equiv of the dendron **11** and an excess of triethylamine with 1 equiv of the TBTU-activated core **8** in DMF gave dendrimer **16** in 79% yield after precipitation in ethyl acetate. The synthesis of dendrimer **17** was performed using similar conditions (reaction of 3.2 equiv of **12** with 1 equiv of **8**) as for the synthesis of **16**. After first step of purification by precipitation in ethyl acetate, dendrimer **17** was obtained in 88% yield. Then, small amounts of **17** were purified by flash chromatography to separate **17** from residual dendron **12**. Coupling of 1 equiv of TBTU-activated core **8** with 3.3 equiv of the dendron **13** in the presence of excess of triethylamine in DMF gave dendrimer **18** in 83% yield after precipitation in ethyl acetate. Further purification of dendrimer **18** from residual dendron **13** was achieved by flash chromatography.

c. Dendrimers Based on Core Molecule 10. The synthesis of the dendrimer **19** was carried out using the reaction of 3.1 equiv of dendron **11** in the presence of excess of triethylamine with 1 equiv of TBTU-activated core **10** in DMF. After purification, the first generation dendrimer **19** was obtained in 63% yield. Reaction of 1 equiv of TBTU-activated core **10** with 3.2 equiv of the dendron **12** gave the second generation dendrimer **20** in $\leq$78% yield after precipitation in ethyl acetate. **20** was purified by flash chromatography to remove residual dendron **12**. The synthesis of the third generation dendrimer based on dendron **13** and core molecule **10** was successful as proven by NMR, but complete separation of **13** from the resulting dendrimer using flash chromatography could not be achieved.

All isolated dendrimers **14**–**20** as shown in Scheme 4 are well-soluble in DMF, DMAc, and DMSO. Only few milligrams, e.g. of **14**, dissolve in less polar solvents such as dichloromethane or chloroform after prolonged stirring. The inclusion or the adsorption of DMF or DMSO solvent molecules in the dendrimers **14**–**20** was detectable by ^{1}H NMR spectroscopy even after extended drying in a vacuum. This fact was also confirmed in thermogravimetric investigations for most dendrimers. The mass loss found due to the vaporization of residual solvent for the first generation dendrimers **14, 16**, and **19** is higher than for second and third generation dendrimers. This is in contrast to the common assumption that solvent molecules are trapped in the cavities in a large globular dendrimers. In our case it is more likely that solvent molecules are adsorbed at the end groups and outer amide linkages. After vaporization of the residual solvent an increase in thermal stability could be observed for the second generation dendrimers in the range 200–250 °C with **15** having the lowest and **20** the highest stability.

The activating agent TBTU used for the synthesis of the dendrimers **15**–**20** (Scheme 4) enhanced the reactivity of the aliphatic acid groups on **8** and **10** toward amines. The core molecules **8** and **10** activated by CDI and DCC/HOBT showed a lower reactivity toward the primary amines of dendrons **11, 12**, and **13** compared to activation by TBTU.

Characterization of the Dendrimers. a. NMR Spectroscopy. As proven in other convergent syntheses of dendrimers, ^{1}H and ^{13}C NMR spectroscopy are very useful tools in confirming the structure of the final dendritic macromolecules. Figure 1a–c shows the aromatic and amide proton region of the ^{1}H NMR spectra of **16, 17**, and **18**. This selected region of the spectra points to some significant signals of the poly(ether amide) dendrimers. Characteristic chemical shifts were observed for the protons of the core (1) at 8.36 ppm, for the amide group (4) of the core unit at 8.63 ppm, for the aliphatic amide groups (9) at 8.07 ppm, and for the protons of the exterior phenyl groups at approximately 7.6 ppm (13 for **16**, 21 for **17**, and 29 for **18**) and approximately 8.0 ppm (15 for **16**, 23 for **17**, and 31 for **18**). Additionally **17** in Figure 1b and **18** in Figure 1c possess the same chemical shifts for the amide group (17) at approximately 8.7 ppm and the interior phenyl group at approximately 7.5 ppm (13) and at approximately 7.9 ppm (15). In the spectrum of **18** in Figure 1c, additional ^{1}H signals, 29′ and 31′, slightly shifted to low field were observed for the exterior phenyl group. These signals are due to a small amount of impurities in **18,** which was also detected by MALDI-TOF-MS (Figure 2b) and SEC but which could not be removed by any purification procedure. Additional signals for the impurities in **18** did not appear probably due to the low signal intensity. The different chemical shift of the exterior phenyl groups of the impurities may be caused by a different solubilizing behavior compared to **18**. ^{13}C NMR spectroscopy confirmed the identification of the structures of **16, 17**, and **18**.

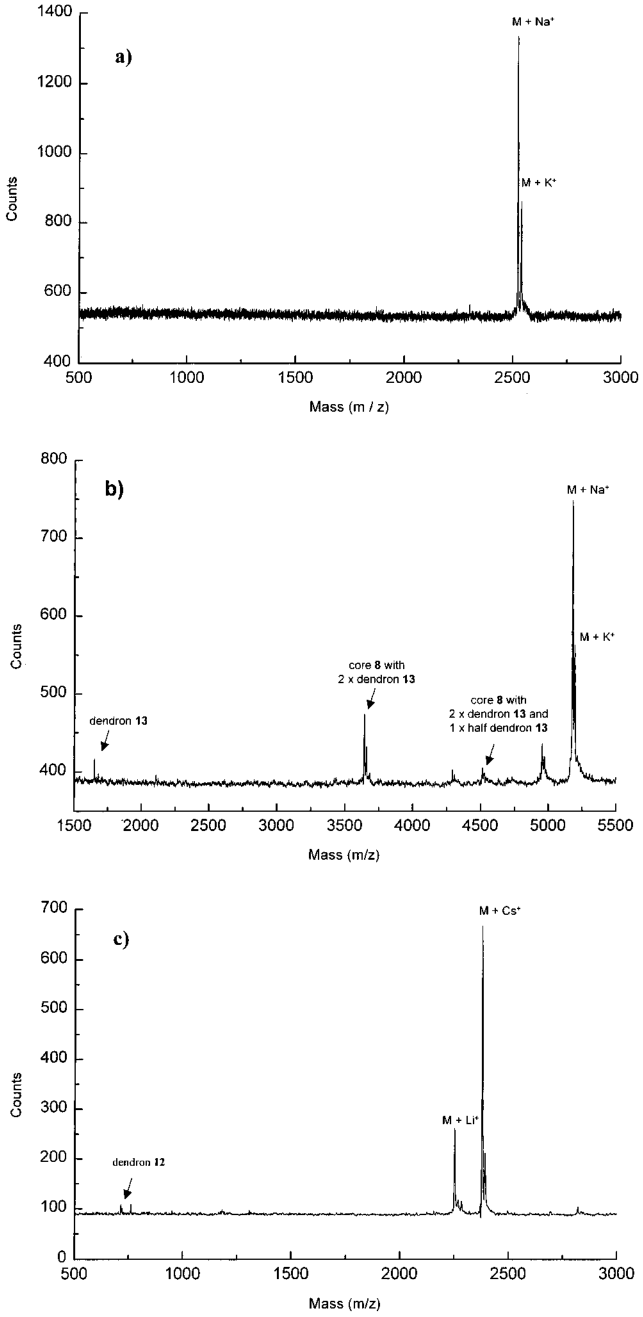


Figure 2. MALDI-TOF mass spectra of (a) **17**, (b) **18**, and (c) **15**.

In general, the signals in the ^{1}H and ^{13}C NMR spectra of the dendrimers **14, 15, 19**, and **20** are not significantly different from the dendrimers **16, 17**, and **18**. Of course, the core molecule **6** without aliphatic spacer resulted in a different chemical shift of the neighboring amide group at the central unit of the dendrimers **14** and **15**. The ^{1}H signal of the corresponding amide group, which

Table 1. Theoretical Molar Masses of the Poly(ether amide) Dendrimers Compared to the Molar Masses Determined by SEC (Solvent: DMF/LiCl) and MALDI-TOF-MS

compd	MM$_{calcd}$ (g/mol)	MALDI-TOF MS m/z	SEC M_p^{a}
14	915.86	917.5	900
15^b	2243.13	2244.2	2200
16	1171.17	1172.5	1100
17	2498.45	2499.0	2790
18^b	5153.00	5154.6	4800
19	1465.74	1466.8	1500
20	2793.01	2793.0	3300

^{a} Molar mass at peak maximum. ^{b} Additional peak in SEC.

is also designated with (4) for **14** and **15** in the experimental part, is observed at approximately 8.9 ppm. Compared to the ^{1}H signal of the amide group (4) for the dendrimers **16, 17**, and **18** as shown in Figure 1a−c, an additional shift of 0.3 ppm to low field was detected for the amide group (4) in **14** and **15**. All ^{1}H and ^{13}C chemical shifts are summarized in the experimental part.

b. SEC and MALDI-TOF-MS. Table 1 provides a comparison of the theoretical molar masses with those obtained from size exclusion chromatography (SEC) and MALDI-TOF-MS. A clear molar mass dependence of elution volume of the different dendritic species could be found. The received MALDI-TOF values for the molar masses of dendrimers **14**−**20** were used for SEC calibration instead of the linear polystyrene (PS) calibration of former investigations.[24] Therefore, the peak maxima (Table 1, M_p) of the SEC agree well with the molar masses determined by MALDI-TOF-MS, and a good correlation between the molar masses of peak maxima determined by SEC (**14**−**20**) and the theoretical calculated values exists. The SEC traces show for **15** and **18** additional peaks of low intensities that appear to be impurities. Therefore, additional experiments by SEC and HPLC in combination with MALDI-TOF-MS are necessary for complete molecular characterization. Also, a strong difference was observed between MALDI-TOF results and SEC results using linear PS standards for the determination of molar masses. The obtained SEC$_{PS}$ values for the molar mass were on average 2 times higher than the molar masses received by MALDI-TOF-MS. Again, this is in contrast to other observations on dendrimers where the globular structure leads to an underestimation and not an overestimation of the molar mass by SEC using calibration with linear standard molecules. One has to assume that the strong polar interactions of the amide and ester groups in the dendritic molecules dominate the behavior more strongly than the globular shape. Work is in progress to explain these unexpected results.[25]

Figure 2a−c outlines the MALDI-TOF mass spectra for dendrimers **17** and **18** based on the core molecule **8** and for dendrimer **15**. The mass spectrum of **17** in Figure 2a shows the mass signals of metal adducts for **17**. No obvious impurities are present. For this sample, there is a good agreement between the determination of structure by NMR, MALDI-TOF-MS, and SEC which show only the desired dendritic molecule. Similar good agreement between NMR, MALDI-TOF-MS, and SEC results is also found for the dendritic poly(ether amide)s **14, 16**, **19,** and **20**. The mass spectrum of **18** in Figure 2b shows impurities at a mass signal of 1651.2 Da corresponding to excess of dendron **13**, at 3641.2 and 3657.2 Da for core molecule **8** with two attached dendrons of **13** (adducts with Na$^+$ and K$^+$), and at 4511.1 Da for core molecule **8** with two attached dendrons of **13** and one attached half-dendron of **13**. The mass spectrum of **15** in Figure 2c corresponds to the desired structure of **15** at 2251.2 Da for M + Li$^+$, at 2267.5 Da for M + Na$^+$, at 2283.4 Da for M + K$^+$, and at 2377.1 Da for M + Cs$^+$ and very low intensities of mass signals at about 700 Da belonging to dendron **12**. The MALDI-TOF results of **15** and **18** correlate with those obtained from SEC measurements. The SEC traces also exhibit additional peaks with very low intensities. However, the MALDI-TOF results confirmed that the desired dendritic poly(ether amide)s were realized with a good level of purity. Nevertheless, the very low differentiation in solubility render the complete purification of the product by chromatography techniques or fractional precipitation very difficult. Therefore, with our dendrimers the high level of purity as described for other dendrimers could not be matched.[26−28]

Table 2. Comparison of T_g Values of the Poly(ether amide) Dendrimers 14−20 Based on Different Core Molecules 6, 8, and 10

dendrimer	compd based on core **6**	T_g (°C)	compd based on core **8**	T_g (°C)	compd based on core **10**	T_g (°C)
1st generation	**14**	82	**16**	70	**19**	20
2nd generation	**15**	83	**17**	97	**20**	83
3rd generation			**18**	114		

In addition, the results obtained from MALDI-TOF-MS show some interesting features[29] when crude samples of the third generation of poly(ether amide) dendrimer **18** were examined. High intensities of the mass signals in MALDI-TOF for the dendron **13** compared to the low signals for the product **18** seem to suggest that the reaction of the dendron **13** with the activated core molecule **8** failed. Nevertheless, SEC of the crude product **18** revealed clear presence of the main product **18** and only low intensity of the signal for the residual dendron **13**. The purified product **18** points out high intensity of the desired mass signal as shown in Figure 2b. Similar preferential detection (based on faster ionization or desorption) of residual dendron **13** by MALDI-TOF-MS in the crude product was also observed for the third generation dendrimer based on core **6**. Again, the MALDI-TOF results were contradicted by SEC measurements. Therefore, MALDI-TOF-MS investigation of crude products should not be used for quantitative analysis of the conversion to the desired dendritic structures. SEC is suited better for control of the qualitative and quantitative composition of dendritic macromolecules before and after working up. Nevertheless, MALDI-TOF-MS analysis is suited best to confirm the presence of molecules of the desired molar mass and is also the most sensitive (but not quantitative) method toward impurities.

c. Differential Scanning Calorimetry. Differential scanning calorimetric analysis of the dendrimers **14**−**20** detected different glass transition temperatures but no melting exotherm. Table 2 summarizes the T_g values. Different trends can be observed comparing dendrimers of increasing generation and with different core molecules. The T_g of **14** and **15** based on the core molecule **6** are similar (82 °C/83 °C), indicating that in this case the T_g's are nearly independent of the molar masses of the dendrons connected. However, the dendrimers **16**−

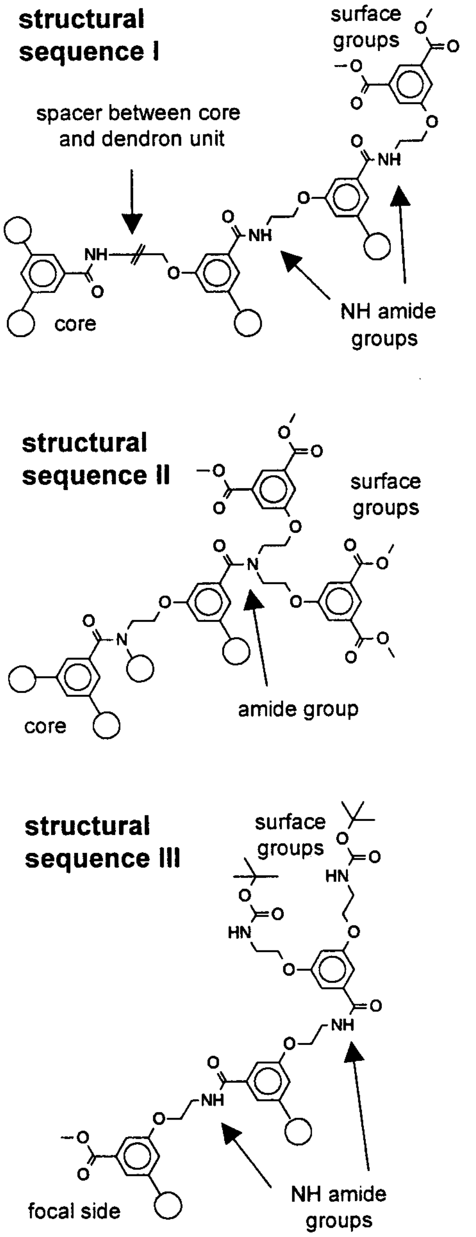
18 based on the core molecule **8** have varying T_g's of 70, 97, and 114 °C. Here, the glass transition temperatures increase with increasing molar mass and are substantially higher than the T_g's of dendrimers **19** and **20** based on the core molecule **10** (20 and 83 °C). In addition, the T_g's decrease within the first generation dendrimers **14, 16**, and **19** with increasing aliphatic chain length in the dendrimer core. As expected, at low generation the flexibility of the core molecule dominates the thermal behavior of the dendritic molecule. The T_g's of the second generation dendrimers **15, 17**, and **20** are all in the range 83–97 °C. Thus, the increasing aliphatic part within the dendrimer has no longer an obvious influence on the T_g. However, the maximum in T_g is not found for the most rigid core in **15** but for **17** with the semiflexible core.

The absence of absolute pure third generation dendrimers based on core molecules **6** and **10** allows only to speculate on their possible T_g since a small amount of impurities can influence strongly the thermal behavior, and thus any experimental investigation of the molecules is meaningless. The T_g value of the third generation dendrimer based on core **6** might be again in the range of 83 °C/84 °C since the results on **14** and **15** point to a low influence of the molar mass of the dendron in this case. Also in the literature it is described theoretically and was observed practically that the T_g values are nearly independent of molar mass for dendritic molecules[30,31] at higher generation when no specific influence of a core molecule or a focal unit is observed. Finally, the third generation dendrimer based on core **10** should exhibit a lower T_g value than **18** (114 °C) based on core **8** but close to or slightly above that of second generation dendrimer **20** (83 °C).

One has to assume that the correlation between the structural features of the dendritic molecules and the glass transition temperatures is very complicated. Flexibility of the structural units, molar mass of the dendrimers, and weight ratio core to dendrons, but also the number and arrangement of strongly interacting groups, e.g., amide functions, have to be taken into account. The latter is probably the main reason for the unexpected results for dendrimers based on core **8**. Here, a continuous increase in T_g with increasing size of the dendrons is found which even exceeds the values for dendrimers with a more rigid core and contradicts previous results that the glass transition should become independent of increasing generation numbers[31] when the influence of the dendrons dominates that of the core molecules. The answer must be found in a special arrangement between the core units and the dendrons.

Comparison of Structural Sequences Based on Different Aromatic Branching Units. A remark seems to be necessary to explain the synthetic difficulties that arose in the synthesis of the presented dendrimers. One has to assume that the educts and products can undergo unfavorable interactions due to the special arrangements of the amide groups. Furthermore, it cannot be excluded that a backfolding tendency of the alkyl spacers of the core molecules may retard the reaction of activated acid groups with the focal amino group of the dendrons. Nevertheless, these problems do not prevent the successful synthesis of dendrimers up to third generation as was proven by NMR and MALDI-TOF-MS. The main problem is to separate dendrimers from residual dendrons and not fully reacted products. The structural features that caused these purification difficulties are shown below (Scheme 5) in comparison with structural sequences of other dendritic poly(ether amide)s.

Scheme 5. Comparison of Functional Groups in Structural Sequence I for Dendrimer 18 with Structural Sequence II for Fourth Generation Dendrimers by Stoddart[21] and Structural Sequence III for Third Generation Dendron by Liskamp[17]



A comparison of the structural sequence I (Scheme 5) for the dendrimers **14**–**20** with the structural sequence II of poly(ether amide) dendrimers described by Stoddart[21] shows that in structure **I** amide groups with free NH functions are present in the inner part of the dendritic macromolecules whereas in structure **II** only dialkylated amide groups can be found in the dendrimer. Both sequences are characterized by methyl esters as surface groups. The NH amide groups in structure **I** can undergo unfavorable interactions (e.g., with residual dendrons or with column chromatography material) during the purification which is reduced in structure **II**. Thus, it was possible to prepare and the purify dendrimers up to generations 4 based on the structure **II**.[21] Additional, the methyl ester groups as end groups allow solubility only in very polar solvents, e.g., DMAc or DMF which are well-known for strong interactions. The structural sequence III in Scheme 5 shows the reversed case of functional groups in a third generation poly(ether amide) dendron which were realized by Liskamp et al.[17] Compared to the structural sequence I of **18**, the methyl ester group is now only at the focal side, and NH amide groups are also present in the inner part of the dendrons, but Boc-protected amino groups form the surface groups. The reversal of the functional groups causes a better solubility in THF, ethyl acetate, or dichloromethane, solvents exhibiting less polar interactions and thus simplifying the purification of larger dendritic macromolecules. The deciding factor for an increased solubility is the voluminous surface group of the dendrons.[17]

Conclusion

This work describes the convergent syntheses of a series of novel poly(ether amide) dendrimers possessing different core molecules. The coupling of these core molecules with three dendrons could be achieved in most cases preferably by TBTU activation. The incorporated core molecules have a significant influence on the properties of the dendrimers and result for example in different T_g values. The values range between 20 and 114 °C for macromolecules having identical aliphatic−aromatic repeating units in the dendrons and identical end groups. These results demonstrate very well the complexity of structure−property relationship in dendrimers.

The above-mentioned structural features did not limit the synthetic growth of the dendrimers but caused major purification difficulties of third generation dendrimers based on core molecules **6** and **10**. To solve such problems, it is necessary to create dendritic poly(ether amide)s with more voluminous surface groups. The future will show that the reaction of Boc-protected amino groups as surface groups in dendrons with defined central units is a helpful tool in order to create pure higher generation poly(ether amide) dendrimers than the dendrimers **14**−**20** presented here.

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