Construction of Well-Defined Multifunctional Dendrimers Using a Trifunctional Core

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Supplementary Information

Experimental Procedures, Spectroscopic Data and ^{1}H NMR and Mass Spectra.

General data.

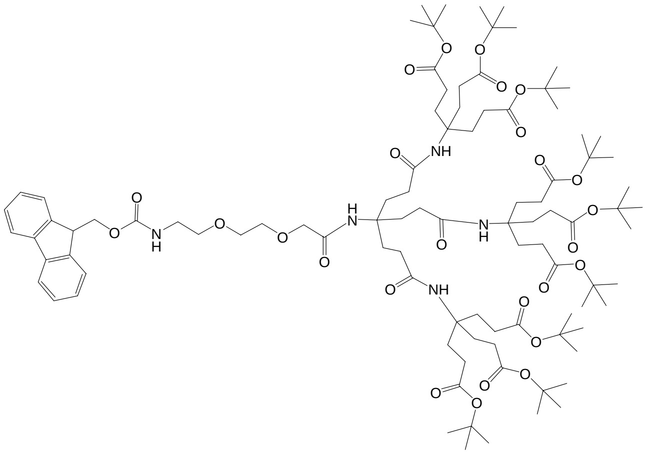
Anhydrous DMF was purchased from Acros, PEG linker **5** from VWR, and dendrons aminotriester and nitrotriester from Frontier Scientific. All compounds were used as received. Compounds **1**,[1] **3**,[1] **4**,[1] **8**[2] and **16**[3] were synthesized according to literature procedures. Dialysis membranes were purchased from SpectrumLabs and used as received.

NMR spectroscopy. ^{1}H NMR spectra were recorded at 25°C on a Bruker AC 400 (400 MHz) spectrometer. ^{13}C NMR spectra were obtained at 100.0 MHz on a Bruker AC 400 spectrometer. All chemical shifts are reported in parts per million (ppm) with reference to solvent residual peaks.

ESI Mass Spectrometry. The ESI mass spectra were obtained in an Agilent 1100 Series Capillary LCMSD Trap XCT Spectrometer.

MALDI-TOF Mass Spectrometry. MALDI-TOF mass spectra were recorded with a Bruker OmniFLEX MALDI-TOF MS Spectrometer.

Synthesis of 6



Dendron **4** (0.460 g, 0.32 mmol), PEG linker **5** (0.200 g, 0.52 mmol) and HATU (0.150 g, 0.41 mmol) were dissolved in 8 mL of dry DMF. Triethylamine (0.1 mL, 0.72 mmol) was added with a syringe and the solution was stirred at room temperature for 16h. The solvent was removed under vacuum and

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[1] SI 1. a) G. R. Newkome; R. K. Behera, C. N. Moorefield, G. R. Baker, *J. Org. Chem*. **1991**, *56*, 7162-7167; b) G. R. Newkome, A. Nayak, R. K. Behera, C. N. Moorefield, G. R. Baker, *J. Org. Chem*. **1992**, *57*, 358-362; c) Michael Brettreich, Andreas Hirsch, *Synlett* **1998**, 1396-1398.

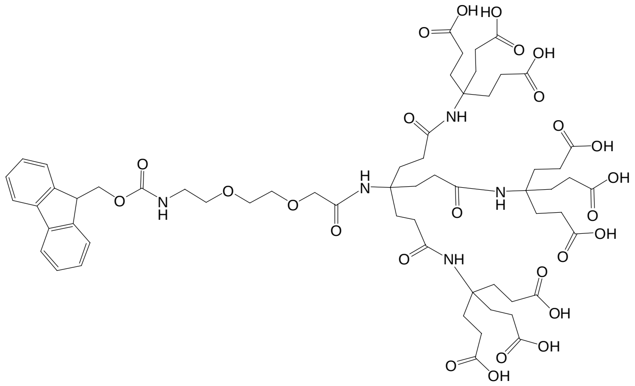
[2] O. E.Vercillo, C. K. Z. Andrade, L. A.Wessjohann, *Org. Lett*. **2008**, *10*, 205-208.

[3] P.-C. Lin, S.-H. Ueng, M.-C. Tseng, J.-L. Ko, K.-T. Huang, S.-C. Yu, A. K. Adak, Y.-J. Chen, C.-C. Lin. Angew. Chem., Int. Ed., **2006**, *45*, 4286-4290.

the product was purified by column chromatography using silica gel and ethyl acetate as eluent. The final product was obtained as a white powder in 92% yield (0.532 g).

^{1}H NMR (MeOD, 400 MHz, δ_ppm *vs.* TMS): 7.80 (d, *J* = 7.5 Hz, arom. C*H* fmoc, 2H), 7.66 (d, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.36 (t, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.29 (t, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.33 (s, CON*H*, 5H), 4.36 (d, *J* = 6.8 Hz, $\mathrm{C}H_2\mathrm{OCONH}$, 2H), 4.22 (t, *J* = 6.7 Hz, $\mathrm{C}H\mathrm{CH_2OCONH}$, 1H), 3.92 (s, $\mathrm{OC}H_2\mathrm{CONH}$, 2H), 3.68 (s, $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$, 4H), 3.60 (t, *J* = 5.4 Hz, $\mathrm{OC}H_2\mathrm{CH_2NHfmoc}$, 2H), 3.34 (s, $\mathrm{OCH_2C}H_2\mathrm{NHfmoc}$, 2H), 2.17 (m, $\mathrm{CH_2C}H_2\mathrm{COO}$, 24H), 1.93 (m, $\mathrm{C}H_2\mathrm{CH_2COO}$, 24H), 1.43 (s, $\mathrm{COOC(C}H_3)_3$, 81H). ^{13}C NMR (MeOD, 100 MHz, δ_ppm *vs.* TMS): 175.3 (*C*ONH), 174.5 (COOtBu), 158.9 ($\mathrm{NH}C\mathrm{OOCH_2}$), 145.5 and 142.7 (arom. C_q), 128.9, 128.3, 126.4 and 121.1 (arom. C*H*), 81.7 ($\mathrm{COO}C\mathrm{(CH_3)_3}$), 72.3, 71.5, 71.2 and 71.1 ($C\mathrm{H_2O}C\mathrm{H_2}$), 67.9 ($\mathrm{NHCOO}C\mathrm{H_2}$), 58.9 ($\mathrm{NHC_q}$), 41.8 ($\mathrm{OOCNH}C\mathrm{H_2CH_2O}$), 32.4 ($\mathrm{CH_2C}H_2\mathrm{CONH}$), 32.1 ($\mathrm{C}H_2\mathrm{CH_2CONH}$), 30.8 ($\mathrm{CH_2C}H_2\mathrm{COOtBu}$), 30.6 ($\mathrm{C}H_2\mathrm{CH_2COOtBu}$), 28.6 ($\mathrm{COOC(}C\mathrm{H_3)_3}$). MS-ESI [MNa$^+$] *m/z* calcd for $\mathrm{C_{97}H_{155}N_5O_{26}Na}$: 1829.1, found 1827.1. Anal. calcd. for $\mathrm{C_{97}H_{155}N_5O_{26}}$: C 64.46, H 8.64; found C 64.19, H 8.53.

Synthesis of 7

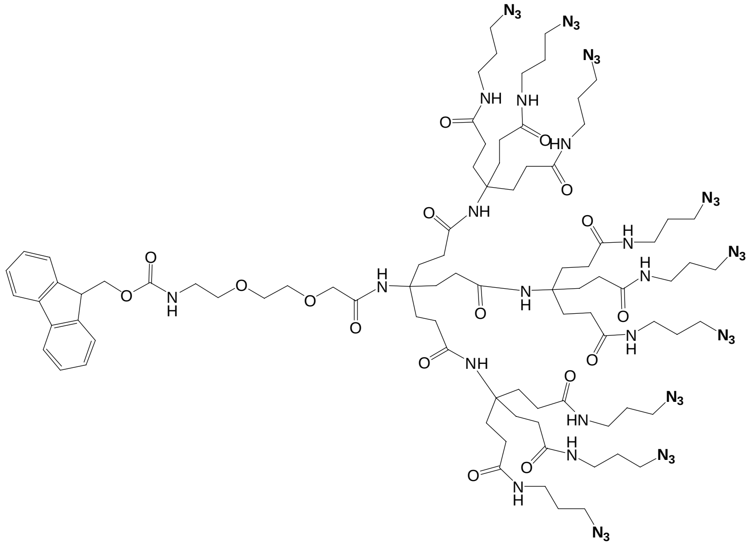


Dendron **6** (0.174 g, 0.096 mmol) was dissolved in 20 mL of formic acid and 2 mL of water were added. The solution was stirred at room temperature for 16h. The solution was evaporated to dryness and the product was washed three times with ethylic ether. The final product was obtained as a white solid in 97% yield (0.121 g).

^{1}H NMR (MeOD, 400 MHz, δ_ppm *vs.* TMS): 8.09 (s, CON*H*, 5H), 7.79 (d, *J* = 7.5 Hz, arom. C*H* fmoc, 2H), 7.64 (d, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.38 (t, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.31 (t, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 4.38 (d, *J* = 6.8 Hz, $\mathrm{C}H_2\mathrm{OCONH}$, 2H), 4.21 (t, *J* = 6.7 Hz, $\mathrm{C}H\mathrm{CH_2OCONH}$, 1H), 3.93 (s, $\mathrm{OC}H_2\mathrm{CONH}$, 2H), 3.67 (s, $\mathrm{OC}H_2\mathrm{C}H_2\mathrm{O}$, 4H), 3.58 (t, *J* = 5.4 Hz,

$\mathrm{OC}\mathit{H}_2\mathrm{CH_2NHfmoc}$, 2H), 3.33 (m, $\mathrm{OCH_2C}\mathit{H}_2\mathrm{NHfmoc}$, 2H), 2.27 (m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{COOH}$, 18H), 2.17 (m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CONH}$, 6H), 2.02 (m, $\mathrm{C}\mathit{H}_2\mathrm{CH_2COO}$, 24H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 177.2 (COOH), 175.5 ($\mathit{C}\mathrm{ONH}$), 159.1 ($\mathrm{NH}\mathit{C}\mathrm{OOCH_2}$), 145.5 and 142.7 (arom. C_q), 128.9, 128.3, 126.3 and 121.1 (arom. $\mathrm{C}\mathit{H}$), 72.3, 71.5, 71.2 and 71.1 ($\mathit{C}\mathrm{H_2O}\mathit{C}\mathrm{H_2}$), 67.8 ($\mathrm{NHCOO}\mathit{C}\mathrm{H_2}$), 58.7 ($\mathrm{NHC_q}$), 41.7 ($\mathrm{OOCNH}\mathit{C}\mathrm{H_2CH_2O}$), 32.2 ($\mathrm{CH_2C}\mathit{H}_2\mathrm{CONH}$), 31.9 ($\mathrm{C}\mathit{H}_2\mathrm{CH_2CONH}$), 30.6 ($\mathrm{CH_2C}\mathit{H}_2\mathrm{COOH}$), 29.4 ($\mathrm{C}\mathit{H}_2\mathrm{CH_2COOH}$). MS-ESI [$\mathrm{MNa^+}$] *m/z* calcd for $C_{61}H_{83}N_5O_{26}Na$: 1324.5, found 1324.4. Anal. calcd. for $C_{61}H_{83}N_5O_{26}$: C 56.26, H 6.42; found C 55.87, H 6.33.

Synthesis of 9

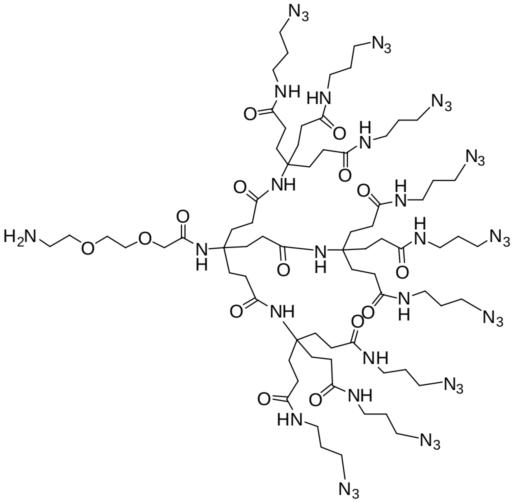


Dendron **7** (0.058 g, 0.045 mmol) and HATU (0.187 g, 0.53 mmol) were dissolved in 6 mL of dry DMF. Triethylamine (0.15 mL, 1.1 mmol) and 3-aminopropyl azide **8** (0.080 g, 0.80 mmol) were successively added with a syringe and the solution was stirred at room temperature for 24h. The solvent was removed under vacuum and the product was purified by column chromatography using silica gel and CH_2Cl_2/methanol (90/10) as eluent. The final product was obtained as a colorless waxy product in 92% yield (0.083 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 7.86 and 7.32 (s, $\mathrm{CON}\mathit{H}$, 14H), 7.81 (d, *J* = 7.5 Hz, arom. C*H* fmoc, 2H), 7.67 (d, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.40 (t, *J* = 7.4 Hz, arom. C*H* fmoc, 2H), 7.33 (t, overlapped with singlet of CON*H*, arom. C*H* fmoc, 2H), 4.33 (d, *J* = 7.0 Hz, $\mathrm{C}\mathit{H}_2\mathrm{OCONH}$, 2H), 4.22 (t, *J* = 7.0 Hz, $\mathrm{C}\mathit{H}\mathrm{CH_2OCONH}$, 1H), 3.96 (s, $\mathrm{OC}\mathit{H}_2\mathrm{CONH}$, 2H), 3.70 and 3.68 (s, $\mathrm{OC}\mathit{H}_2\mathrm{C}\mathit{H}_2\mathrm{O}$, 4H), 3.59 (t, *J* = 5.9 Hz, $\mathrm{OC}\mathit{H}_2\mathrm{CH_2NHfmoc}$, 2H), 3.34 (t, *J* = 6.7 Hz, $\mathrm{OCH_2C}\mathit{H}_2\mathrm{NHfmoc}$ and $\mathrm{C}\mathit{H}_2\mathrm{N_3}$, 20H), 3.23 (t, *J* = 6.6 Hz, $\mathrm{NHC}\mathit{H}_2\mathrm{CH_2CH_2N_3}$, 18H), 2.17 (m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{CONH}$, 24H), 1.99 (m, $\mathrm{C}\mathit{H}_2\mathrm{CH_2CONH}$, 24H), 1.74 (m, $\mathrm{NHCH_2C}\mathit{H}_2\mathrm{CH_2N_3}$, 18H). ^{13}C NMR

(MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 175.5 (*C*ONH), 159.2 (NH*C*OOCH$_2$), 145.5 and 142.7 (arom. *C*$_q$), 128.9, 128.3, 126.3 and 121.2 (arom. C*H*), 72.3, 71.6, 71.2 and 71.1 (*C*H$_2$O*C*H$_2$), 67.7 (NHCOO*C*H$_2$), 58.9 (NHC$_q$), 50.3 (*C*H$_2$N$_3$), 41.7 (OOCNH*C*H$_2$CH$_2$O), 38.1 (NH*C*H$_2$CH$_2$CH$_2$N$_3$), 31.7 (CH$_2$C*H*$_2$CONH), 31.4 (C*H*$_2$CH$_2$CONH), 29.8 (NHCH$_2$*C*H$_2$CH$_2$N$_3$). MS-ESI [MH$^+$] *m/z* calcd for $C_{88}H_{138}N_{41}O_{17}$: 2041.1, found 2042.2. Anal. calcd. for $C_{88}H_{137}N_{41}O_{176}$: C 51.78, H 6.76; found C 51.49, H 6.68.

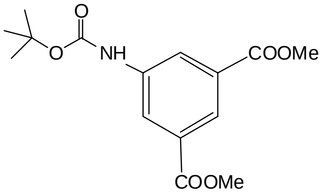
Synthesis of 10



Dendron **9** (0.076 g, 0.037 mmol) was dissolved in 2 mL of DMF and 0.4 mL of piperidine was added. The solution was stirred at room temperature for 30 min. The solvent was removed and the product was purified by dialysis against water (3 x 1L) using a Spectra-Por MWCO 500-1000 dialysis membrane. The final product was obtained as a colorless waxy product in 98% yield (0.066 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 3.95 (s, OC*H*$_2$CONH, 2H), 3.77 (t, *J* = 5.0 Hz, OC*H*$_2$CH$_2$NH$_2$, 2H) 3.64 (s, OC*H*$_2$C*H*$_2$O, 4H), 3.34 (t, *J* = 6.7 Hz, C*H*$_2$N$_3$, 18H), 3.23 (t, *J* = 6.8 Hz, NHC*H*$_2$CH$_2$CH$_2$N$_3$, 18H), 2.19 (m, CH$_2$C*H*$_2$CONH, 24H), 2.00 (m, C*H*$_2$CH$_2$CONH, 24H), 1.74 (m, NHCH$_2$C*H*$_2$CH$_2$N$_3$, 18H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 175.6 (*C*ONH), 72.1, 71.4, 71.2 and 70.3 (*C*H$_2$O*C*H$_2$), 59.3 (NHC$_q$), 50.2 (*C*H$_2$N$_3$), 41.6 (NH$_2$*C*H$_2$CH$_2$O), 38.0 (NH*C*H$_2$CH$_2$CH$_2$N$_3$), 31.7 (CH$_2$C*H*$_2$CONH), 31.4 (C*H*$_2$CH$_2$CONH), 29.8 (NHCH$_2$*C*H$_2$CH$_2$N$_3$). MS-ESI [MH$^+$] *m/z* calcd for $C_{73}H_{128}N_{41}O_{15}$: 1819.0, found 1819.3. Anal. calcd. for $C_{73}H_{127}N_{41}O_{15}$: C 48.20, H 7.04; found C 47.92, H 6.96.

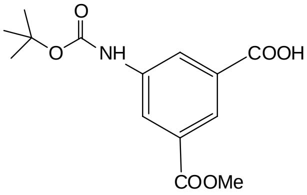
Synthesis of 12:



Dimethyl 5-aminoisophthalate (2.00 g, 9.56 mmol) was dissolved in 100 mL of dry methylene chloride. Triethylamine (3.05 mL, 28.7 mmol) and di-tert-butyl dicarbonate (4.39 mL, 19.1 mmol) were successively added and the solution was stirred at room temperature for 16h. Solvent was removed under vacuum giving a yellow solid. The product was purified by column chromatography using silica gel and hexane/ethyl acetate (80/20) as eluent. The final product was obtained as a white powder in 66% yield (1.95 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.30 (s, arom. C*H*, 2H), 8.23 (s, arom. C*H*, 1H), 3.93 (s, COOC*H*$_3$, 6H), 1.54 (s, C(C*H*$_3$)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 167.7 (*C*OOCH$_3$), 155.1 (*C*OOtBu), 141.9 (arom. *C*NH), 132.6 (arom. *C*COOCH$_3$), 125.2 and 124.4 (arom. *C*H), 81.6 (*C*(CH$_3$)$_3$), 53.1 (COO*C*H$_3$), 28.8 (C(*C*H$_3$)$_3$). MS-ESI [M$^-$] *m/z* calcd for $C_{15}H_{18}NO_6$: 308.1, found 308.4. Anal. calcd. for $C_{15}H_{18}NO_6$: C 58.25, H 6.19; found C 58.47, H 6.29.

Synthesis of 13:

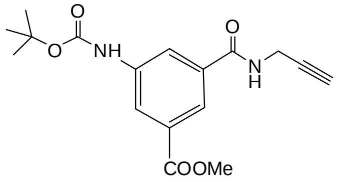


Product **12** (1.21 g, 3.91 mmol) was dissolved in 90 mL of methanol and an aqueous solution of sodium hydroxide (0.156 g, 3.91 mmol in 10 mL of water) was added. The solution was stirred at room temperature for 24h and the solvent was removed under vacuum. The product was purified by column chromatography using silica gel and ethyl acetate/MeOH (96/4) as eluent. The final product was obtained as a white powder in 77% yield (0.89 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.32, 8.29 and 8.25 (s, arom. C*H*, 3H), 3.93 (s, COOC*H*$_3$, 3H), 1.53 (s, C(C*H*$_3$)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 168.8 (*C*OOCH$_3$), 167.7

(*C*OOH), 155.0 (*C*OOtBu), 141.6 (arom. *C*NH), 133.2 (arom. *C*COOH), 132.3 (arom. *C*COOCH$_3$), 125.5, 124.8 and 124.3 (arom. *C*H), 81.6 (*C*(CH$_3$)$_3$), 53.0 (COO*C*H$_3$), 28.8 (C(*C*H$_3$)$_3$). MS-ESI [M$^-$] *m/z* calcd for $C_{14}H_{16}NO_6$: 294.1, found 293.8. Anal. calcd. for $C_{14}H_{17}NO_6$: C 56.94, H 5.80; found C 57.16, H 5.69.

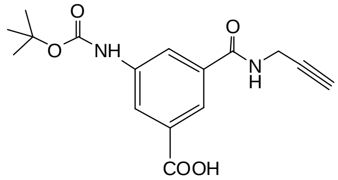
Synthesis of 14:



Product **13** (0.200 g, 0.68 mmol) and HATU (0.283 g, 0.75 mmol) were dissolved in 12 mL of dry DMF. Propargylamine (0.065 mL, 1.02 mmol) and diisopropylethylamine (0.24 mL, 1.35 mmol) were added with a syringe and the solution was stirred at room temperature for 16h. The solvent was removed under vacuum and the product was purified by column chromatography using silica gel and CH_2Cl_2/MeOH (98/2) as eluent. The final product was obtained as a white powder in 98% yield (0.22 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.27 (s, arom. C*H*, 1H), 8.08 (s, arom. C*H*, 2H), 4.15 (d, *J* = 2.5 Hz, NHC*H*$_2$C≡CH, 2H), 3.93 (s, COOC*H*$_3$, 3H), 2.61 (s, C≡C*H*, 1H), 1.54 (s, C(C*H*$_3$)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 168.9 (*C*OOCH$_3$), 167.8 (*C*ONHCH$_2$), 155.2 (*C*OOtBu), 141.8 (arom. *C*NH), 136.6 (arom. *C*CONH), 132.5 (arom. *C*COOCH$_3$), 123.4, 123.2 and 122.9 (arom. *C*H), 81.7 (*C*(CH$_3$)$_3$), 80.7 (*C*≡CH), 72.3 (C≡*C*H), 53.0 (COO*C*H$_3$), 30.2 (NH*C*H$_2$), 28.8 (C(*C*H$_3$)$_3$). MS-ESI [M(H$_2$O)$^+$] *m/z* calcd for $C_{17}H_{22}N_2O_6$: 350.1, found 349.3. Anal. calcd. for $C_{17}H_{20}N_2O_5$: C 61.44, H 6.01; found C 61.23, H 6.16.

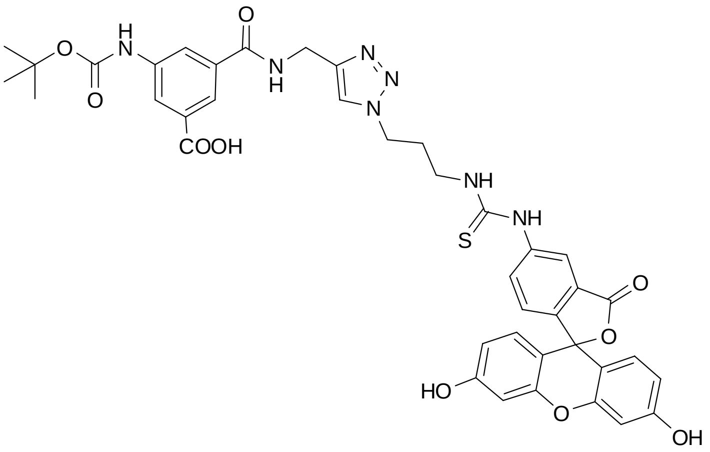
Synthesis of 15:



Product **14** (0.200 g, 0.60 mmol) was dissolved in 20 mL of methanol and an aqueous solution of sodium hydroxide (0.036 g, 0.90 mmol, in 1 mL of water) was added. The solution was stirred at room temperature for 48h and the solvent was removed under vacuum. The product was purified by column chromatography using silica gel and $\mathrm{CH_2Cl_2}$/MeOH (80/20) as eluent. The final product was obtained as a beige powder in 87% yield (0.17 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.07 (s, arom. C*H*, 2H), 8.02 (s, arom. C*H*, 1H), 4.15 (d, *J* = 2.2 Hz, NHCH_2C≡CH, 2H), 2.62 (s, C≡C*H*, 1H), 1.52 (s, C(CH_3)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 169.7 (*C*OOH and *C*ONHCH$_2$), 155.2 (*C*OOtBu), 141.0 (arom. *C*NH), 135.9 (arom. *C*CONH), 130.5 (arom. *C*COOH) 123.8, 123.2 and 120.8 (arom. *C*H), 81.2 (*C*(CH$_3$)$_3$), 81.0 (*C*≡CH), 72.3 (C≡*C*H), 30.1 (NH*C*H$_2$), 28.8 (C(*C*H$_3$)$_3$). MS-ESI [M$^-$] *m/z* calcd for $\mathrm{C_{16}H_{17}N_2O_5}$: 317.3, found 317.3. Anal. calcd. for $\mathrm{C_{16}H_{18}N_2O_5}$: C 60.37, H 5.70; found C 60.07, H 5.61.

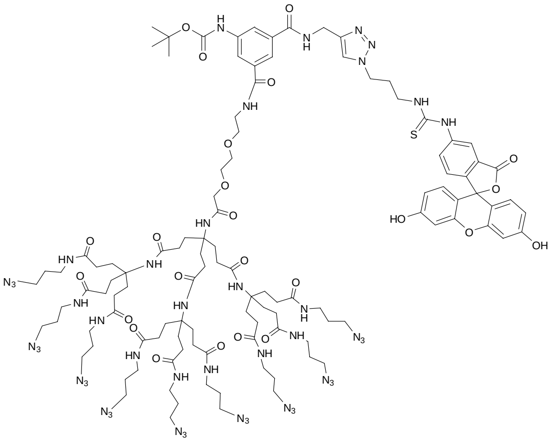
Synthesis of 17



Products 1**5** (0.088 g, 0.28 mmol) and **16** (0.085 g, 0.17mmol) were dissolved in 200 mL of $\mathrm{CH_2Cl_2/EtOH/H_2O}$ (1:1:2) solvent mixture. Aqueous solutions of $\mathrm{CuSO_4.5H_2O}$ (0.050 g, 0.20 mmol) and sodium ascorbate (0.079 g, 0.40 mmol) were successively added and the solution was stirred at room temperature for 24h. The solvent was removed under vacuum and the product was purified by reverse-phase column using methanol as eluent. The product was obtained as a yellow solid in 62% yield (0.085 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.10 (s, arom. C*H*, 2H), 8.05 (s, arom. C*H*, 1H), 7.84 (s, triazole C*H*, 1H), 7.51 (m, arom. C*H*, 1H), 7.31 (m, arom. C*H*, 1H), 6.98 (m, arom. C*H*, 2H), 6.69 (s, arom. C*H*, 2H), 6.20 (m, arom. C*H*, 2H), 4.64 (s, triazole-CH_2CH$_2$, 2H), 4.53 (s, NHCH_2-triazole, 2H), 3.49 (m, NHCH_2CH$_2$CH$_2$-triazole, 2H), 1.92 (m, NHCH$_2$CH_2CH$_2$-triazole, 2H), 1.51 (s, C(CH_3)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 182.7 (NH*C*=S), 173.8 (*C*OO), 169.7 (*C*OOH and *C*ONHCH$_2$), 158.5 (arom. C_qOH), 155.2 (*C*OOtBu), 142.3 and 123.2 (*C*H of triazole), 141.1 (arom. *C*NH), 141.6, 139.5, 130.5, 126.8 and 124.4 (arom. C_{q} of FITC), 135.9 (arom. *C*CONH), 132.4, 121.1 and 104.3 (arom. *C*H of FITC), 130.5 (arom. *C*COOH), 123.7, 123.1 and 120.6 (arom. *C*H of core), 81.2 (*C*(CH_3)$_3$), 57.6 (NH*C*H_2-triazole), 51.0 (NHCH_2CH_2*C*H_2-triazole), 38.9 (NH*C*H_2CH_2CH_2), 29.0 (NHCH_2*C*H_2CH_2), 28.8 (C(*C*H_3)$_3$). MS MALDI-TOF [MH^+] *m/z* calcd for $C_{40}H_{38}N_7O_{10}S$: 808.1, found: 808.6. Anal. calcd. for $C_{40}H_{37}N_7O_{10}S$: C 59.47, H 4.62; found C 59.49, H 4.69.

Synthesis of 18

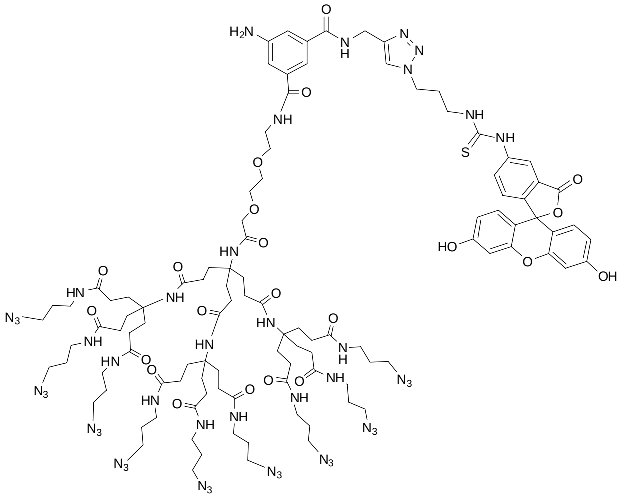


Product **17** (0.016 g, 0.018 mmol), dendron **10** (0.040 g, 0.022 mmol) and HATU (0.0084 g, 0.024 mmol) were dissolved in 5 mL of dry DMF and diisopropylethylamine (0.007 mL, 0.040 mmol) was added. The solution was stirred at room temperature for 24h. The solvent was removed under vacuum and the product was purified by dialysis against methanol (3 x 1L), using a Spectra-Por MWCO 2000 dialysis membrane. The product was obtained as a yellow waxy product in 72% yield (0.039 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 7.97 (s, arom. C*H*, 3H), 7.87 (s, triazole C*H*, 1H), 7.70 (s, CON*H*, 16H), 7.64 (d, *J* = 8.2 Hz, arom. C*H*, 1H), 7.43 (s, arom. C*H*, 1H), 7.29 (d, *J* = 8.2 Hz, arom. C*H*, 1H), 6.72 (s, arom. C*H*, 2H), 6.55 (d, *J* = 7.3 Hz, arom. C*H*, 2H), 4.64 (s, triazole-C*H*$_2$CH_2, 2H), 4.55 (s, NHC*H*$_2$-triazole, 2H), 3.97 (s, OC*H*$_2$CONH, 2H), 3.78 (t, *J* = 4.9 Hz, OC*H*$_2$CH_2NHCO, 2H), 3.66 (s, OC*H*$_2$C*H*$_2$O, 4H), 3.50 (t, *J* = 6.5 Hz, NHC*H*$_2$CH_2CH_2-triazole, 2H), 3.36 (t, *J* = 6.7 Hz, C*H*$_2$$N_3$, 18H), 3.25 (t, *J* = 6.8 Hz, NHC*H*$_2$CH_2C$H_2$$N_3$, 18H), 2.19 (m, C$H_2$C*H*$_2$CONH, 24H), 2.00 (m, C*H*$_2$CH_2CONH and NHCH_2C*H*$_2$CH_2-triazole, 26H), 1.76 (m, NHCH_2C*H*$_2$C$H_2$$N_3$, 18H), 1.52 (s, C(C*H*$_3$)$_3$, 9H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 182.7 (NH*C*=S), 175.6 (*C*ONH), 169.7 (*C*ONHCH_2), 158.5 (arom. C_qOH), 155.1 (*C*OOtBu), 142.3 and 123.2 (*C*H of triazole), 141.2 (arom. *C*NH), 141.6, 139.5, 130.4, 126.6 and 124.5 (arom. C_q of FITC), 135.9 (arom. *C*CONH), 132.4, 121.1 and 104.3 (arom. *C*H of FITC), 123.7, 123.1 and 120.5 (arom. *C*H of core), 81.2 (*C*(CH_3)$_3$), 72.2, 71.5, 71.3 and 70.4 (*C*H_2O*C*H_2), 59.3 (NHC_q), 57.4 (NH*C*H_2-triazole), 51.0 (NHCH_2CH_2*C*H_2-

triazole), 50.3 ($\mathit{C}H_2N_3$), 41.6 ($NH_2\mathit{C}H_2CH_2O$), 38.8 ($NH\mathit{C}H_2CH_2CH_2$), 38.0 ($NH\mathit{C}H_2CH_2CH_2N_3$), 31.7 ($CH_2C\mathit{H}_2CONH$), 31.4 ($C\mathit{H}_2CH_2CONH$), 29.8 ($NHCH_2\mathit{C}H_2CH_2N_3$), 29.2 ($NHCH_2\mathit{C}H_2CH_2$), 28.8 ($C(\mathit{C}H_3)_3$). MS MALDI-TOF [MH$^+$] *m/z* calcd for $C_{113}H_{163}N_{48}O_{24}S$: 2608.3, found: 2609.6. Anal. calcd. for $C_{113}H_{162}N_{48}O_{24}S$: C 52.02, H 6.26; found C 51.83, H 6.15.

Synthesis of 19

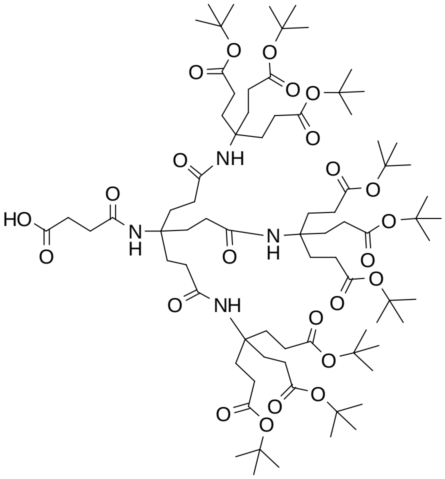


Dendron **18** (0.030 g, 0.011 mmol) was dissolved in 20 mL of formic acid and 2 mL of water was added. The solution was stirred at room temperature for 16h. The solution was evaporated to dryness and the product was washed three times with ethylic ether. The final product was obtained as a yellow waxy product in 95% yield (0.027 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 7.97 (s, arom. C*H*, 1H), 7.87 (s, triazole C*H*, 1H), 7.70 (s, CON*H*, 16H), 7.64 (d, *J* = 8.2 Hz, arom. C*H*, 1H), 7.43 (s, arom. C*H*, 3H), 7.29 (d, *J* = 8.1 Hz, arom. C*H*, 1H), 6.72 (s, arom. C*H*, 2H), 6.55 (s, arom. C*H*, 2H), 4.64 (s, triazole-$C\mathit{H}_2CH_2$, 2H), 4.55 (s, $NHC\mathit{H}_2$-triazole, 2H), 3.97 (s, $OC\mathit{H}_2CONH$, 2H), 3.78 (m, $OC\mathit{H}_2CH_2NHCO$, 2H), 3.66 (s, $OC\mathit{H}_2C\mathit{H}_2O$, 4H), 3.50 (m, $NHC\mathit{H}_2CH_2CH_2$-triazole, 2H), 3.36 (t, *J* = 6.7 Hz, $C\mathit{H}_2N_3$, 18H), 3.25 (t, *J* = 6.8 Hz, $NHC\mathit{H}_2CH_2CH_2N_3$, 18H), 2.19 (m, $CH_2C\mathit{H}_2CONH$, 24H), 2.00 (m, $C\mathit{H}_2CH_2CONH$ and $NHCH_2C\mathit{H}_2CH_2$-triazole, 26H), 1.76 (m, $NHCH_2C\mathit{H}_2CH_2N_3$, 18H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 182.7 (NH*C*=S), 175.6 (*C*ONH), 169.7 ($\mathit{C}ONHCH_2$), 158.5 (arom. C_qOH), 148.2 (arom. *C*NH), 142.3 and 123.2 (*C*H of triazole), 141.6, 139.5, 130.4, 126.6 and 124.5 (arom. C_q of FITC), 135.9 (arom. *C*CONH), 132.4, 121.1 and 104.3 (arom. *C*H of FITC), 116.0, 115.7 and 115.1 (arom. *C*H of core), 72.2, 71.5, 71.3 and 70.4 ($\mathit{C}H_2O\mathit{C}H_2$), 59.3 ($NHC_q$), 57.4 ($NH\mathit{C}H_2$-triazole), 51.0 ($NHCH_2CH_2\mathit{C}H_2$-triazole), 50.3 ($\mathit{C}H_2N_3$), 41.6 ($NH_2\mathit{C}H_2CH_2O$), 38.8 ($NH\mathit{C}H_2CH_2CH_2$), 38.0 ($NH\mathit{C}H_2CH_2CH_2N_3$), 31.7 ($CH_2C\mathit{H}_2CONH$), 31.4 ($C\mathit{H}_2CH_2CONH$), 29.8 ($NHCH_2\mathit{C}H_2CH_2N_3$), 29.2

(NHCH$_2$*C*H$_2$CH$_2$). MS MALDI-TOF [MH$^+$] *m/z* calcd for $C_{108}H_{155}N_{48}O_{22}S$: 2508.2, found: 2509.3. Anal. calcd. for $C_{108}H_{154}N_{48}O_{22}S$: C 51.71, H 6.19; found C 51.52, H 6.11.

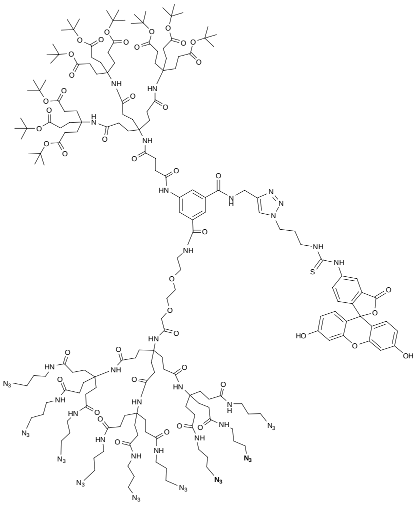
Synthesis of 20



Dendron **4** (0.140 g, 0.097 mmol) was dissolved in 5 mL of pyridine and succinic anhydride (0.020 g, 0.194 mmol) was added. The solution was stirred at room temperature for 48h. The solvent was removed and the product was purified by column chromatography using silica gel and ethyl acetate as eluent. Dendron **20** was obtained as a white solid in 92% yield (0.138 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 7.49 and 7.28 (s, CON*H*, 4H), 2.63 (t, *J* = 6.5 Hz, CH$_2$C*H*$_2$COOH, 2H), 2.46 (t, *J* = 6.5 Hz, C*H*$_2$CH$_2$COOH, 2H), 2.17 (m, C$_q$CH$_2$C*H*$_2$CO, 24H), 1.94 (m, C$_q$C*H*$_2$CH$_2$CO, 24H), 1.45 (s, COOC(C*H*$_3$)$_3$, 81H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 175.3 (*C*ONH), 174.5 (*C*OOtBu), 173.8 (*C*OOH), 81.5 (COO*C*(CH$_3$)$_3$), 58.8 (NHC$_q$), 32.5 (CH$_2$*CH*$_2$CONH), 32.2 (C*H*$_2$CH$_2$CONH), 30.6 (CH$_2$C*H*$_2$COOtBu), 30.4 (C*H*$_2$CH$_2$COOtBu), 30.0 (CH$_2$*C*H$_2$COOH), 29.6 (*C*H$_2$CH$_2$COOH), 28.3 (COOC(*C*H$_3$)$_3$). MS-ESI [M$^-$] *m/z* calcd for $C_{80}H_{138}N_4O_{24}$: 1539.0, found 1538.3. Anal. calcd. for $C_{80}H_{138}N_4O_{24}$: C 62.39, H 9.03; found C 62.32, H 9.01.

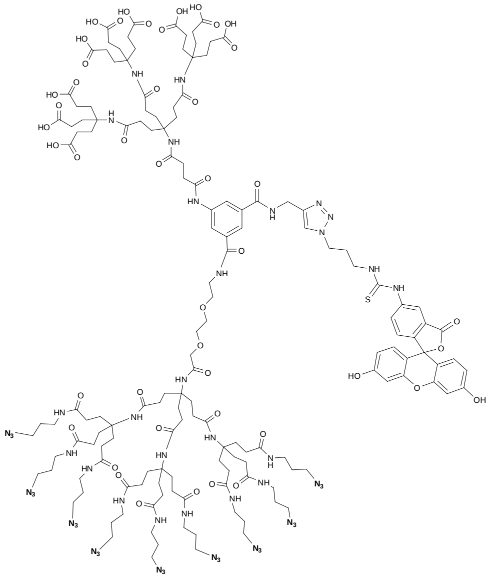
Synthesis of 21



Product **19** (0.020 g, 0.0080 mmol) and dendron **20** (0.015 g, 0.010 mmol) were dissolved in 5 mL of dry DMF. HATU (0.0034 g, 0.010 mmol) and diisopropylethylamine (0.003 g, 0.020 mmol) were added, and the solution was stirred at room temperature for 24h. The solvent was removed under vacuum and the product was purified by dialysis against methanol (3 x 1L), using a Spectra-Por MWCO 2000 dialysis membrane. Dendrimer **21** was obtained as a yellow waxy product in 81% yield (0.026 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.01-6.41 (arom. C*H* and CON*H*, 20H), 4.61 (s, triazole-C*H*$_2$CH$_2$, 2H), 4.58 (s, NHC*H*$_2$-triazole, 2H), 3.96 (s, OC*H*$_2$CONH, 2H), 3.90 (s, OC*H*$_2$CH$_2$NHCO, 2H), 3.66 and 3.64 (s, OC*H*$_2$C*H*$_2$O, 4H), 3.45 (m, NHC*H*$_2$CH$_2$CH$_2$-triazole, 2H), 3.36 (t, *J* = 6.6 Hz, C*H*$_2$N$_3$, 18H), 3.25 (t, *J* = 6.7 Hz, NHC*H*$_2$CH$_2$CH$_2$N$_3$, 18H), 2.64 (m, CH$_2$C*H*$_2$CONH, 2H), 2.47 (m, C*H*$_2$CH$_2$CONH, 2H), 2.18 (m, CH$_2$C*H*$_2$CONH and CH$_2$C*H*$_2$COOtBu, 48H), 2.00 (m, C*H*$_2$CH$_2$CONH, C*H*$_2$CH$_2$COOtBu and NHCH$_2$C*H*$_2$CH$_2$-triazole, 50H), 1.76 (m, NHCH$_2$C*H*$_2$CH$_2$N$_3$, 18H), 1.45 (s, COOC(C*H*$_3$)$_3$, 81H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 182.7 (NH*C*=S), 175.5, 175.3, 174.4 and 169.6 (*C*=O), 158.5 (arom. *C$_q$*OH), 148.1 (arom. *C*NH), 142.2 and 123.2 (*C*H of triazole), 141.6, 139.5, 130.4, 126.5 and 124.4 (arom. *C*$_q$ of FITC), 135.9 (arom. *C*CONH), 132.5, 121.2 and 104.2 (arom. *C*H of FITC), 116.1, 115.8 and 115.7 (arom. *C*H of core), 81.4 (COO*C*(CH$_3$)$_3$), 72.2, 71.5, 71.2 and 70.2 (*C*H$_2$O*C*H$_2$), 59.3 (NH*C*$_q$), 57.4 (NH*C*H$_2$-triazole), 51.0 (NHCH$_2$CH$_2$*C*H$_2$-triazole), 50.2 (*C*H$_2$N$_3$), 41.6 (NH$_2$*C*H$_2$CH$_2$O), 38.7 (NH*C*H$_2$CH$_2$CH$_2$), 37.9 (NH*C*H$_2$CH$_2$CH$_2$N$_3$), 31.7 (CH$_2$C*H*$_2$CONH), 31.4 (C*H*$_2$CH$_2$CONH), 30.5 (CH$_2$C*H*$_2$COOtBu), 30.3 (C*H*$_2$CH$_2$COOtBu), 29.7 (NHCH$_2$*C*H$_2$CH$_2$N$_3$), 29.2 (NHCH$_2$*C*H$_2$CH$_2$), 28.3 (COOC(*C*H$_3$)$_3$). MS MALDI-TOF [MH$^+$] *m/z* calcd for $C_{188}H_{291}N_{52}O_{45}S$: 4029.2, found: 4030.1. Anal. calcd. for $C_{188}H_{290}N_{52}O_{45}S$: C 56.02, H 7.25; found C 55.74, H 7.16.

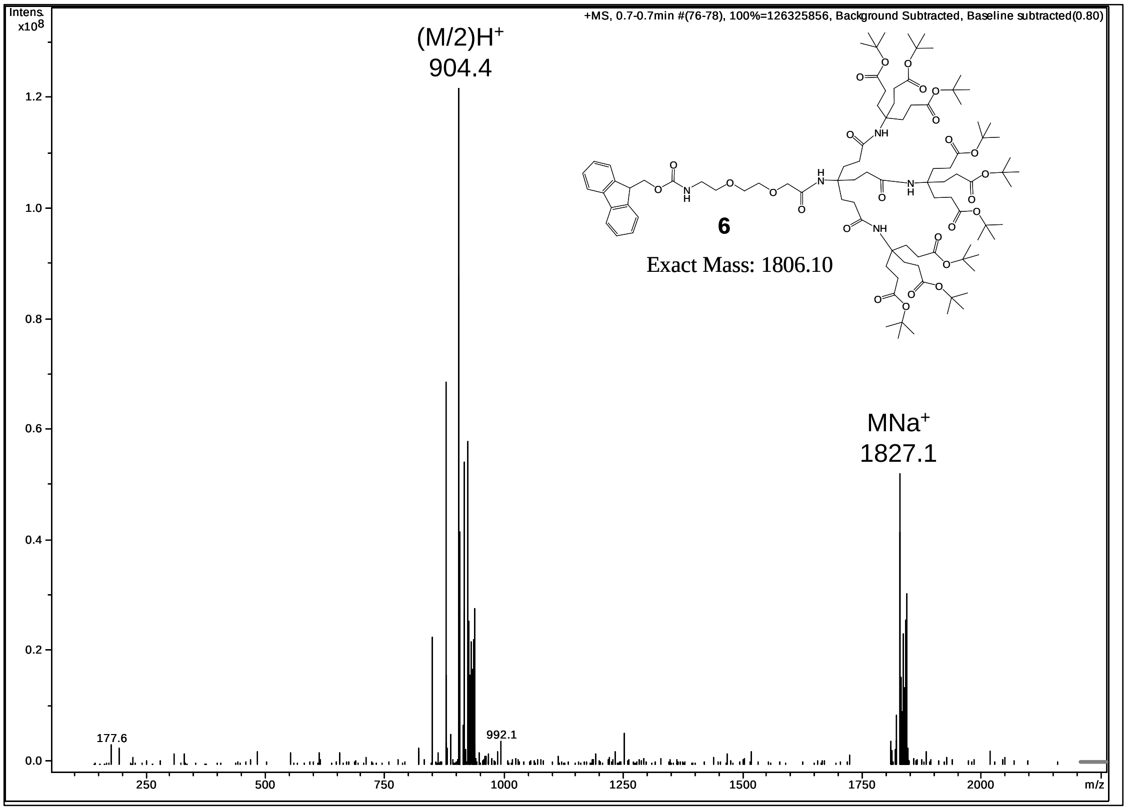
Synthesis of 22

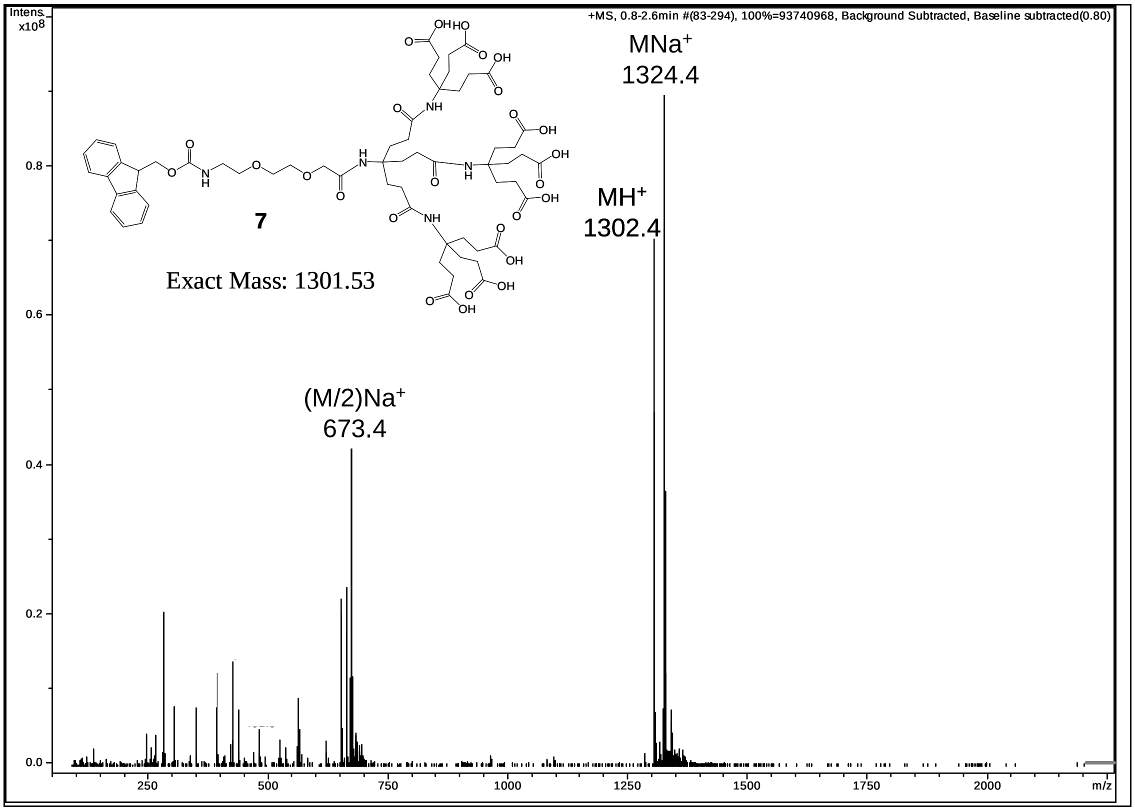


Dendrimer **21** (0.020 g, 0.0050 mmol) was dissolved in 20 mL of formic acid and 2 mL of water were added. The solution was stirred at room temperature for 16h. The solution was evaporated to dryness and the product was washed three times with ethylic ether. Dendrimer **22** was obtained as a yellow waxy product in 96% yield (0.017 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.01-6.41 (arom. C*H* and CON*H*, 20H), 4.61 (s, triazole-CH_2CH$_2$, 2H), 4.58 (s, NHCH_2-triazole, 2H), 3.95 (s, OCH_2CONH, 2H), 3.90 (s, OCH_2CH$_2$NHCO, 2H), 3.70-3.48 (m, OCH_2CH_2O and NHCH_2CH$_2$CH$_2$-triazole, 6H), 3.35 (t, *J* = 5.5 Hz, CH_2N$_3$, 18H), 3.24 (t, *J* = 6.3 Hz, NHCH_2CH$_2$CH$_2$N$_3$, 18H), 2.64 (m, CH$_2$CH_2CONH, 2H), 2.47 (m, CH_2CH$_2$CONH, 2H), 2.27 (m, CH$_2$CH_2COOH, 18H), 2.17 (m, CH$_2$CH_2CONH, 24H), 2.00 (m, CH_2CH$_2$CONH, CH_2CH$_2$COOH and NHCH$_2$CH_2CH$_2$-triazole, 50H), 1.76 (m, NHCH$_2$CH_2CH$_2$N$_3$, 18H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 182.8 (NH*C*=S), 175.5, 175.3, 174.4, 173.2 and 169.6 (*C*=O), 158.4 (arom. C_qOH), 148.0 (arom. *C*NH), 142.2 and 123.3 (*C*H of triazole), 141.6, 139.5, 130.5, 126.5 and 124.3 (arom. C_{q} of FITC), 135.8 (arom. *C*CONH), 132.5, 121.2 and 104.2 (arom. *C*H of FITC), 116.1, 115.8 and 115.7 (arom. *C*H of core), 72.3, 71.6, 71.2 and 70.4 (*C*H$_2$O*C*H$_2$), 59.4 (NHC_{q}), 57.4 (NH*C*H$_2$-triazole), 51.0 (NHCH$_2$CH$_2$*C*H$_2$-triazole), 50.2 (*C*H$_2$N$_3$), 41.6 (NH$_2$*C*H$_2$CH$_2$O), 38.7 (NH*C*H$_2$CH$_2$CH$_2$), 37.8 (NH*C*H$_2$CH$_2$CH$_2$N$_3$), 31.7 (CH$_2$CH_2CONH), 31.4 (CH_2CH$_2$CONH), 30.5 (CH$_2$CH_2COOH), 30.6 (CH_2CH$_2$COOH), 29.7 (NHCH$_2$*C*H$_2$CH$_2$N$_3$), 29.4 (CH_2CH$_2$COOH), 29.2 (NHCH$_2$*C*H$_2$CH$_2$). MS MALDI-TOF [MH$^+$] *m/z* calcd for $C_{152}H_{219}N_{52}O_{45}S$: 3524.6, found: 3524.2. Anal. calcd. for $C_{152}H_{218}N_{52}O_{45}S$: C 56.02, H 7.25; found C 55.81, H 7.12.

Mass Spectra

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x10^8
+MS, 0.8-2.6min #(83-294), 100%=93740968, Background Subtracted, Baseline subtracted(0.80)
MNa+
1324.4
MH+
1302.4
(M/2)Na+
673.4
7
Exact Mass: 1301.53
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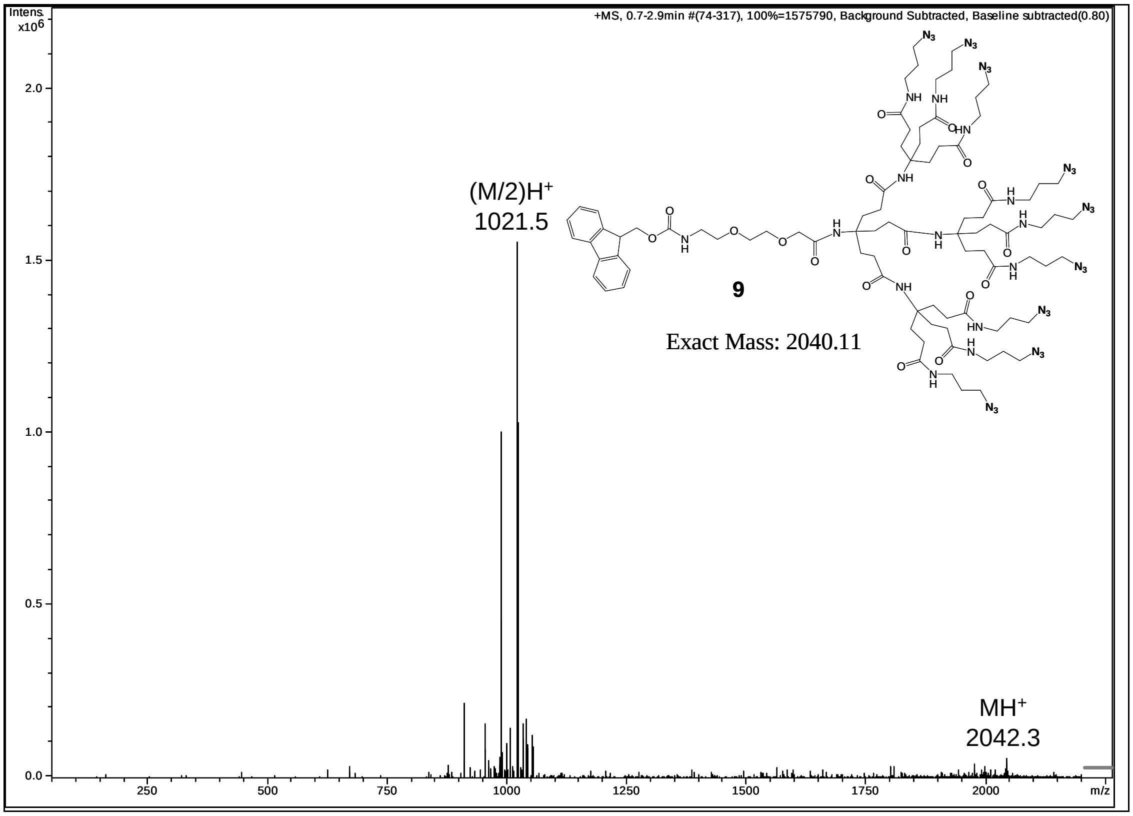
0.2
0.4
0.6
0.8
250
500
750
1000
1250
1500
1750
2000
m/z


Intens.
x10^6
+MS, 0.7-2.9min #(74-317), 100%=1575790, Background Subtracted, Baseline subtracted(0.80)
(M/2)H+
1021.5
MH+
2042.3
9
Exact Mass: 2040.11
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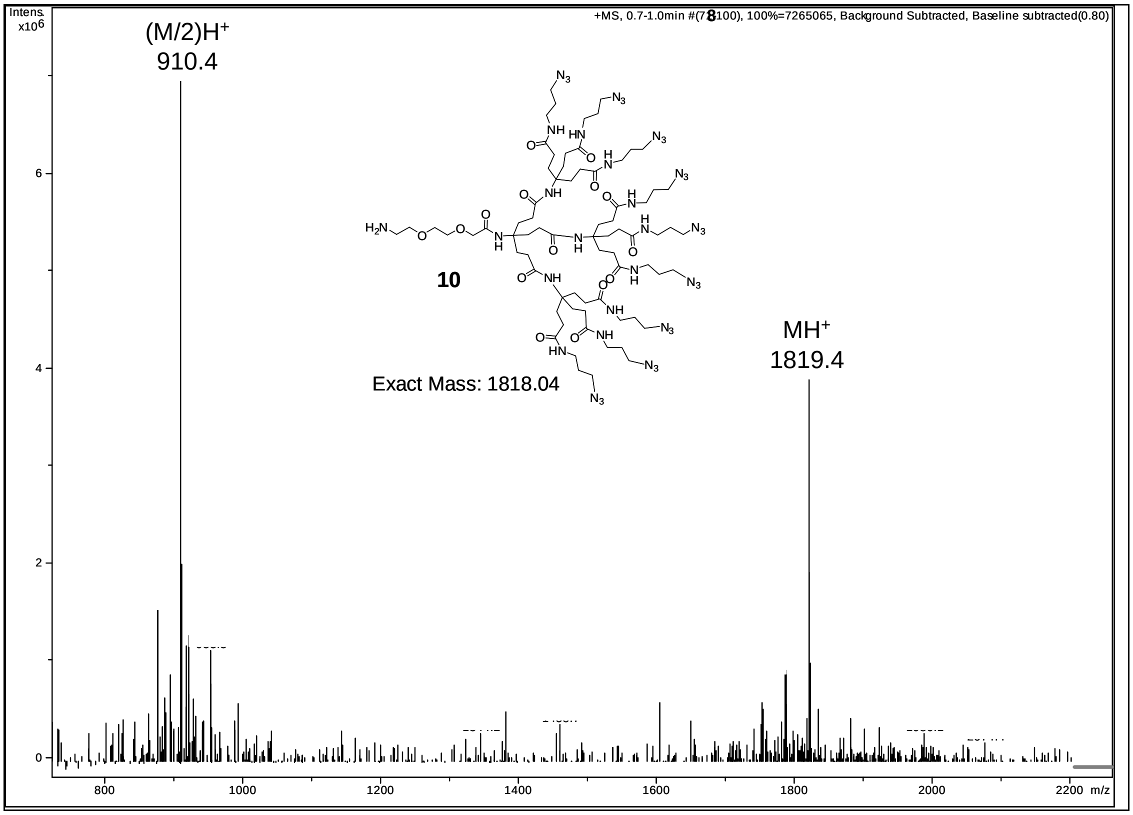
1.0
1.5
2.0
250
500
750
1000
1250
1500
1750
2000
m/z


Intens.
x10^6
+MS, 0.7-1.0min #(78-100), 100%=7265065, Background Subtracted, Baseline subtracted(0.80)
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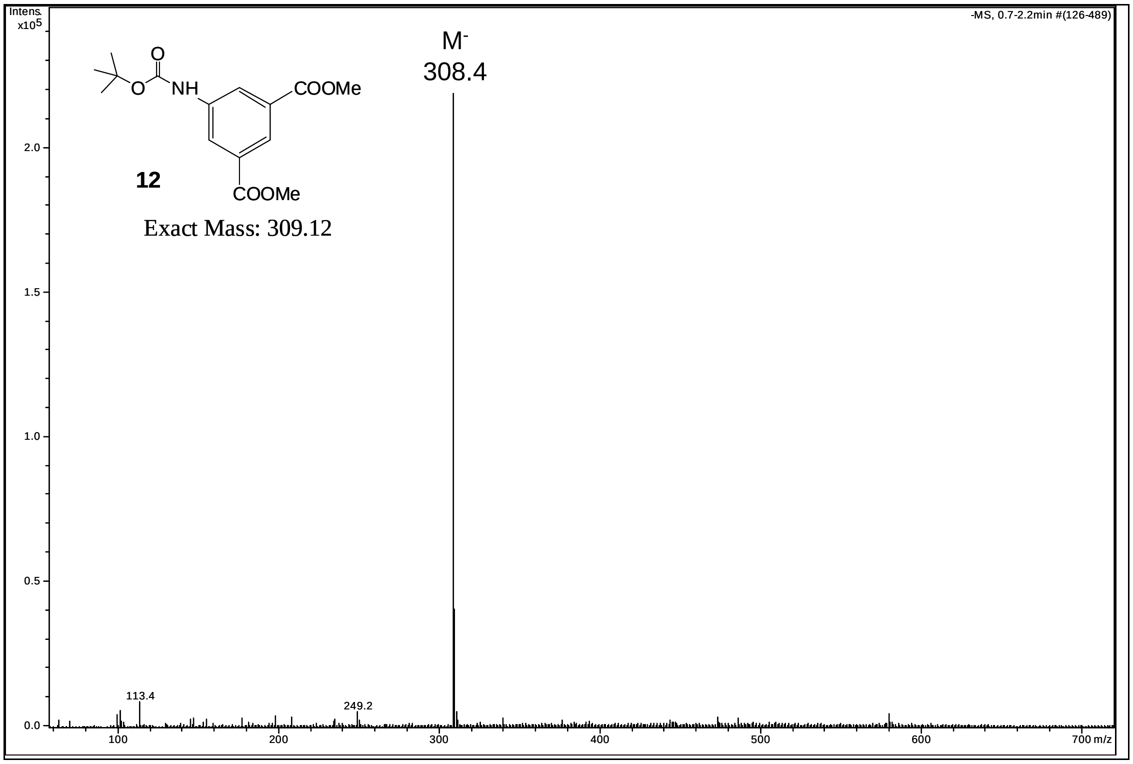
910.4
MH+
1819.4
10
Exact Mass: 1818.04
H2N
O
N
H
NH
N3
0
2
4
6
800
1000
1200
1400
1600
1800
2000
2200
m/z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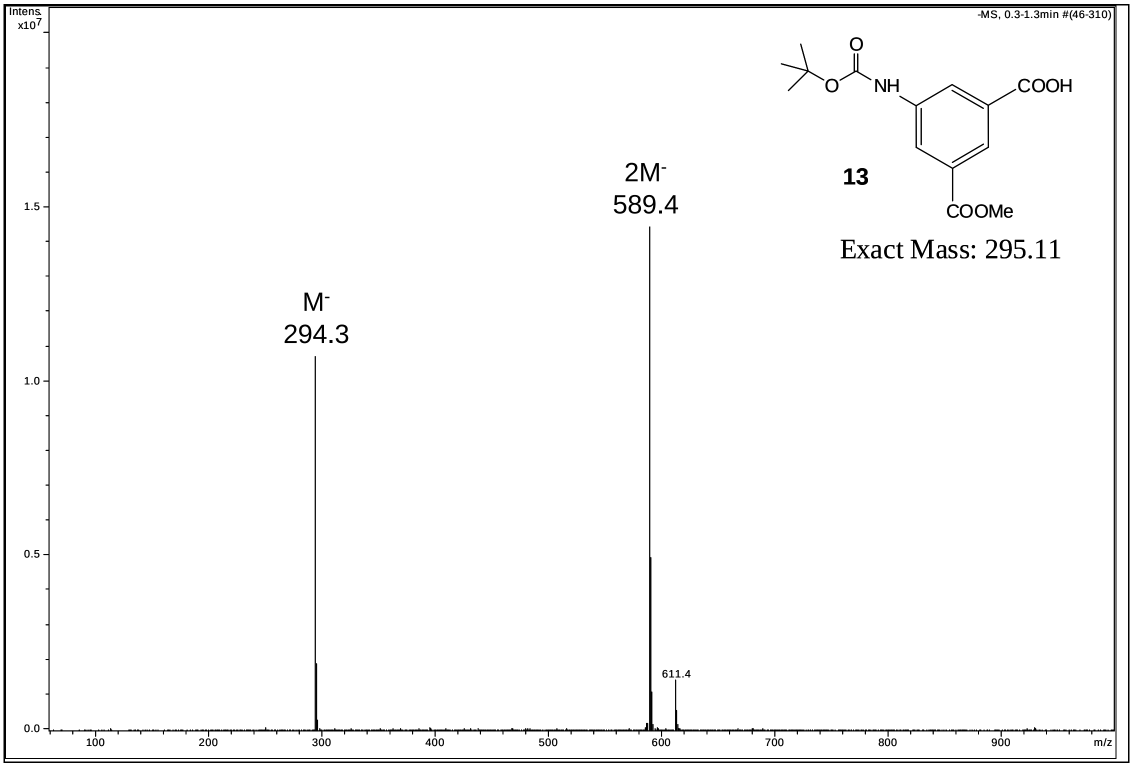
x10^5
-MS, 0.7-2.2min #(126-489)
M-
308.4
12
COOMe
NH
O
Exact Mass: 309.12
113.4
249.2
0.0
0.5
1.0
1.5
2.0
100
200
300
400
500
600
700
m/z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x10^7
-MS, 0.3-1.3min #(46-310)
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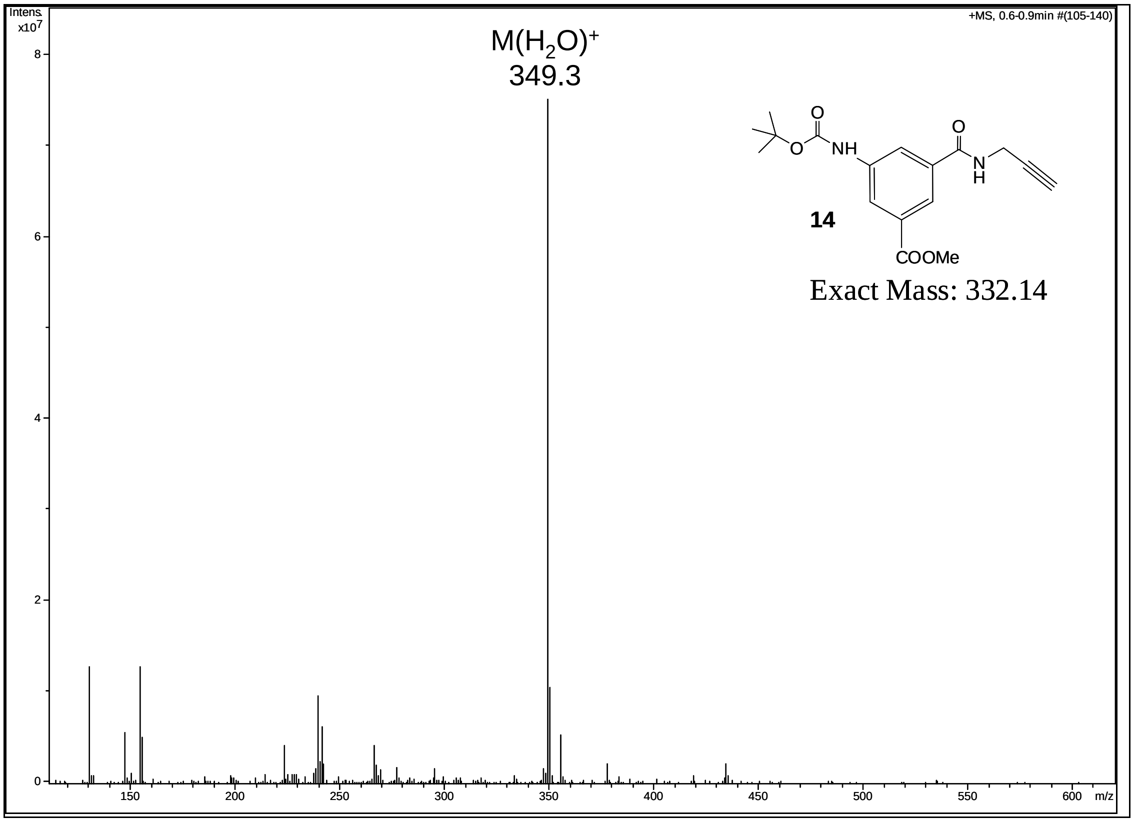
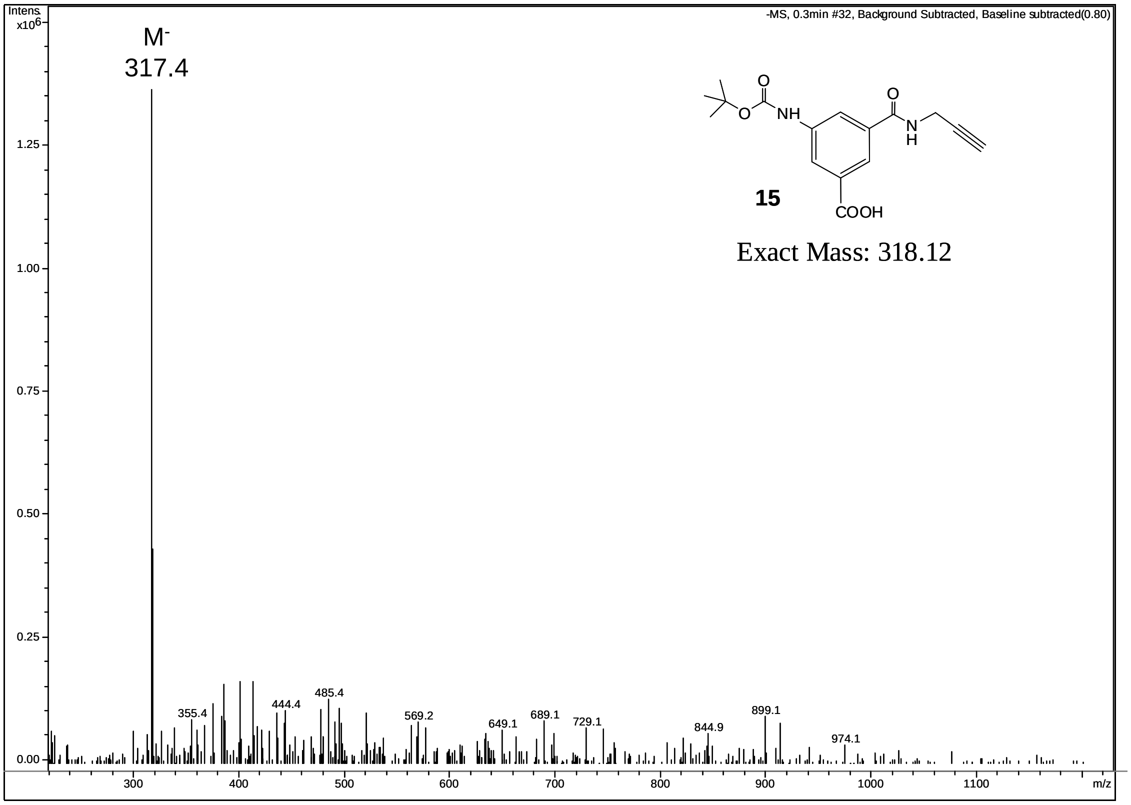
1.0
0.5
0.0
100
200
300
400
500
600
700
800
900
m/z
M-
294.3
2M-
589.4
611.4
O
O
NH
COOH
13
COOMe
Exact Mass: 295.11


Intens.
x10^7
+MS, 0.6-0.9min #(105-140)
8
6
4
2
0
150
200
250
300
350
400
450
500
550
600
m/z
M(H2O)+
349.3
O
O
NH
O
N
H
14
COOMe
Exact Mass: 332.14


Intens.
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M-
317.4
O
O
NH
O
N
H
15
COOH
Exact Mass: 318.12
1.25
1.00
0.75
0.50
0.25
0.00
355.4
444.4
485.4
569.2
649.1
689.1
729.1
844.9
899.1
974.1
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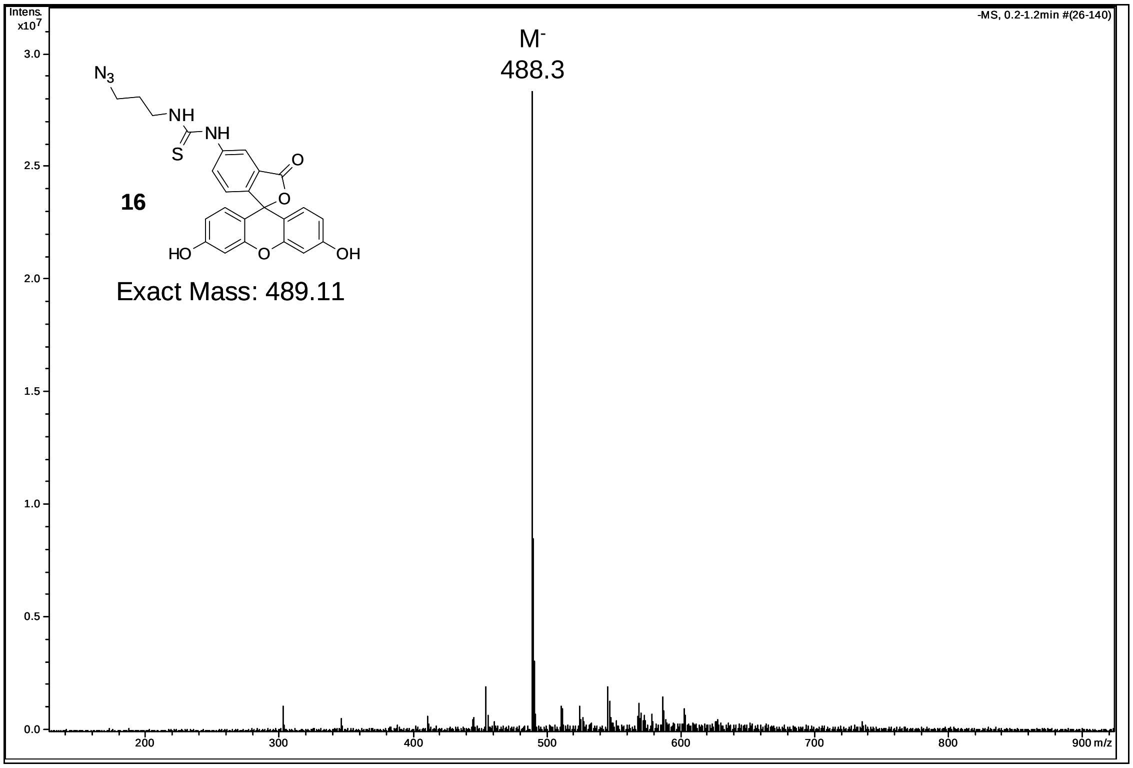
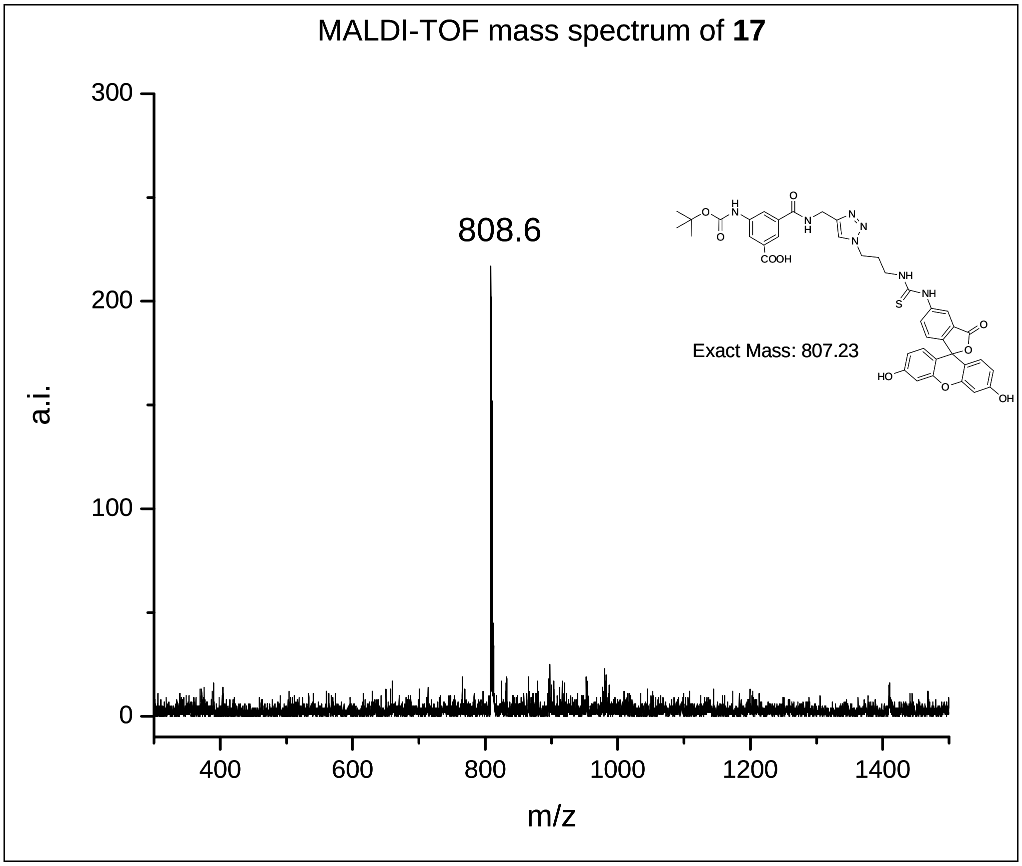
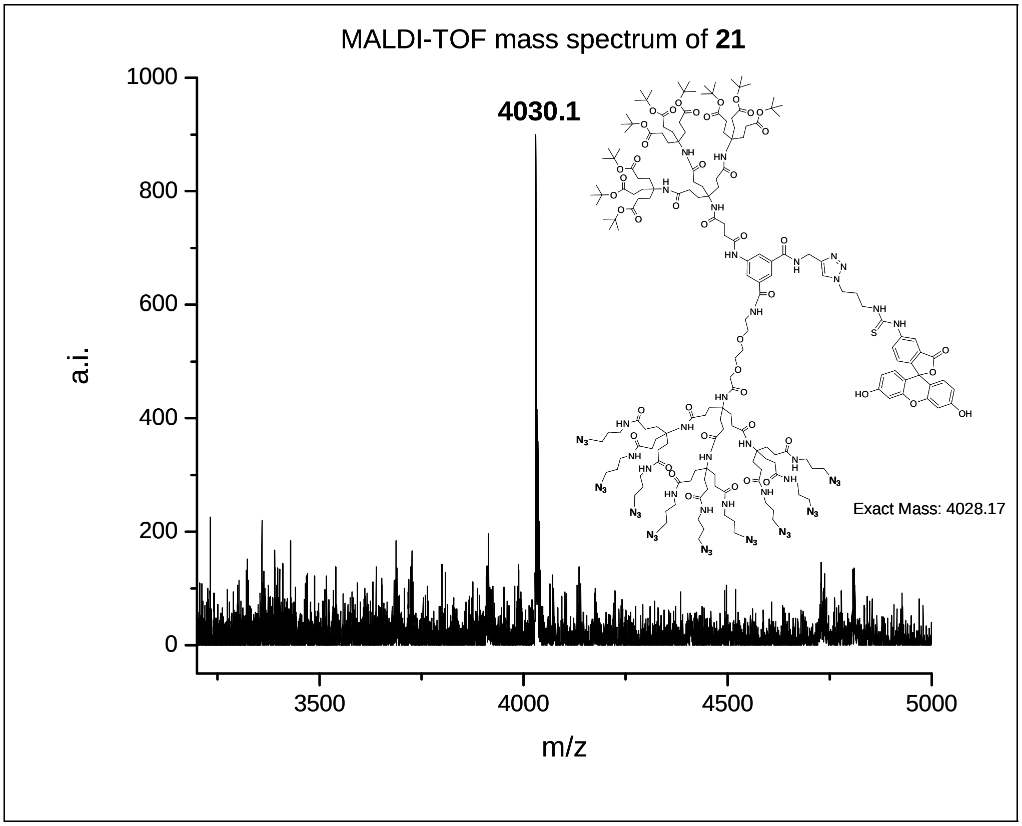
800
900
1000
1100
m/z


Intens.
x10^7
-MS, 0.2-1.2min #(26-140)
M-
488.3
N3
NH
NH
S
O
O
16
HO
O
OH
Exact Mass: 489.11
3.0
2.5
2.0
1.5
1.0
0.5
0.0
200
300
400
500
600
700
800
900 m/z

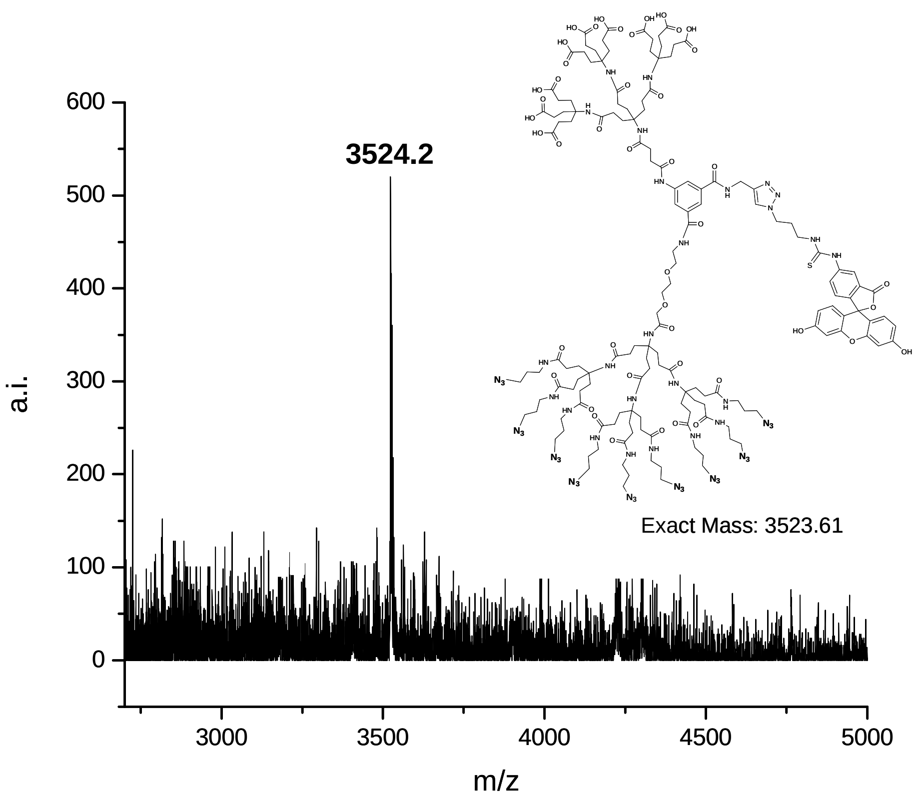


MALDI-TOF mass spectrum of **17**



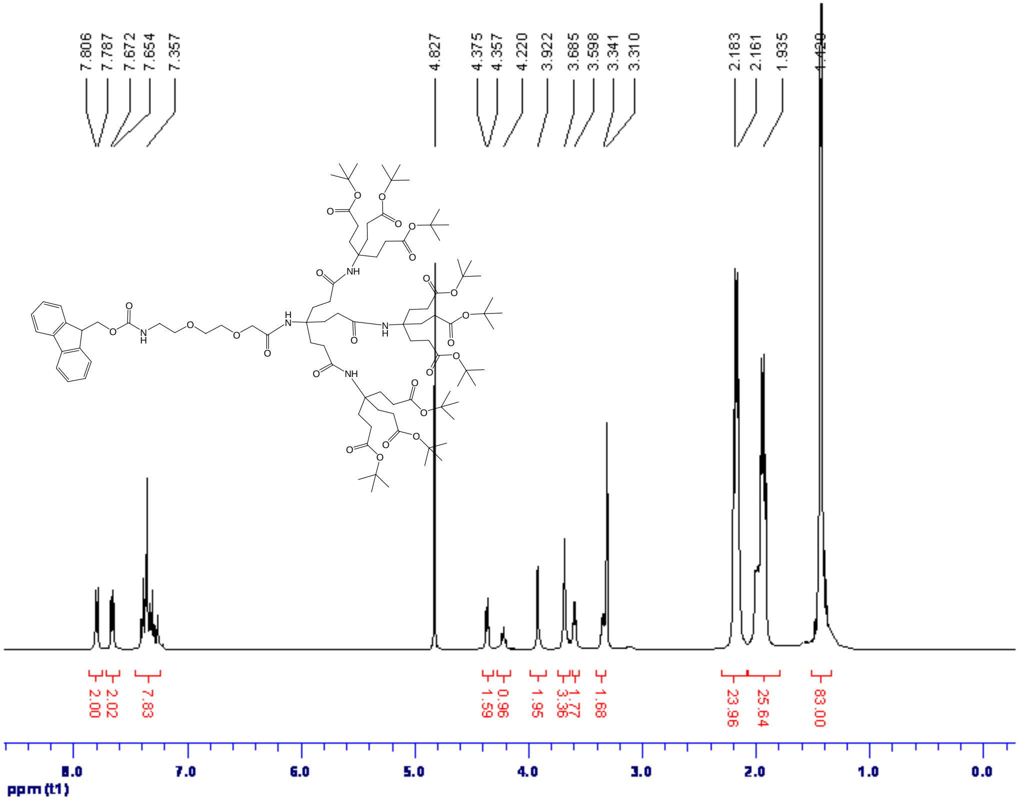
MALDI-TOF mass spectrum of **21**

MALDI-TOF mass spectrum of **22**

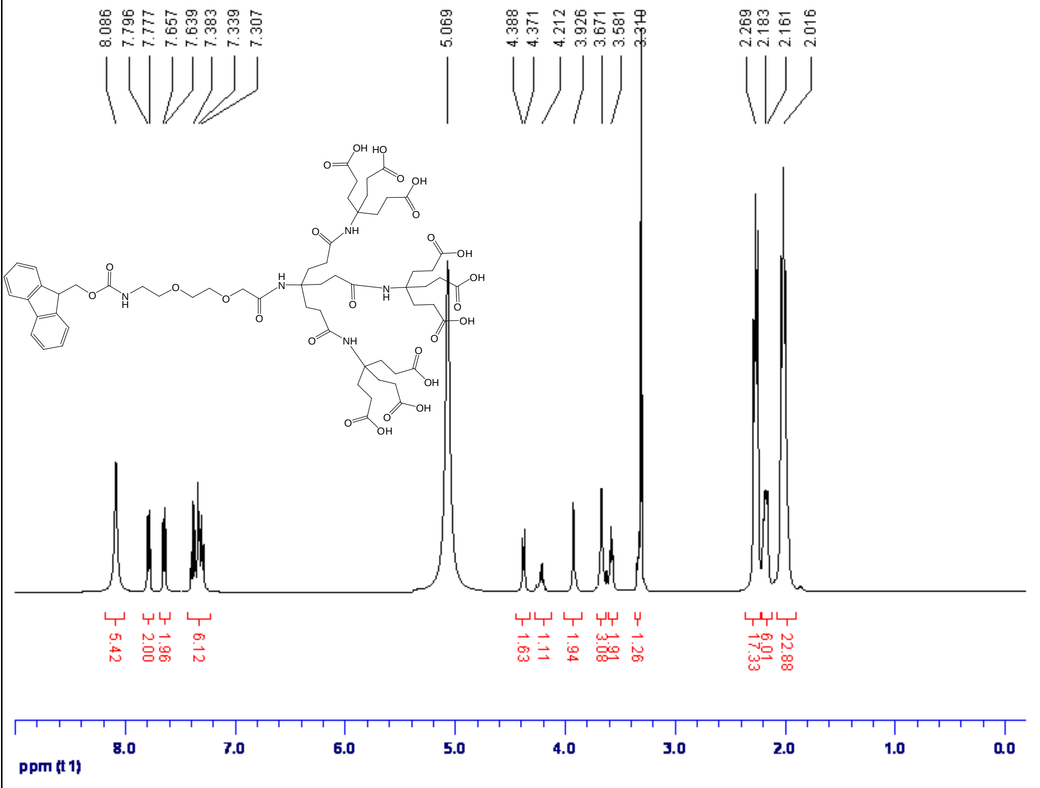


^{1}H NMR Spectra

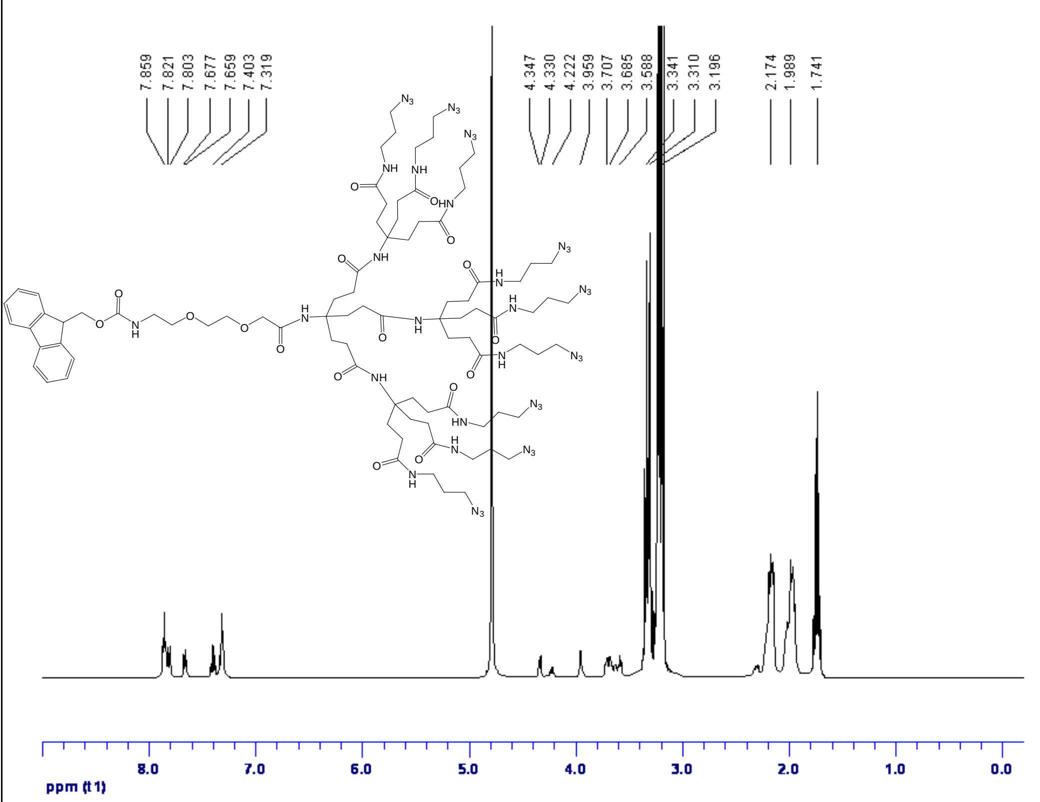
^{1}H NMR spectrum of product **6**



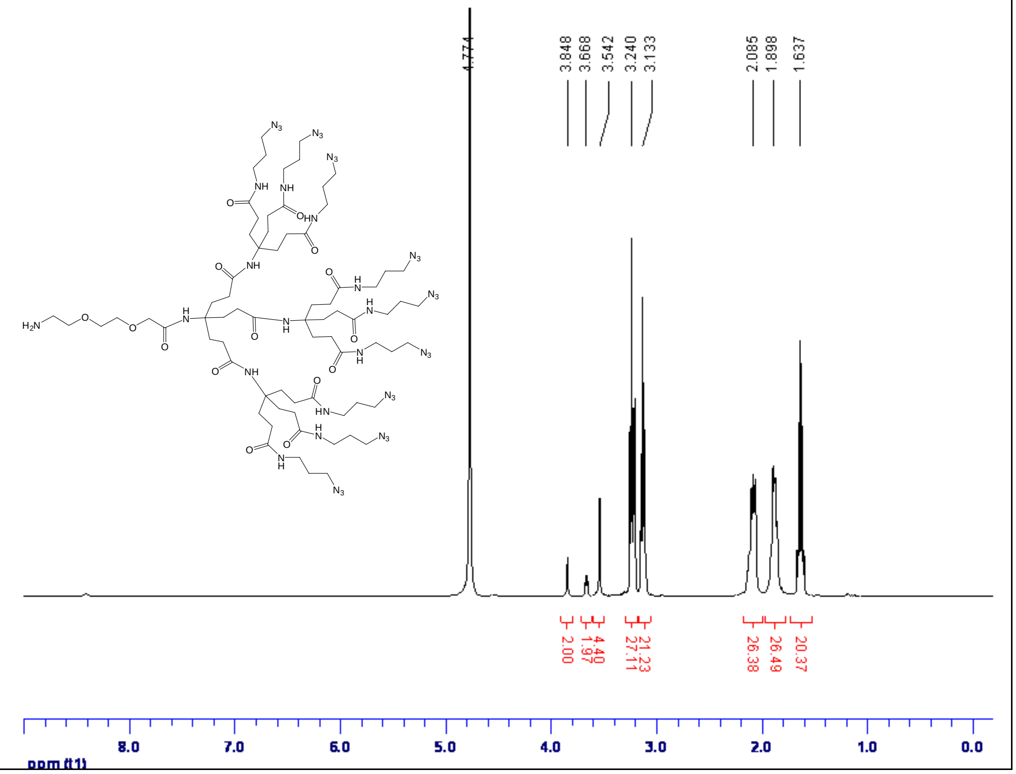
^{1}H NMR spectrum of product **7**



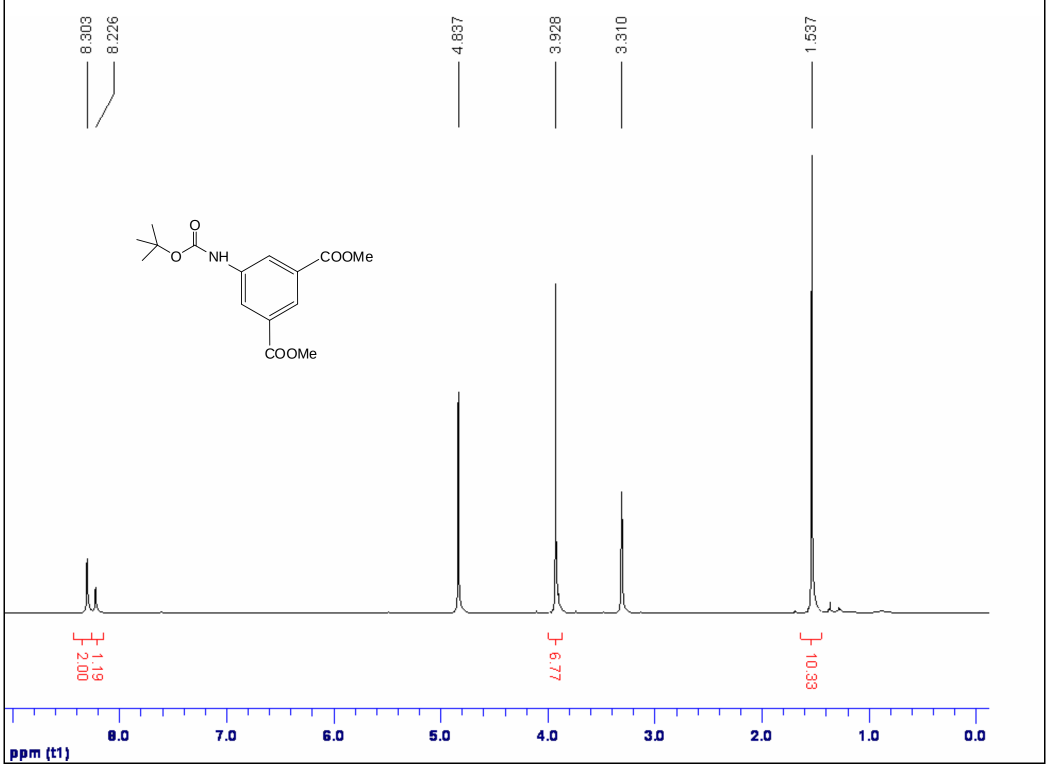
^{1}H NMR spectrum of product **9**



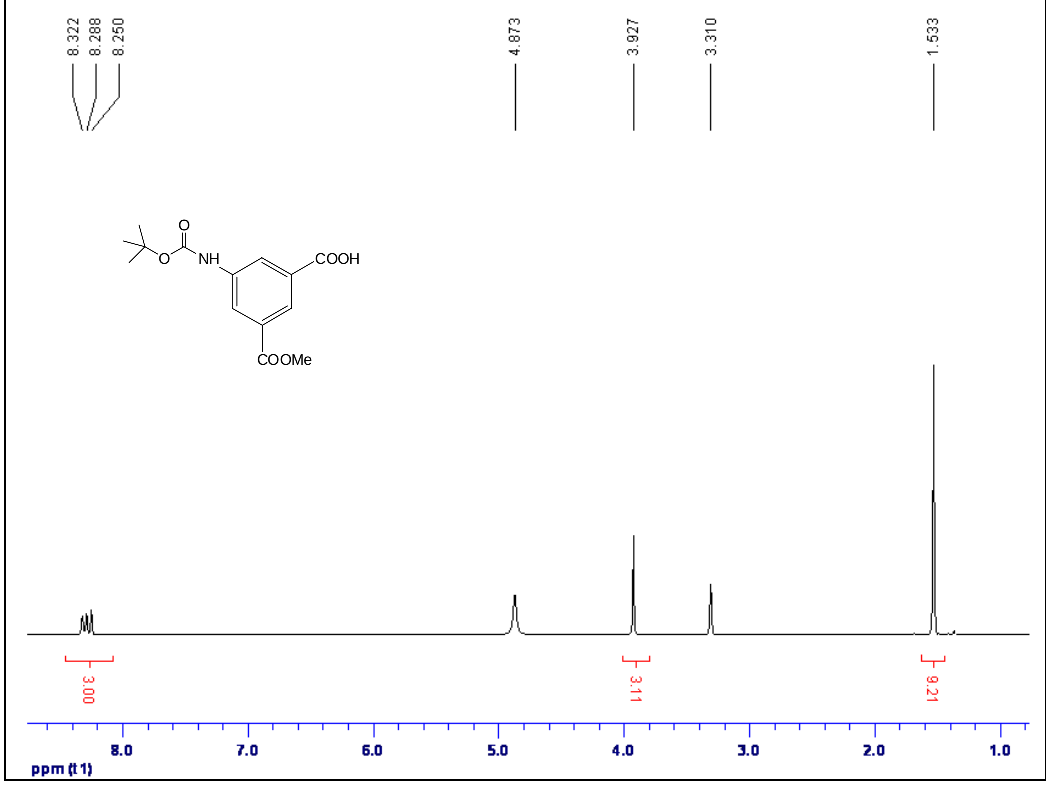
^{1}H NMR spectrum of product **10**



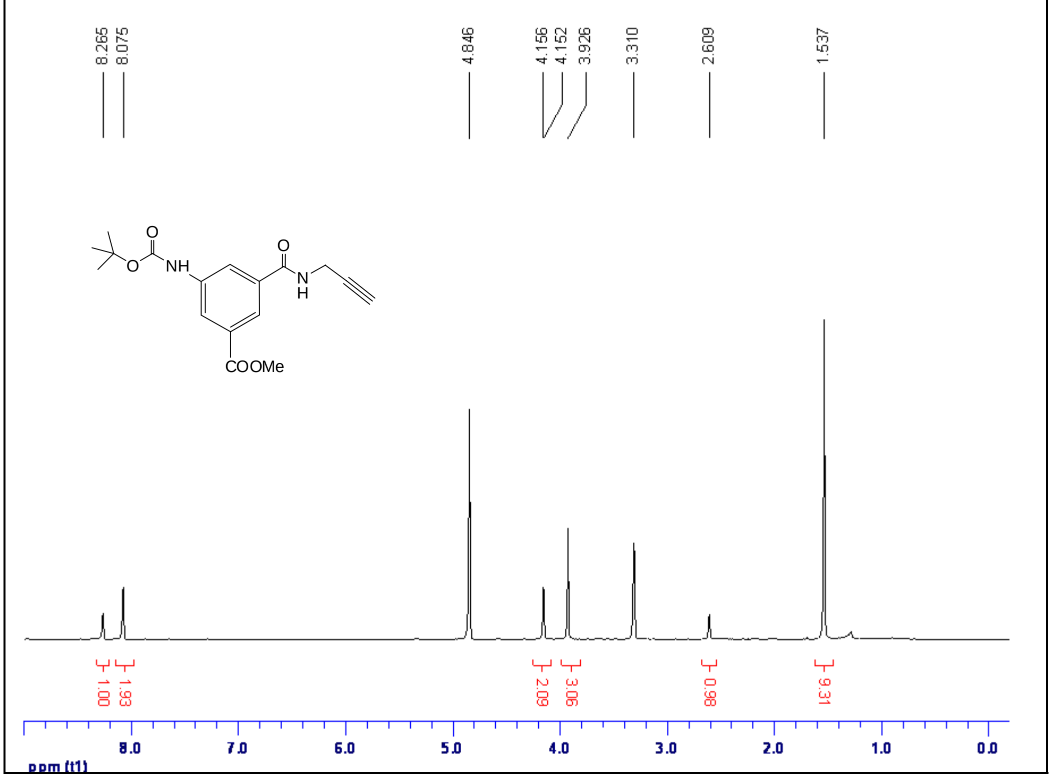
^{1}H NMR spectrum of product **12**



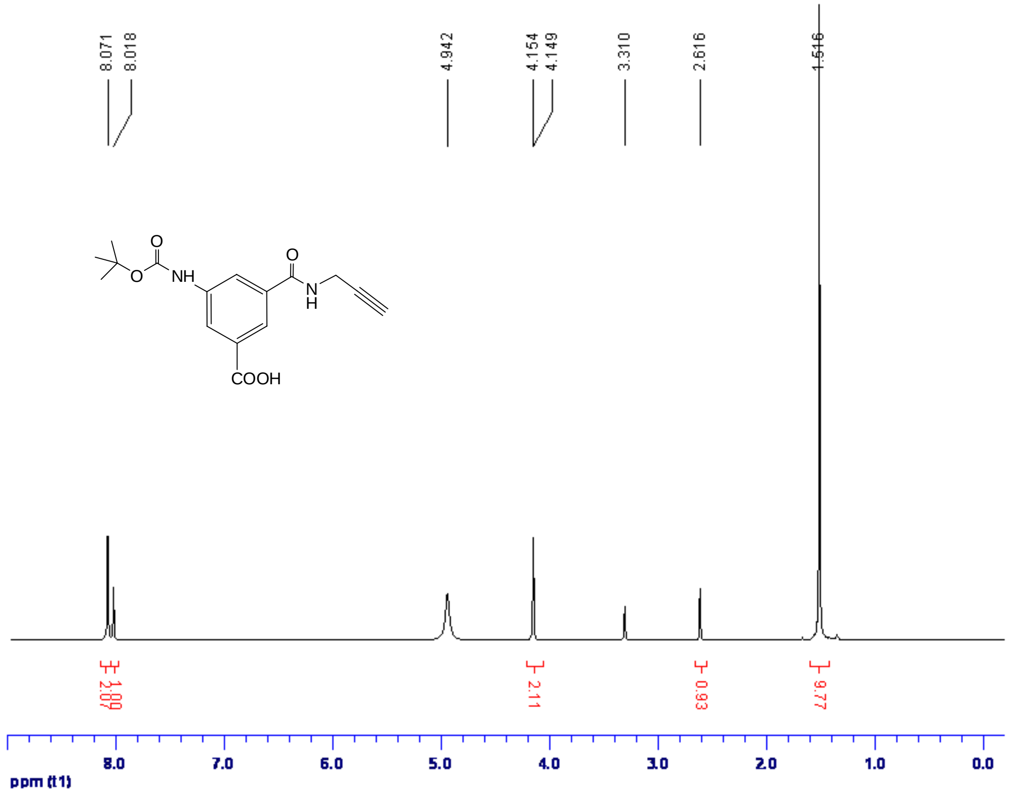
^{1}H NMR spectrum of product **13**



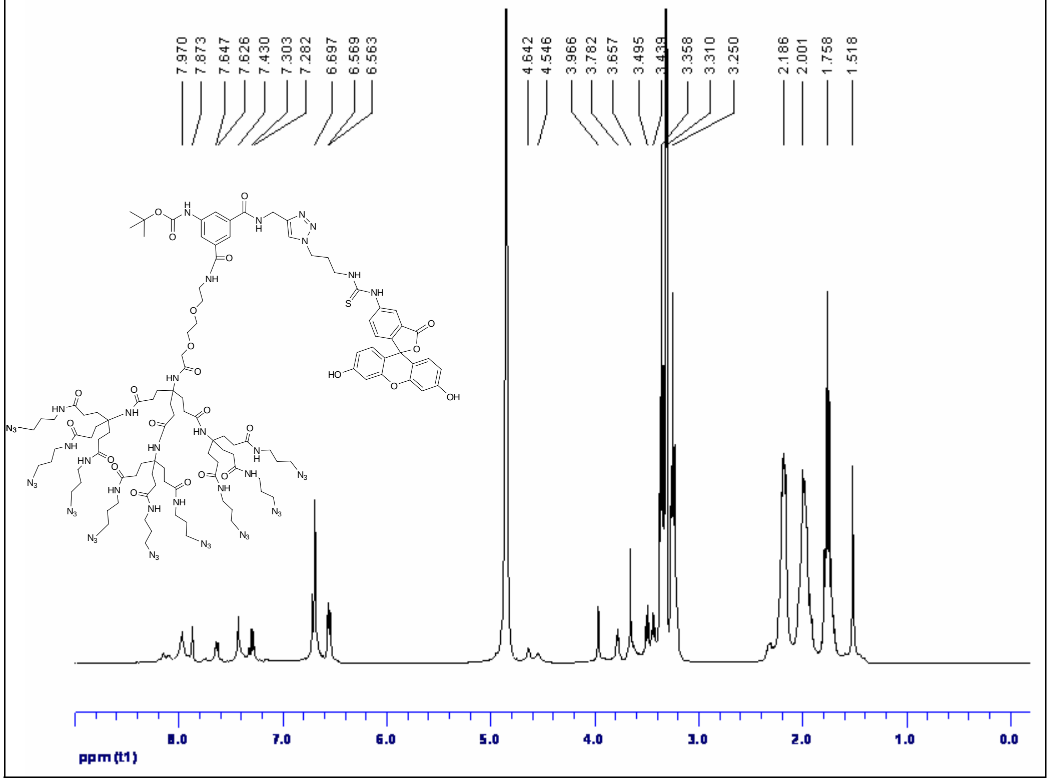
^{1}H NMR spectrum of product **14**



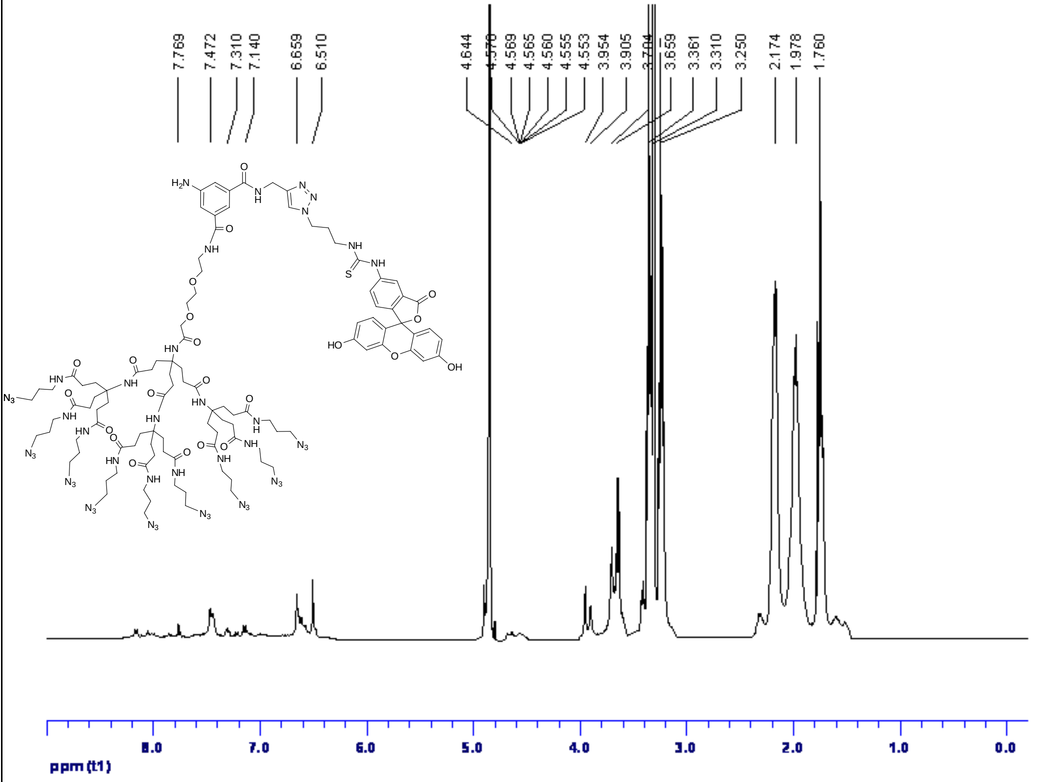
^{1}H NMR spectrum of product **15**



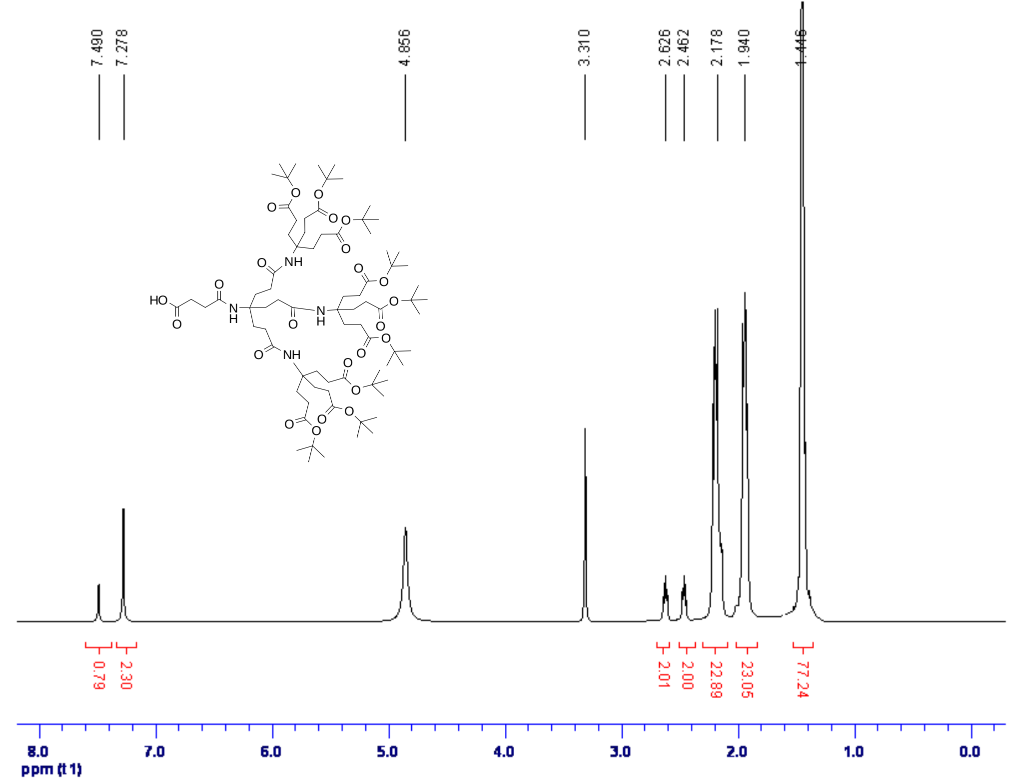
^{1}H NMR spectrum of product **18**



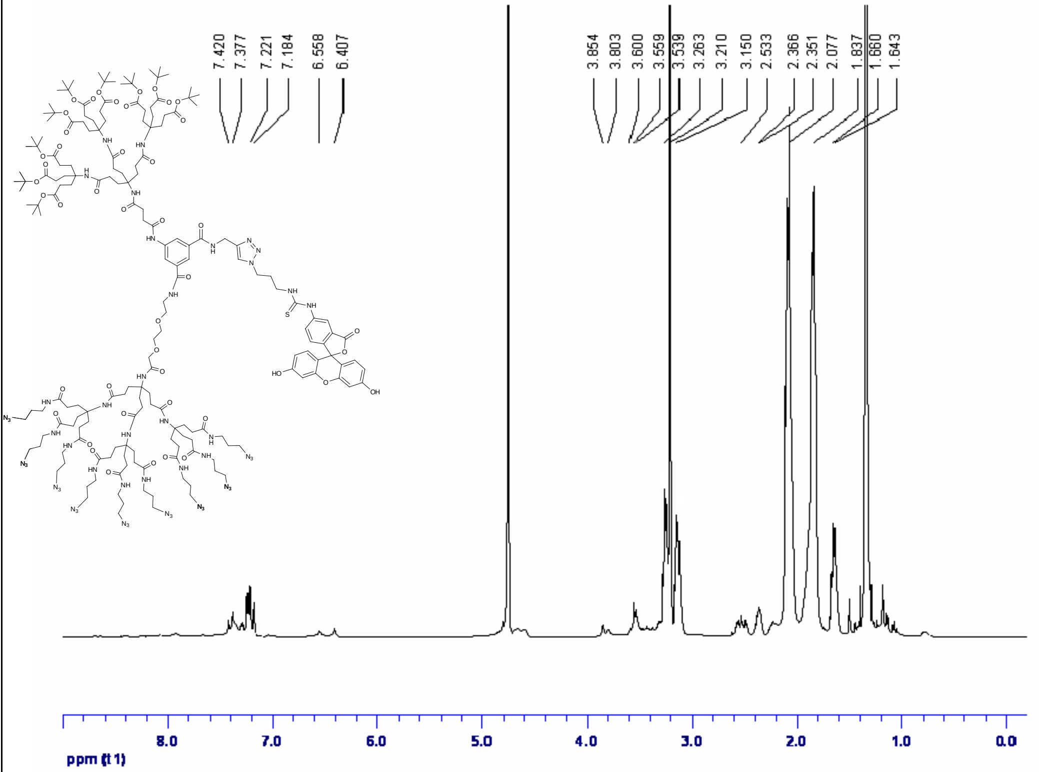
^{1}H NMR spectrum of product **19**



^{1}H NMR spectrum of product **20**



^{1}H NMR spectrum of product **21**



^{1}H NMR spectrum of product **22**