Strain-Promoted Alkyne Azide Cycloaddition for the Functionalization of Poly(amide)-based Dendrons and Dendrimers

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Supporting Information

General data.

Triethyleneglycol monomethyl ether (95%), propargyl bromide (80 wt. % in toluene), diisopropylethylamine (DIPEA), sodium hydride (60% dispersion in mineral oil), sulfonated bathophenanthroline, diacid-PEG linker **10** (3,6,9-trioxaundecanedioic acid, > 70%), octadecyl-functionalized silica (C18-silica) were purchased from sigma-aldrich. Anhydrous dimethylformamide (DMF), 2-(7-Aza-1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU), 1-Hydroxybenzotriazole (HOBt), diisopropylcarbodiimide (DIC), *t*-butanol (^{t}BuOH) and Cu wire (1 mm diameter, 99.9 %) were purchased from VWR. Dendrons nitrotriester **1** and aminotriester **5** were purchased from Frontier Scientific.

Dendron triacid **2** was obtained by deprotection of the acid groups on commercial dendron nitrotriester **1**; the reaction was carried out by stirring **1** in formic acid/water (9:1) for 24h as previously described.[1] 3-aminopropyl azide **3** was synthesized according to literature procedures.[2]

Dialysis. Dialysis membrane Spectra/Por® 6 MWCO (molecular weight cut-off) 2000 (38 mm flat width) was purchased from SpectrumLabs and used as received. About 10 cm of dialysis membrane was used for each purification. For dendrimers **11** and **13**: a methanol solution of dendrimer was introduced inside the dialysis bag that was then introduced in 1L of methanol and gently stirred for about 5h. The exterior methanol solution was replaced for fresh methanol and stirred for about 10h, then replaced again and finally stirred for about 15h.

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 using methanol solutions of the products.

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

Elemental analysis was performed in a PERKIN ELMER 2400, Series II CHNSO analyzer. For dendrons **15** and **17**, CHNCu analysis were obtained at Galbraith Laboratories using ICP-ms for Cu analysis.

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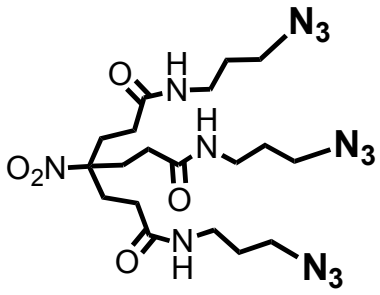
[1] SI 1. a) G. R. Newkome; R. K. Behera, C. N. Moorefield, G. R. Baker, *J. Org. Chem*. **1991**, *56*, 7162-7167; b) G. R. Newkome, A. Nayak, R. K. Behera, C. N. Moorefield, G. R. Baker, *J. Org. Chem*. **1992**, *57*, 358-362; c) M. Brettreich, A. Hirsch, *Synlett* **1998**, 1396-1398.

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

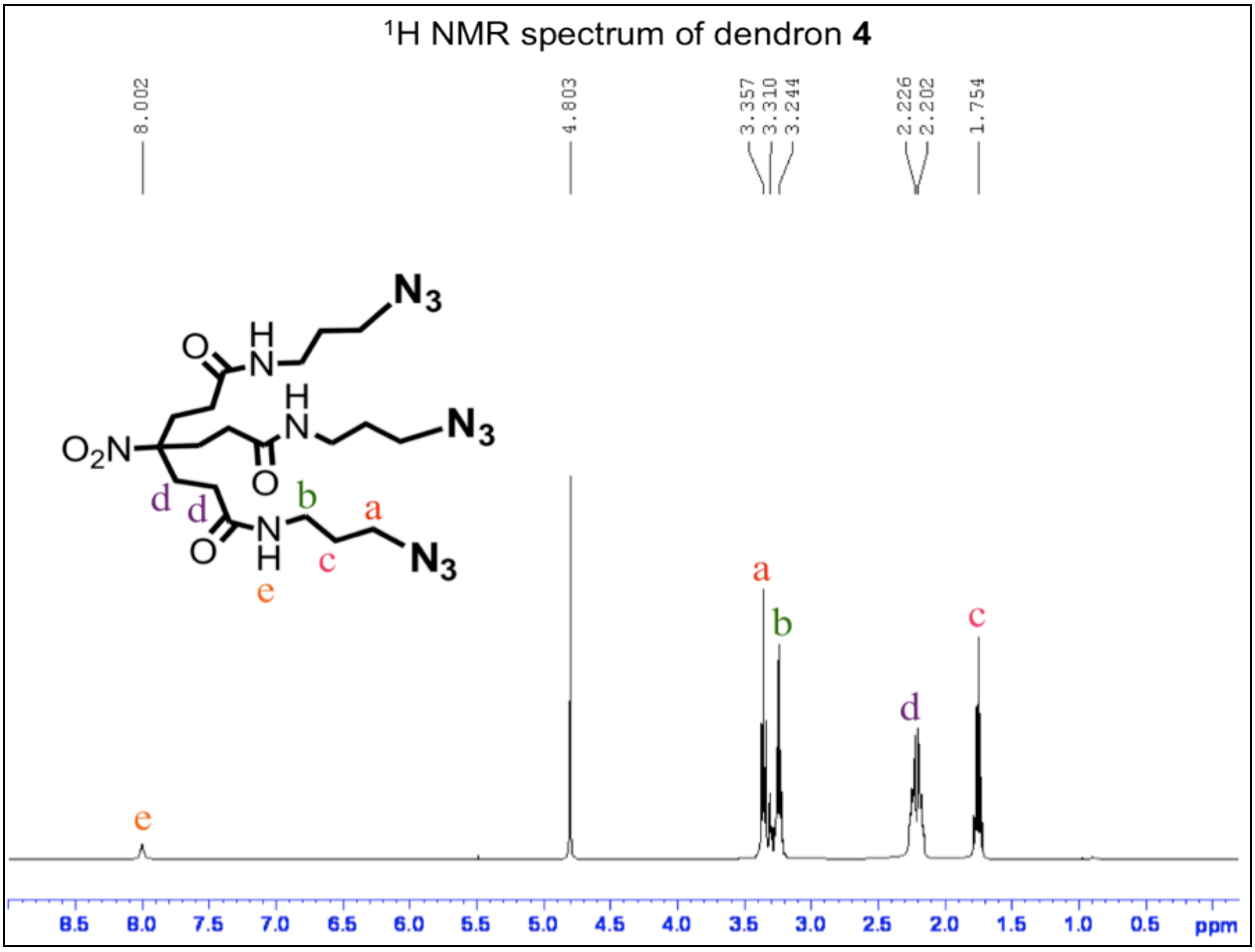
Synthesis of dendron 4

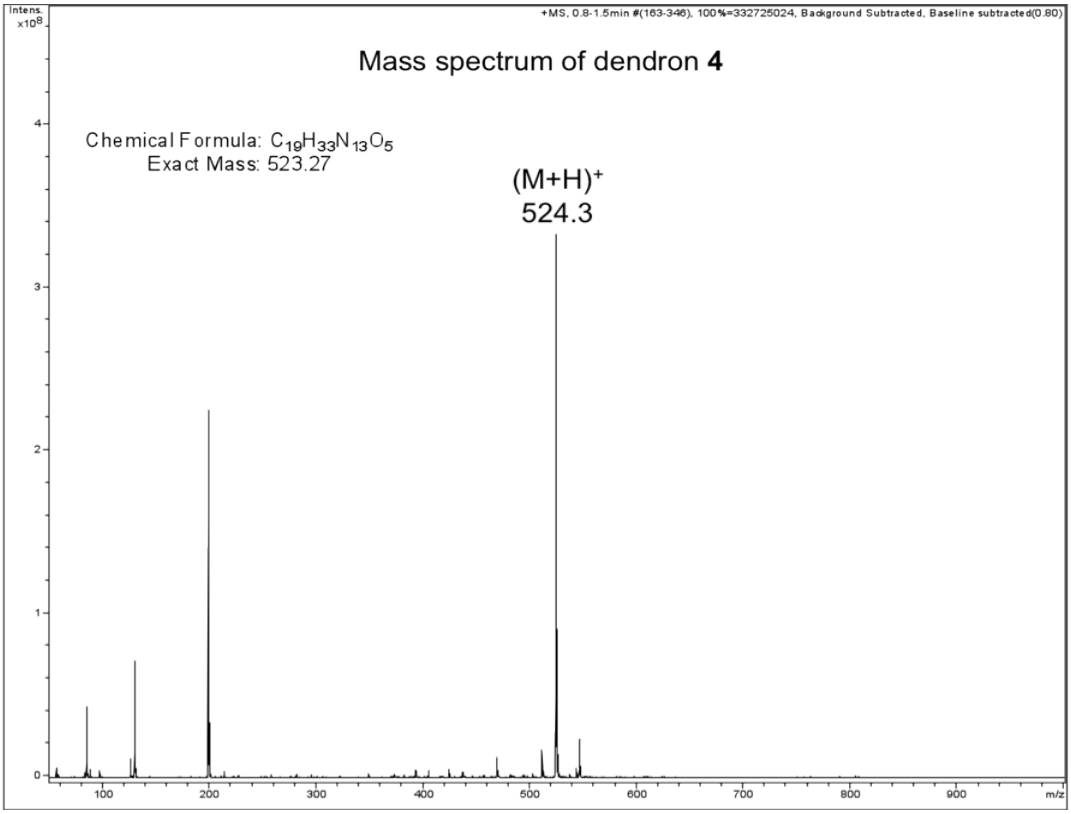


Chemical Formula: $C_{19}H_{33}N_{13}O_5$
Molecular Weight: 523.55

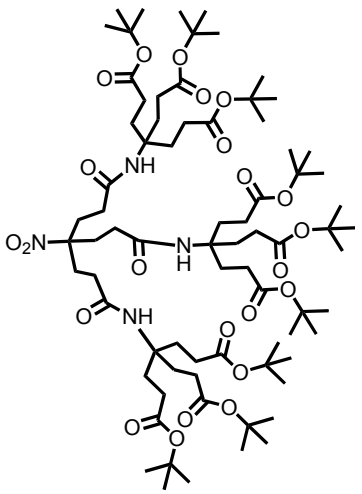
Dendron **2** (0.500 g, 1.80 mmol) and HATU (2.53 g, 7.21 mmol) were dissolved in 15 mL of dry DMF. Diisopropylethylamine (2.5 mL, 14.43 mmol) and 3-aminopropyl azide **3** (1.08g, 10.82 mmol) were successively added with a syringe. The solution was stirred at room temperature for 24h. Then, the solvent was removed under vacuum and the resulting brown oil was dissolved in methylene chloride and washed with an aqueous solution of $NaHCO_3$ and water. The organic phase was dried over sodium sulfate, filtered through paper and evaporated to dryness. The product was purified by column chromatography (silica gel) using CH_2Cl_2/MeOH (90/10) as eluent. Dendron **4** was obtained as a colorless oil in 93% yield (0.880 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs*. TMS): 8.00 (s, CON*H*, 3H), 3.36 (t, *J* = 6.68 Hz, CH_2N$_3$, 3H), 3.24 (t, *J* = 6.80 Hz, CH_2CH$_2$CH$_2$N$_3$, 6H), 2.23 and 2.20 (m, CH_2CH_2CONH, 12H), 1.75 (m, CH$_2$CH_2CH$_2$N$_3$, 6H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs*. TMS): 174.2 (*C*=O), 94.4 (NO$_2$*C*$_q$), 50.2 (*C*H$_2$N$_3$), 38.0 (*C*H$_2$CH$_2$CH$_2$N$_3$), 32.2 (CH$_2$*C*H$_2$CONH) and 31.3 (*C*H$_2$CH$_2$CONH), 29.7 (CH$_2$*C*H$_2$CH$_2$N$_3$). Infrared υ_{N3}: 2098.10 cm^{-1}. MS-ESI (M+H)$^+$ *m/z* calcd for $C_{19}H_{34}N_{13}O_5$: 524.3, found 524.3. Anal. calcd. for $C_{19}H_{33}N_{13}O_5$: C 43.59, H 6.35; found C 43.31, H 6.22.


¹H NMR spectrum of dendron 4
8.002
4.803
3.357
3.310
3.244
2.226
2.202
1.754
N3
O2N
d
d
b
a
c
e
a
b
c
d
e
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Intens.
x10⁸
+MS, 0.8-1.5min #(163-346), 100%=332725024, Background Subtracted, Baseline subtracted(0.80)
Mass spectrum of dendron 4
Chemical Formula: C19H33N13O5
Exact Mass: 523.27
(M+H)+
524.3
4
3
2
1
0
100 200 300 400 500 600 700 800 900 m/z

Synthesis of dendron 6[1]

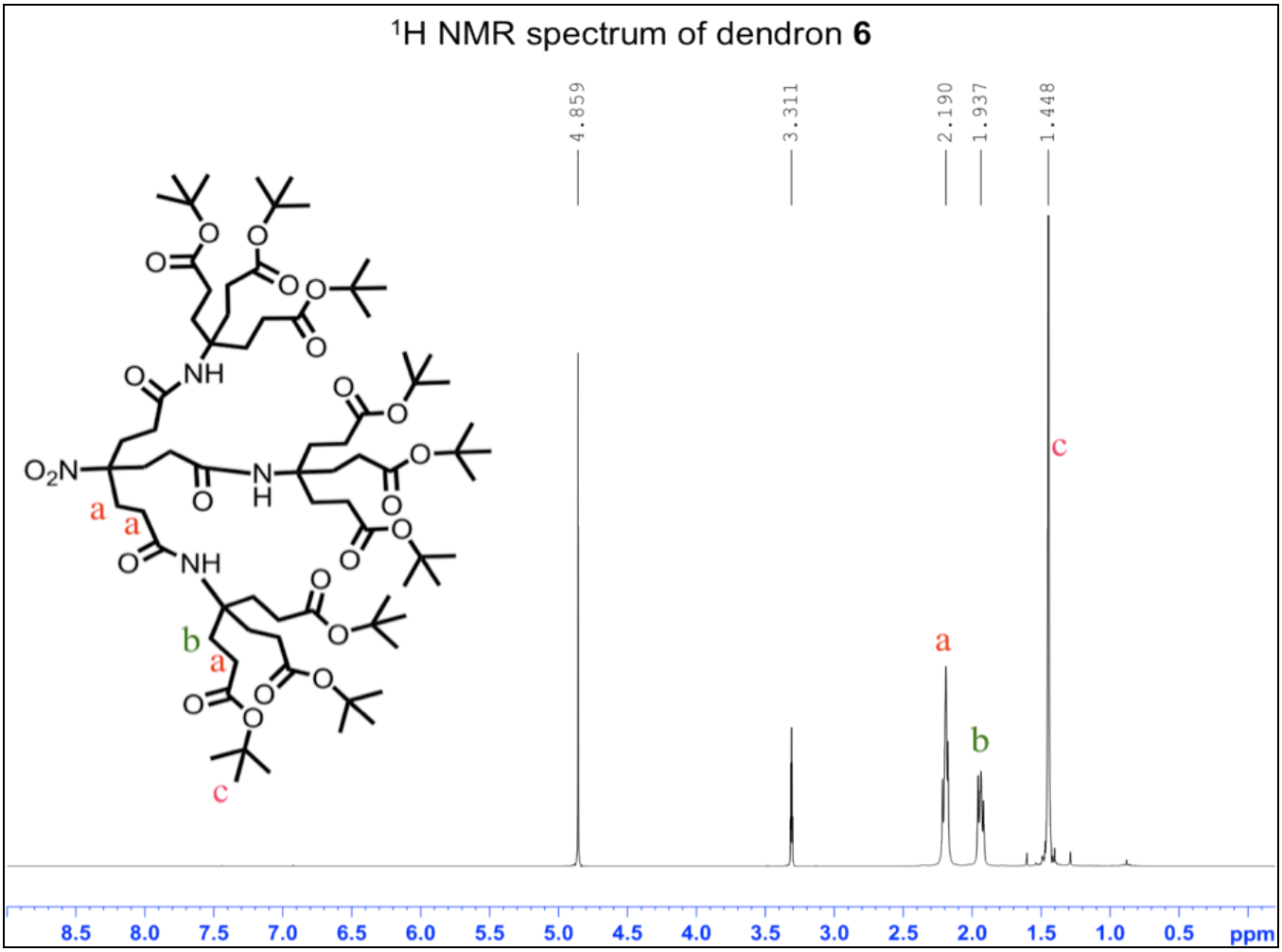


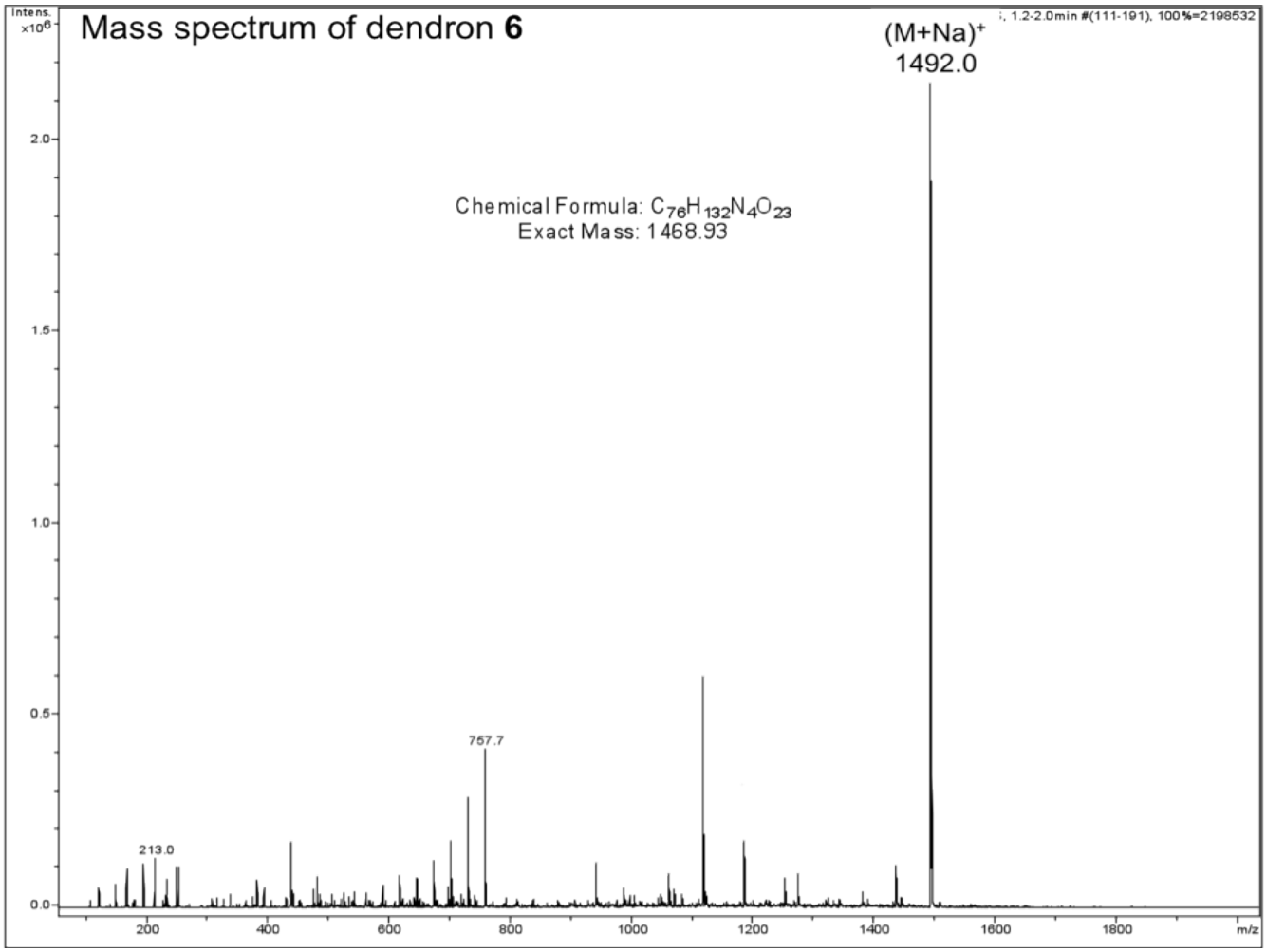
Chemical Formula: $C_{76}H_{132}N_4O_{23}$
Molecular Weight: 1469.87

Dendron nitrotriacid **2** (0.500 g, 1.80 mmol) and dendron aminotriester **5** (3.00 g, 7.21 mmol) were introduced in a Schlenk flask and 40 mL of dry DMF was added. HOBt (0.974 g, 7.21 mmol) and DIC (0.910 g, 7.21 mmol) were successively added and the solution was stirred at room temperature for 48h. Solvent was removed under vacuum and the product was purified by column chromatography (silica gel) using hexane/ethyl acetate (60:40) as eluent. Dendron **6** was obtained as a white powder in 92% yield (2.43 g).

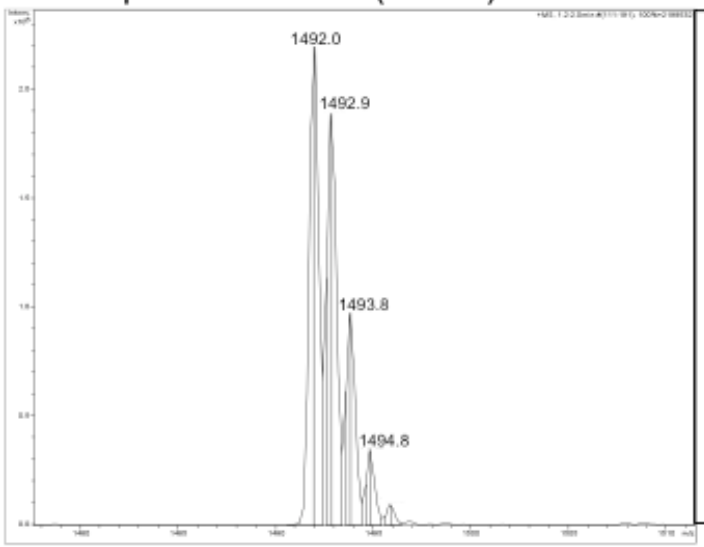
Note: The column chromatography was followed by TLC using anisaldehyde stain. Dendron **6** is the first product coming out of the column followed by dendron aminotriester **5** used in excess (both dendrons give blue spots on TLC using the anisaldehyde stain.

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 2.19 (t, J = 7.98 Hz, $NO_2C_qCH_2CH_2$ and CH_2COO^tBu, 30H), 1.94 (m, $CH_2CH_2COO^tBu$, 18H), 1.45 (s, $COO(CH_3)_3$, 81H). MS-ESI $(M+Na)^+$ *m/z* calcd for $C_{76}H_{132}N_4O_{23}$: 1491.9, found 1491.6.

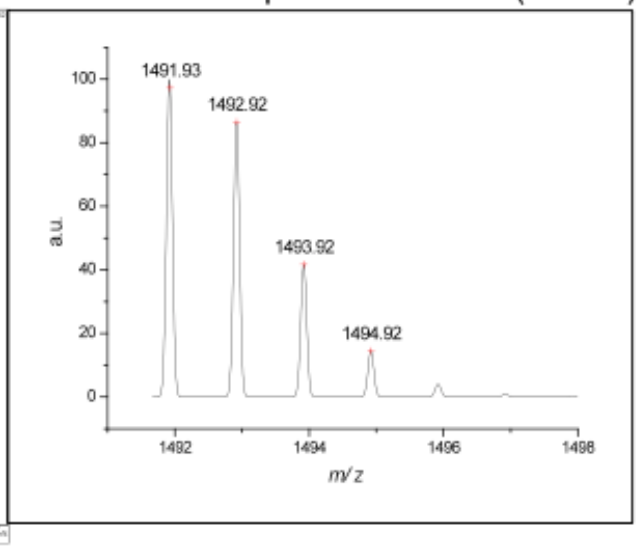

¹H NMR spectrum of dendron 6
4.859
3.311
2.190
1.937
1.448
a
b
c
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm



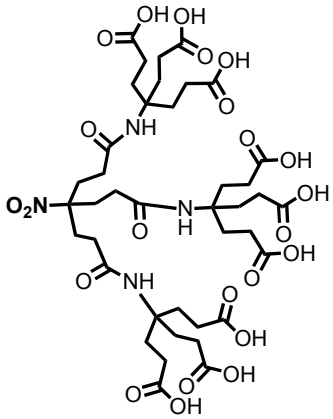
Isotopic distribution (M+Na)



Theoretical isotopic distribution (M+Na)



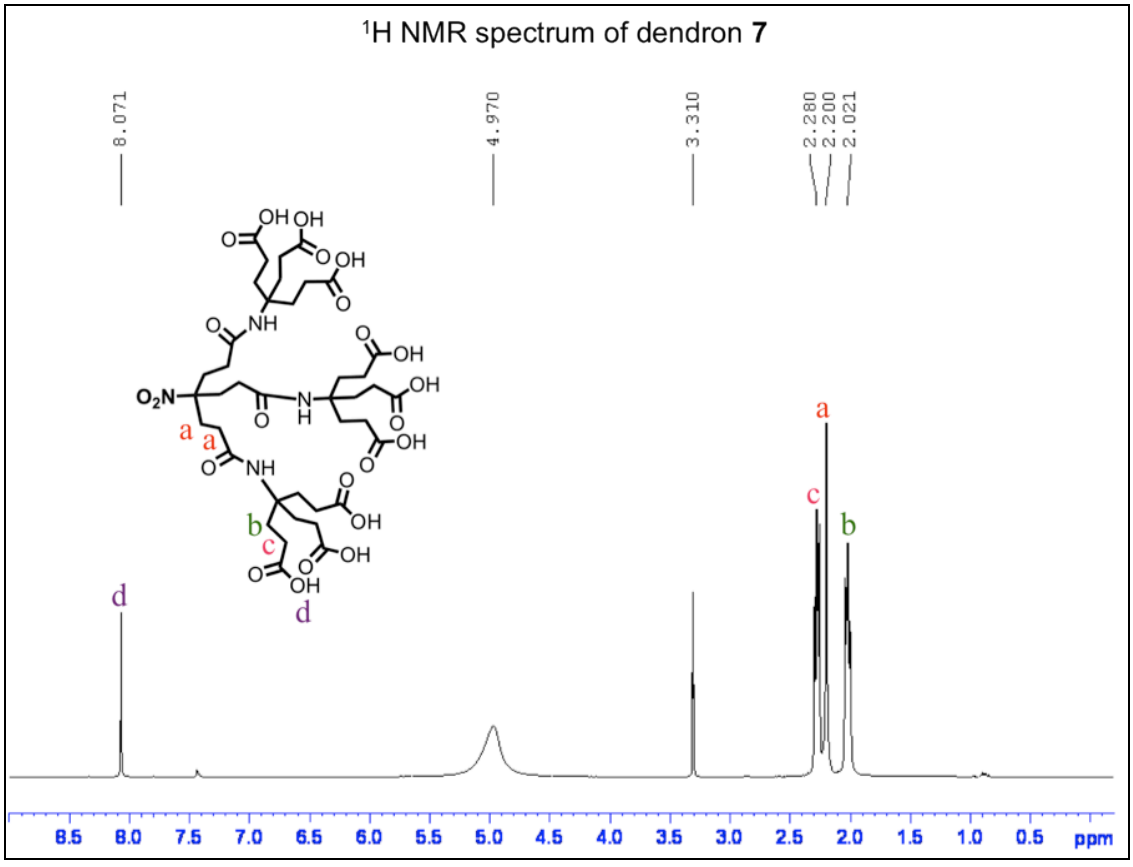
Synthesis of dendron 7[1]

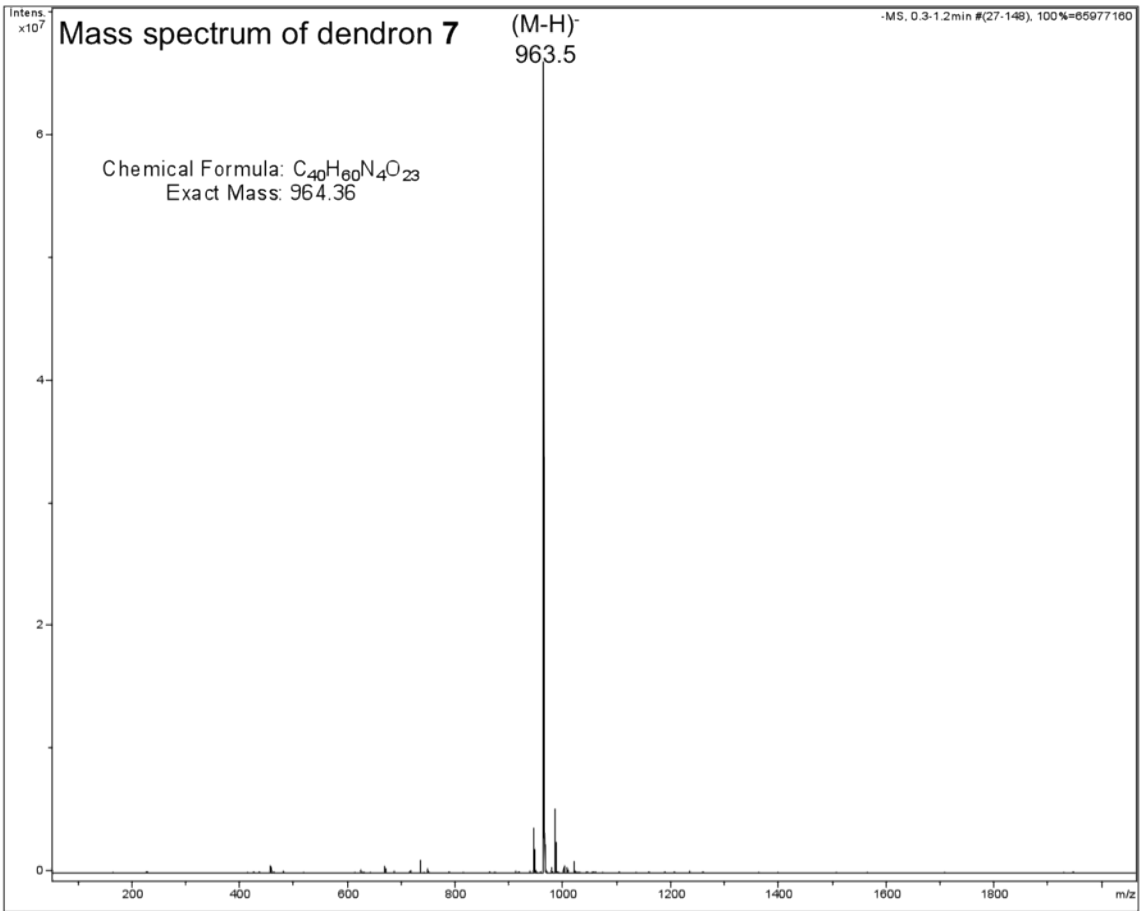


Chemical Formula: $C_{40}H_{60}N_4O_{23}$
Molecular Weight: 964.92

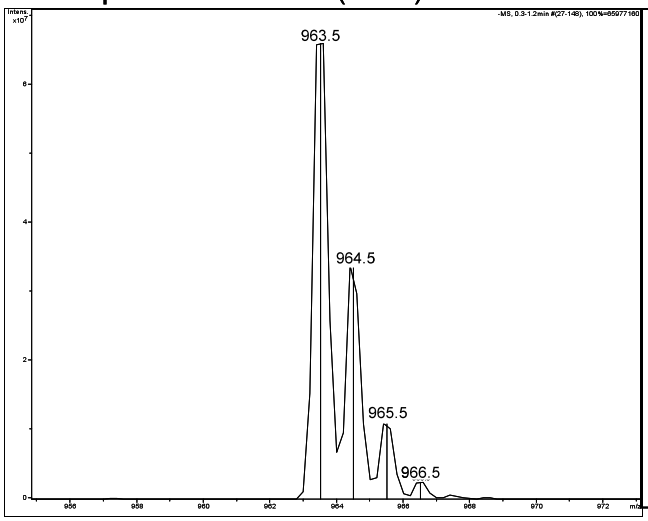
Dendron **6** (2.00 g, 1.36 mmol) was dissolved in 60 mL of formic acid/water (9:1) and the solution was stirred at room temperature for 24h. After removing the solvent, product washed twice with ethyl ether and dried under vacuum. Dendron **7** was obtained as a white powder in 97% yield (1.28 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.07 (COO*H*), 2.28 (t, *J* = 8.00 Hz, CH_2COOH, 18H), 2.20 (s, $NO_2C_qCH_2CH_2$, 12H), 2.02 (t, CH_2CH_2COOH, 18H). MS-ESI (M-H)$^-$ *m/z* calcd for $C_{40}H_{59}N_4O_{23}$: 963.4, found 963.1.

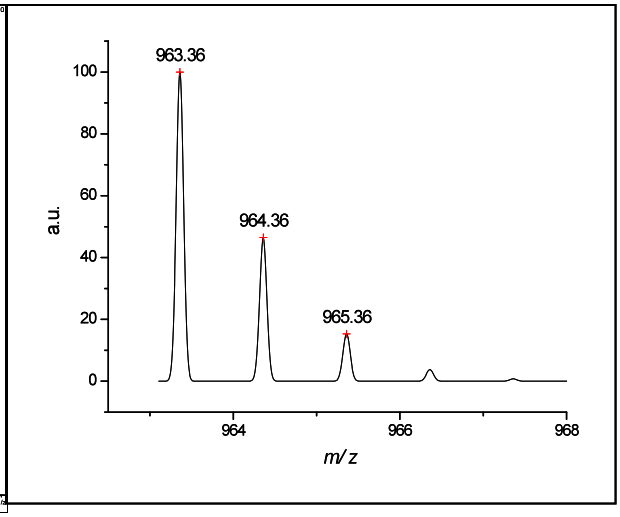




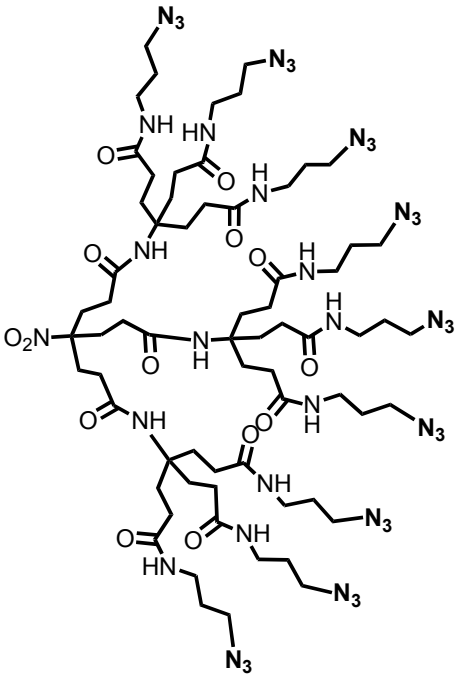
Isotopic distribution $(M-H)^-$



Theoretical isotopic distribution $(M-H)^-$



Synthesis of dendron 8

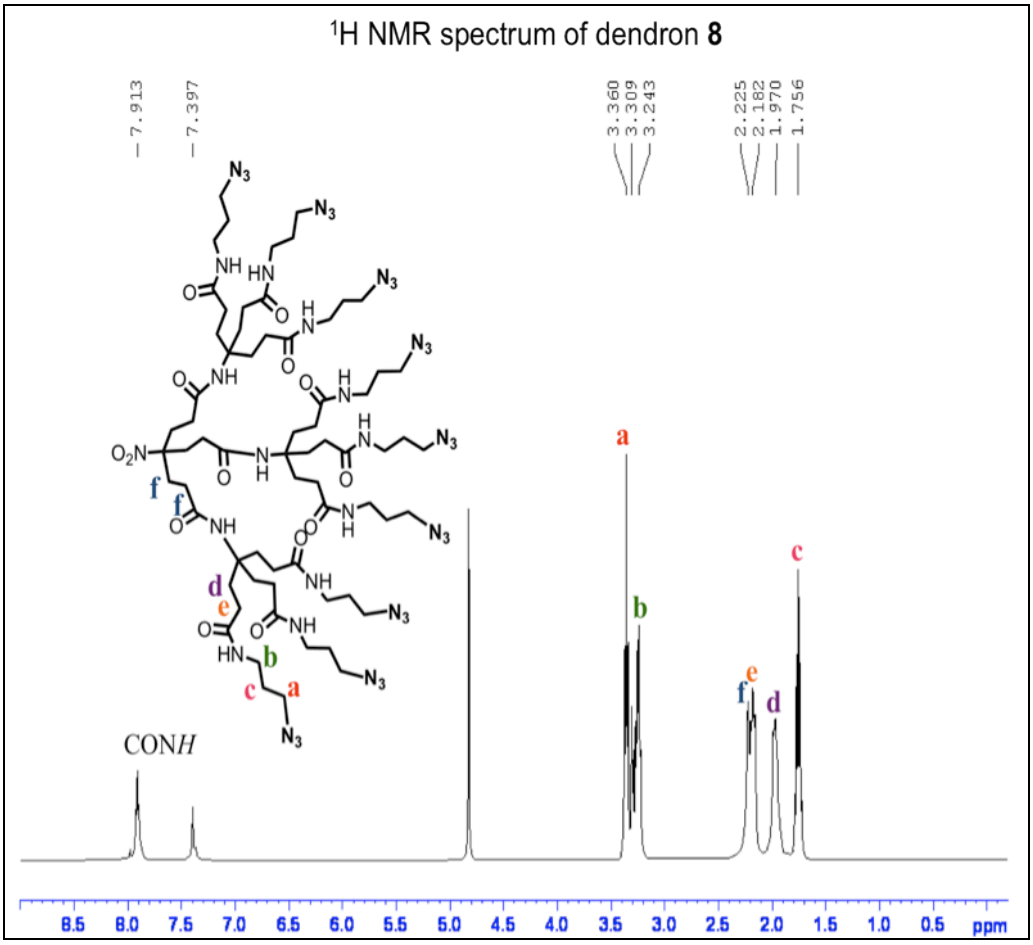


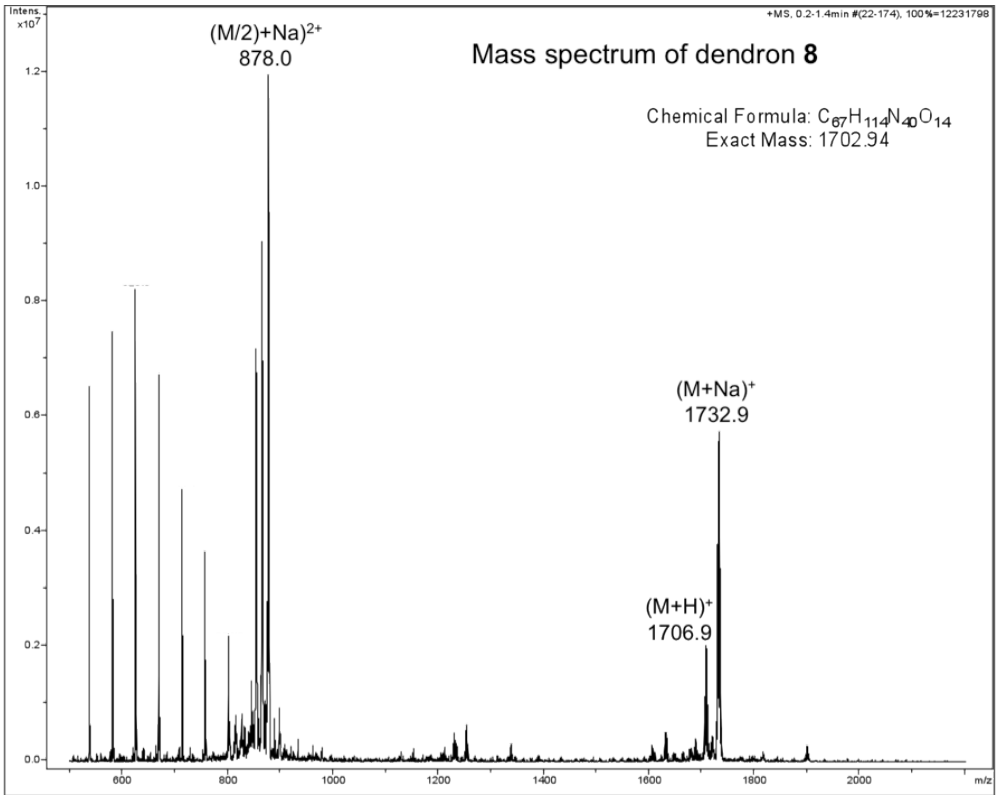
Chemical Formula: $C_{67}H_{114}N_{40}O_{14}$
Molecular Weight: 1703.88

Dendron nonacid **7** (0.300 g, 0.311 mmol) and HATU (1.31 g, 3.73 mmol) were dissolved in 20 mL of dry DMF. Diisopropylethylamine (1.0 mL, 5.74 mmol) and 3-aminopropyl azide **3** (0.723 g, 5.60 mmol) were successively added with a syringe. The solution was stirred at room temperature for 24h. Then, the solvent was removed under vacuum and the resulting brown oil was dissolved in methylene chloride and washed with an aqueous solution of $NaHCO_3$ and with water. The organic phase was dried over sodium sulfate, filtered through paper and evaporated to dryness. The product was purified by column chromatography (silica gel) using CH_2Cl_2/MeOH (80/20) as eluent. Dendron **8** was obtained as a colorless oil in 87% yield (0.460 g).

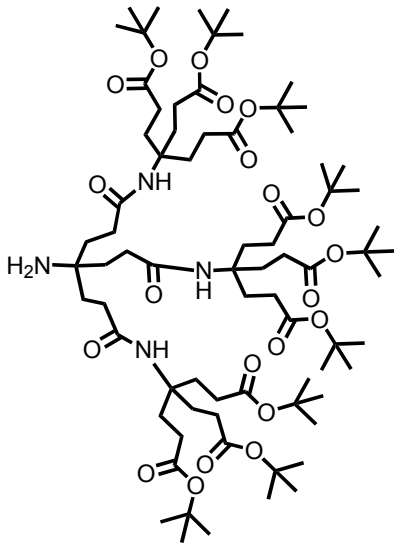
Note: A yellow oil (impurity) came out of the column with CH_2Cl_2/MeOH (98/2).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs*. TMS): 7.91 and 7.40 (s, CON*H*, 12H), 3.36 (t, J = 6.68 Hz, CH_2N$_3$, 18H), 3.24 (t, J = 5.86 Hz, CH_2CH$_2$CH$_2$N$_3$, 18H), 2.23 (s, NO$_2$C$_q$CH_2CH_2, 12H), 2.18 (t, J = 7.90 Hz, CH_2CONH, 18H), 1.97 (m, CH_2CH$_2$CONH, 18H), 1.76 (m, CH$_2$CH_2CH$_2$N$_3$, 18H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs*. TMS): 175.8 and 173.7 (*C*=O), 94.5 (NO$_2$*C*$_q$), 59.3 (CONHC$_q$), 50.2 (*C*H$_2$N$_3$), 38.0 (*C*H$_2$CH$_2$CH$_2$N$_3$), 32.3 (inner CH$_2$*C*H$_2$CONH), 32.0 (inner *C*H$_2$CH$_2$CONH), 31.7 (outer CH$_2$*C*H$_2$CONH), 31.4 (outer *C*H$_2$CH$_2$CONH), 29.9 (CH$_2$*C*H$_2$CH$_2$N$_3$). Infrared υ_{N3}: 2098.30 cm^{-1}. MS-ESI (M+H)$^+$ *m/z* calcd for $C_{67}H_{114}N_{40}O_{14}Na$: 1725.9, found 1732.9. Anal. calcd. for $C_{67}H_{114}N_{40}O_{14}$: C 46.60, H 6.65; found C 46.15, H 6.42.


^{1}H NMR spectrum of dendron **8**
7.913
7.397
3.360
3.309
3.243
2.225
2.182
1.970
1.756
CONH
a
b
c
d
e
f
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Mass spectrum of dendron **8**
(M/2)+Na)$^{2+}$
878.0
Chemical Formula: $C_{67}H_{114}N_{40}O_{14}$
Exact Mass: 1702.94
(M+Na)$^+$
1732.9
(M+H)$^+$
1706.9
m/z

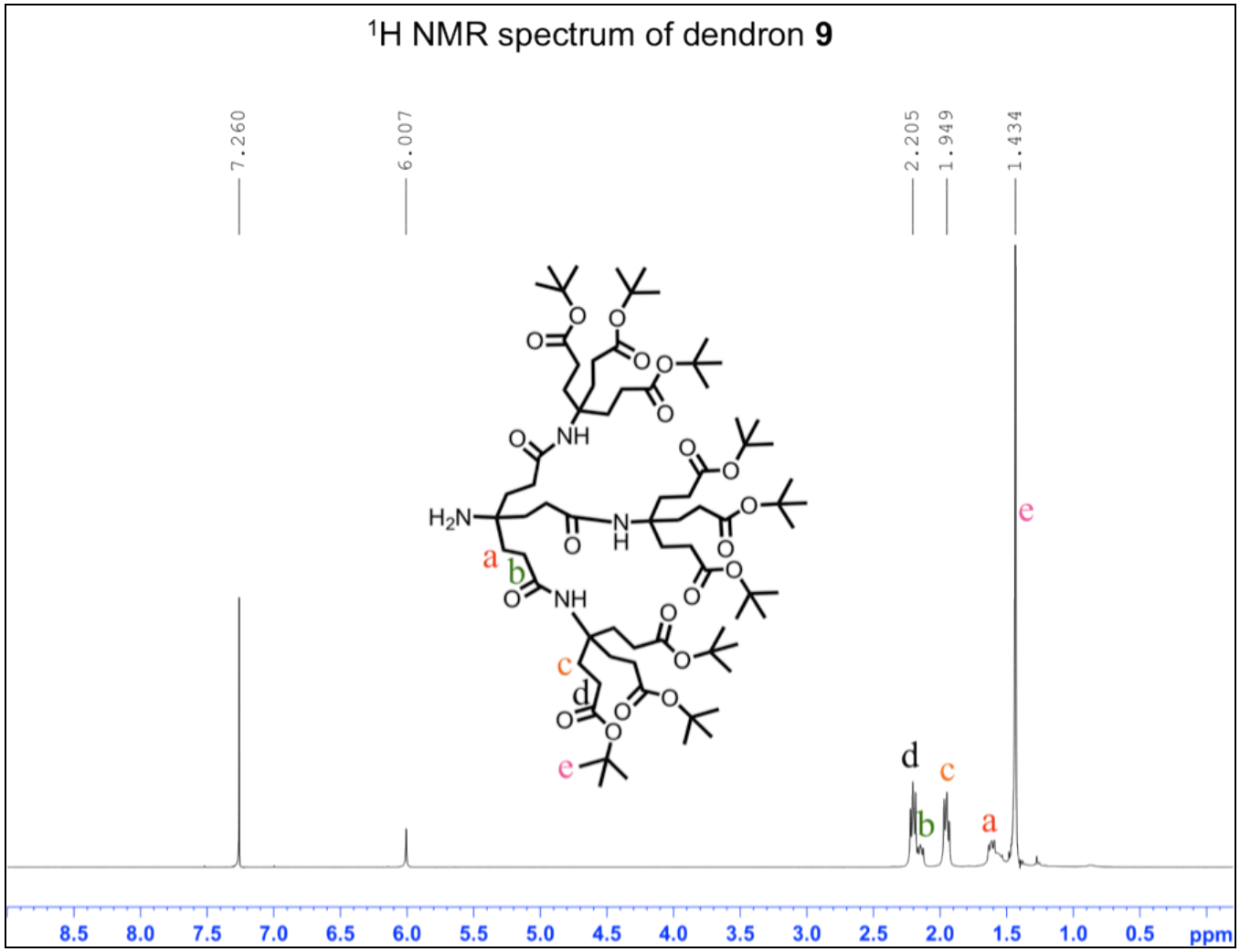
Synthesis of dendron 9[1]

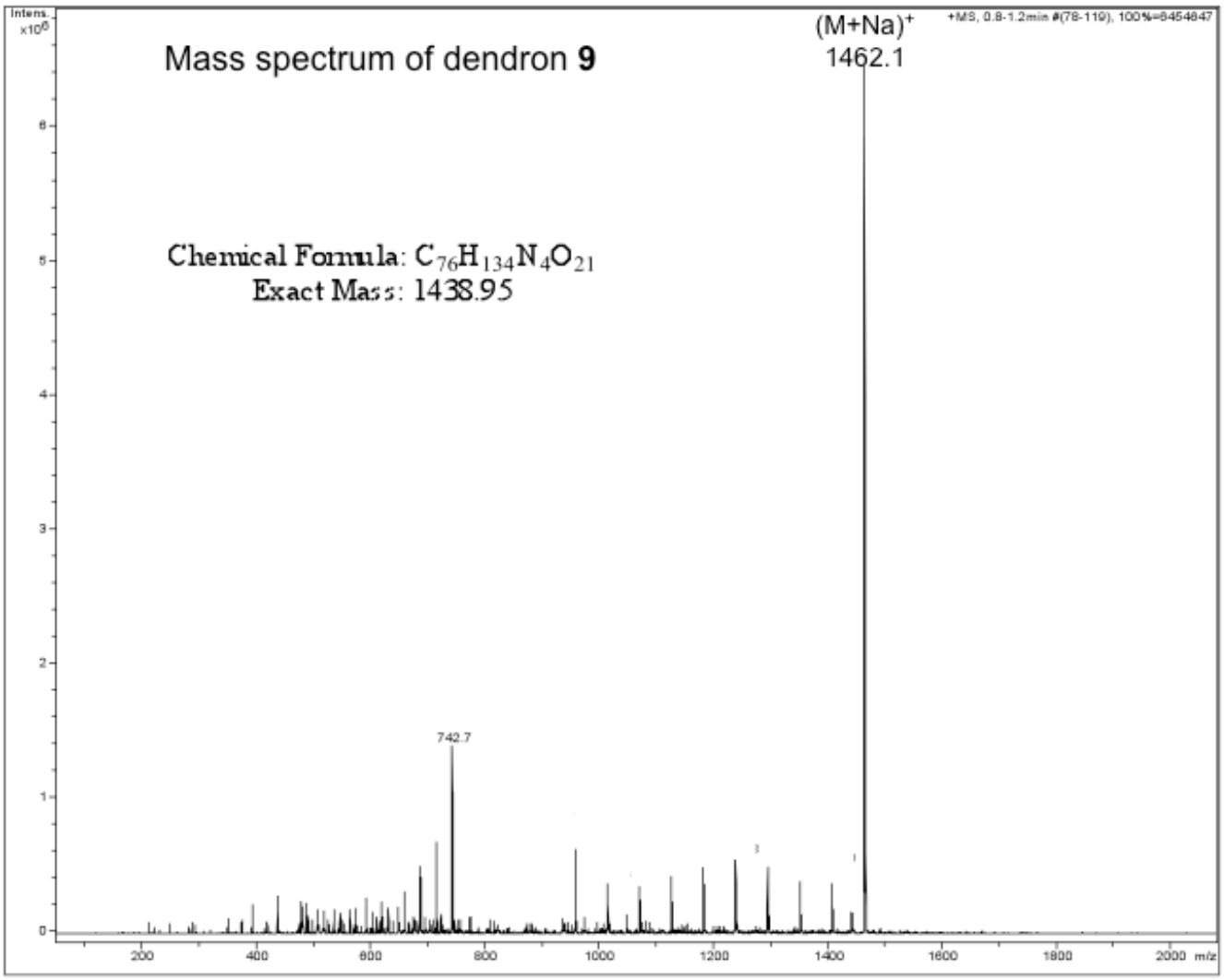


Chemical Formula: $C_{76}H_{134}N_4O_{21}$
Molecular Weight: 1439.89

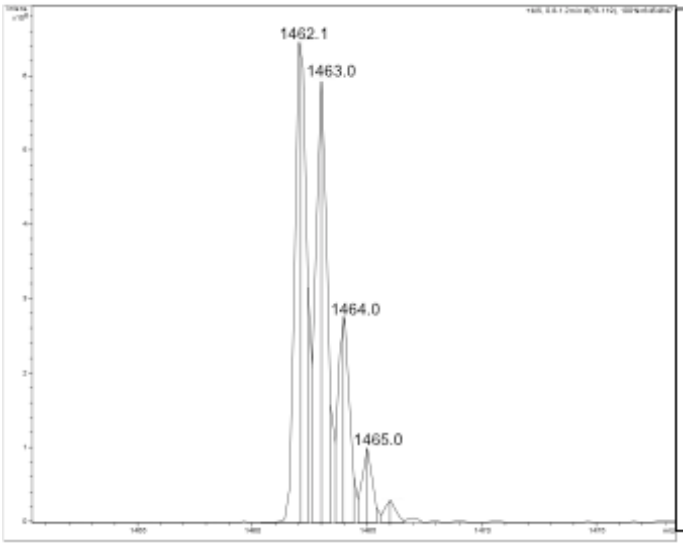
Dendron **6** (0.500 g, 0.340 mmol) was dissolved in 200 mL of ethanol and Raney-Ni catalyst was added. The solution was stirred at 45psi H_2 and 55ºC for 24h. The solution was cooled to room temperature, filtered through celite to remove the catalyst and solvent was removed under vacuum. Product was dissolved in CH_2Cl_2, filtered again through celite and evaporated to dryness. Dendron **9** was obtained as a white powder in 89% yield (0.437 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 2.21 (t, C*H*$_2$COO^{t}Bu, 18H), 2.16 (t, C*H*$_2$CONH, 6H), 1.95 (t, C*H*$_2$CH$_2$COO^{t}Bu, 18H), 1.60 (t, NH$_2$C$_q$C*H*$_2$, 6H), 1.45 (s, COO(C*H*$_3$)$_3$, 81H). MS-ESI $(M+Na)^+$ *m/z* calcd for $C_{76}H_{134}N_4O_{21}Na$: 1462.0, found 1462.1.

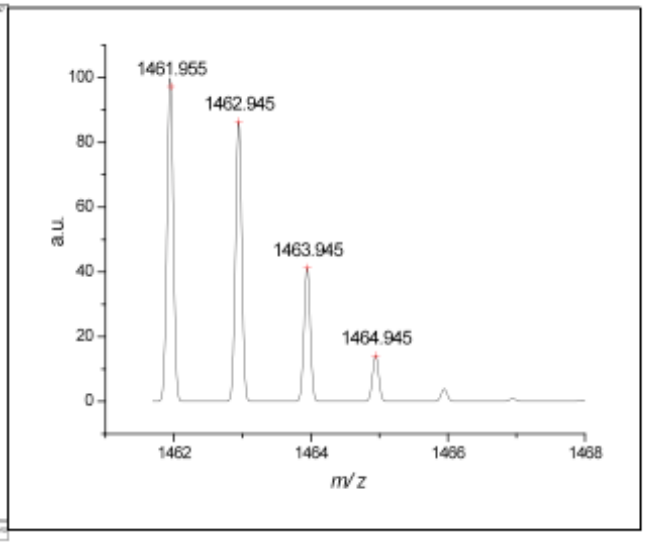

¹H NMR spectrum of dendron 9
7.260
6.007
2.205
1.949
1.434
a
b
c
d
e
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm



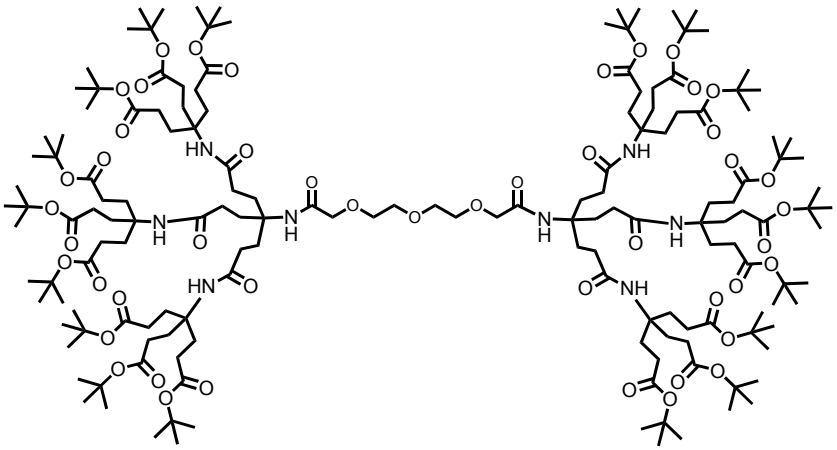
Isotopic distribution $(M+Na)^+$



Theoretical isotopic distribution $(M+Na)^+$



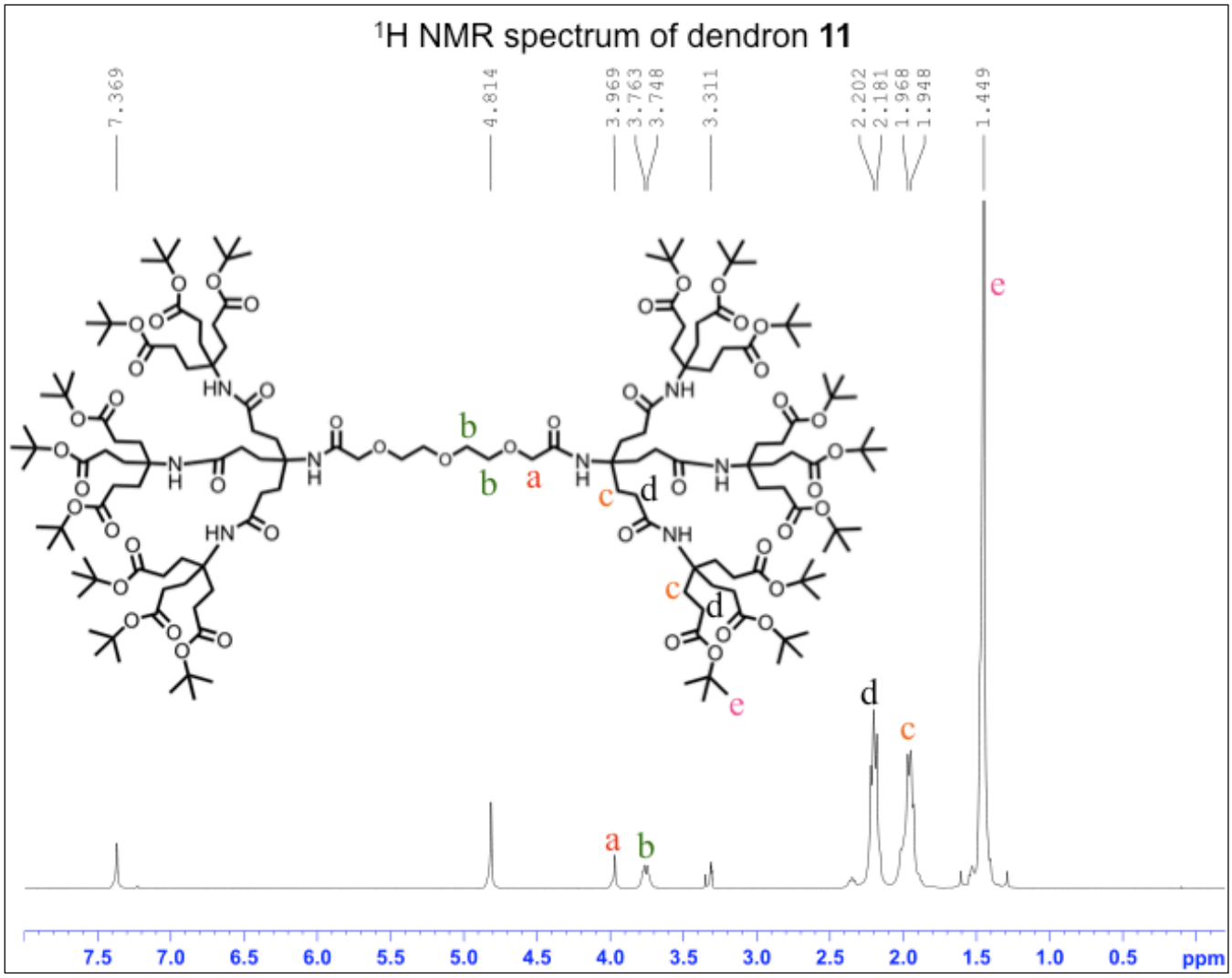
Synthesis of dendrimer 11

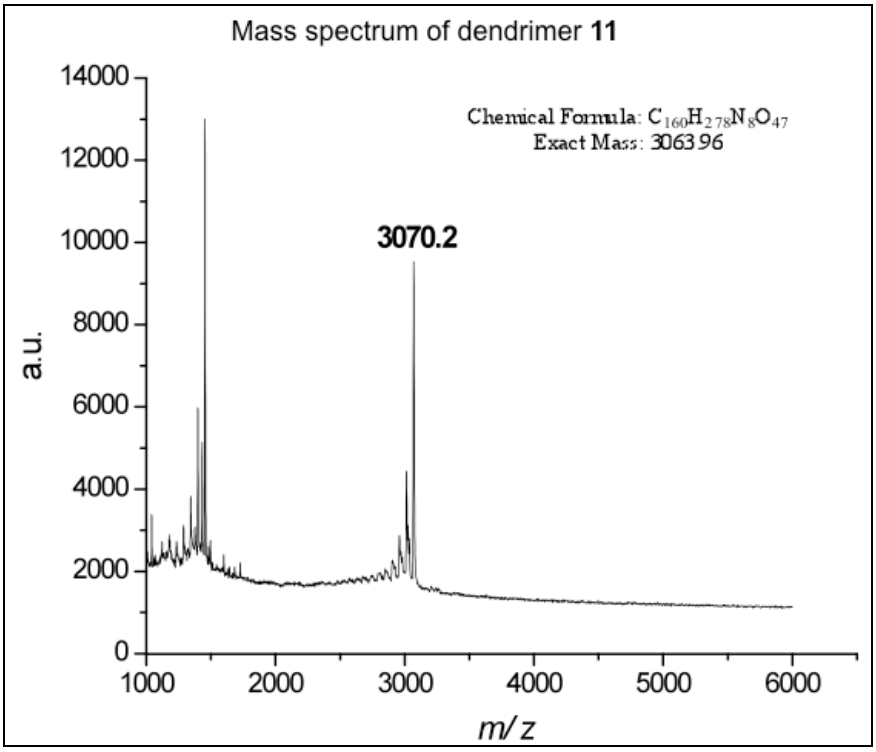


Chemical Formula: $C_{160}H_{278}N_8O_{47}$
Molecular Weight: 3065.94

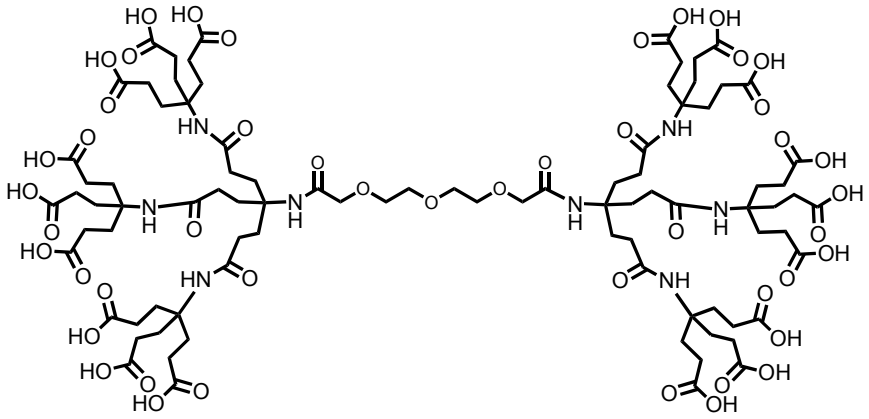
Dendron **9** (0.544 g, 0.378 mmol) and compound **10** (0.035 g, 0.158 mmol) were dissolved in 10 mL of DMF. HATU (0.132 g, 0.378 mmol) and DIPEA (0.3 mL, 17.2 mmol) were successively added and the solution was stirred at room temperature for 48h. The solvent was removed under vacuum and the product was purified by dialysis against methanol using a MWCO 2000 dialysis membrane. Dendrimer **11** was obtained as colorless waxy product in 85% yield (0.410 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs*. TMS): 7.37 (s, CON*H*, 8H), 3.97 (s, OCH_2CONH, 4H), 3.75 (m, OCH_2CH_2O, 8H), 2.20 (m, CH$_2$CH_2CO, 48H), 1.95 (m, CH_2CH$_2$CO, 48H), 1.45 (s, C(CH_3)$_3$, 162H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs*. TMS): 175.3 and 174.5 (*C*=O), 81.7 (*C*(CH$_3$)$_3$), 72.4 (O*C*H$_2$CO), 71.6 (O*C*H$_2$*C*H$_2$O), 58.9 (CONH*C*$_q$), 32.5 (inner CH$_2$*C*H$_2$CONH), 32.2 (inner *C*H$_2$CH$_2$CONH), 30.8 (outer CH$_2$*C*H$_2$CONH), 30.6 (outer *C*H$_2$CH$_2$CONH), 28.6 (C(*C*H$_3$)$_3$). MALDI-TOF (M+H)$^+$ *m*/*z* calcd for $C_{160}H_{279}N_8O_{47}$: 3065.0, found 3070.2. Anal. calcd. for $C_{160}H_{278}N_8O_{47}$: C 62.68, H 9.14; found C 62.32, H 9.06.


¹H NMR spectrum of dendron 11
7.369
4.814
3.969
3.763
3.748
3.311
2.202
2.181
1.968
1.948
1.449
a
b
c
d
e
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


Mass spectrum of dendrimer 11
Chemical Formula: C160H278N8O47
Exact Mass: 3063.96
3070.2
a.u.
m/z
14000
12000
10000
8000
6000
4000
2000
0
1000
2000
3000
4000
5000
6000

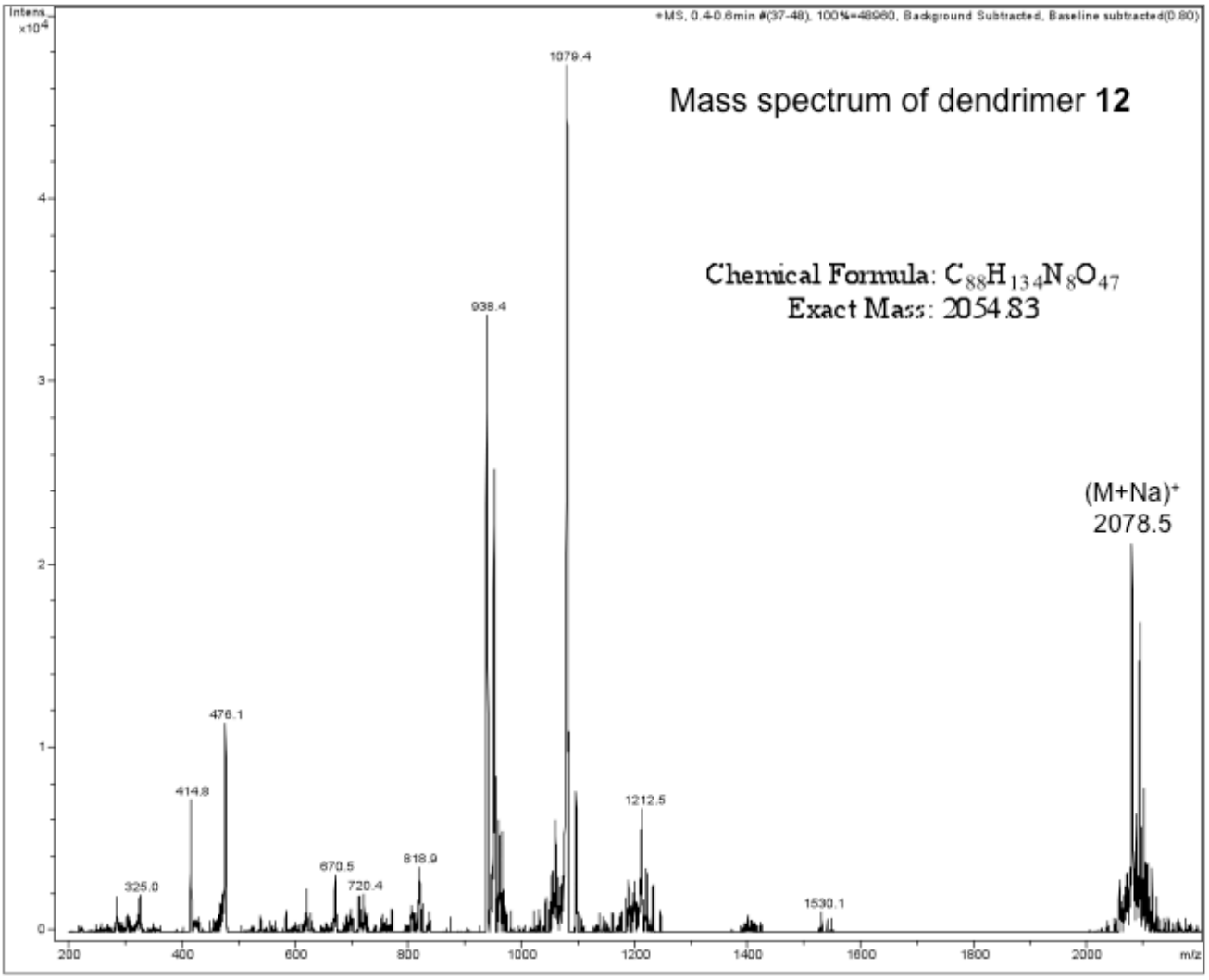
Synthesis of dendrimer 12



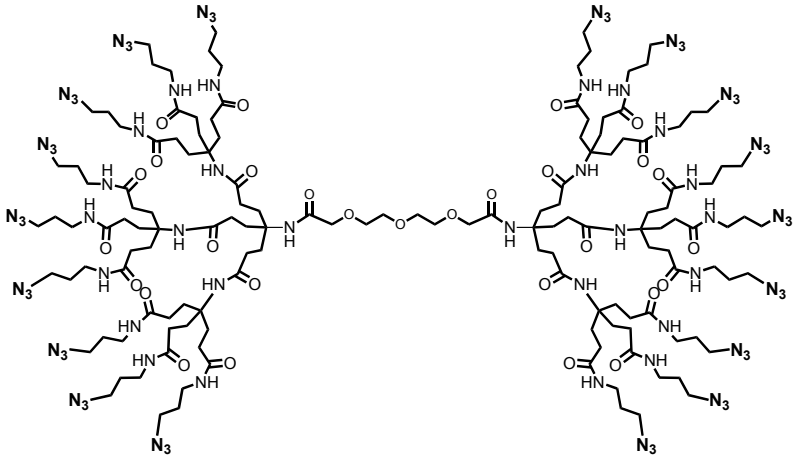
Chemical Formula: $C_{88}H_{134}N_8O_{47}$
Molecular Weight: 2056.03

Dendrimer **11** (0.300 g, 0.0978 mmol) was dissolved in 55 mL of formic acid/water (9:1) and the solution was stirred at room temperature for 24h. After removal of the solvent, the resulting product was washed twice with ethyl ether and dried under vacuum. Dendrimer **12** was obtained as a colorless waxy product in 97% yield (0.195 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.09 (s, COO*H*, 18H), 7.32 (s, CON*H*, 8H), 3.98 (s, OCH_2CONH, 4H), 3.74 (m, OCH_2CH_2O, 8H), 2.31 (m, CH_2COOH, 36H), 2.21 (m, CH_2CH_2CONH, 12H), 2.03 (m, CH_2CH_2CO, 48H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 177.3 (*C*OOH), 175.5 and 174.5 (*C*ONH), 72.2 (O*C*H_2CO), 71.5 (O*C*$H_2C$$H_2$O), 59.3 and 58.5 (CONH$C_q$), 32.2 (inner CH_2*C*H_2CONH), 32.0 (inner *C*H_2CH_2CONH), 30.6 (CH_2*C*H_2COOH), 30.6 (*C*H_2CH_2COOH). MS-ESI $(M+Na)^+$ *m/z* calcd for $C_{88}H_{134}N_8O_{47}Na$: 2077.8, found 2078.5. Anal. calcd. for $C_{88}H_{134}N_8O_{47}$: C 51.48, H 6.57; found C 51.10, H 6.31.


Intens.
x10^4
+MS, 0.4-0.6min #(37-48), 100%=48960, Background Subtracted, Baseline subtracted(0.80)
Mass spectrum of dendrimer 12
Chemical Formula: C88H134N8O47
Exact Mass: 2054.83
(M+Na)+
2078.5
1079.4
938.4
476.1
414.8
325.0
670.5
720.4
818.9
1212.5
1530.1
m/z

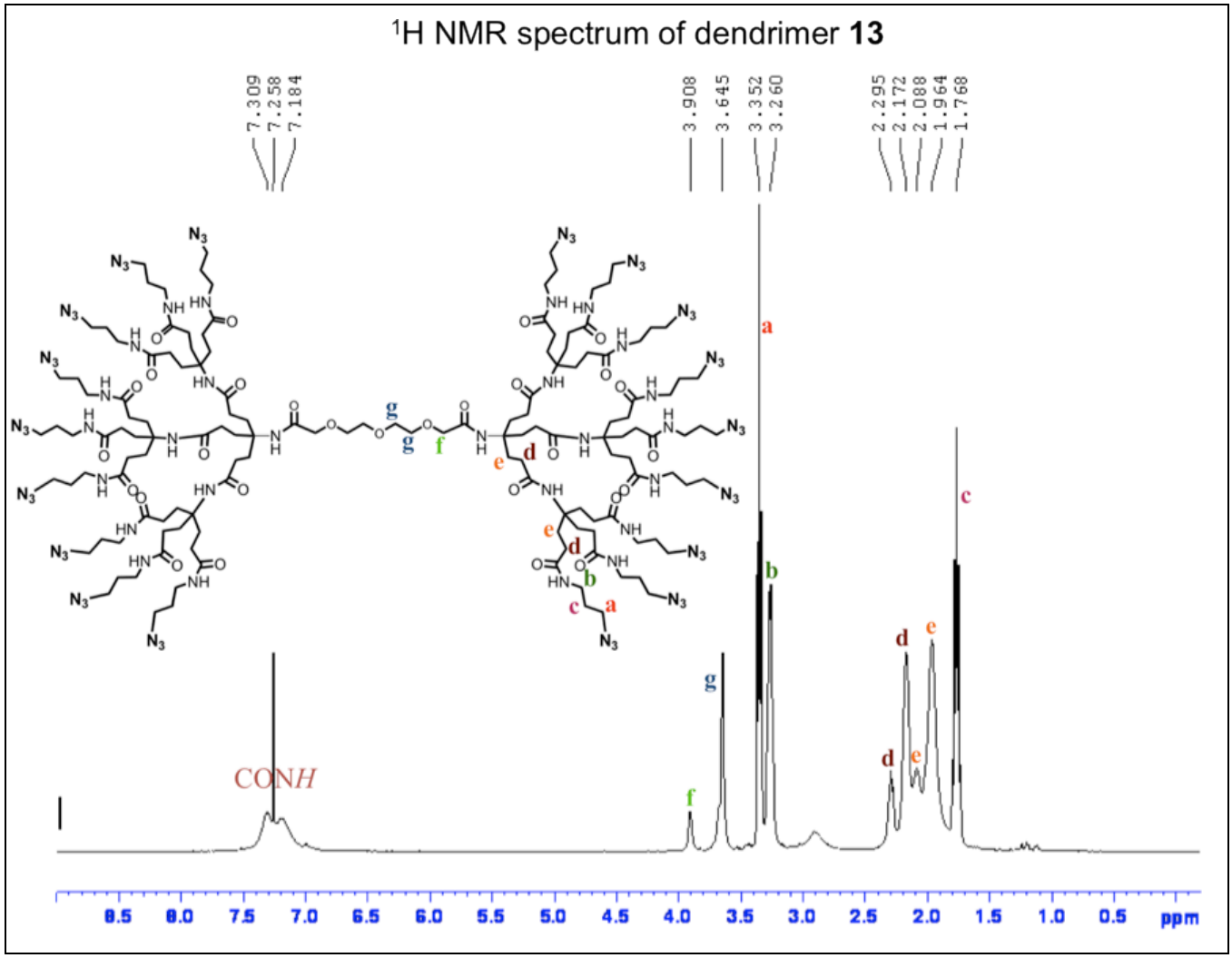
Synthesis of dendrimer 13



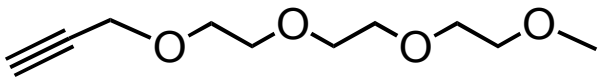
Chemical Formula: $C_{142}H_{242}N_{80}O_{29}$
Molecular Weight: 3533.96

Dendrimer **12** (0.050 g, 0.0243 mmol) and HATU (0.187 g, 0.535 mmol) were dissolved in 10 mL of DMF. Diisopropylethylamine (0.150 mL, 0.875 mmol) and 3-aminopropyl azide **3** (0.088 g, 0.875 mmol) were successively added with a syringe. The solution was stirred at room temperature for 48h. Then, the solvent was removed under vacuum and the product was purified by dialysis against methanol using a MWCO 2000 dialysis membrane. Dendrimer **13** was obtained as a colorless oil in 76% yield (0.065 g).

^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm} *vs*. TMS): 7.42 and 7.21 (s, CON*H*, 26H), 3.91 (s, OCH_2CONH, 4H), 3.65 (m, OCH_2CH_2O, 8H), 3.35 (t, J = 6.58 Hz, CH_2N$_3$, 36H), 3.27 (d, J = 5.52 Hz, CH_2CH$_2$CH$_2$N$_3$, 36H), 2.30 and 2.17 (m, CH_2CONH, 48H), 2.09 and 1.97 (m, CH_2CH$_2$CONH, 48H), 1.76 (m, CH$_2$CH_2CH$_2$N$_3$, 36H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm} *vs*. TMS): 173.9, 72.2 (O*C*H$_2$CO), 71.5 (O*C*H$_2$*C*H$_2$O), 58.4 (CONH*C*$_q$), 49.3 (*C*H$_2$N$_3$), 37.1 (*C*H$_2$CH$_2$CH$_2$N$_3$), 30.8 (*C*H$_2$*C*H$_2$CONH), 28.9 (CH$_2$*C*H$_2$CH$_2$N$_3$). Infrared υ_{N3}: 2098.20 cm^{-1}. Anal. calcd. for $C_{142}H_{242}N_{80}O_{29}$: C 48.26, H 6.90; found C 48.03, H 6.84.


^{1}H NMR spectrum of dendrimer **13**
7.309
7.258
7.184
3.908
3.645
3.352
3.260
2.295
2.172
2.088
1.964
1.768
CONH
a
b
c
d
e
f
g
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

Synthesis of alkyne derivative 14

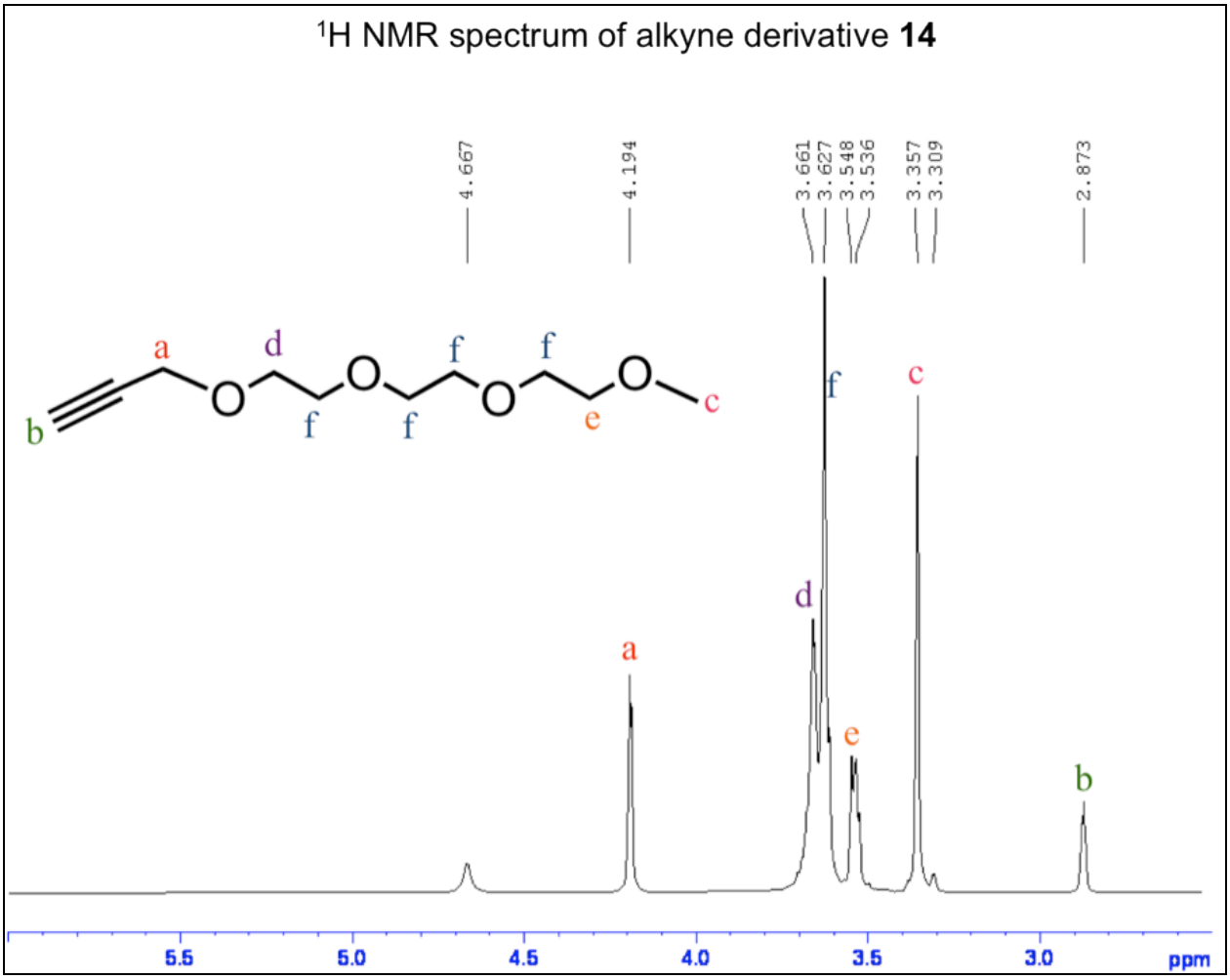


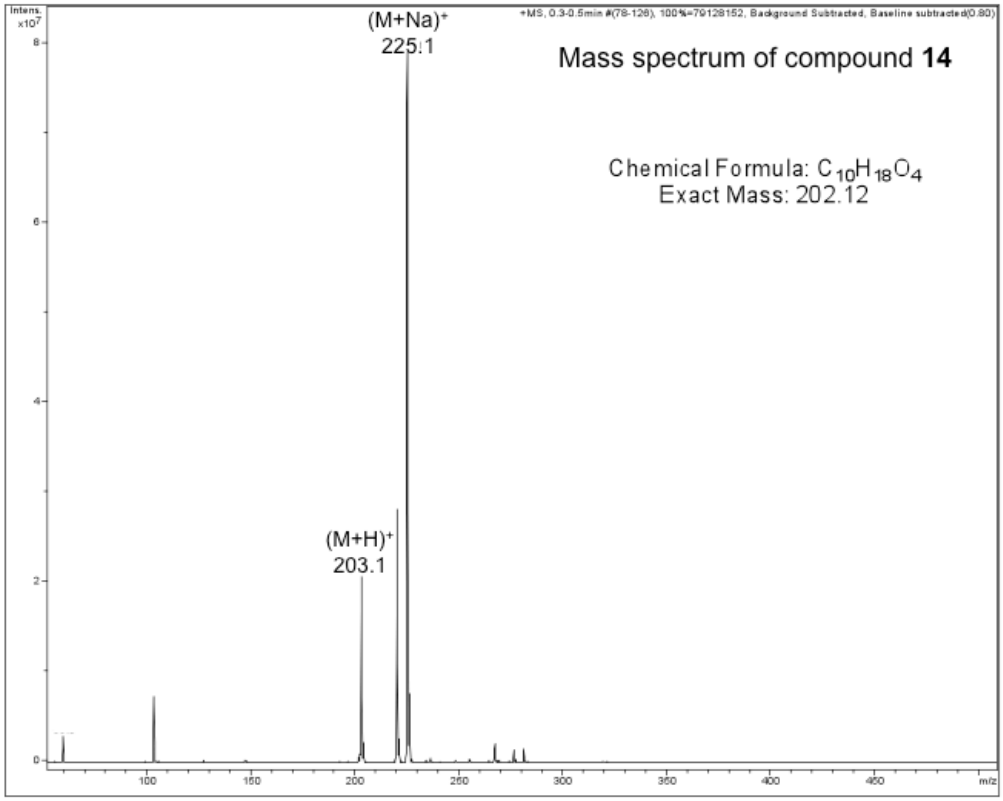
Chemical Formula: $C_{10}H_{18}O_4$
Molecular Weight: 202.25

Triethyleneglycol monomethyl ether (5 mL, 31.24 mmol) was introduced in a Schlenk flask and dried under vaccum. Dry DMF (50 mL) and propargyl bromide (7 mL, 62.50 mmol, 80 wt. % in toluene) were successively added. At room temperature, sodium hydride (2.25 g, 93.73 mmol, 60% dispersion in mineral oil) was slowly added and the solution was heated at 80ºC for 24h. The reaction was carefully quenched with cold water and concentrated under reduced pressure. Methylene chloride (200 mL) was added and the reaction was washed with water (3 x 200 mL). The separated organic layer was dried over sodium sulfate, filtered through paper and concentrated. The product was purified by column chromatography (silica gel) using hexane/ethyl acetate (gradient from 90:10 until 50:50) as eluent. Product **14** was obtained as a colorless oil in 58% yield (3.66 g).

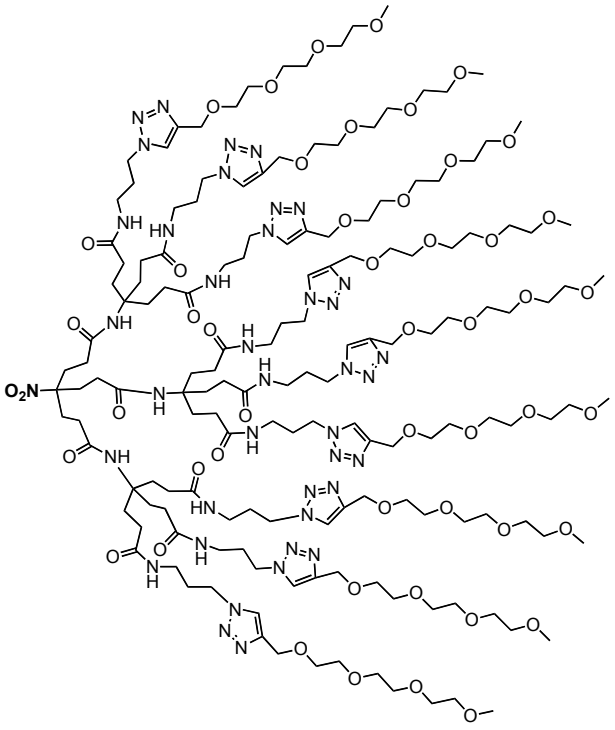
Note: The column chromatography was followed by TLC using potassium permanganate stain.

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 4.19 (m, C*H*$_2$C≡CH, 2H), 3.66, 3.63 and 3.54 (m, OC*H*$_2$C*H*$_2$O, 12H), 3.36 (s, OC*H*$_3$, 3H), 2.87 (C≡C*H*, 1H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 80.8 (*C*≡CH), 76.2 (C≡*C*H), 73.0, 71.6, 71.4 and 70.2 (O*C*H$_2$*C*H$_2$O), 59.2 (C*H*$_2$C≡CH), 59.1 (O*C*H$_3$). MS-ESI (M+Na)$^+$ *m/z* calcd for $C_{10}H_{18}O_4Na$: 225.1, found 225.1. Anal. calcd. for $C_{10}H_{18}O_4$: C 59.39, H 8.97; found C 59.61, H 9.02.


¹H NMR spectrum of alkyne derivative 14
4.667
4.194
3.661
3.627
3.548
3.536
3.357
3.309
2.873
a
b
c
d
e
f
5.5
5.0
4.5
4.0
3.5
3.0
ppm


(M+Na)⁺
225.1
Mass spectrum of compound 14
Chemical Formula: C10H18O4
Exact Mass: 202.12
(M+H)⁺
203.1
m/z

Synthesis of dendron 15 by "click" chemistry



Chemical Formula: $C_{157}H_{276}N_{40}O_{50}$
Molecular Weight: 3524.11

Method A. To a methylene chloride solution (10 mL) of dendron **8** (0.156 g, 0.0916 mmol) and alkyne derivative **14** (0.259 g, 1.28 mmol), 5 mL of an aqueous solution of $CuSO_4 \bullet 5H_2O$ (0.206 g, 0.824 mmol) was added. Under vigorous stirring 5 mL of an aqueous solution of sodium ascorbate (0.326 g, 1.65 mmol) was added dropwise. The solution was stirred at room temperature under nitrogen for 24h. Several workup procedures were attempted in order to isolate dendron **15** from the copper catalyst:

(i) Extraction: an aqueous solution of ammonium hydroxide was added to the heterogeneous solution and stirred for 5 minutes. The methylene chloride phase was separated from the aqueous phase but the product remained in the aqueous phase together with the copper catalyst and sodium ascorbate. The aqueous phase was then evaporated to dryness resulting in a brown solid. The residue was dissolved in methanol resulting in a green solution with a green precipitate. The solution was filtered through celite and the solvent was removed resulting in a light green waxy product. The green coloration suggested the presence of copper.

(ii) Column chromatography (SiO_2): the green waxy product from (i) was dissolved in methanol and filtered through a plug of silica gel. A green layer remained on top of the silica and a green solution eluted from the column. The solvent was removed and the product was dissolved in acetonitrile and filtered through a syringe filter to remove silica traces. A light green waxy product was obtained. The green coloration still suggested the presence of copper.

(iii) Reverse-phase column chromatography (octadecyl-functionalyzed silica): The light green waxy product from (i) was dissolved in methanol/water (50:50) and introduced to reverse-phase column chromatography (using C18-silica). Several combinations of solvents methanol/acetonitrile/water were used but only one green fraction was obtained. A thin green layer remained on top of the column suggesting the removal of a significant amount of copper. A light green waxy product was obtained also suggesting the contamination with copper.

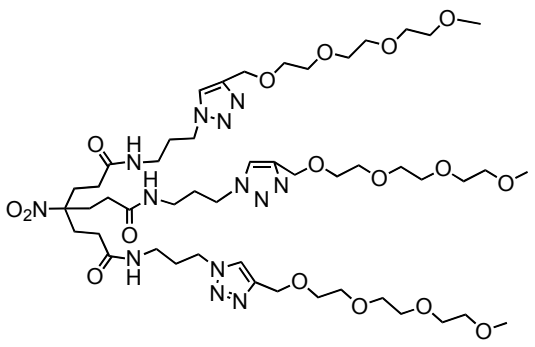
(iv) Dialysis: the green waxy product from (i) was dissolved in water and introduced into a dialysis membrane. The dialysis membrane was introduced in a 4 L beaker containing distilled water for three days. After three days, the green coloration of the product inside the dialysis bag remained. The same procedure was also used using aqueous solution of ammonium hydroxide or EDTA with no success.

Anal. calcd. for $C_{157}H_{276}N_{40}O_{50}$: C 53.51, H 7.89, N 15.90; found C 44.54, H 6.75, N 9.77. Anal. found for Cu 0.50 %.

Method B. Dendron **8** (0.050 g, 0.0293 mmol) and alkyne derivative **14** (0.083 g, 0.411 mmol) were dissolved in 10 mL of methylene chloride. In a second flask, CuI (0.050 g, 0.264 mmol), sodium ascorbate (0.104 g, 0.528 mmol) and sulfonated bathophenanthroline (0.312 g, 0.528 mmol) were dissolved in 10 mL of a degassed mixture of ethanol/water (1:1) and heated to reflux for 3 minutes resulting in a dark red solution. The red aqueous "click" solution was added to the methylene chloride solution containing the dendron and the alkyne derivative, and the mixture was stirred at room temperature for 24h. Similarly to method A, several workup procedures were attempted in order to isolate dendron **15** from the copper catalyst, resulting in a light green waxy product (see method A for workup procedures). Anal. calcd. for $C_{157}H_{276}N_{40}O_{50}$: C 53.51, H 7.89, N 15.90; found C 40.92, H 6.11, N 9.57. Anal. found for Cu 0.007 %.

Method C. Dendron **8** (0.050 g, 0.0293 mmol) and alkyne derivative **14** (0.083 g, 0.411 mmol) were dissolved in 10 mL of ^{t}BuOH/water (1:1). Five pieces of copper wire (around 5 mm each), sulfonated bathophenanthroline (0.028 g, 0.053 mmol) and sodium ascorbate (0.021 g, 0.106 mmol) were added successively. The solution was vigorously stirred at room temperature for 48h. Similarly to methods A and B, several workup procedures were attempted in order to isolate product **15** from the copper catalyst resulting in a light green waxy product (see method A for workup procedures). Anal. calcd. for $C_{157}H_{276}N_{40}O_{50}$: C 53.51, H 7.89, N 15.90; found C 49.50, H 7.16, N 18.71. Anal. found for Cu 0.004%.

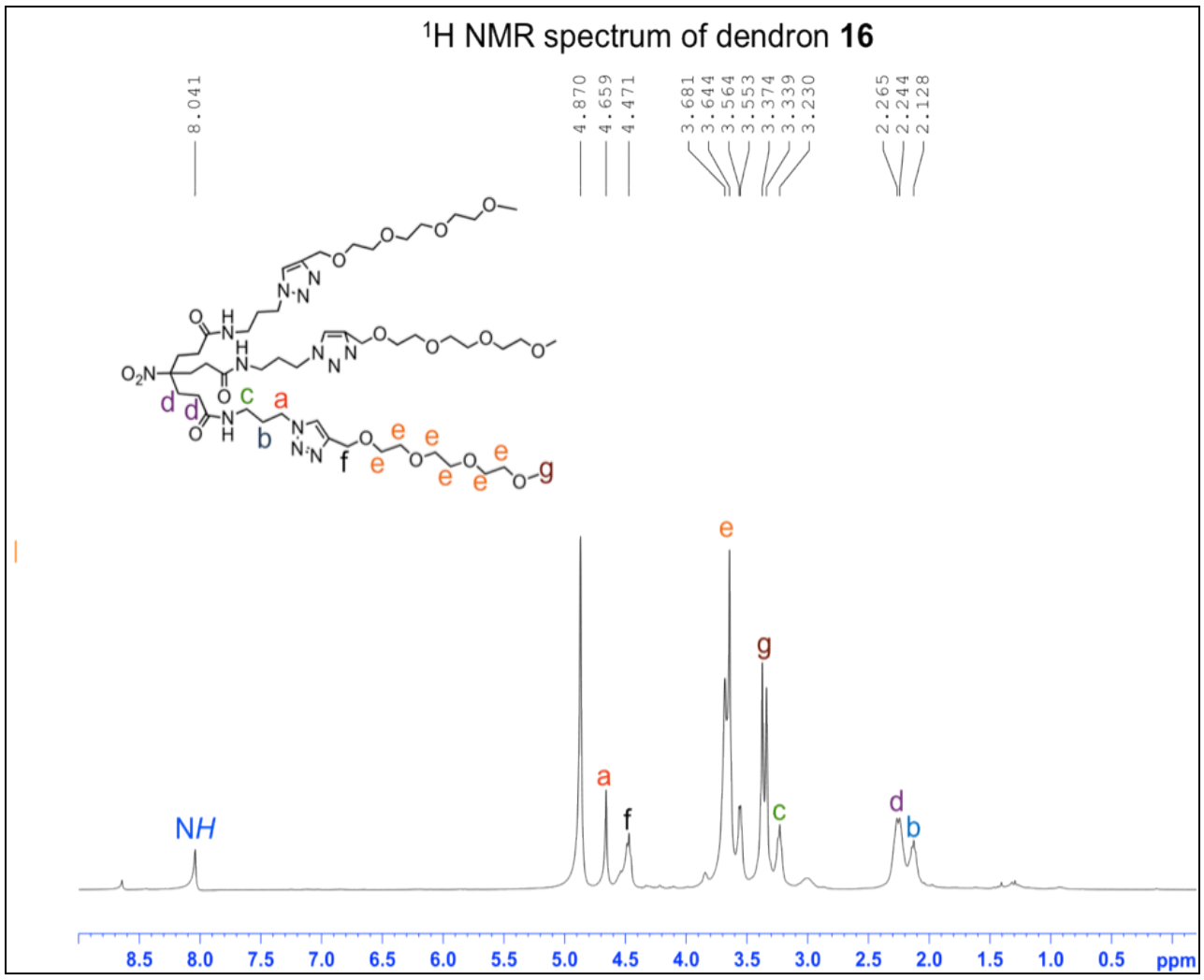
Synthesis of dendron 16

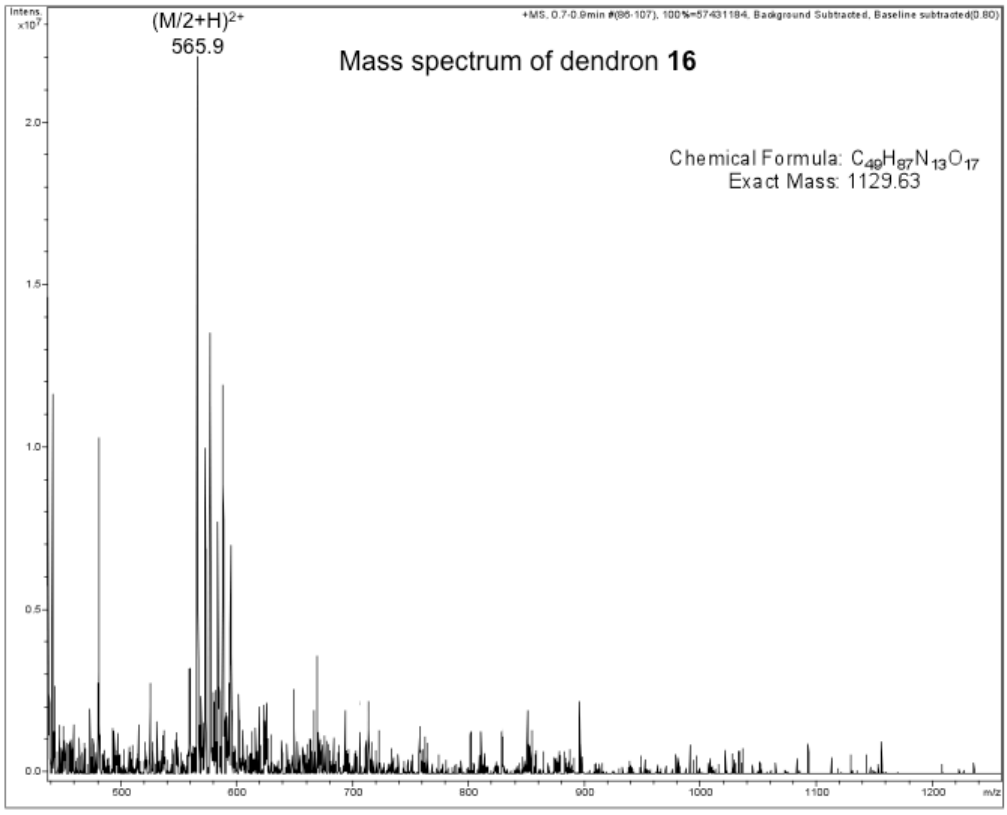


Chemical Formula: $C_{49}H_{87}N_{13}O_{17}$
Molecular Weight: 1130.29

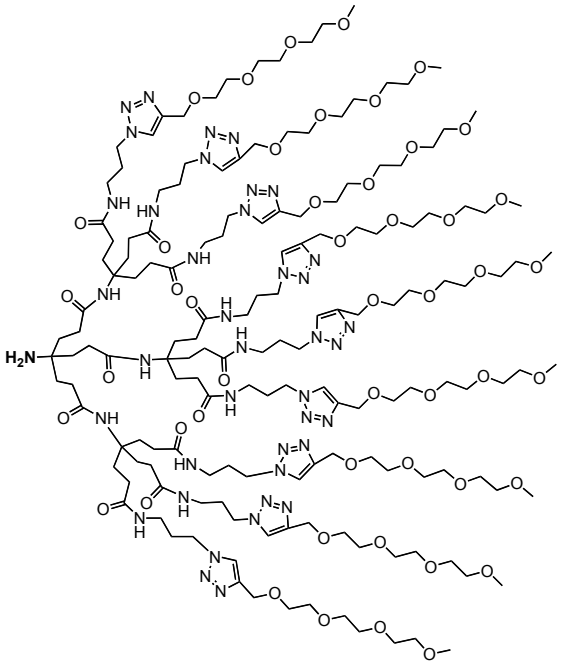
Dendron **4** (0.100 g, 0.191 mmol) and alkyne derivative **14** (0.155 g, 0.764 mmol) were dissolved in 10 mL of ^{t}BuOH/water (1:1). Five pieces of copper wire (around 5 mm each) sulfonated bathophenanthroline (0.062 g, 0.115 mmol) and sodium ascorbate (0.045 g, 0.230 mmol) were successively added. The solution was vigorously stirred at room temperature for 48h. Copper wire was removed and the solution was evaporated to dryness. Methylene chloride was added and the solution was filtered through celite. The solvent was removed under *vacuum* and washed three times with hexanes in order to remove the alkyne derivative added in excess. Dendron **16** was obtained as a colorless waxy product in 92% yield (0.205 g).

^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.04 (s, C*H* of triazole, 3H), 4.66 (s, CH_2CH_2-triazole, 6H), 4.47 (s, OCH_2-triazole, 6H), 3.68, 3.64 and 3.56 (m, OCH_2CH_2O, 36H), 3.37 and 3.34 (s, OCH_3, 9H), 3.23 (s, $CH_2CH_2CH_2$-triazole, 6H), 2.27 and 2.24 (m, $NO_2C_qCH_2CH_2$, 24H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 175.8 (*C*=O), 146.1 (C_q of triazole), 125.3 (*C*H of triazole), 73.0, 71.5, 71.3 and 70.8 (OCH_2CH_2O), 65.0 (OCH_2-triazole), 59.1 (OCH_3), 37.6 (CH_2-triazole), 31.4 and 31.0 (CH_2CH_2CONH). MS-ESI (M^{2+}+Na) *m/z* calcd for $C_{49}H_{87}N_{13}O_{17}Na^{2+}$: 587.8, found 587.8. Anal. calcd. for $C_{49}H_{87}N_{13}O_{17}$: C 52.07, H 7.76; found C 52.21, H 7.83.


1H NMR spectrum of dendron 16
8.041
4.870
4.659
4.471
3.681
3.644
3.564
3.553
3.374
3.339
3.230
2.265
2.244
2.128
NH
a
f
e
g
c
d
b
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

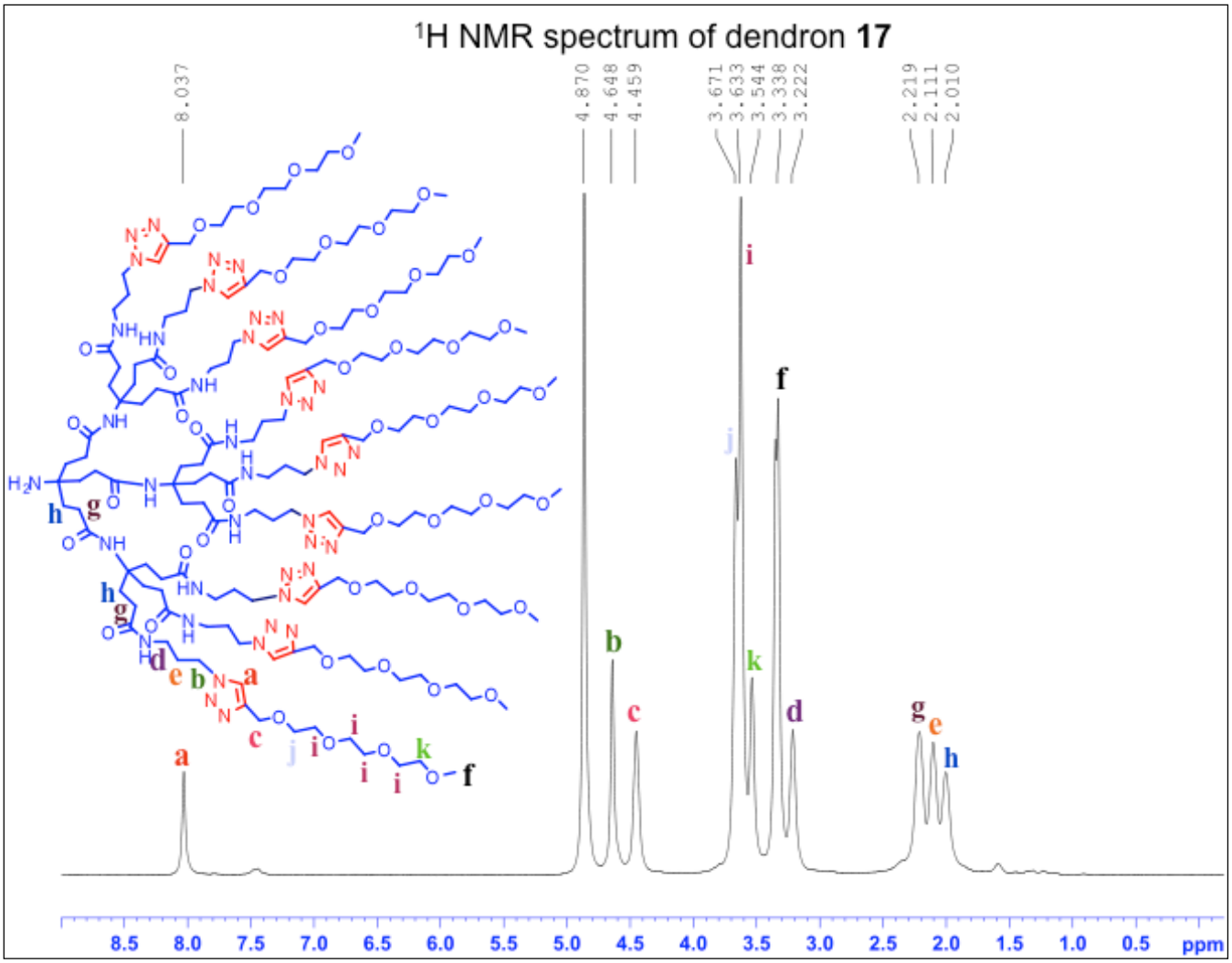

(M/2+H)2+
565.9
Mass spectrum of dendron 16
Chemical Formula: C49H87N13O17
Exact Mass: 1129.63
500
600
700
800
900
1000
1100
1200
m/z

Synthesis of dendron 17

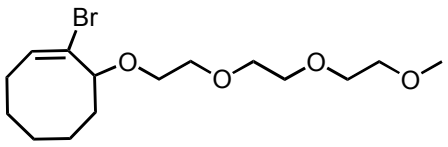


Chemical Formula: $C_{157}H_{278}N_{40}O_{48}$
Molecular Weight: 3494.13

The light green waxy product obtained from synthesis of dendron **15** (0.100 g, 0.028 mmol) was dissolved in 20 mL of ethanol and $CuSO_4$•$5H_2O$ (0.007g, 0.028 mmol) was added resulting in a green solution. The solution was heated to reflux and $NaBH_4$ (0.006 g, 0.142 mmol) was added slowly. The solution readily turned to dark brown and after 15 minutes a black precipitate formed. After refluxing the solution for 1h, it was cooled to room temperature, filtered through celite and the solvent was removed. The product was dissolved in methylene chloride and filtered again through celite to remove the salts. After removal of the solvent, dendron **17** was obtained as a yellow waxy product in 71% yield (0.070 g). ^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs.* TMS): 8.04 (s, C*H* of triazole, 9H), 4.65 (s, $CH_2C\mathit{H}_2$-triazole, 18H), 4.46 (s, $OC\mathit{H}_2$-triazole, 18H), 3.67, 3.63 and 3.54 (m, $OC\mathit{H}_2C\mathit{H}_2O$, 108H), 3.34 (s, $OC\mathit{H}_3$, 27H), 3.22 (s, $C\mathit{H}_2CH_2CH_2$-triazole, 18H), 2.22 (s, $CH_2C\mathit{H}_2CONH$, 24H), 2.11 (m, $CH_2C\mathit{H}_2CH_2$-triazole, 18H), 2.01 (s, $C\mathit{H}_2CH_2CONH$, 24H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs.* TMS): 175.8 (*C*=O), 146.0 (C_q of triazole), 125.2 (*C*H of triazole), 72.9, 71.4, 71.3 and 70.8 ($OC\mathit{H}_2C\mathit{H}_2O$), 65.1 ($OC\mathit{H}_2$-triazole), 59.2 ($OC\mathit{H}_3$), 37.6 ($C\mathit{H}_2$-triazole), 31.5 and 31.2 ($C\mathit{H}_2C\mathit{H}_2CONH$). MS-ESI $(M+Na)^+$ *m/z* calcd for $C_{157}H_{278}N_{40}O_{48}Na$: 3516.0, found 3517.1. Anal. calc. for $C_{157}H_{278}N_{40}O_{48}$: C 53.97, H 8.02; found C 51.23, H 7.21. Anal. found for Cu 0.001 %.


^{1}H NMR spectrum of dendron **17**
8.037
4.870
4.648
4.459
3.671
3.633
3.544
3.338
3.222
2.219
2.111
2.010
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

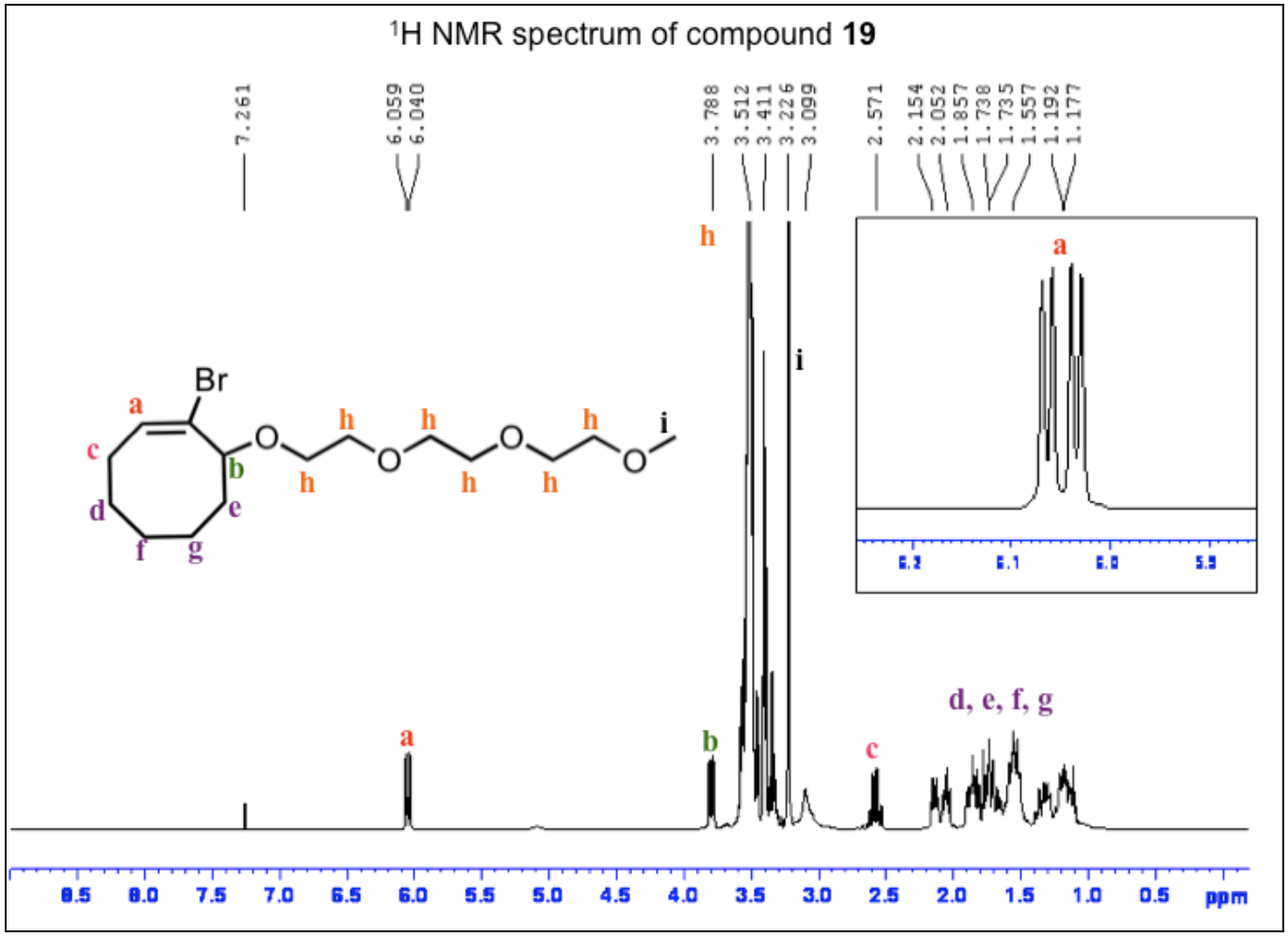
Synthesis of 19



Chemical Formula: $C_{15}H_{27}BrO_4$
Molecular Weight: 351.28

Triethyleneglycol monomethyl ether (7.35 g, 44.8 mmol), $AgClO_4$ (2.30 g, 11.1 mmol), anhydrous pyridine (3.2 mL) and anhydrous toluene (6.0 mL) were introduced in a Schlenk flask under an argon atmosphere. A toluene solution (2.4 mL) of bicyclic compound **18** (1.00 g, 3.7 mmol) was added under argon. The mixture was refluxed for 4h in the dark. The solvent was removed under *vacuum* and the residue was dissolved in hexanes/ethyl acetate (3:1) and filtered through a silica plug. The product was purified by flash column chromatography using hexanes/ethyl acetate (3:1). Compound **19** was obtained as a yellow oil in 95% yield (1.23 g). *Note.* The reaction was carried out under argon atmosphere. Prior to use, triethyleneglycol monomethyl ether was dried overnight under *vacuum* at 60ºC in order to remove traces of water. Prior to use, $AgClO_4$ was dissolved in toluene and dried overnight under *vacuum* in order to remove traces of water. The column chromatography was followed by TLC using the anisaldehyde stain.

^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm} *vs.* TMS): 6.06 (m, vinyl proton, 1H), 3.79 (m, C*H*-O, 1H), 3.51-3.30 (m, OCH_2CH_2O, 12H), 3.23 (s, OCH_3, 3H), 2.57 (m, CH_2CH=CBr, 2H), 2.15-1.18 (m, CH_2 of cyclooctyne ring, 8H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm} *vs.* TMS): 134.4 (*C*Br), 127.9 (*C*=CBr), 85.0 (*C*H-O), 72.4, 71.7, 70.4, 70.3, 68.0 and 67.7 (O*C*H_2*C*H_2O), 58.8 (O*C*H_3), 39.4, 36.3, 33.1, 27.9 and 26.2 (*C*H_2 of cyclooctyne ring). MS-ESI (M+Na) *m/z* calcd for $C_{15}H_{27}BrO_4Na$: 373.1, found 373.2. Anal. calc. for $C_{15}H_{27}BrO_4$: C 51.29, H 7.75; found C 51.03, H 7.61.


¹H NMR spectrum of compound 19
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6.059
6.040
3.788
3.512
3.411
3.226
3.099
2.571
2.154
2.052
1.857
1.738
1.735
1.557
1.192
1.177
Br
a
b
c
d
e
f
g
h
i
d, e, f, g
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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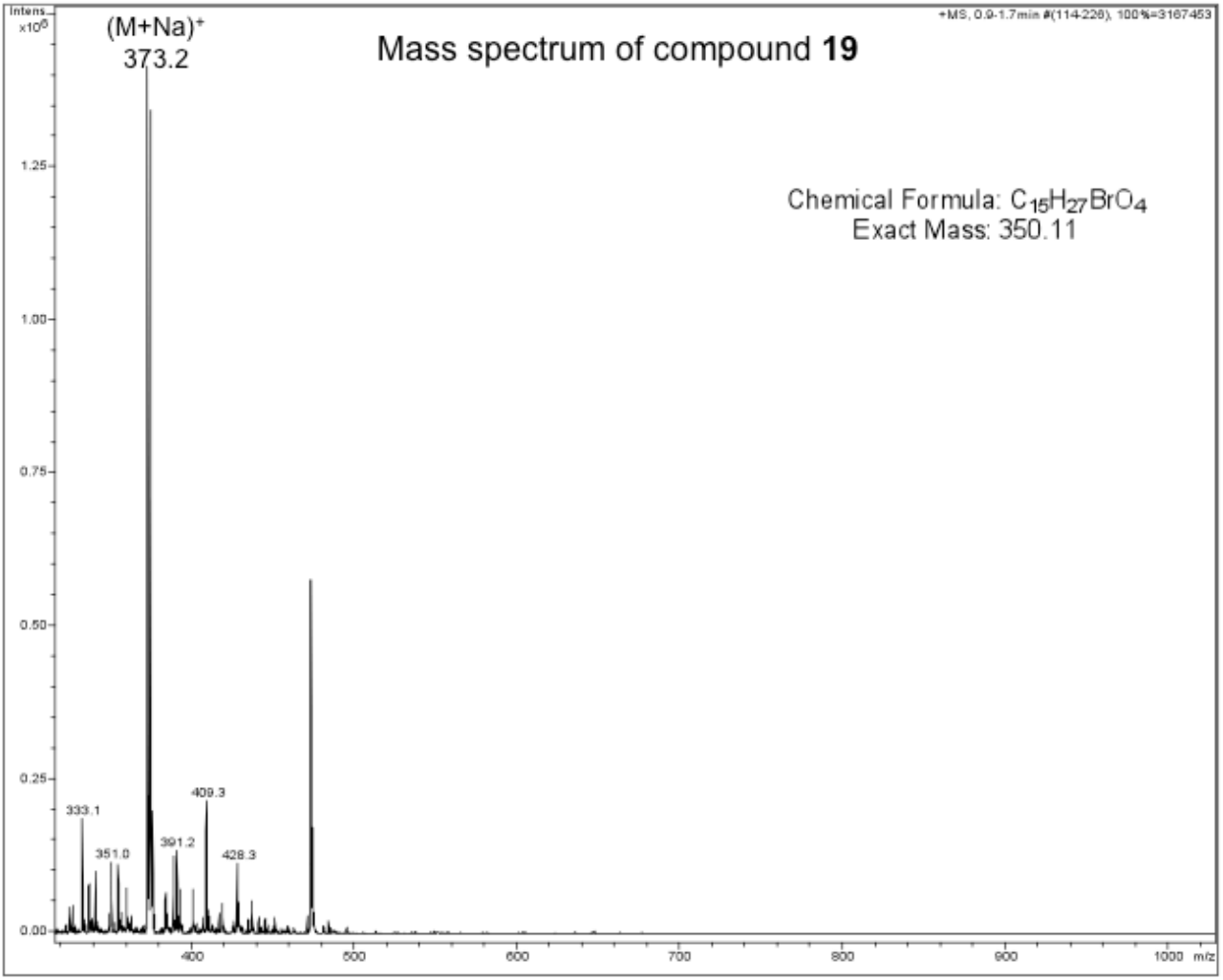
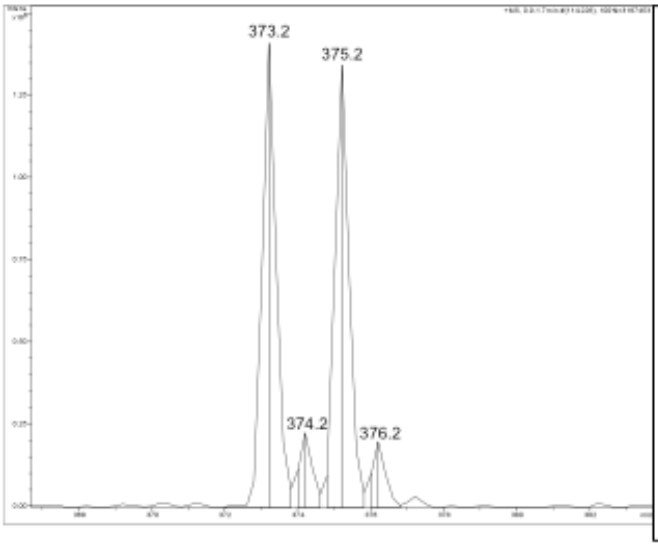
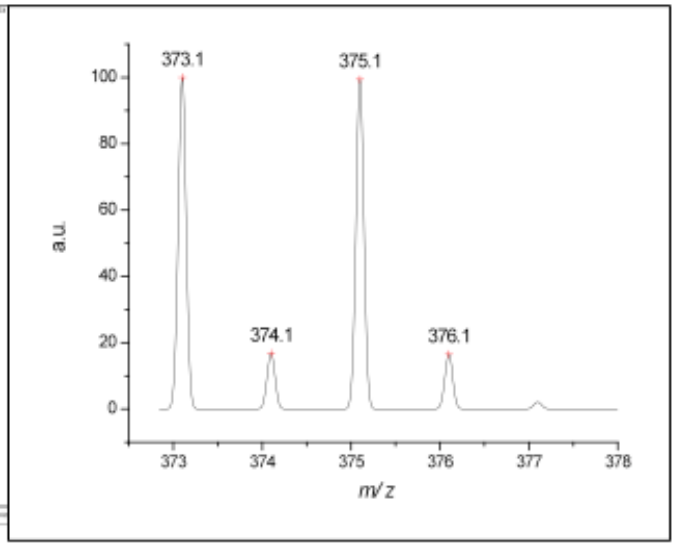
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm



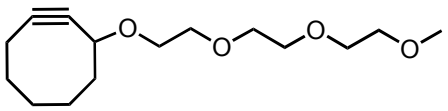
Isotopic distribution $(M+Na)^+$



Theoretical isotopic distribution $(M+Na)^+$



Synthesis of 20

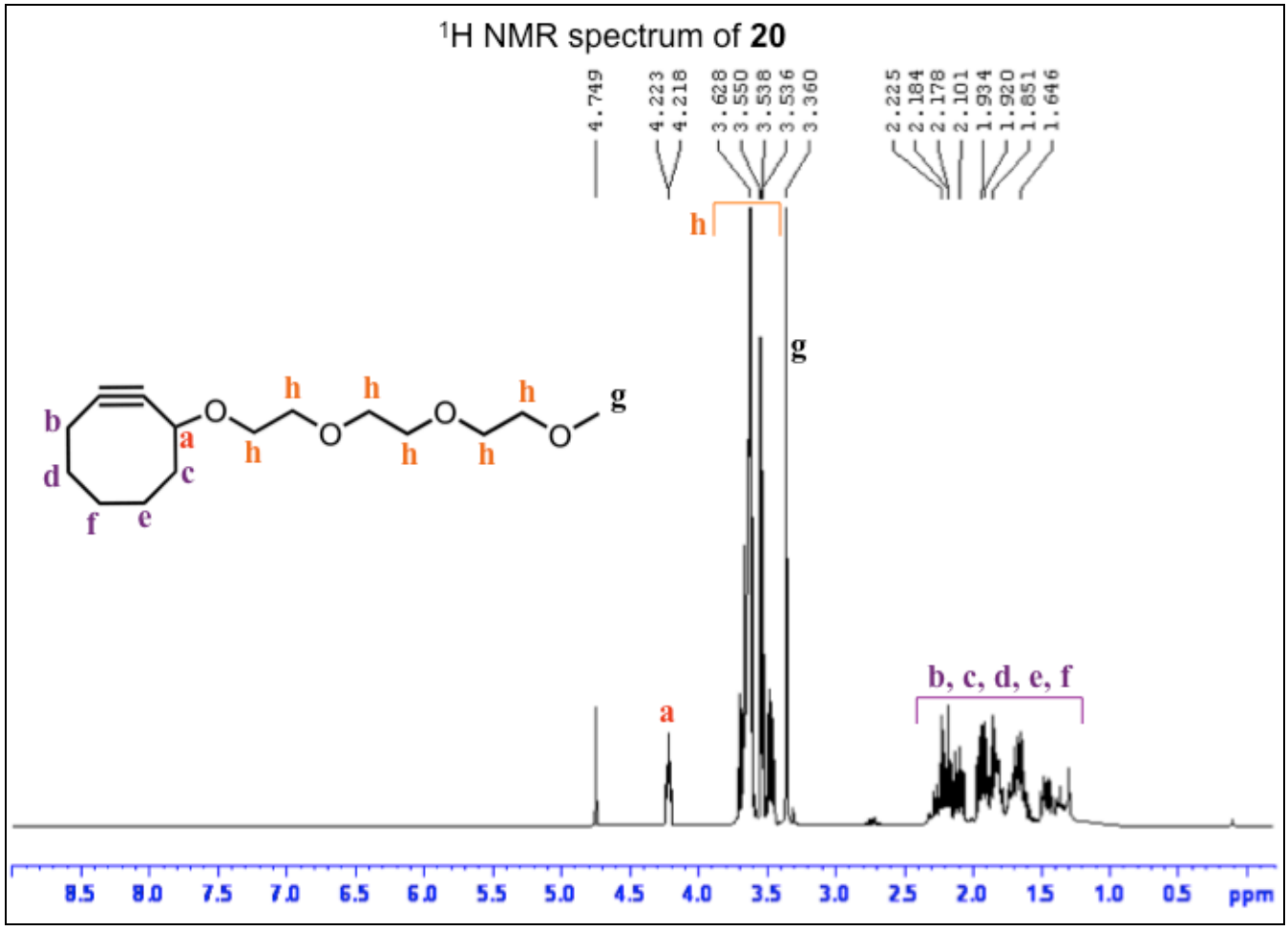


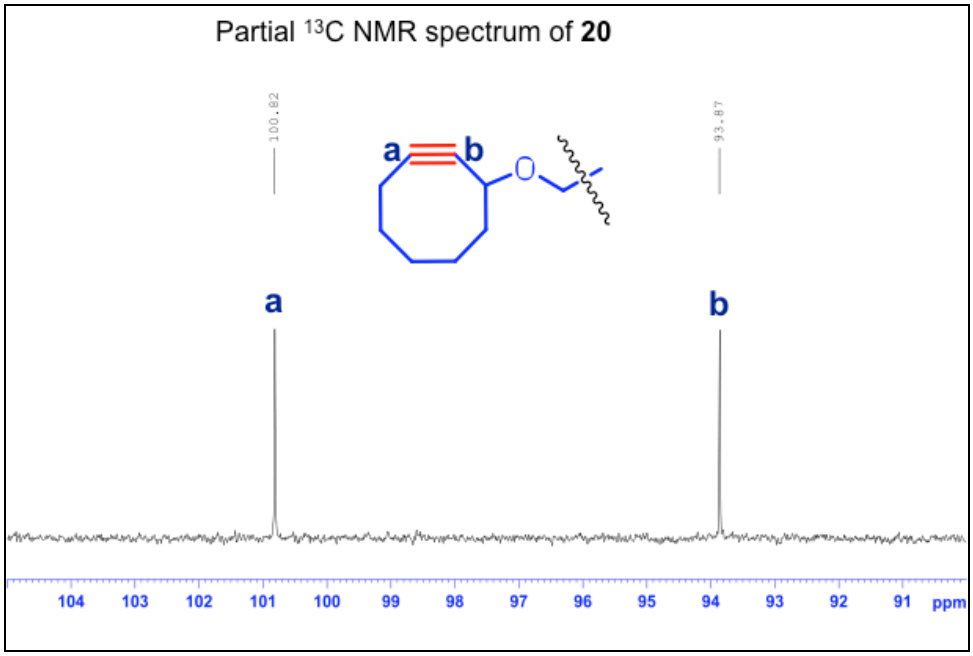
Chemical Formula: $C_{15}H_{26}O_4$
Molecular Weight: 270.36

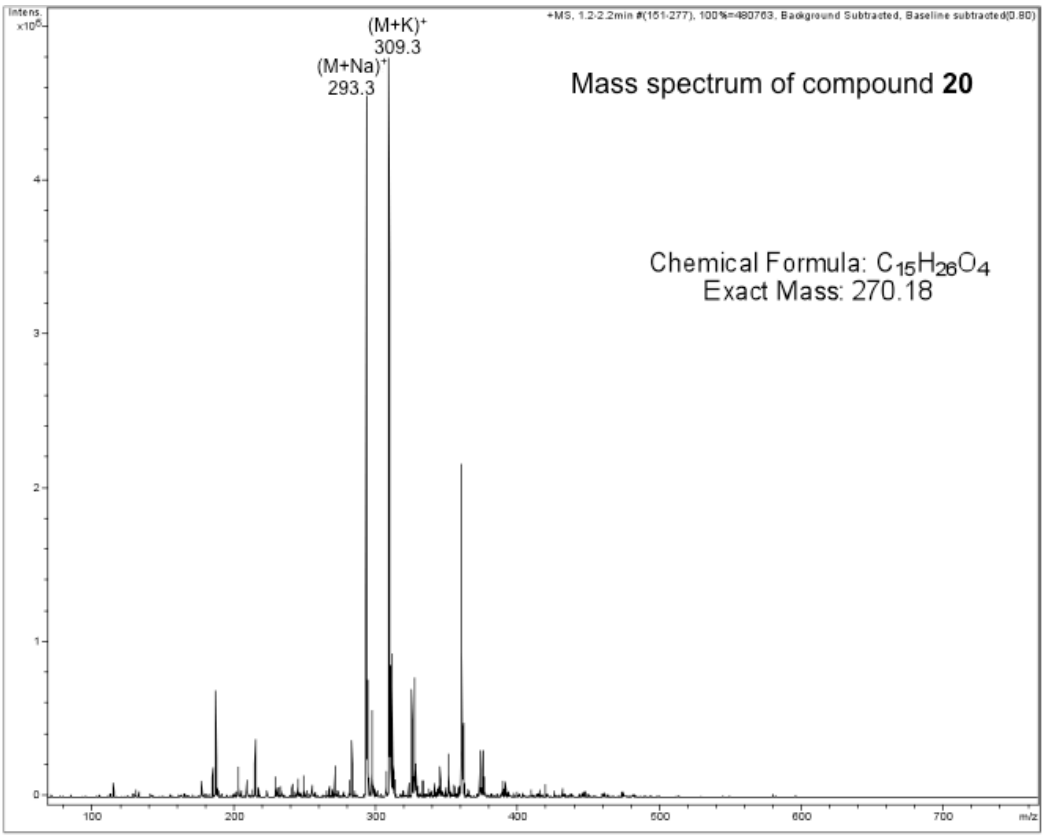
Compound **19** (0.484 g, 1.38 mmol) was dissolved in dry DMSO (10 mL) and DBU (2.14 mL, 13.8 mmol) was added. The reaction mixture was heated overnight at 60ºC. Water (200 mL) was added and the product was extracted three times with ethyl acetate. The organic layer was dried over sodium sulfate, filtered through paper and concentrated under *vacuum*. The product was purified by column chromatography using hexane/ethyl acetate (3:1) as eluent. Compound **20** was obtained as a colorless oil in 87% yield (0.325 g).

Note. Column chromatography was followed by TLC using phosphomolybdic acid stain (PMA).

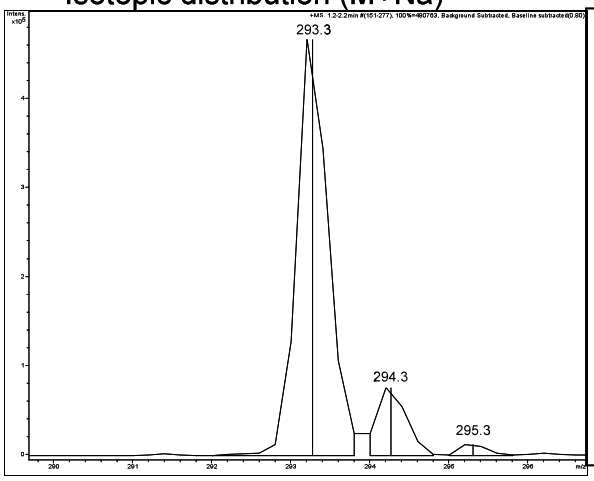
^{1}H NMR (MeOD, 400 MHz, δ_{ppm} *vs*. TMS): 4.22 (m, C*H*-O, 1H), 3.62-3.40 (m, OCH_2CH_2O, 12H), 3.36 (s, OCH_3, 3H), 2.23-1.20 (m, CH_2 of cyclooctyne ring, 8H). ^{13}C NMR (MeOD, 100 MHz, δ_{ppm} *vs*. TMS): 100.8 (*C*≡CCHO), 93.9 (C≡*C*CHO), 73.8 (*C*H-O), 73.1, 71.7, 71.6, 71.5, and 69.6 (O*C*H_2*C*H_2O), 59.3 (O*C*H_3), 39.1, 35.5, 31.1, 27.6 and 21.4 (*C*H_2 of cyclooctyne ring). MS-ESI (M+Na) *m/z* calcd for $C_{15}H_{26}O_4$Na: 293.2, found 293.3. Anal. calc. for $C_{15}H_{26}O_4$: C 66.64, H 9.69; found C 66.32, H 9.61.


¹H NMR spectrum of 20
4.749
4.223
4.218
3.628
3.550
3.538
3.536
3.360
2.225
2.184
2.178
2.101
1.934
1.920
1.851
1.646
h
g
a
b, c, d, e, f
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

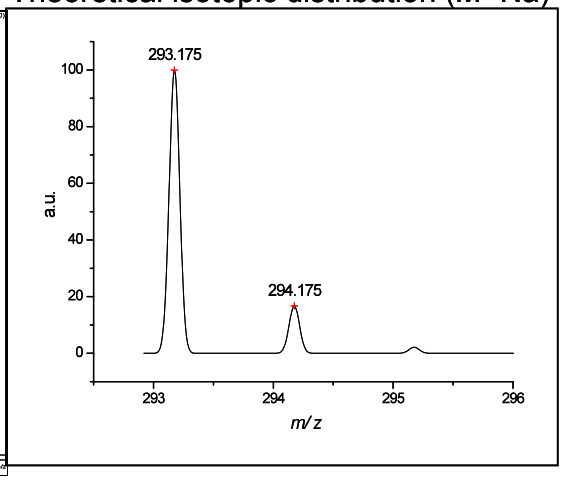

Partial ¹³C NMR spectrum of 20
100.82
93.87
a
b
104
103
102
101
100
99
98
97
96
95
94
93
92
91
ppm



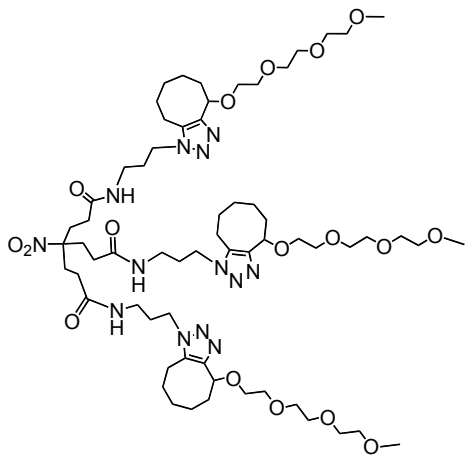
Isotopic distribution $(M+Na)^+$



Theoretical isotopic distribution $(M+Na)^+$



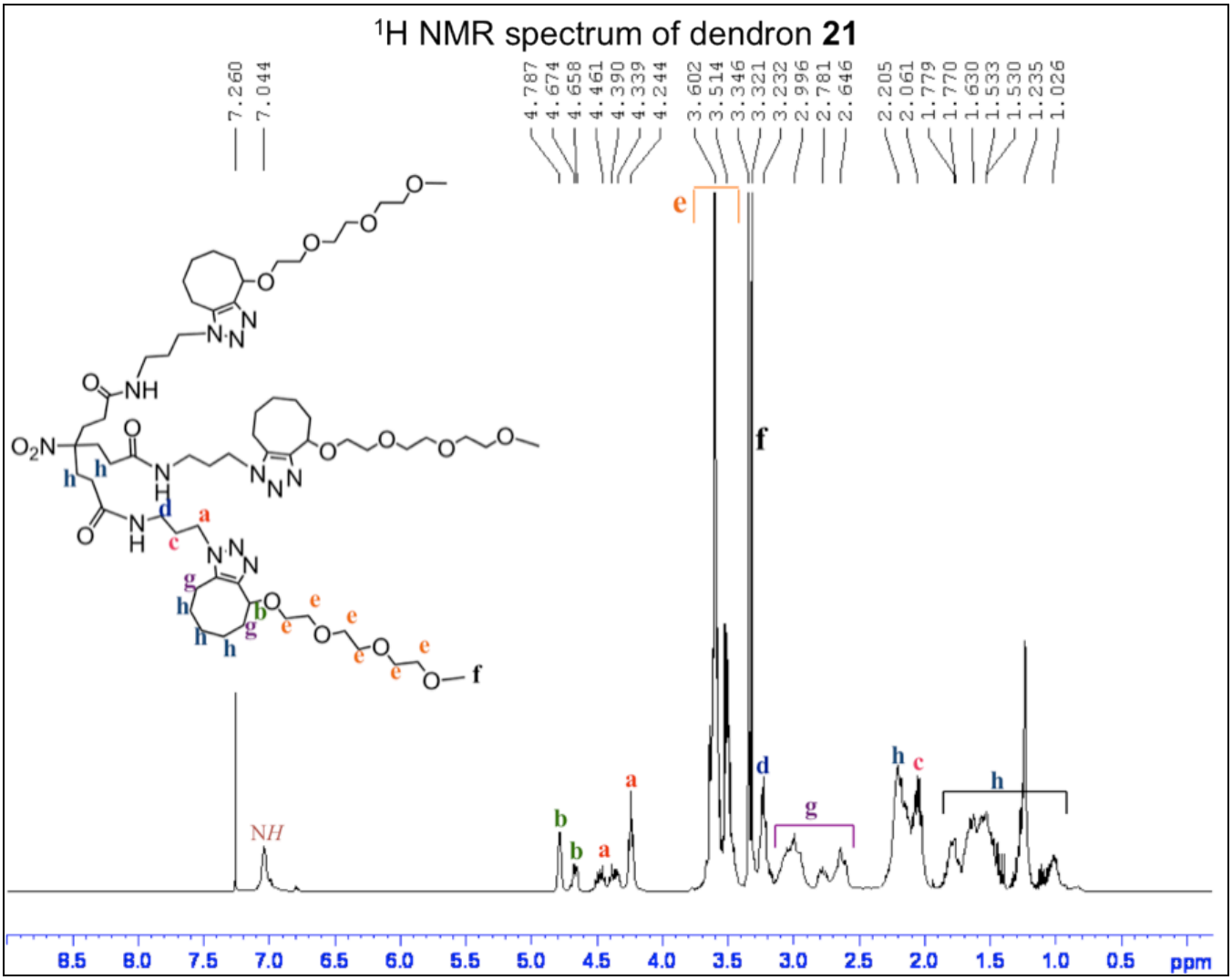
Synthesis of dendron 21

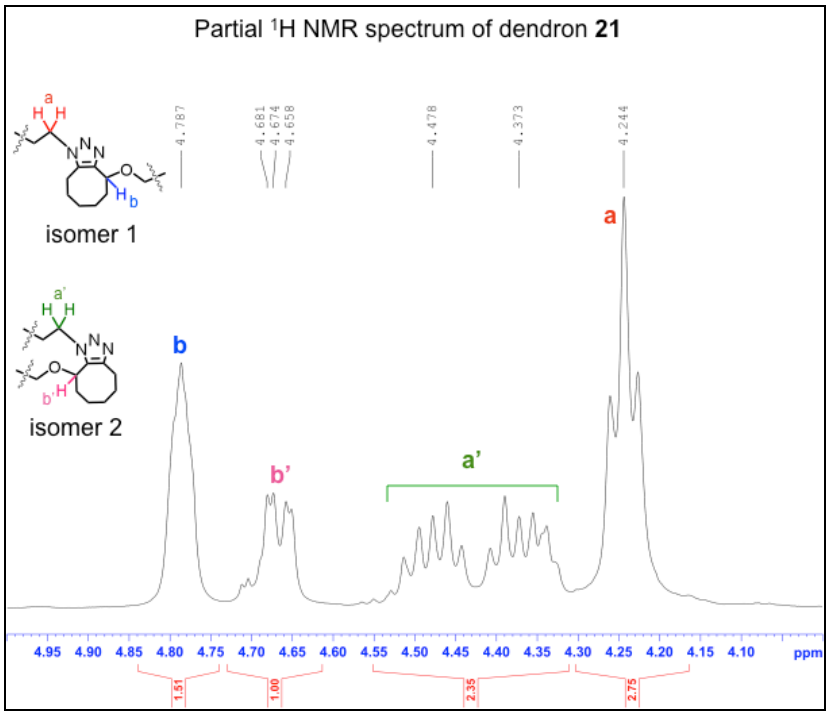


Chemical Formula: $C_{64}H_{111}N_{13}O_{17}$
Molecular Weight: 1334.64

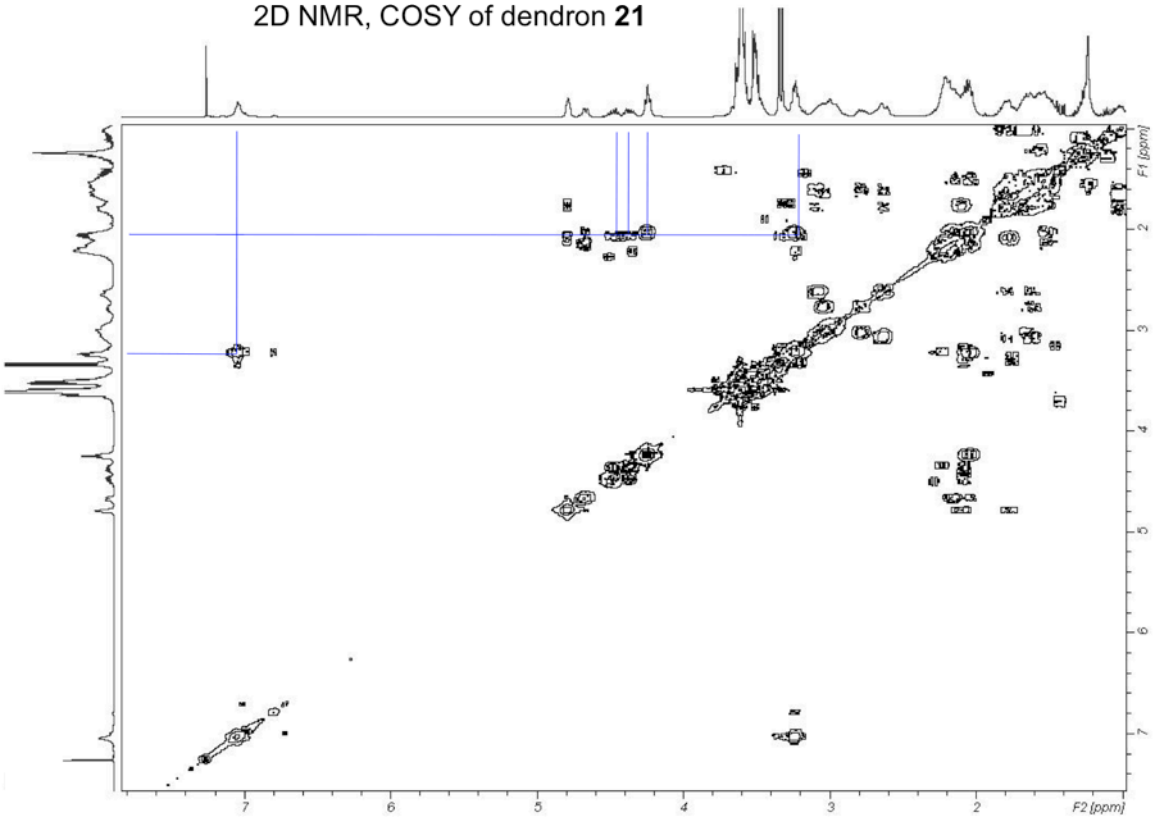
Dendron tris-azide **4** (0.012 g, 0.022 mmol) and cyclooctyne **20** (0.027 g, 0.100 mmol) were dissolved in 1 mL of ethanol. Water was added (1mL) and the solution became cloudy. The solution was stirred at room temperature for 24h resulting in a colorless solution. The solvents were removed and the product was washed twice with hexanes and precipitated from CH_2Cl_2/hexanes in order to remove the cyclooctyne that was added in excess. Dendron **21** was obtained as a colorless waxy product in 98% yield (0.029 g).

^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm} *vs.* TMS): 7.04 (s, CON*H*, 3H), 4.79 (s, C=CC*H*-O, isomer 1), 4.67 (m, C=CC*H*-O, isomer 2), 4.48 and 4.37 (m, CH_2-triazole, isomer 2), 4.24 (t, J = 6.78 Hz, CH_2-triazole, isomer 1), 3.64-3.4 (m, OCH_2CH_2O, 36H), 3.35 and 3.32 (s, OCH_3, 9H), 3.24 (m, CONHCH_2, 6H), 3.02-2.65 (m, CH_2C=CCHCH_2 of cyclooctene ring, 12H), 2.21 (m, CH_2CH_2NHCO, 12H), 2.06 (m, CONHCH_2, 6H), 1.78-1.02 (m, CH_2 of cyclooctene ring, 18H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm} *vs.* TMS): 171.9 and 171.6 (*C*=O), 145.7 and 144.4 (CH_2NC_q of triazole ring, both isomers), 134.1 and 133.3 ($CH_2N_3C_q$ of triazole ring, both isomers), 93.2 (NO_2C_q), 74.7 and 72.0 (*C*H-O of cyclooctene ring), 70.8-70.6 and 68.0 (O*C*H$_2$*C*H$_2$O), 59.1 (O*C*H$_3$), 46.8 and 45.4 (*C*H$_2$-triazole, both isomers), 36.0 (*C*H$_2$CH$_2$CH$_2$-triazole), 35.6 (CH$_2$*C*H$_2$CH$_2$-triazole), 31.7-17.5 (*C*H$_2$ of cyclooctene ring and *C*H$_2$*C*H$_2$CONH). MS-ESI $(M+Na)^+$ *m/z* calcd for $C_{64}H_{111}N_{13}O_{17}Na$: 1356.8, found 1357.0. Anal. calc. for $C_{64}H_{111}N_{13}O_{17}$: C 57.59, H 8.38; found C 57.68, H 8.42.

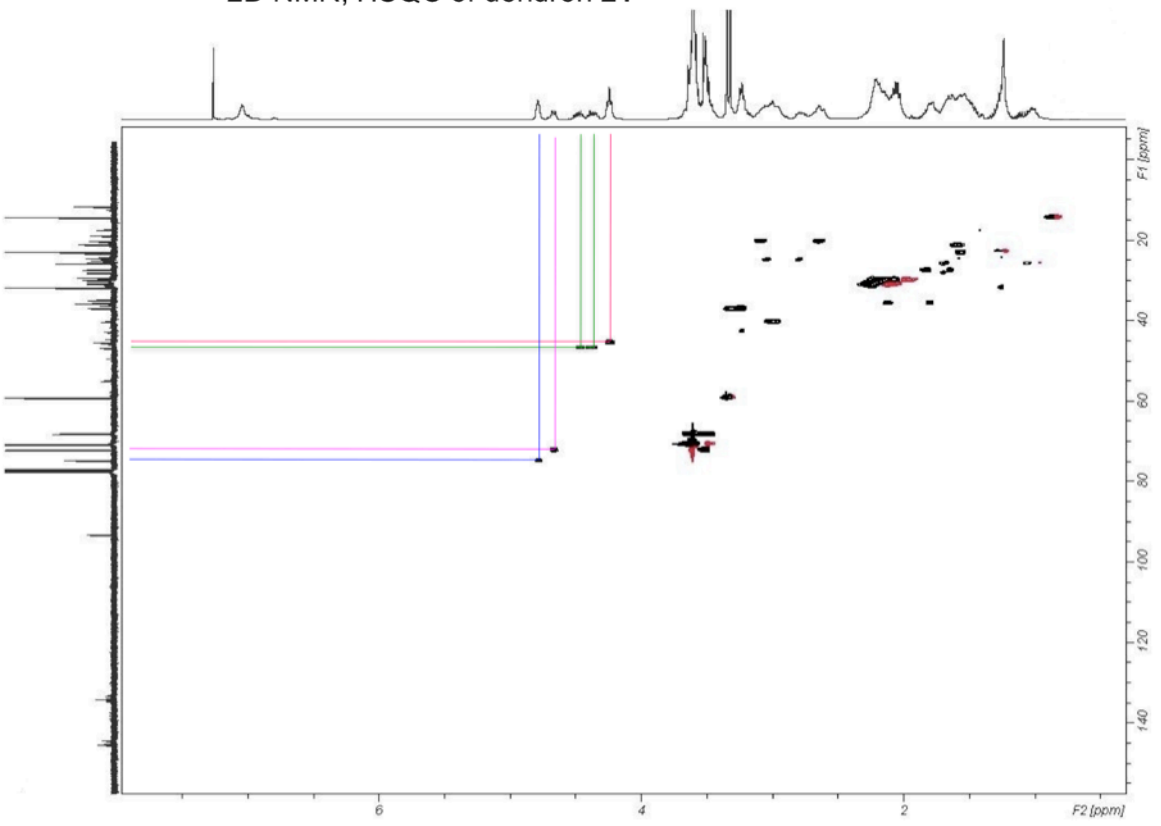

^{1}H NMR spectrum of dendron **21**
7.260
7.044
4.787
4.674
4.658
4.461
4.390
4.339
4.244
3.602
3.514
3.346
3.321
3.232
2.996
2.781
2.646
2.205
2.061
1.779
1.770
1.630
1.533
1.530
1.235
1.026
NH
ppm

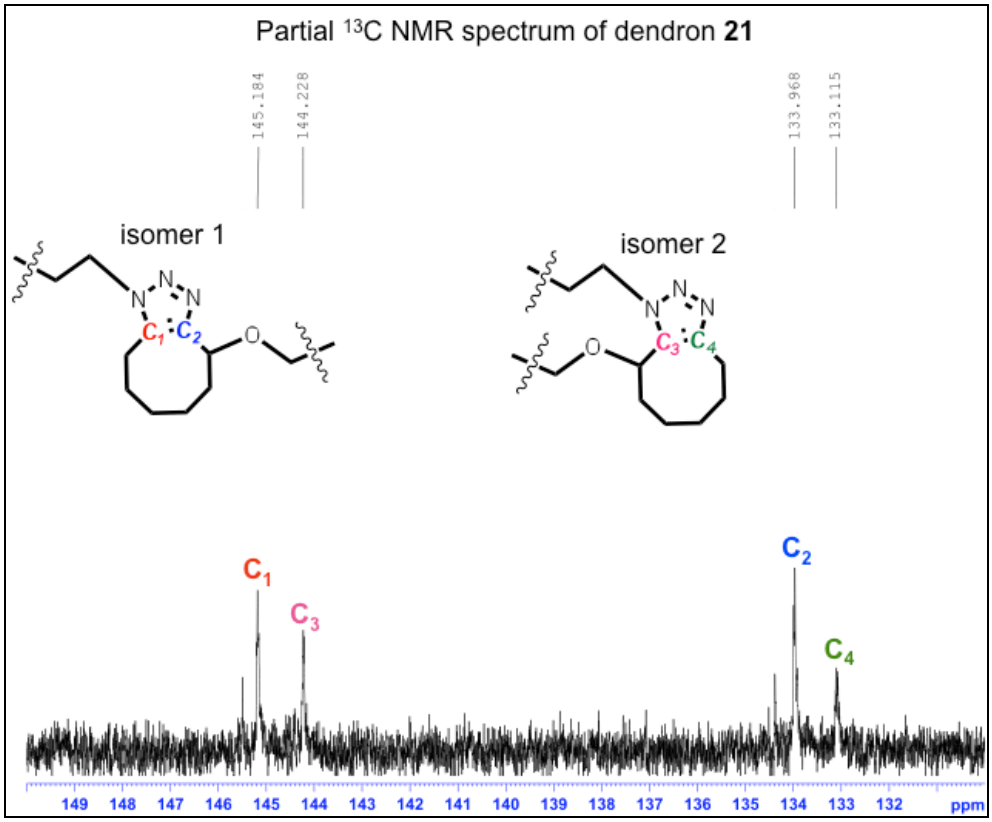

Partial ^{1}H NMR spectrum of dendron **21**
isomer 1
isomer 2
4.787
4.681
4.674
4.658
4.478
4.373
4.244
ppm

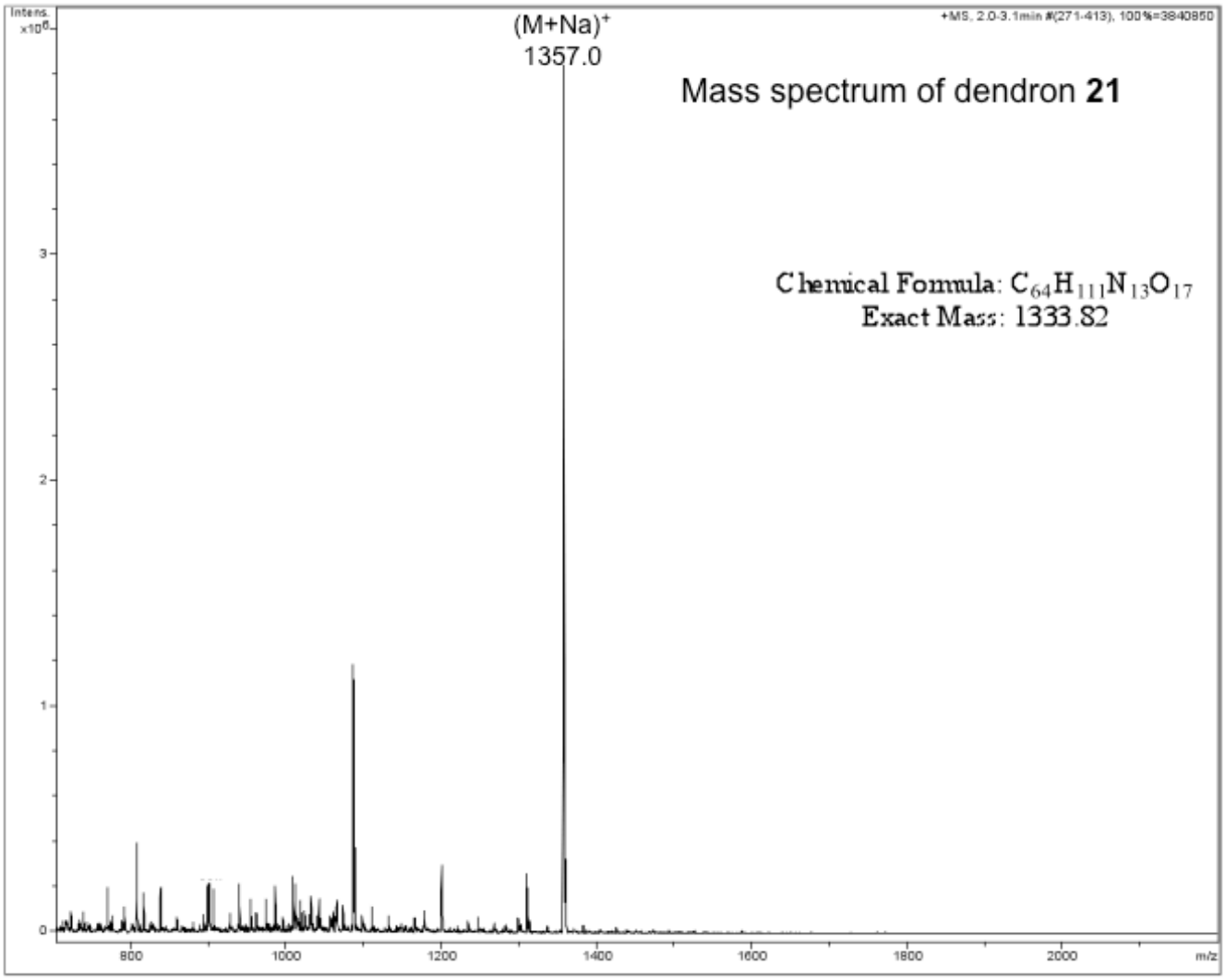
2D NMR, COSY of dendron **21**



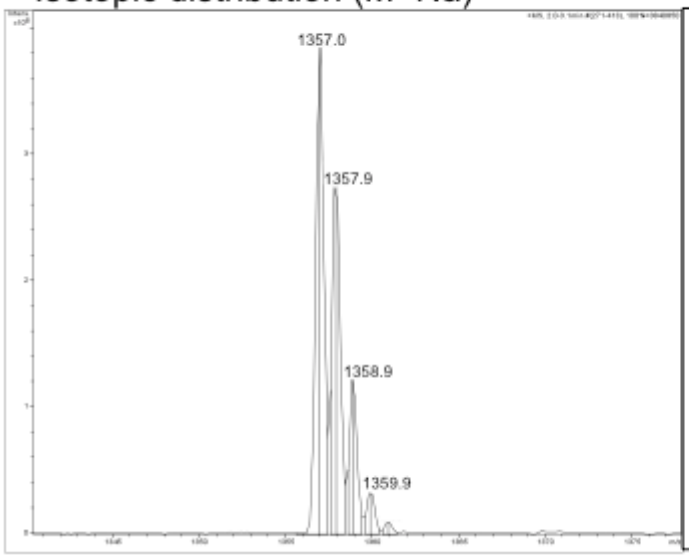
2D NMR, HSQC of dendron **21**



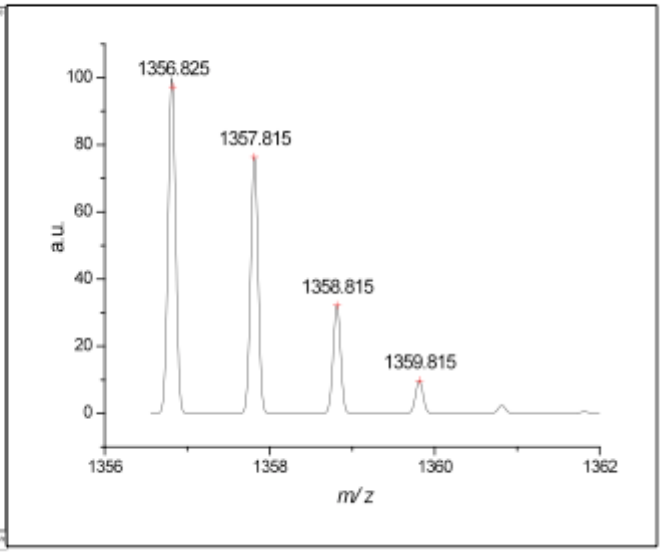

Partial ^{13}C NMR spectrum of dendron **21**
145.184
144.228
133.968
133.115
isomer 1
isomer 2
C_1
C_2
C_3
C_4
149 148 147 146 145 144 143 142 141 140 139 138 137 136 135 134 133 132 ppm



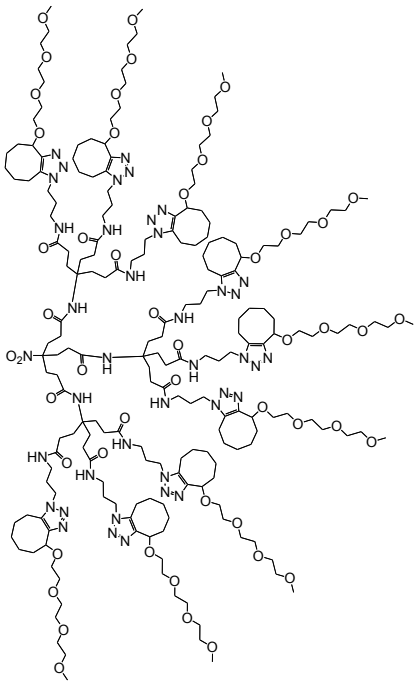
Isotopic distribution $(M+Na)^+$



Theoretical isotopic distribution $(M+Na)^+$



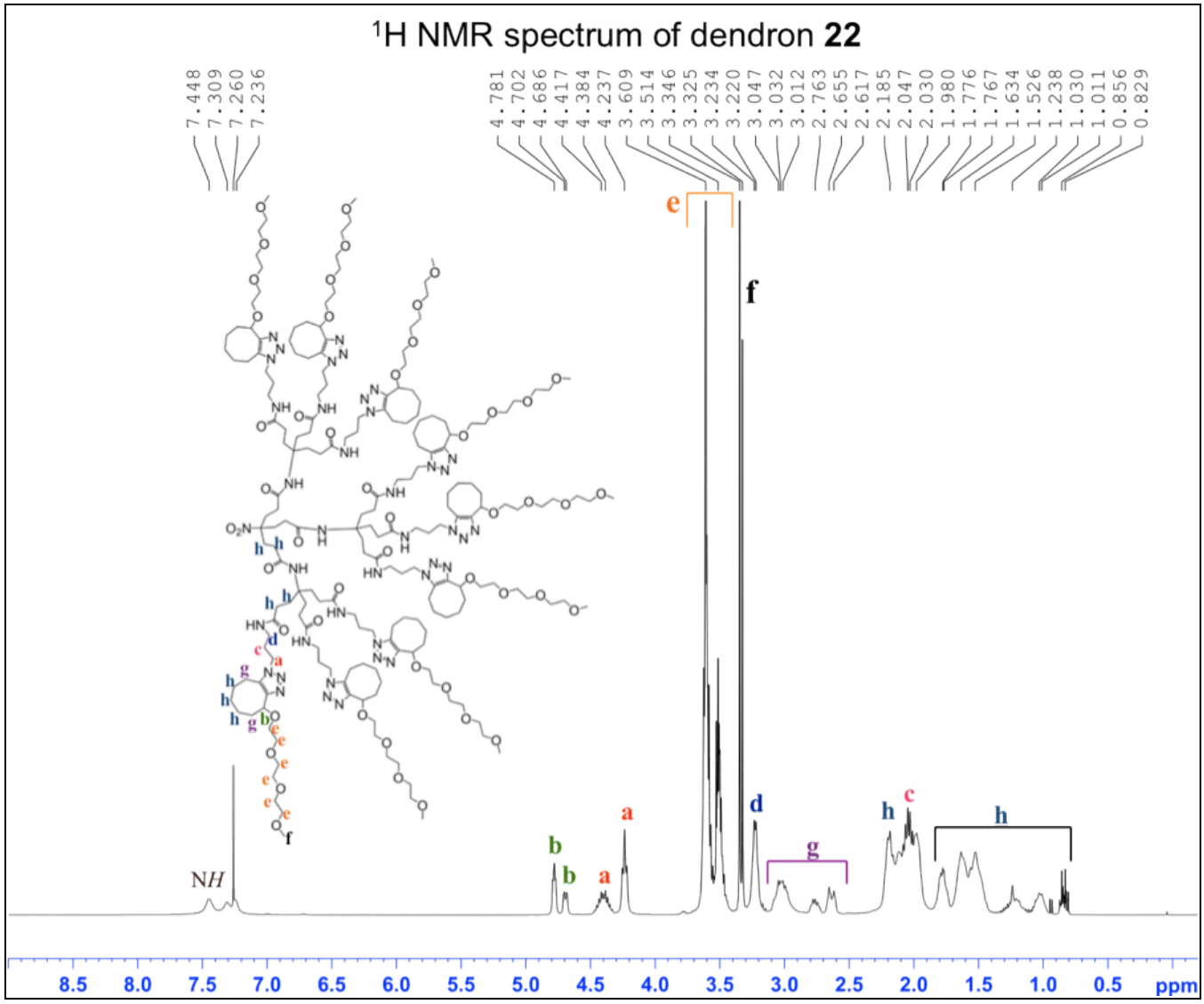
Synthesis of dendron 22

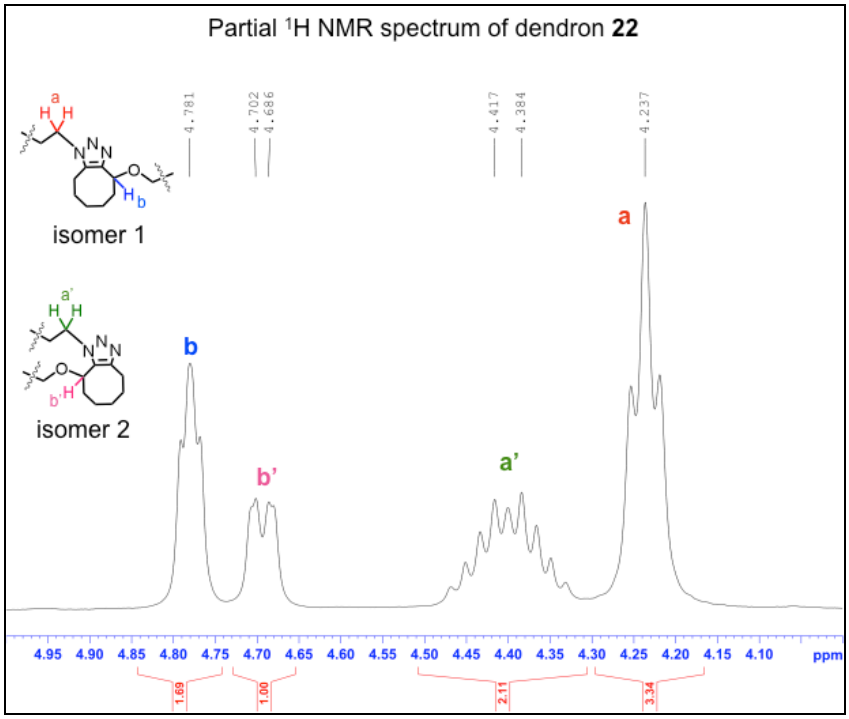


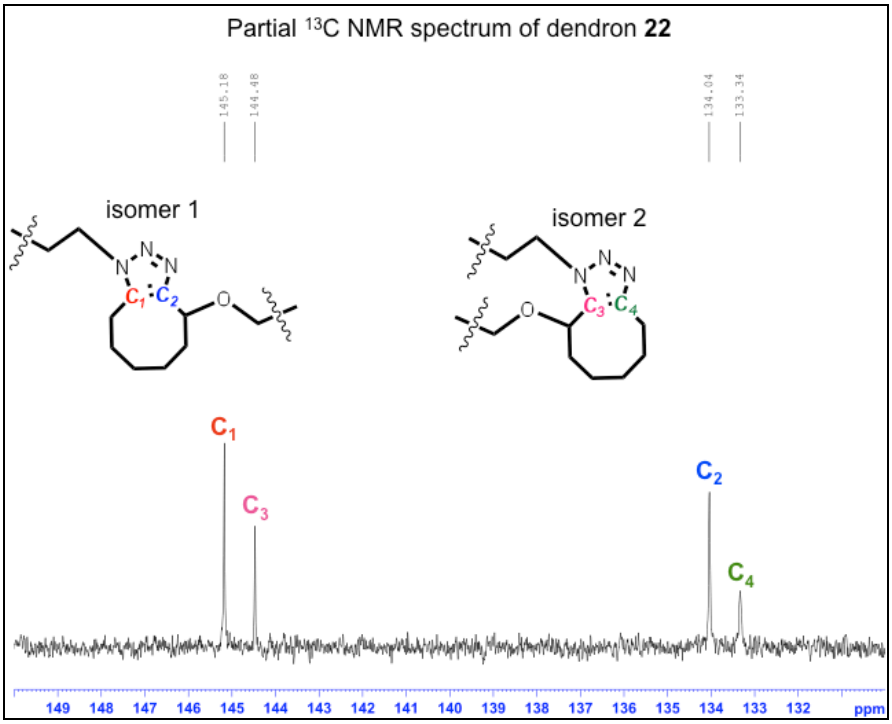
Chemical Formula: $C_{202}H_{348}N_{40}O_{50}$
Molecular Weight: 4137.16

Dendron nona-azide **8** (0.020 g, 0.012 mmol) and cyclooctyne **20** (0.029 g, 0.106 mmol) were dissolved in 1 mL of ethanol. Water was added (1mL) and the solution became cloudy. The solution was stirred at room temperature for 24h resulting in a colorless solution. The solvent was removed and the product was washed twice with hexanes and precipitated from CH_2Cl_2/hexanes in order to remove the cyclooctyne that was added in excess. Dendron **22** was obtained as a colorless waxy product in 97% yield (0.048 g).

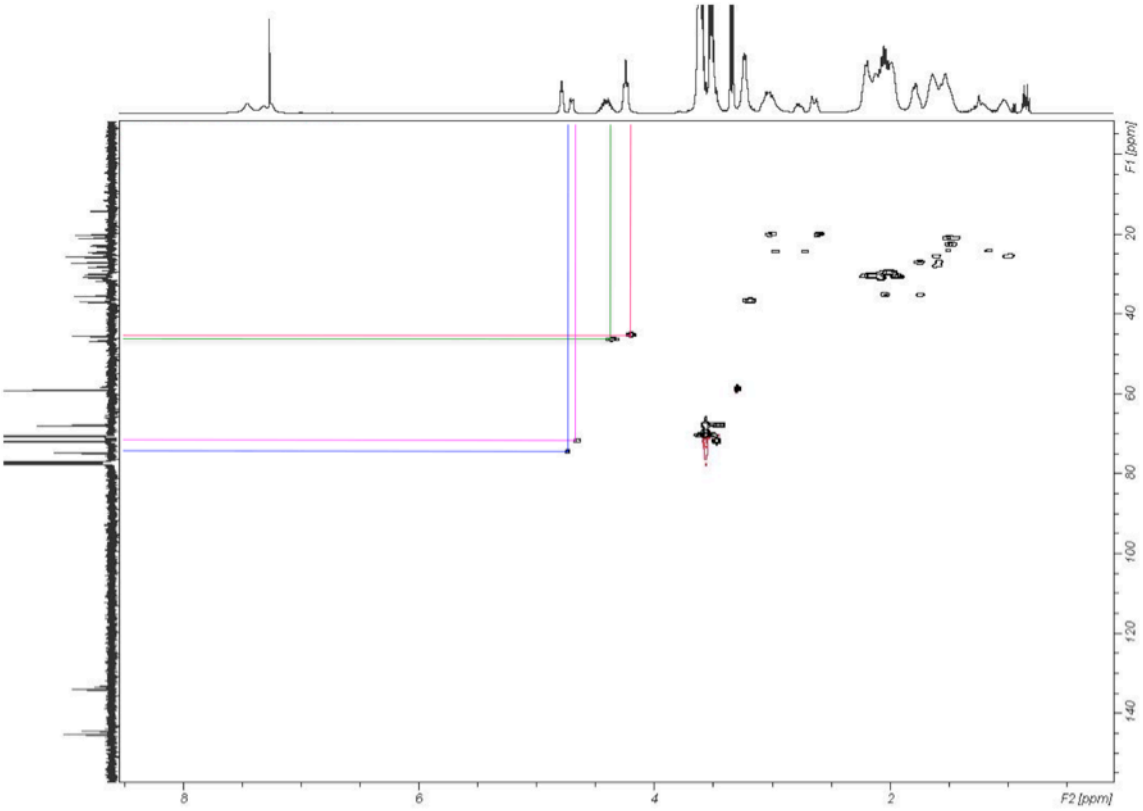
^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm} *vs.* TMS): 7.45 (s, CON*H*, 12H), 4.78 (s, C=CC*H*-O, isomer 1), 4.69 (m, C=CC*H*-O, isomer 2), 4.40 (m, CH_2-triazole, isomer 2), 4.24 (t, J = 6.88 Hz, CH_2-triazole, isomer 1), 3.62-3.45 (m, OCH_2CH_2O, 108H), 3.35 and 3.33 (s, OCH_3, 27H), 3.23 (m, CONHCH_2, 18H), 3.02-2.62 (m, CH_2C=CCHCH_2 of cyclooctene ring, 36H), 2.19 and 1.98 (m, CH_2CH_2NHCO, 48H), 2.04 (m, CONHCH_2, 18H), 1.78-1.02 (m, CH_2 of cyclooctene ring, 54H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm} *vs.* TMS): 173.9 and 173.7 (*C*=O), 145.2 and 144.5 (CH_2NC_q of triazole ring, both isomers), 134.1 and 133.3 ($CH_2N_3C_q$ of triazole ring, both isomers), 74.7 and 72.0 (*C*H-O of cycloctene ring), 70.8-70.6 and 68.0 (O*C*H_2*C*H_2O), 59.2 and 59.1 (O*C*H_3), 46.8 and 45.5 (*C*H_2-triazole, both isomers), 36.9 (*C*H_2CH$_2$CH$_2$-triazole), 35.6 (CH$_2$*C*H_2CH$_2$-triazole), 31.7-17.5 (*C*H_2 of cyclooctene ring and *C*H_2*C*H_2CONH). MALDI-TOF $(M+H)^+$ *m/z* calcd for $C_{202}H_{349}N_{40}O_{50}$: 4134.6, found 4135.7. Anal. calc. for $C_{202}H_{348}N_{40}O_{50}$: C 58.63, H 8.48; found C 58.77, H 8.51.

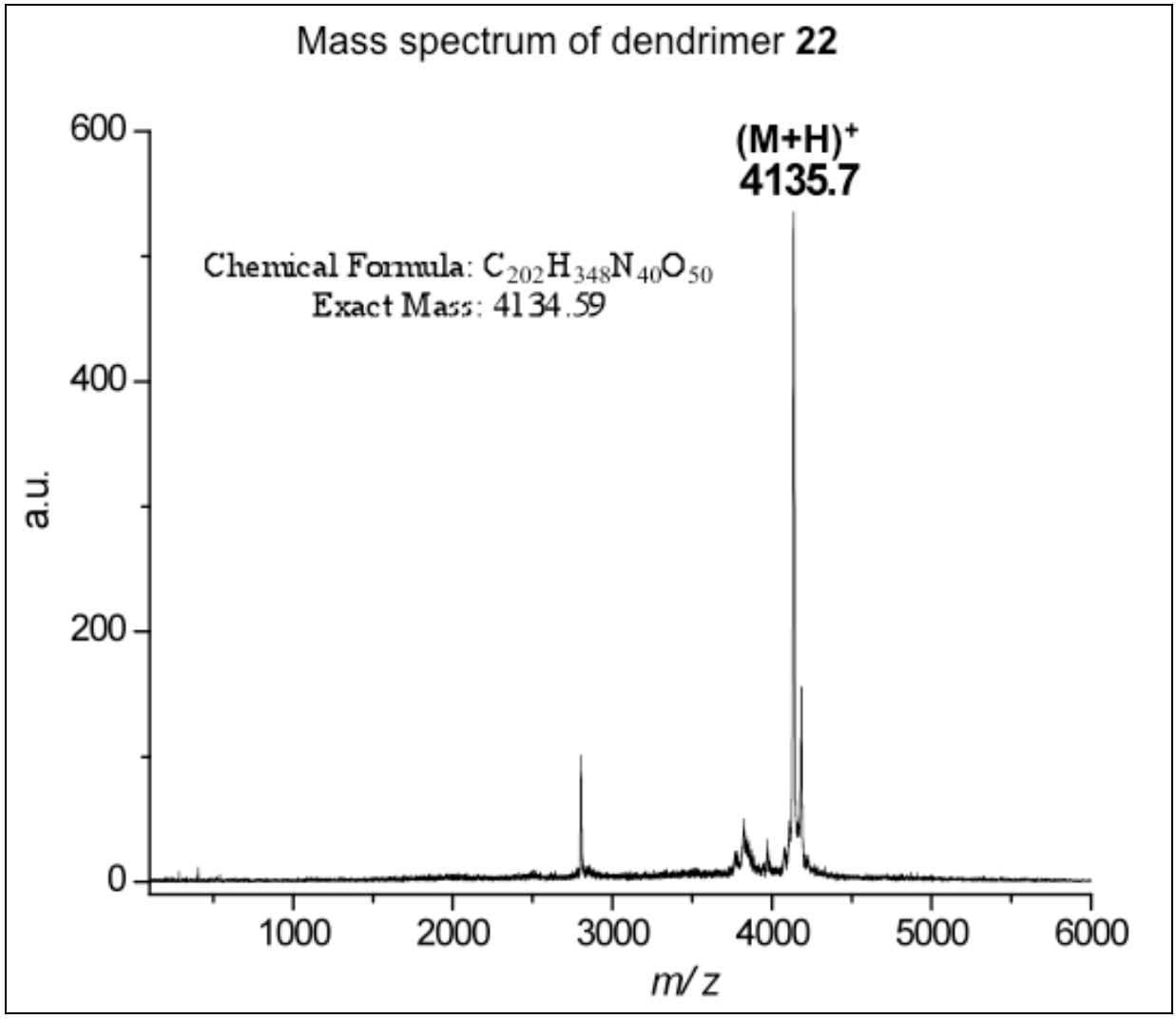

^{1}H NMR spectrum of dendron **22**
7.448
7.309
7.260
7.236
4.781
4.702
4.686
4.417
4.384
4.237
3.609
3.514
3.346
3.325
3.234
3.220
3.047
3.032
3.012
2.763
2.655
2.617
2.185
2.047
2.030
1.980
1.776
1.767
1.634
1.526
1.238
1.030
1.011
0.856
0.829
NH
b
b
a
a
e
f
d
g
h
c
h
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


Partial ^{1}H NMR spectrum of dendron **22**
isomer 1
isomer 2
4.781
4.702
4.686
4.417
4.384
4.237
a
b
b'
a'
4.95
4.90
4.85
4.80
4.75
4.70
4.65
4.60
4.55
4.50
4.45
4.40
4.35
4.30
4.25
4.20
4.15
4.10
ppm
1.69
1.00
2.11
3.34

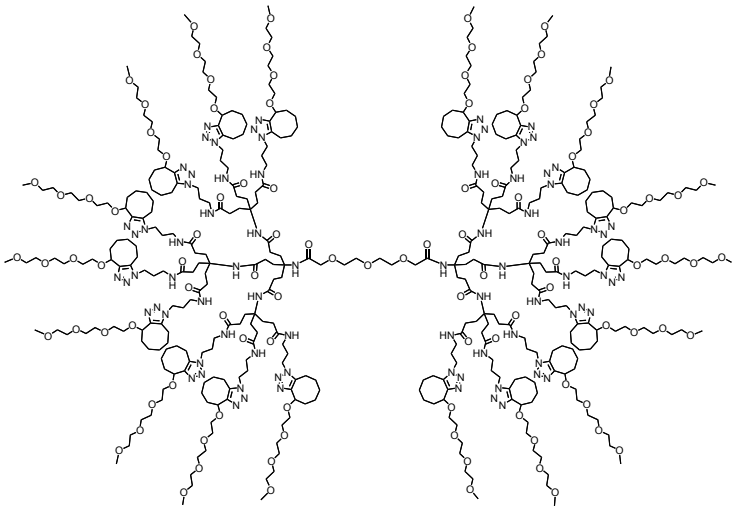


2D NMR, HSQC of dendron **22**




Mass spectrum of dendrimer 22
(M+H)+
4135.7
Chemical Formula: C202H348N40O50
Exact Mass: 4134.59
600
400
200
0
a.u.
1000
2000
3000
4000
5000
6000
m/z

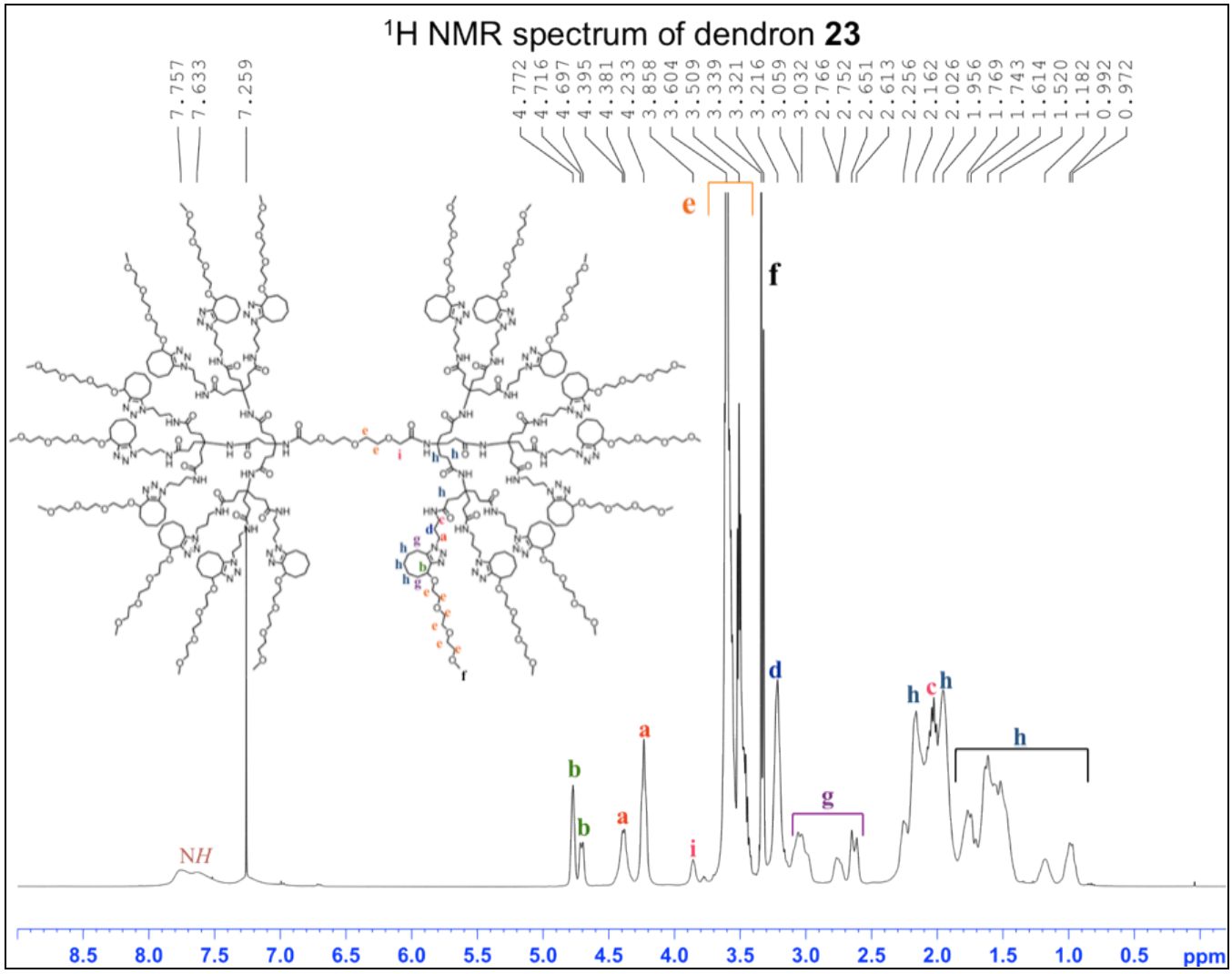
Synthesis of dendrimer 23

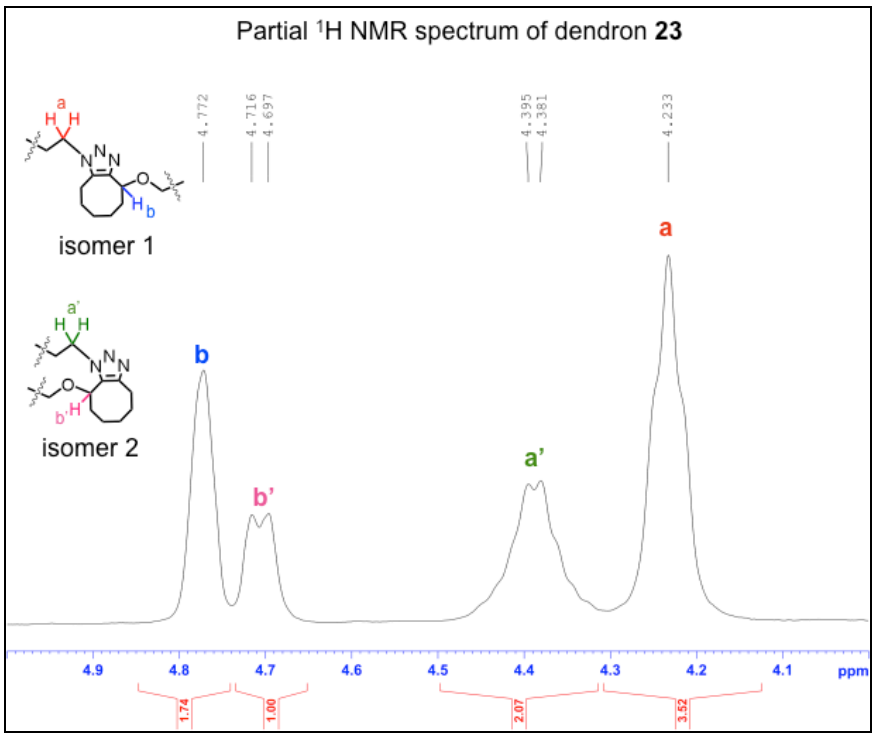


Chemical Formula: $C_{412}H_{710}N_{80}O_{101}$
Molecular Weight: 8400.52

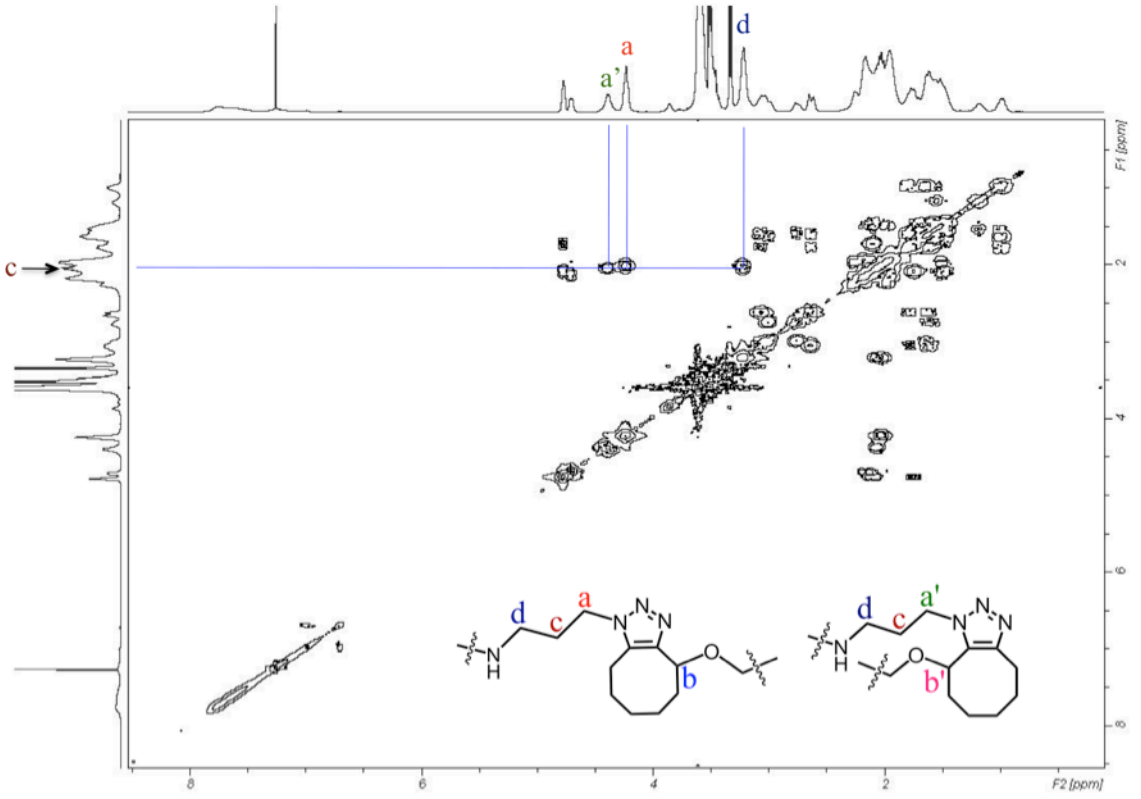
Dendrimer eighteen-azide **13** (0.013 g, 0.0037 mmol) and cyclooctyne **20** (0.027 g, 0.100 mmol) were dissolved in 1 mL of ethanol. Water was added (1mL) and the solution became cloudy. The solution was stirred at room temperature for 24h resulting in a colorless solution. The solvent was removed and the product was washed twice with hexanes and precipitated from CH_2Cl_2/hexanes in order to remove the cyclooctyne that was added in excess. Dendrimer **23** was obtained as a colorless waxy product in 95% yield (0.030 g).

^{1}H NMR ($CDCl_3$, 400 MHz, δ_{ppm} *vs.* TMS): 7.76 (s, CON*H*, 26H), 4.77 (s, C=CC*H*-O, isomer 1), 4.70 (m, C=CC*H*-O, isomer 2), 4.39 (m, CH_2-triazole, isomer 2), 4.23 (t, J = 6.84 Hz, CH_2-triazole, isomer 1), 3.89 (s, OCH_2CONH, 4H), 3.65-3.45 (m, OCH_2CH_2O, 224H), 3.34 and 3.32 (s, OCH_3, 54H), 3.22 (m, CONHCH_2, 36H), 3.06-2.62 (m, CH_2C=CCHCH_2 of cyclooctene ring, 72H), 2.25, 2.16 and 1.96 (m, CH_2CH_2NHCO, 96H), 2.03 (m, CONHCH_2, 36H), 1.77-0.97 (m, CH_2 of cyclooctene ring, 108H). ^{13}C NMR ($CDCl_3$, 100 MHz, δ_{ppm} *vs.* TMS): 174.2-173.4 (*C*=O), 145.2 and 144.5 (CH_2NC_q of triazole ring, both isomers), 134.1 and 133.4 ($CH_2N_3C_q$ of triazole ring, both isomers), 74.7 and 72.0 (*C*H-O of cycloctene ring), 70.4-70.6 and 68.0 (O*C*H$_2$*C*H$_2$O and O*C*H$_2$NHCO), 59.2 (O*C*H$_3$), 46.7 and 45.5 (*C*H$_2$-triazole, both isomers), 37.0 (*C*H$_2$CH$_2$CH$_2$-triazole), 35.6 (CH$_2$*C*H$_2$CH$_2$-triazole), 31.7-20.2 (*C*H$_2$ of cyclooctene ring and *C*H$_2$*C*H$_2$CONH). MALDI-TOF $(M+H)^+$ *m/z* calcd for $C_{412}H_{710}N_{80}O_{101}$: 8396.1, found 8395.3. Anal. calc. for $C_{412}H_{710}N_{81}O_{101}$: C 58.91, H 8.52; found C 59.11, H 8.59.

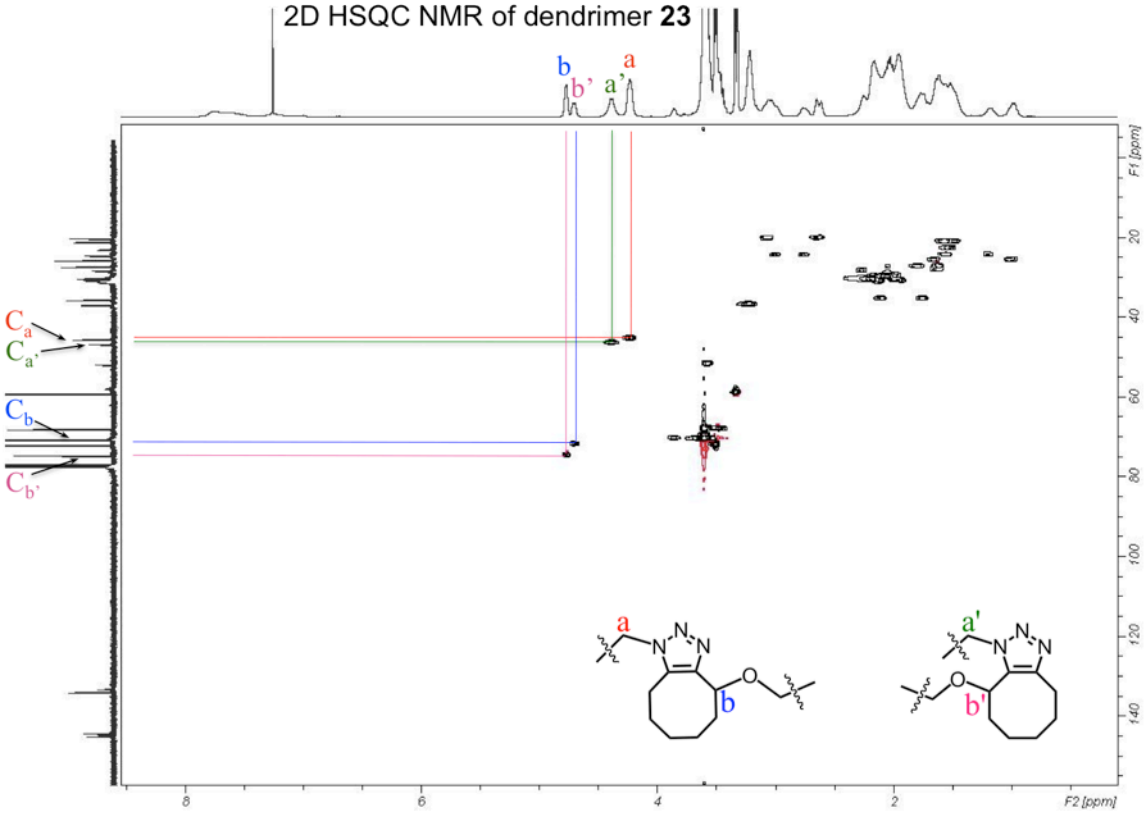

¹H NMR spectrum of dendron 23
7.757
7.633
7.259
4.772
4.716
4.697
4.395
4.381
4.233
3.858
3.604
3.509
3.339
3.321
3.216
3.059
3.032
2.766
2.752
2.651
2.613
2.256
2.162
2.026
1.956
1.769
1.743
1.614
1.520
1.182
0.992
0.972
NH
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

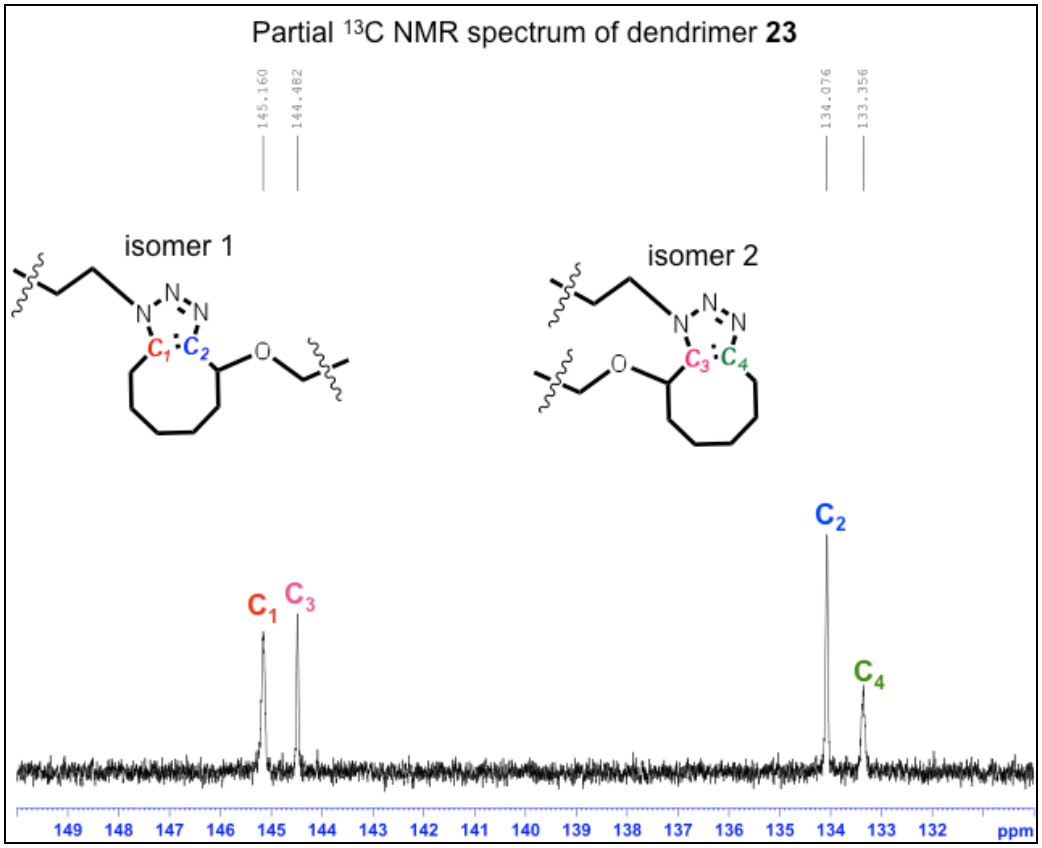

Partial ¹H NMR spectrum of dendron 23
isomer 1
isomer 2
4.772
4.716
4.697
4.395
4.381
4.233
4.9
4.8
4.7
4.6
4.5
4.4
4.3
4.2
4.1
ppm
1.74
1.00
2.07
3.52

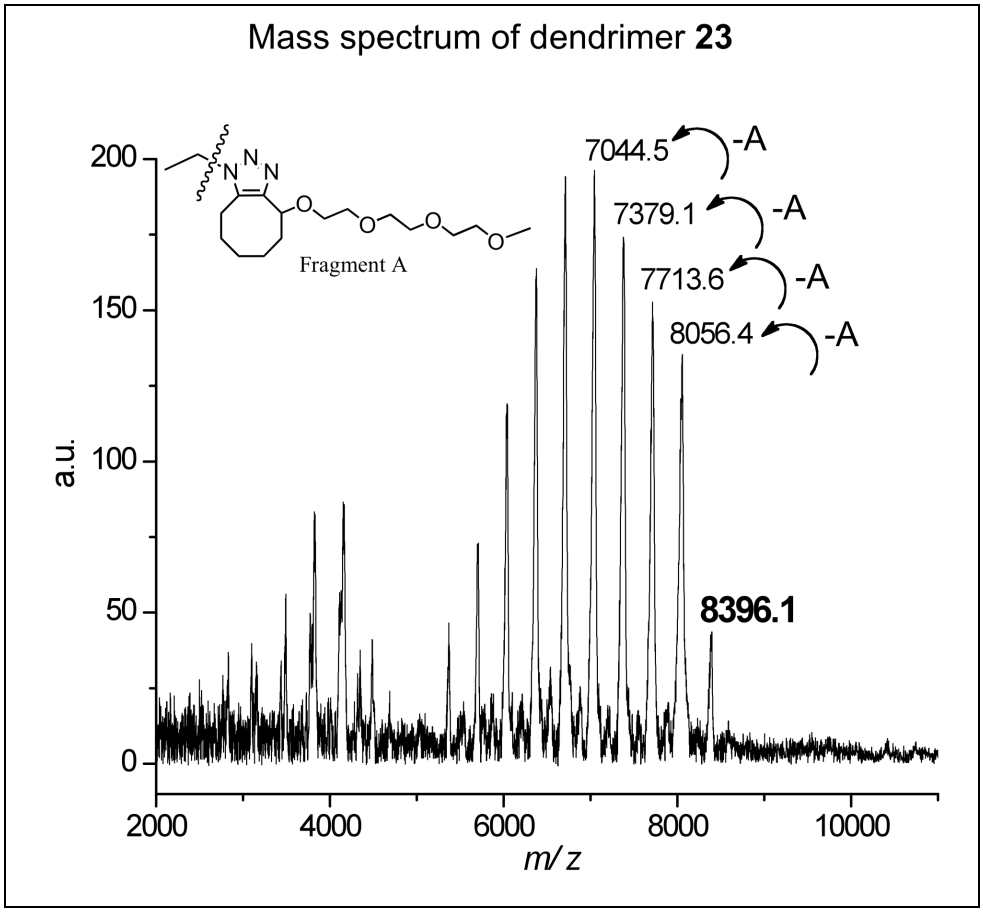
2D COSY NMR of dendrimer **23**



2D HSQC NMR of dendrimer **23**




Partial 13C NMR spectrum of dendrimer 23
145.160
144.482
134.076
133.356
isomer 1
isomer 2
C1
C2
C3
C4
149 148 147 146 145 144 143 142 141 140 139 138 137 136 135 134 133 132 ppm


Mass spectrum of dendrimer 23
Fragment A
7044.5
7379.1
7713.6
8056.4
-A
8396.1
a.u.
200
150
100
50
0
2000
4000
6000
8000
10000
m/z