Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Influence of linker groups on the solubility of triazine dendrimers

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Contributions

A. Enciso performed all of the experimental work and contributed to the design of the studies and preparation of the manuscript. M. Garzoni performed the computational studies that are reported and contributed to the preparation of the manuscript. G. Pavan supervised the computational portions of the work and its final communication. E. Simanek supervised the experimental portions of this work and its final communication.

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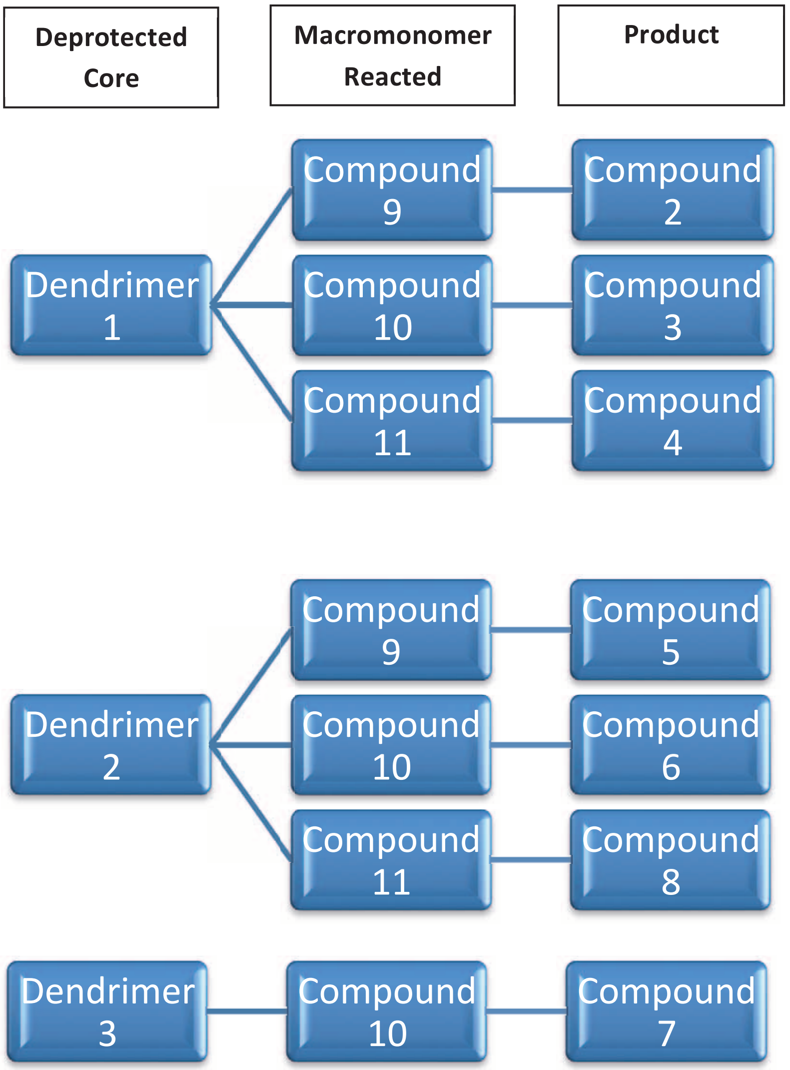
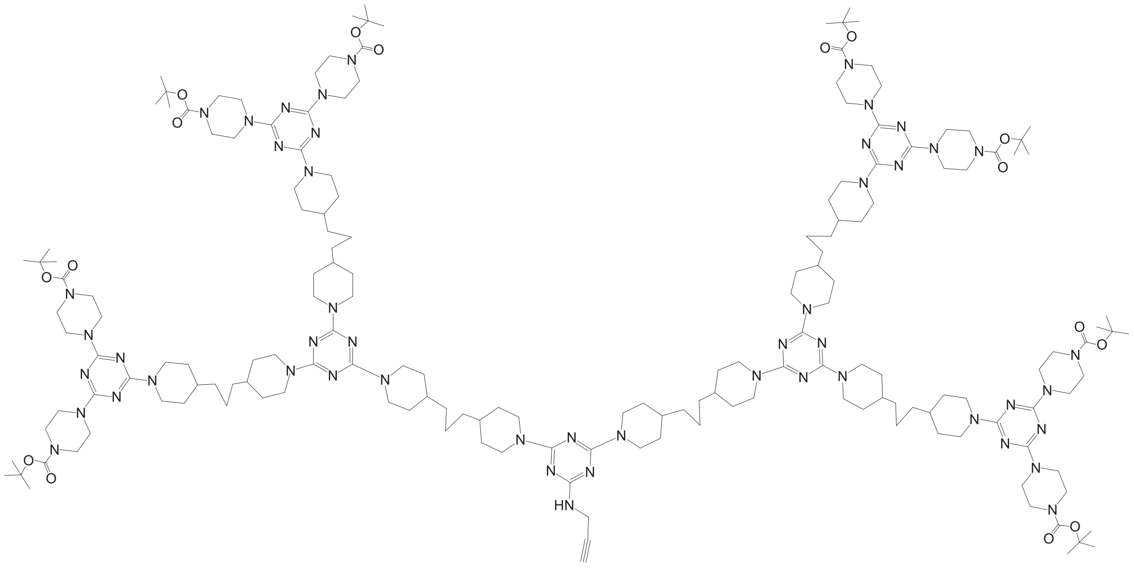
General Synthesis Procedure

The general procedure of synthesis consisted of reacting dendrimers with three different classes of macromonomers (compounds **9**, **10** and **11**) respectively, from 4 to 6 days in a capped pressure vessel at 75ºC in order to generate the hybrid dendrimers. After work up and purification, the hybrid dendrimers were deprotected using a 1:1 solution of MeOH and concentrated HCl; followed by a neutralization with 5 M NaOH (*aq.*).

All reactions were monitored by TLC, mass spectroscopy and NMR when allowed by solubility.

Mass spectra were collected at TCU (ESI-TOF) and the Laboratory for Biological Mass Spectrometry at Texas A&M University (MALDI-TOF).





Compound 1-Boc

A solution of **15** (1.82g, 1.14mmol), DIPEA (0.47 mL, 2.7mmol), 4,6-dichloro-N-(prop-2-yn-1-yl)-1,3,5-triazin-2-amine (0.109g, 0.54mmol)in 6mL of THF were stirred and heated at 75°C for 2 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine, the organic layer was dried over $MgSO_4$, filtered and evaporated under vacuum. The solid was purified by silica gel chromatography (from hexanes to hexanes:EtOAc= 3:2) to provide a white solid: **1-Boc** (1.67g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.72 (bs, 24H, equatorial C**H**N-triazine of dipiperidine), 4.18 (s, 2H, NHC**H₂**CCH), 3.73 (s, 32H, triazine-$NCH_2C\mathbf{H_2}NBoc$), 3.44 (s, 32H, triazine-$NC\mathbf{H_2}CH_2NBoc$), 2.71 (bs, 24H, equatorial C**H**CH_2N-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.67 (s, 24H, axial C**H**N-triazine of dipiperidine), 1.48 (s, 72H, $C(C\mathbf{H_3})_3$), 1.33-0.85 (m, 72H, axial C**H**CH_2N-triazine of dipiperidine (24H), C**H₂**-trimethylene (12H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (36H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.6, 165.4, 165.1 ($N_3\mathbf{C}_3$), 154.9 (**C**O), 79.9 (**C**$(CH_3)_3$), 43.6 ($CHCH_2\mathbf{C}H_2N$), 43.6, ($NCH_2\mathbf{C}H_2N$-triazine), 43.1 ($N\mathbf{C}H_2CH_2N$-triazine), 36.9 (H**C**-trimethylene), 36.4 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.3 ($\mathbf{C}H_2CH_2N$), 28.5 ($C(\mathbf{C}H_3)_3$), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{174}H_{284}N_{50}O_{16}$: 3332.24; found 3332.34 $(M + H)^+$.

Figure S1. ^{1}H NMR Spectrum of **1-Boc**.

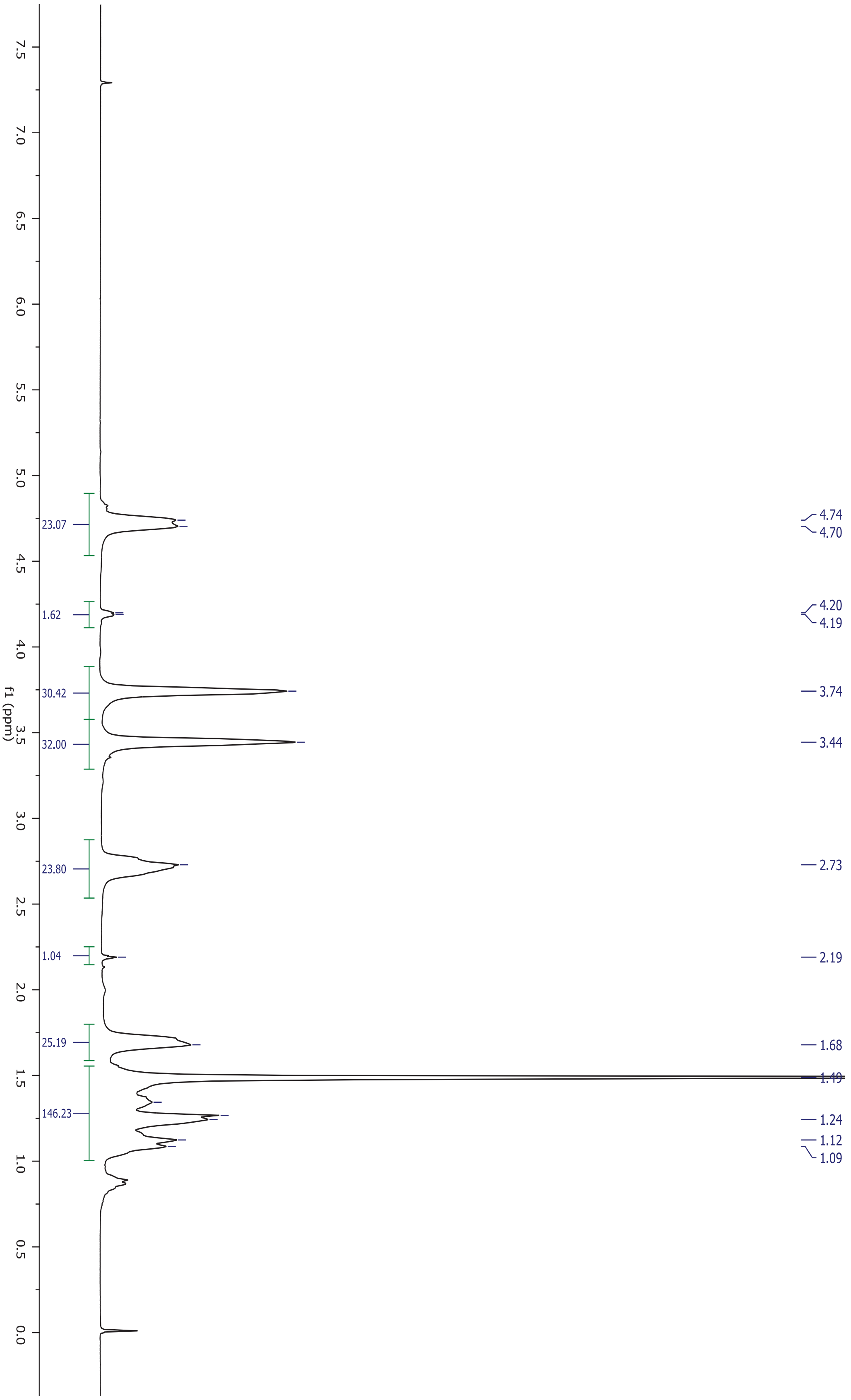


Figure S2. ^{13}C NMR Spectrum of **1-Boc**.

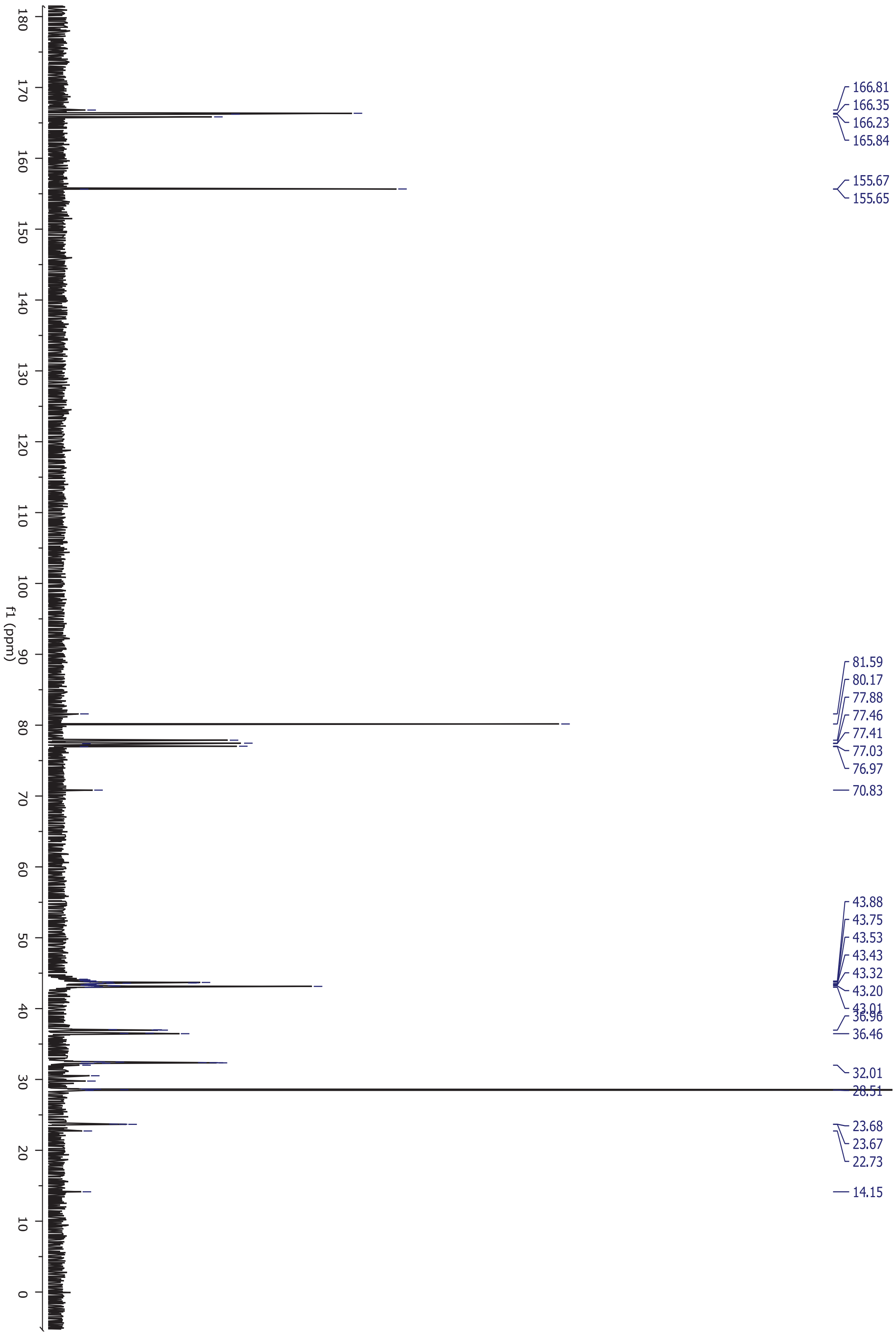


Figure S3. Mass Spectrum of **1-Boc** (ESI-TOF).

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Inj Vol	-1	**InjPosition**		**SampleType**	Sample	**IRM Calibration Status**	All Ions Missed
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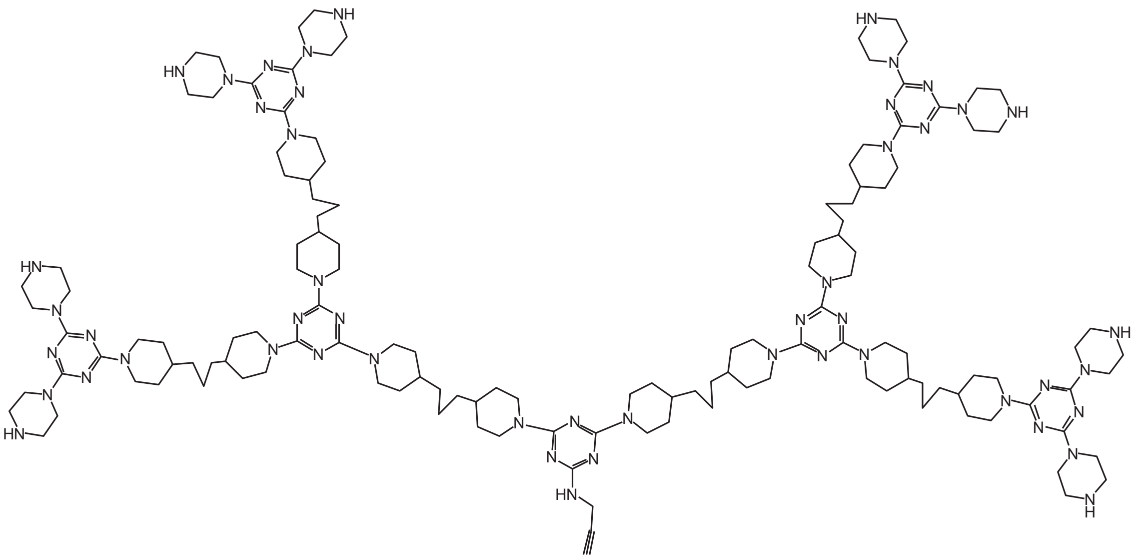


Dendrimer 1

A solution of compound **1-Boc** (0.417g, 0.125mmol) in concentrated HCl (3mL) and methanol (3mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, evaporated under vacuum to yield Dendrimer **1** (0.316g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.71 (d, *J = 12Hz*, 24H, equatorial C**H**N-triazine of dipiperidine), 4.19 (s, 2H, NHC**H₂**CCH), 3.75 (bs, 32H, triazine-$NCH_2C\mathbf{H_2}NH$), 2.88 (bs, 32H, triazine-$NC\mathbf{H_2}CH_2NH$), 2.71 (t, *J = 12Hz*, 24H, equatorial C**H**CH_2N-triazine of dipiperidine), 2.27 (bs, 8H, N**H**), 2.18 (s, 1H, $NHCH_2CC\mathbf{H}$), 1.68 (d, *J = 12Hz*, 24H, axial C**H**N-triazine of dipiperidine), 1.43-1.08 (m, 72H, axial C**H**CH_2N-triazine of dipiperidine (24H), C**H**-trimethylene of dipiperidine (12H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (36H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.5, 165.4, 165.2 ($N_3\mathbf{C_3}$), 46.1 ($CHCH_2\mathbf{C}H_2NH$), 44.4 ($NCH_2\mathbf{C}H_2N$-triazine), 43.5 ($HNCH_2\mathbf{C}H_2N$-triazine), 36.9 (H**C**-trimethylene), 36.4 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.3 ($\mathbf{C}H_2CH_2N$), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{134}H_{220}N_{50}$: 2531.43; found 2530.87 $(M + H)^+$.

Figure S4. ^{1}H NMR Spectrum of **1**

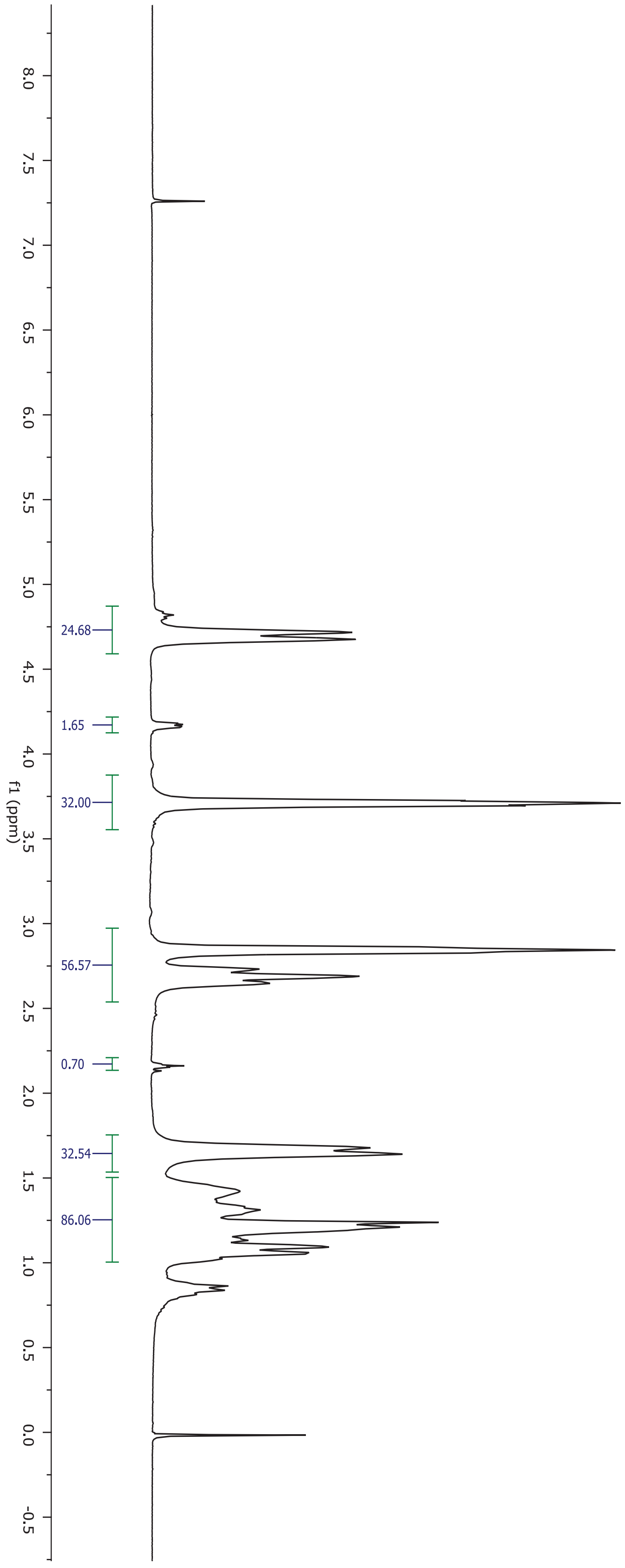


Figure S5. ^{13}C NMR Spectrum of Dendrimer **1**

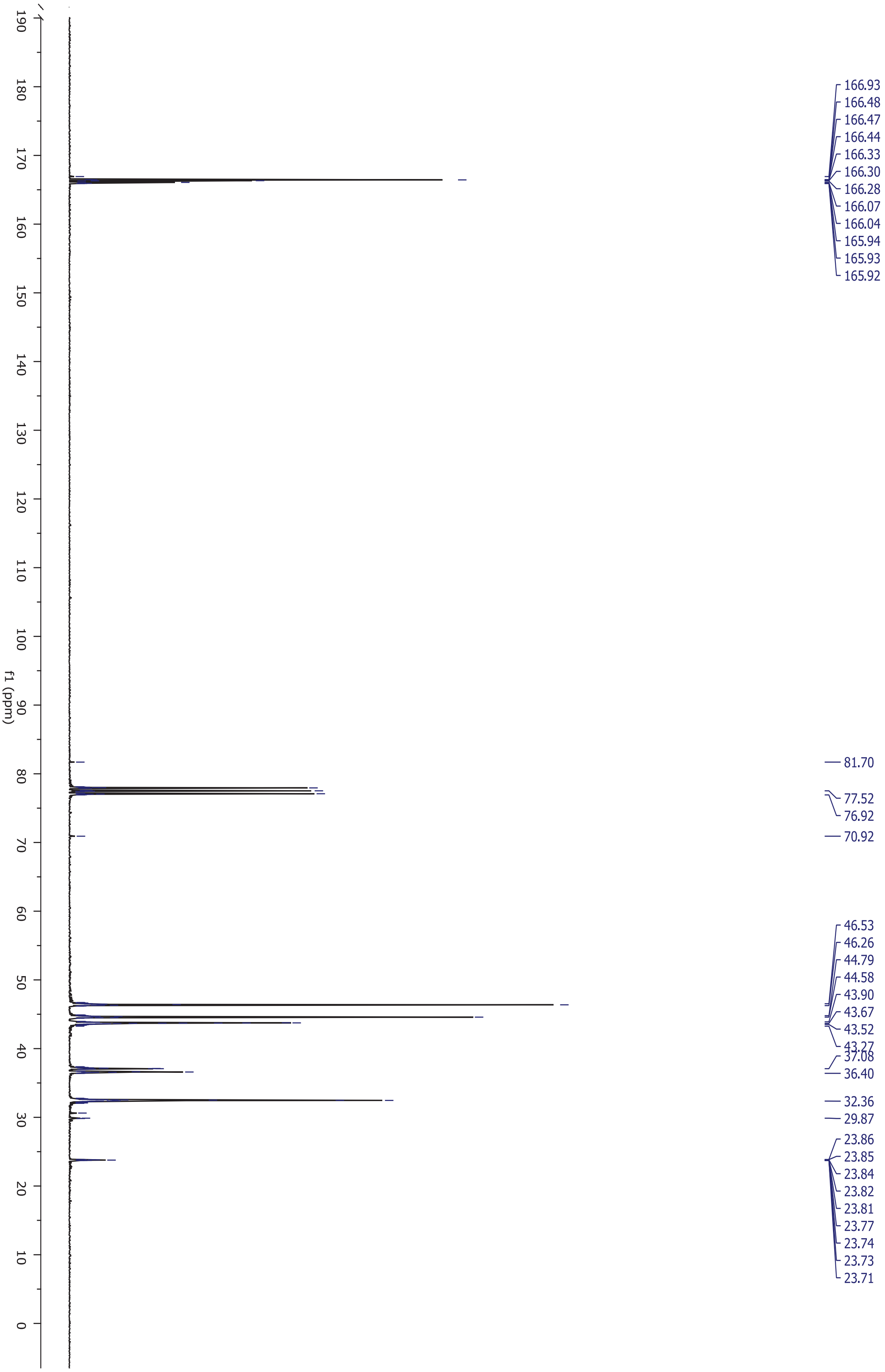
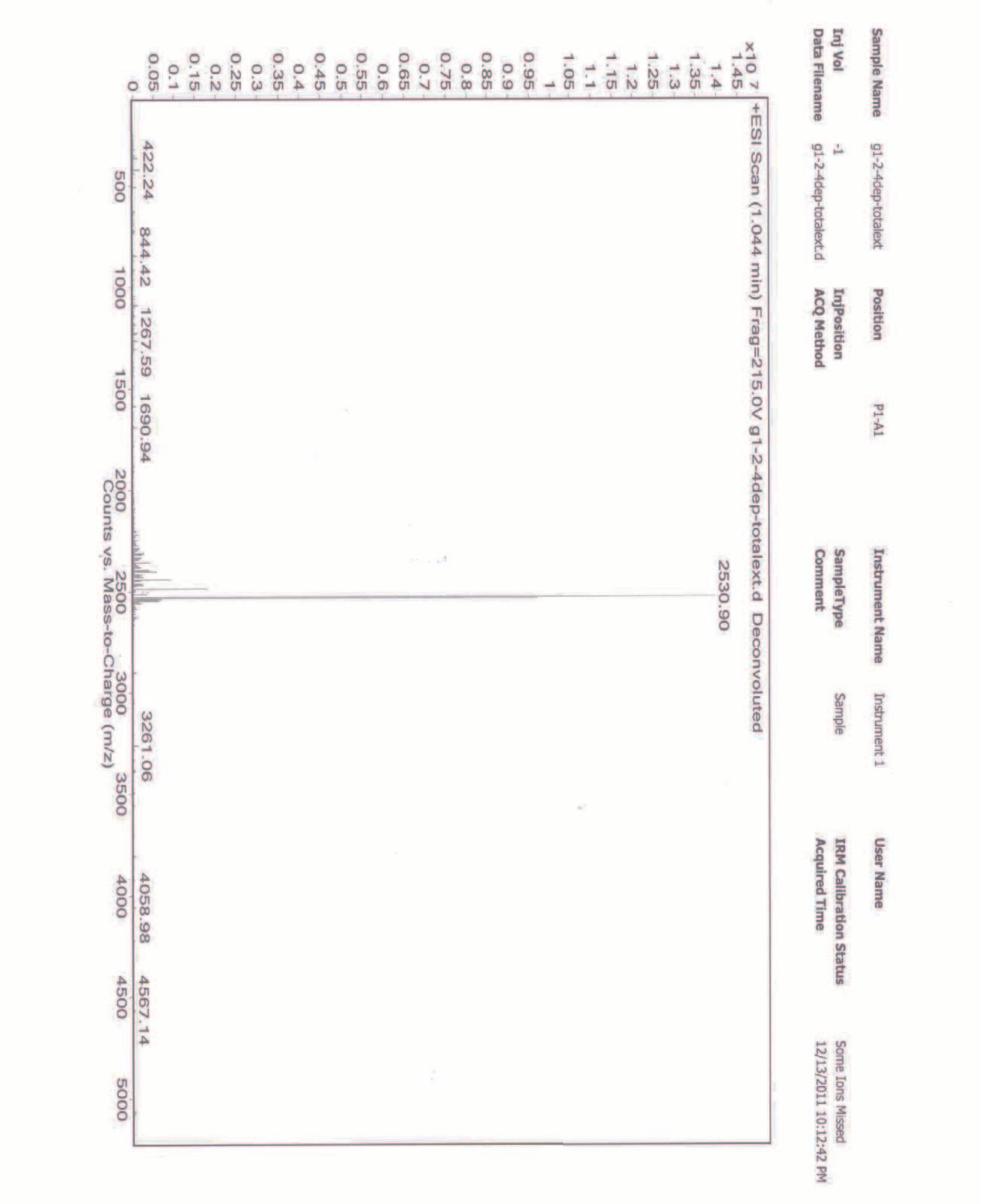


Figure S6. Mass Spectrum of **1**



Sample Name	g1-2-4dep-totalext	**Position**	P1-A1	**Instrument Name**	Instrument 1	**User Name**	
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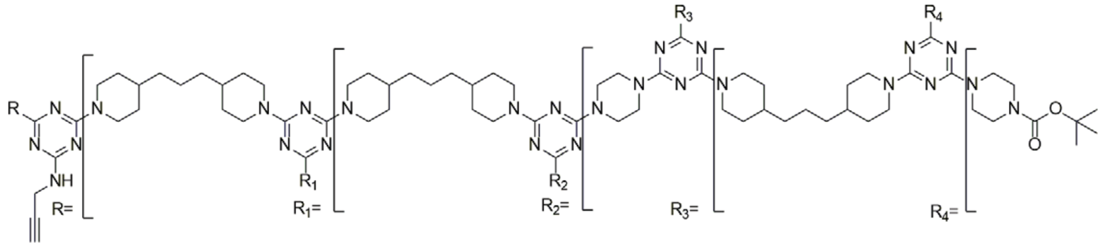


Compound **2-Boc**

A solution of **1** (0.160g, 0.063mmol), **9** (1.44g, 1.01 mmol), and DIPEA (0.19 mL, 1.1 mmol) in 0.6mL of THF was stirred and heated at 75°C for 6 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by silica gel chromatography (from 100% dichloromethane to dichloromethane:methanol= 9:1).Compound **12** (0.576g, 67%) was recovered as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.73 (bs, 88H, equatorial C**H**N-triazine of dipiperidine), 4.18 (s, 2H, $NHC\mathbf{H_2}CCH$), 3.74 (s, 192H, (128H) triazine-$NCH_2C\mathbf{H_2}NBoc$, (64H) triazine-$NC\mathbf{H_2}C\mathbf{H_2}$-triazine), 3.44 (s, 128H, triazine-$NC\mathbf{H_2}CH_2NBoc$), 2.72 (bs, 88H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.68 (s, 88H, axial C**H**N-triazine of dipiperidine), 1.48-1.08 (552H (288H) $C(C\mathbf{H_3})_3$, (88H) axial $C\mathbf{H}CH_2N$-triazine of dipiperidine, (44H) C**H**-trimethylene, (132H) $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.3, 165.92 ($N_3\mathbf{C}_3$), 155.78 (**C**O), 80.24 ($\mathbf{C}(CH_3)_3$), 44.19 ($CHCH_2\mathbf{C}H_2N$), 44.19, ($NCH_2\mathbf{C}H_2N$-triazine), 43.09 ($N\mathbf{C}H_2CH_2N$-triazine), 36.67 (H**C**-trimethylene), 36.49 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.38 ($\mathbf{C}H_2CH_2N$), 28.59 ($C(\mathbf{C}H_3)_3$), 23.8 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI-TOF) calculated for $C_{702}H_{1140}N_{218}O_{64}$: 13592.45; found 13592.45 $(M + H)^+$.

Figure S7. ^{1}H NMR Spectrum of **2-Boc**

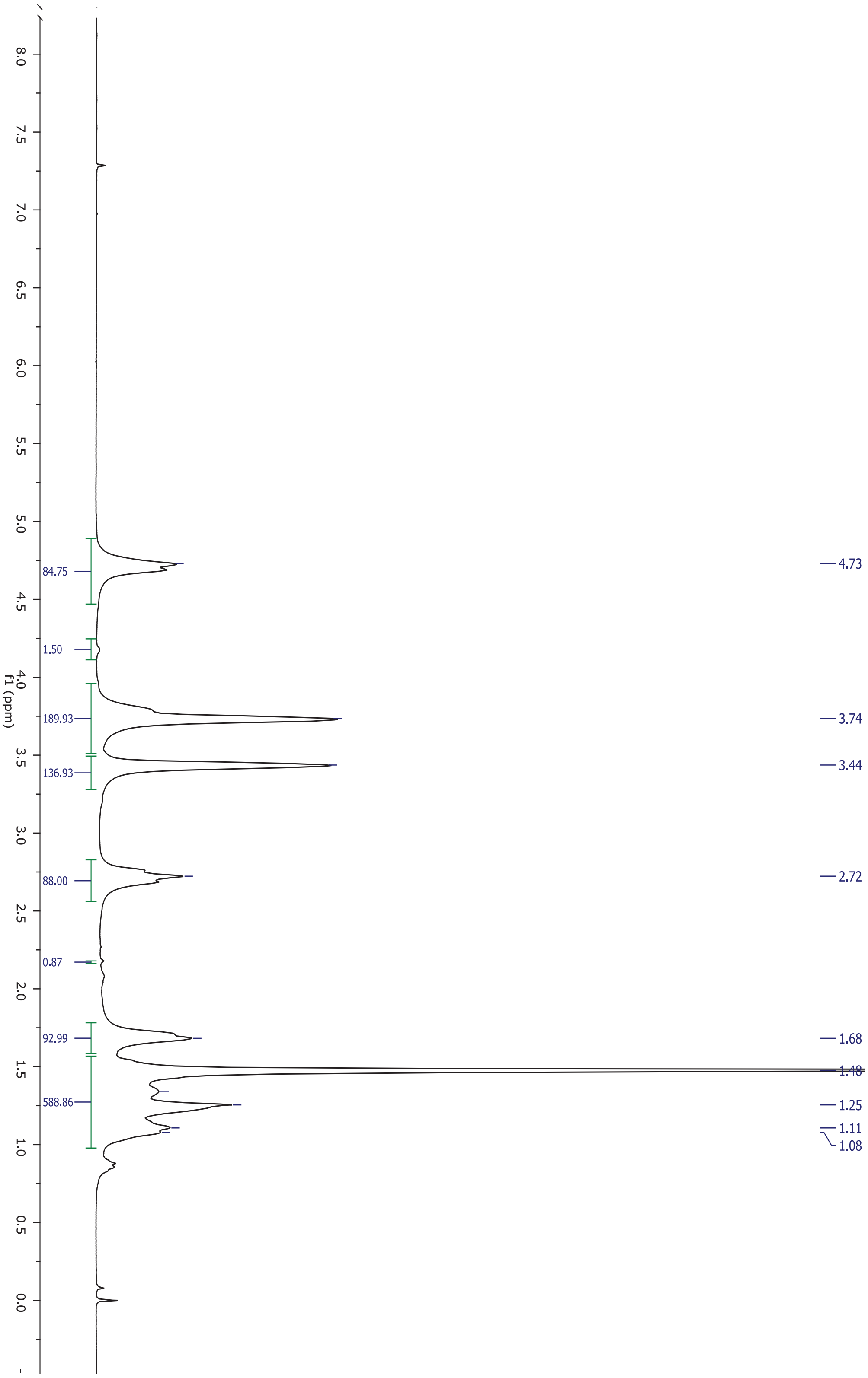


Figure S8. ^{13}C NMR Spectrum of **2-Boc**

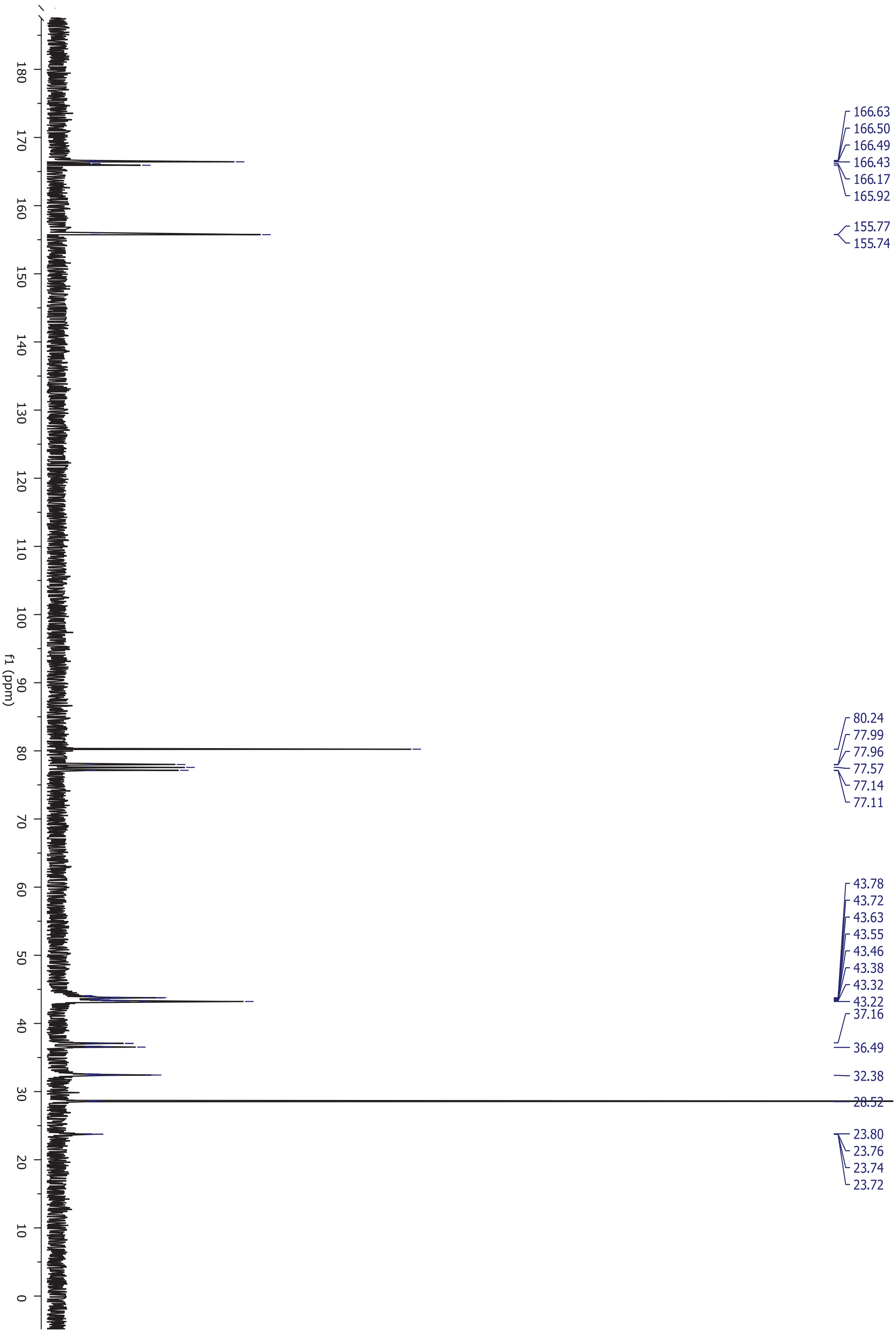
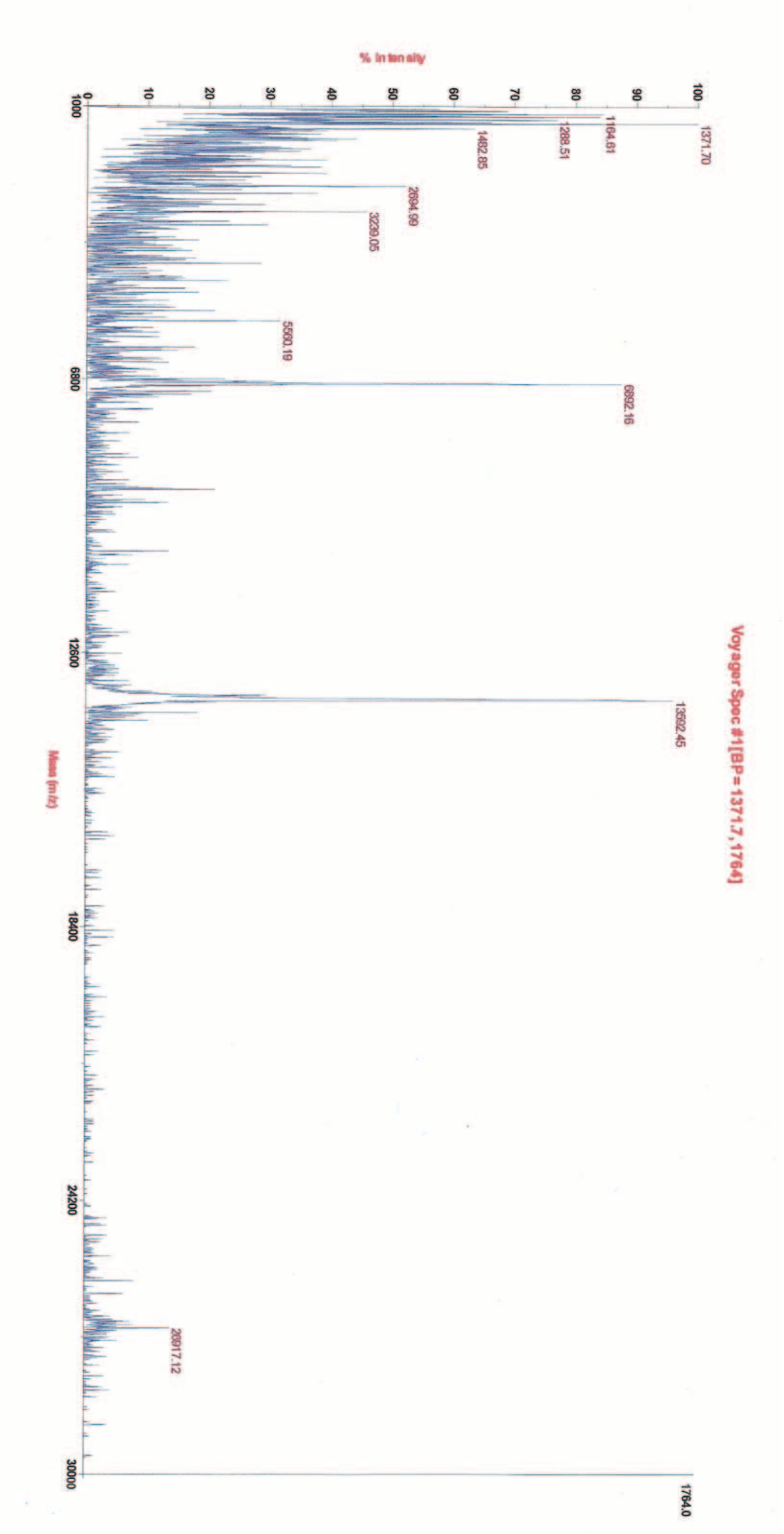
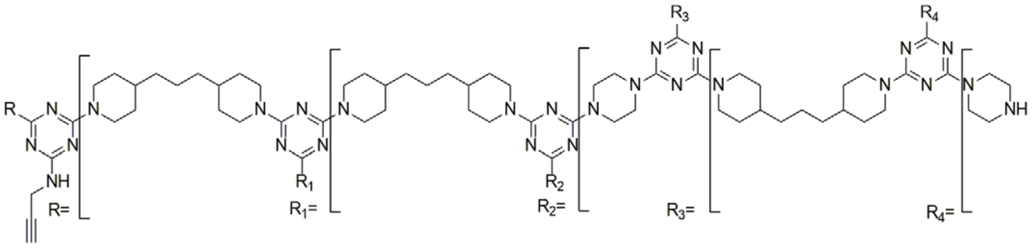


Figure S9. Mass Spectrum of **2-Boc** (MALDI-TOF)

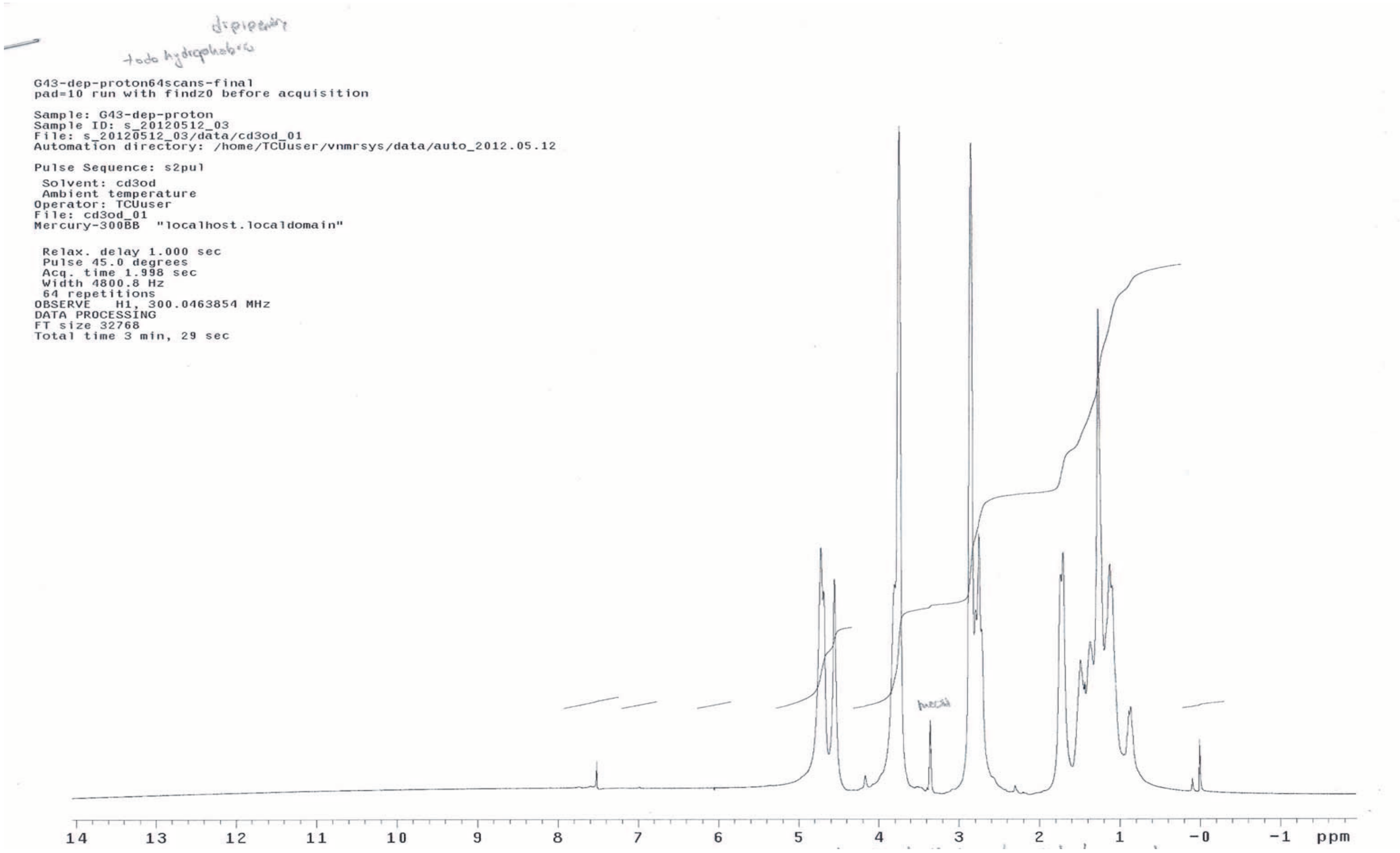




Dendrimer 2

A solution of **2-Boc** (0.100g, 0.0073mmol) in concentrated HCl (2mL) and methanol (2mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, and evaporated under vacuum to yield **13** (0.076g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.72-4.55 (bs, 88H, equatorial C**H**N-triazine of dipiperidine), 4.17 (s, 2H, NHC$\mathbf{H_2}$CCH), 3.75 (s, 192H, (128H) triazine-NCH$_2$C$\mathbf{H_2}$NH, (64H) triazine-NC$\mathbf{H_2}$C$\mathbf{H_2}$-triazine), 2.85 (s, 128H, triazine-NC$\mathbf{H_2}$CH$_2$NH), 2.79 (bs, 88H, equatorial C**H**CH$_2$N-triazine of dipiperidine), 2.3 (bt, 1H, NHCH$_2$CC**H**), 1.71 (s, 88H, axial C**H**N-triazine of dipiperidine), 1.44-1.13 (264H (288H) axial C**H**CH$_2$N-triazine of dipiperidine (88H), C**H**-trimethylene (44H), C$\mathbf{H_2}$C$\mathbf{H_2}$C$\mathbf{H_2}$ (132H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.53, 165.18 164.91 ($N_3\mathbf{C}_3$), 45.30 (NCH$_2$**C**H$_2$NH), 43.76 (NCH$_2$**C**H$_2$N-triazine), 43.12 (N**C**H$_2$CH$_2$N-triazine), 36.75 (H**C**-trimethylene), 36.25 (**C**H$_2$CH$_2$**C**H$_2$), 32.18 (CH**C**H$_2$CH$_2$N), 28.59 (CH2**C**H2N-triazine-piperidine-NH), 23.8 (CH$_2$**C**H$_2$CH$_2$). MS (MALDI-TOF) calcd for $C_{542}H_{884}N_{218}$: 10447.59; found 10489.26 $(M + H)^+$.

Figure S10. ^{1}H NMR Spectrum of **2**



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todo hydrophobico

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 Ambient temperature
Operator: TCUuser
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Figure S11. ^{13}C NMR Spectrum of **2**

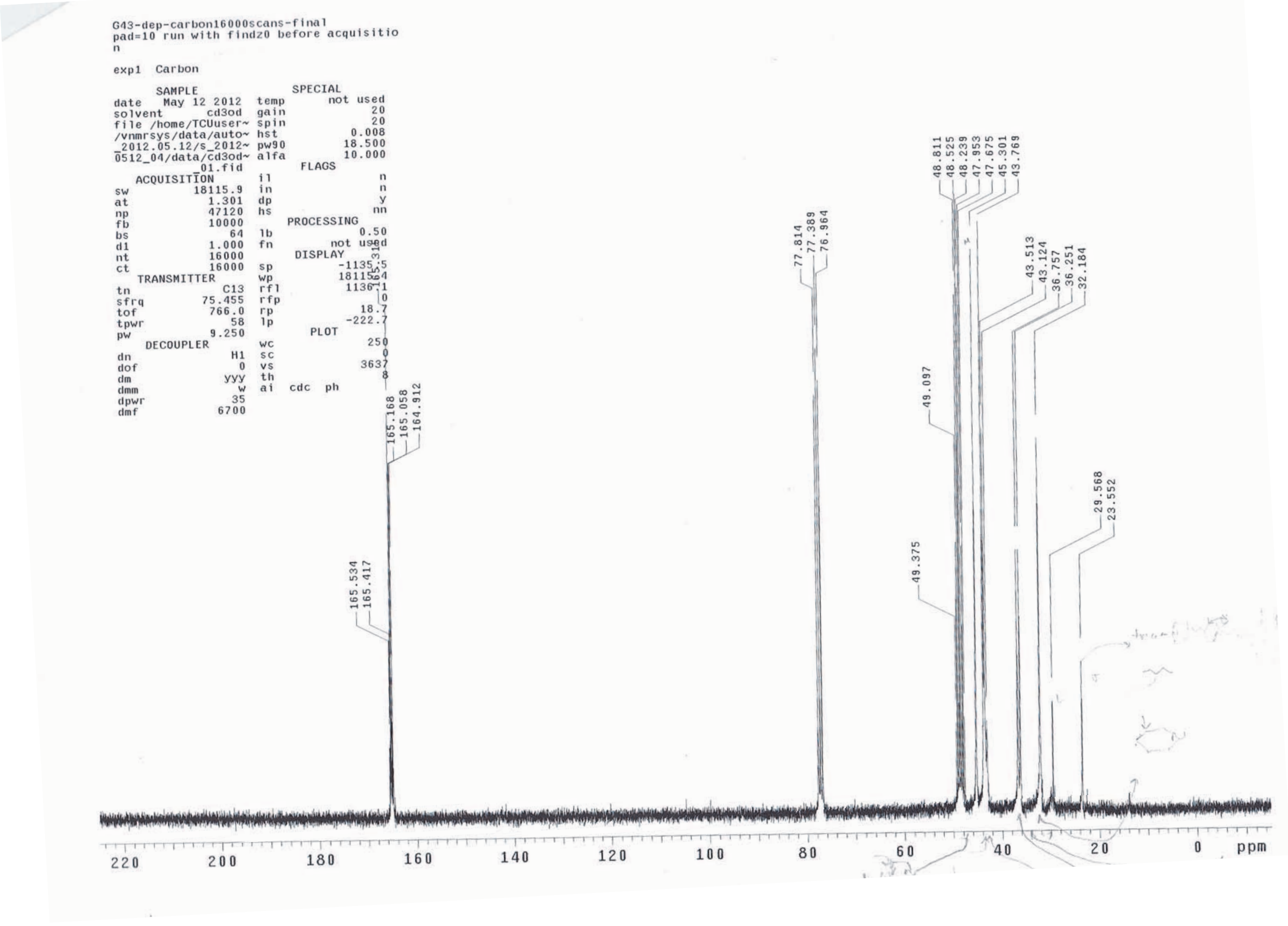

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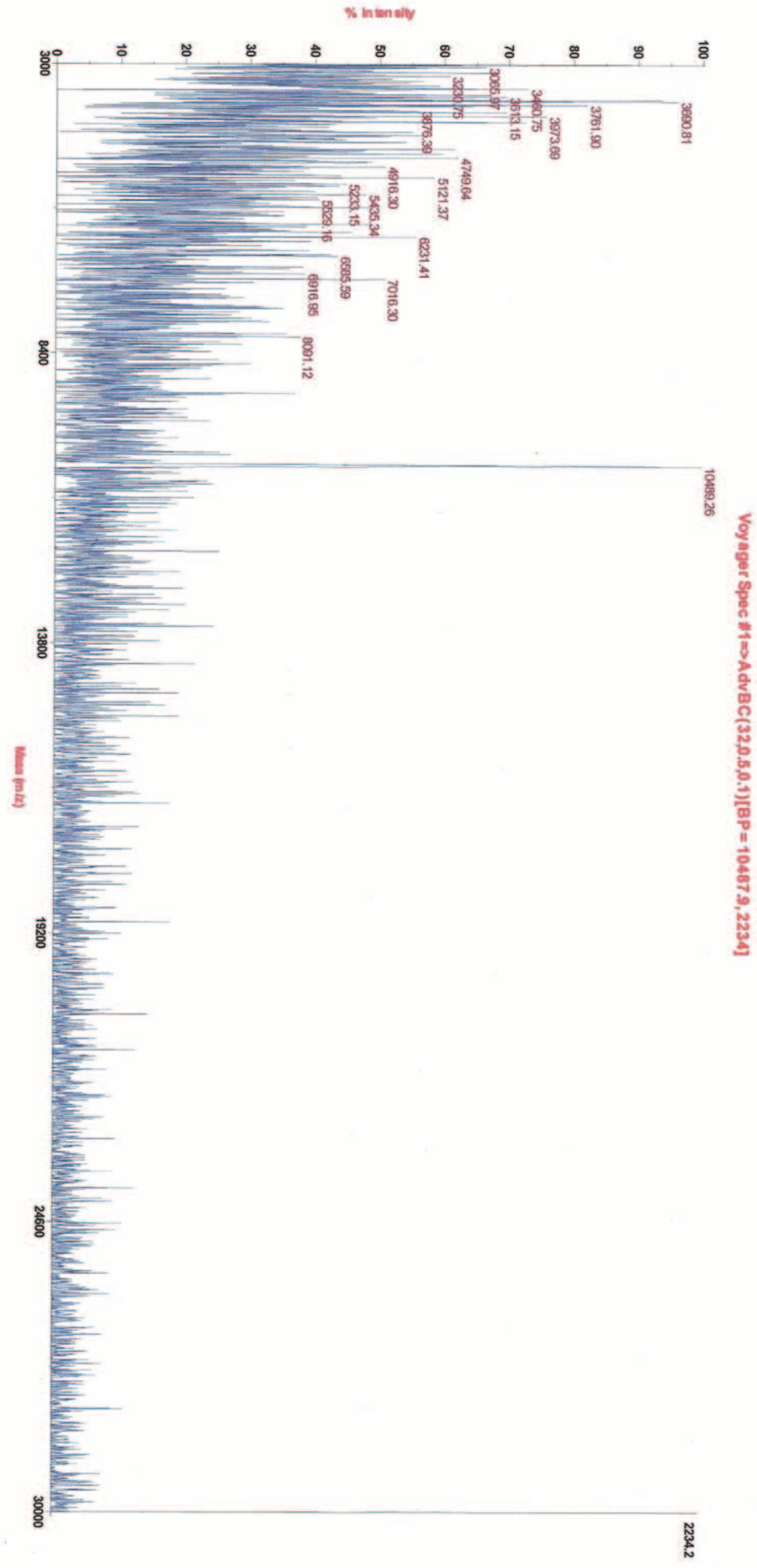
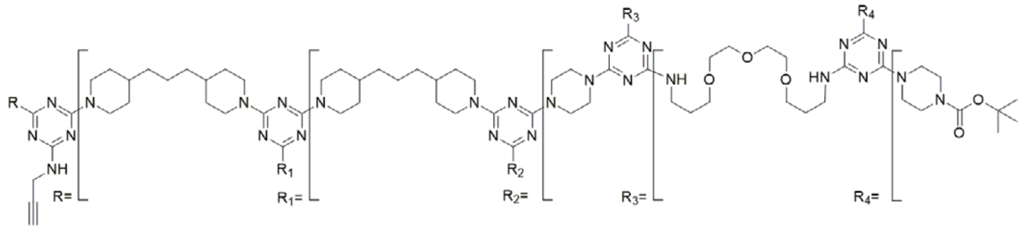
Figure S12. Mass Spectrum of **2** (MALDI-TOF)





Compound 3-Boc

A solution of compound **1** (0.146g, 0.058mmol), **10** (1.805g, 1.25mmol), and DIPEA (0.165mL, 0.95mmol) in 2.5mL of THF was stirred at 75°C for 4 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by silica gel chromatography (from 100% dichloromethane to dichloromethane: methanol = 9:1). Compound **3-Boc** (0.643g, 81%) was recovered as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.72 (bs, 24H, equatorial C**H**N-triazine of dipiperidine), 4.18 (s, 2H, NHC$\mathbf{H_2}$CCH), 3.72-3.4 (b, 576 H, (64H) triazine-NC$\mathbf{H_2}$CH$_2$N-triazine, (192H) C$\mathbf{H}_2$OC$\mathbf{H}_2$C$\mathbf{H}_2$OC$\mathbf{H}_2$C$\mathbf{H}_2$OC$\mathbf{H}_2$, (128H) NC$\mathbf{H}_2$CH$_2$NBoc, (64H) NHC$\mathbf{H_2}$CH$_2$CH$_2$O, (128H) NCH$_2$C$\mathbf{H_2}$NBoc), 2.7 (bs, 24H, equatorial C**H**CH$_2$N-triazine of dipiperidine), 2.18 (bt, 1H, NHCH$_2$CC**H**), 1.9-1.68 (b, 88H, (64H) OCH$_2$C$\mathbf{H_2}$CH$_2$NH, (24) axial C**H**N-triazine of dipiperidine), 1.47 (s, 288H, C(C**H**$_3$)$_3$), 1.33-0.85 (m, 72H, axial C**H**CH$_2$N-triazine of dipiperidine (24H), C**H**-trimethylene (12H), C$\mathbf{H_2}$C$\mathbf{H_2}$C$\mathbf{H_2}$ (36H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.2, 165.45, 164.9 (**C**$_3$N$_3$), 154.76 (**C**O), 79.8 (**C**(CH3)3), 70.57 (O**C**H$_2$**C**H$_2$O), 69.27 (NHCH$_2$CH$_2$**C**H$_2$O), 44.0 (trimethylene-CHCH$_2$**C**H$_2$N), 43.6, (NCH$_2$**C**H$_2$N-triazine), 43.63 (BocN**C**H$_2$CH$_2$N-triazine), 42.5 (N**C**H$_2$CH$_2$N-triazine), 36.9 (H**C**-trimethylene), 36.32 (NH**C**H2CH2CH2O), 36.3 (**C**H$_2$CH$_2$**C**H$_2$), 32.2 (**C**H$_2$CH$_2$N), 29.0 (NHCH$_2$**C**H$_2$CH$_2$O), 28.3 (C(**C**H$_3$)$_3$), 23.7 (CH$_2$**C**H$_2$CH$_2$). (MALDI-TOF) calcd for $C_{654}H_{1108}N_{218}O_{112}$: 13808.77; found 13808.47 $(M + H)^+$.

Figure S13. ^{1}H NMR Spectrum of **3-Boc**

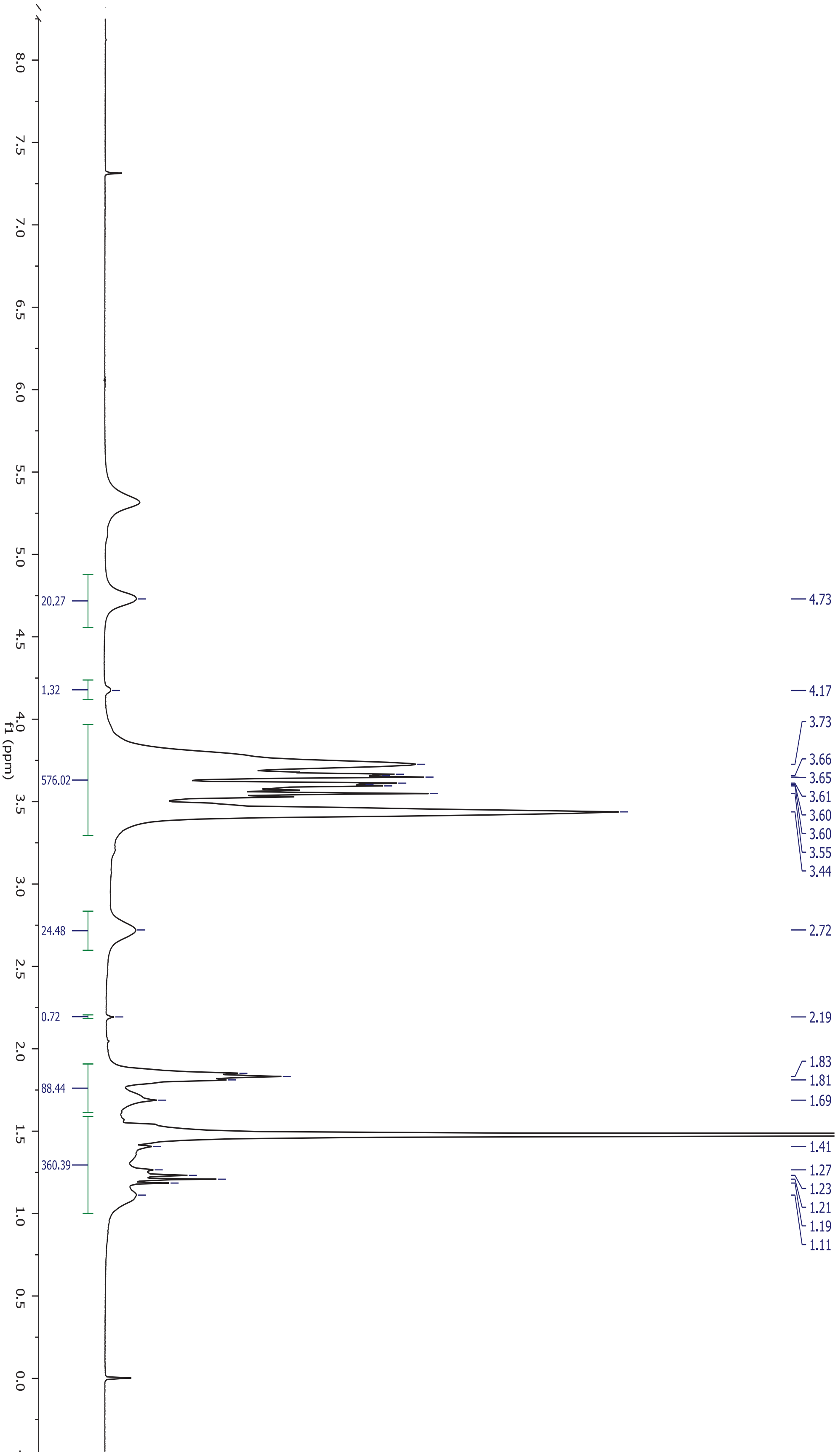


Figure S14. ^{13}C NMR Spectrum of **3-Boc**

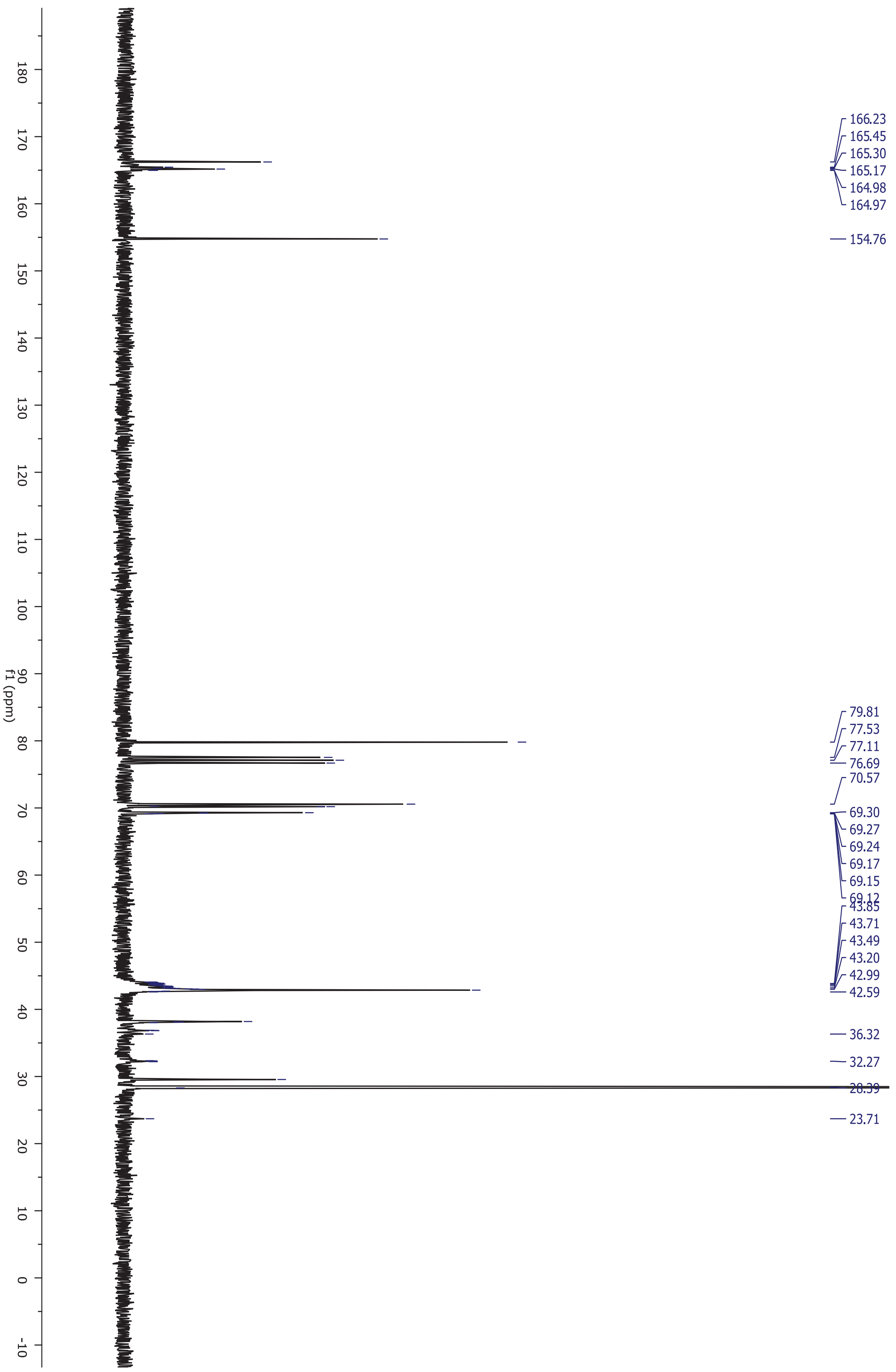
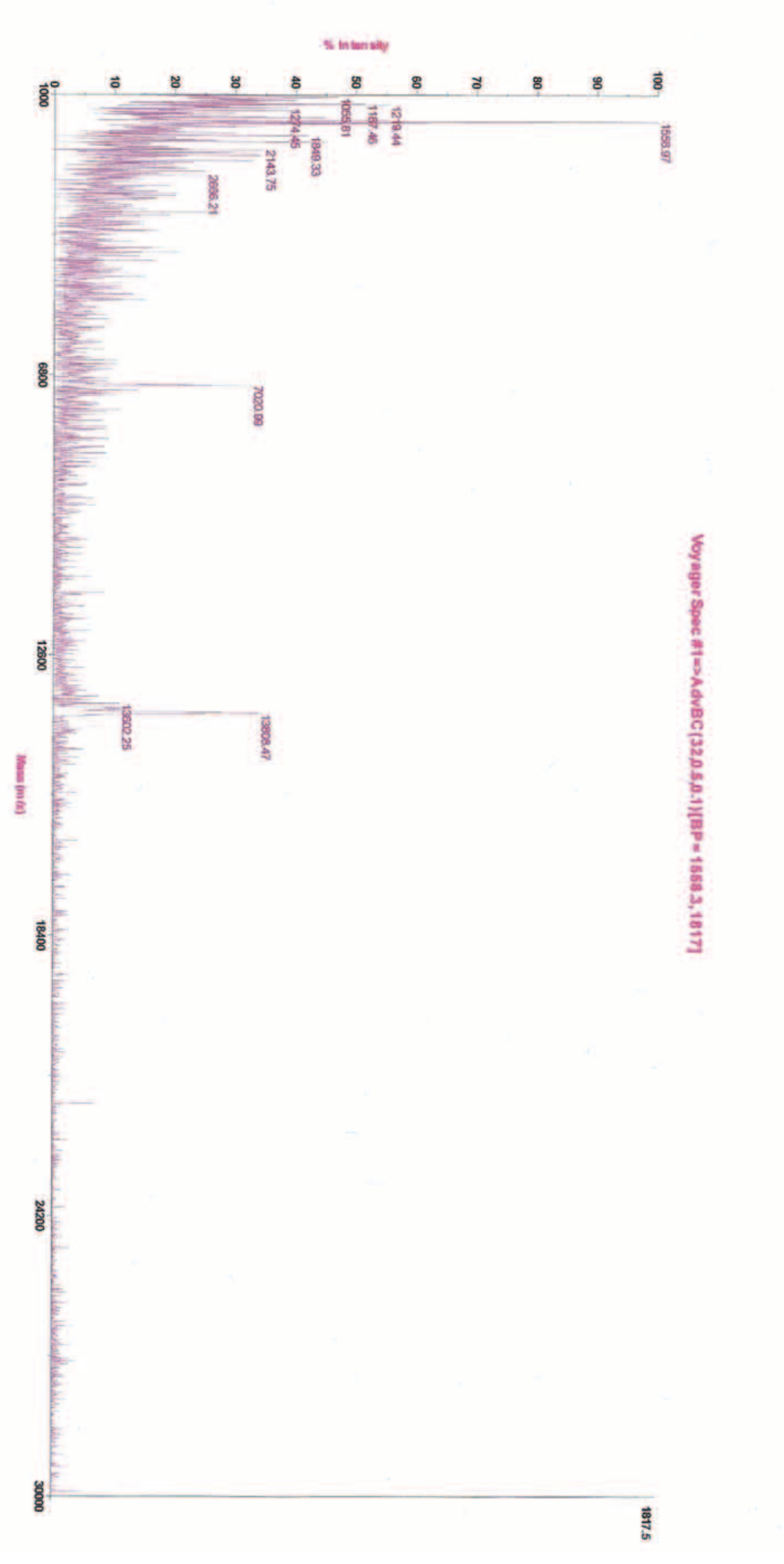
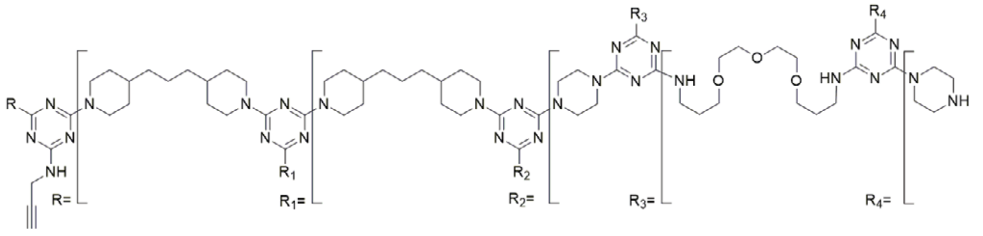


Figure S15. Mass Spectrum of **3-Boc** (MALDI-TOF)





Dendrimer 3

A solution of **3-Boc** (0.195g, 0.014mmol) in concentrated HCl (2mL) and methanol (2mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, and evaporated under vacuum to yield Dendrimer **3** (0.149g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.71 (bs, 24H, equatorial C**H**N-triazine of dipiperidine), 4.17 (s, 2H, $NHC\mathbf{H_2}CCH$), 3.76-3.43 (b, 448 H, (64H) triazine-$NC\mathbf{H_2}CH_2N$-triazine,(192H) $C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}$, (64H) $NHC\mathbf{H_2}CH_2CH_2O$, (128H) triazine-$NC\mathbf{H_2}CH_2NH_2$), 2.84 (bs, 128H $NCH_2C\mathbf{H_2}NH_2$), 2.71 (t, *J = 12Hz*, 24H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.8-1.68 (b, 88H, (64H) $OCH_2C\mathbf{H_2}CH_2NH$, (24) axial C**H**N-triazine of dipiperidine), 1.33-0.85 (m, 72H, axial $C\mathbf{H}CH_2N$-triazine of dipiperidine (24H), C**H**-trimethylene (12H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (36H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 167.3, 166.15 ($\mathbf{C}_3N_3$), 71.01 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 69.74 ($NHCH_2CH_2\mathbf{C}H_2O$), 46.31 ($H_2N\mathbf{C}H_2CH_2N$-triazine), 43.6 ($H_2NCH_2\mathbf{C}H_2N$-triazine), 38.36 (trimethylene-$CHCH_2\mathbf{C}H_2N$), 38.25 ($N\mathbf{C}H_2CH_2N$-triazine), 37.09 (H**C**-trimethylene), 36.37 (NH**C**H2CH2CH2O), 36.57 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.43 ($\mathbf{C}H_2CH_2N$), 29.8 ($NHCH_2\mathbf{C}H_2CH_2O$), 23.8 ($CH_2\mathbf{C}H_2CH_2$). (ESI-TOF) calcd for $C_{494}H_{852}N_{218}O_{48}$: 10607.09; found 10604.87 $(M + H)^+$.

Figure S16. ^{1}H NMR Spectrum of **3**

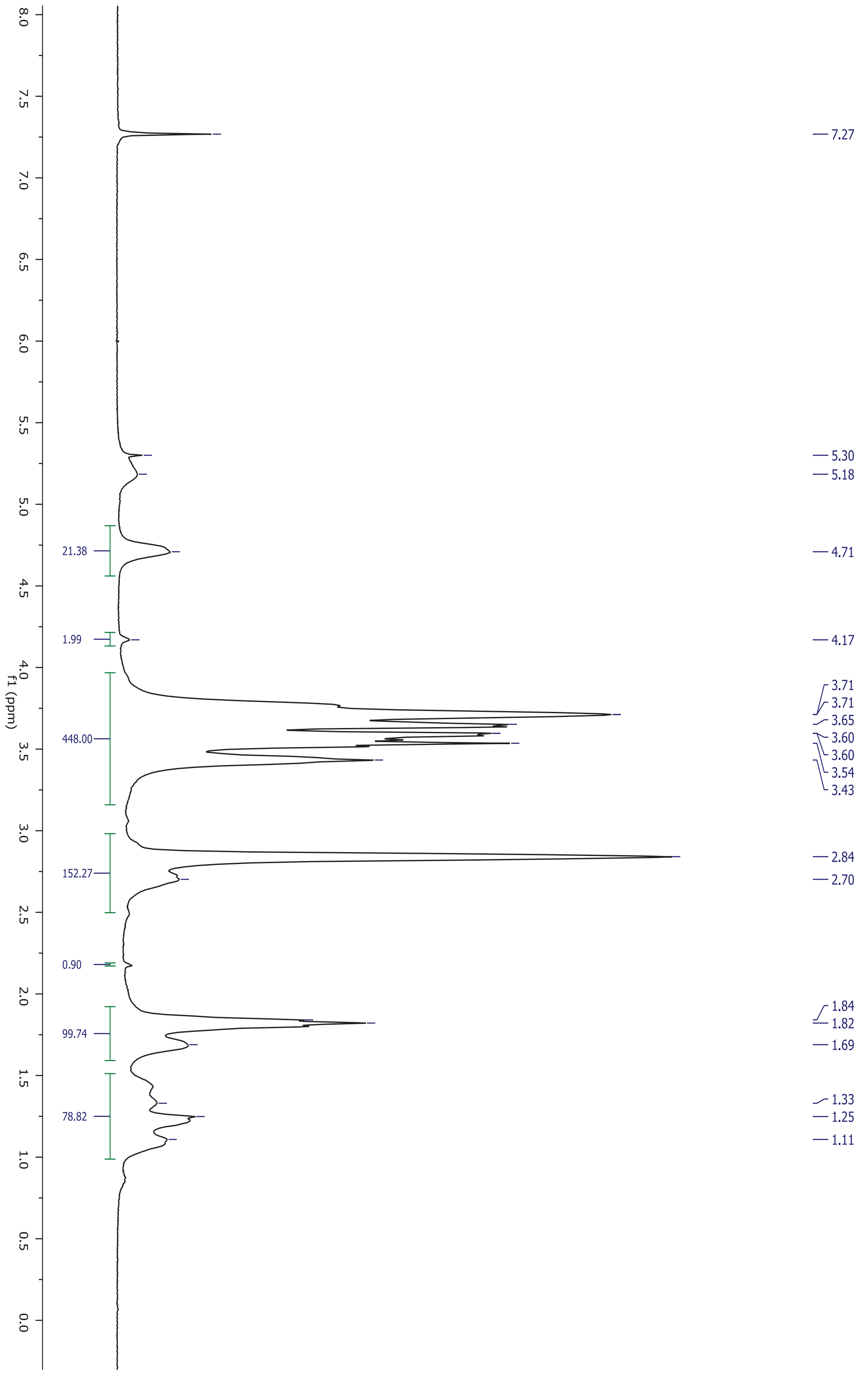


Figure S17. ^{13}C NMR Spectrum of **3**

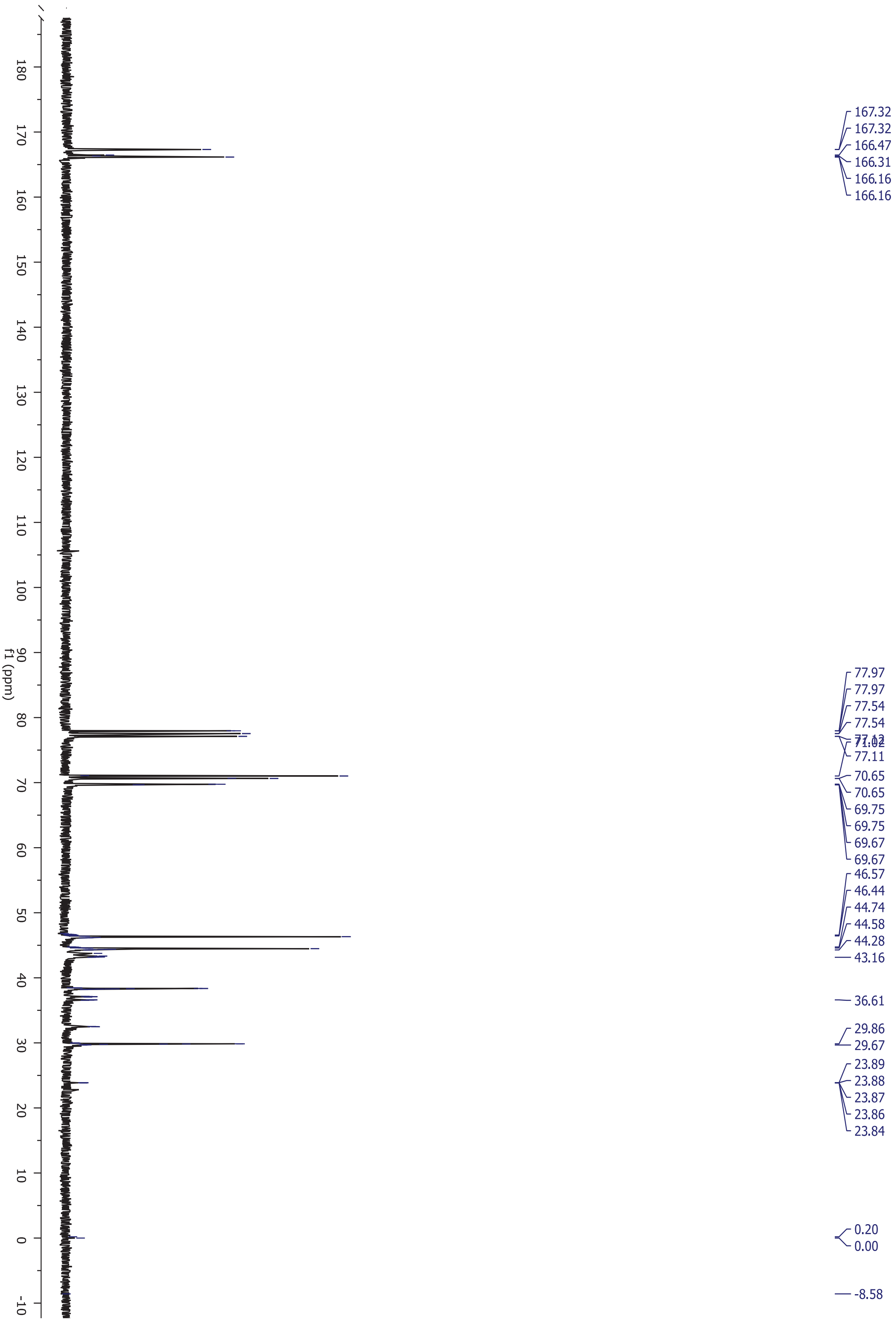
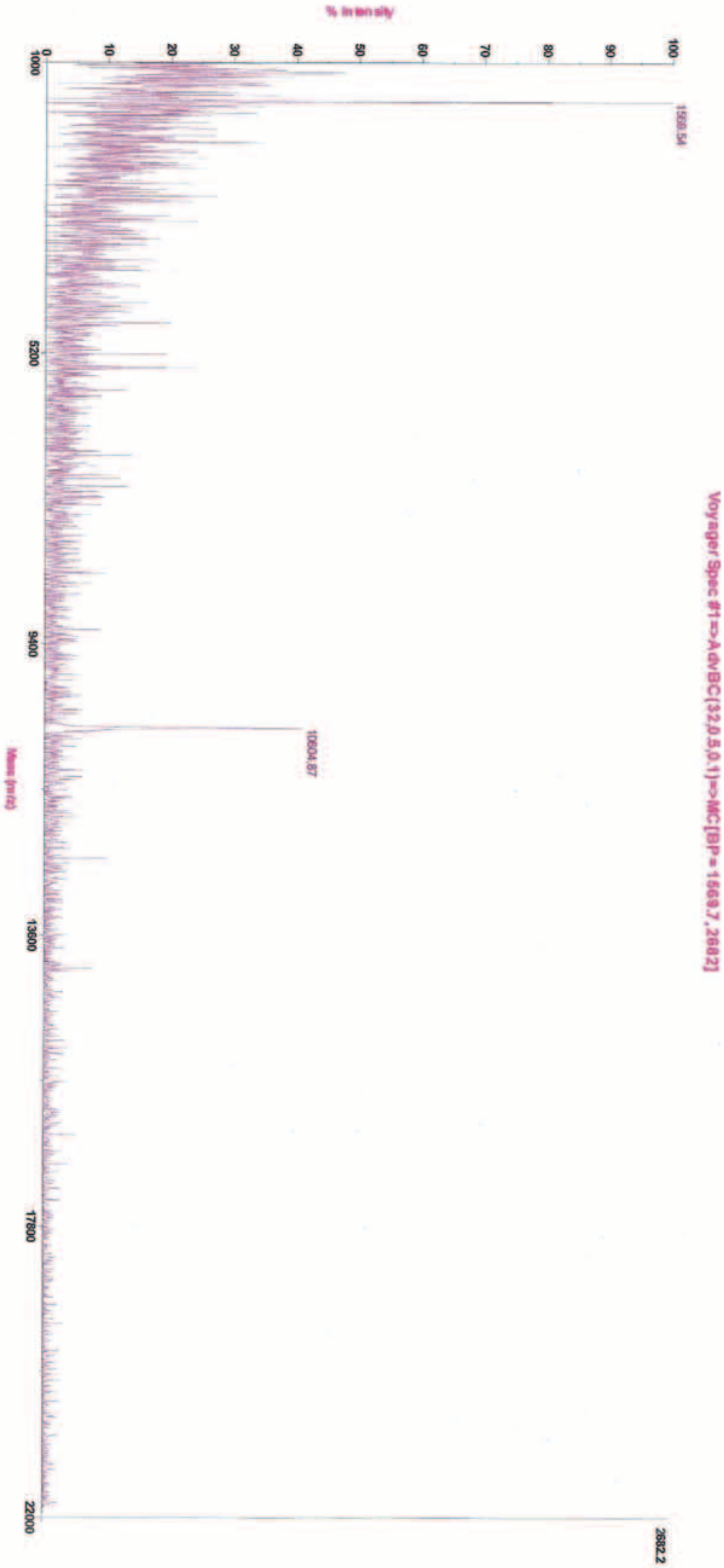
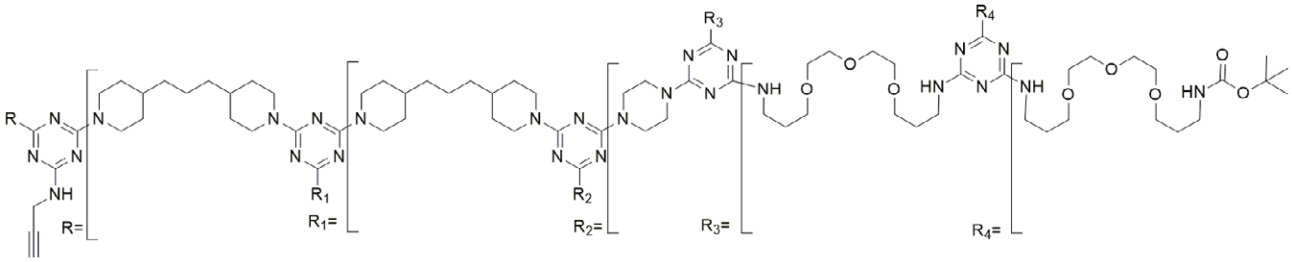


Figure S18. Mass Spectrum of **3** (MALDI-TOF)





Compound 4-Boc

A solution of compound dendrimer **1** (0.038g, 0.0150mmol), **11** (0.476g, 0.24mmol), and DIPEA (0.04mL, 0.24mmol) in 1.2mL of THF was stirred and heated at 75°C during 4 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by precipitation EtOAc/ hexanes. Compound **4-Boc** (0.225g, 83%) was recovered as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.72 (bs, 24H, equatorial $C\mathbf{H}N$-triazine of dipiperidine), 4.18 (s, 2H, $NHC\mathbf{H_2}CCH$), 3.64-3.43 (b, 768 H, (m, (608H), $C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}$, (96) C_3N_3-$NHC\mathbf{H_2}CH_2CH_2O$) (64H) triazine-$NC\mathbf{H_2}CH_2N$-triazine,), 3.21 (br m, 64H, $BocNHC\mathbf{H_2}$), 2.71 (bs, 24H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.82-1.73 (b, 216H, (192H) $OCH_2C\mathbf{H_2}CH_2NH$, (24) axial $C\mathbf{H}N$-triazine of dipiperidine), 1.43 (s, 288H, $C(C\mathbf{H_3})_3$), 1.23-1.10 (m, 72H, axial $C\mathbf{H}CH_2N$-triazine of dipiperidine (24H), $C\mathbf{H}$-trimethylene (12H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (36H)). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 166.91, 166.3, 166.14, 165.96, 165.83 ($\mathbf{C}_3N_3$), 156.8 ($\mathbf{C}O$), 79.02 ($\mathbf{C}$(CH3)3), 70.7 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.4 (two lines, $O\mathbf{C}H_2\mathbf{C}H_2O$), 69.7 ($CH_2CH_2\mathbf{C}H_2O$), 69.45 ($CH_2CH_2\mathbf{C}H_2O$), 43.13 (trimethylene-$CHCH_2\mathbf{C}H_2N$), 38.76, ($NCH_2\mathbf{C}H_2N$-triazine), 38.11 ($N\mathbf{C}H_2CH_2N$-triazine), 36.91 ($H\mathbf{C}$-trimethylene), 36.39 ($\mathbf{C}H_2CH_2N$), 36.3 not found ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.25 ($NH\mathbf{C}H_2CH_2CH_2O$), 30.0 ($NHCH_2\mathbf{C}H_2CH_2O$), 28.43 ($C(\mathbf{C}H_3)_3$), 23.67 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{846}H_{1556}N_{218}O_{208}$: 18110.74; found 18111.48 $(M + H)^+$.

Figure S19. ^{1}H NMR Spectrum of **4-Boc**

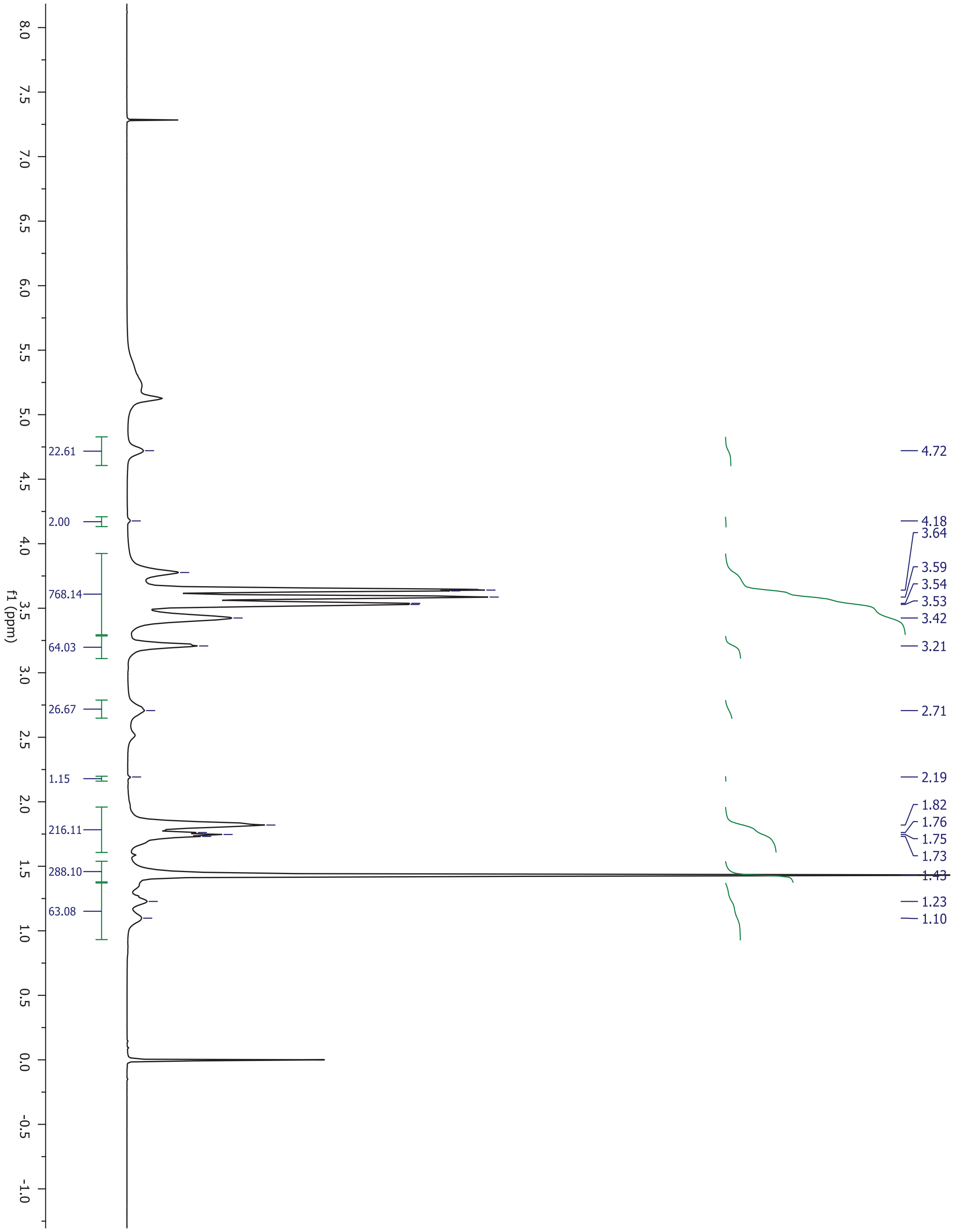


Figure S20. ^{13}C NMR Spectrum of **4-Boc**

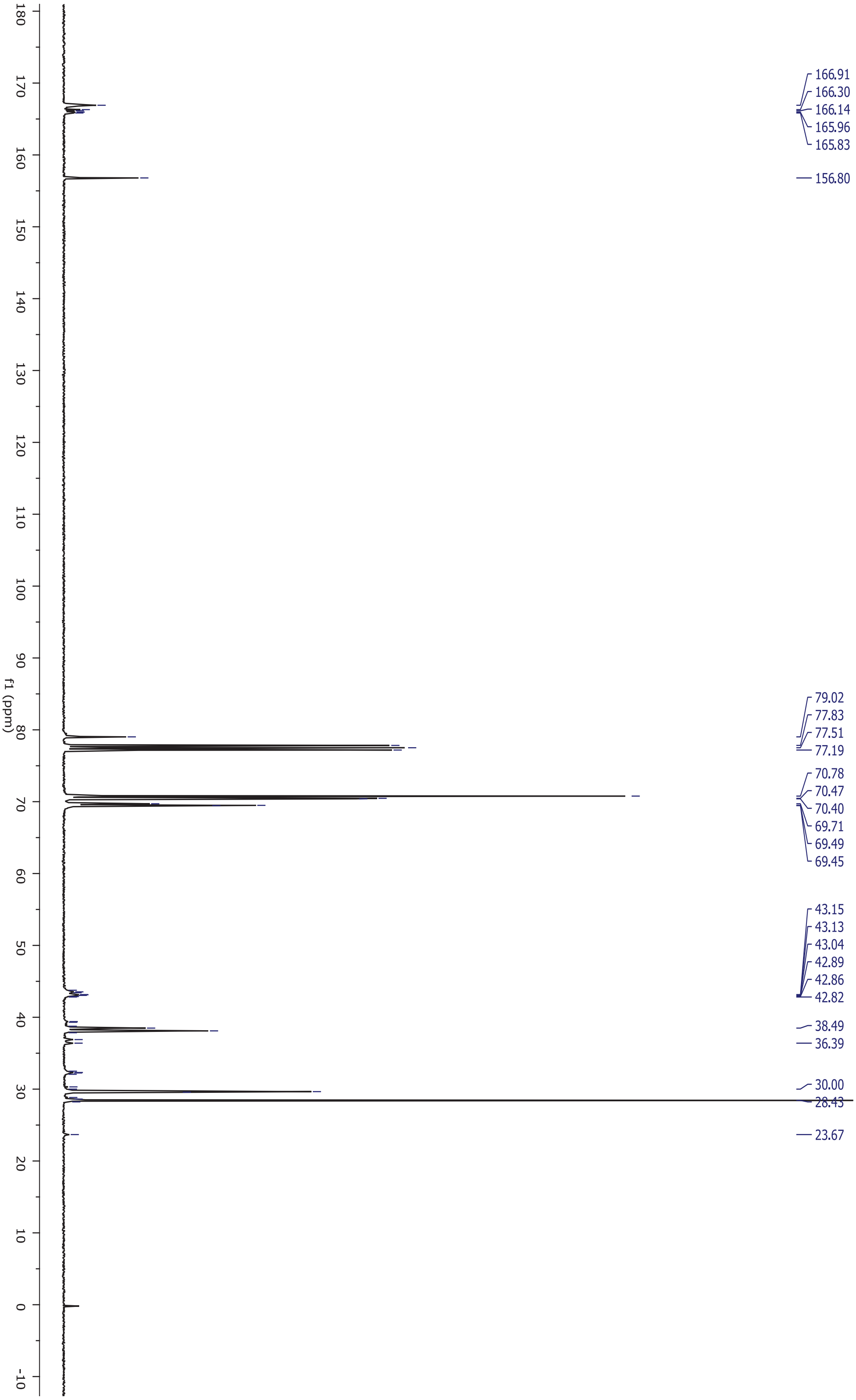
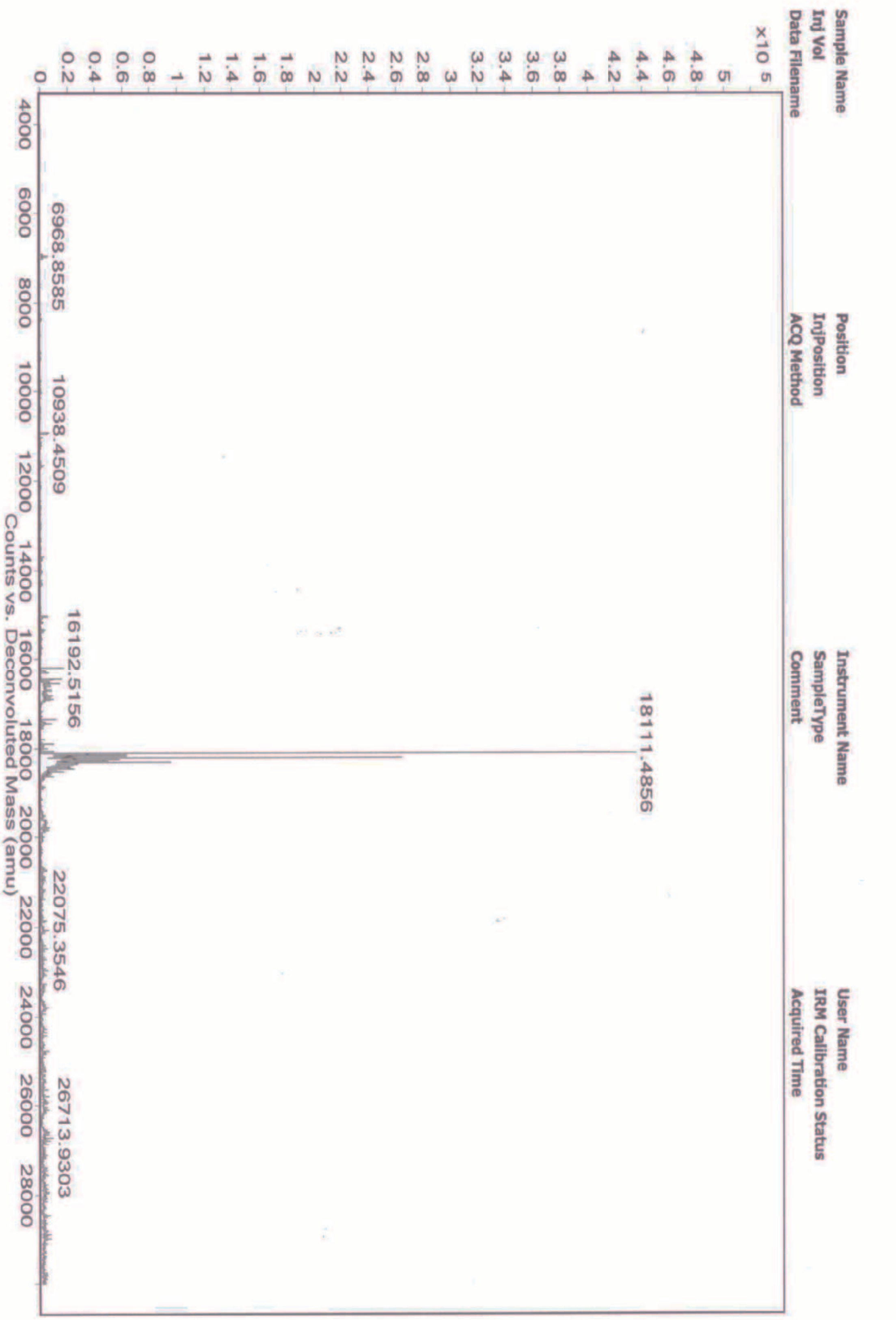
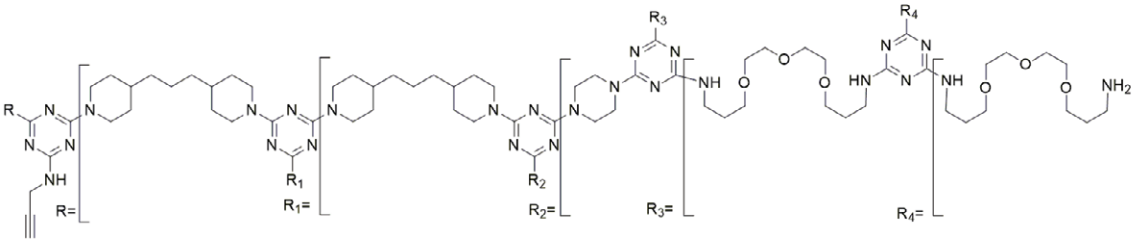


Figure S21. Mass Spectrum of **4-Boc** (ESI-TOF)





Dendrimer 4

A solution of compound **4-Boc** (0.226g, 0.012mmol) in concentrated HCl (2mL) and methanol (2mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, and evaporated under vacuum to yield dendrimer **4** as a white wax (0.186g, quantitative). ^1H NMR (400 MHz, $CDCl_3$, δ): 4.72 (bs, 24H, equatorial $C\mathbf{H}N$-triazine of dipiperidine), 4.18 (s, 2H, $NHC\mathbf{H_2}CCH$), 3.77-3.41 (b, 768 H, (m, (608H), $C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}C\mathbf{H_2}OC\mathbf{H_2}$, (96H) C_3N_3-$NHC\mathbf{H_2}CH_2CH_2O$) (64H) triazine-$NC\mathbf{H_2}CH_2N$-triazine), 2.77 (br m, 64H, $BocNHC\mathbf{H_2}$), 2.71 not found (bs, 24H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.81-0.88 (b, 288H, (192H) $OCH_2C\mathbf{H_2}CH_2NH$, (24) axial $C\mathbf{H}N$-triazine of dipiperidine, $C\mathbf{H}CH_2N$-triazine of dipiperidine (24H), $C\mathbf{H}$-trimethylene (12H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (36H)). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 167.12, 166.50, 166.34, 166.16, 166.04 ($\mathbf{C}_3N_3$), 71.02 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.6 (two lines, $O\mathbf{C}H_2\mathbf{C}H_2O$), 69.8 ($CH_2CH_2\mathbf{C}H_2O$), 69.67 ($CH_2CH_2\mathbf{C}H_2O$), 44.01 (trimethylene-$CHCH_2\mathbf{C}H_2N$), 39.26, ($NCH_2\mathbf{C}H_2N$-triazine), 38.26 ($N\mathbf{C}H_2CH_2N$-triazine), 37.08 ($H\mathbf{C}$-trimethylene), 36.59 ($\mathbf{C}H_2CH_2N$), 36.3 not found ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 33.6 ($NH_2\mathbf{C}H_2CH_2CH_2O$), 32.50 ($NH\mathbf{C}H_2CH_2CH_2O$), 29.86 ($NHCH_2\mathbf{C}H_2CH_2O$), 23.84 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{683}H_{1300}N_{218}O_{144}$: 14898.11; found 14908.11 $(M + H)^+$.

Figure S22. ^{1}H NMR Spectrum of **4**

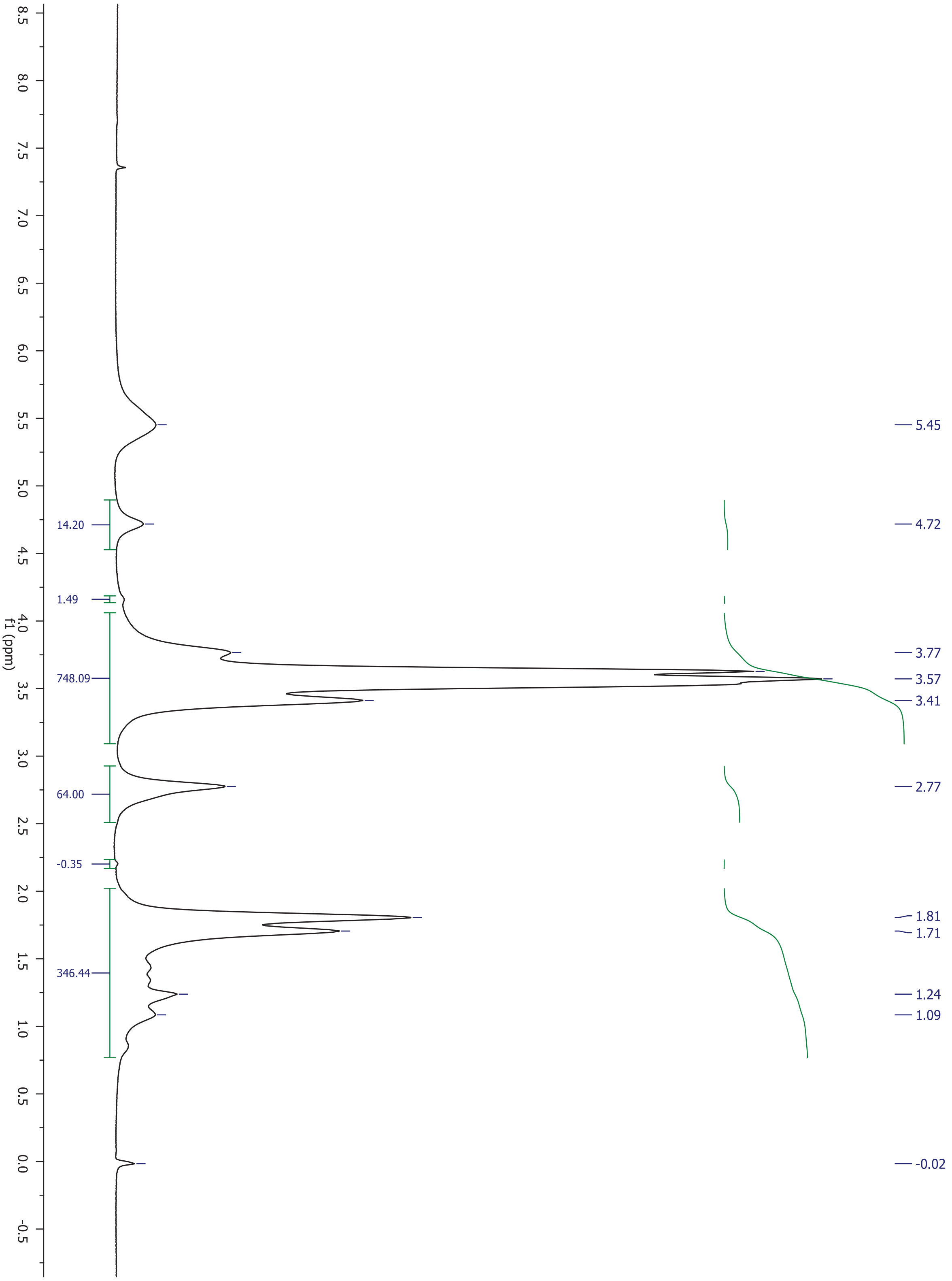


Figure S23. ^{13}C NMR Spectrum of **4**

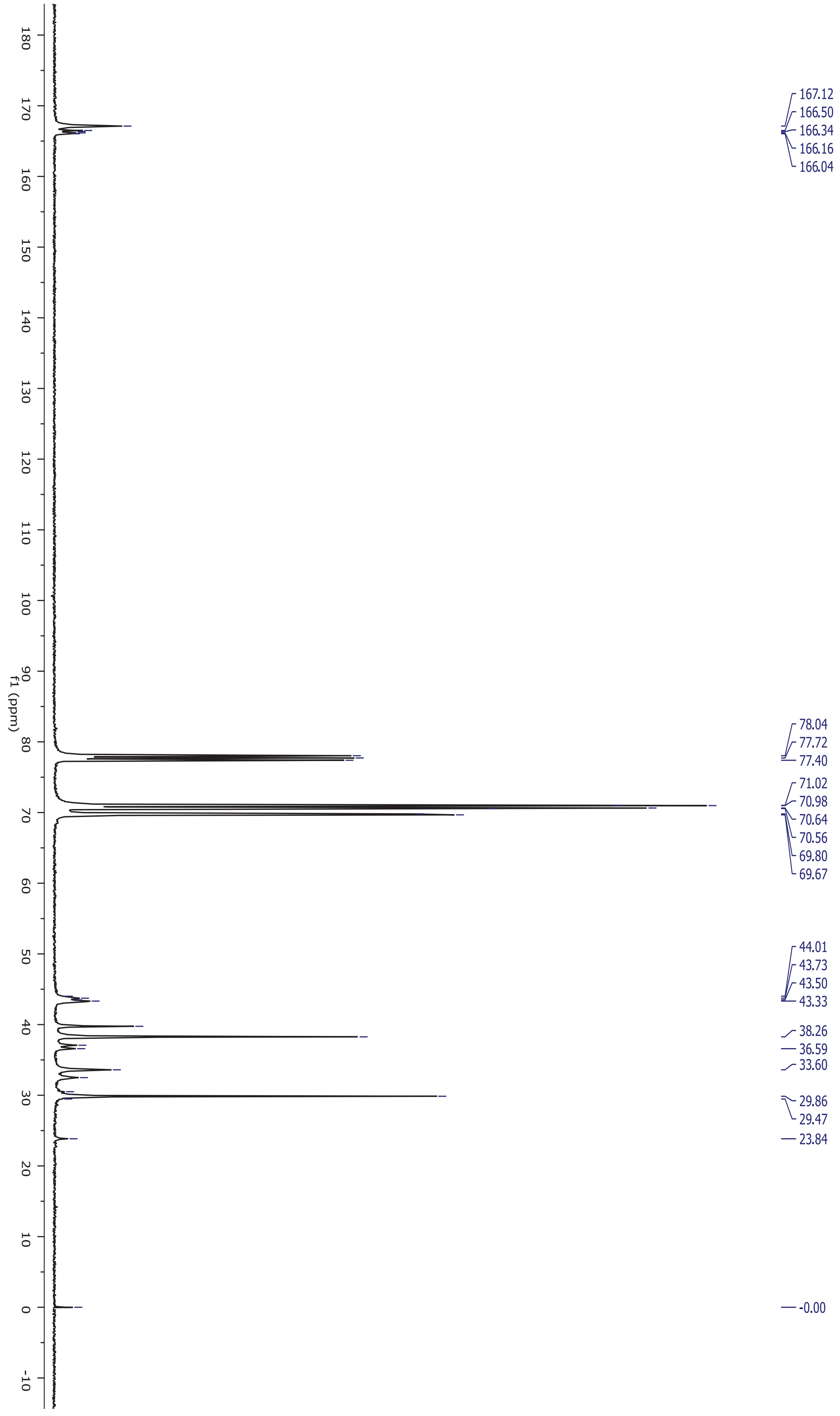
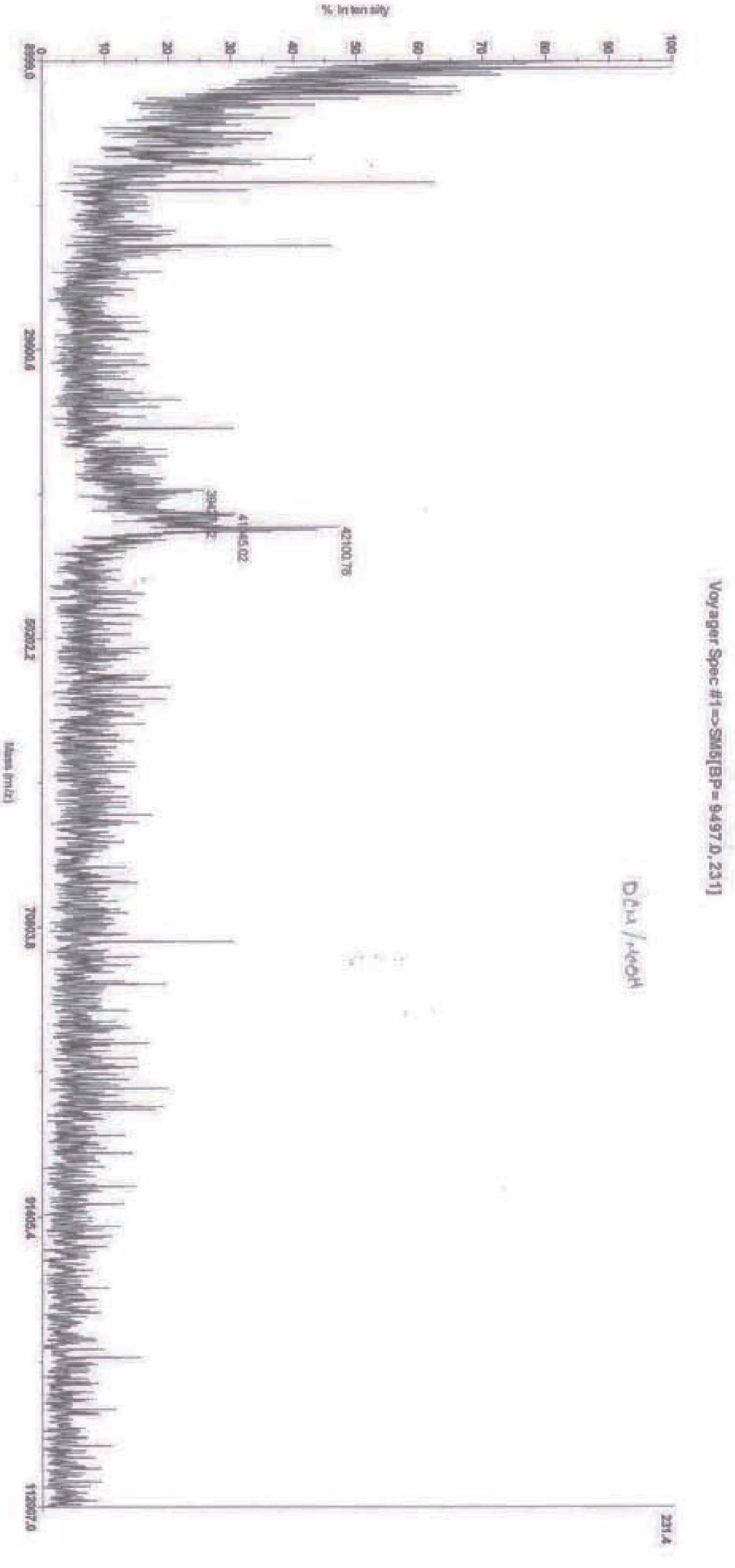
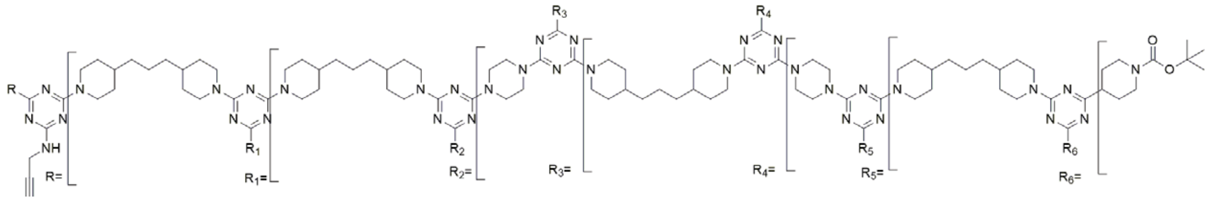


Figure S24. Mass Spectrum of **4** (MALDI-TOF)





Compound 5-Boc

A solution of compound dendrimer **2** (0.088g, 0.0084mmol), **9** (0.769g, 0.54mmol), DIPEA (0.094mL, 0.54mmol) in 0.5mL of THF and 0.2mL of MeOH was stirred and heated at 75°C during 6 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine, the organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by precipitation EtOAc/ hexanes. Compound **5-Boc** (0.32g, 70%) was recovered as a white solid. . ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.73 (bs, 344H, equatorial C**H**N-triazine of dipiperidine), 4.18 (s, 2H, $NHC\mathbf{H_2}CCH$, not found), 3.80-3.74 (s, 704H, (512H) triazine-$NCH_2C\mathbf{H_2}NBoc$, (192H) triazine-$NC\mathbf{H_2}C\mathbf{H_2}$-triazine), 3.45 (s, 512H, triazine-$NC\mathbf{H_2}CH_2NBoc$), 2.74-2.71 (bs, 344H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 (bt, 1H, $NHCH_2CC\mathbf{H}$**,** not found), 1.72 (s, 344H, axial C**H**N-triazine of dipiperidine), 1.49-1.09 (2696H (1152H) $C(C\mathbf{H_3})_3$, (856H) axial $C\mathbf{H}CH_2N$-triazine of dipiperidine, (172H) C**H**-trimethylene, (516H) $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.5,165.2,165.0 ($N_3\mathbf{C}_3$), 154.8 (**C**O), 79.8 ($\mathbf{C}(CH_3)_3$), 43.5 ($CHCH_2\mathbf{C}H_2N$), 43.5, ($NCH_2\mathbf{C}H_2N$-triazine), 43.0 ($N\mathbf{C}H_2CH_2N$-triazine), 36.8 (H**C**-trimethylene), 36.3 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 32.2 ($\mathbf{C}H_2CH_2N$), 28.4 ($C(\mathbf{C}H_3)_3$), 23.6 ($CH_2\mathbf{C}H_2CH_2$). MS (MALDI-TOF) calculated for $C_{2814}H_{4564}N_{890}O_{256}$: 54825.15; not found.

Figure S25. ^{1}H NMR Spectrum of **5-Boc**

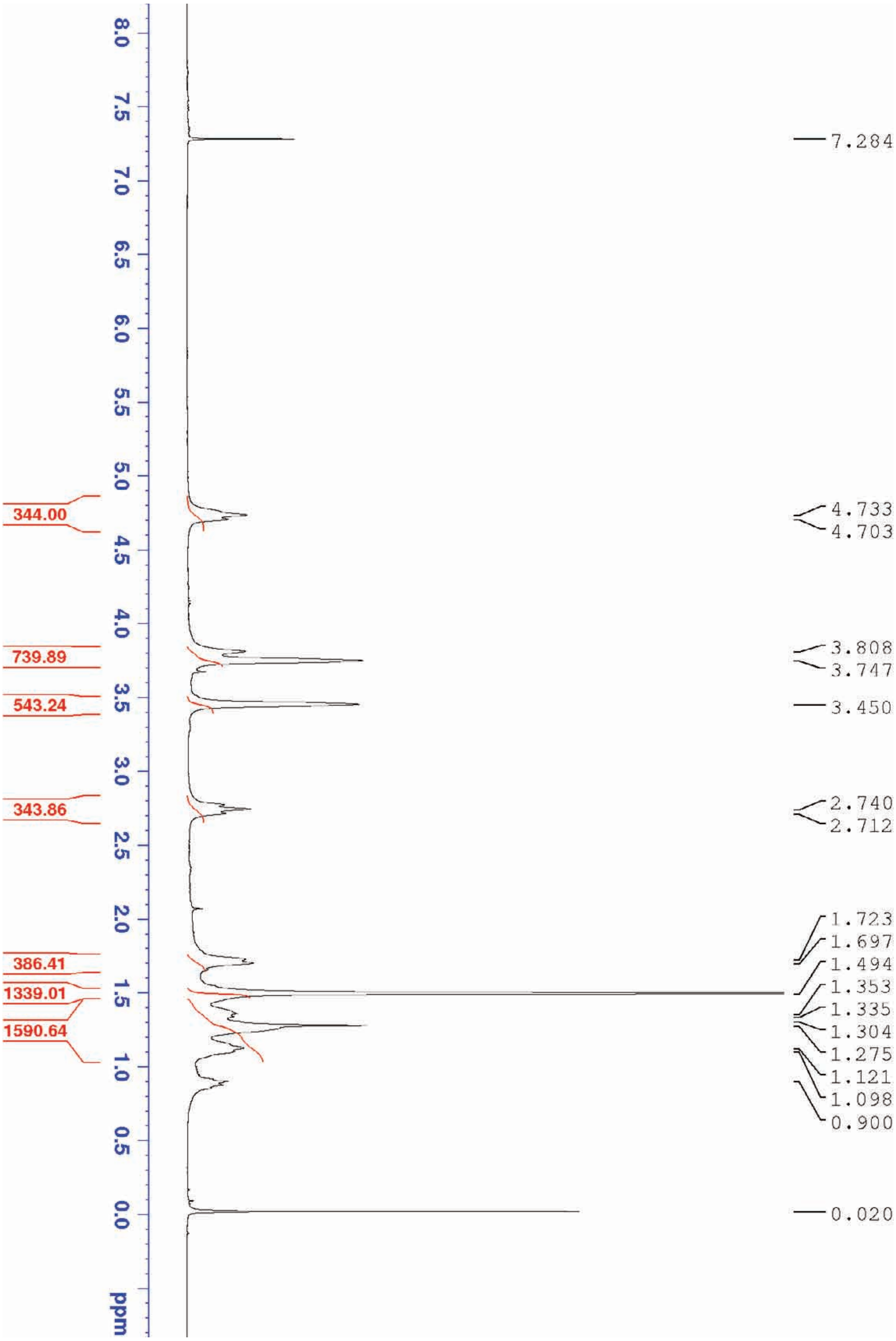
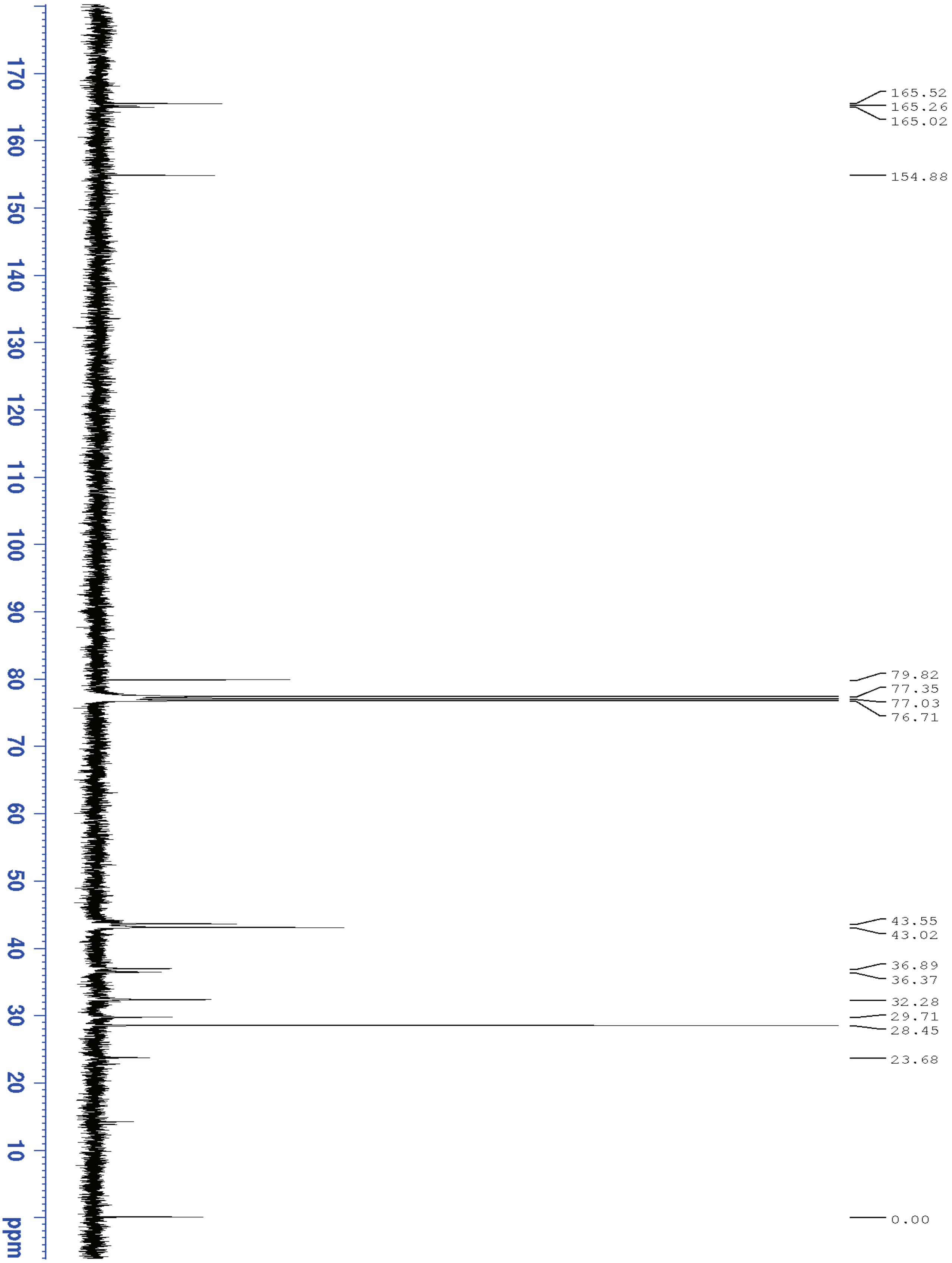
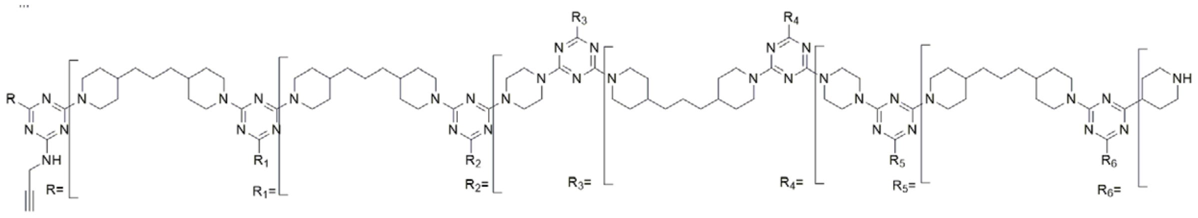


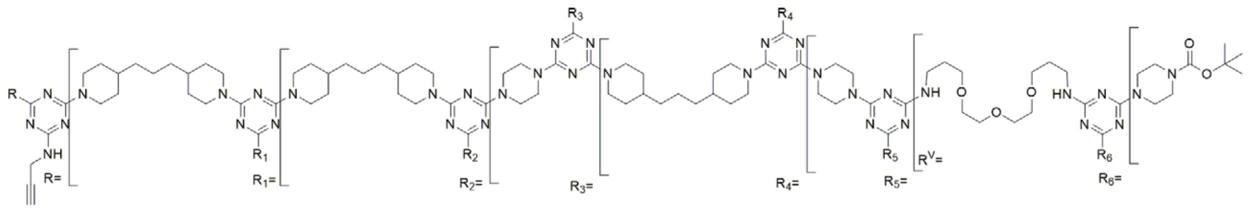
Figure S26. ^{13}C NMR Spectrum of **5-Boc**





Dendrimer 5

A solution of compound **5-Boc** (0.015g, 0.00027mmol) in concentrated HCl (0.5mL) and methanol (0.5mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq*.), passed through a phase separator from Whatman, evaporated under vacuum to yield **5** (0.011g, quant.). After evaporation the white solid recovered could not be redissolved. No characterization data is available. The structure of the product is assumed.



Compound 6-Boc

A solution of compound dendrimer **2** (0.074g, 0.0070mmol), **10** (0.392g, 0.271mmol), and DIPEA (0.08mL, 0.46mmol) in 1.8mL of THF and 0.5mL of MeOH was stirred at 75°C for 4 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by precipitation EtOAc/ hexanes. Compound **6-Boc** (0.37g, 95%) was recovered as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 4.73 (bs, 88H, equatorial C**H**N-triazine of dipiperidine), 4.18 not found (s, 2H, $NHC\mathbf{H_2}CCH$), 3.65-3.43 (b, 2368 H, (320H) triazine-$NC\mathbf{H_2}CH_2N$-triazine, (768H) $C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2$, (512H) $NC\mathbf{H}_2CH_2NBoc$, (256H) $NHC\mathbf{H_2}CH_2CH_2O$, (512H) $NCH_2C\mathbf{H_2}NBoc$), 2.73 (bs, 88H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine), 2.18 not found (bt, 1H, $NHCH_2CC\mathbf{H}$), 1.82-1.63 (b, 344H, (256H) $OCH_2C\mathbf{H_2}CH_2NH$, (88) axial C**H**N-triazine of dipiperidine), 1.47 (s, 1152H, $C(C\mathbf{H}_3)_3$), 1.33-0.85 (m, 264H, axial $C\mathbf{H}CH_2N$-triazine of dipiperidine (88H), C**H**-trimethylene (44H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (132H)). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 167.61, 166.53 ($\mathbf{C}_3N_3$), 156.05 (**C**O), 80.63 (**C**(CH3)3), 71.34 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.01 ($NHCH_2CH_2\mathbf{C}H_2O$), 44.51 (trimethylene-$CHCH_2CH_2N$), 43.65 ($NCH_2\mathbf{C}H_2N$-triazine), 43.46 ($BocN\mathbf{C}H_2CH_2N$-triazine), 38.77 ($N\mathbf{C}H_2CH_2N$-triazine), 37.49 (H**C**-trimethylene), 36.98 (NH**C**H2CH2CH2O), 32.86 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 30.08 ($\mathbf{C}H_2CH_2N$), 29.09 ($NHCH_2\mathbf{C}H_2CH_2O$), 28.9 ($C(\mathbf{C}H_3)_3$), 24.36 ($CH_2\mathbf{C}H_2CH_2$). (MALDI-TOF) calcd for $C_{2622}H_{4436}N_{890}O_{448}$: 55563.17; found (due to the high voltage the BOC groups were cleaved during the analysis and the deprotected mass is observed) 42754.46 $(M + H)^+$.

Figure S27. ^{1}H NMR Spectrum of **6-Boc**

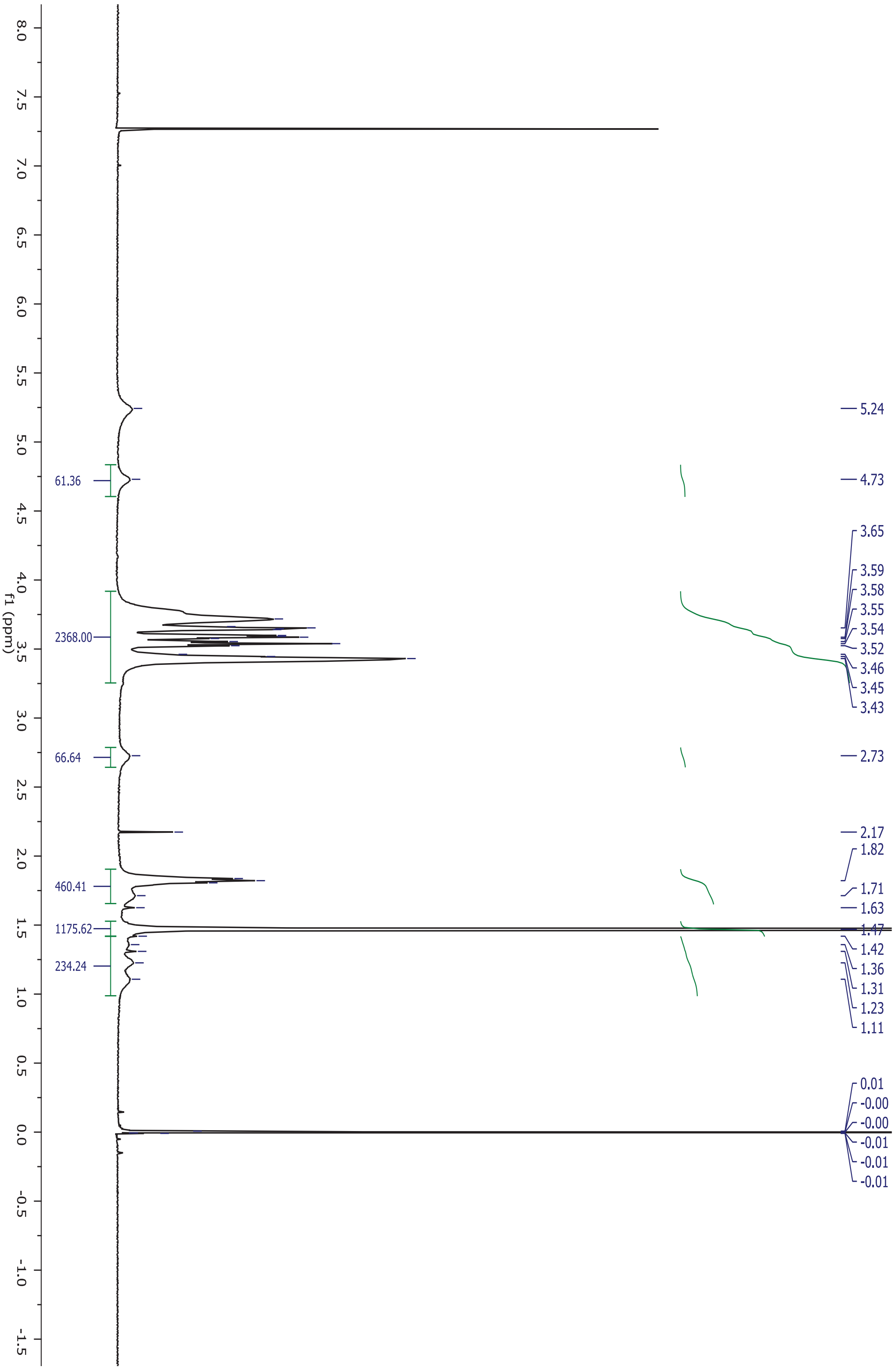


Figure S28. ^{13}C NMR Spectrum of **6-Boc**

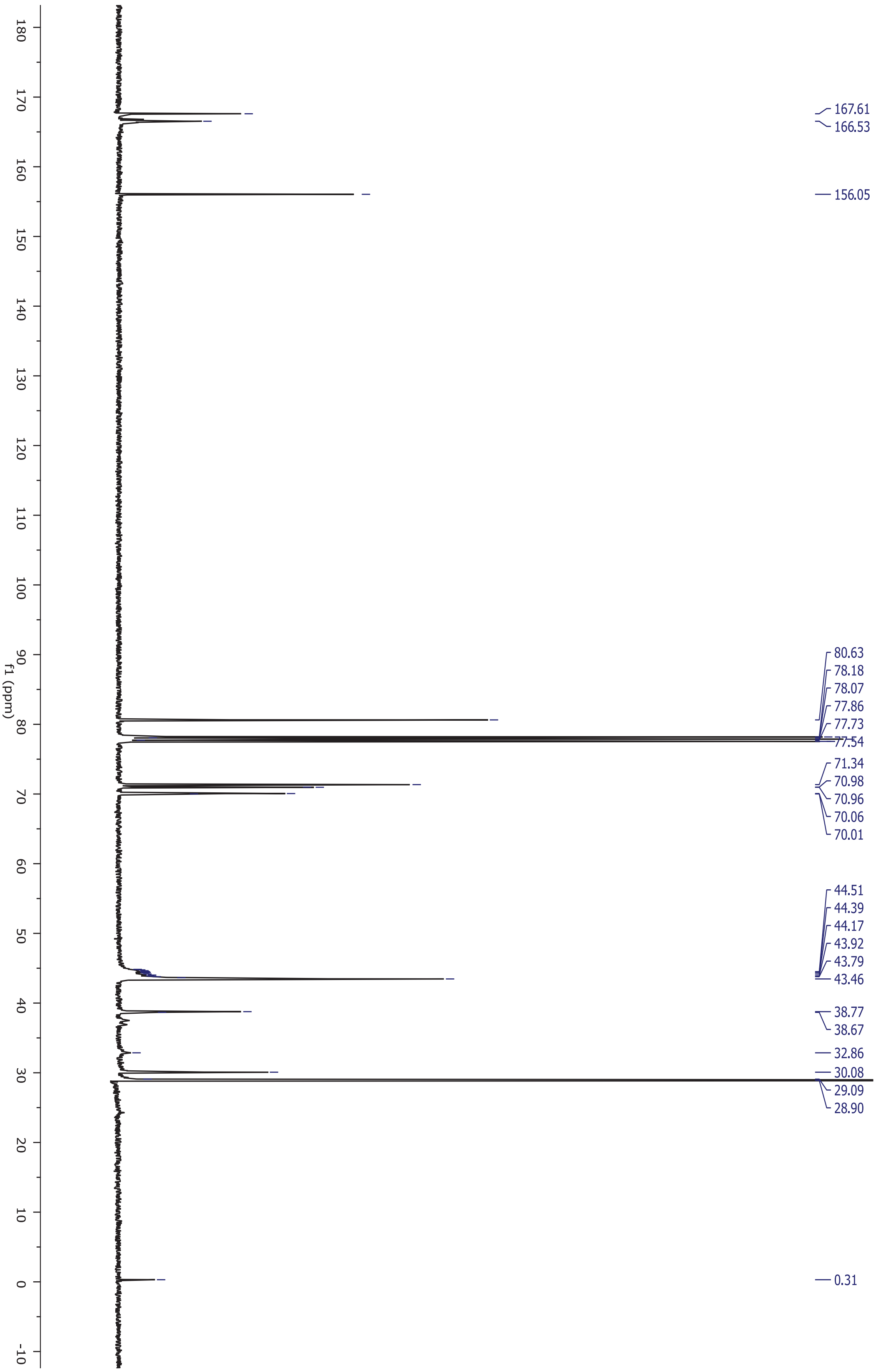
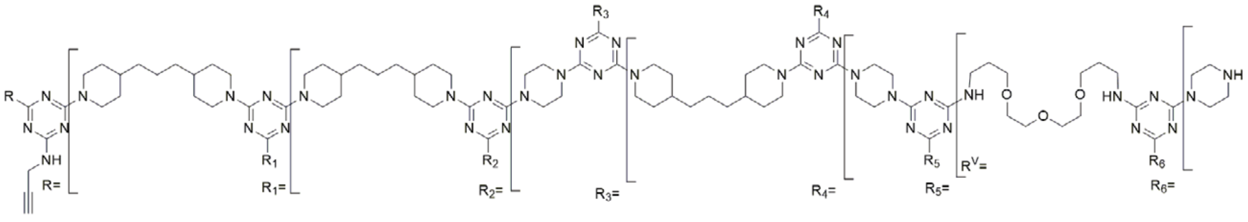


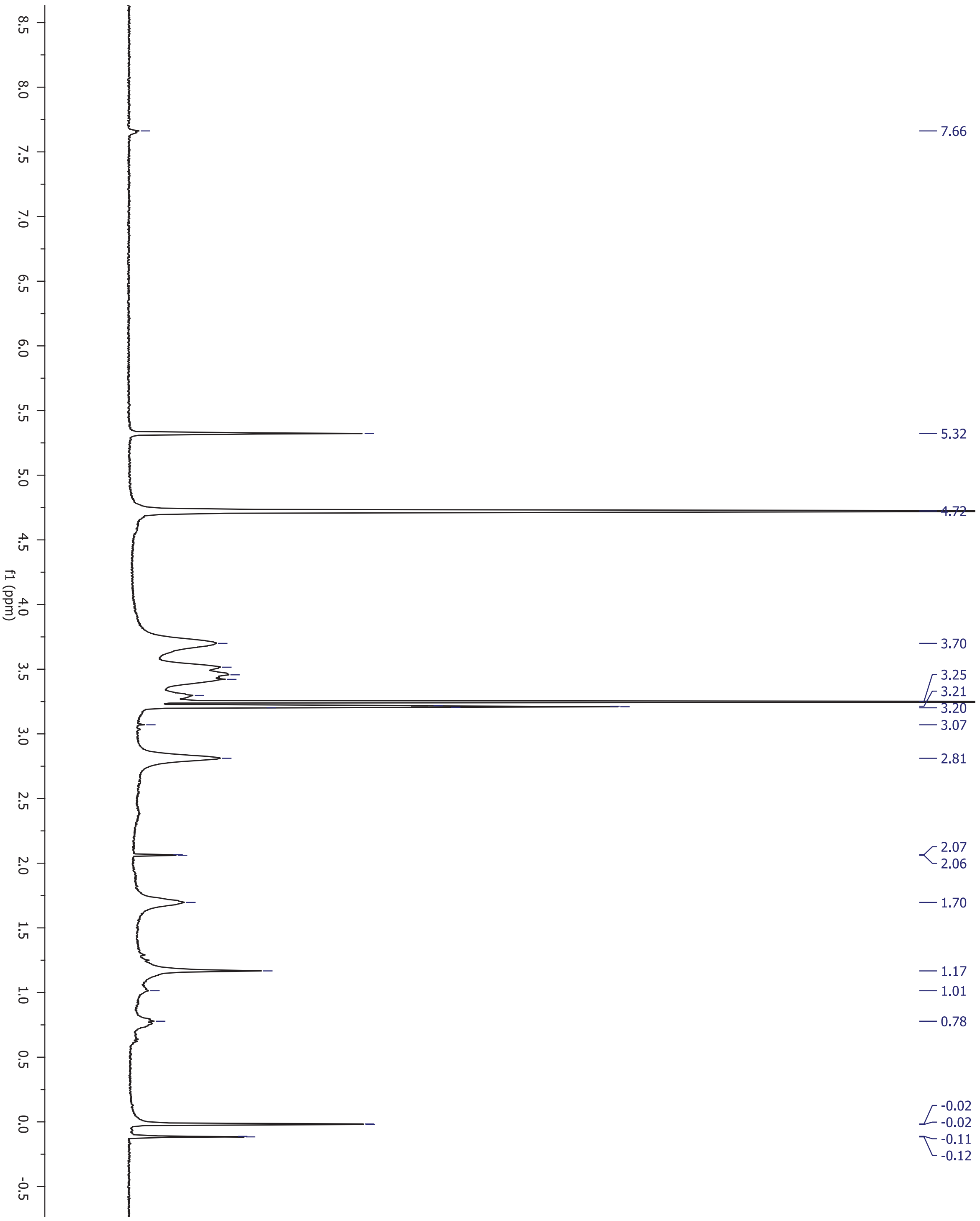
Figure S29. Mass Spectrum of **6-Boc** (MALDI-TOF). Loss of BOC is evident.

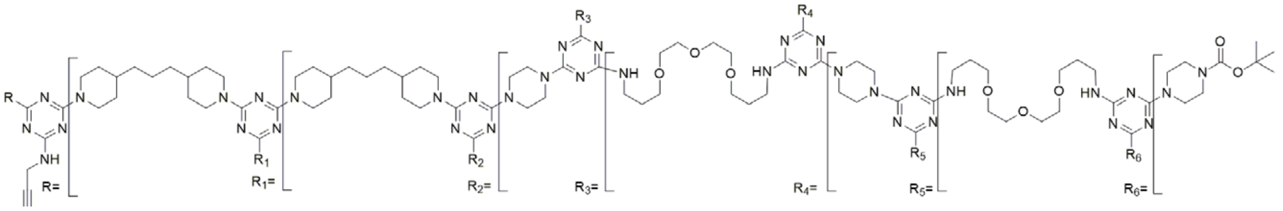


Dendrimer 6

A solution of compound **6-Boc** (0.147g, 0.0026mmol) in concentrated HCl (2mL) and methanol (2mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, and evaporated under vacuum to yield dendrimer **6** (0.113g, quant.). ^{1}H NMR (400 MHz, CDCl$_3$, δ): 4.73 (bs, 88H, equatorial C**H**N-triazine of dipiperidine), 4.18 not found (s, 2H, NHC$\mathbf{H_2}$CCH), 3.7-3.20 (b, 2368 H, (320H) triazine-NC$\mathbf{H_2}$CH$_2$N-triazine, (768H) C$\mathbf{H_2}$OC$\mathbf{H_2}$C$\mathbf{H_2}$OC$\mathbf{H_2}$C$\mathbf{H_2}$OC$\mathbf{H_2}$, (512H) NC$\mathbf{H_2}$CH$_2$NH$_2$, (256H) NHC$\mathbf{H_2}$CH$_2$CH$_2$O, (512H) NCH$_2$C$\mathbf{H_2}$NH$_2$), 2.81 (bs, 88H, equatorial C**H**CH$_2$N-triazine of dipiperidine), 2.18 not found (bt, 1H, NHCH$_2$CC**H**), 1.70 (b, 344H, (256H) OCH$_2$C$\mathbf{H_2}$CH$_2$NH, (88) axial C**H**N-triazine of dipiperidine), 1.17-0.78 (m, 264H, axial C**H**CH$_2$N-triazine of dipiperidine (88H), C**H**-trimethylene (44H), C$\mathbf{H_2}$C$\mathbf{H_2}$C$\mathbf{H_2}$ (132H)).MALDI-TOF) calcd for $C_{1984}H_{3414}N_{890}O_{192}$: 42754.54; not found

Figure S30. ^{1}H NMR Spectrum of **6**





Compound 7-Boc

A solution of compound dendrimer **3** (0.056g, 0.0053mmol), **10** (0.488g, 0.34 mmol), and DIPEA (0.057mL, 0.34 mmol) in 1.5 mL of THF and 0.2mL MeOH was stirred at 75°C during 4 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by multiple precipitations of EtOAc against hexanes. Compound **7-Boc** (0.156g, 53%) was recovered as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.72-3.4 (b, 2624H, (320H) triazine-$NC\mathbf{H_2}CH_2N$-triazine, (960H) $C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2$, (512H) $NC\mathbf{H}_2CH_2NBoc$, (64H) $NHC\mathbf{H_2}CH_2CH_2O$, (512H) $NCH_2C\mathbf{H_2}NBoc$), 1.84-1.82 (b, 320H $OCH_2C\mathbf{H_2}CH_2NH$), 1.47 (s, 1152H, $C(C\mathbf{H}_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.268, 165.198 ($\mathbf{C}_3N_3$), 154.77 (**C**O), 79.8 (**C**(CH3)3), 70.58 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.2 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 69.29 ($NHCH_2CH_2\mathbf{C}H_2O$), 43.8 ($NCH_2\mathbf{C}H_2N$-triazine), 43.87 (Boc$N\mathbf{C}H_2CH_2N$-triazine), 42.87 ($N\mathbf{C}H_2CH_2N$-triazine), 38.19 ($NH\mathbf{C}H_2CH_2CH_2O$), 29.5 ($NHCH_2\mathbf{C}H_2CH_2O$), 28.4 ($C(\mathbf{C}H_3)_3$) MS (MALDI-TOF) calcd for $C_{2574}H_{4404}N_{890}O_{496}$: 55722.67; found 562004.38 $(M + H)^+$.

Figure S31. ^{1}H NMR Spectrum of **7-Boc**

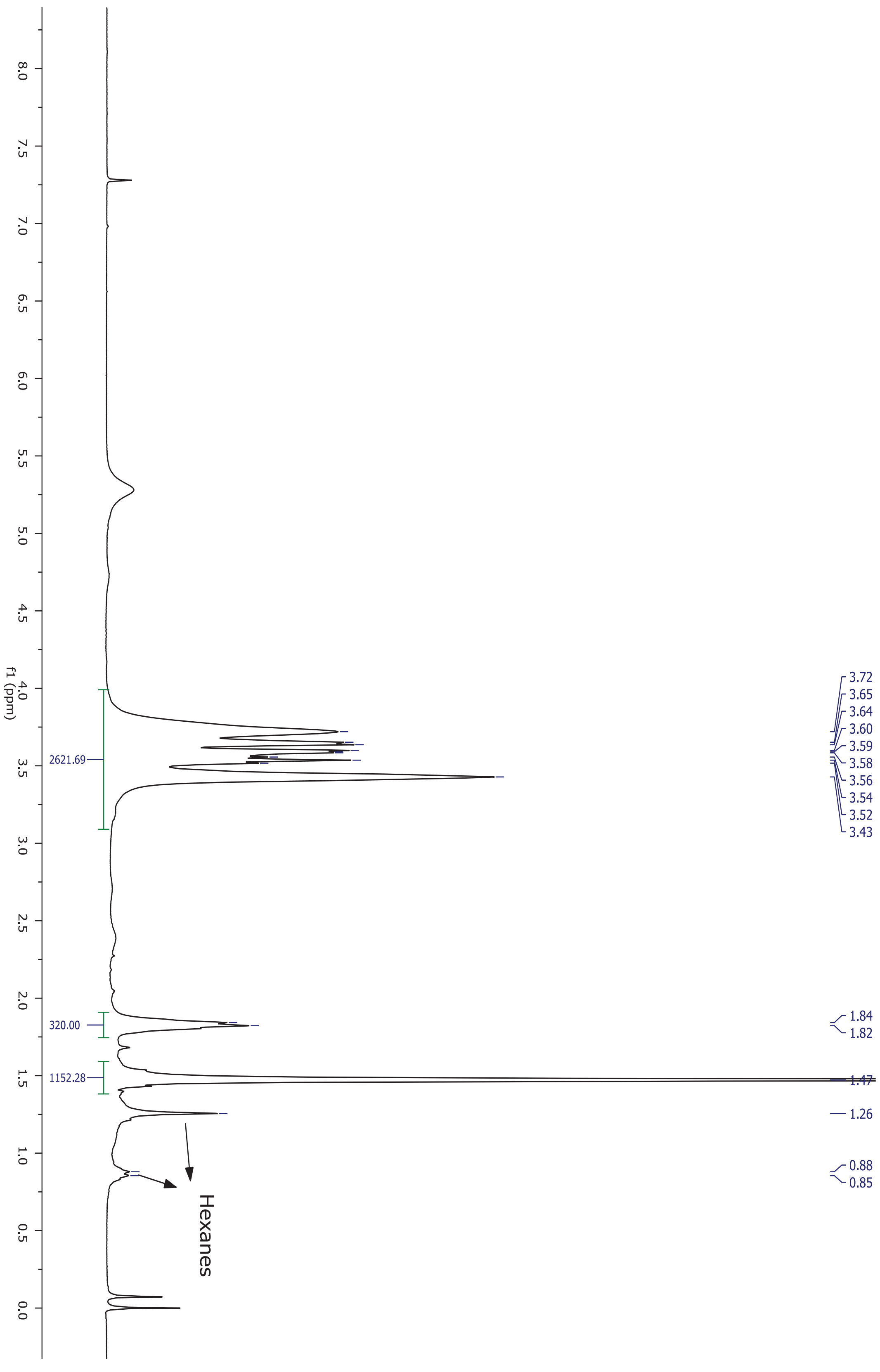


Figure S32. ^{13}C NMR Spectrum of **7-Boc**

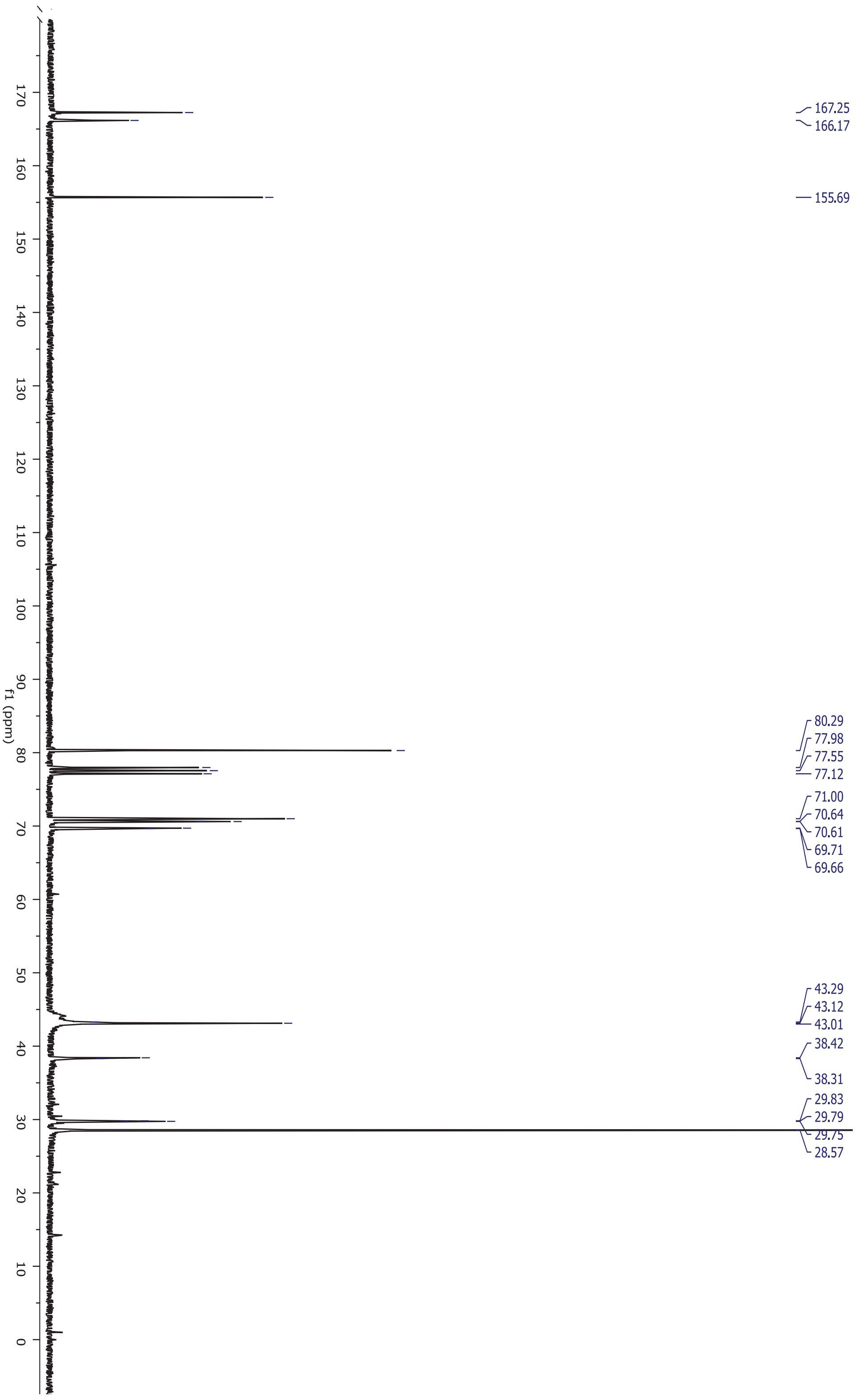
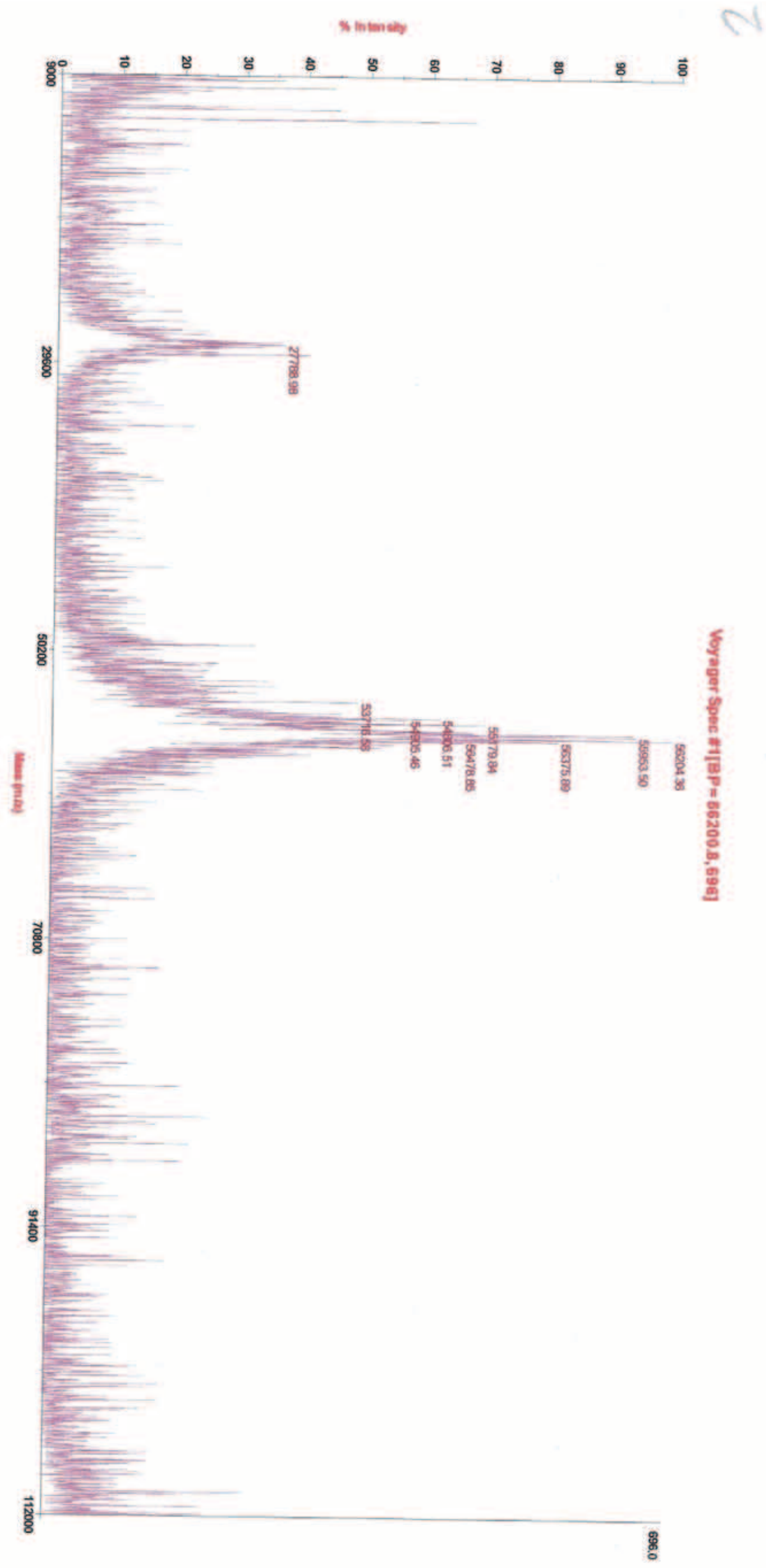
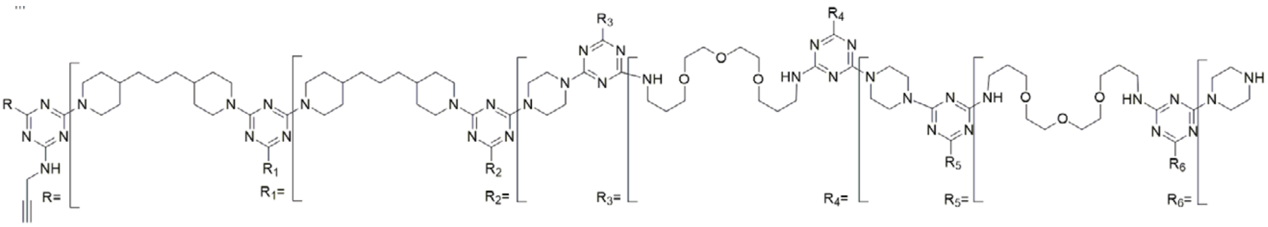


Figure S33. Mass Spectrum of **7-Boc** (MALDI-TOF)





Dendrimer 7

A solution of compound **7-Boc** (0.200g, 0.0036mmol) in concentrated HCl (5mL) and methanol (5mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whaltman, and evaporated under vacuum to yield **7** (0.15g, quantitative). ^{1}H NMR (300 MHz, $CDCl_3$, δ): 3.72-3.43 (b, 2112H, (320H) triazine-$NC\mathbf{H_2}CH_2N$-triazine, (960H) $C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2$, (512H) $NC\mathbf{H}_2CH_2NH$, (64H) $NHC\mathbf{H_2}CH_2CH_2O$), 2.85 (b, 512H $NCH_2C\mathbf{H_2}NH$), 1.82 (b, 320H $OCH_2C\mathbf{H_2}CH_2NH$). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 166.31, 165.1 ($\mathbf{C}_3N_3$),70.01 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 69.64 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 68.67 ($NHCH_2CH_2\mathbf{C}H_2O$), 43.64 ($NCH_2\mathbf{C}H_2N$-triazine), 42.23 ($HN\mathbf{C}H_2CH_2N$-triazine), 42.18 ($N\mathbf{C}H_2CH_2N$-triazine), 37.28 ($NH\mathbf{C}H_2CH_2CH_2O$), 29.0 ($NHCH_2\mathbf{C}H_2CH_2O$). MS (MALDI-TOF) calcd for $C_{1936}H_{3380}N_{890}O_{240}$: 42915.96; found 43499.86 $(M + H)^+$.

Figure S34. ^{1}H NMR Spectrum of **7**

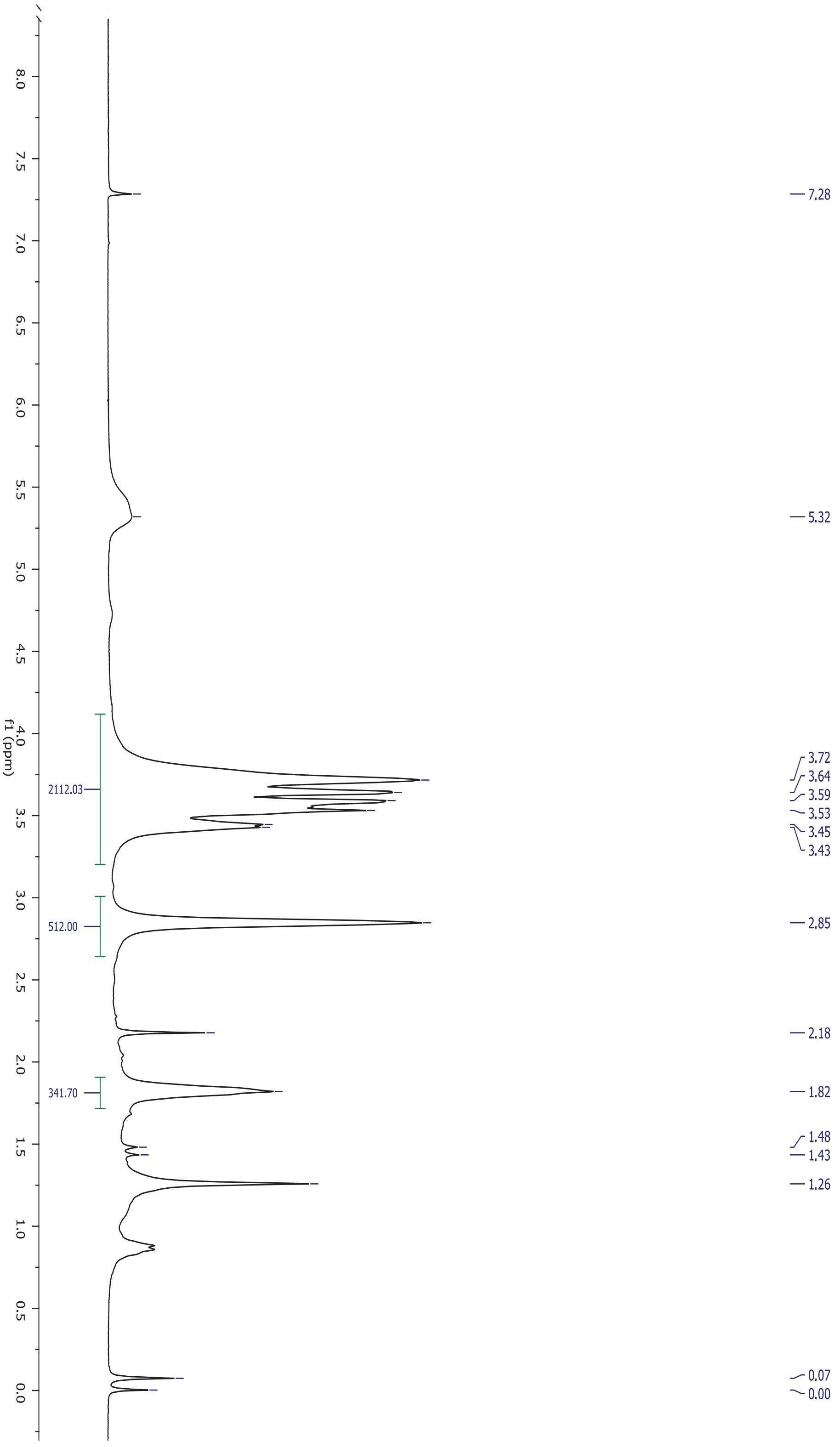


Figure S35. ^{13}C NMR Spectrum of **7**

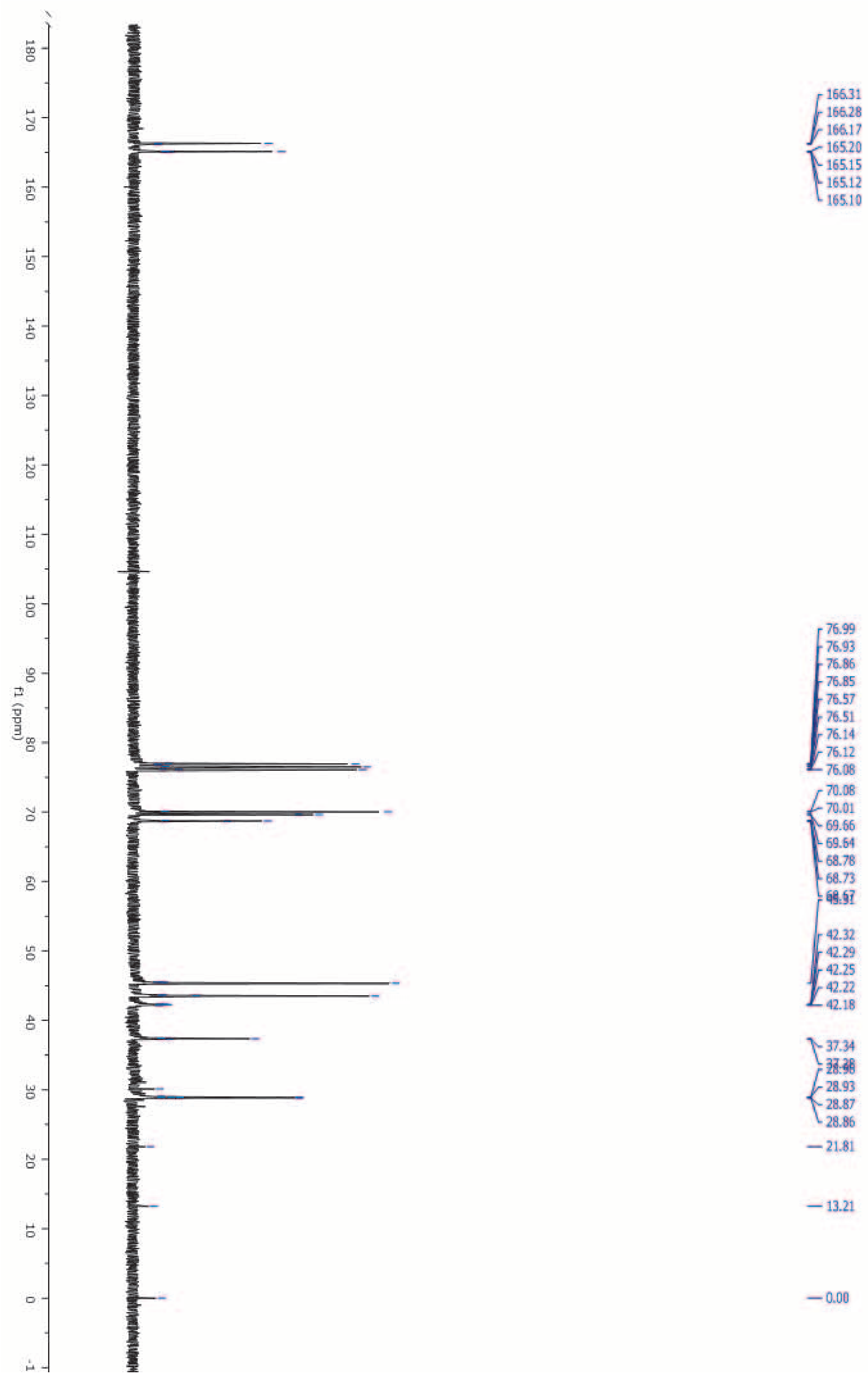
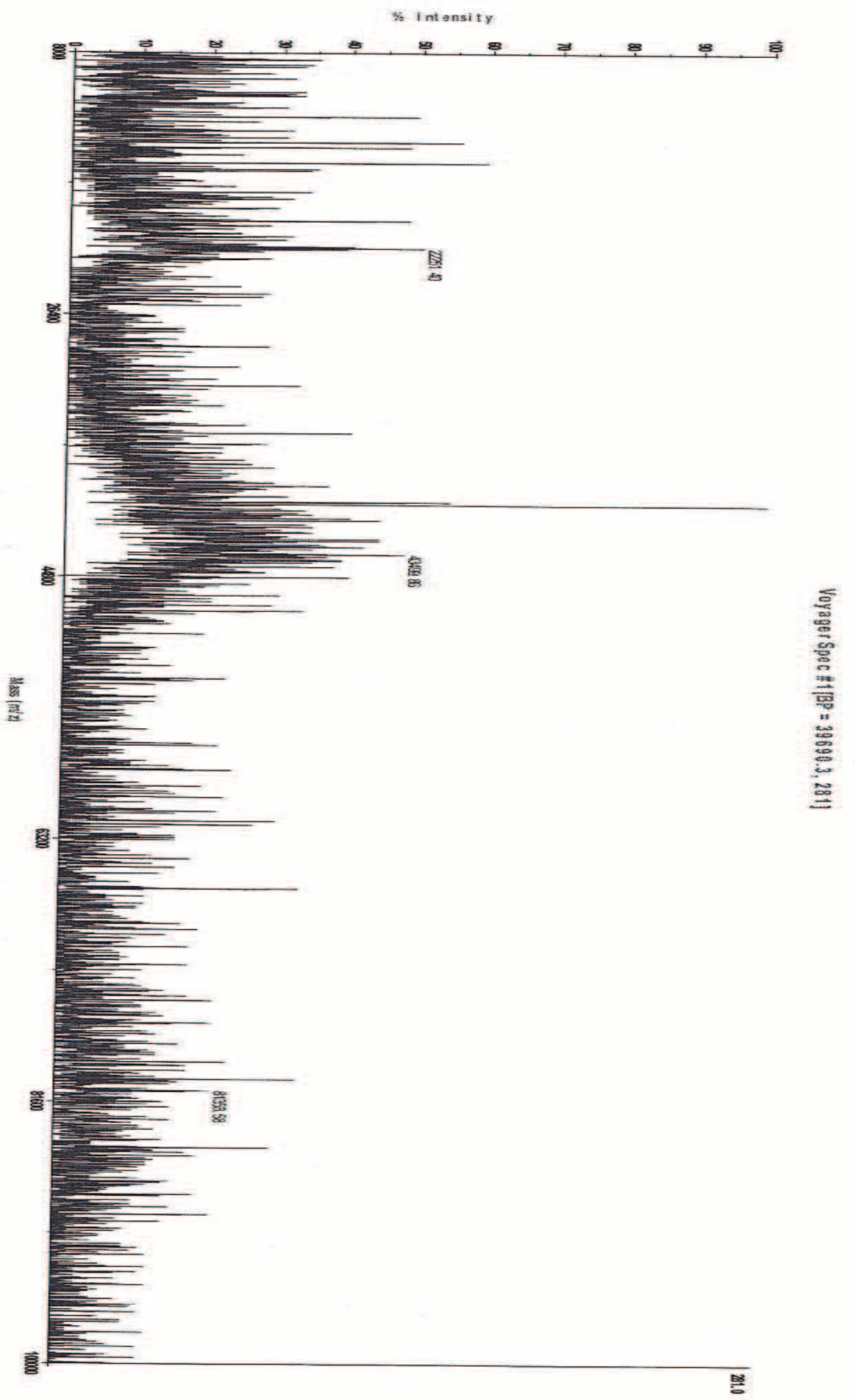
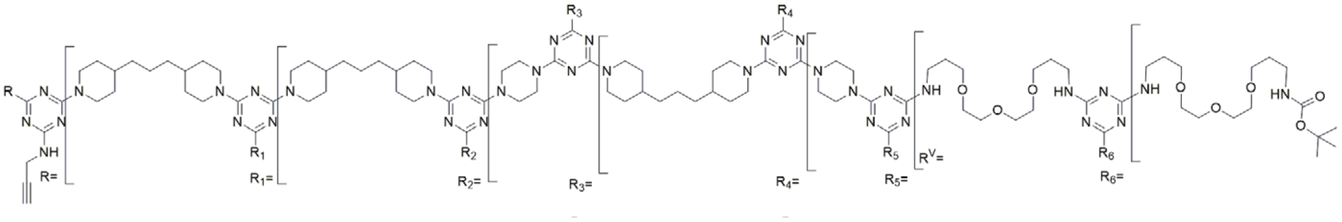


Figure S36. Mass Spectrum of **7** (MALDI-TOF)





Compound 8-Boc

A solution of dendrimer **2** (0.073g, 0.0070mmol), **11** (0.888 g, 0.448mmol), and DIPEA (0.08mL, 0.448mmol) in 1 mL of THF, 0.8mL of MeOH and 0.2mL of water, was stirred at 75°C for 6 days in a pressure relief reaction vial. The crude product was dissolved in dichloromethane and washed with brine. The organic layer was passed through a phase separator from Whatman, and evaporated under vacuum. The solid was purified by precipitation DCM/diethyl ether. Compound **8-Boc** (0.408g, 80%) was recovered as a white wax. ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.5-3.0 (b, 3200 H, (2304H) C**H**$_2$OC**H**$_2$C**H**$_2$OC**H**$_2$C**H**$_2$OC**H**$_2$, (640H) NHC**H$_2$**CH$_2$CH$_2$O, (256H) NCH$_2$C**H$_2$**NBoc), 3.01 (br m, 256H, BocNHC**H$_2$**), 1.63-1.26 (b, 768H OCH$_2$C**H$_2$**CH$_2$NH, 1.23 (s, 1152H, C(C**H**$_3$)$_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ): 166.3, 165.26 (**C**$_3$N$_3$), 156.04 (**C**O), 78.79 (**C**(CH$_3$)$_3$), 70.57 (two lines, O**C**H$_2$**C**H$_2$O), 69.25 (CH$_2$CH$_2$**C**H$_2$O), 43.0 (trimethylene-CHCH$_2$**C**H$_2$N), 38.5 (**C**H$_2$CH$_2$CH$_2$O), 38.07 (**C**H$_2$CH$_2$CH$_2$O), 29.62 (NHCH$_2$**C**H$_2$CH$_2$O), 28.47 (C(**C**H$_3$)$_3$). (ESI-TOF) calcd for $C_{3390}H_{6228}N_{890}O_{832}$: 72727.24; not found.

Figure S37. ^{1}H NMR Spectrum of **8-Boc**

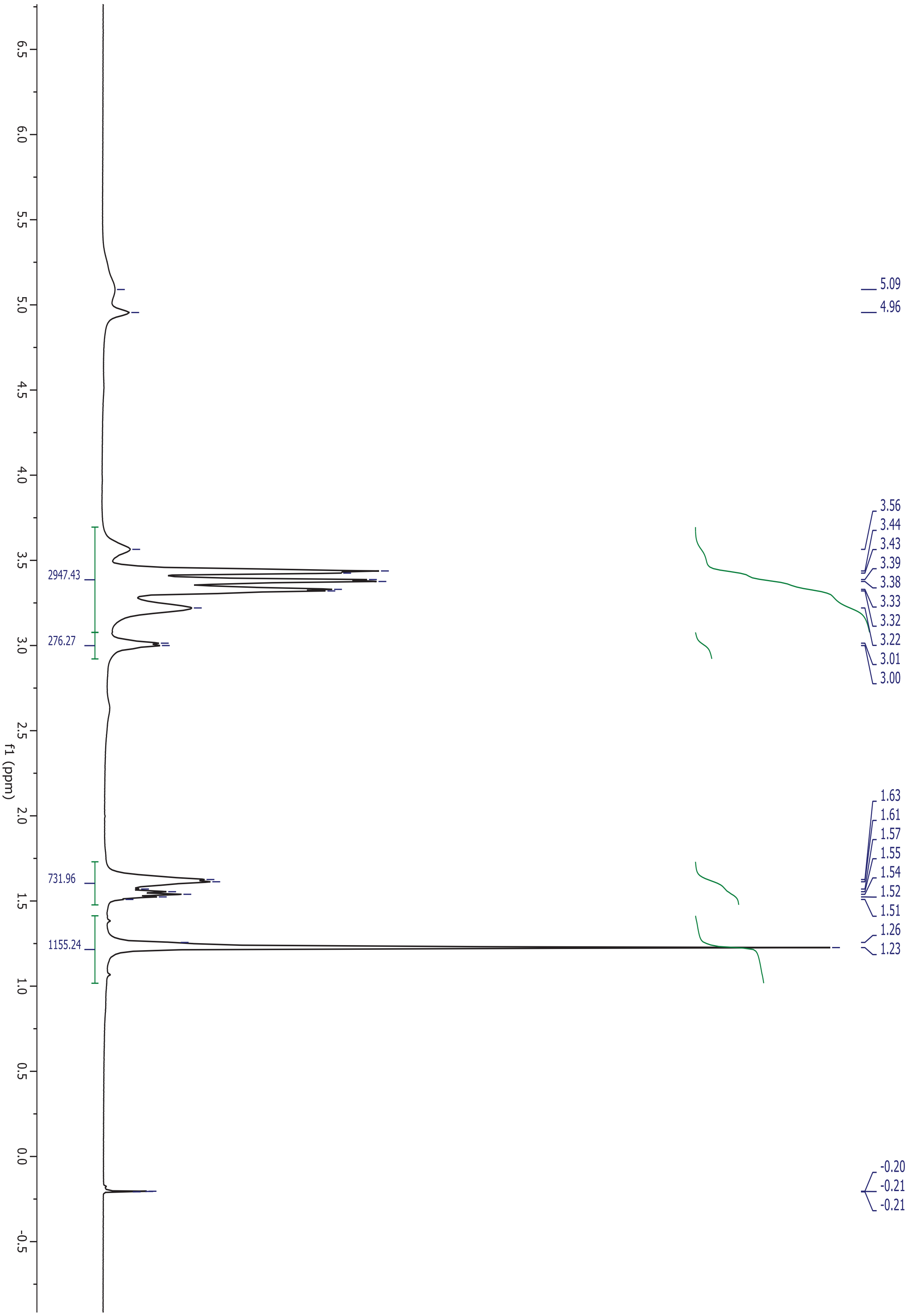
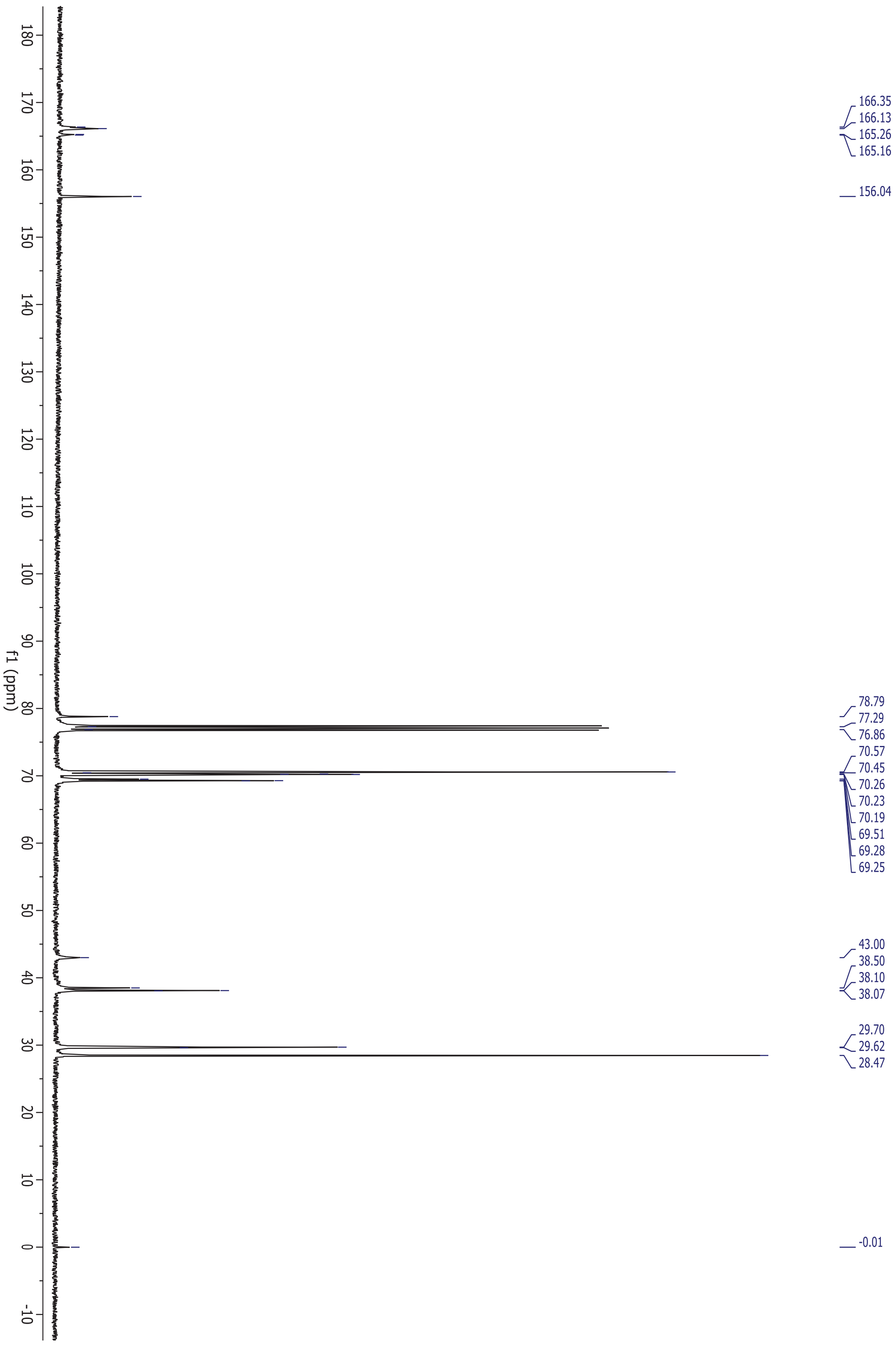
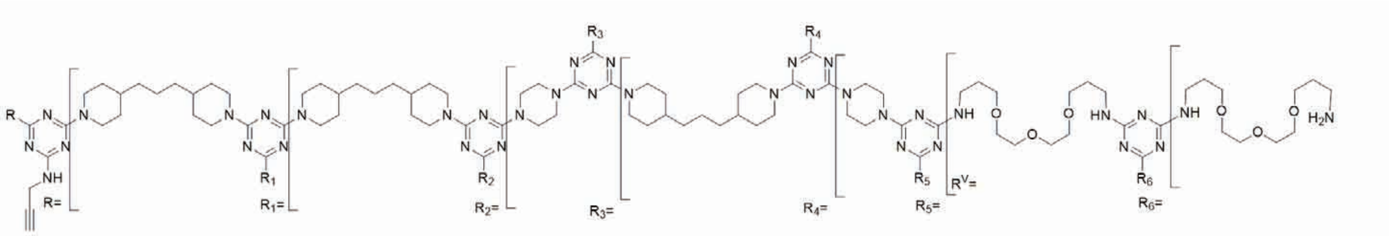


Figure S38. ^{13}C NMR Spectrum of **8-Boc**





Dendrimer 8

A solution of compound **8-Boc** (0.400g, 5.49 umol) in concentrated HCl (2mL) and methanol (2mL) was stirred for 15 h at room temperature and then evaporated under vacuum. The residue was dissolved in dichloromethane, washed with 5 M NaOH (*aq.*), passed through a phase separator from Whatman, evaporated under vacuum to yield **8** as a white wax (0.314g, 95%). ^{1}H NMR (400 MHz, $CDCl_3$, δ): 3.76-3.42 (b, 3200 H, (2304H) $C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2$, (640H) $NHC\mathbf{H_2}CH_2CH_2O$, (256H) $NCH_2C\mathbf{H_2}NBoc$), 2.79-2.77 (br m, 256H, $BocNHC\mathbf{H_2}$), 1.85-1.70 (b, 768H $OCH_2C\mathbf{H_2}CH_2NH$. ^{13}C NMR (100 MHz, $CDCl_3$, δ): 166.16, 165.27 ($\mathbf{C}_3N_3$), 70.63 (two lines, $O\mathbf{C}H_2\mathbf{C}H_2O$), 69.42 ($CH_2CH_2\mathbf{C}H_2O$), 43.0 (trimethylene-$CHCH_2\mathbf{C}H_2N$), 39.57 ($\mathbf{C}H_2CH_2CH_2O$) 38.09 ($\mathbf{C}H_2CH_2CH_2O$), 33.40 ($OCH_2\mathbf{C}H_2CH_2NH_2$), 29.72 ($NHCH_2\mathbf{C}H_2CH_2O$). (ESI-TOF) calcd for $C_{2750}H_{5204}N_{890}O_{576}$: 59920.53; not found.

Figure S39. ^{1}H NMR Spectrum of **8**

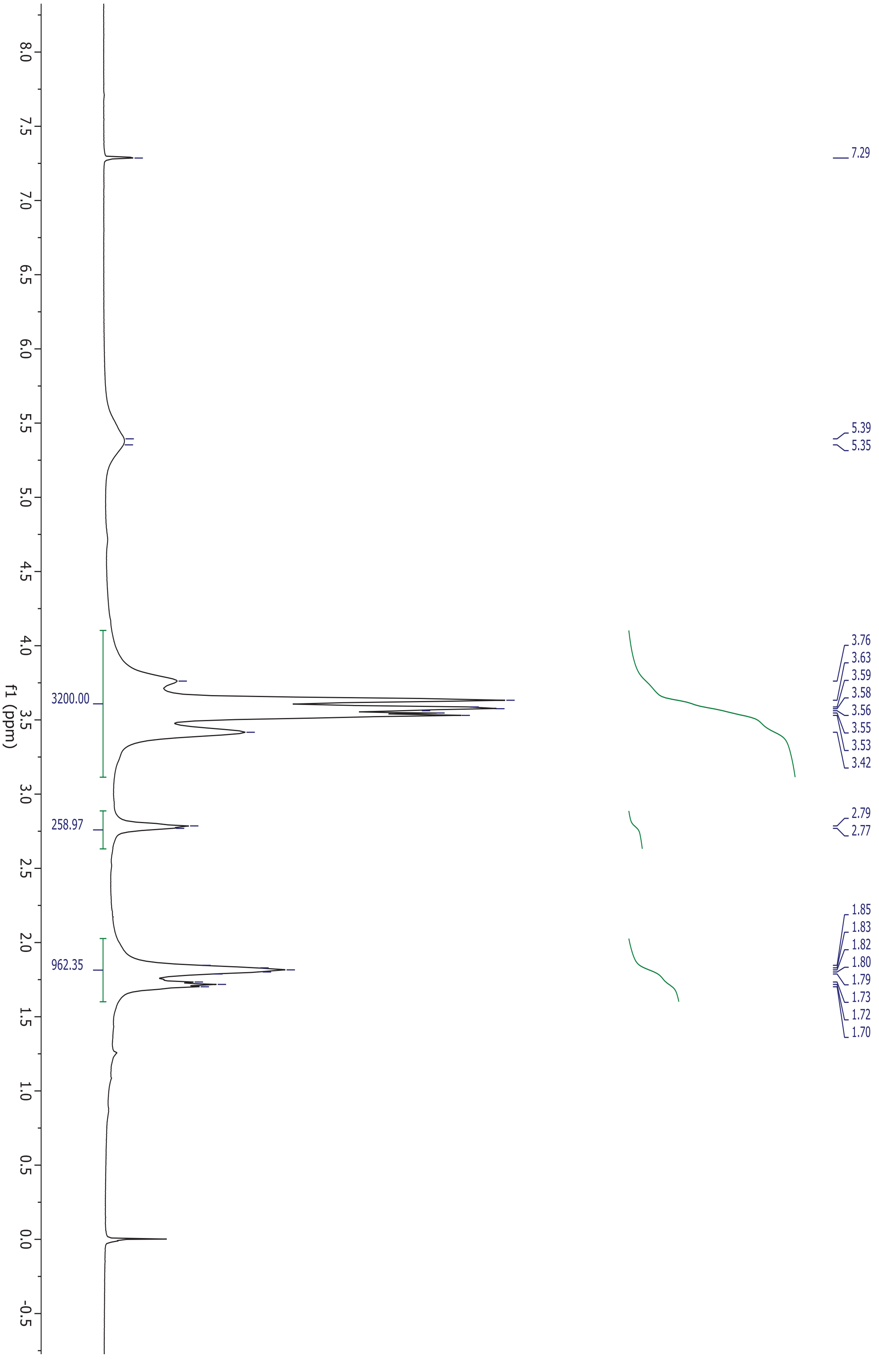
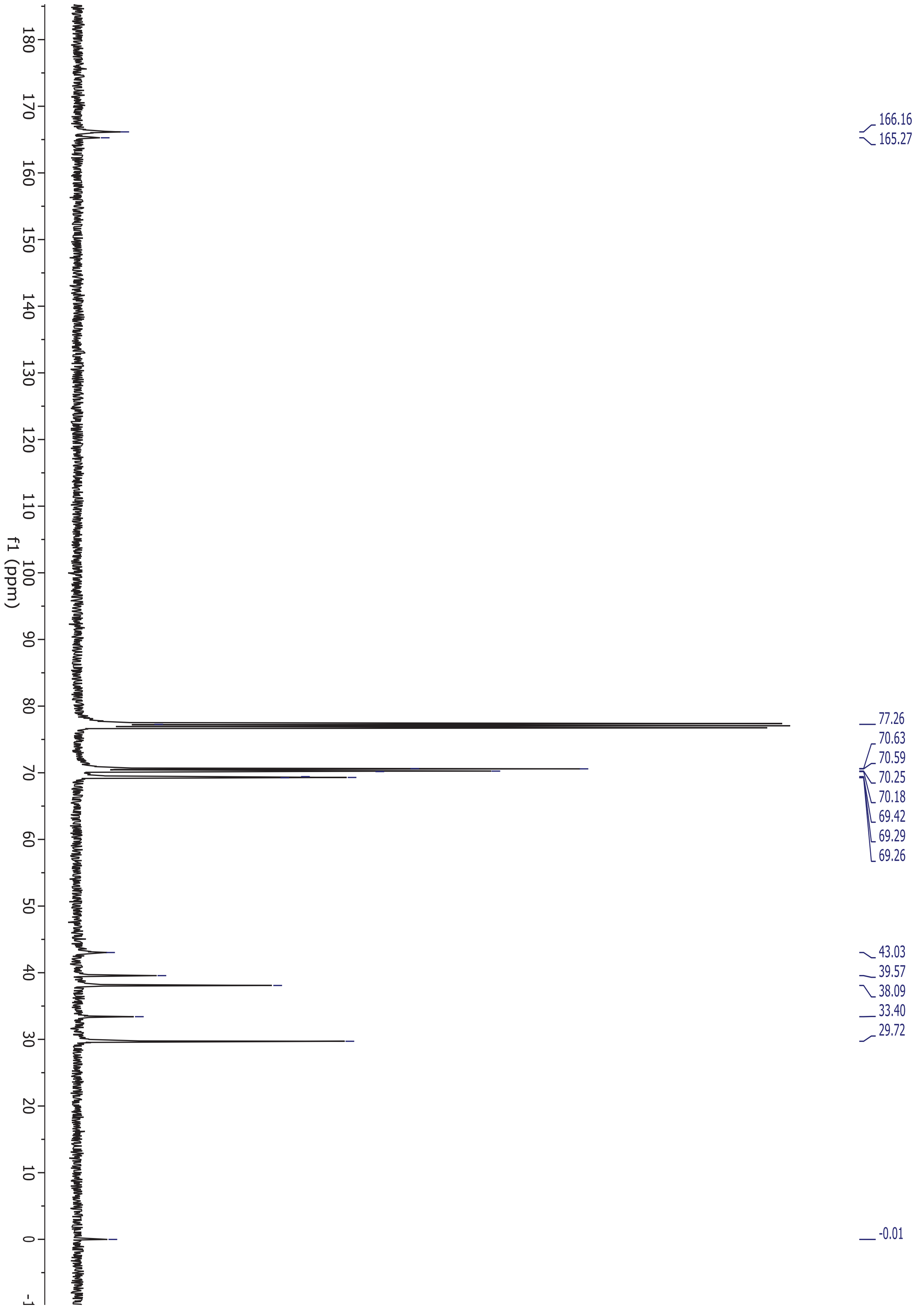
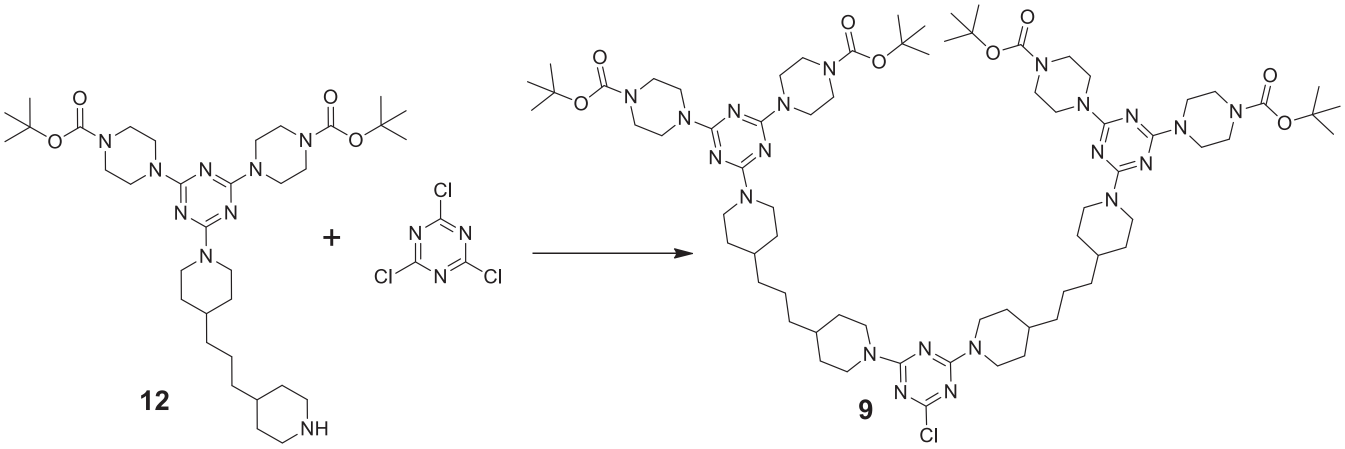


Figure S40. ^{13}C NMR Spectrum of **8**





Compound 9

Cyanuric chloride (0.476g, 2.58mmol) was added to a solution of **12** (3.5g, 5.32mmol) and DIPEA (3.7mL, 21.2mmol) in dichloromethane (25mL). After stirring 12 h, the solution was washed with brine, dried over $MgSO_4$, filtered, and evaporated under vacuum. The crude was purified by silica gel chromatography (from hexanes:EtOAc= 5:1 to hexanes: EtOAc= 2:1) to obtain **9** (3.4g, 92%) as a white solid. Melting point: 123-125 °C. ^{1}H NMR (300 MHz, $CDCl_3$, δ): 4.71 (d, *J = 12Hz*, 8H, equatorial C**H**N-triazine of dipiperidine (4H), equatorial C**H**N-C_3N_3Cl of dipiperidine (4H)), 3.74 (s, 16H, triazine-$NCH_2C\mathbf{H_2}NBoc$), 3.44 (s, 16H, triazine-$NC\mathbf{H_2}CH_2NBoc$), 2.83 – 2.69 (m, 8H, equatorial C**H**CH_2N-triazine of dipiperidine (4H), equatorial C**H**CH_2N-C_3N_3Cl of dipiperidine (4H)), 1.98-1.55 (m, 8H, axial C**H**N-triazine of dipiperidine (4H), axial C**H**N-C_3N_3Cl of dipiperidine (4H)), 1.46 (s, 36H, $C(C\mathbf{H_3})_3$)), 1.36 – 1.08 (m, 24H, axial C**H**CH_2N-triazine of dipiperidine (4H), axial C**H**CH_2N-C_3N_3Cl of dipiperidine (4H), C**H**-trimethylene (4H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (12H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.6, 165.1, 164.2 ($N_3\mathbf{C}_3$), 155.0 (**C**O), 79.8 ($\mathbf{C}(CH_3)_3$), 44.0 ($CHCH_2\mathbf{C}H_2N$), 43.6, ($NCH_2\mathbf{C}H_2N$-triazine), 43.1 ($N\mathbf{C}H_2CH_2N$-triazine), 36.9, 36.7 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 36.4, 36.2 (H**C**-trimethylene), 32.3 ($\mathbf{C}H_2CH_2N$), 28.5 ($C(\mathbf{C}H_3)_3$), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{71}H_{116}ClN_{21}O_8$: 1425.90; found 1426.88 $(M + H)^+$.

Compound 12 has been reported: Patra, S.; Kozura, B.; Huang, A. Y.-T.; Enciso, A. E.; Sun, X.; Hsieh, J.-T.; Kao, C.-L.; Chen, H.-T.; Simanek, E. E. Org. Lett., **2013,** 15, 3808.

Figure S41. ^{1}H NMR Spectrum of **9**

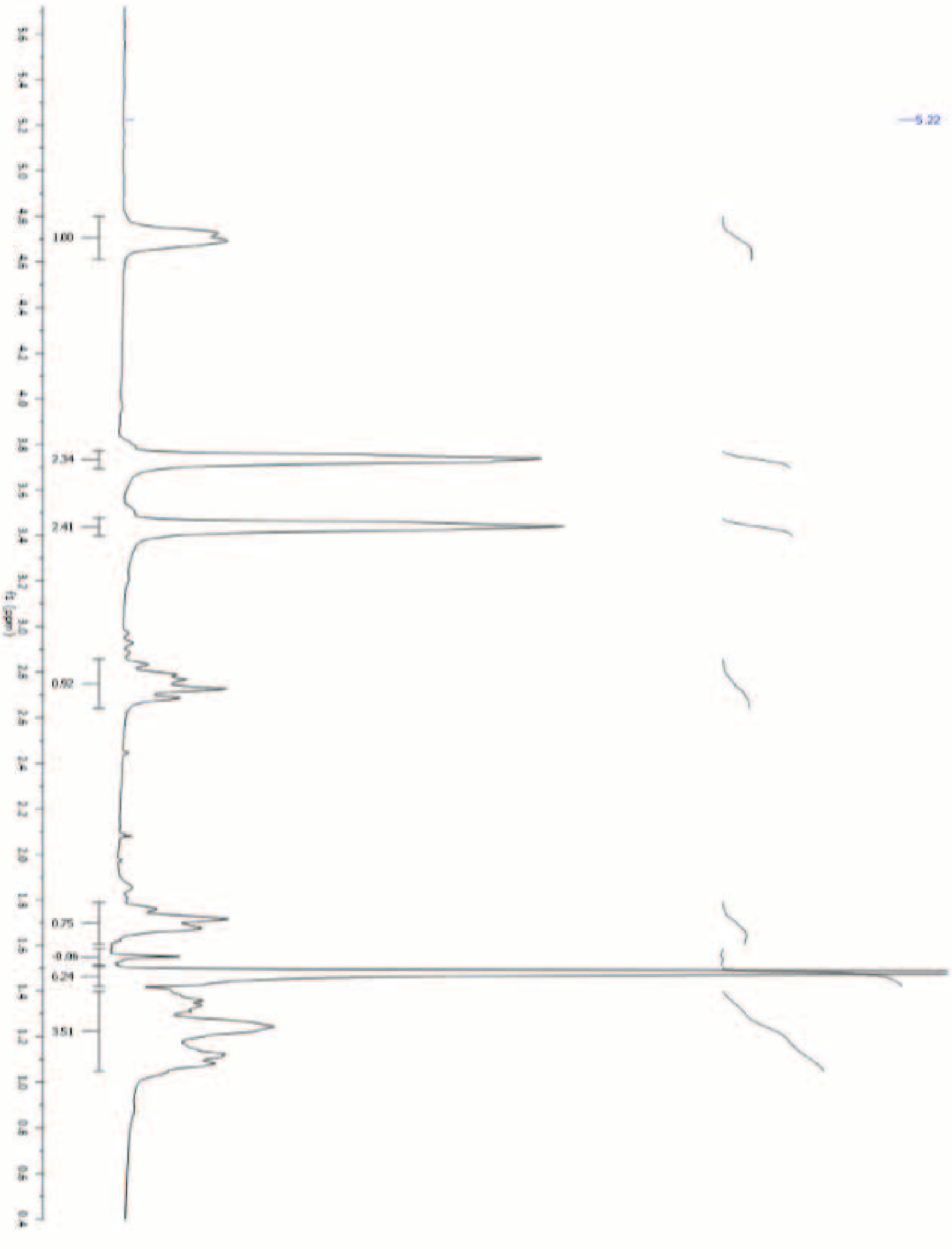


Figure S42. ^{13}C NMR Spectrum of **9**

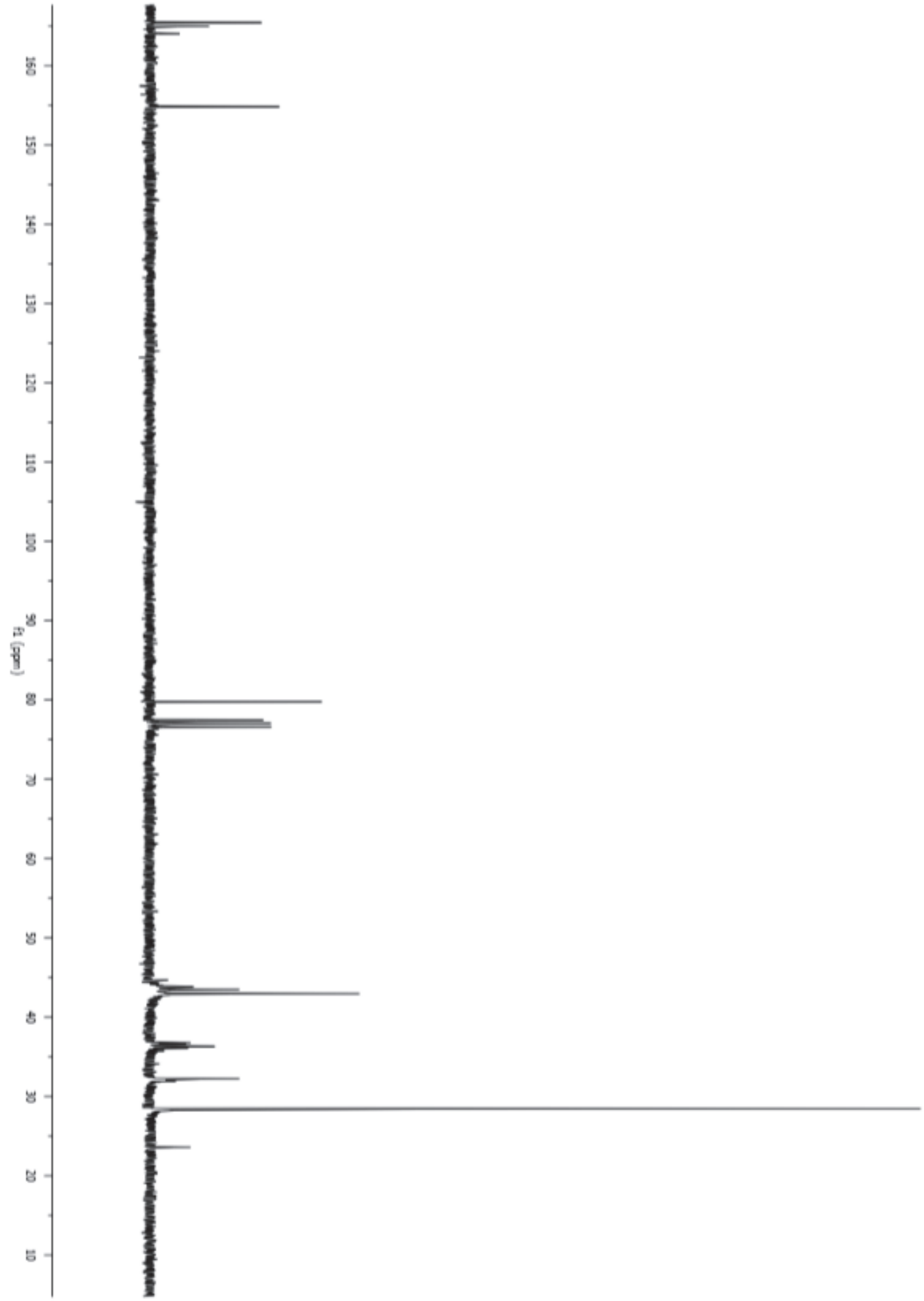
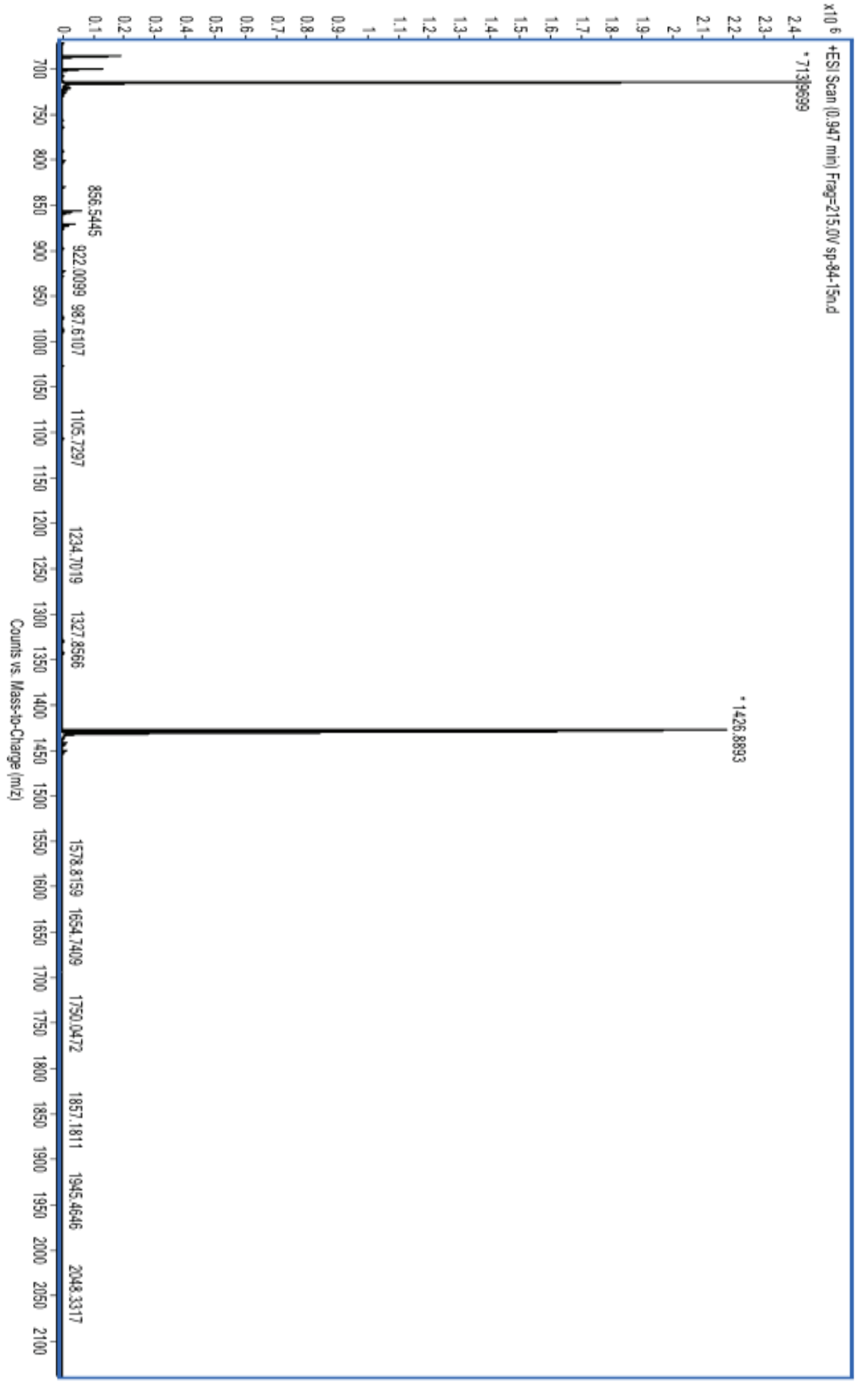
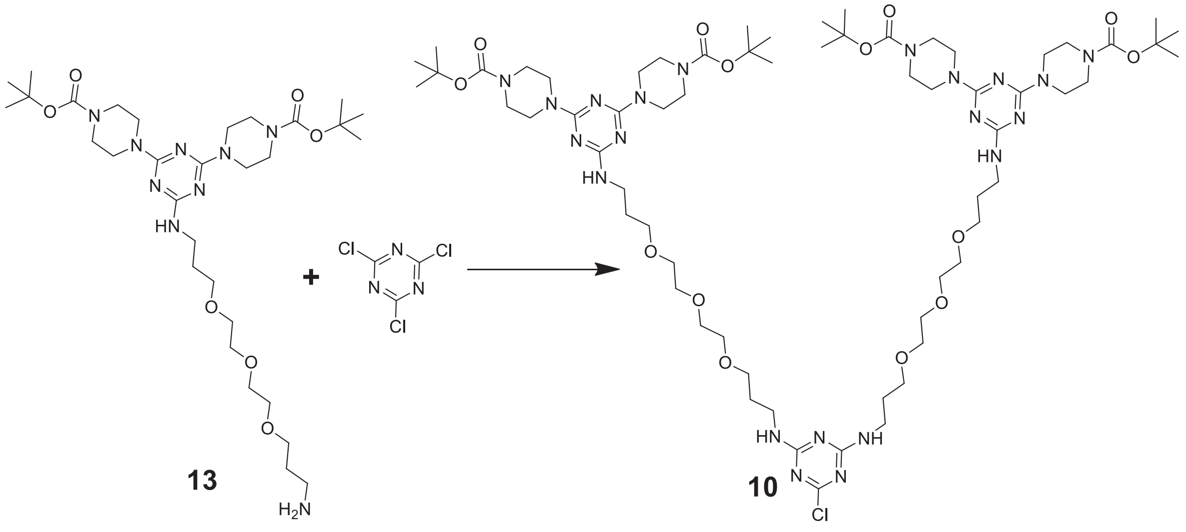


Figure S43. Mass Spectrum of **9** (ESI-TOF)





Compound 10

A solution of compound **13** (5.51g, 8.25mmol), and DIPEA (2.87mL, 4.12mmol) in THF (42mL) was cooled down to 0°C. Later, cyanuric chloride (0.76g, 4.12mmol) was added slowly to the solution and the reaction was left to reach room temperature and reacted for 24hrs. The reaction crude was evaporated under vacuum, washed with brine, and passed through a phase separator filter from Whatman. After that, it was evaporated under vacuum. The crude solid was purified by silica gel chromatography (from hexanes: EtOAc= 2:3 to 100% EtOAc). Compound **10** (4.87g, 81%) was obtained as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.70 (br, 16H, $NC\mathbf{H}_2CH_2NBoc$), 3.63-3.53 (m, 24H, $C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2C\mathbf{H}_2OC\mathbf{H}_2$), 3.40 (br, 24H, $NHC\mathbf{H}_2CH_2CH_2O$, $NCH_2C\mathbf{H}_2NBoc$), 1.81 (m, 8H, $OCH_2C\mathbf{H}_2CH_2NH$), 1.45 (s, 36H, $C(C\mathbf{H}_3)_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.4 ($\mathbf{C}_3N_3$), 165.9 ($\mathbf{C}_3N_3$), 165.4 ($\mathbf{C}_3N_3$), 154.9 ($\mathbf{C}O$), 80.0 ($\mathbf{C}(CH_3)_3$), 70.7 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.4 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 69.5 ($NHCH_2CH_2\mathbf{C}H_2O$), 43.1 (piperazine), 39.1 ($NHCH_2CH_2\mathbf{C}H_2O$), 38.4 ($NHCH_2CH_2\mathbf{C}H_2O$), 29.7 ($NH\mathbf{C}H_2CH_2CH_2O$), 29.0 ($NHCH_2\mathbf{C}H_2CH_2O$), 28.5 ($C(\mathbf{C}H_3)_3$); MS (MALDI-TOF) calcd for $C_{65}H_{112}ClN_{21}O_{14}$ 1445.83, found 1446.80 $(M + H)^+$.

Compound **13** has been reported: Lim, J.; Mintzer, M. A.; Perez, L. M.; Simanek, E. E. Org. Lett., **2010**, 12, 1148.

Figure S44. ^{1}H NMR Spectrum of **10**

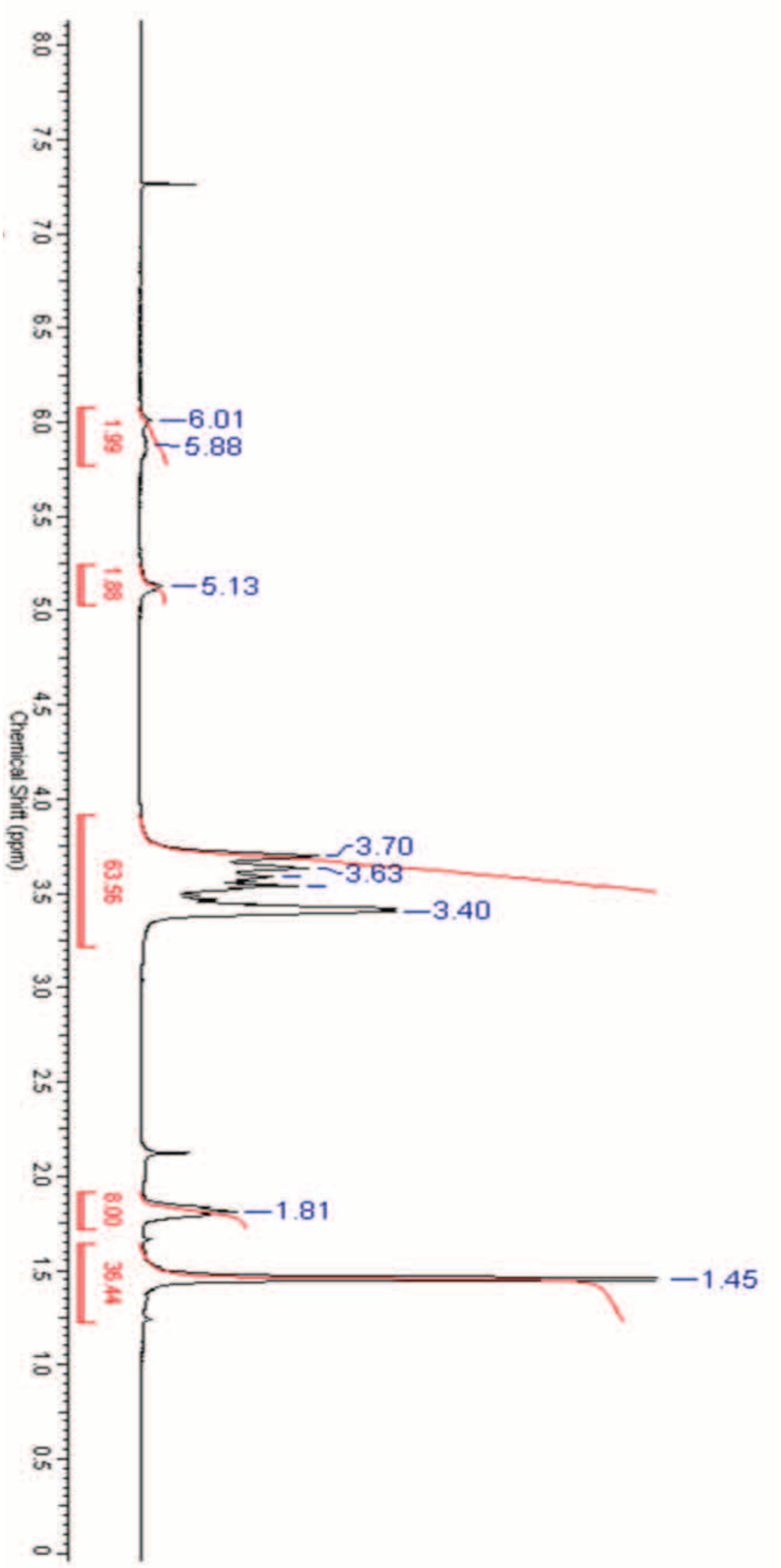


Figure S45. ^{13}C NMR Spectrum of **10**

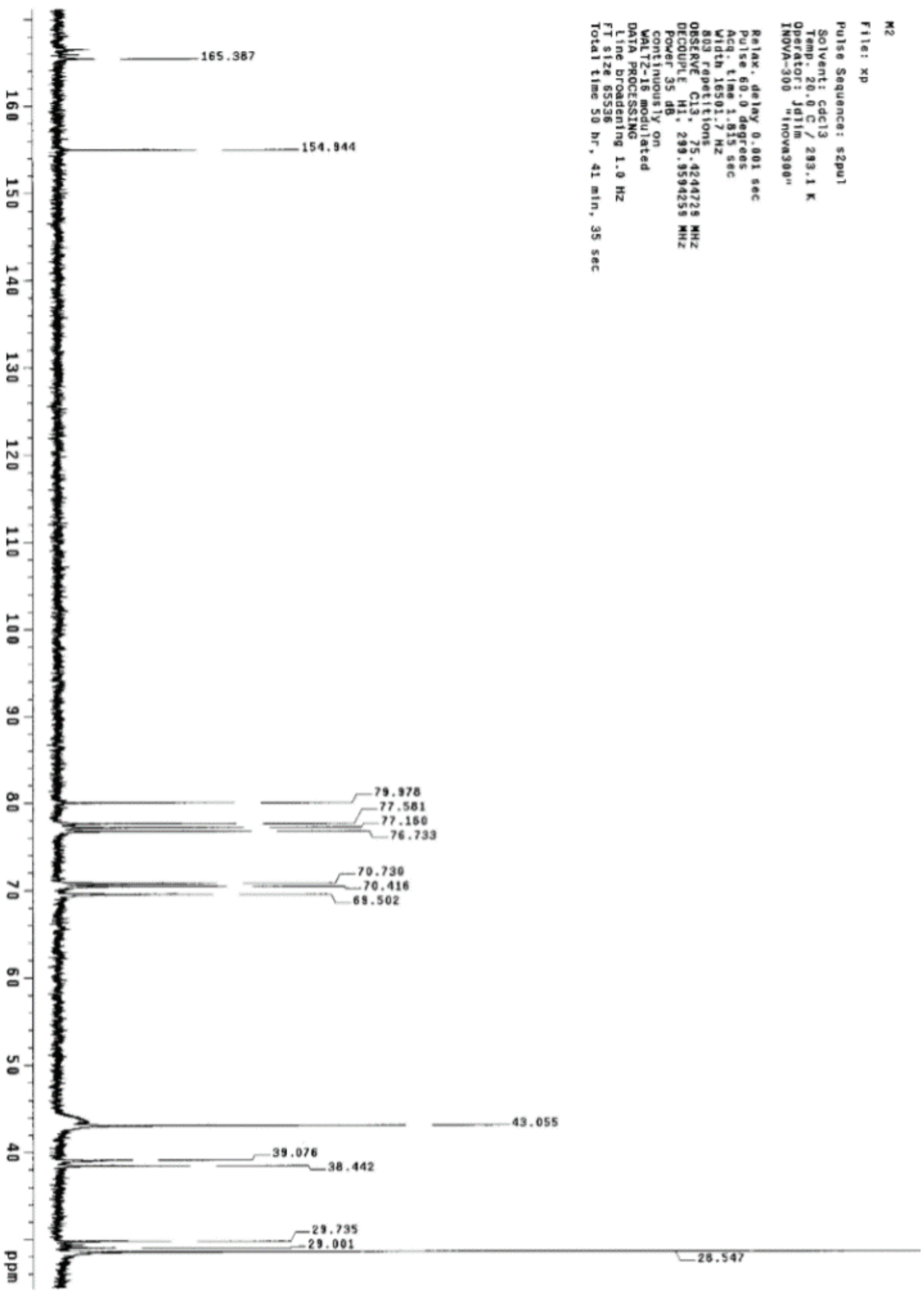
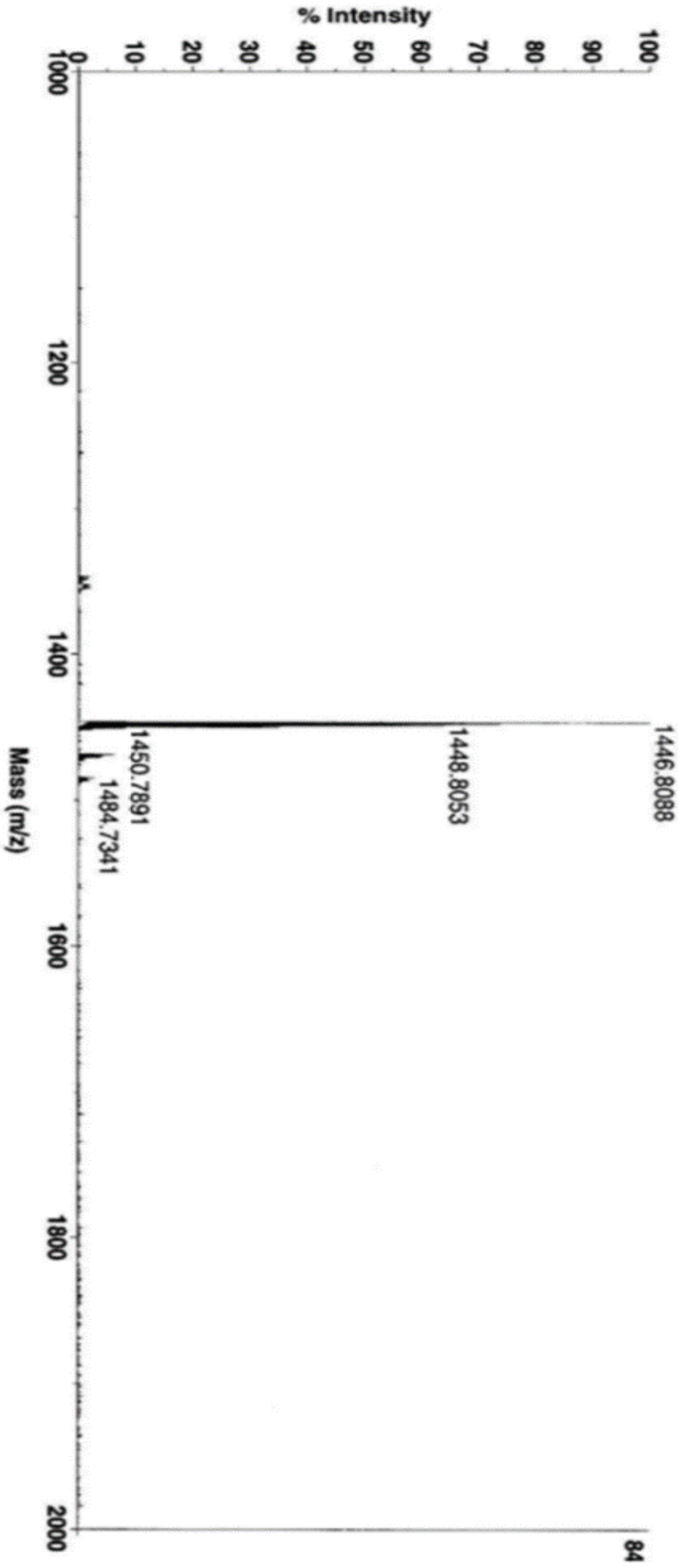
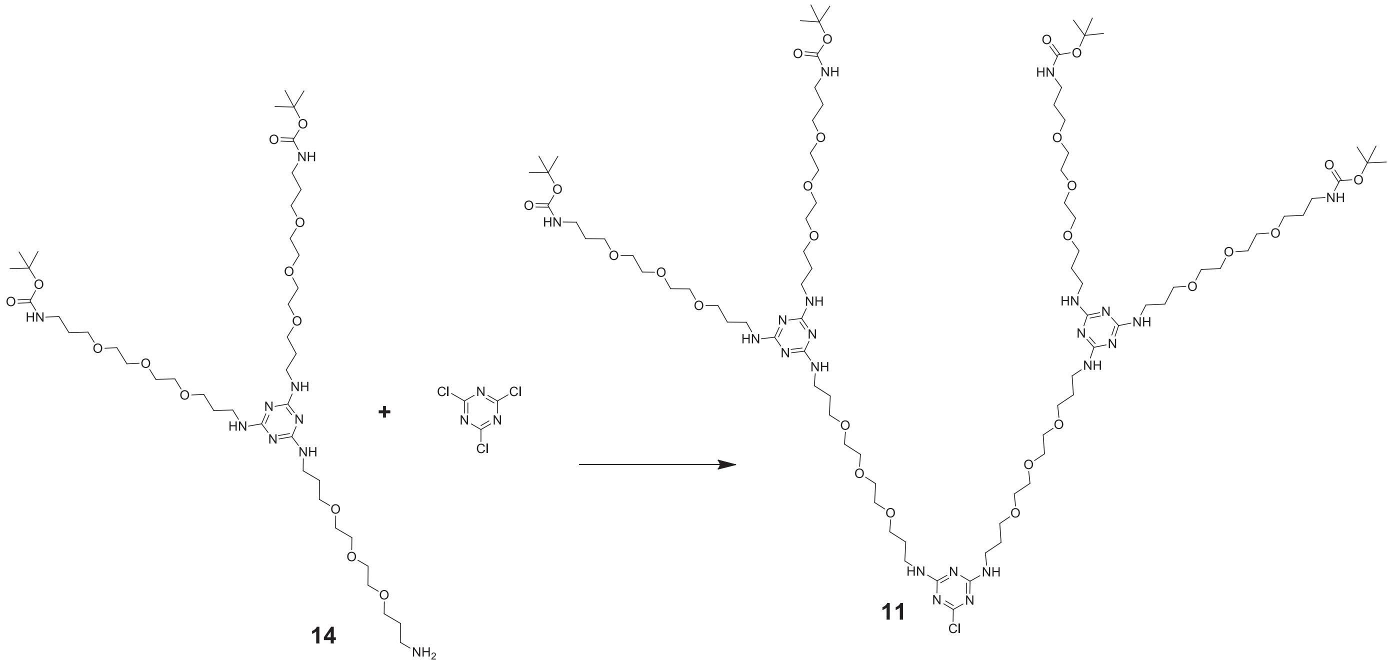


Figure S46. Mass Spectrum of **10** (ESI-TOF)





Compound 11. Compound **14** (4.08 g, 4.36 mmol) was added to a solution of cyanuric chloride (0.366 g, 1.98 mmol) in THF (20 mL). Afterwards, DIPEA (3.2 mL, 9.32 mmol) was added dropwise, and the solution was stirred for 2 minutes in order to allow reagents to mix. Then, the solution was irradiated in the microwave while stirring for 10 minutes at 60ºC using dynamic mode. The solvent system (in column volumes) used was the following: 1 CV (100% DCM to 95:5= DCM: MeOH), 15CV (95:5= DCM: MeOH), 10CV (90:10= DCM: MeOH), 20CV (85:15= DCM: MeOH) to give **11** (3.85g, 98%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.65-3.43 (m, 88H, $\mathbf{CH_2OCH_2CH_2OCH_2CH_2OCH_2}$, C_3N_3-NHC$\mathbf{H_2}$$CH_2CH_2O$), 3.21 (br m, 8H, BocNHC$\mathbf{H_2}$), 1.83-1.70 (m, 24H, $OCH_2C\mathbf{H_2}CH_2$), 1.44 (s, 36H, $C(C\mathbf{H_3})_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.9 ($\mathbf{C}_3N_3$), 165.6 ($\mathbf{C}_3N_3$), 156.1 (**C**O), 78.8 ($\mathbf{C}(CH_3)_3$), 70.5 ($O\mathbf{C}H_2\mathbf{C}H_2O$), 70.2 (two lines, $O\mathbf{C}H_2CH_2O$), 69.5 ($CH_2CH_2\mathbf{C}H_2O$), 69.3 ($CH_2CH_2\mathbf{C}H_2O$), 38.4 ($\mathbf{C}H_2CH_2CH_2O$), 38.1 ($\mathbf{C}H_2CH_2CH_2O$), 29.6 ($NHCH_2\mathbf{C}H_2CH_2O$), 28.4 ($C(\mathbf{C}H_3)_3$); MS (ESI-TOF) calcd for $C_{89}H_{168}ClN_{21}O_{26}$ 1982.2158, found 1984.4671 $(M + H)^+$.

Compound **14** has been reported: *Rapid, Semi-automated Convergent Synthesis of Low Generation Triazine Dendrimers using Microwave Assisted Reactions*. Enciso, A.E.; Abid, Z.M.; Simanek, E.E. *Polymer Chem*. **2014**, *5*, 4635-40.

Figure S47. ^{1}H NMR Spectrum of **11**

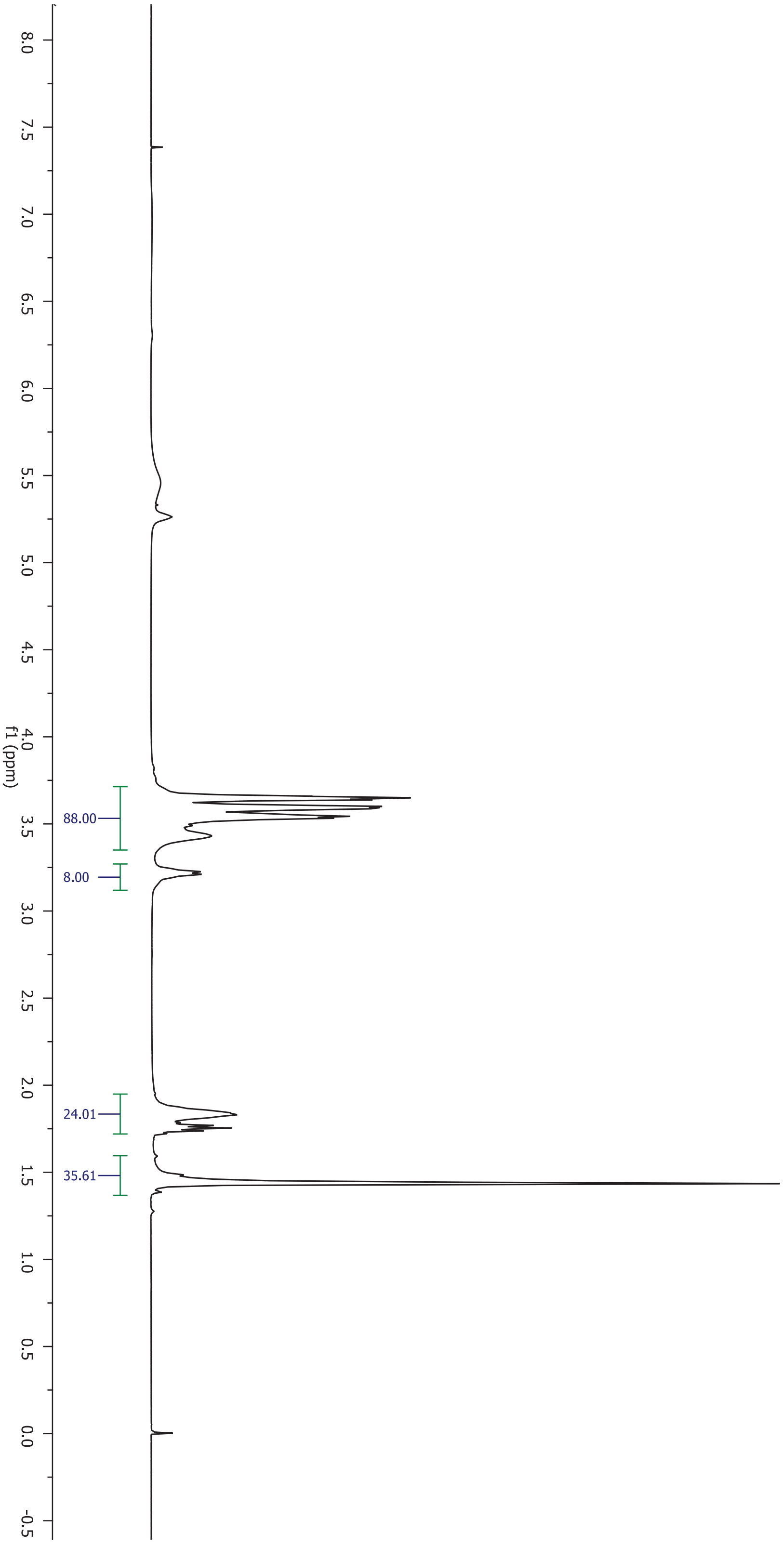


Figure S48. ^{13}C NMR Spectrum of **11**

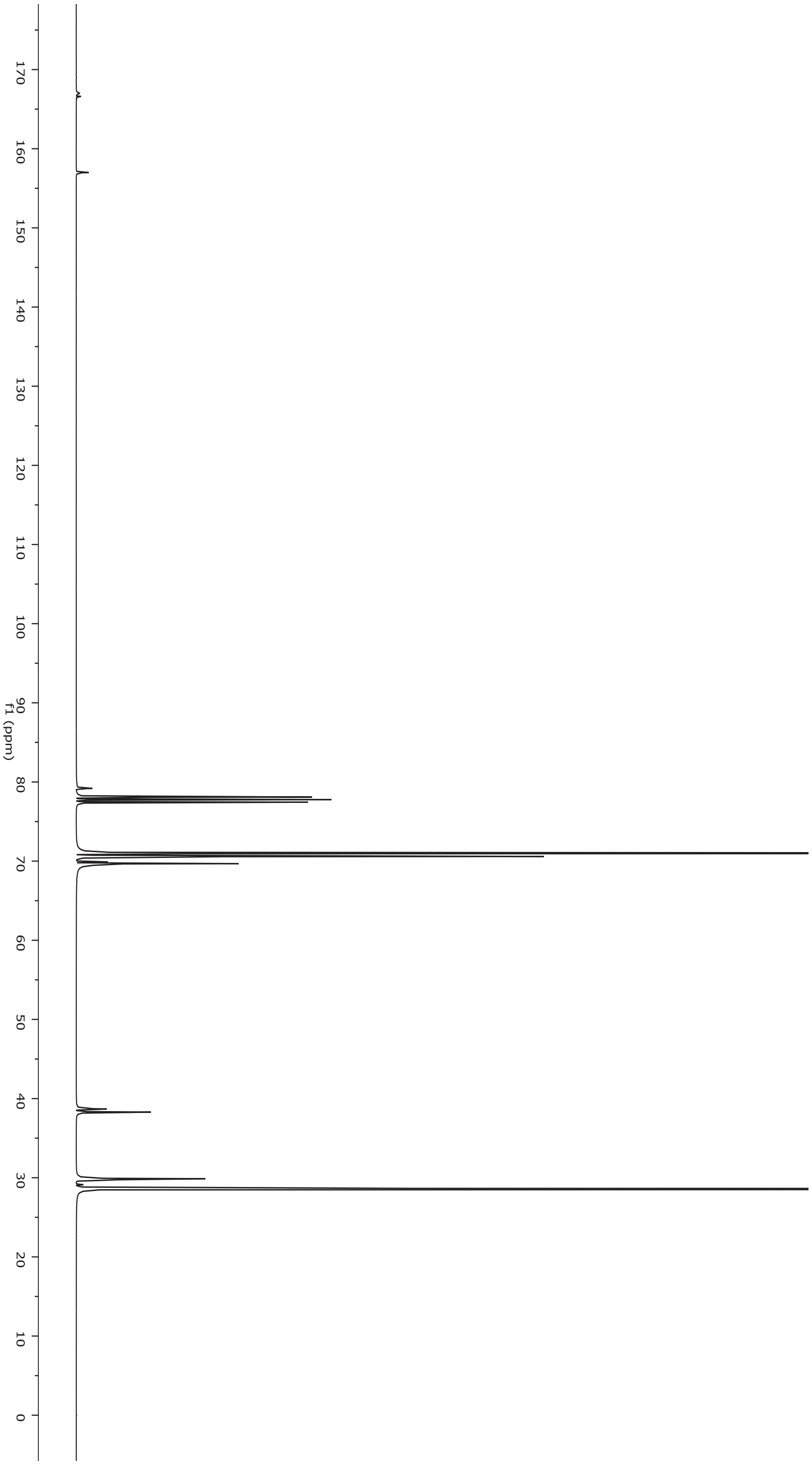
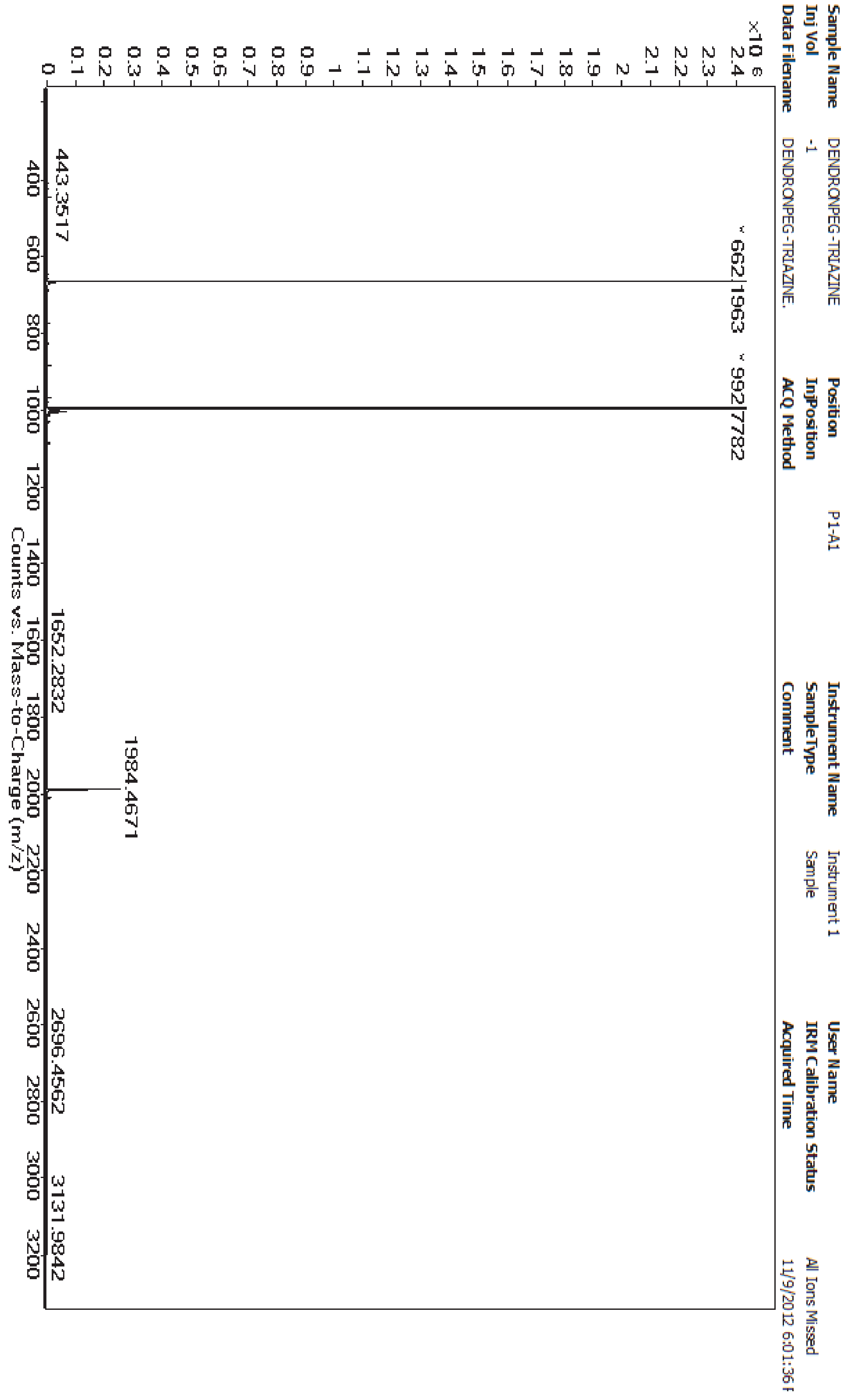


Figure S49. Mass Spectrum of **11** (ESI-TOF)



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Instrument Name Instrument 1
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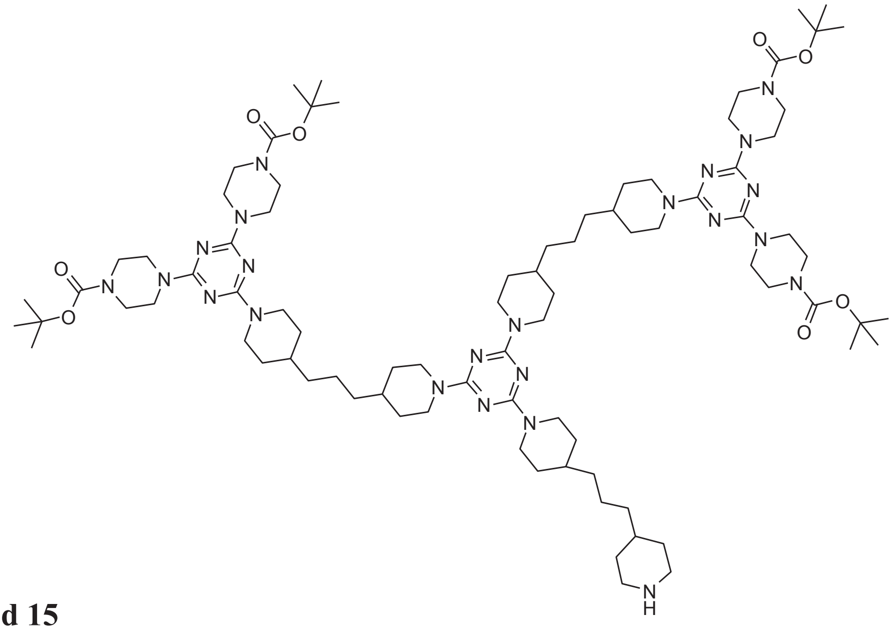
ACQ Method
Comment
Acquired Time 11/9/2012 6:01:36 F



Compound 15

Compound **9** (4g, 2.8mmol) was added to a solution of trimethylene dipiperidine (4.72g, 22.4mmol) in dichloromethane at room temperature and stirred overnight. The solution was washed with brine, dried over $MgSO_4$, filtered and evaporated under vacuum. The crude product was purified by silica gel chromatography (from hexanes:EtOAc = 4:1 to hexanes: EtOAc= 1:1 and later flushed with DCM 8:1 w/ 1% NH_4OH) to yield 4(3.35g, 75%) as a white solid. Melting point: 129-130 °C. ^1H NMR (300 MHz, $CDCl_3$, δ): 4.72 (d, *J = 12Hz*, 12H, equatorial C**H**N-triazine of dipiperidine (10H), equatorial-C**H**NH (2H)), 3.74 (s, 16H, triazine-$NCH_2C\mathbf{H_2}NBoc$), 3.44 (s, 16H, triazine-$NC\mathbf{H_2}CH_2NBoc$), 2.77–2.58 (m, 13H, equatorial $C\mathbf{H}CH_2N$-triazine of dipiperidine (10H), equatorial $C\mathbf{H}CH_2NH$ (2H), N**H** (1H)), 1.67 (bs, 12H, axial C**H**N-triazine of dipiperidine (10H), axial C**H**NH (2H)), 1.33 (s, 36H, $C(C\mathbf{H_3})_3$)), 1.32-1.09 (m, 36H, axial $C\mathbf{H}CH_2N$-triazine of dipiperidine (10H), axial $C\mathbf{H}CH_2NH$ (2H), C**H**-trimethylene (6H), $C\mathbf{H_2}C\mathbf{H_2}C\mathbf{H_2}$ (18H)). ^{13}C NMR (75 MHz, $CDCl_3$, δ): 165.6, 165.5, 165.1 ($N_3\mathbf{C}_3$), 155.1 (**C**O), 80.0 ($\mathbf{C}(CH_3)_3$), 47.1 ($\mathbf{C}H_2NH$), 43.71 ($CHCH_2\mathbf{C}H_2N$), 43.71, ($NCH_2\mathbf{C}H_2N$-triazine), 43.2 ($N\mathbf{C}H_2CH_2N$-triazine), 37.6 ($H\mathbf{C}CH_2CH_2NH$), 37.1 (H**C**-trimethylene), 36.5, 36.4 ($\mathbf{C}H_2CH_2\mathbf{C}H_2$), 33.9 ($\mathbf{C}H_2CH_2NH$), 32.4 ($\mathbf{C}H_2CH_2N$), 28.5 ($C(\mathbf{C}H_3)_3$), 23.7 ($CH_2\mathbf{C}H_2CH_2$). MS (ESI-TOF) calcd for $C_{84}H_{141}N_{23}O_8$: 1601.16; found 1602.13 $(M + H)^+$.

Compound 9 has been reported: Patra, S.; Kozura, B.; Huang, A. Y.-T.; Enciso, A. E.; Sun, X.; Hsieh, J.-T.; Kao, C.-L.; Chen, H.-T.; Simanek, E. E. Org. Lett., **2013,** 15, 3808.

Figure S50. ^{1}H NMR Spectrum of **15**

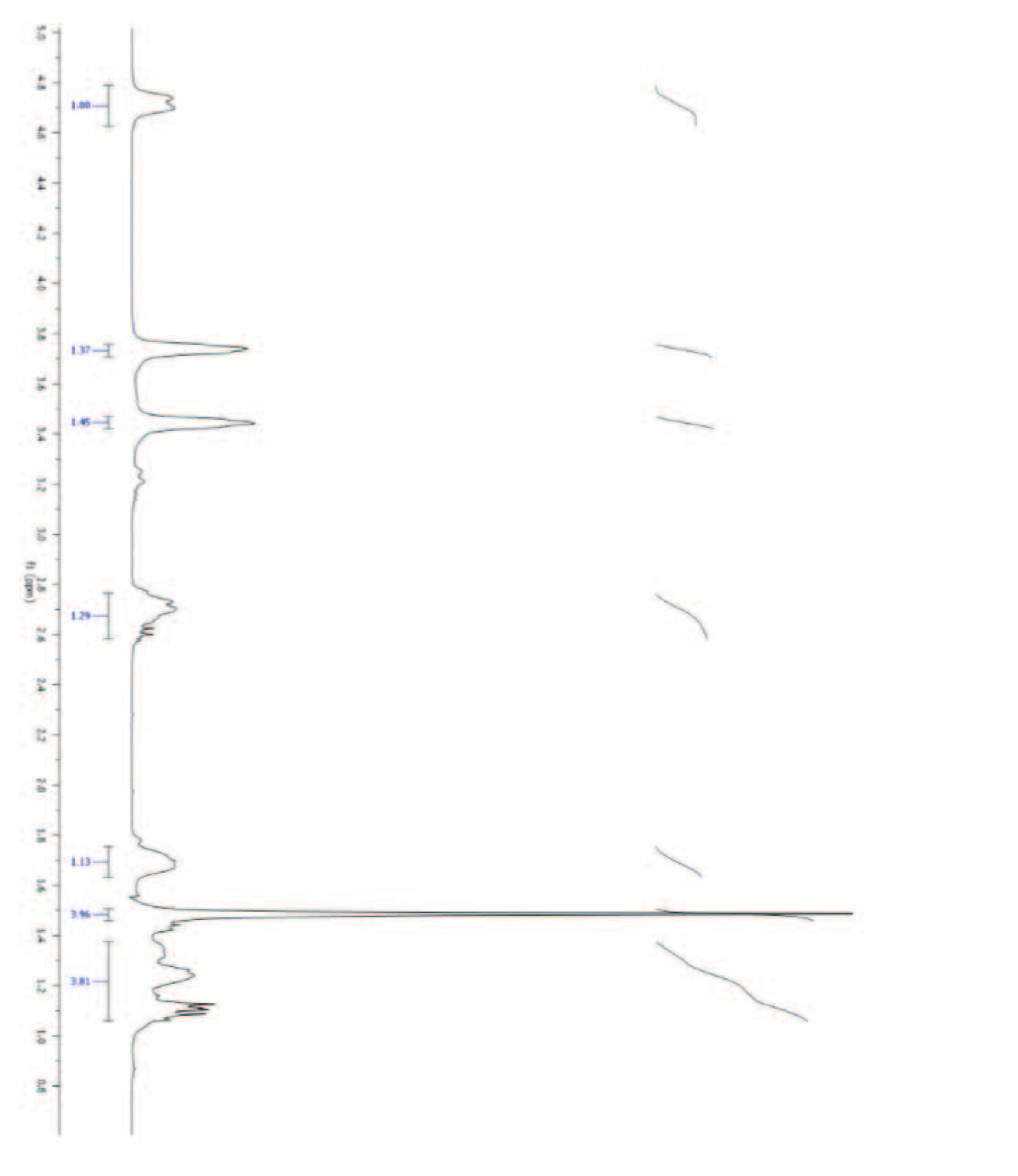


Figure S51. ^{13}C NMR Spectrum of **15**

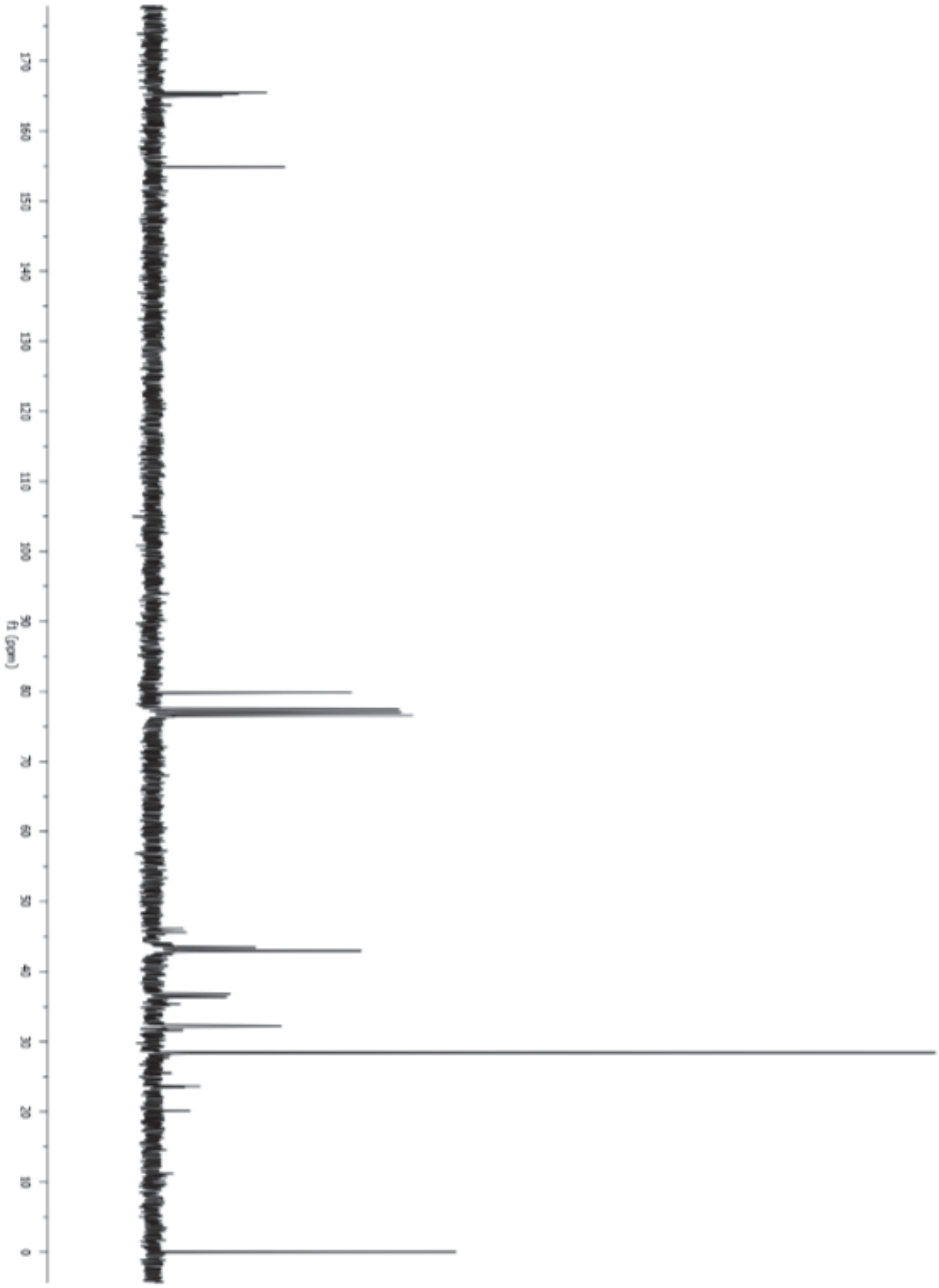
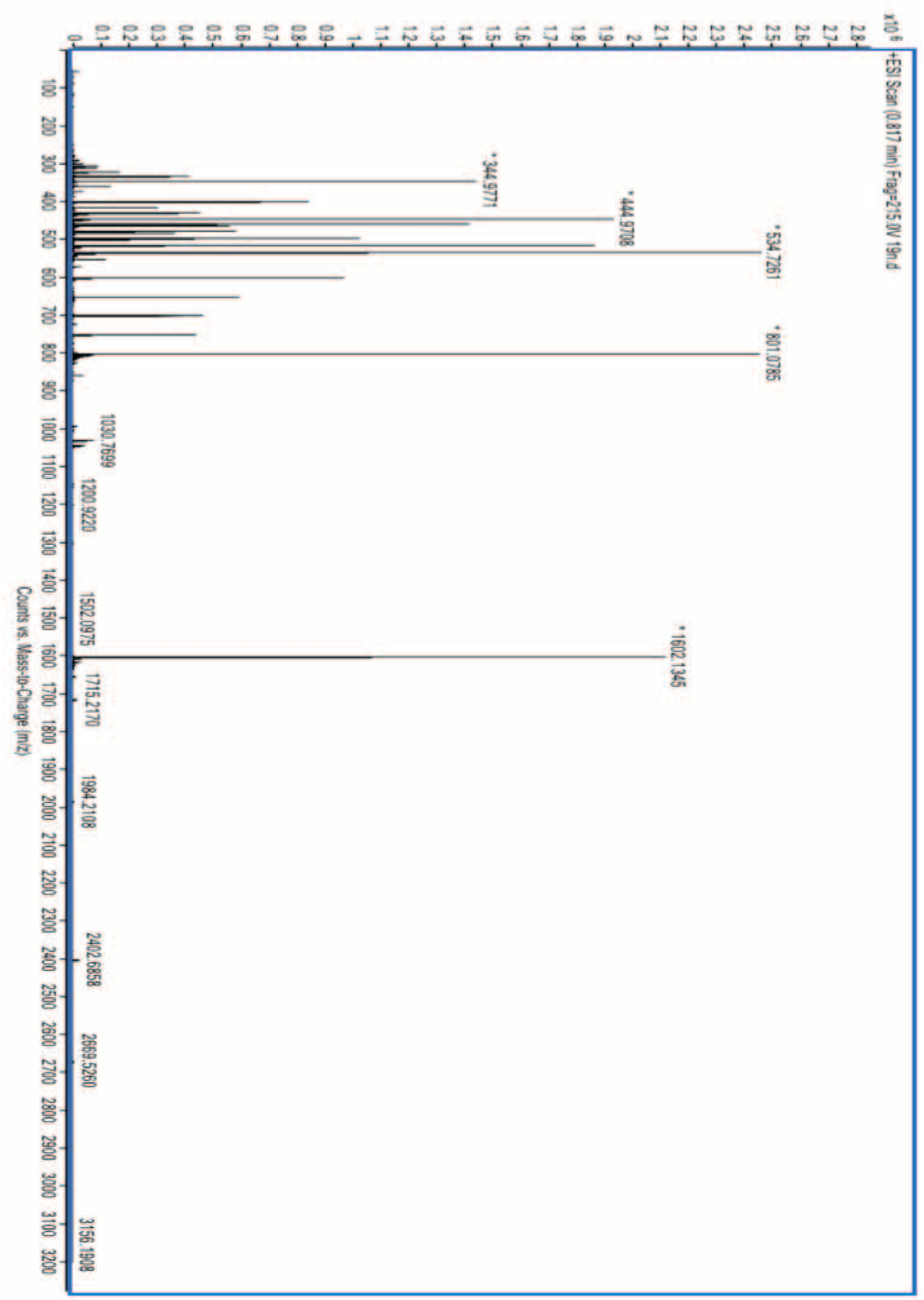


Figure S52. Mass Spectrum of **15** (ESI-TOF). Multiply-charged adducts are visible.

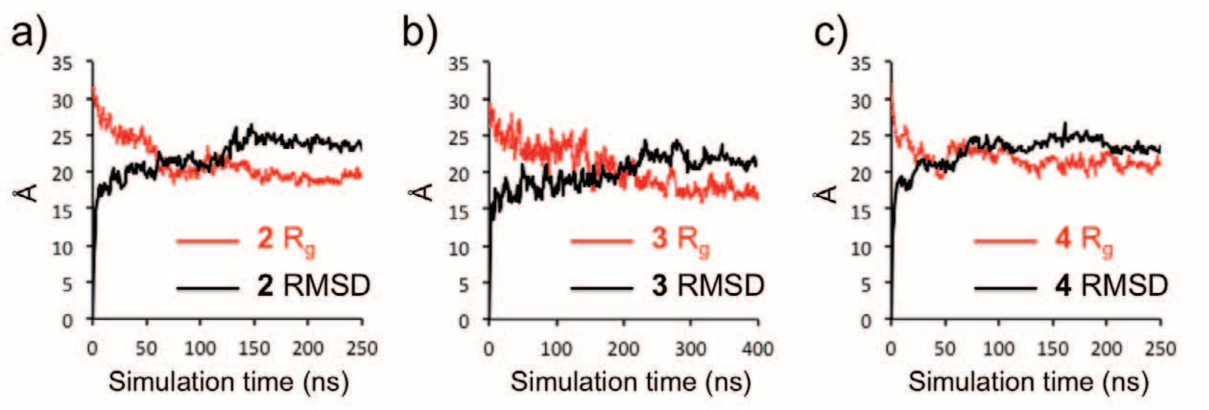


Data from Computational Simulations

Table T1. Main features of the molecular systems simulated in this study

Molecular system	Simulation temperature (K)	MW (Da)	Dendrimer charge[a] (e)	Box volume (Å^3)	Number of Cl$^-$ and Na$^+$ ions in the system[b]	Number of water molecules in the system	Total number of atom in the system	Simulation time for each MD run (ns)
2	300	10487	+32	834397	72	26881	82495	250
3	300	10646	+32	610229	52	19553	60443	400
4	300	14940	+32	1308294	114	42214	129222	250

[a] All surface amino groups were considered as +1 e charged in the systems - the overall charge present on each dendrimer is +32 e. [b] Number of Cl$^-$ and Na$^+$ ions in the system to guarantee overall neutrality and to reproduce the experimental ionic strength of 150 mM [NaCl] in solution.



Plot P1. Root mean square deviation (RMSD) and radius of gyration (R$_g$) data obtained from the MD simulations of **2** (a), **3** (b) and **4** (c) and expressed as a function of simulation time.