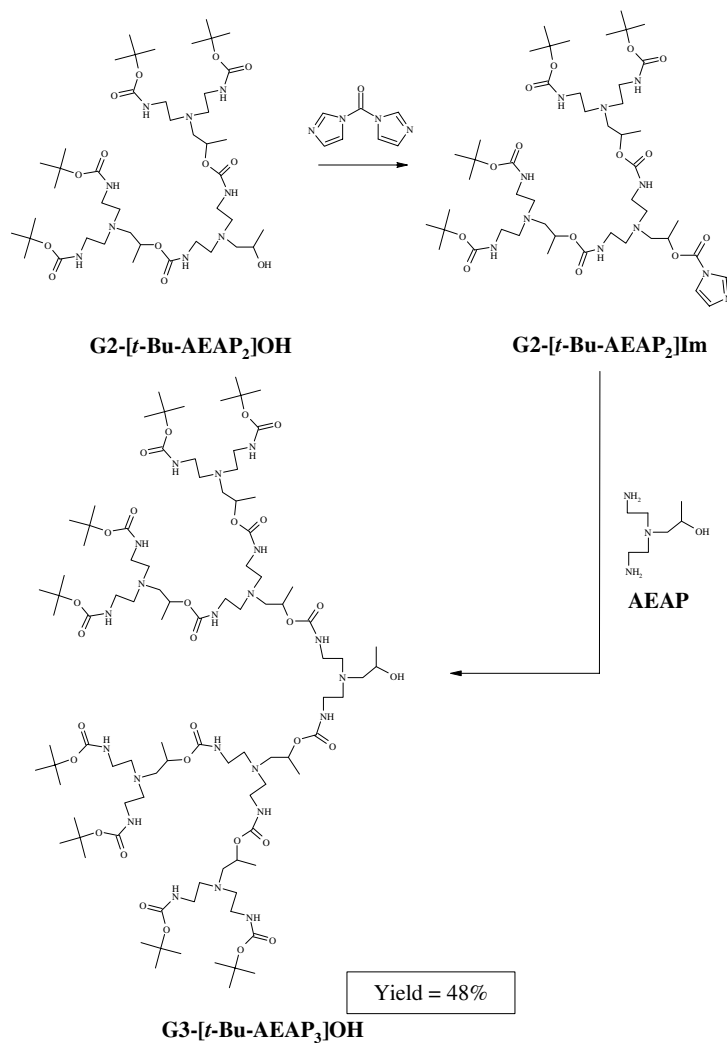


# Selective Convergent Synthesis of Aliphatic Polyurethane Dendrimers

W. James Feast<sup>†</sup>, Steve P. Rannard\* and Alison Stoddart<sup>‡</sup>

## Supplementary Information



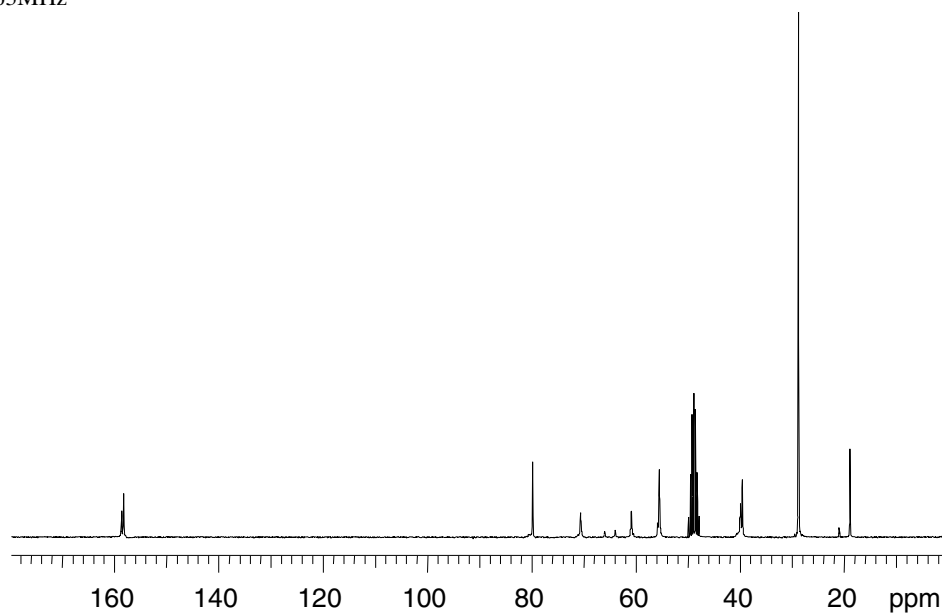
### Synthesis of **G3-[t-Bu-AEAP<sub>3</sub>]OH**:

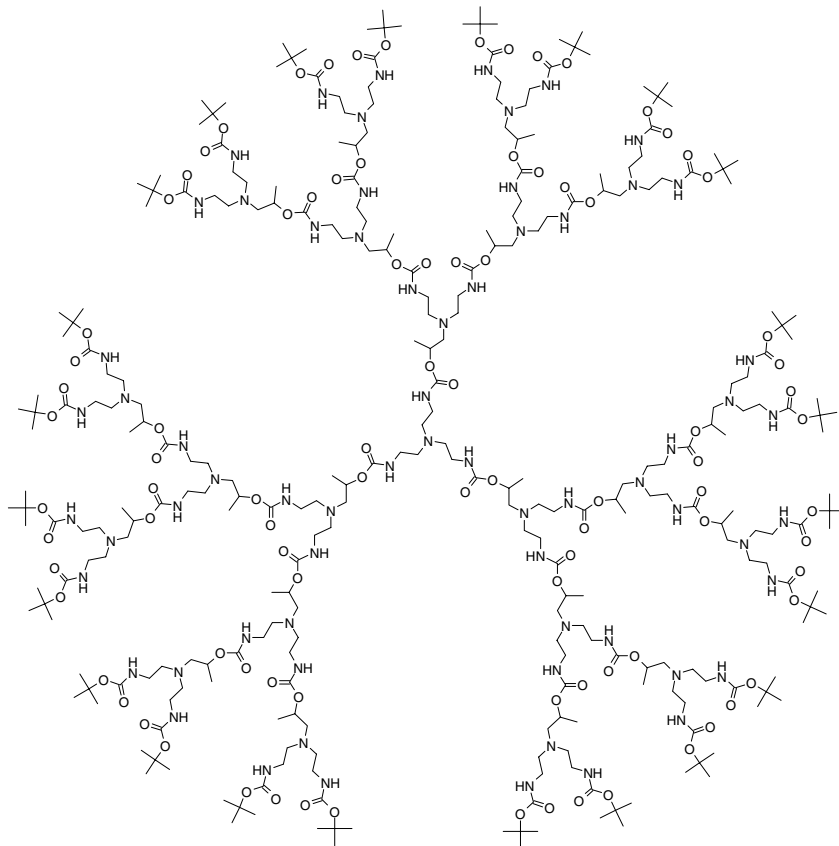
CDI (4.62 mmol) was added to a stirred solution of **G2-[t-Bu-AEAP<sub>2</sub>]OH**, (3.89 mmol) in toluene (50 mL). The mixture was heated at 60°C for 4 hrs. Subsequently, the reaction mixture was analysed by <sup>1</sup>H NMR spectroscopy and interpretation of the spectrum indicated there was no evidence of the starting materials (*i.e.* G2-[t-Bu-

AEAP<sub>2</sub>]OH or CDI). The branching unit **AEAP** (1.95 mmol) was added and the solution was heated for 1 day at 60°C. The reaction mixture was concentrated *in vacuo* and redissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The organic phase was subsequently washed with water (3 x 100 mL), dried over MgSO<sub>4</sub> and the solvent removed using the rotary evaporator. The oil obtained was purified by column chromatography (silica gel, eluting with EtOAc increasing to EtOAc:MeOH, 100:5) and then purified by preparative GPC (Biobeads, eluting with toluene) to give compound **G3-[*t*-Bu-AEAP<sub>3</sub>]OH** as a colourless amorphous solid (48%). *T<sub>g</sub>* = 40.0°C. Found C, 54.16; H, 9.08; N, 13.83%. C<sub>95</sub>H<sub>185</sub>O<sub>29</sub>N<sub>21</sub> requires, C, 54.71; H, 8.94; N, 14.10%. <sup>13</sup>C NMR (62.9 MHz, CD<sub>3</sub>OD) δ 19.0, 21.0, 28.9, 39.6, 40.0, 55.6, 55.9, 61.0, 64.0, 66.0, 70.7, 79.9, 158.3, 158.7, 158.8. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 1.12 (d, J=6Hz, 3H), 1.20 (d, J=6.4Hz, 18H), 1.44 (s, 72H), 2.41-2.64 (m, 42H), 3.04-3.24 (m, 28H), 3.78 (m, 1H), 4.85 (m, obscured by water peak, 6H), 6.42 (s, br, O(CO)NHCH<sub>2</sub>CH<sub>2</sub>), 6.71 (s, br, O(CO)NHCH<sub>2</sub>CH<sub>2</sub>), 6.85 (s, br, O(CO)NHCH<sub>2</sub>CH<sub>2</sub>). *m/z* (ES MS) 2108.2 [M+Na]<sup>+</sup>, 1054.4 [M+2H]<sup>2+</sup>, 1065.4 [M+H+Na]<sup>2+</sup>. *m/z* (MALDI TOF (Voyager) MS) 2086 [M+H]<sup>+</sup>, 2108 [M+Na]<sup>+</sup>, 2124 [M+K]<sup>+</sup> calculated *M<sub>w</sub>* = 2085.61. GPC; *M<sub>w</sub>* = 2300, *Pd* = 1.00.

<sup>13</sup>CNMR spectrum of **G3-[*t*-Bu-AEAP<sub>3</sub>]OH**

CD<sub>3</sub>OD  
63MHz





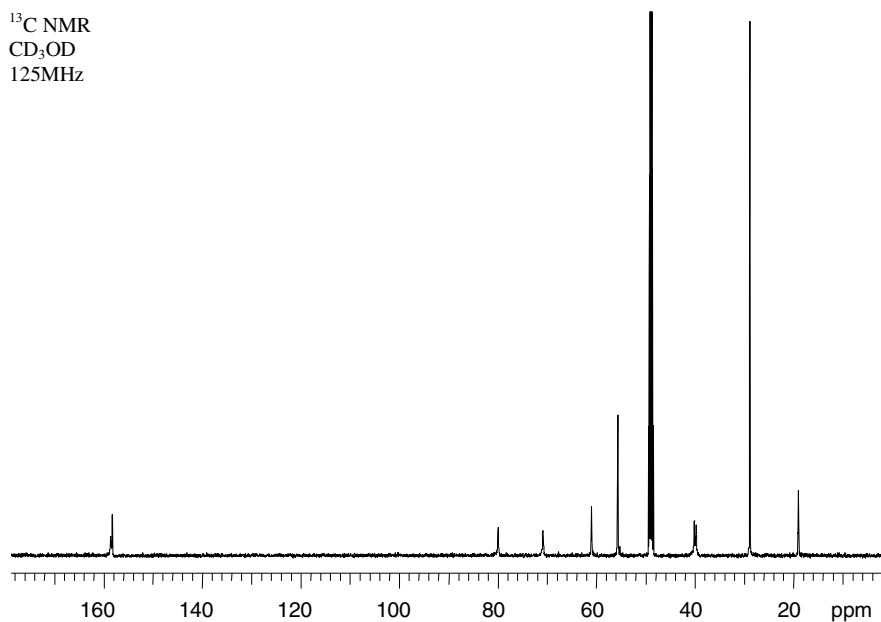
#### Synthesis of G3-[*t*-Bu-AEAP<sub>3</sub>]TAEA:

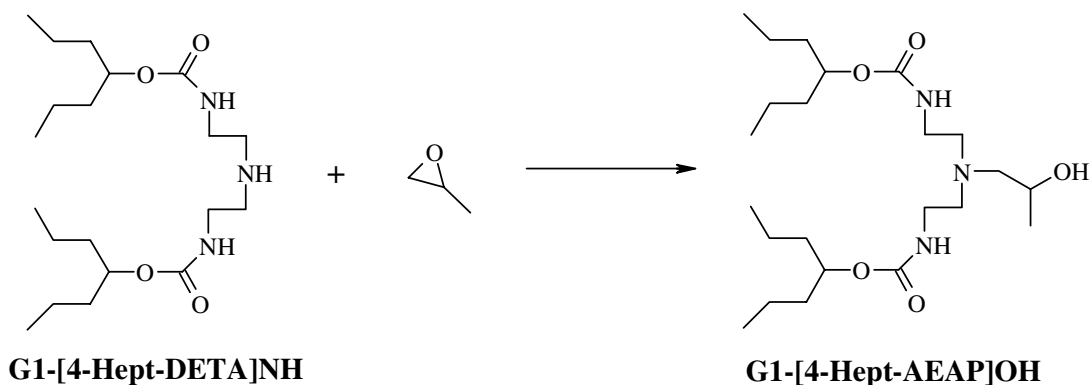
CDI (0.57 mmol) was added to a stirred solution of G3-[*t*-Bu-AEAP<sub>3</sub>]OH (0.47 mmol) in toluene (40 mL) and the mixture was heated at 60°C for 4 hours. Subsequently, the reaction mixture was analysed by <sup>1</sup>H NMR spectroscopy and interpretation of the spectrum indicated no evidence of the presence of starting materials (*i.e.* G3-[*t*-Bu-AEAP<sub>3</sub>]OH or CDI). **TAEA** (0.16 mmol) was added to the solution and the mixture was heated for 1 day at 60°C. The reaction mixture was concentrated *in vacuo* and redissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The organic phase was subsequently washed with water (3 x 100 mL), dried over MgSO<sub>4</sub> and the solvent removed using the rotary evaporator. The yellow oil obtained was purified by column chromatography (silica gel, eluting with EtOAc:MeOH 100:5 increasing to EtOAc:MeOH 100:10). The colourless oil obtained was purified further by preparative GPC (Biobeads, eluting with toluene) to give compound G3-[*t*-Bu-

AEAP<sub>3</sub>]TAEA was isolated as a white amorphous solid (20%).  $T_g = 48.9^\circ\text{C}$ . Found C, 54.46; H, 8.74; N, 13.41%.  $\text{C}_{294}\text{H}_{567}\text{O}_{90}\text{N}_{67}$  requires, C, 54.48; H, 8.82; N, 14.48%.  $^{13}\text{C}$  NMR (125 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  19.1, 29.0, 39.9, 40.2, 55.6, 55.7, 61.1, 70.9, 80.0, 158.3, 158.6.  $^1\text{H}$  NMR (400 MHz,  $\text{CD}_3\text{OD}$ )  $\delta$  1.20 (d,  $J=6.4\text{Hz}$ , 63H), 1.44 (s, 216H), 2.48-2.63 (m, 132H), 3.05-3.25 (m, 90H), 4.85 (m, obscured by water peak, 21H), 6.42 (s, br,  $\text{OC(O)NHCH}_2$ ), 6.71 (s, br,  $\text{OC(O)NHCH}_2$ ).  $m/z$  (ES MS) 3235.8  $[\text{M}+2\text{H}]^{2+}$ , 3246.9  $[\text{M}+\text{H}+\text{Na}]^{2+}$ , 3257.9  $[\text{M}+2\text{Na}]^{2+}$ .  $m/z$  (MALDI TOF (Kratos) MS) 6469  $[\text{M}+\text{H}]^+$ , calculated  $M_w = 6481.05$ . GPC;  $M_w = 4980$ ,  $P_d = 1.06$ .

$^{13}\text{C}$  NMR spectrum of third generation dendrimer G3-[*t*-Bu-AEAP<sub>3</sub>]TAEA

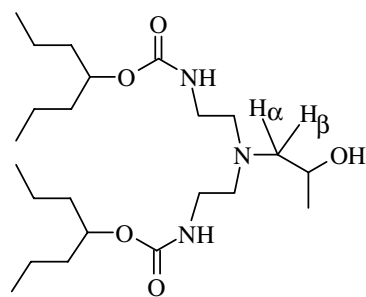
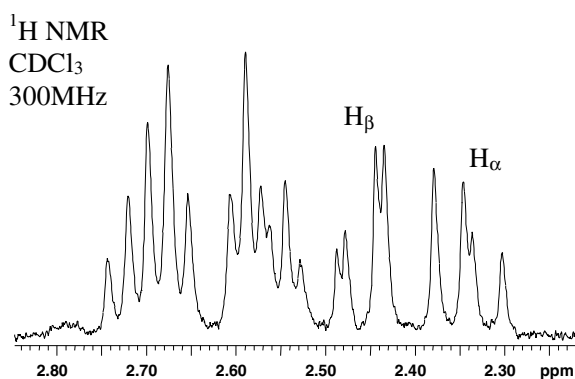
$^{13}\text{C}$  NMR  
 $\text{CD}_3\text{OD}$   
 125MHz





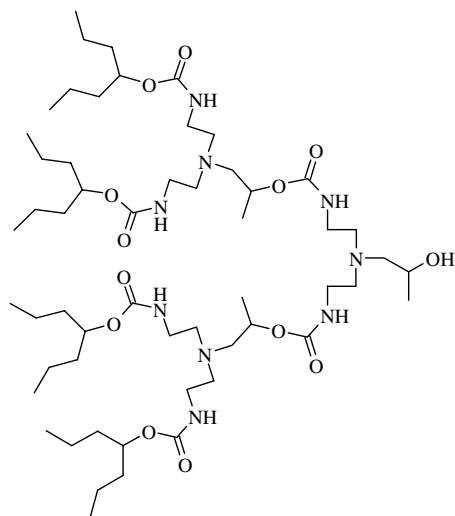
#### Synthesis of G1-[4-Hept-AEAP]OH :

To a stirred solution of G1-[4-Hept-DETA]NH (67.5 mmol) in ethanol, (200 mL) propylene oxide (11.8 g, 202 mmol) was added and the mixture heated at 30°C for 20 hrs. The solvent was removed using the rotary evaporator and the oil dried under vacuum ( $10^{-1}$  mbar) for 1 day. Purification by column chromatography (silica gel, eluting with EtOAc) gave G1-[4-Hept-AEAP]OH as a colourless oil (23.8 g, 91%).  $T_g = -39.5^\circ\text{C}$ . Found C, 61.90; H, 10.61; N, 9.43%.  $\text{C}_{23}\text{H}_{47}\text{N}_3\text{O}_5$  requires, C, 61.99; H, 10.63; N, 9.43%.  $^{13}\text{C}$  NMR (62.9 MHz,  $\text{CDCl}_3$ )  $\delta$  14.0, 18.5, 20.0, 36.7, 39.2, 55.1, 63.2, 64.1, 74.4, 157.2.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  0.91 (t,  $J=7.2\text{Hz}$ , 12H), 1.12 (d,  $J=6.3\text{Hz}$ , 3H), 1.33 (m, 8H), 1.47 (m, 8H), 1.63 (s, br, OH), 2.34 (dd,  $J=12.9\text{Hz}$ ,  $J=9.9\text{Hz}$ , 1H), 2.46 (dd,  $J=13.2\text{Hz}$ ,  $J=3\text{Hz}$ , 1H), 2.56 (dt,  $J=13.2\text{Hz}$ ,  $J=5.4\text{Hz}$ , 2H), 2.67 (m, 2H), 3.23 (m, 4H), 3.73 (m, 1H), 4.76 (qn,  $J=6\text{Hz}$ , 2H), 5.07 (s, br,  $\text{O}(\text{CO})\text{NHCH}_2$ ).  $m/z$  (GC, EI) 446  $[\text{M}+\text{H}]^+$ , calculated  $M_w = 445.64$ .



**G1-[4-Hept-AEAP]OH**

$^1\text{H}$  NMR spectrum of G1-[4-Hept-AEAP]OH demonstrating coupling of  
diastereotopic hydrogens

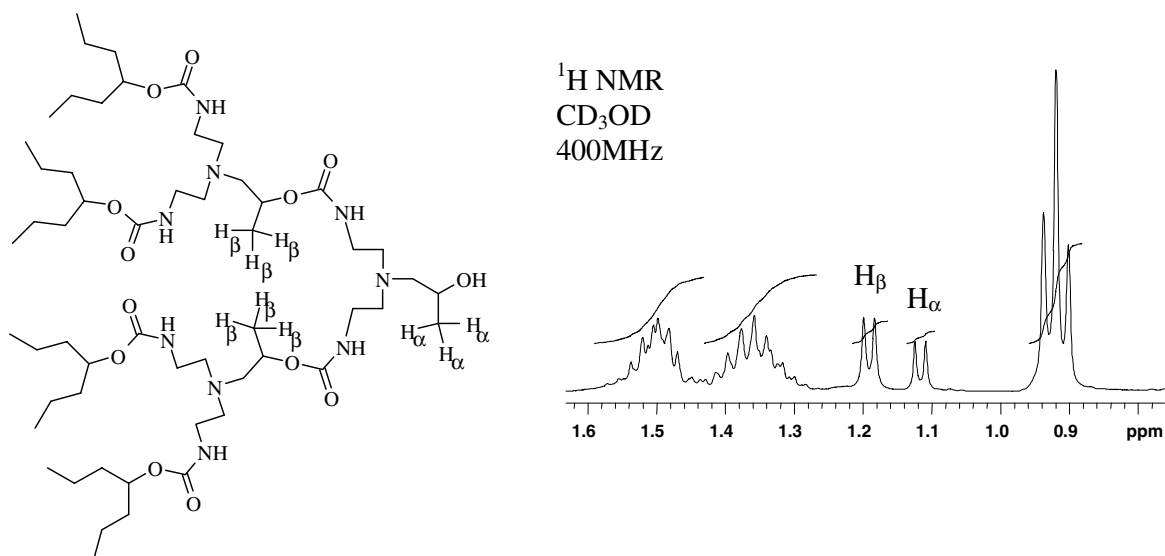


**G2-[4-Hept-AEAP<sub>2</sub>]OH**

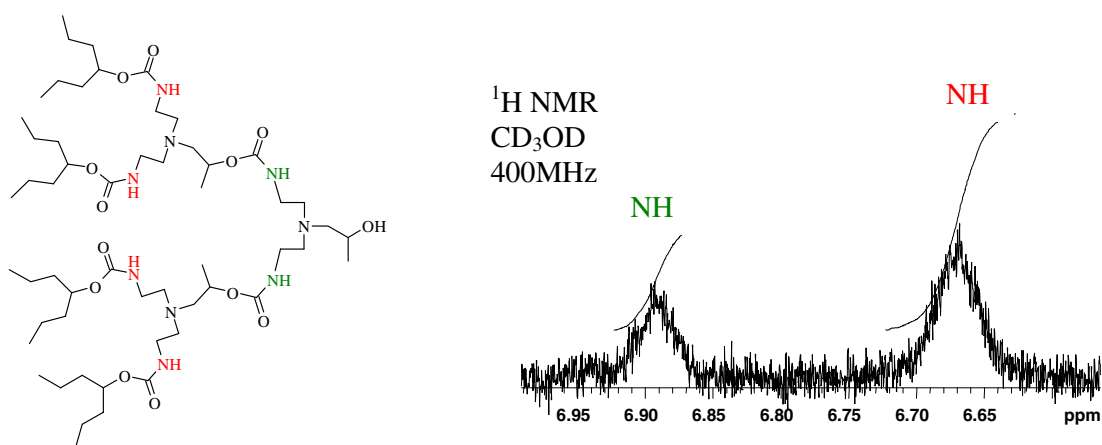
#### Synthesis of **G2-[4-Hept-AEAP<sub>2</sub>]OH**:

CDI (28.1 mmol) was added to a stirred solution of G1-[4-Hept-AEAP]OH (24.4 mmol) in toluene (100 mL). The mixture was heated at 60°C for 6 hrs. Subsequently, the reaction mixture was analysed by <sup>1</sup>H NMR spectroscopy and interpretation of the spectrum indicated there was no evidence of the starting materials (G1-[4-Hept-AEAP]OH or CDI). The branching unit **AEAP** (13.4 mmol) was added and the solution was heated for 20 hrs. The reaction mixture was concentrated *in vacuo* and redissolved in CH<sub>2</sub>Cl<sub>2</sub> (200 mL). The organic phase was subsequently washed with water (3 x 250 mL), dried over MgSO<sub>4</sub> and the solvent removed using the rotary evaporator. The resulting pale yellow oil was purified by column chromatography (silica gel, eluting with EtOAc:C<sub>6</sub>H<sub>12</sub> 1:23) and the colourless oil obtained was dried under vacuum (10<sup>-1</sup> mbar) to give compound G2-[4-Hept-AEAP<sub>2</sub>]OH as a sticky colourless oil (49%). *T<sub>g</sub>* = -4.3°C. Found C, 59.54; H, 9.91; N, 11.20%. C<sub>55</sub>H<sub>109</sub>N<sub>9</sub>O<sub>13</sub> requires, C, 59.81; H, 9.95; N, 11.41%. <sup>13</sup>C NMR (62.9 MHz, CD<sub>3</sub>OD) δ 14.5, 18.9, 19.5, 20.9, 37.8, 39.9 (resonances from two distinct carbons overlap), 55.5, 55.9, 60.9, 64.0, 65.8 (split into 3 peaks), 70.6, 74.9, 158.6, 158.9. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 0.92 (t, J=7.2Hz, 24H), 1.12 (d, J=6.4Hz, 3H), 1.19 (d, J=6.4 Hz, 6H), 1.30-1.41 (m, 16H), 1.47-1.54 (m, 16H), 2.38-2.68 (m, 18H), 3.09-3.28 (m, 12H), 3.77 (m, 1H), 4.73 (m, 4H), 4.85 (m, 2H), 6.67 (s, br, O(CO)NHCH<sub>2</sub>CH<sub>2</sub>), 6.89 (s, br, O(CO)NHCH<sub>2</sub>CH<sub>2</sub>). *m/z* (ES MS) 1105 [M+H]<sup>+</sup>, 1127 [M+Na]<sup>+</sup>, 1143

$[M+K]^+$ , 553  $[M+2H]^{2+}$ , 564  $[M+H+Na]^{2+}$ , 575  $[M+2Na]^{2+}$ .  $m/z$  (MALDI-TOF (Kratos) MS) 1105  $[M+H]^+$ , 1127  $[M+Na]^+$ , calculated  $M_w = 1104.51$ . GPC;  $M_w = 1180$ ,  $Pd = 1.00$ .



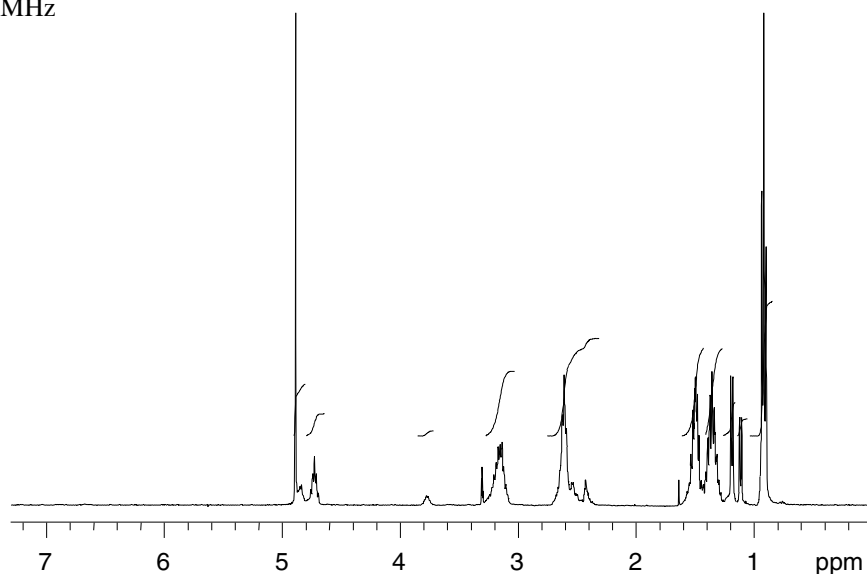
Methyl group hydrogens of G2-[4-Hept-AEAP<sub>2</sub>]OH



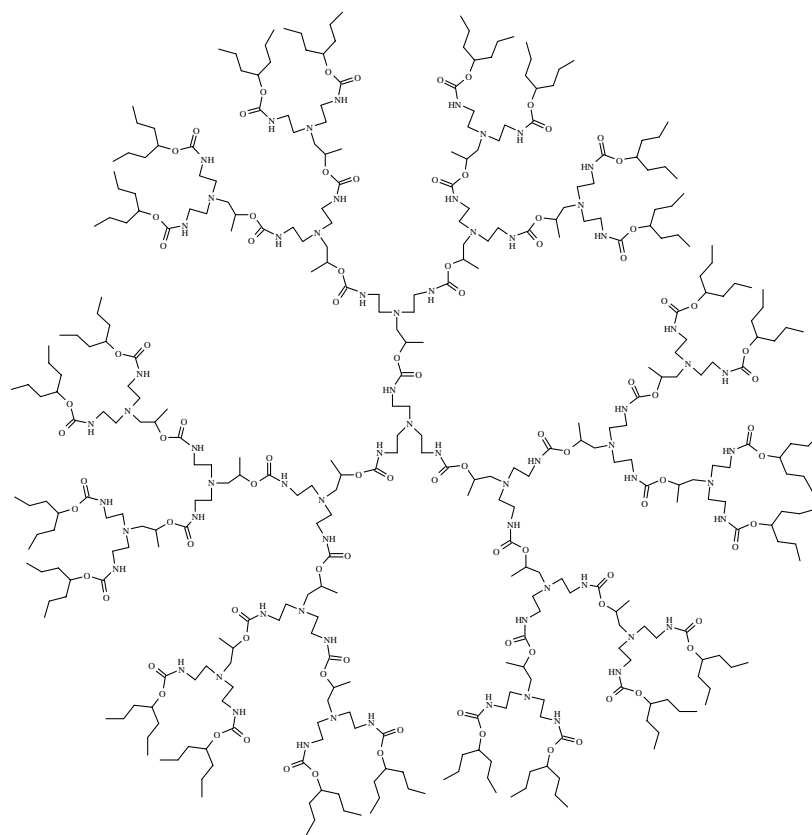
Urethane N-H resonances of G2-[4-Hept-AEAP<sub>2</sub>]OH

$^1\text{H}$  NMR Spectrum of G2-[4-Hept-AEAP<sub>2</sub>]OH

$\text{CD}_3\text{OD}$   
400 MHz





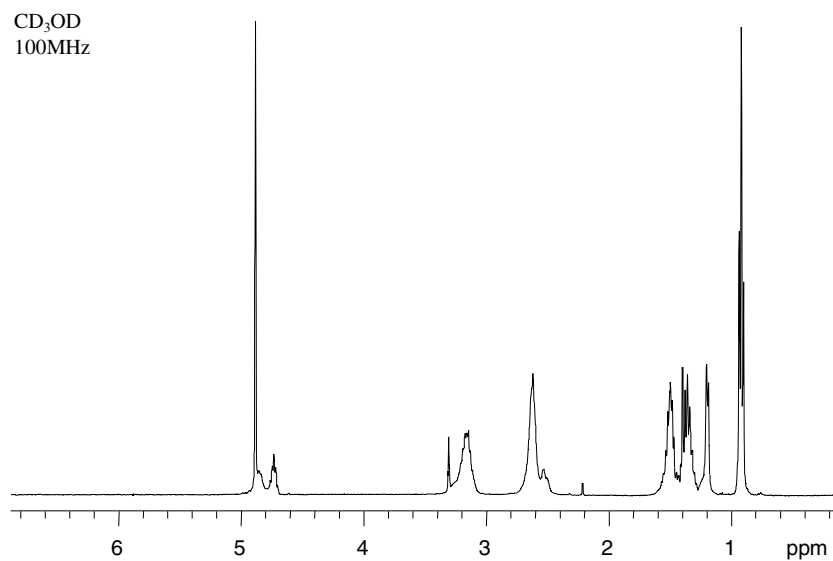


#### Synthesis of G3-[4-Hept-AEAP<sub>3</sub>]TAEA:

CDI (0.57 mmol) was added to a stirred solution of G3-[4-Hept-AEAP<sub>3</sub>]OH (0.47 mmol) in toluene (40 mL) and the mixture was heated at 60°C for 4 hours. Subsequently, the reaction mixture was analysed by <sup>1</sup>H NMR spectroscopy and interpretation of the spectrum indicated no evidence of the presence of starting materials (i.e. G3-[4-Hept-AEAP<sub>3</sub>]OH or CDI). TAEA (0.16 mmol) was added to the solution and the mixture was heated for 1 day at 60°C. The reaction mixture was concentrated in vacuo and redissolved in CH<sub>2</sub>Cl<sub>2</sub> (100 mL). The organic phase was subsequently washed with water (3 x 100 mL), dried over MgSO<sub>4</sub> and the solvent removed using the rotary evaporator. The yellow oil obtained was purified by column chromatography (silica gel, eluting with EtOAc:MeOH 100:5 increasing to EtOAc:MeOH 100:10). The colourless oil obtained was purified further by preparative GPC (Biobeads, eluting with toluene) to give compound G3-[4-Hept-AEAP<sub>3</sub>]TAEA as an extremely sticky oil (280 mg, 24%). *T<sub>g</sub>* = 19.4°C. Found C, 57.37; H, 9.50; N, 11.88%. C<sub>366</sub>H<sub>711</sub>O<sub>90</sub>N<sub>67</sub> requires, C, 58.68; H, 9.57; N, 12.53%. <sup>13</sup>C NMR (100 MHz, CD<sub>3</sub>OD) δ 14.6, 19.1, 19.7, 40.0, 40.1, 55.7, 61.0, 70.7, 75.2, 158.7, 158.8, 159.3. <sup>1</sup>H NMR (400 MHz, CD<sub>3</sub>OD) δ 0.92 (t, *J*=7.2Hz, 144H), 1.20 (d, *J*=6Hz, 63H), 1.36 (m, 96H), 1.50 (m, 96H), 2.51-2.66 (m, 132H), 3.12-3.20 (m, 90H), 4.74 (m, 24H), 4.85 (m, obscured by water peak, 9H), 6.46 (s, br, OC(O)NHCH<sub>2</sub>), 6.76 (s, br, OC(O)NHCH<sub>2</sub>). *m/z* (ES MS) 7511.4 [M+Na]<sup>+</sup>, 7527.5

$[M+K]^+$ , calculated  $M_w = 7490.96$  and an impurity at 5063.6 corresponding to the two-armed dendrimer. GPC;  $M_w = 6410$ ,  $Pd = 1.01$ .

$^1H$  NMR Spectrum of G3-[4-Hept-AEAP<sub>3</sub>]TAEA:



MALDI-TOF (Voyager) mass spectrum of G3-[4-Hept-AEAP<sub>3</sub>]TAEA

