Synthesis and Characterisation of Polyamide Dendrimers with Systematically Varying Surface Functionality

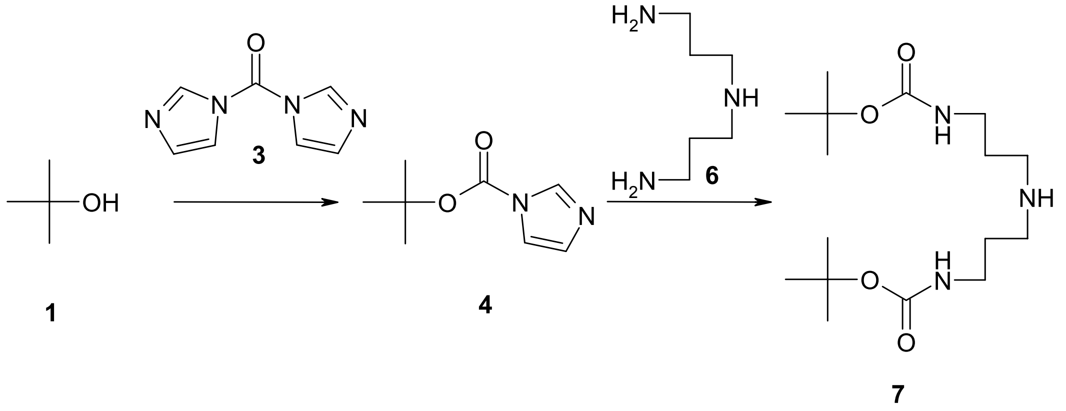
Helen Willcock, Andrew I Cooper, Dave J Adams and Steve P Rannard*

Supporting information.

NOTE: - CDI purity.

The purity of CDI (**3**) may vary from as little as 60% up to 98% between commercial samples of purchased material (identical nominal grade). This is possibly due to hydrolysis during storage. To ensure accuracy during syntheses, purity was determined by measuring CO_2 evolved when CDI was reacted with water. The measured purity was used to modify the nominal weight (and therefore nominal moles) of CDI added to each reaction. In all experiments that follow, the stated molar quantities of CDI used are nominal figures (based on actual weight of material added to the reaction) and have been adjusted to ensure stoichiometry after purity analysis.

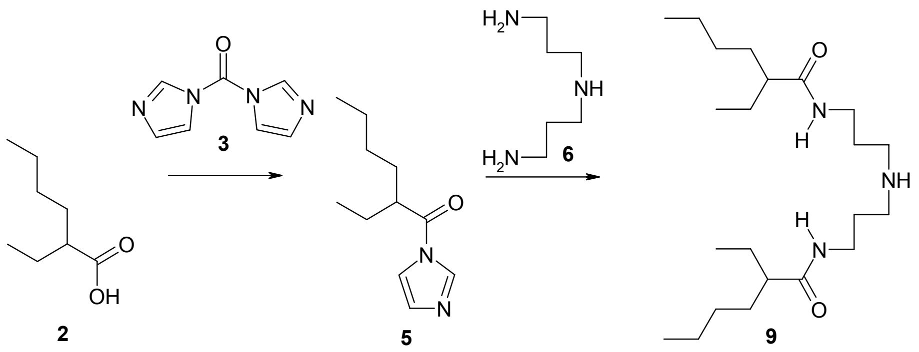
Synthesis of symmetric first generation polyamide dendron 7.



Scheme S1 - Synthesis of symmetric first generation polyamide dendron 7.

Dry toluene (100mL) and *t*-butanol (**1**) (11.91 g, 161 mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. CDI (**3**) (13.60 g, 84 mmol) was added via a powder addition funnel and the mixture was heated to 60°C with stirring for 5 h. A solution of DPTA (**6**) (5.77 g, 44 mmol) in dry toluene (60 mL) was added dropwise via a pressure equalising dropping funnel. The reaction mixture was stirred at 60°C for 18 h, then left to cool and concentrated *in vacuo*. The resulting liquid was dissolved in CH_2Cl_2 (60 mL) and washed 3 times with distilled water (3 x 60 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give **7** as a white powder (12.02g, 86%). Found C, 57.77; H, 10.19; N, 12.77%. $C_{16}H_{33}N_3O_4$ requires, C, 57.98; H, 10.04; N, 12.68%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.8, 30.2, 39.3, 47.8, 79.4, 156.6. ^1H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 18H, $COOC(C\underline{H}_3)_3$) 1.64 (m, 4H, $CH_2C\underline{H}_2CH_2$), 2.65 (t, 4H, $NH(C\underline{H}_2)_2$), 3.21 (q, 4H, $OCONHC\underline{H}_2$), 5.15 (br, $OCON\underline{H}$). *m/z* (ES+ MS) 332 $[M+H]^+$.

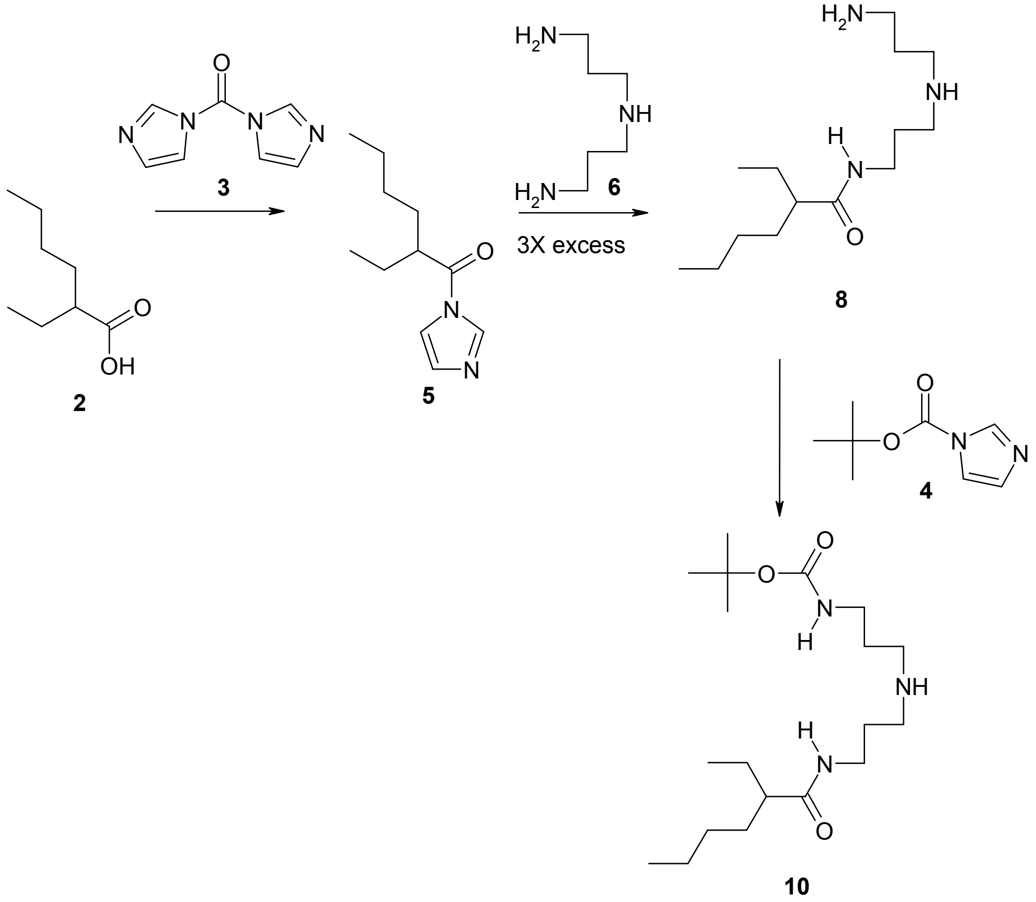
Synthesis of symmetric first generation polyamide dendron 9.



Scheme S2 - Synthesis of symmetric first generation polyamide dendron ***9****.*

Dry toluene (90mL) and CDI (**3**) (9.32 g, 57.5 mmol, 1.15 X excess) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. The mixture was heated to 60°C and a solution of **2** (7.20 g, 50 mmol) in toluene (10 mL) was added slowly (to control CO_2 evolution) via a pressure equalising dropping funnel. After the addition was complete, the mixture was stirred at 60°C whilst being purged with dry N_2 for 30 mins. A solution of DPTA (**6**) (3.7 mL, 26.25 mmol) in toluene (5 mL) was added dropwise via a pressure equalising dropping funnel. The reaction mixture was stirred at 60°C for 18 h, then left to cool and concentrated *in vacuo*. The resulting liquid was dissolved in CH_2Cl_2 (50 mL) and washed 3 times with water (3 x 50 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give **9** as a semicrystalline solid (9.19g, 96%). Found C, 68.68; H, 11.89; N, 11.02%. $C_{22}H_{45}N_3O_2$ requires, C, 68.88; H, 11.82; N, 10.95%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 14.8, 21.9, 24.1, 27.6, 30.7, 31.4, 34.1, 38.4, 48.3, 50.6, 179.2. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (m, 12H, $CH_2C\underline{H}_3$), 1.25-1.70 (overlapping m, 20H, $C\underline{H}_2$), 2.07 (m, 2H, $COC\underline{H}(CH_2)_2$) 2.59 (t, 4H, $NH(C\underline{H}_2)_2$), 3.24 (t, 4H, $CONHC\underline{H}_2$) 6.65 (t, $CHCON\underline{H}$). *m/z* (CI+ MS NH_4) 384 $[M+H]^+$.

Synthesis of asymmetric first generation polyamide dendron 10.



*Scheme S3 - Synthesis of asymmetric first generation dendron **10**.*

Dry toluene (100 mL) and CDI (**3**) (9.32 g, 57.5 mmol, 1.15 X excess) were added to a 250mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. The mixture was heated to 60°C and a solution of **2** (7.20 g, 50 mmol) in toluene (10 mL) was added slowly (to control CO_2 evolution) via a pressure equalising dropping funnel. After the addition was complete, the mixture was stirred at 60°C whilst being purged with dry N_2 for 30 mins. This solution was then added slowly dropwise to a stirred solution of DPTA (**6**) (21.2 mL, 150 mmol, 3X excess) in dry toluene (50 mL) at 60°C. The reaction mixture was stirred at 60°C for 16 h, after which it was cooled and extracted into distilled water (50 mL). The volume of water was reduced in *vacuo* to 20 mL and the product was extracted using DCM (50 mL). The solution was dried using anhydrous Na_2SO_4 and the solvent removed in *vacuo* to give **8** as a colourless oil (12.2 g, 95%) that was used without further purification for the next step. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (m, 6H, $CH_2C\underline{H}_3$), 1.27 (m, 4H, $C\underline{H}_2$), 1.42-1.58 (d of m, 4H, $C\underline{H}_2$), 1.65 (m, 4H, $C\underline{H}_2$), 1.96 (m, 1H, $COC\underline{H}(CH_2)_2$), 2.67 (m, 4H, $NH(C\underline{H}_2)_2$), 2.79 (t, 2H, $C\underline{H}_2NH_2$), 3.36 (q, 2H, $CONHC\underline{H}_2$), 7.25 (t, $N\underline{H}$). *m/z* (CI+ MS NH_4) 258 $[M+H]^+$.

Dry toluene (100 mL) and *t*-butanol (**1**) (4.44 g, 60 mmol, 1.5 X excess) were added to a 250mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. CDI (**3**) (7.1 g, 44 mmol, 1.1X excess) was added via a powder addition funnel and the mixture was heated to 60°C with stirring for 5 h. **8** (10.79g, 42mmol) was added and the reaction mixture was stirred at 60°C for 18 h, then left to cool and concentrated *in vacuo*. The resulting liquid was dissolved in CH_2Cl_2 (60 mL) and washed 3 times with distilled water (3 x 60 mL) and once with a saturated NaCl solution (60 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give **10** as a clear colourless, viscous liquid (12.02g, 84%). Found C, 62.72; H, 11.01; N, 12.10%. $C_{22}H_{46}N_4O_2$ requires, C, 63.83; H, 10.99; N, 11.75%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 14.8, 21.9, 24.1, 28.8, 30.2, 39.3, 47.8, 50.6, 79.4, 156.5, 176.4. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (overlapping t, 6H, $CH_2C\underline{H}_3$) 1.27 (m, 4H, $C\underline{H}_2$), 1.44 (s, 9H, $COOC(C\underline{H}_3)_3$), 1.40-1.71 (overlapping m, 8H, $C\underline{H}_2$), 1.91 (m, 1H $COC\underline{H}(CH_2)_2$), 2.66 (overlapping t, 4H, $NH(C\underline{H}_2)_2$), 3.21 (q, 2H, $OCONHC\underline{H}_2$), 3.36 (q, 2H, $CHCONHC\underline{H}_2$), 5.20 ($OCON\underline{H}$), 6.53 ($CHCON\underline{H}$). *m/z* (ES+ MS) 358 $[M+H]^+$.

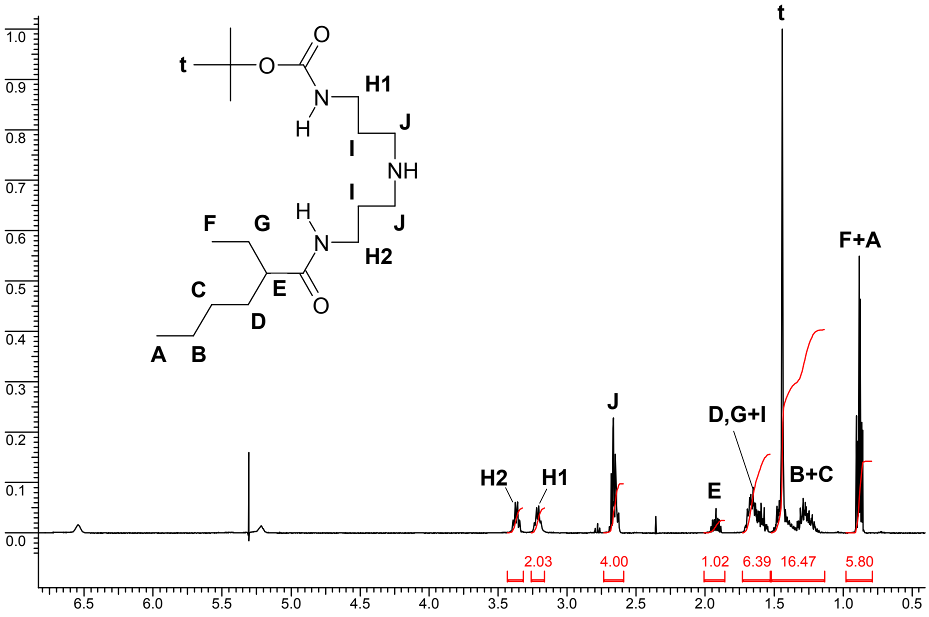


*Figure S1 - ^{1}H NMR of asymmetric first generation dendron **10** in $CDCl_3$*

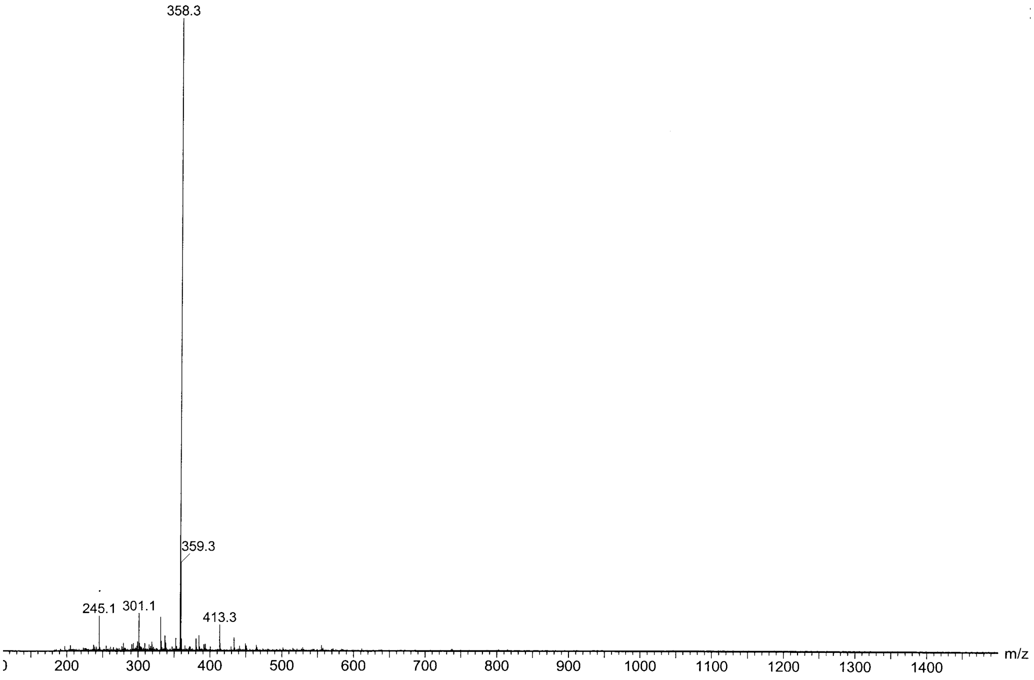
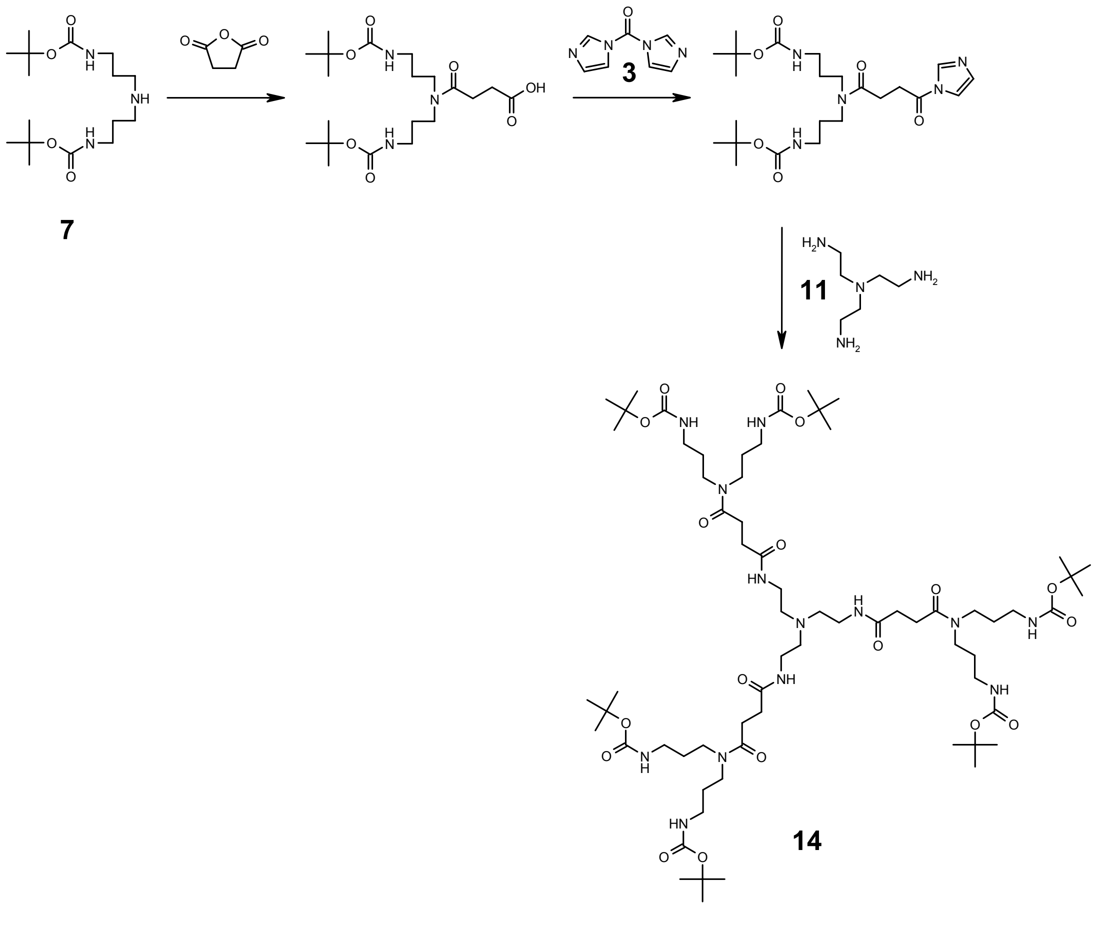


Figure S2 - Electrospray mass spectrum of **10** *showing $[M+H]^+$ (actual mass 357).*

Synthesis of Polyamide Dendrimer14.



*Scheme S4 – Synthesis of symmetric first generation polyamide dendrimer **14**.*

Dry toluene (100 mL) and **7** (16.55 g, 50 mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. Succinic anhydride (5.0 g, 50 mmol) was added and the mixture was heated to 60°C until the solid anhydride had completely disappeared. CDI (**3**) (8.1 g, 50 mmol) was added slowly such that the CO_2 evolution was controlled. After the complete addition of **3**, the solution was purged with dry N_2 whilst stirring at 60°C for 30 minutes. The solution was then transferred to a 3-necked round-bottomed flask containing TAEA (**11**) (2.43 g, 16.6 mmol) and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and concentrated *in* *vacuo*. The resulting viscous liquid was dissolved in CH_2Cl_2 (40 mL) and washed 3 times with water (3 x 40 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*, then purified by silica gel chromatography eluting with ethyl acetate:methanol (9:1) to give **14** as a foamed solid (20.2g, 88%) Found C, 57.23; H, 8.93; N, 13.07%. $C_{66}H_{123}N_{13}O_{18}$ requires, C, 57.16; H, 8.94; N, 13.13%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.3, 29.4, 31.3, 37.8, 38.4, 38.7, 43.0, 45.5, 54.7, 156.5, 173.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (d, 54H, $COOC(C\underline{H}_3)_3$), 1.65-1.83 (d of m, 12H, $CH_2C\underline{H}_2CH_2$), 2.54 (m, 6H, $N(C\underline{H}_2)_3$), 2.54-2.69 (d of m, 12H, $CON(C\underline{H}_2)_2$), 3.04 (m, 6H, $(CH_2)_2NCOC\underline{H}_2$), 3.15 (m, 6H, $NHCOC\underline{H}_2$), 3.23 (m, 6H, $N(CH_2C\underline{H}_2)_3$), 3.37 (m, 12H, $OCONHC\underline{H}_2$), 5.26 (br, $OCON\underline{H}$), 5.34 (br, $OCON\underline{H}$), 7.52 (br, $CH_2CON\underline{H}$). *m/z* (ES+ MS) 1386 $[M+H]^+$, 1408 $[M+Na]^+$. GPC; M_w = 1682, PDI = 1.08.

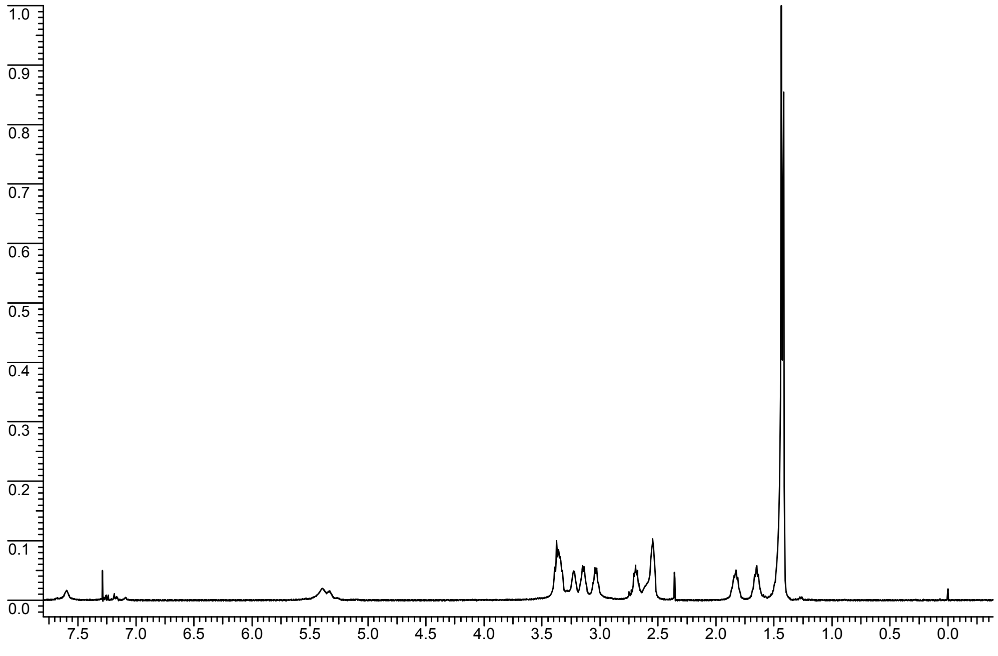


*Figure S3 - ^{1}H NMR of symmetric first generation dendrimer **14** in $CDCl_3$.*

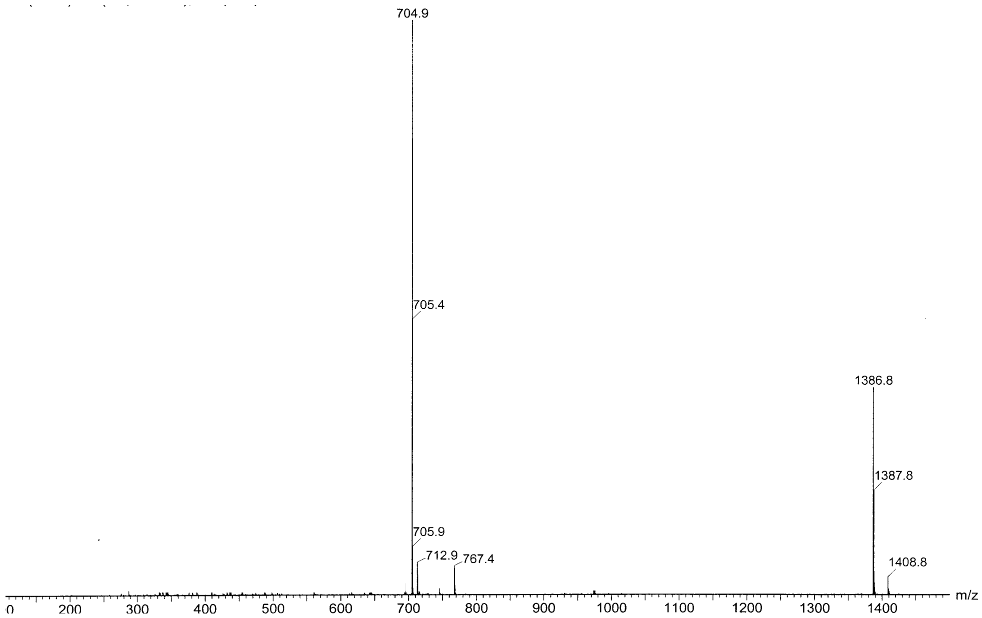


Figure S4 - Electrospray mass spectrum of **14** *showing* $[M+Na+H]^{2+}$ *at m/z 704 and* $[M+H]^{+}$ *at 1386 (actual mass 1385).*

Synthesis of Polyamide Dendrimer 16.

The procedure was similar to that described for the synthesis of **14**, but using **10** as the starting material. The purification step was achieved by silica gel chromatography (eluting with ethyl acetate:methanol 9:1 increasing to 1:1) to give **16** as a foamed solid (3.22 g, 53%). Found C, 59.60; H, 9.50; N, 12.60%. $C_{75}H_{141}N_{13}O_{15}$ requires, C, 61.49; H, 9.70; N, 12.43%. ^{13}C NMR (100 MHz, MeOD) δ 12.6, 14.4, 23.1, 26.4, 29.5, 32.8, 36.9, 45.6, 49.7, 156.4, 173.9, 176.4, 177.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (m, 18H, $C\underline{H}_3$), 1.28-2.00 (overlapping m, 66H, $(CH_2)_2$, aliphatic $C\underline{H}_2$, $COOC(C\underline{H}_3)_3$, $CON(CH_2C\underline{H}_2CH_2)_2$), 2.54 – 2.70 (overlapping m, 18H, $N(C\underline{H}_2CH_2)_3$, $CON(C\underline{H}_2CH_2CH_2)_3$), 3.20 – 3.38 (overlapping m, 30H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$, $C\underline{H}_2NHCO(EH)$, $C\underline{H}_2NHCOO(CH_3)_3$), 6.53 (br, $N\underline{H}$), 6.83 (br, $N\underline{H}$), 7.55 (br, $N\underline{H}$), 7.65 (br, $N\underline{H}$). *m/z* (ES+ MS) 755 $[M+2Na]^{2+}$, 1487 $[M+Na]^{+}$. GPC; $M_w = 1604$, PDI = 1.02.

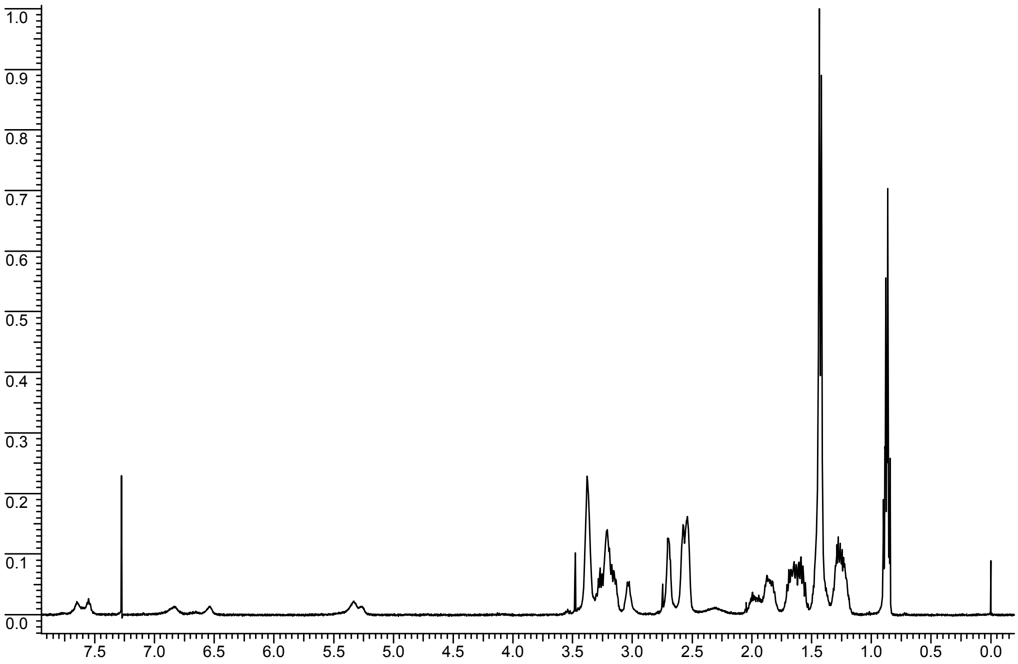


*Figure S5 - ^{1}H NMR of symmetric first generation dendrimer **16** in $CDCl_3$.*

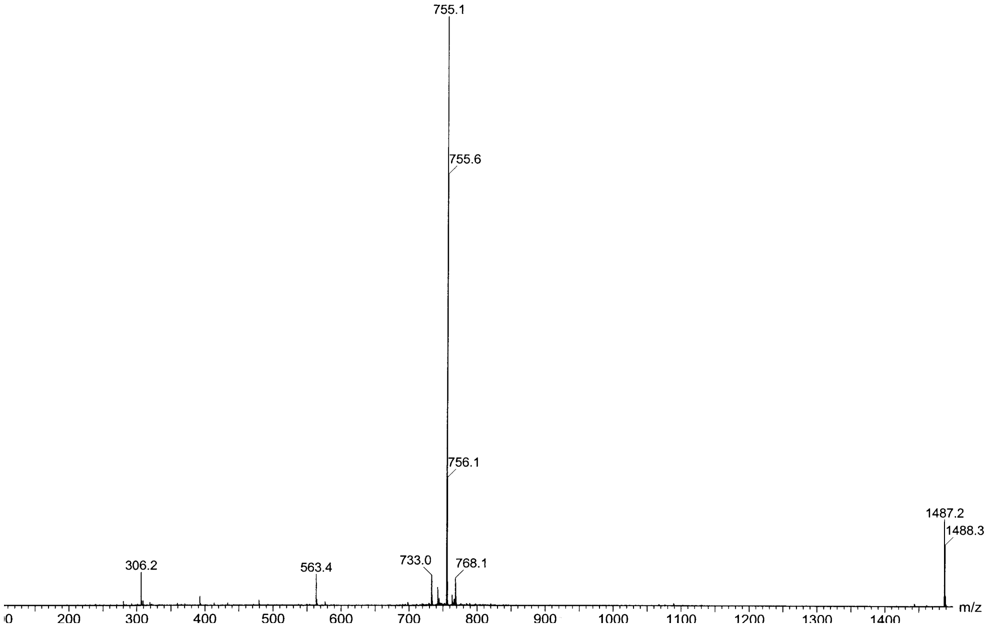


Figure S6 - Electrospray mass spectrum of **16** *showing $[M+2Na]^{2+}$ at m/z 755 and $[M+Na]^{+}$ at m/z 1487 (actual mass 1463).*

Synthesis of Polyamide Dendrimer 18.

The procedure was similar to that described for the synthesis of **14**, but using **9** as the starting material and THF as the solvent. During the reaction the material gelled the solvent several times, vigorous stirring with a spatula was required before addition of further reactants. The material was purified by silica gel chromatography eluting with EtOAc:MeOH (7:3) to give **18** as a sticky solid (5.1 g, 81%). Found C, 65.13; H, 10.44; N, 11.72%. $C_{84}H_{159}N_{13}O_{12}$ requires, C, 65.38; H, 10.38; N, 11.80%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.4, 23.1, 26.4, 28.2, 30.7, 32.9, 36.8, 38.7, 43.0, 45.5, 49.7, 54.7, 173.1, 176.5, 177.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (m, 36H, $C\underline{H}_3$), 1.26 – 1.58 (overlapping m, 48H, aliphatic $C\underline{H}_2$), 1.69 – 1.86 (d of m, 12H, $CON(CH_2C\underline{H}_2CH_2)_3$), 1.98 (m, 6H, $NHCOC\underline{H}(CH_2)_2$), 2.53 (m, 6H, $N(C\underline{H}_2)_3$), 2.58 – 2.68 (d of m, 12H, $CON(C\underline{H}_2)_2$), 3.20 – 3.27 (overlapping m, 18H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$), 3.39 (m, 12H, $C\underline{H}_2NHCO(EH)$)), 6.58 (t, N$\underline{H}$), 6.83 (t, N$\underline{H}$), 7.57 (t, N$\underline{H}$), *m/z* (ES+ MS) 783 $[M+H+Na]^{2+}$, 794 $[M+2Na]^{2+}$. (GPC data not obtained as material gelled THF).

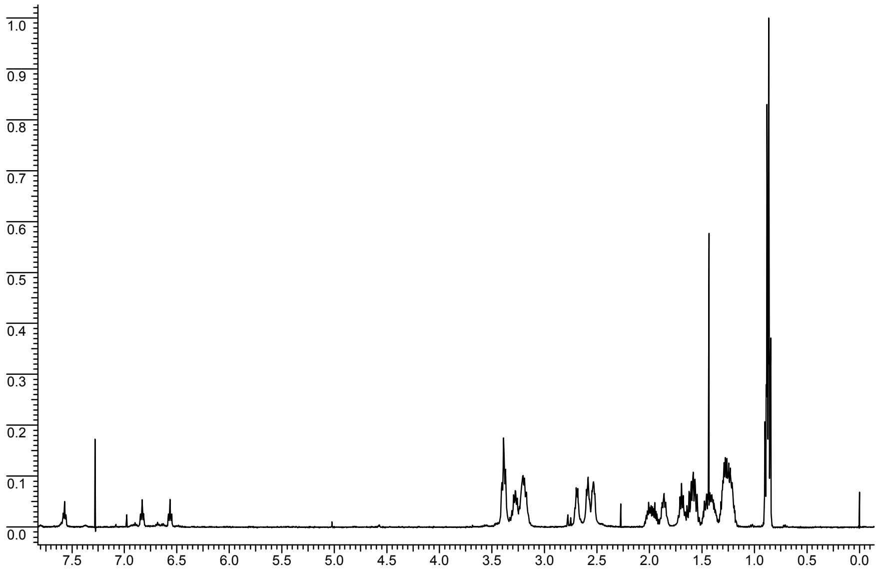


*Figure S7 - ^{1}H NMR of symmetric first generation dendrimer **18** in $CDCl_3$.*

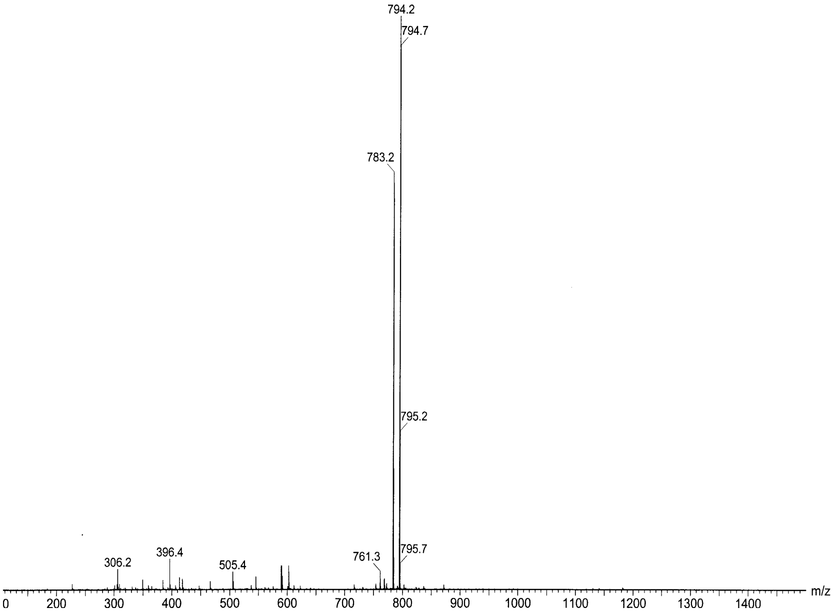


Figure S8 - Electrospray mass spectrum of **18** *showing* $[M+H+Na]^{2+}$ *at m/z 783 and* $[M+2Na]^{2+}$ *at m/z 794 (actual mass 1541).*

Synthesis of Polyamide Dendrimer 19.

The procedure was similar to that described for the synthesis of **14**, but using bis(2-ethyl hexyl) amine (BEHA) as the starting material. The purification step was achieved by silica gel chromatography (eluting with ethyl acetate:methanol 9:1 increasing to 1:1) to give **19** as a viscous liquid (16.30 g, 88%). Found C, 70.42; H, 11.79; N, 8.47%. $C_{66}H_{129}N_7O_6$ requires, C, 70.98; H, 11.64; N, 8.78%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 14.5, 23.5, 24.2, 29.1, 30.9, 31.7, 37.4, 38.6, 49.3, 51.5, 54.4, 172.9, 173.2. ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (m, 36H, $C\underline{H}_3$), 1.26 (m, 48H, aliphatic $C\underline{H}_2$), 1.63 (m, 6H, $C\underline{H}(CH_2)_3$), 2.53 (m, 6H, $N(C\underline{H}_2)_3$), 2.53-2.69 (d of m, 12H, $CONC\underline{H}_2CH(CH_2)_2$), 3.20-3.32 (overlapping t and m, 18H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$), 7.54 (t, NH – disappears on addition of a drop of D_2O). *m/z* (ES+ MS) 1117 $[M+H]^+$. GPC; M_w = 1712, PDI = 1.18.

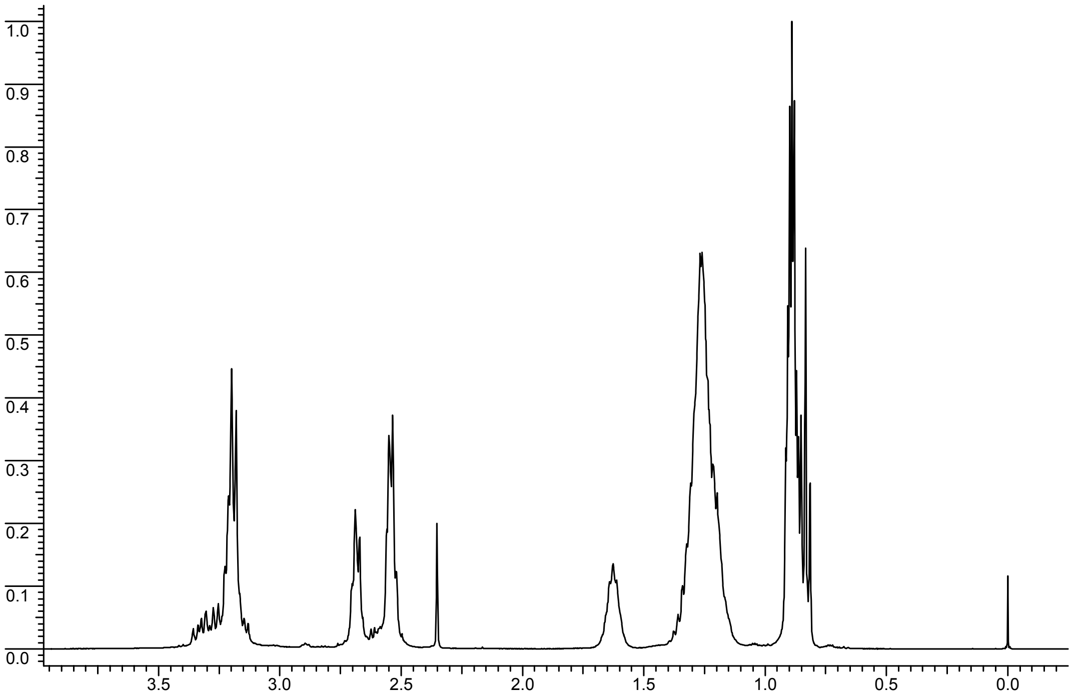


*Figure S9 - ^{1}H NMR of symmetric first generation dendrimer **19** in CDCl$_3$.*

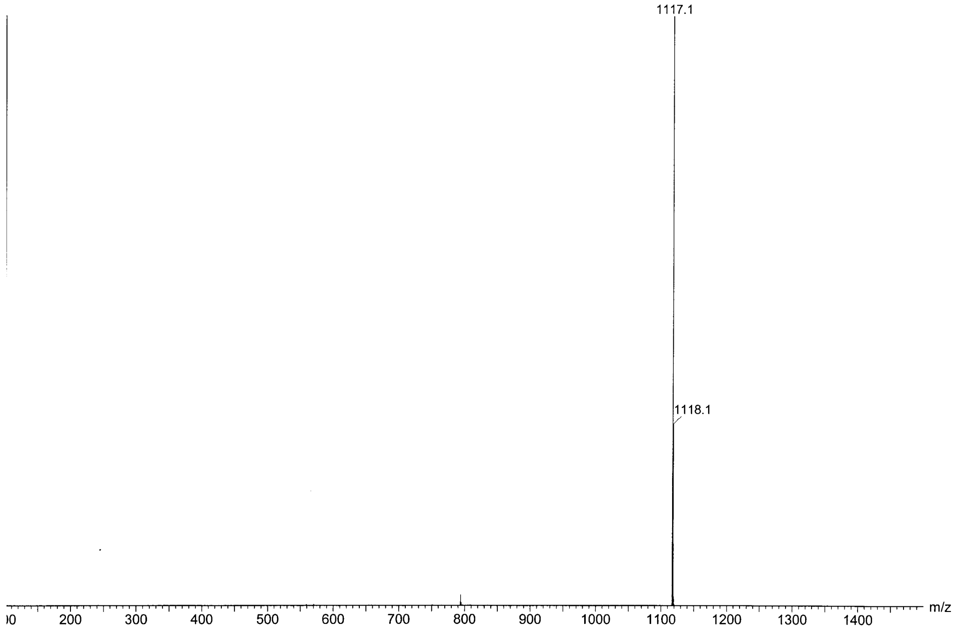
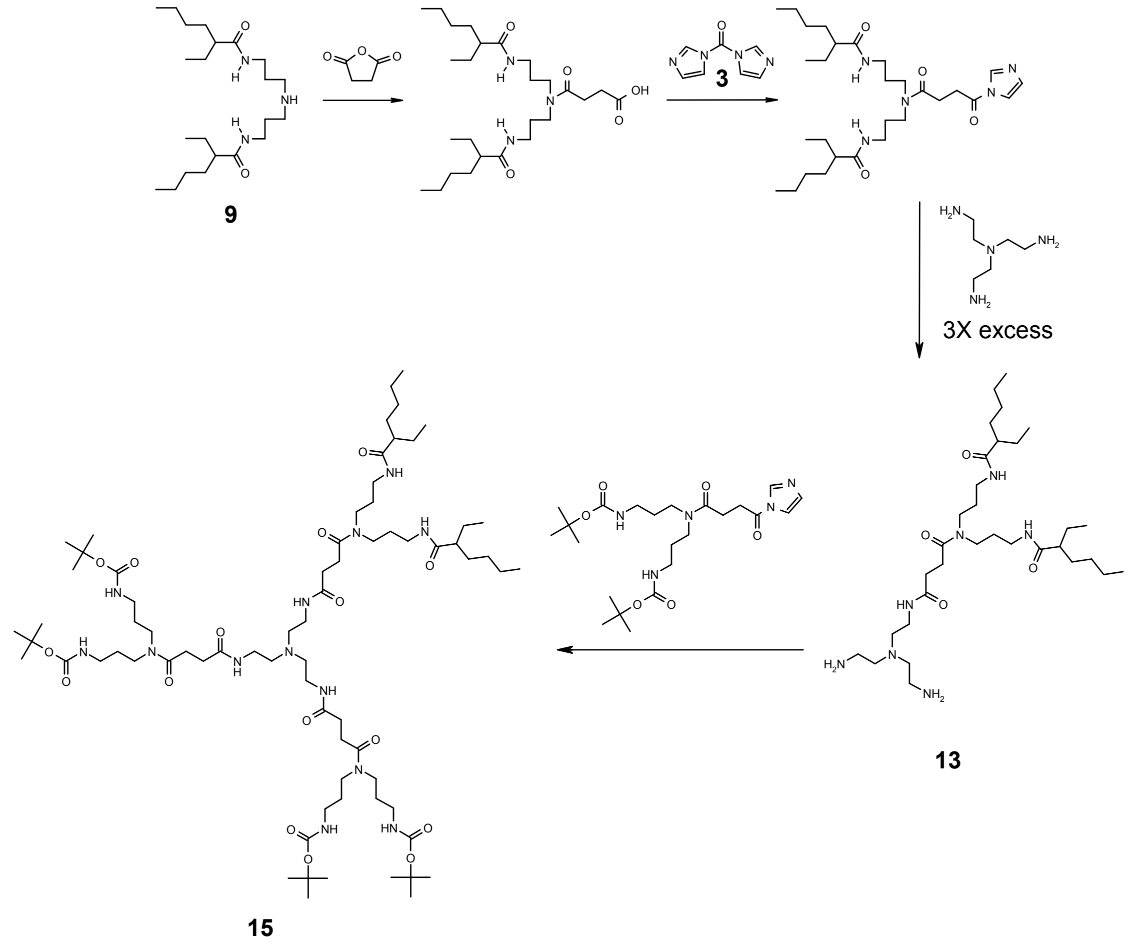


Figure S10 - Electrospray mass spectrum of **19** *showing [M+H]$^+$ at m/z 1117 (actual mass 1116).*

Synthesis of Polyamide Dendrimer 15.



*Scheme S5 - Synthesis of asymmetric first generation dendrimer **15**.*

Dry THF (40 mL) and **9** (4.38 g, 11.4 mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. Succinic anhydride (1.14 g, 11.4 mmol) was added and the mixture was heated to 60°C until the solid anhydride had completely disappeared. **3** (1.95 g, 12 mmol, 1.05 X excess, 95% purity) was added slowly such that the CO_2 evolution was controlled. After the complete addition of **3**, the solution was purged with dry N_2 whilst stirring at 60°C for 30 minutes. During the reaction the material gelled the solvent several times, vigorous stirring with a spatula was required before addition of further reactants. The solution was then added slowly dropwise to a round bottomed flask containing TAEA (**11**) (5.2 g, 30 mmol, 3 X excess) in THF (50 mL) and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and concentrated *in vacuo*. The resulting viscous liquid was dissolved in CH_2Cl_2 (30 mL) and washed 3 times with water (3 x 50 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo* to give **13** as a viscous liquid (4.56 g, 65%) that was used without further purification for the next step. *m/z* (ES+ MS) 612 $[M+H]^+$, 634 $[M+Na]^+$.

Dry toluene (30 mL) and **7** (4.68g, 14.1mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. Succinic anhydride (1.41 g, 14.1 mmol) was added and the mixture was heated to 60°C until the solid anhydride had completely disappeared. CDI (**3**) (2.40 g, 14.8 mmol, 1.05 X excess, 95% purity) was added slowly such that the CO_2 evolution was controlled. After the complete addition of CDI, the solution was purged with dry N_2 whilst stirring at 60°C for 1h. **13** (4.32 g, 7.1 mmol) in toluene (20 mL) was added and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and concentrated *in vacuo*. The resulting viscous liquid was dissolved in CH_2Cl_2 (60 mL) and washed 3 times with water (3 x 60 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*, then purified by silica gel chromatography eluting with EtOAc:MeOH (9:1 increasing to 1:1) to give **15** as a crispy pale yellow solid (4.4g, 43%). Found C, 59.47; H, 9.32; N, 12.60%. $C_{72}H_{165}N_{13}O_{16}$ requires, C, 60.10; H, 9.46; N, 12.65%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.3, 23.1, 26.4, 28.2, 30.7, 32.5, 36.8, 38.7, 43.1, 45.5, 49.7, 54.6, 156.2, 173.1, 176.5, 177.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (m, 12H, $C\underline{H}_3$), 1.20-1.99 (overlapping m, 74H, integration higher than expected due to water overlapping peak, $NHCOC\underline{H}(CH_2)_2$, aliphatic $C\underline{H}_2$, $COOC(C\underline{H}_3)_3$, $CON(CH_2C\underline{H}_2CH_2)_2$), 2.54-2.70 (overlapping m, 18H, $N(C\underline{H}_2CH_2)_3$, $CON(C\underline{H}_2CH_2CH_2)_3$), 3.03-3.38 (overlapping m, 30H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$, $C\underline{H}_2NHCO(EH)$, $C\underline{H}_2NHCOO(CH_3)_3$), 5.25 (br, NH), 5.34 (br, N$\underline{H}$), 6.62 (br, N$\underline{H}$), 6.83 (br, N$\underline{H}$), 7.58 (br, NH). *m/z* (ES+ MS) 742 $[M+2Na]^{2+}$, 1461 $[M+Na]^+$. GPC; $M_w = 1890$, PDI = 1.10.

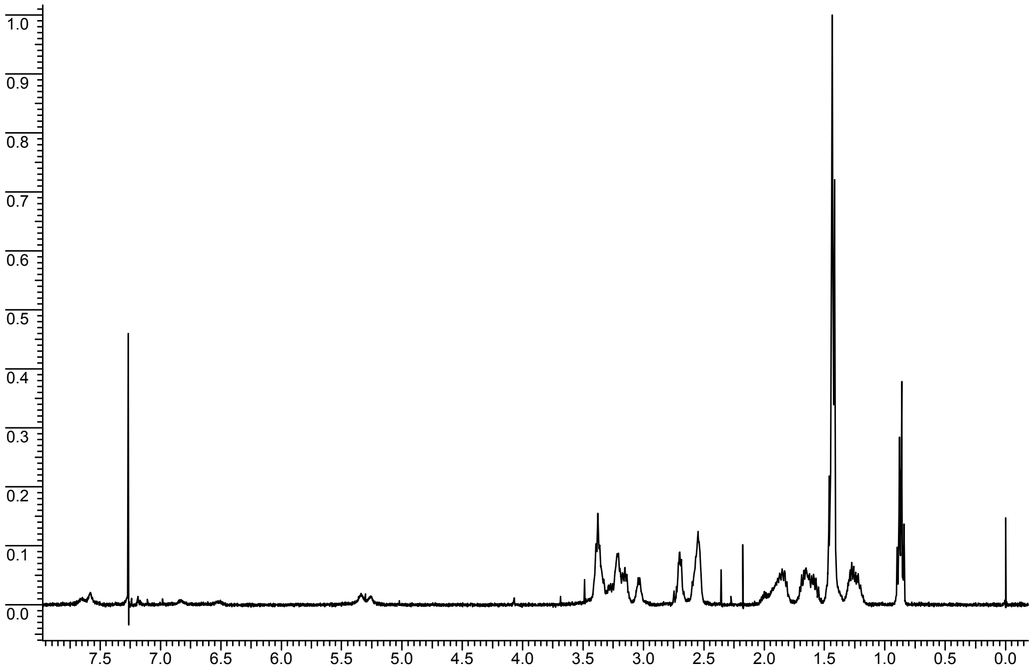


*Figure S11 – NMR spectrum of asymmetric first generation dendrimer **15** in $CDCl_3$.*

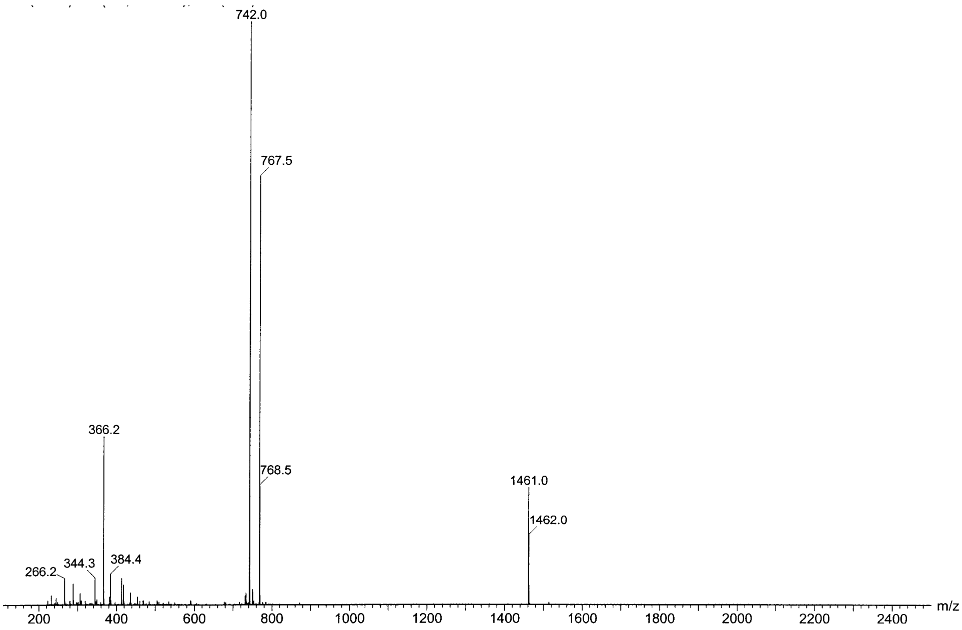
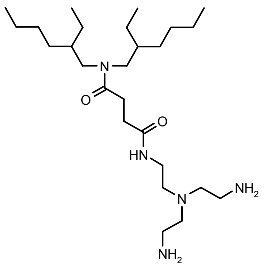


Figure S12 - Electrospray mass spectrum of **15** *showing [M+2Na]$^{2+}$ at m/z 742 and [M+Na]$^{+}$ at m/z 1461 (actual mass 1438).*

Synthesis of asymmetric polyamide Dendrimer 20.

The procedure was similar to that described for the synthesis of **13**, but using BEHA as the starting material, to give **S24** as a viscous liquid (22.37g, 95%). Found C, 65.42; H, 11.71; N, 13.69%. $C_{26}H_{55}N_5O_2$ requires, C, 65.88; H, 11.80; N, 13.91%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.2, 14.7, 21.8, 23.4, 24.1, 29.4, 31.8, 37.3, 38.0, 39.9, 49.2, 51.6, 56.2, 173.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.89 (m, 12H), 1.26 (m, 16H), 1.63 (m, 2H), 2.54 (m, 8H), 2.66 (m, 2H), 2.76 (t, 4H), 3.18 (t, 2H), 3.28 (m, 4H). *m/z* (ES+ MS) 470 [M+H]$^{+}$,492 [M+Na]$^{+}$.



S24

Figure S13 – Structure of monosubstituted intermediate **S24**.

The procedure was similar to that described for the synthesis of **15**, using **S24** in the place of **13**. Purification was achieved by silica gel chromatography eluting with EtOAc:MeOH (95:5 increasing to 1:1) to give **20** as a glassy solid (6.87g, 50.5%). Found C, 61.04; H, 9.82; N, 11.61%. $C_{66}H_{125}N_{11}O_{14}$ requires, C, 61.13; H, 9.72; N, 11.88%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.3, 14.4, 23.5, 24.4, 29.1, 30.9, 31.7, 37.4, 38.5, 49.3, 51.5, 54.4, 156.5, 172.9, 173.0. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83-0.90 (m, 12H, $C\underline{H}_3$), 1.26 (m, 16H, aliphatic $C\underline{H}_2$), 1.44 (d, 36H, $COOC(C\underline{H}_3)_3$), 1.65 – 1.83 (overlapping m, 10H, $CH_2C\underline{H}_2CH_2NHCOO$ and $C\underline{H}(CH_2)_3)$), 2.55 (m, 6H, $N(C\underline{H}_2)_3$), 2.55 - 2.70 (d of m, 12H, $CON(C\underline{H}_2)_2$), 3.04-3.20 (overlapping m, 18H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$), 3.37 (m, 8H, $OCONHC\underline{H}_2$), 5.38 (br, $OCON\underline{H}$), 5.43 (br, $OCON\underline{H}$), 7.58 (br, $CH_2CON\underline{H}$). *m/z* (ES+ MS) 1297 $[M+H]^+$. GPC; $M_w = 2047$, PDI = 1.04.

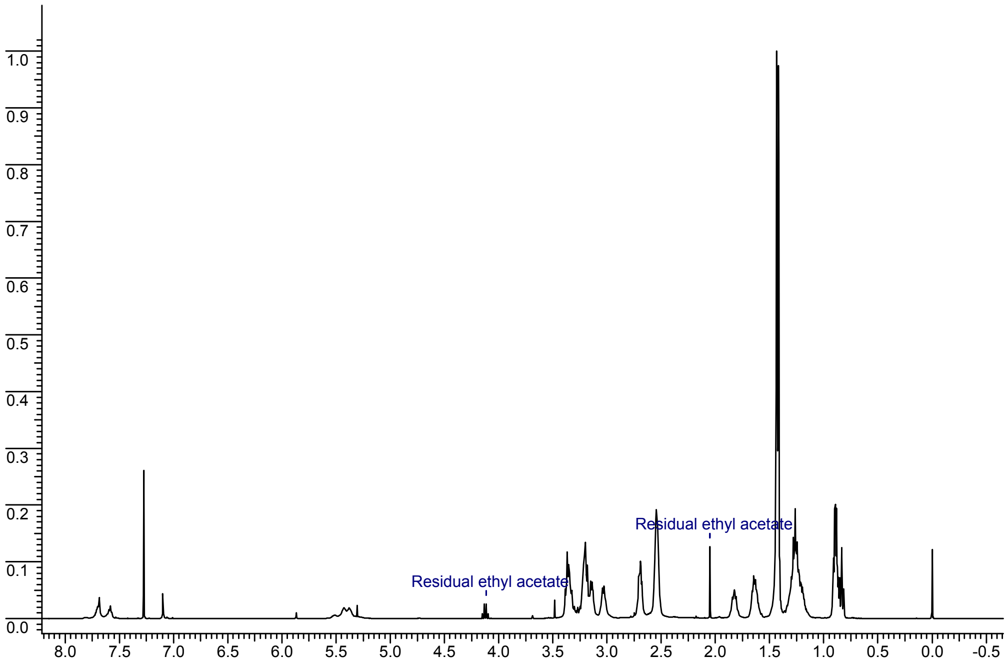


*Figure S14 - NMR spectrum of asymmetric first generation dendrimer **20** in $CDCl_3$.*

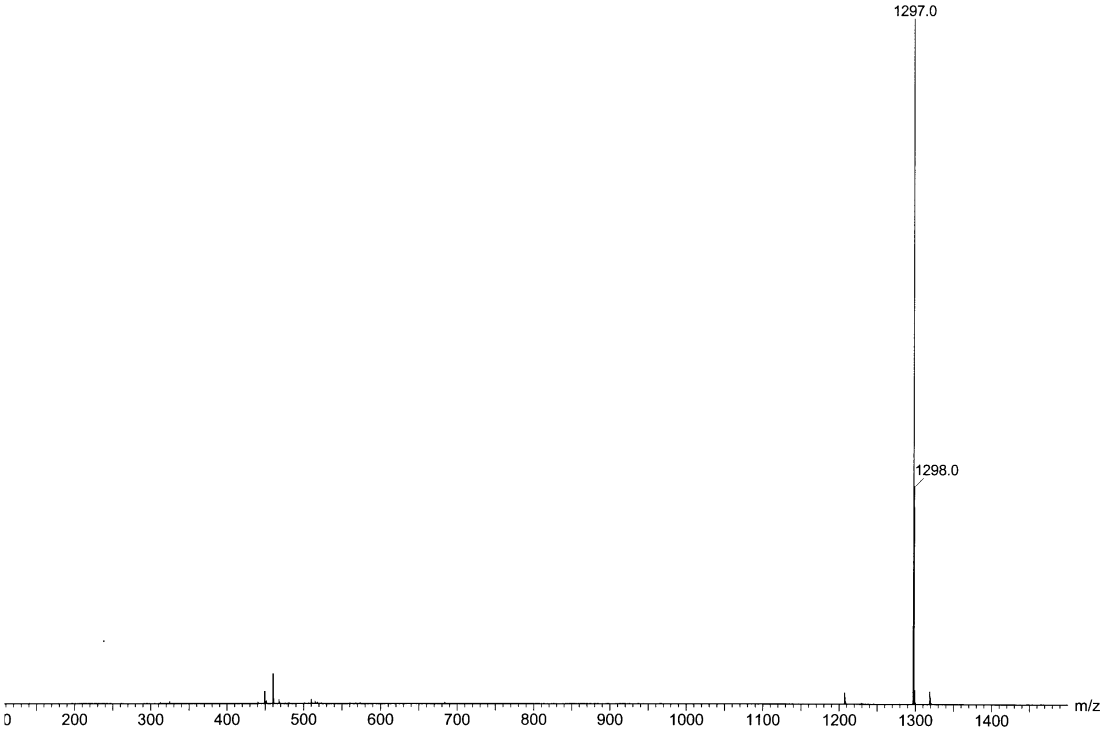


*Figure S15 - Electrospray mass spectrum of **20** showing $[M+H]^+$ at m/z 1297 (actual mass 1296).*

Synthesis of Polyamide Dendrimer 17.

The procedure was similar to that described for the synthesis of **13**, using toluene as the solvent and **7** as the starting material, to give **12** as a glassy solid which was used without further purification for the next steps (63%) *m/z* (ES+ MS) 560 $[M+H]^+$.

Dry toluene (100 mL) and **9** (3.72 g, 9.7 mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. Succinic anhydride (0.97 g, 9.7 mmol) was added and the mixture was heated to 60°C until the solid anhydride had completely disappeared. CDI (**3**) (1.64 g, 10.2 mmol, 1.05 X excess, 95% purity) was added slowly such that the CO_2 evolution was controlled. After the complete addition of CDI (**3**), the solution was purged with dry N_2 whilst stirring at 60°C for 1h. **12** (2.35 g, 4.2 mmol) in toluene (20 mL) was added and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and concentrated *in vacuo*. The resulting viscous liquid was dissolved in CH_2Cl_2 (40mL) and washed 3 times with water (3 x 40mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*, then purified by silica gel chromatography eluting with EtOAc:MeOH (9:1 increasing to 1:1) to give **17** as a sticky solid (2.25g, 36%). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.4, 23.1, 26.4, 28.2, 30.7, 32.9, 36.8, 38.7, 43.0, 45.5, 49.7, 54.7, 156.2, 173.1, 176.5, 177.0. ^1H NMR (400 MHz, $CDCl_3$) δ 0.88 (m, 24H, $C\underline{H}_3$), 1.20-1.99 (overlapping m, 66H, integration higher than expected due to overlapping water peak, $NHCOC\underline{H}(CH_2)_2$, aliphatic $C\underline{H}_2$, $COOC(C\underline{H}_3)_3$, $CON(CH_2C\underline{H}_2CH_2)_2$), 2.54-2.70 (overlapping m, 18H, $N(C\underline{H}_2CH_2)_3$, $CON(C\underline{H}_2CH_2CH_2)_3$), 3.03-3.38 (overlapping m, 30H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$, $C\underline{H}_2NHCO(EH)$, $C\underline{H}_2NHCOO(CH_3)_3$), 5.24 (br, $N\underline{H}$), 5.34

(br, N*H*), 6.51 (br, N*H*), 6.79 (br, N*H*), 7.60 (br, N*H*). *m/z* (ES+ MS) 768 $[M+2Na]^{2+}$,1514 $[M+Na]^{+}$. GPC; M_w = 1776, PDI = 1.11.

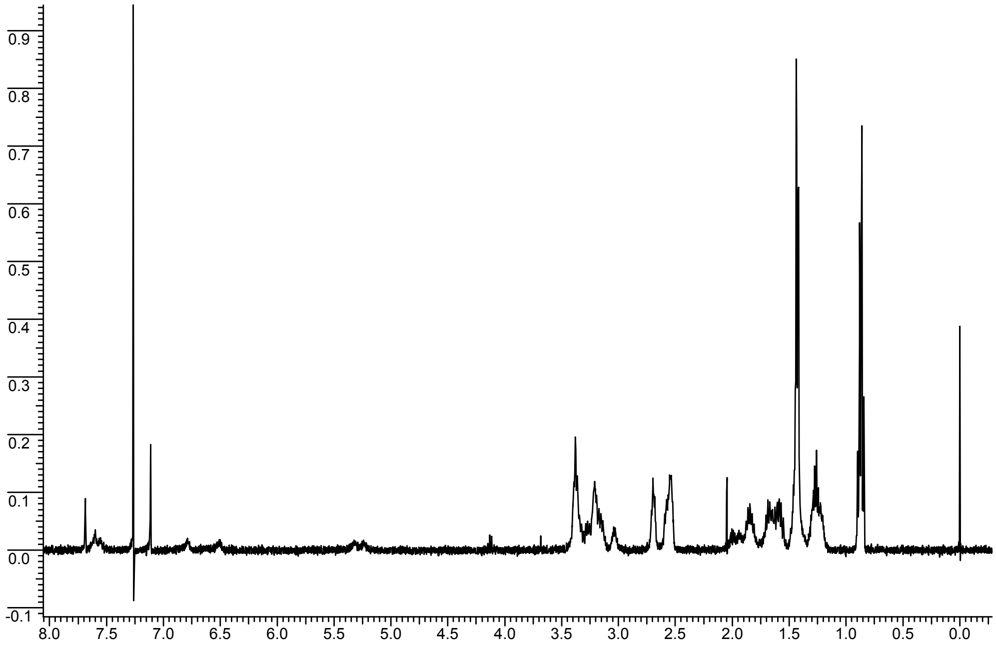


Figure S16 - NMR spectrum of asymmetric first generation dendrimer ***17*** *in* $CDCl_3$.

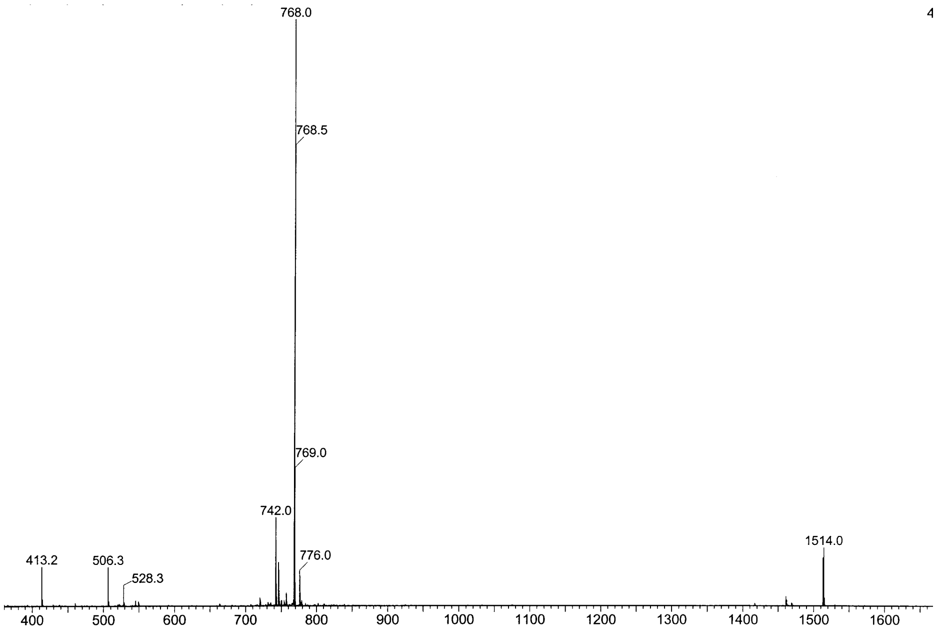
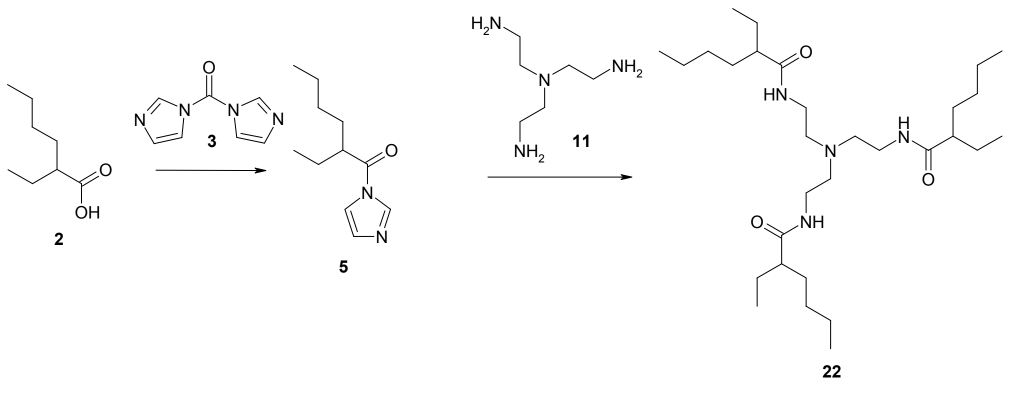


Figure S17 - Electrospray mass spectrum of **17** *showing* $[M+2Na]^{2+}$ *at m/z 768 and* $[M+Na]^{+}$ *at m/z 1514 (actual mass 1491).*

Synthesis of Polyamide Dendrimer 21.

The procedure was similar to that described for the synthesis of **17**, using BEHA (2.33 g, 9.7 mmol) in the place of **9**. The crude material was purified by silica gel chromatography eluting with EtOAc:MeOH (9:1 increasing to 1:1) to give **21** as a sticky solid (2.23 g, 44%). Found C, 64.02; H, 10.44; N, 11.05%. $C_{66}H_{127}N_9O_{10}$ requires, C, 65.69; H, 10.61; N, 10.45%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.5, 14.4, 23.5, 24.4, 29.3, 30.9, 31.7, 37.4, 38.5, 49.3, 51.5, 54.4, 156.4, 172.8, 173.1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83-0.90 (m, 24H, $C\underline{H}_3$), 1.26 (m, 32H, aliphatic $C\underline{H}_2$), 1.44 (d, 18H, $COOC(C\underline{H}_3)_3$), 1.65-1.82 (overlapping m, 8H, $CH_2C\underline{H}_2CH_2NHCOO$ and $C\underline{H}(CH_2)_3$), 2.55 (m, 6H, $N(C\underline{H}_2)_3$), 2.55 - 2.70 (d of m, 12H, $CON(C\underline{H}_2)_2$), 3.05-3.20 (m, 18H, $N(CH_2C\underline{H}_2NHCOC\underline{H}_2C\underline{H}_2)_3$), 3.36 (m, 4H, $OCONHC\underline{H}_2$), 5.40 (br, NH, $OCON\underline{H}$), 7.70 (br, NH, $CH_2CON\underline{H}$). *m/z* (ES+ MS) 1207 $[M+H]^+$,1229 $[M+Na]^+$. GPC; M_w = 2155, PDI = 1.05.

Synthesis of Polyamide Dendrimer 22.



Scheme S6 – Synthesis of symmetric zero generation dendrimer ***22****.*

Dry toluene (100 mL) and CDI (**3**) (9.31 g, 57.5 mmol) were added to a 250 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. A solution of **2** (7.2 g, 50 mmol) in toluene (20 mL) was added slowly dropwise to control CO_2 evolution. After complete addition the mixture was purged with dry N_2 whilst stirring at 60°C for 30 minutes, to ensure the complete consumption of the reagent and to aid the removal of any dissolved CO_2. The solution was then transferred to a 3-necked round-bottomed flask containing TAEA (**11**) (2.43 g, 16.6 mmol) and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and the resulting solution was washed 3 times with water (3 x 50 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*, then purified by silica gel chromatography eluting with ethyl acetate:methanol 9:1 to give **22** as a white rubbery solid (7.20 g, 83%). Found C, 68.56; H, 11.59; N, 10.62%. $C_{30}H_{60}N_4O_3$ requires C, 68.66; H, 11.52; N, 10.68%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 14.4, 23.2, 26.3, 30.3, 32.8, 37.9, 49.6, 55.1, 176.9. ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (m, 18H, $C\underline{H}_3$), 1.26 – 1.55 (overlapping m, 24H, aliphatic $C\underline{H}_2$), 2.12 (m, 3H, $NHCOC\underline{H}(CH_2)_2$), 2.62 (t, 6H, $N(C\underline{H}_2)_3$), 3.27 (t, 6H, $CONHC\underline{H}_2$), 6.64 (br, $N\underline{H}$). *m/z* (ES+ MS) 525 $[M+H]^+$, 547 $[M+Na]^+$. GPC; $M_w = 572$, PDI = 1.15.

Synthesis of Polyurethane Dendrimer 23.

Dry toluene (250 mL) and CDI (**3**) (27.20 g, 167 mmol) were added to a 500 mL 3-necked round-bottomed flask fitted with dry N_2 inlet and magnetic stirrer. A solution of *t*-butanol (**1**) (23.83 g, 322 mmol, 2 X excess) in toluene (20 mL) was added dropwise and the mixture was stirred at 60°C for 5 hours. The solution was then transferred to a 3-necked round-bottomed flask containing TAEA (**11**) (7.1 g, 48.6 mmol) and the mixture was stirred at 60°C for a further 18 hours. The solution was cooled and concentrated *in vacuo*. The resulting liquid was dissolved in CH_2Cl_2 (50 mL) and washed 3 times with water (3 x 50 mL). The solution was dried with anhydrous Na_2SO_4, filtered and concentrated *in vacuo*, then purified by silica gel chromatography eluting with ethyl acetate (100%) to give **23** as a crystalline solid (16.31 g, 75%) Found C, 56.47; H, 9.47; N, 12.60%. $C_{21}H_{42}N_4O_6$ requires, C, 56.48; H, 9.48; N, 12.55%. ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 39.0, 54.6, 79.6, 156.7. ^1H NMR (400 MHz, $CDCl_3$) δ 1.46 (s, 27H, $COOC(C\underline{H}_3)_3$), 2.53 (t, 6H, $N(C\underline{H}_2)_3$), 3.16 (q, 6H, $N(CH_2C\underline{H}_2)_3$), 5.19 (br, $N\underline{H}$), *m/z* (ES+ MS) 447 $[M+H]^+$, 469 $[M+Na]^+$. GPC; $M_w = 540$, PDI = 1.11.

Preliminary Organogelation Studies[a]

Material	Solvent			
	DCM	THF	Toluene	MeOH
18	Gel at 100mg/mL (10% w/v)	Ambient Temperature Gel at 1mg/mL (0.1% w/v) Up to 60°C Gel at 200mg/mL (20% w/v)	Up to 60°C Gel at 200mg/mL (20% w/v)	Gel at high concentration
17	Gel at 150mg/mL (15% w/v)	S	S	S
16	S	S	S	S
15	S	S	S	S
14	S	S	S	S
9	S	Up to 60°C Gel at 150mg/mL (15% w/v)	Up to 60°C Gel at 150mg/mL (15% w/v)	S
9 (CO_2H)[b]	-[d]	Up to 60°C Gel at 190mg/mL (19% w/v)	Up to 60°C Gel at 190mg/mL (19% w/v)	-
9 (Imid)[c]	-	Up to 60°C Gel at 210mg/mL (21% w/v)	Up to 60°C Gel at 210mg/mL (21% w/v)	-
7	S	S	S	S
10	S	S	S	S
22	S	S	S	S
23	S	S	S	S

[a] *Observations of organogelation during the synthesis and characterisation of the systematically varying series of polyamide dendrons and dendrimers. Detailed studies have not been conducted and the concentrations presented are not limiting.*

[b] *Acid functional dendron 9 after reaction with succinic anhydride*

[c] *Imidazolide of dendron 9 after reaction with succinic anhydride and subsequent reaction with CDI (**3**)*
[d] *Not tested*

Table S1 – Conditions under which organogelation was observed for polyamide dendrons and dendrimers

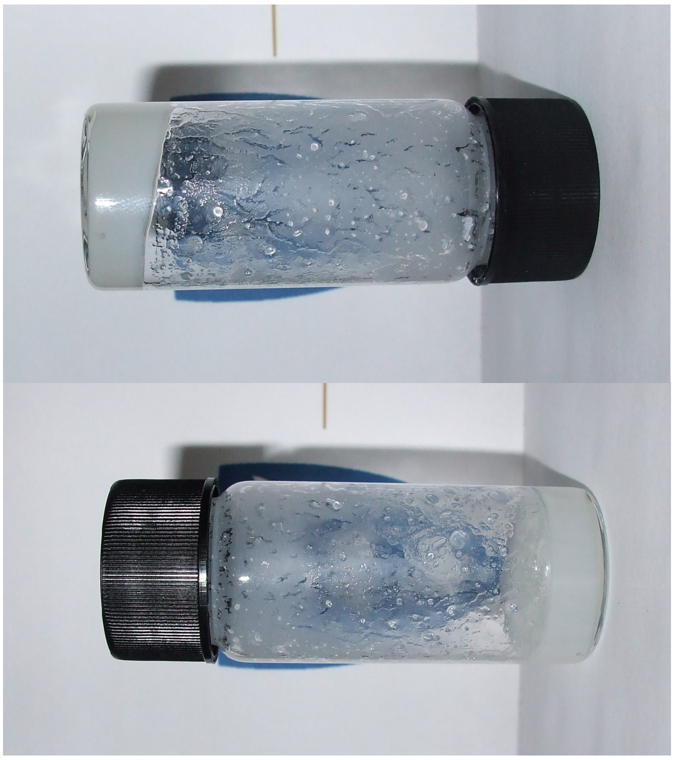


Figure S18– Organogelation of dichloromethane with Polyamide Dendrimer ***18***