Nanometer-Sized Amino Acids for the Synthesis of Nanometer-Scale Water-Soluble Molecular Rods of Precise Length

Chris M. Gothard, Nosheen A. Rao, and James S. Nowick*

Department of Chemistry, University of California, Irvine, Irvine, California 92697-2025.

Supporting Information Table of Contents

Synthetic Intermediates (**1**, **3**-**8**)

H-(Abc^{2K})$_1$-NH_2 **9a**

H-(Abc^{2K})$_2$-NH_2 **9b**

H-(Abc^{2K})$_3$-NH_2 **9c**

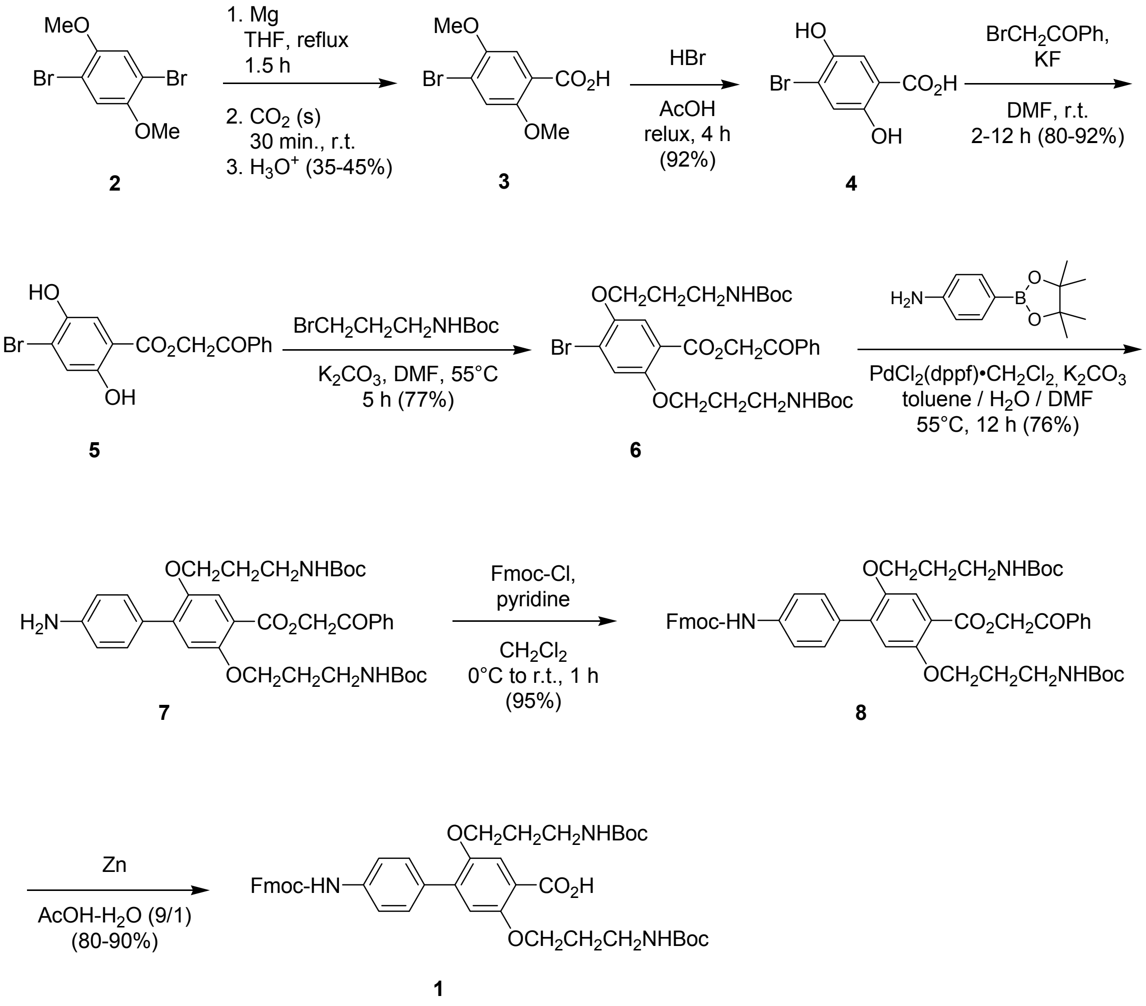
H-(Abc^{2K})$_4$-NH_2 **9d**

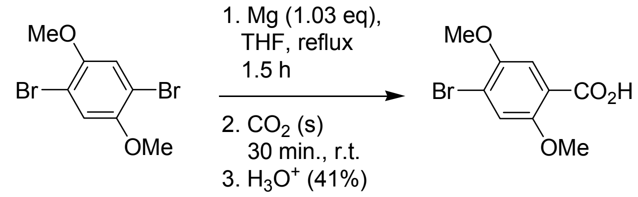
H-(Abc^{2K})$_5$-NH_2 **9e**

H-(Abc^{2K})$_6$-NH_2 **9f**

General Procedures. Commercial solvents and reagents were used without further purification, unless otherwise stated. Reactions were carried out under an atmosphere of nitrogen. Solution-phase reactions were monitored by thin-layer chromatography (TLC) and carried out on 250 µm silica gel polyester plates on fluorescent silica gel with UV visualization. Column chromatography was performed on 40–63 µm silica gel (EMD Science) using flash chromatography. Solvents were removed by rotary evaporation. Residual solvents were removed under vacuum (< 0.01 mmHg). Precipitated and recrystallized products were dried under vacuum (< 0.01 mmHg) or by air suction through a filter funnel. High resolution mass spectra were obtained by electrospray ionization (ESI) on a Waters Micromass LCT Premier (instrument variation $\sigma < 5$ ppm). NMR spectra were recorded using a 500 MHz Bruker AVANCE^{TM} spectrometer. Chemical shifts are reported in parts per million (ppm) on the δ scale. ^{1}H and ^{13}C NMR spectra in CD_3SOCD_3 were referenced with TMS ($\delta = 0.00$ ppm); ^{1}H NMR spectra in D_2O were referenced to HDO at $\delta = 4.80$ ppm. IR spectra were obtained using a Galaxy Series FTIR 5000. HPLC analysis was performed on an analytical RP-HPLC instrument, using a C_{18} column (Alltech, Platinum Rocket, 3µm packing, 7 mm × 53 mm).

Fmoc-Abc$^{2K(Boc)}$-OH (1) Synthetic Scheme.





1,4-dibromo-2,5-dimethoxybenzene (**2**)

4-bromo-2,5-dimethoxybenzoic acid (**3**)

4-Bromo-2,5-dimethoxybenzoic acid[1] **(3).** A solution of 1,4-dibromo-2,5-dimethoxybenzene (5.00 g, 16.9 mmol) in THF (80 mL) was added in drops over 30 min to a refluxing mixture of magnesium turnings (0.42 g, 17 mmol) and THF (10 mL). The mixture was heated at reflux for an additional hour and then allowed to cool to 25 °C before solid CO_2 (ca. 5 g, 100 mmol) was added in small portions. The mixture was stirred for an additional 15 min, concentrated by rotary evaporation to approximately one fifth of its original volume, and then cooled in an ice-bath. The cooled solution was acidified with concd HCl (aq) to form a white precipitate and then extracted into ether (100 mL). The organic layer was washed with water (ca. 100 mL) and then extracted into aq 1 M KOH (3 × ca. 20 mL). The alkaline solution was acidified with concd HCl (aq), and the solids were washed with water to give a brown solid. Recrystallization from acetic acid–water (ca. 50 mL, 1/1, *v*/*v*) provided 4-bromo-2,5-dimethoxybenzoic acid (**3**) as an off-white solid (1.81 g, 41%): mp 169-171 °C; IR (KBr) 3500-2200 (br), 2634, 1697, 1604, 1569 cm^{-1}; ^1H NMR (500 MHz, CD_3SOCD_3, 298 K) δ 12.87 (s, 1 H), 7.38 (s, 1 H), 7.33 (s, 1 H), 3.82 (s, 3 H), 3.79 (s, 3 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 166.4, 152.3, 148.9, 120.9, 117.8, 114.9, 113.8, 56.6, 56.5; HRMS (ESIMS) *m/z* for $C_9H_9BrO_4Na$ $[M+Na]^+$ calcd 282.9582, found 282.9573.

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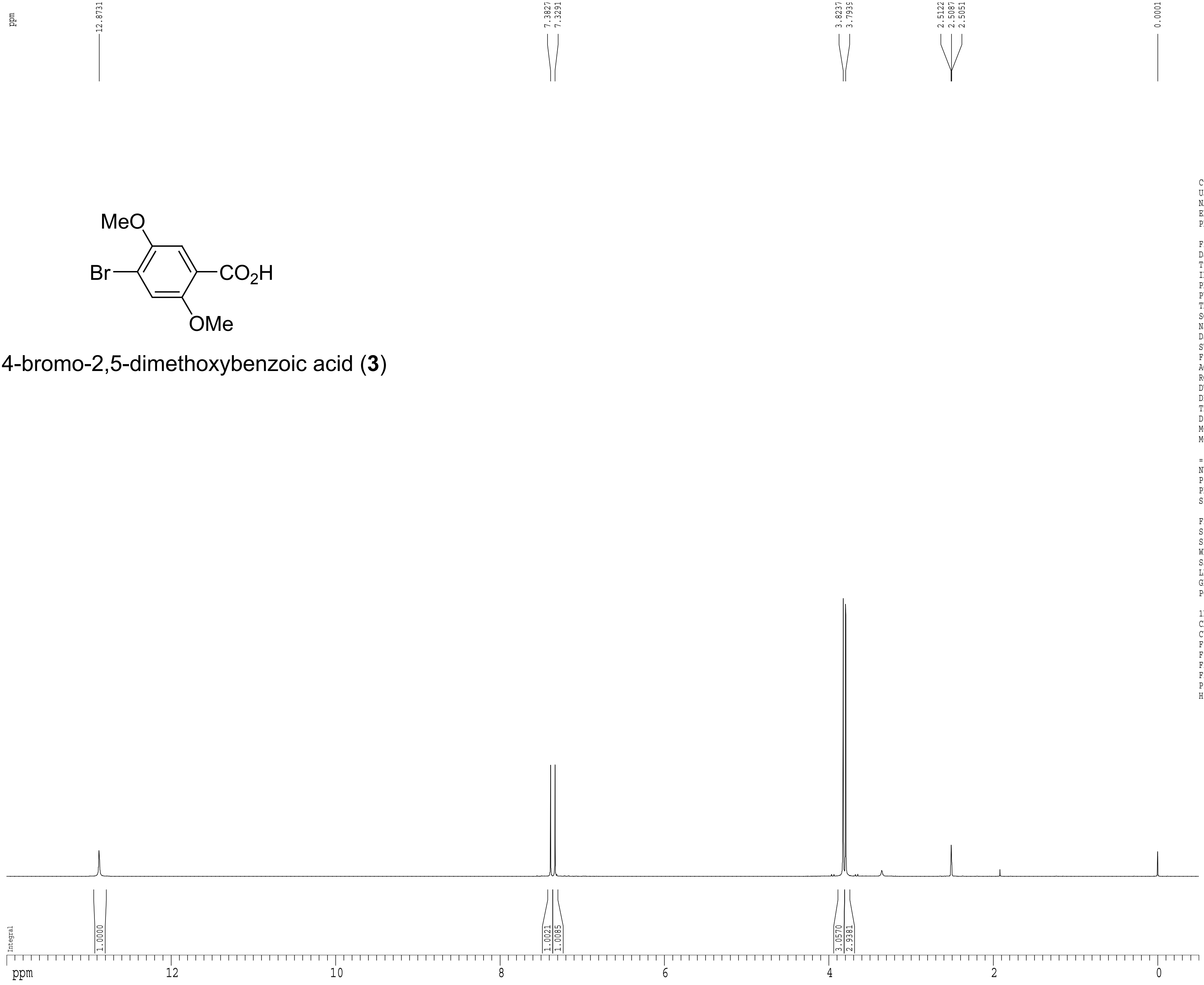
[1] Bortnik, S. P.; Landau, M. A.; Siryachenko, B. V.; Dubov, S. S.; Yarovenko, N. N. *Zh. Org. Khim.* **1972**, *8*, 340-341.

1H spectrum

4-bromo-2,5-dimethoxybenzoic acid (**3**)



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F1               7003.08 Hz
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F2               -250.11 Hz
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HZCM           318.12241 Hz/cm
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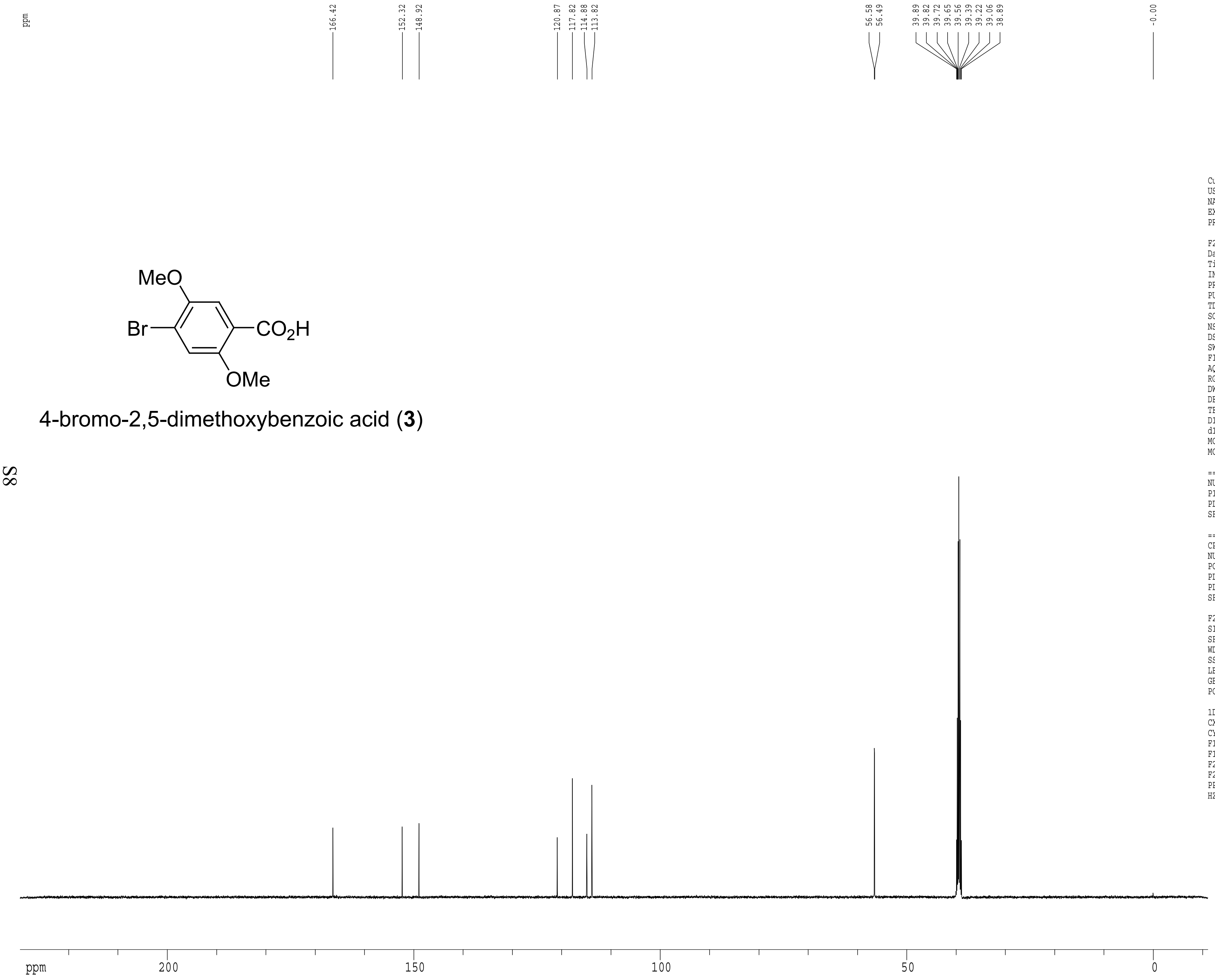
13C spectrum with 1H decoupling



4-bromo-2,5-dimethoxybenzoic acid (**3**)

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DS                     4
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FIDRES          0.463222 Hz
AQ             1.0794470 sec
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NUC2                  1H
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SFO2         500.2225011 MHz

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GB                     0
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1D NMR plot parameters
CX                 22.80 cm
CY                  8.10 cm
F1P              229.870 ppm
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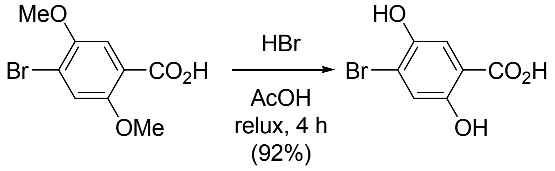
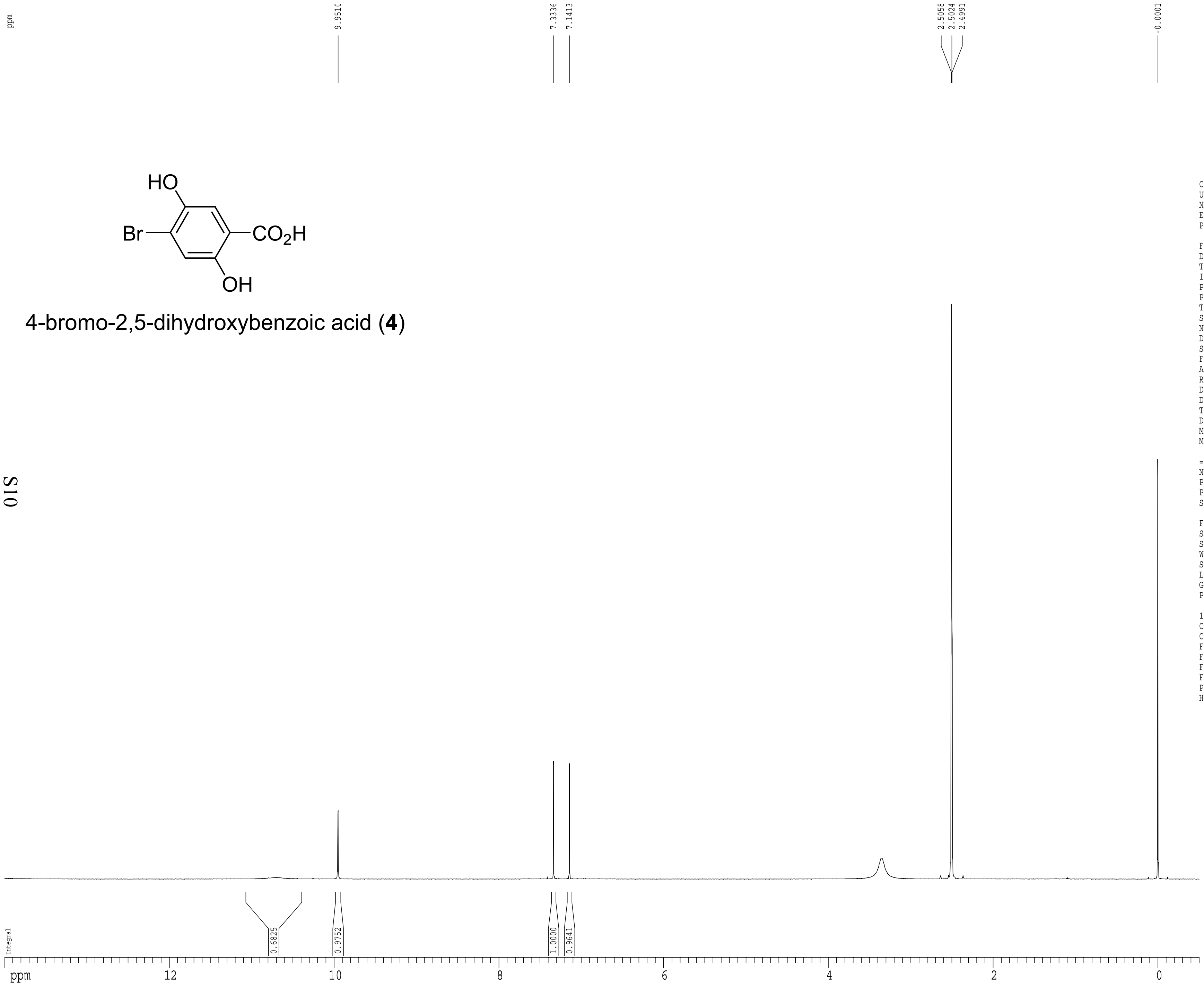


4-bromo-2,5-dimethoxy-benzoic acid (**3**)

4-bromo-2,5-dihydroxy-benzoic acid (**4**)

4-Bromo-2,5-dihydroxybenzoic acid (**4**). A solution of 4-bromo-2,5-dihydroxybenzoic acid (**3**) (6.75 g, 25.9 mmol), 48% aq HBr (130 mL) and acetic acid (30 mL) was heated at reflux for 4 h. The mixture was then concentrated by rotary evaporation to remove most of the acetic acid and then extracted with ether (3 × 200 mL). The organic layer was washed with 6 N HCl (200 mL) and then extracted with 2 M NaOH (3 × 50 mL). Acidification with concd HCl and filtration with water gave 4-bromo-2,5-dihydroxybenzoic acid (**4**) as a tan-colored solid (5.55 g, 92%): mp 229-230 °C; IR (KBr) 3700-2000 (br), 1690, 1611 cm^{-1}; ^{1}H NMR, (500 MHz, CD_3SOCD_3, 298 K) δ 10.70 (br. s, 1 H), 9.95 (s, 1 H), 7.33 (s, 1 H), 7.14 (s, 1 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 171.0, 153.7, 146.5, 120.7, 117.4, 115.2, 112.5; HRMS (ESIMS) *m/z* for $C_7H_4BrO_4$ $[M-H]^-$ calcd 230.9293, found 230.9283.



4-bromo-2,5-dihydroxybenzoic acid (**4**)

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TD                 81728
SOLVENT             DMSO
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                 456.1
DW                62.400 usec
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TE                 298.0 K
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======== CHANNEL f1 ========
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PL1                 1.60 dB
SFO1         500.2235015 MHz

F2 - Processing parameters
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SF           500.2200119 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 10.98 cm
F1P               14.000 ppm
F1               7003.08 Hz
F2P               -0.500 ppm
F2               -250.11 Hz
PPMCM            0.63596 ppm/cm
HZCM           318.12241 Hz/cm
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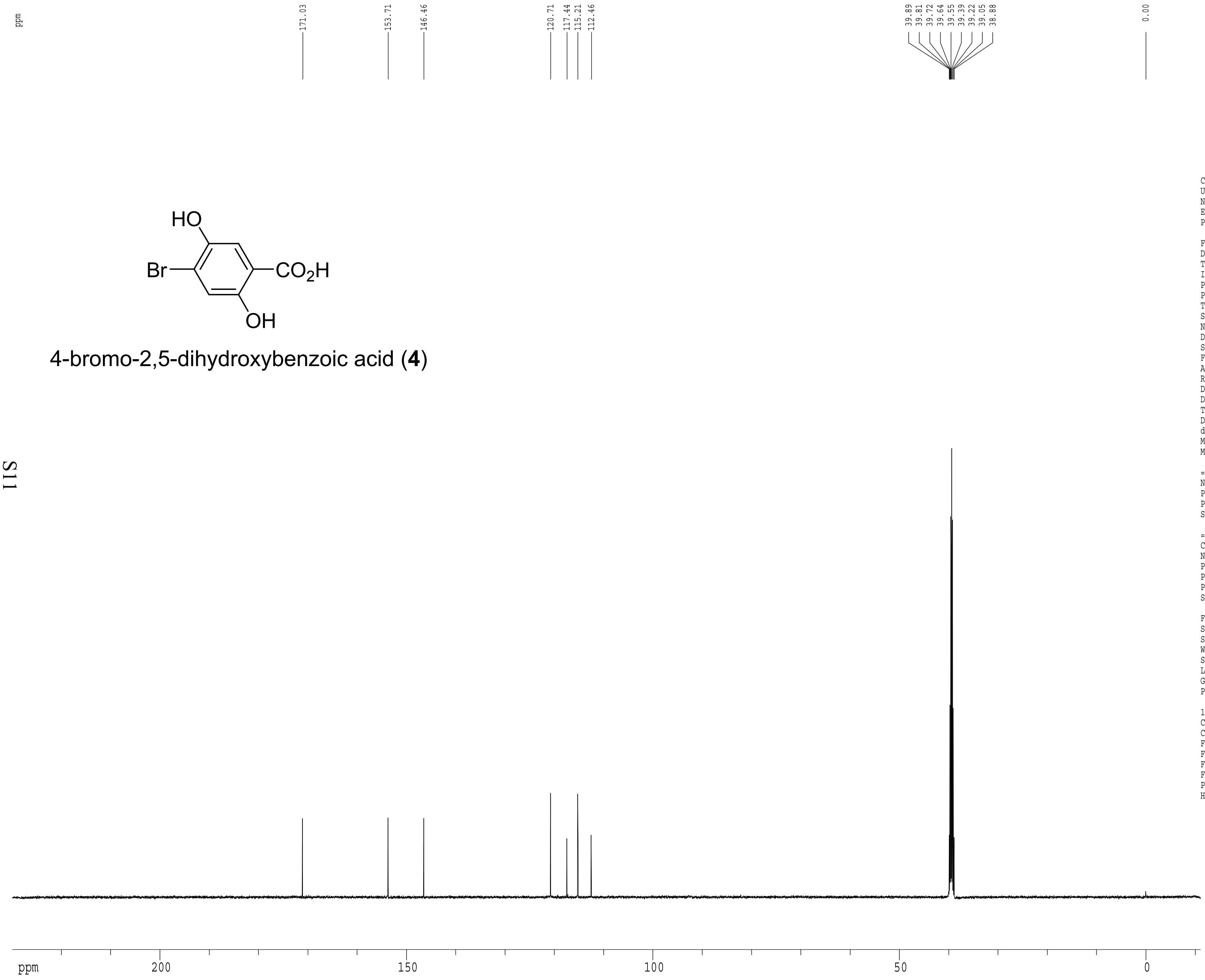
13C spectrum with 1H decoupling



4-bromo-2,5-dihydroxybenzoic acid (**4**)

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PULPROG          zgdc30
TD                 65418
SOLVENT             DMSO
NS                   177
DS                     4
SWH            30303.031 Hz
FIDRES          0.463222 Hz
AQ             1.0794635 sec
RG                  6502
DW                16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
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P1                 15.00 usec
PL1                -1.00 dB
SFO1         125.7942548 MHz

======== CHANNEL f2 ========
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NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

F2 - Processing parameters
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GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                  8.63 cm
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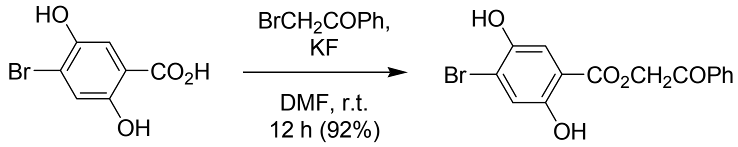
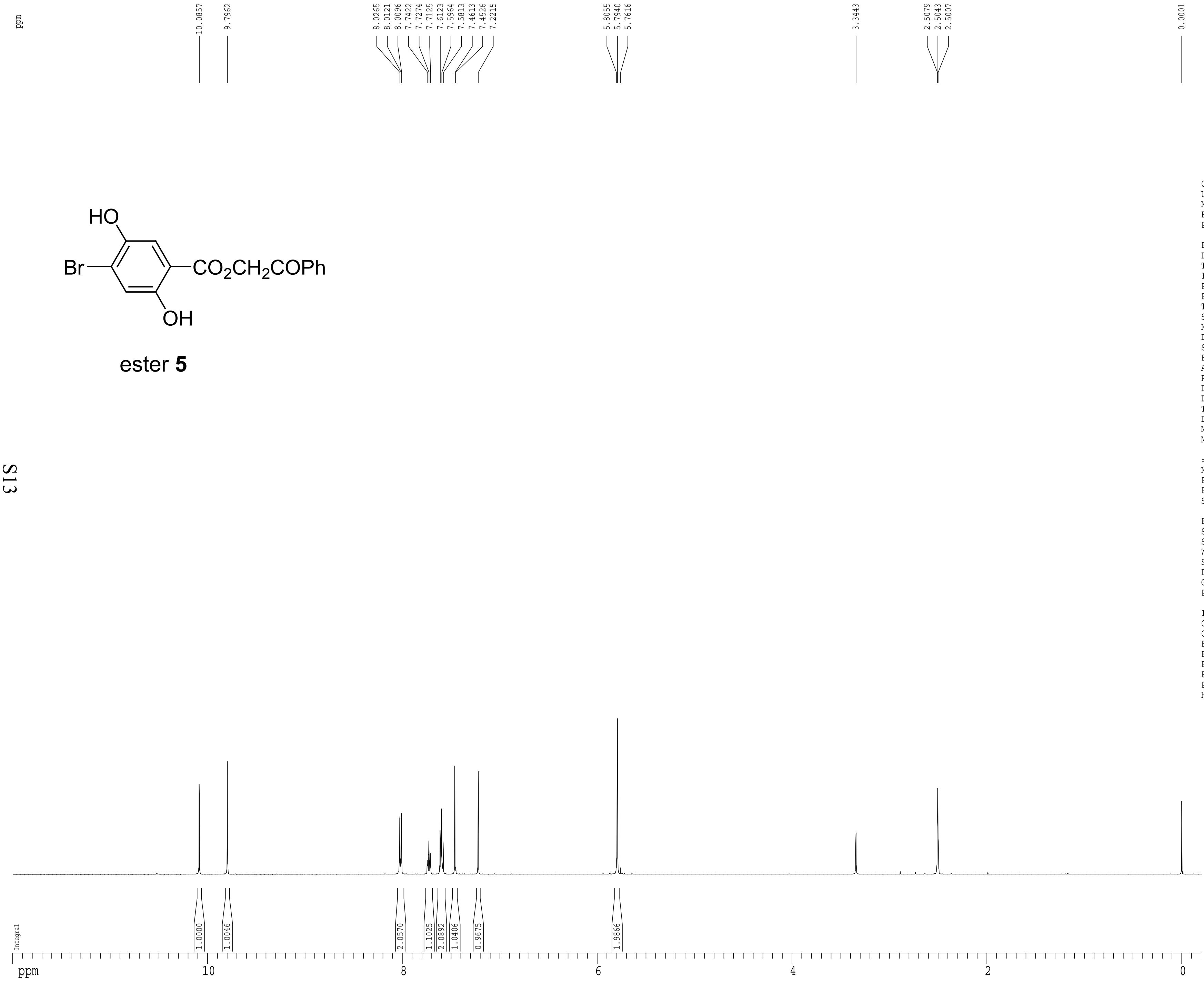


4-bromo-2,5-dihydroxy-benzoic acid (**4**)

ester **5**

Ester 5. A solution of 4-bromo-2,5-dihydroxybenzoic acid (**4**) (4.21 g, 18.1 mmol), 2-bromoacetophenone (3.60 g, 18.1 mmol), potassium fluoride (2.31 g, 39.8 mmol), and DMF (100 mL) was stirred under an atmosphere of nitrogen for ca. 12 h at 25 °C. The reaction mixture was then partitioned between water (100 mL) and CH_2Cl_2 (100 mL) and the organic layer was extracted with CH_2Cl_2 (2 × 50 mL). The combined organic layers were washed with saturated aq sodium chloride (250 mL), dried (Na_2SO_4, 2 h), filtered, and concentrated by rotary evaporation to provide a yellow solid. The yellow solid was dissolved in CH_2Cl_2 (20 mL) and ethyl acetate (20 mL), and precipitated with hexanes (100 mL) to provide ester **5** as an off-white solid (5.86 g, 92%): mp 184-186 °C; IR (KBr) 3408, 3061, 2920, 1721, 1692, 1616, 1592 cm^{-1}; ^1H NMR, (500 MHz, CD_3SOCD_3, 298 K) δ 10.09 (s, 1 H), 9.80 (s, 1 H), 8.02 (d, J = 7.2 Hz, 2 H), 7.71 (t, J = 7.4 Hz, 1 H), 7.59 (t, J = 7.8 Hz, 2 H) 7.46 (s, 1 H), 7.22 (s, 1 H), 5.79 (s, 2 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 192.3, 166.7, 152.3, 146.7, 134.1, 133.6, 128.9, 127.8, 121.3, 117.7, 115.3, 112.7, 67.3; HRMS (ESIMS) *m/z* for $C_{15}H_{11}BrO_5Na$ $[M+Na]^+$ calcd 372.9688, found 372.9675.

1H spectrum



ester **5**

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TD                 81728
SOLVENT             DMSO
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PL1                 1.60 dB
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1D NMR plot parameters
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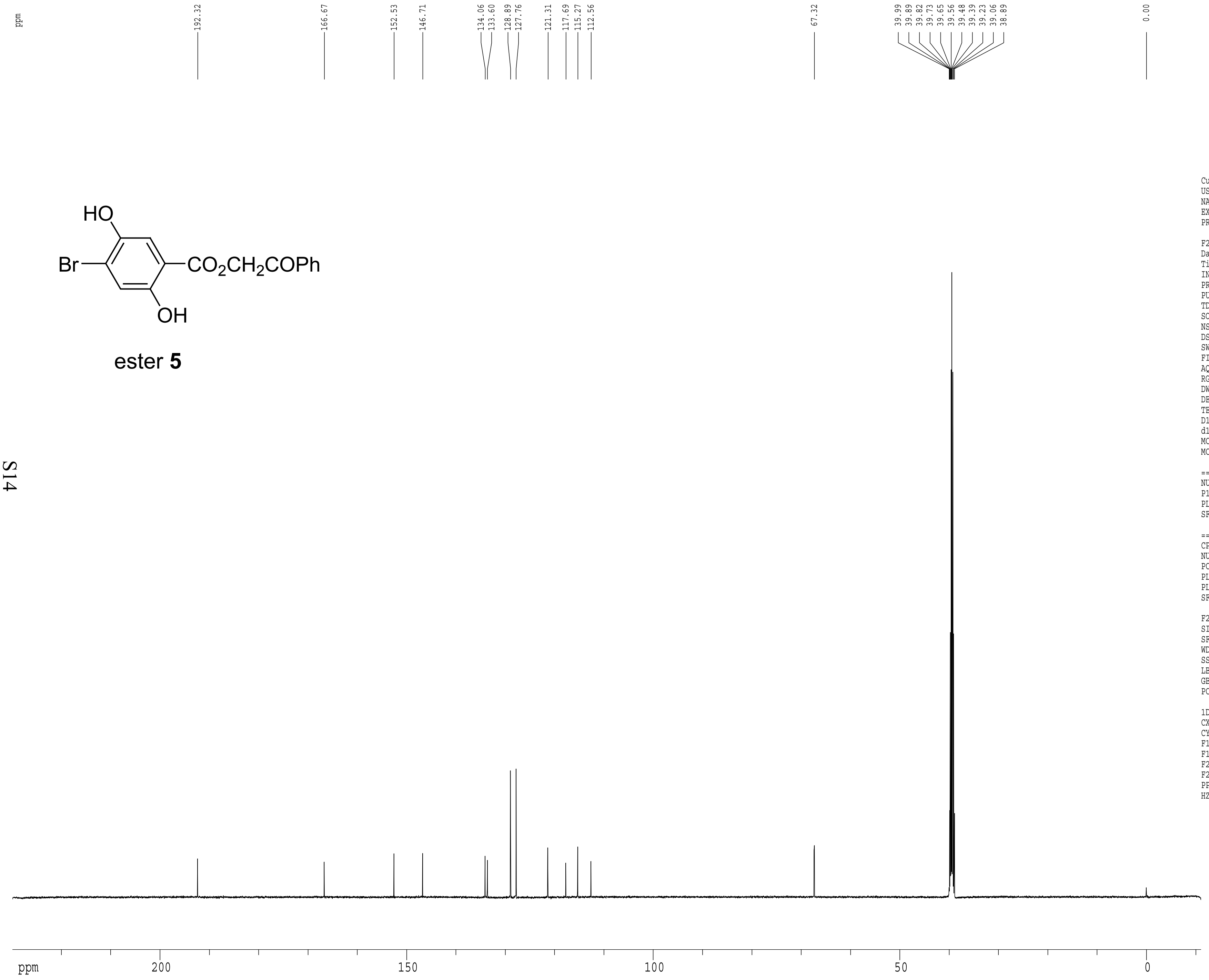
13C spectrum with 1H decoupling

ester **5**



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PROCNO                 1

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TD                 65418
SOLVENT             DMSO
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FIDRES          0.463222 Hz
AQ             1.0794635 sec
RG                5792.6
DW                16.500 usec
DE                  6.00 usec
TE                 298.0 K
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MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
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PL1                -1.00 dB
SFO1         125.7942548 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

F2 - Processing parameters
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1D NMR plot parameters
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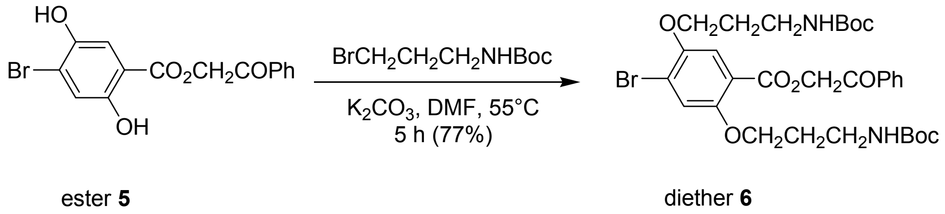

Diether 6. A solution of ester **5** (2.21 g, 6.29 mmol), *t*-butyl-3-bromopropylcarbamate[2] (5.24 g, 22.0 mmol), dry K_2CO_3 (5.22 g, 37.7 mmol), and DMF (100 mL) was stirred at 50 °C for 5 h under an atmosphere of nitrogen. Saturated aq sodium chloride (ca. 100 mL) was then added to the mixture and the solution was extracted with CH_2Cl_2 (3 × 40 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated by rotary evaporation to give a yellow solid. The yellow solid was dissolved in warm ethyl acetate (ca. 50 mL), precipitated with hexanes (ca. 100 mL), and the resultant solid was filtered to provide diether **6** as a white powder (3.22 g, 77%): mp 159-161 °C; IR (KBr) 3356, 2984, 2937, 2877, 1740, 1674, 1524 cm^{-1}; ^{1}H NMR, (500 MHz, CD_3SOCD_3, 298 K) δ 8.02 (d, *J* = 7.2 Hz, 2 H), 7.72 (t, *J* = 7.4 Hz, 1 H), 7.59 (t, *J* = 7.8 Hz, 2 H), 7.45 (d, *J* = 10.4 Hz, 2 H), 6.90 (t, *J* = 5.3 Hz, 1 H), 6.83 (t, *J* = 5.4 Hz, 1 H), 5.71 (s, 2 H), 4.04 (appar. t, *J* = 5.4 Hz, 4 H), 3.15-3.08 (m, 4 H), 1.87 (quintet, *J* = 6.5 Hz, 2 H), 1.79 (quintet, *J* = 6.4 Hz, 2 H), 1.37 (s, 9 H), 1.33 (s, 9 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 192.6, 164.0, 155.5, 152.6, 148.6, 133.87, 133.86, 128.8, 127.7, 119.5, 119.0, 117.1, 115.3, 77.4, 77.3, 67.6, 67.3, 67.0, 36.9, 36.8, 29.1, 28.2, 28.1; HRMS (ESIMS) *m/z* for $C_{31}H_{41}BrN_2O_9Na$ $[M+Na]^+$ calcd 687.1893, found 687.1873.

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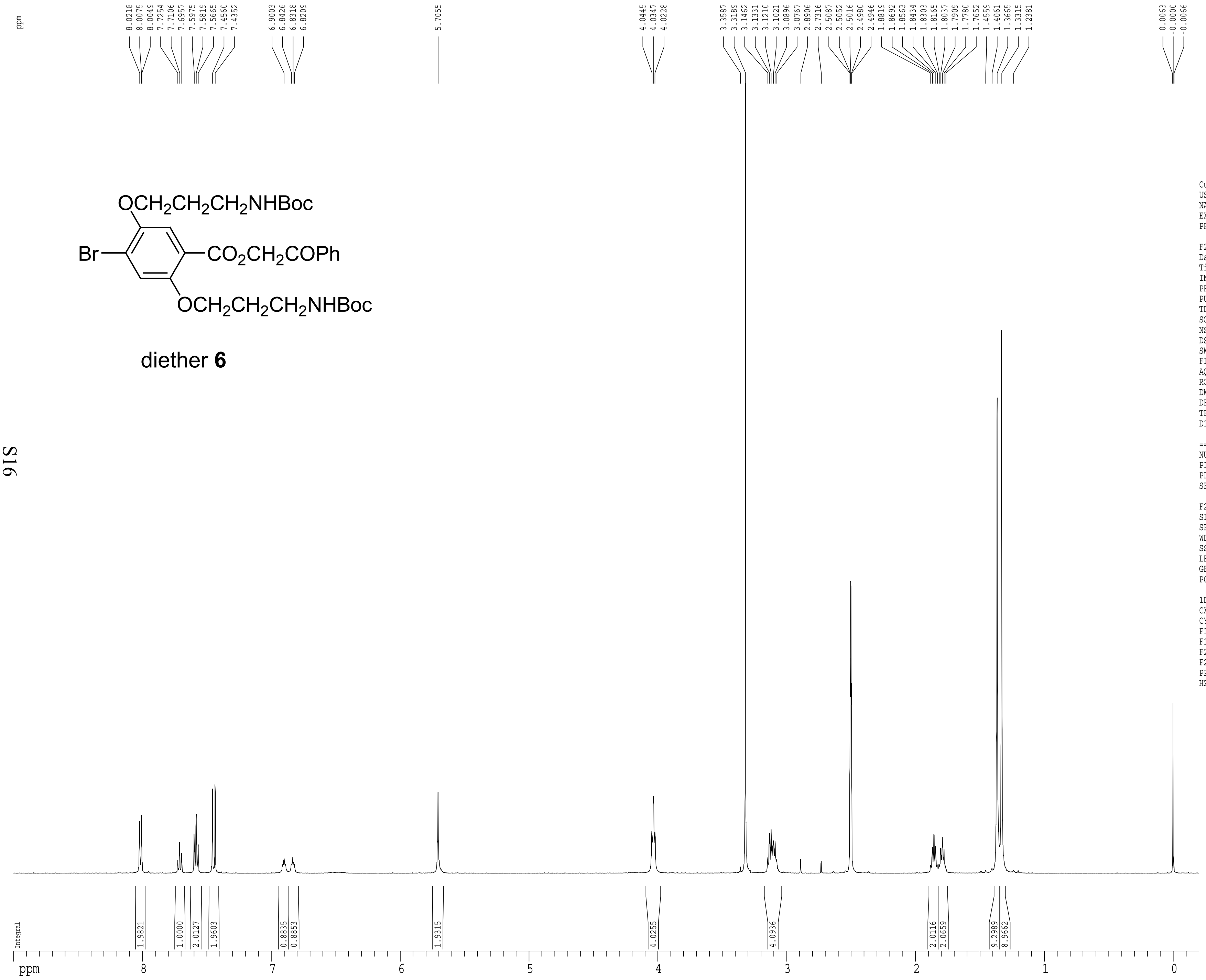
[2] Zych, A. J.; Iverson, B. L. *J. Am. Chem. Soc.* **2000**, *122*, 8898-8909.



diether **6**

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PC                  4.00

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F1               4500.36 Hz
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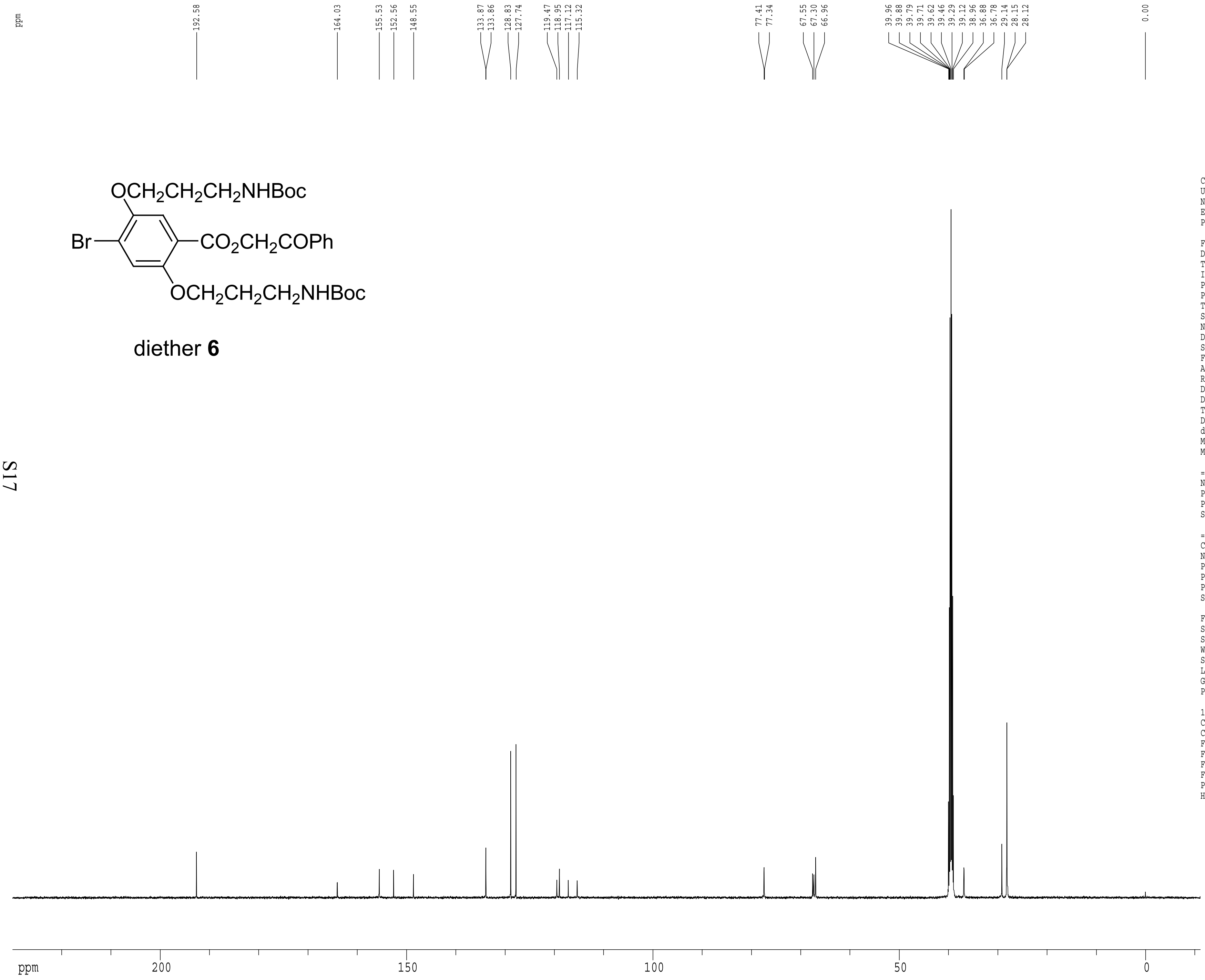
13C spectrum with 1H decoupling



diether **6**

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TE                 298.0 K
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MCREST        0.00000000 sec
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======== CHANNEL f1 ========
NUC1                 13C
P1                  7.00 usec
PL1                 0.00 dB
SFO1        125.7213258 MHz

======== CHANNEL f2 ========
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NUC2                  1H
PCPD2              80.00 usec
PL2                -3.00 dB
PL12               15.00 dB
SFO2        499.9324997 MHz

F2 - Processing parameters
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1D NMR plot parameters
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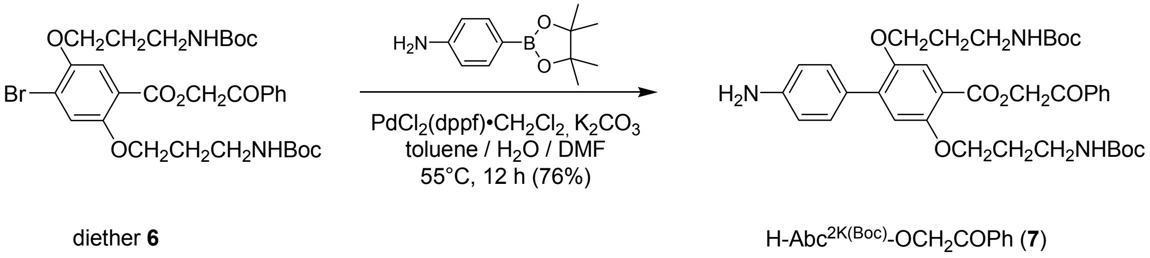

H-Abc$^{2K(Boc)}$-OCH$_2$COPh (7). Diether **6** (7.55 g, 11.5 mmol), 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)aniline (2.52 g, 11.5 mmol), PdCl$_2$(dppf)•CH$_2$Cl$_2$[3] (0.38 g, 0.46 mmol), K$_2$CO$_3$ (7.95 g, 57.6 mmol) were dissolved in a mixture of toluene (245 mL), water (70 mL), and DMF (35 mL) and was stirred at 55 ^{o}C for ca. 12 h under an atmosphere of nitrogen. The suspension was then concentrated by rotary evaporation to remove most of the toluene and then diluted with CH$_2$Cl$_2$ (250 mL). The organic layer was washed with water (ca. 250 mL), saturated aq sodium chloride (ca. 250 mL), and dried (Na$_2$SO$_4$). After filtration and concentration by rotary evaporation, a brown oil was obtained and was purified using column chromatography (silica gel, ethyl acetate–hexanes, 2/1, *v*/*v*) to provide H-Abc$^{2K(Boc)}$-OCH$_2$COPh (**7**) as an off-white solid (6.55 g, 84%): mp 149-151 °C; IR (KBr) 3477, 3366, 2974, 2930, 2874, 1736, 1681 cm^{-1}; ^{1}H NMR, (500 MHz, CD$_3$SOCD$_3$, 298 K) δ 8.03 (d, *J* = 7.0 Hz, 2 H), 7.71 (t, *J* = 7.3 Hz, 1 H), 7.59 (t, *J* = 7.8 Hz, 2 H), 7.43 (s, 1 H), 7.35 (d, *J* = 8.5 Hz, 2 H), 7.02 (s, 1 H), 6.88 (t, *J* = 5.3 Hz, 1 H), 6.83 (t, *J* = 5.5 Hz, 1 H), 6.63 (d, *J* = 8.5 Hz, 2 H), 5.69 (s, 2 H), 5.30 (s, 2 H), 4.06 (t, *J* = 6.0 Hz, 2 H), 3.92 (t, *J* = 6 Hz, 2 H), 3.12 (q, *J* = 6.3 Hz, 2 H), 3.07 (q, *J* = 6.2 Hz, 2 H), 1.83-1.77 (m, 4 H), 1.37 (s, 9 H), 1.33 (s, 9 H); ^{13}C NMR (125 MHz, CD$_3$SOCD$_3$, 298 K) δ 192.9, 164.3, 155.5, 153.0, 148.8, 148.5, 136.6, 134.0,

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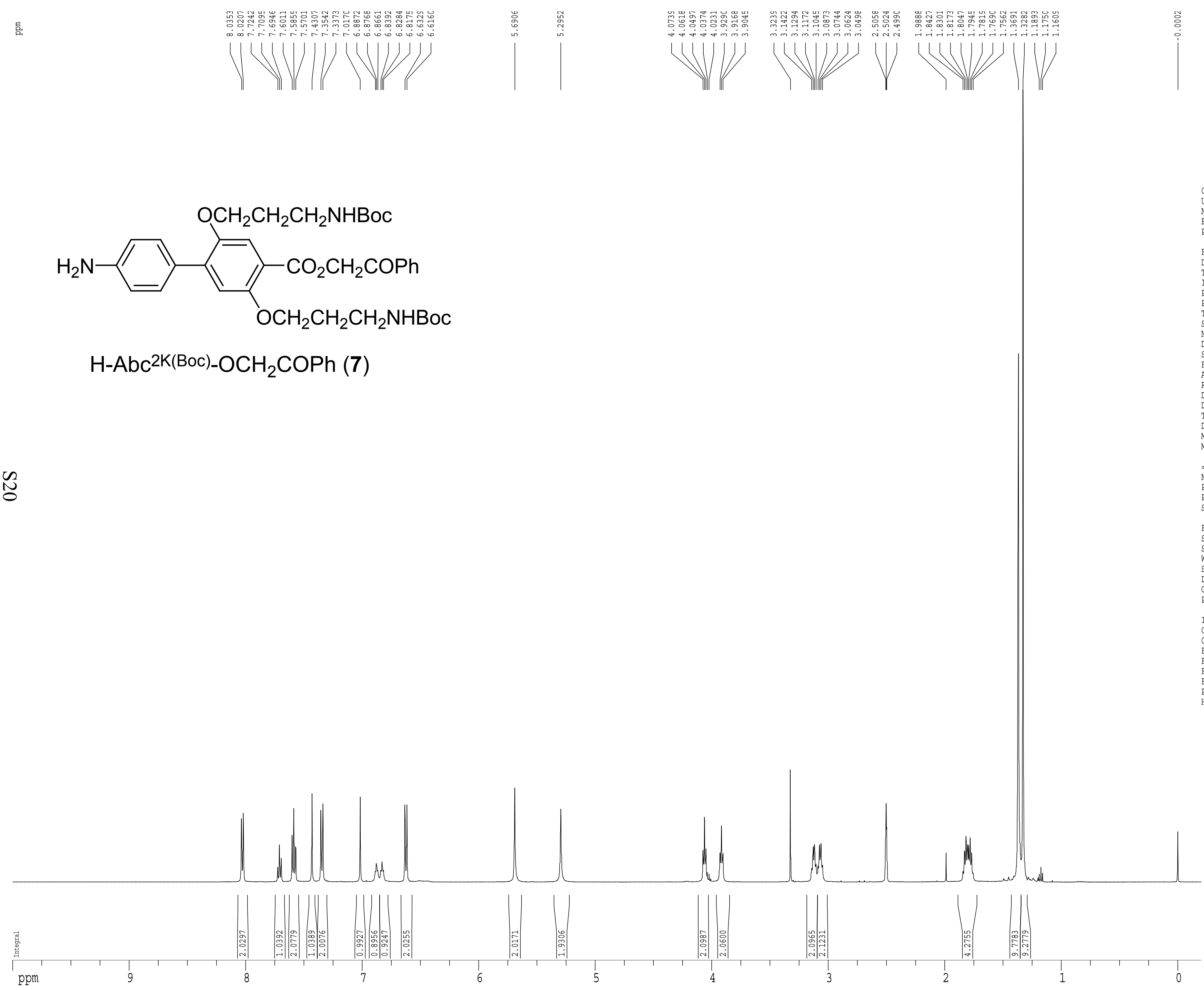
[3] Hayashi, T.; Konishi, M.; Kobori, Y.; Kumada, M.; Higuchi, T.; Hirotsu, K. *J. Am. Chem. Soc.* **1984**, *106*, 158-163.

133.8, 130.0, 128.8, 127.7, 123.8, 116.4, 115.9, 115.3, 113.2, 77.4, 77.3, 67.2, 66.7, 66.2, 37.1, 36.8, 29.3, 29.2, 28.2, 28.1; HRMS (ESIMS) *m/z* for $C_{37}H_{47}N_3O_9Na$ $[M+Na]^+$ calcd 700.3210, found 700.3205.

H-Abc$^{2K(Boc)}$-OCH$_2$COPh (**7**)



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SSB                  0
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GB                   0
PC                4.00

1D NMR plot parameters
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CY               16.88 cm
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HZCM         223.65291 Hz/cm
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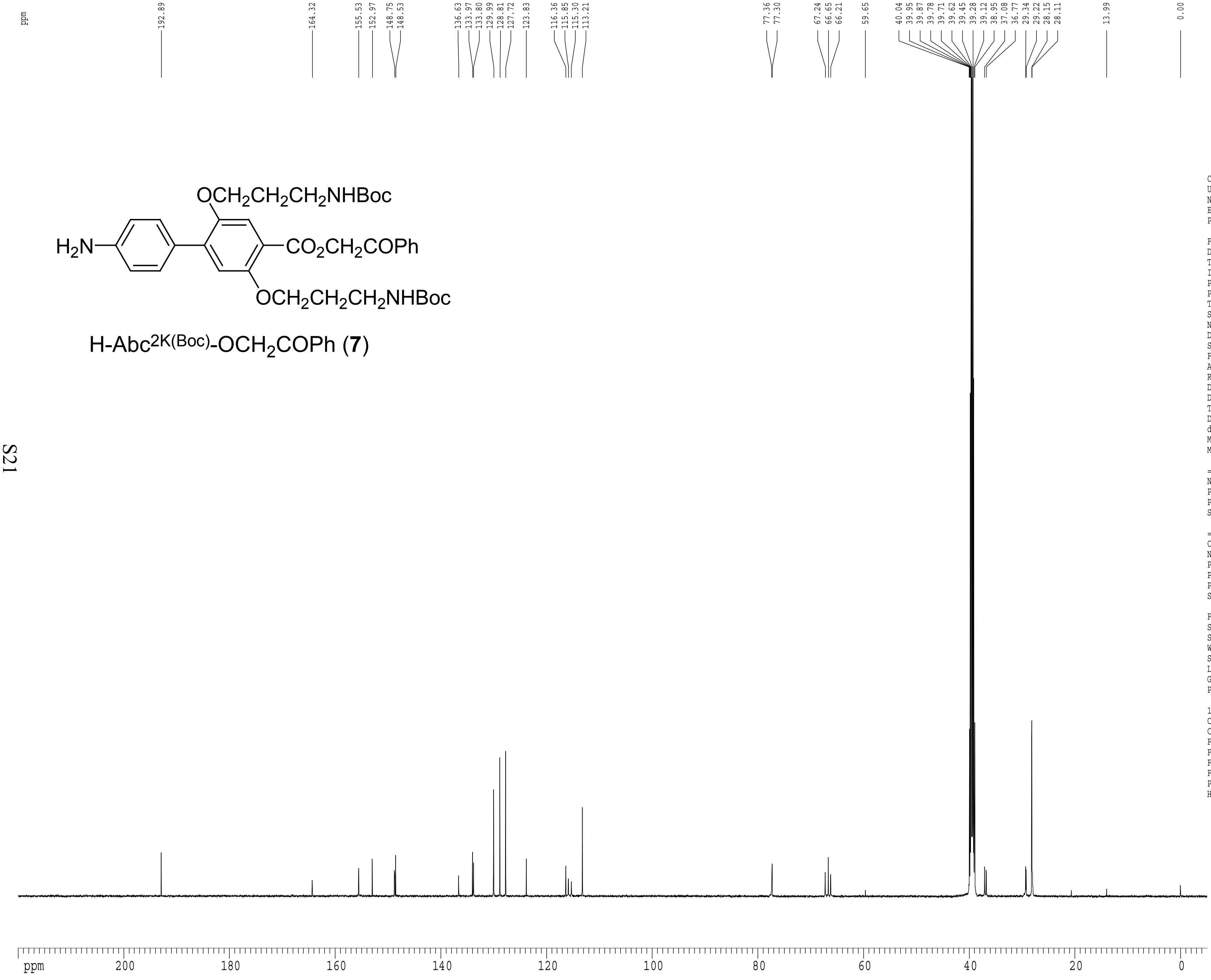

H-Abc$^{2K(Boc)}$-OCH$_2$COPh (**7**)

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SOLVENT            CDCl3
NS                 10654
DS                     4
SWH            30303.031 Hz
FIDRES          0.462388 Hz
AQ             1.0813940 sec
RG                1625.5
DW                16.500 usec
DE                  4.50 usec
TE                 298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                  7.00 usec
PL1                 0.00 dB
SFO1         125.7213258 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              80.00 usec
PL2                -3.00 dB
PL12               15.00 dB
SFO2         499.9324997 MHz

F2 - Processing parameters
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SF           125.7075716 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 22.84 cm
F1P              220.000 ppm
F1              27655.67 Hz
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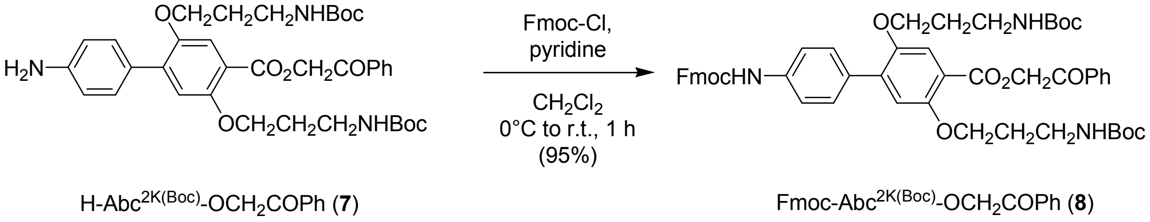
HZCM          1240.53528 Hz/cm
```

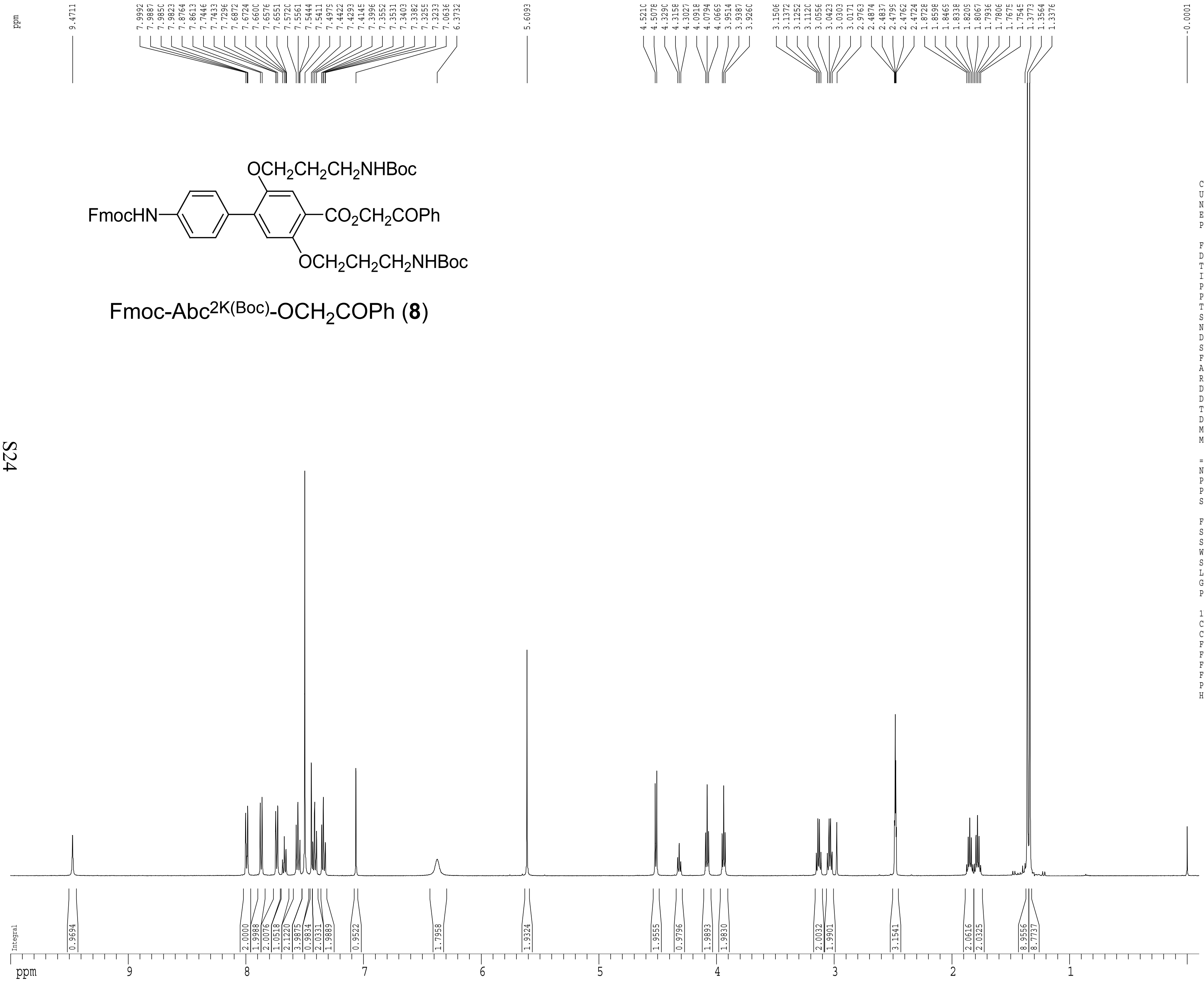


H-Abc$^{2K(Boc)}$-OCH$_2$COPh (**7**) Fmoc-Abc$^{2K(Boc)}$-OCH$_2$COPh (**8**)

Fmoc-Abc$^{2K(Boc)}$-OCH$_2$COPh (8). A solution of H-Abc$^{2K(Boc)}$-OCH$_2$COPh (**7**) (6.55 g, 9.66 mmol), pyridine (0.95 mL, 11.6 mmol), and CH_2Cl_2 (200 mL) was cooled to 0 °C in an ice-bath. Fmoc-Cl (2.75 g, 10.6 mmol) in CH_2Cl_2 (50 mL) was added in drops over 5 min. After 30 min, the solution was allowed to warm to 25 °C and stirred for an additional 30 min. The mixture was then washed with water (100 mL), dried (Na_2SO_4), filtered, and the filtrate was concentrated by rotary evaporation to give a yellow oil. The yellow oil was dissolved in CH_2Cl_2 (ca. 15 mL), precipitated using ethyl acetate (ca. 50 mL) and hexanes (ca. 100 mL), and filtered to provide Fmoc-Abc$^{2K(Boc)}$-OCH$_2$COPh (**8**) as a white solid (8.82 g, 95%): mp 108-110 °C; IR (KBr) 3349, 2980, 2935, 2873, 1732, 1698, 1596 cm^{-1}; ^{1}H NMR, (500 MHz, CD_3SOCD_3, 358 K) δ 9.47 (s, 1 H), 7.99 (d, *J* = 8.5 Hz, 2 H), 7.87 (d, *J* = 7.5 Hz, 2 H), 7.74 (d, *J* = 7.5 Hz, 2 H), 7.67 (t, *J* = 7.4 Hz, 1 H), 7.56 (t, *J* = 7.7 Hz, 2 H), 7.50 (s, 4 H), 7.44 (s, 1 H), 7.42 (t, *J* = 7.4 Hz, 2 H), 7.34 (td, *J* = 7.4, 1.1 Hz, 2 H), 7.06 (s, 1 H), 6.37 (br. s, 2 H), 5.61 (s, 2 H), 4.51 (d, *J* = 6.6 Hz, 2 H), 4.32 (t, *J* = 6.6 Hz, 1 H), 4.08 (t, *J* = 6.2 Hz, 2 H), 3.94 (t, *J* = 6.3 Hz, 2 H), 3.13 (q, *J* = 6.4 Hz, 2 H), 3.04 (q, *J* = 6.4 Hz, 2 H), 1.85 (quintet, *J* = 6.5 Hz, 2 H), 1.78 (quintet, *J* = 6.5 Hz, 2 H), 1.36 (s, 9 H), 1.34 (s, 9 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 192.8, 164.3, 155.53, 155.51, 153.3, 152.7, 148.8, 143.7, 140.7, 138.6, 135.2, 133.90, 133.85, 130.8, 129.7, 128.8, 127.7, 127.6, 127.0, 125.0, 120.1, 117.7, 117.6, 116.5, 115.0, 77.4, 77.3, 67.2, 66.8, 66.1, 65.5, 46.5, 37.0, 36.6, 29.2, 29.1, 28.1, 28.0; HRMS (ESIMS) *m/z* for $C_{52}H_{57}N_3O_{11}Na$ $[M+Na]^+$ calcd 922.3891, found 922.3874.

T = 358 K

Fmoc-Abc$^{2K(Boc)}$-OCH$_2$COPh (**8**)



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NUC1                  1H
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PL1                -3.00 dB
SFO1         499.9334995 MHz

F2 - Processing parameters
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SF           499.9300219 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 22.04 cm
F1P               10.000 ppm
F1               4999.30 Hz
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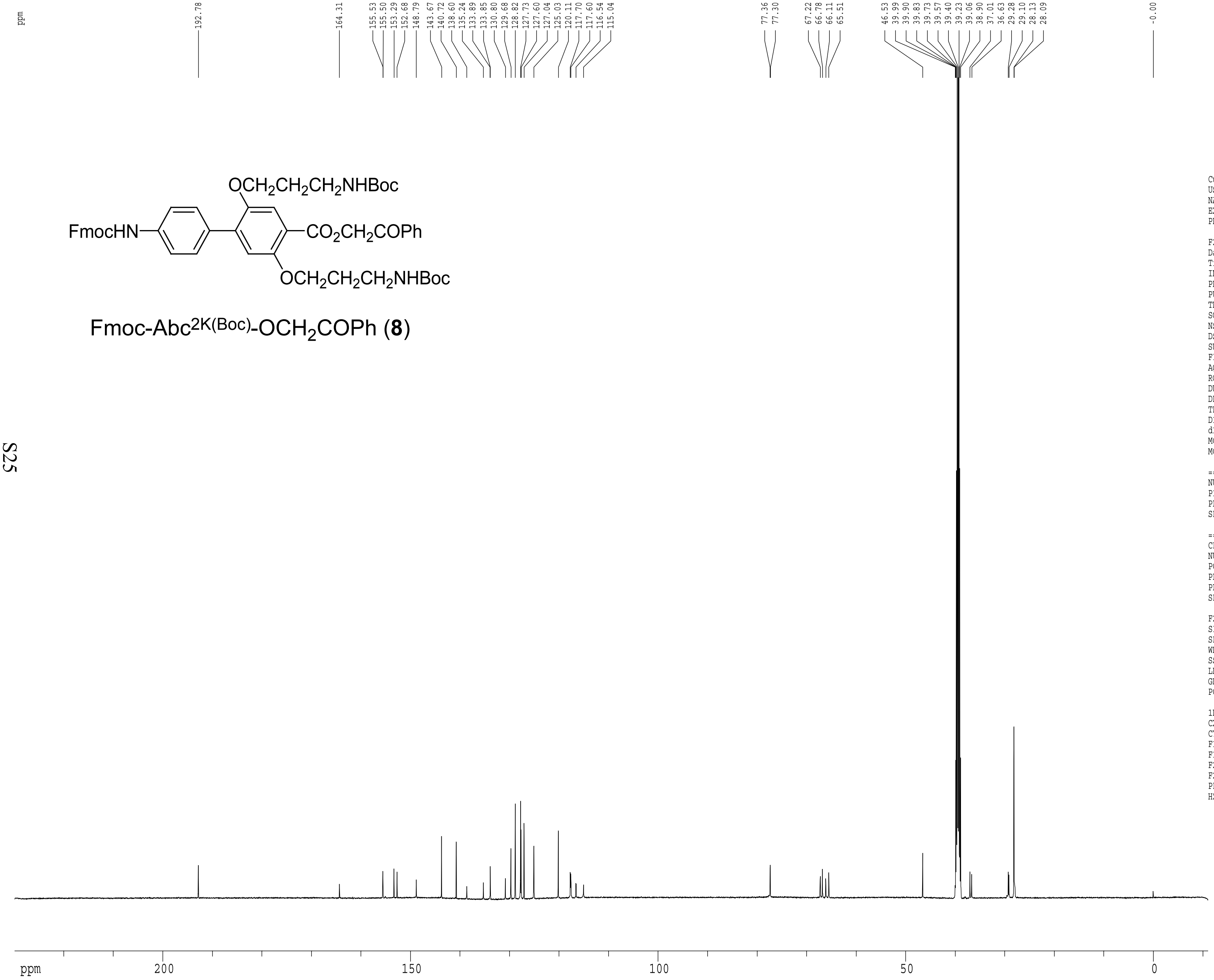
13C spectrum with 1H decoupling



Fmoc-Abc$^{2K(Boc)}$-OCH$_2$COPh (**8**)

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SWH            30303.031 Hz
FIDRES          0.463222 Hz
AQ             1.0794470 sec
RG                  8192
DW                16.500 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.25000000 sec
d11           0.03000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 15.00 usec
PL1                -1.00 dB
SFO1         125.7942548 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

F2 - Processing parameters
SI                 65536
SF           125.7804942 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
CX                 22.80 cm
CY                 19.35 cm
F1P              229.862 ppm
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F2              -1390.87 Hz
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HZCM          1329.08032 Hz/cm
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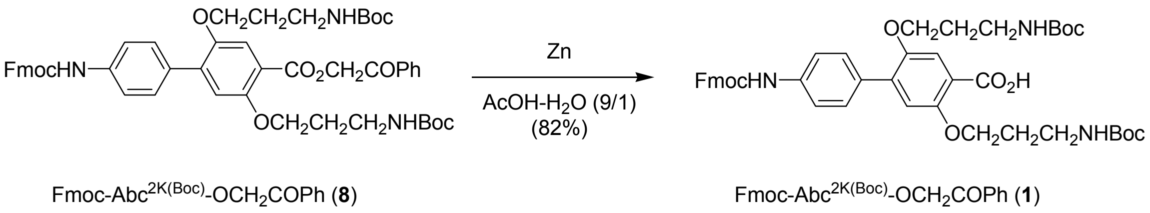

Fmoc-Abc$^{2K(Boc)}$-OH (1). Zn dust (31.1 g, 460 mmol) was added to a solution of Fmoc-Abc$^{2K(Boc)}$-OCH_2COPh (**8**) (8.28 g, 9.20 mmol), AcOH (100 mL), and H_2O (10 mL) and was stirred at 25 °C for 18 h.[4] The suspension was then diluted with CH_2Cl_2 (ca. 100 mL) and stirred for an additional 30 min before the solids were removed by filtering the mixture through a bed of Celite®. The filtrate was concentrated by rotary evaporation and the resultant yellow oil was dissolved in CH_2Cl_2 (300 mL), washed with 0.2 N HCl (250 mL), H_2O (250 mL), and saturated aq sodium chloride (250 mL). The organic layer was dried over Na_2SO_4 and concentrated by rotary evaporation to give a yellow oil. Purification was performed by dissolving the yellow oil in ether (ca. 50 mL) and precipitating with hexanes (ca. 200 mL) to provide Fmoc-Abc$^{2K(Boc)}$-OH (**1**) as a white solid (5.9 g, 82 %): mp 108-110 °C; IR (KBr) 3366, 2978, 2874, 1712, 1689, 1608, 1590, 1533 cm^{-1}; ^{1}H NMR, (500 MHz, CD_3SOCD_3, 328 K) δ 12.32 (s, 1 H), 9.63 (s, 1 H), 7.89 (d, J = 7.5 Hz, 2 H), 7.75 (d, J = 7.5 Hz, 2 H), 7.48 (s, 4 H), 7.42 (t, J = 7.4 Hz, 2 H), 7.35 (td, J = 7.4, 1.1 Hz, 2 H), 7.33 (s, 1 H), 7.01 (s, 1 H), 6.63 (br. s, 2 H), 4.51 (d, J = 6.6 Hz, 2 H), 4.32 (t, J = 6.7 Hz, 1 H), 4.05 (t, J = 6.3 Hz, 2 H), 3.92 (t, J = 6.3 Hz, 2 H), 3.11 (q, J = 6.6 Hz, 2 H), 3.02 (q, J = 6.5 Hz, 2 H), 1.83 (quintet, J = 6.5 Hz, 2 H), 1.75 (quintet, J = 6.5 Hz, 2 H), 1.36 (s, 18 H); ^{13}C NMR (125 MHz, CD_3SOCD_3, 298 K) δ 166.7, 155.5, 153.3, 151.9, 148.8, 143.7, 140.7, 138.4, 134.0, 131.0, 129.6, 127.6, 127.0,

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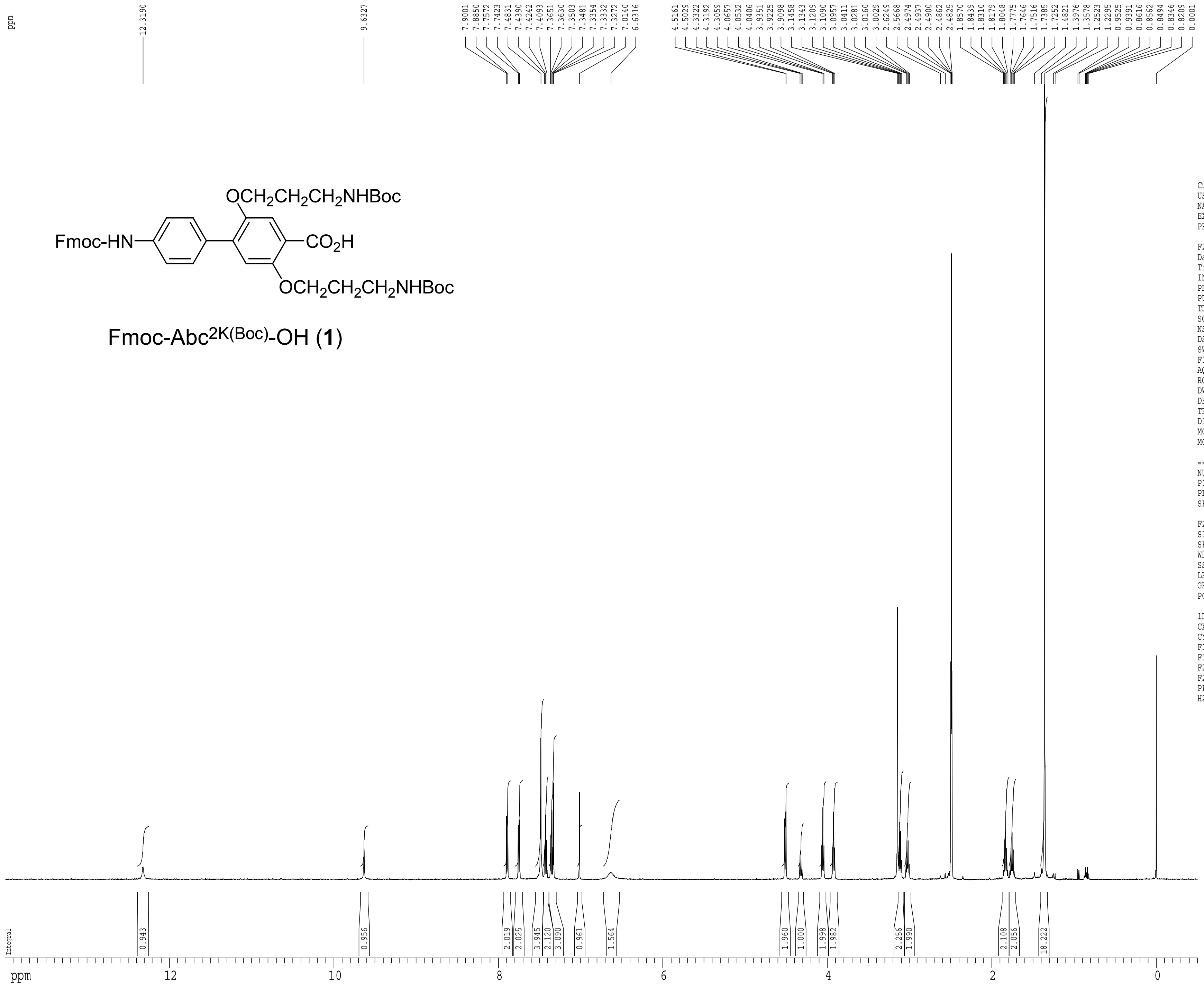
[4] Hendrickson, J. B.; Kandall, C. *Tetrahedron Lett.* **1970**, *5*, 343-344.

125.0, 120.2, 120.1, 117.6, 116.5, 114.9, 77.4, 67.2, 66.1, 65.5, 46.5, 36.9, 36.7, 29.2, 29.1, 28.1; HRMS (ESIMS) *m/z* for $C_{44}H_{51}N_3O_{10}Na$ $[M+Na]^+$ calcd 804.3472, found 804.3456.



Fmoc-Abc$^{2K(Boc)}$-OH (**1**)

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SOLVENT             DMSO
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DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                  1024
DW                62.400 usec
DE                  6.00 usec
TE                 328.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                 12.00 usec
PL1                -3.00 dB
SFO1         499.9334995 MHz

F2 - Processing parameters
SI                 65536
SF           499.9300170 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 28.75 cm
F1P               14.000 ppm
F1               6999.02 Hz
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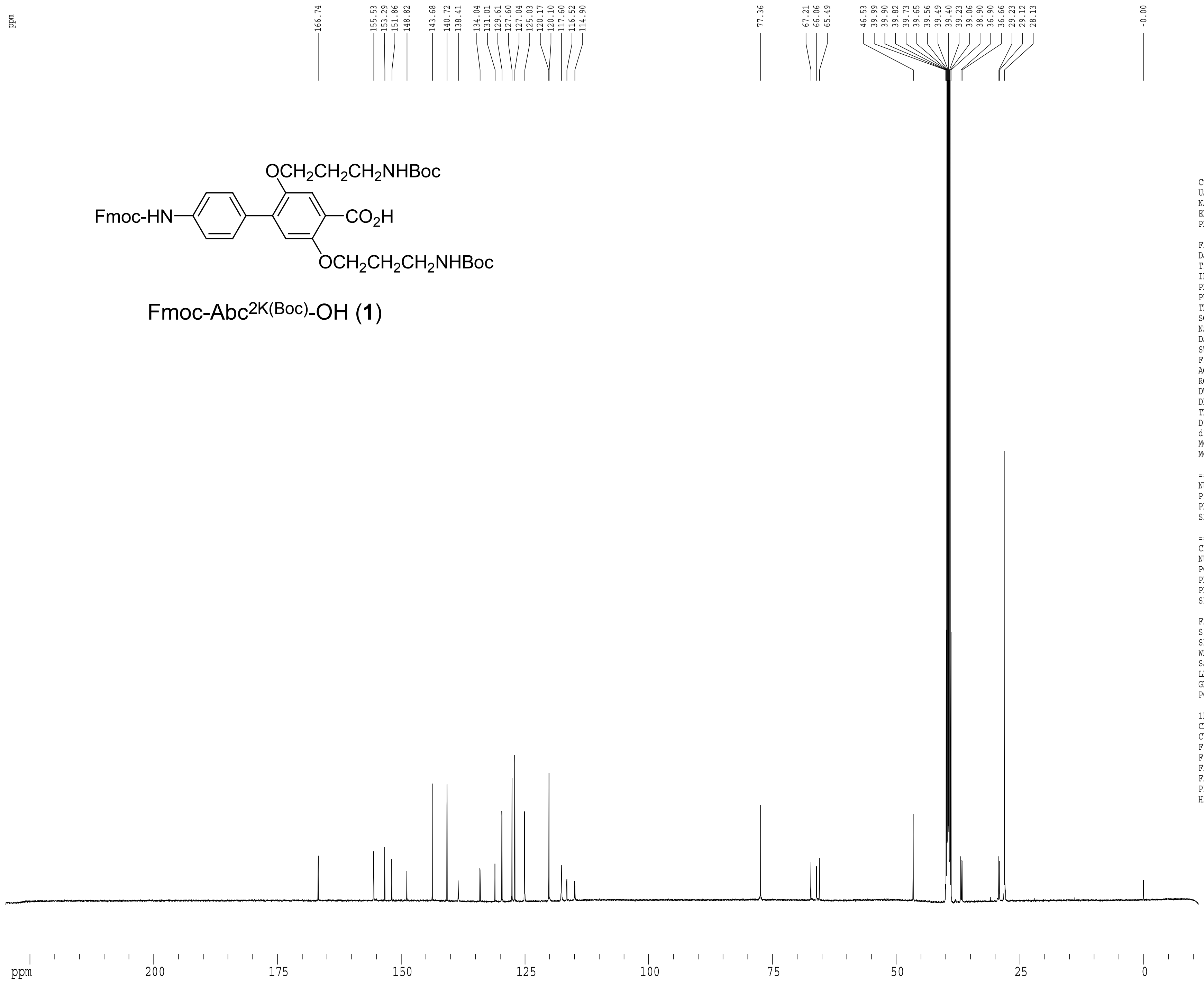
13C spectrum with 1H decoupling



Fmoc-Abc$^{2K(Boc)}$-OH (**1**)

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NS                  5000
DS                     4
SWH           30303.031 Hz
FIDRES         0.463222 Hz
AQ            1.0794470 sec
RG                  6502
DW               16.500 usec
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TE                298.0 K
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d11          0.03000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                 13C
P1                 15.00 usec
PL1                -1.00 dB
SFO1         125.7942548 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2             100.00 usec
PL2                 1.60 dB
PL12               23.54 dB
SFO2         500.2225011 MHz

F2 - Processing parameters
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SF           125.7804937 MHz
WDW                   EM
SSB                    0
LB                  1.00 Hz
GB                     0
PC                  2.00

1D NMR plot parameters
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CY                 37.75 cm
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F1              28912.62 Hz
F2P              -11.054 ppm
F2              -1390.41 Hz
PPMCM           10.56666 ppm/cm
HZCM          1329.08032 Hz/cm
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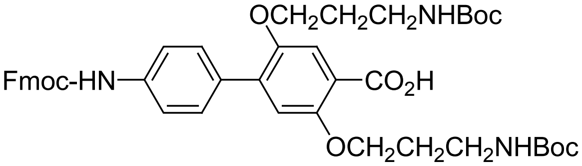
Fmoc-Abc$^{2K(Boc)}$-OH (**1**)
Analytical RP-HPLC chromatograph

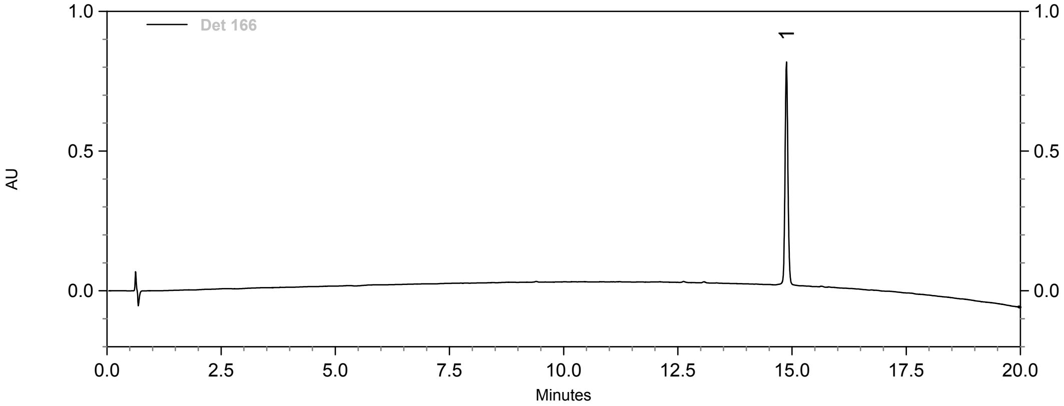


Analytical RP-HPLC (5-90% acetonitrile with 0.1% TFA over 20 min, λ = 214)

Sample ID: Fmoc-Abc2KBoc-OH 2nd recry
Filename : D:\32Karat\Projects\Default\Data\Chris\cg-10-216 fmoc-Abc2K(Boc)-OH Synthesis\Fmoc-Abc2KBoc-OH 2nd recry

Method : Rocket Platinum Column 5-90% B in 20 min (214 nm)

Date Inj. : 10/15/2006 6:37:54 PM



Det 166 Results

Time	Area	Area %	Height	Height %	Pk #
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Totals					
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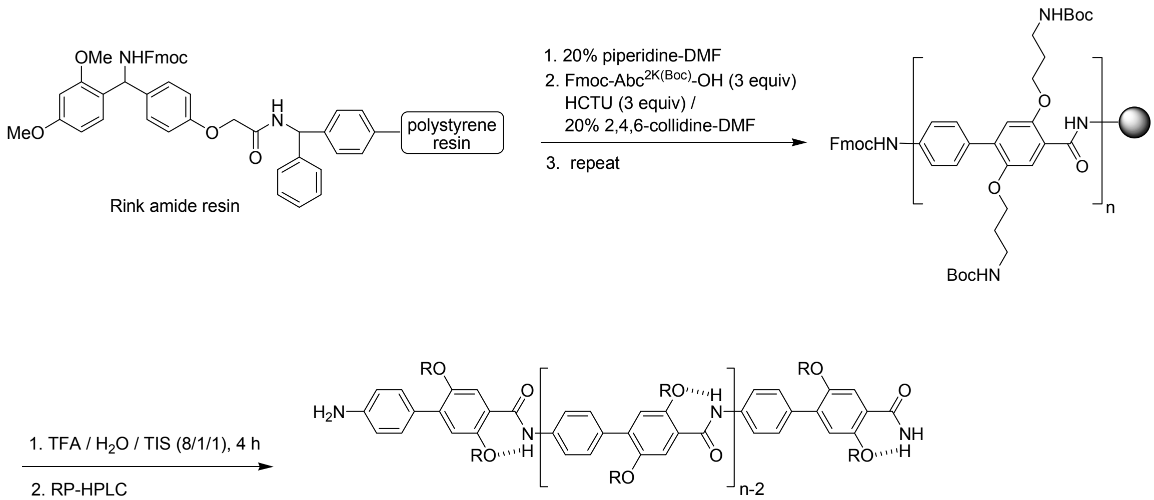

R = $CH_2CH_2CH_2NH_3^+$ $CF_3CO_2^-$

9a n=1; **9b** n=2; **9c** n=3; **9d** n=4; **9e** n=5; **9f** n=6; **9g** n=7; **9h** n=8; **9i** n=10

Synthesis of Abc^{2K} Oligomers 9a-9i. A Bio-Rad Poly-Prep chromatography column containing 47 mg of Rink amide resin (0.64 mmol/g., Novabiochem, Rink Amide resin co. 100-200 mesh, 1% DVB) was soaked with DMF (3 × ca. 5 mL, 1 min each) and then drained under nitrogen pressure. The Fmoc group was removed by adding a solution of 20% piperidine–DMF (1 × ca. 5 mL for 1 min, 1 × ca. 5 mL for 20 min) to the resin, capping the column on both ends, and gently agitating the resin. The piperidine solution was drained, and the resin was washed with DMF (6 × ca. 5 mL, 1 min each) and CH_2Cl_2 (6 × ca. 5 mL, 1 min each). Coupling of Fmoc-Abc$^{2K(Boc)}$-OH (**1**) to the resin was accomplished by pre-activating Fmoc-Abc$^{2K(Boc)}$-OH (70 mg, 0.09 mmol) with diisopropylcarbodiimide (13 μL, 0.085 mmol) and HOAt (12 mg, 0.09 mmol) in DMF–CH_2Cl_2 (ca. 0.5 mL / ca. 0.2 mL). After 2-3 min, the coupling solution was added to the resin and the resin was gently agitated for ca. 12 h. (Fmoc-Abc$^{2K(Boc)}$-OH (**1**) (3 equiv) was also coupled using HCTU[5] (3 equiv) in a solution of 20% 2,4,6-collidine–DMF and became the preferred method of coupling.) The reaction vessel was then drained and the

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[5] Marder, O.; Shvo, Y.; Albericio, F. *Chim. Oggi* **2002**, *20*, 37-41.

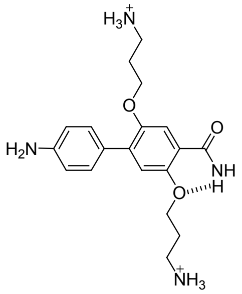
resin was washed with DMF (6 × ca. 5 mL, 1 min each) and then with CH_2Cl_2 (3 × ca. 5 mL, 1 min each).

To monitor the completeness of the couplings, a small amount of resin was cleaved in a new Bio-Rad column using a ca. 1-mL solution of CF_3COOH/water/triisopropylsilane, 8/1/1, *v*/*v*/*v*) and was vigorously agitated for ca. 2 h. The solution was then drained, concentrated by rotary evaporation, and the residue was dissolved in a mixture of water and CH_3CN and injected into an analytical RP-HPLC instrument to determine if any remaining aniline was present. (If any uncoupled aniline was observed on the chromatograph, an additional coupling was carried out. Typically, only the longer oligomers (n = 7–10) required an additional coupling and were required less often when the HCTU coupling method was used.)

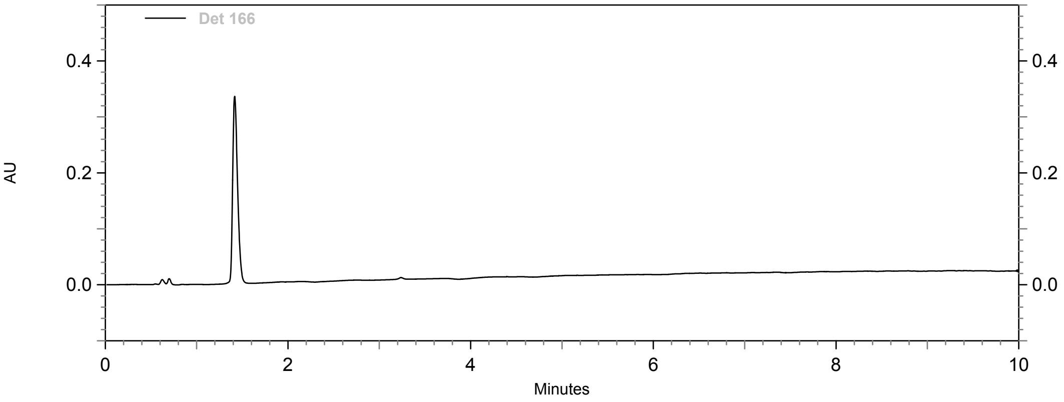
The above procedure was repeated until the desired length of Abc^{2K} oligomer was obtained. After final Fmoc deprotection using 20% piperidine–DMF, washing with DMF (5×) and CH_2Cl_2 (5×), the resin was transferred to a small round bottomed flask equipped with a magnetic stirring bar and treated with ca. 10 mL of CF_3COOH/water/triisopropylsilane (8/1/1, *v*/*v*/*v*) for 2–4 h. The resin was then filtered off using a fritted filter funnel and washed several times with the cleavage cocktail. The solution was concentrated by rotary evaporation. The resultant oil was dissolved in a mixture of water and CH_3CN, and the oligomer was purified by preparative RP-HPLC (water–CH_3CN buffers with 0.1 % TFA). (The oligomers typically eluted between 20 and 30% CH_3CN.) Pure fractions of the product were concentrated by rotary evaporation to remove most of the CH_3CN, frozen, and then lyophilized to afford a white powder (15–

20 mg). The remaining less pure HPLC fractions were also lyophilized into a white powder (ca. 20 mg) and stored for future use.

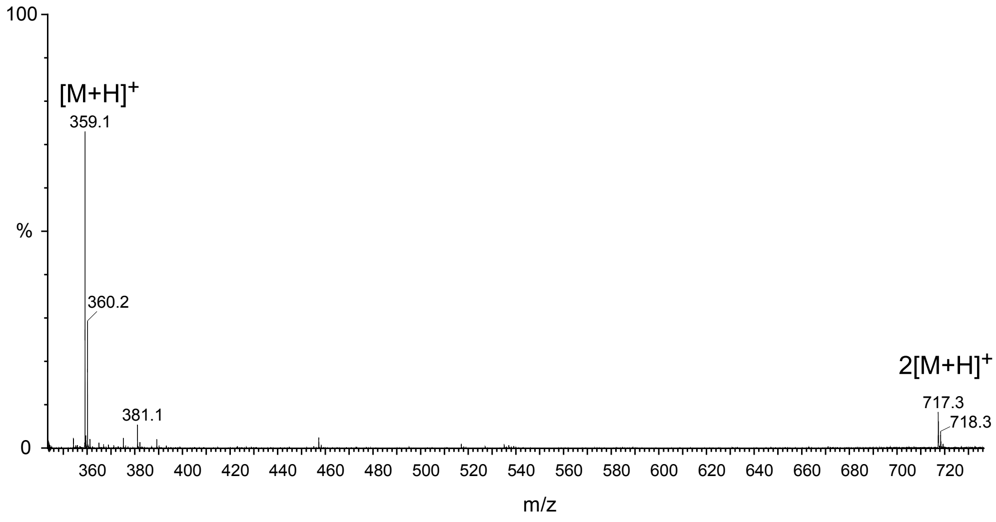
H-(Abc^{2K})$_1$-NH$_2$ TFA salt **9a**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



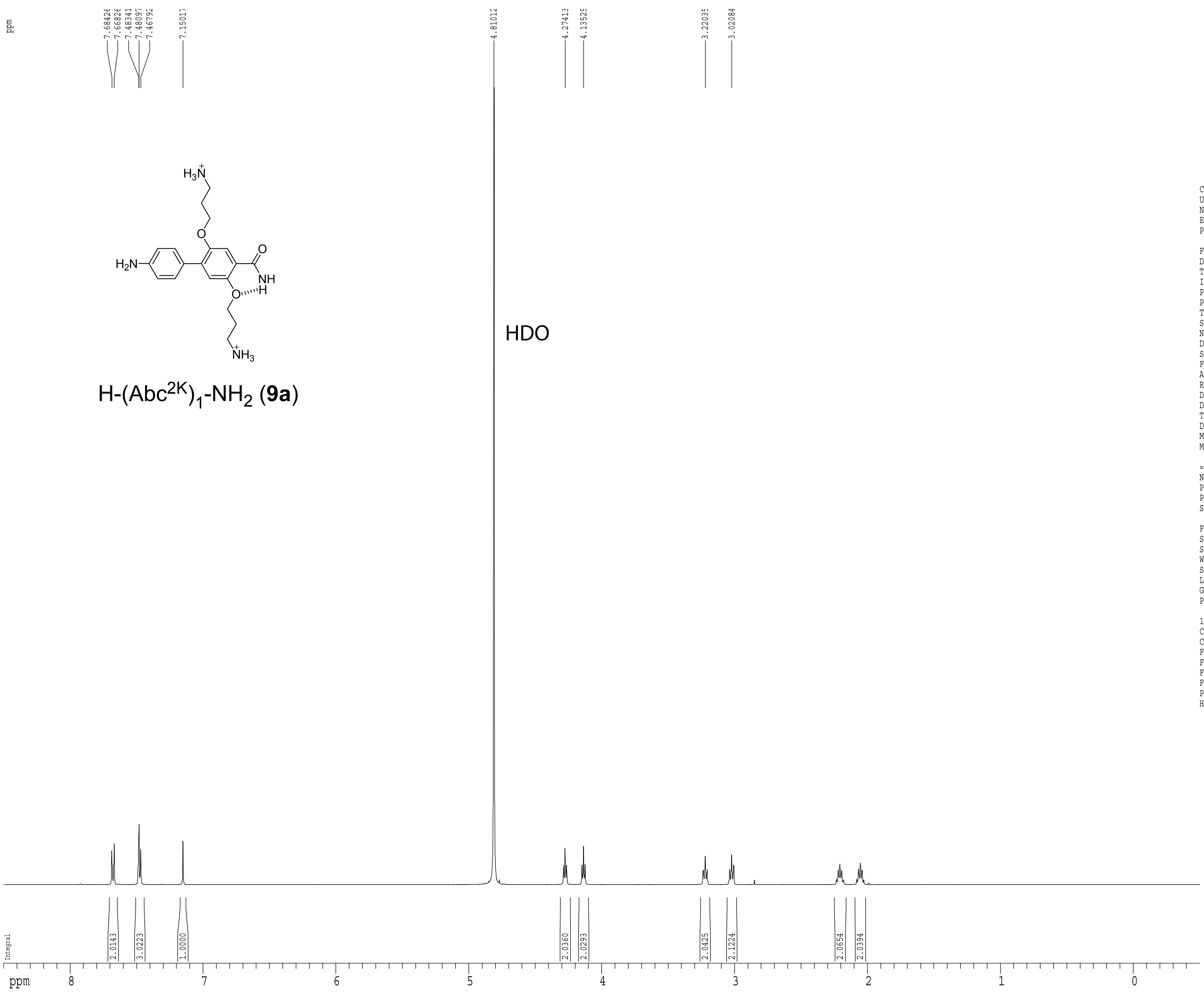
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 10 min, λ = 214)



(b) ESI Mass spectrum. (Calcd exact mass for $C_{19}H_{26}N_4O_3$ [M] = 358.20.)



^1H NMR of Abc^{2K} Monomer H-Abc^{2K}-NH_2 (500 MHz, 298 K, D_2O)



H-$(Abc^{2K})_1$-NH_2 (**9a**)

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Current Data Parameters
USER              cgotha
NAME            na-1-267
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20061111
Time               21.34
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                    32
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                     9
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1        500.2235015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2199992 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 22.86 cm
F1P                8.500 ppm
F1               4251.87 Hz
F2P               -0.500 ppm
F2               -250.11 Hz
PPMCM            0.39474 ppm/cm
HZCM           197.45528 Hz/cm
```
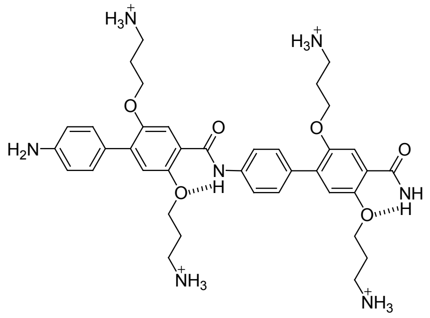
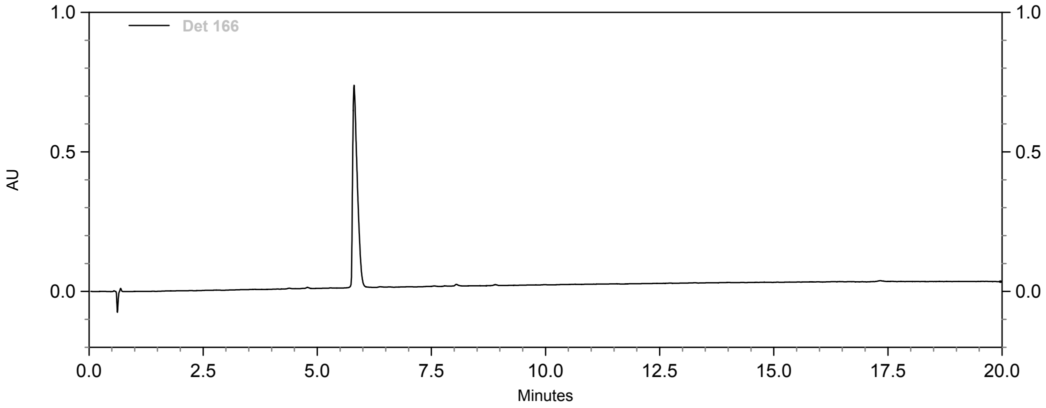
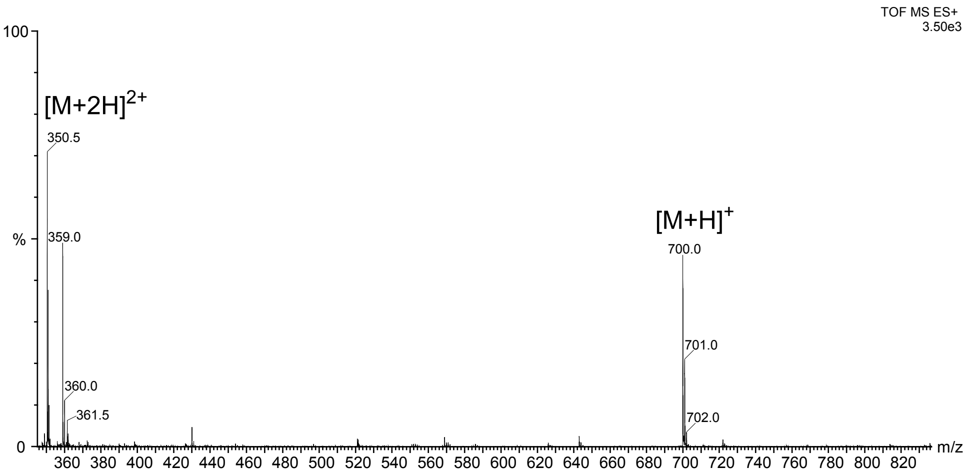

H-(Abc^{2K})$_2$-NH$_2$ TFA salt **9b**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)

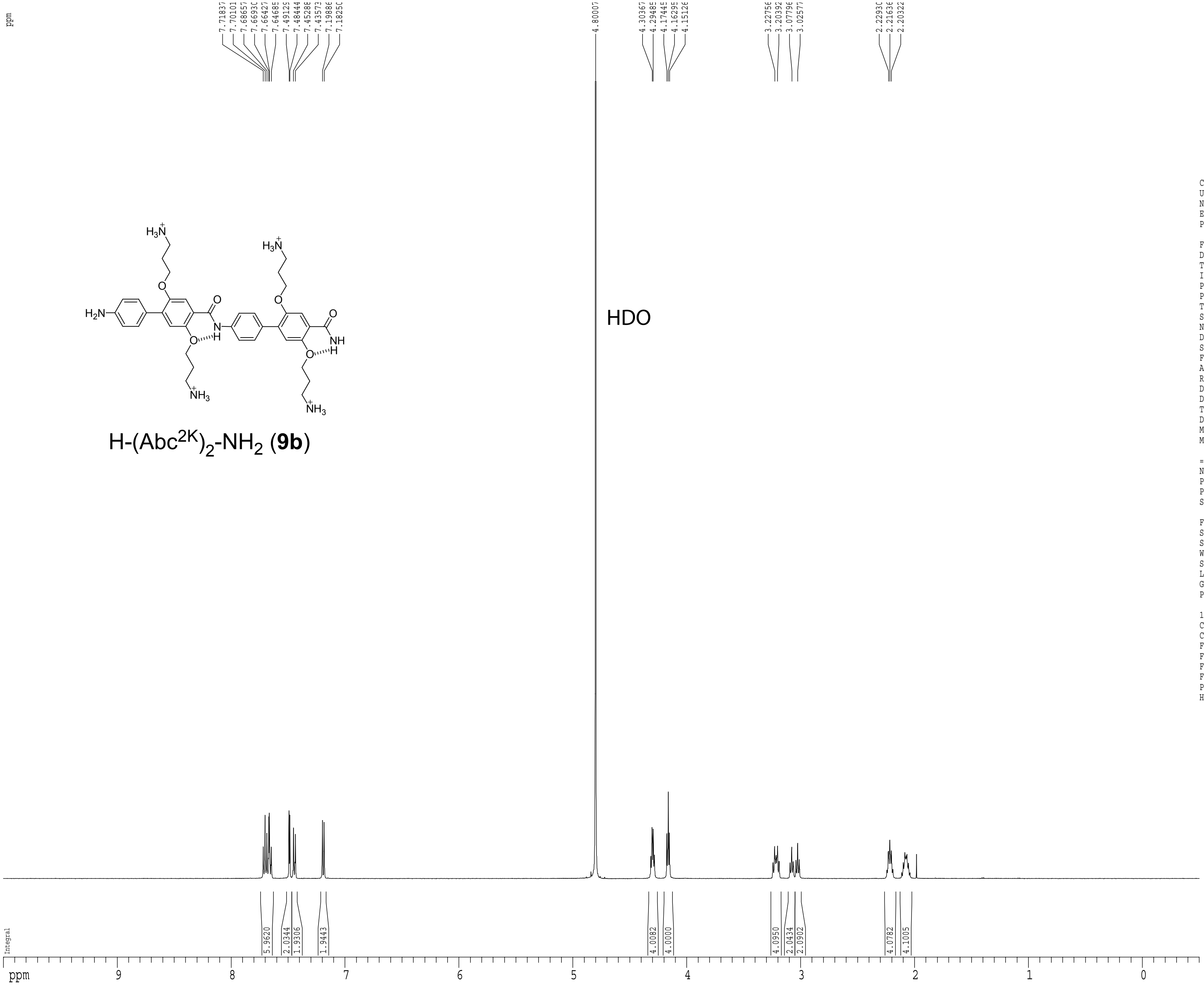


(b) ESI Mass spectrum. (Calcd exact mass for $C_{38}H_{49}N_7O_6$ [M] = 699.37)



^{1}H NMR of Abc^{2K} Dimer H-(Abc^{2K})$_2$-NH$_2$ (500 MHz, 298 K, D$_2$O)

H-(Abc^{2K})$_2$-NH$_2$ (**9b**)



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Current Data Parameters
USER              cgotha
NAME            cg-6-109
EXPNO                  1
PROCNO                 1

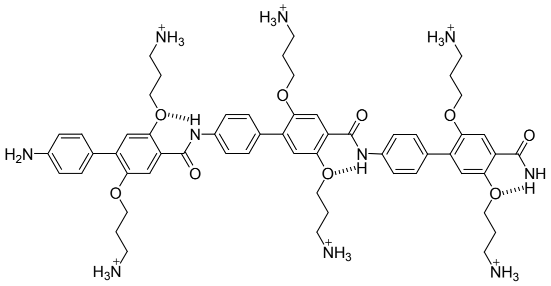
F2 - Acquisition Parameters
Date_           20060810
Time               23.48
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                    44
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                     9
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1         500.2235015 MHz

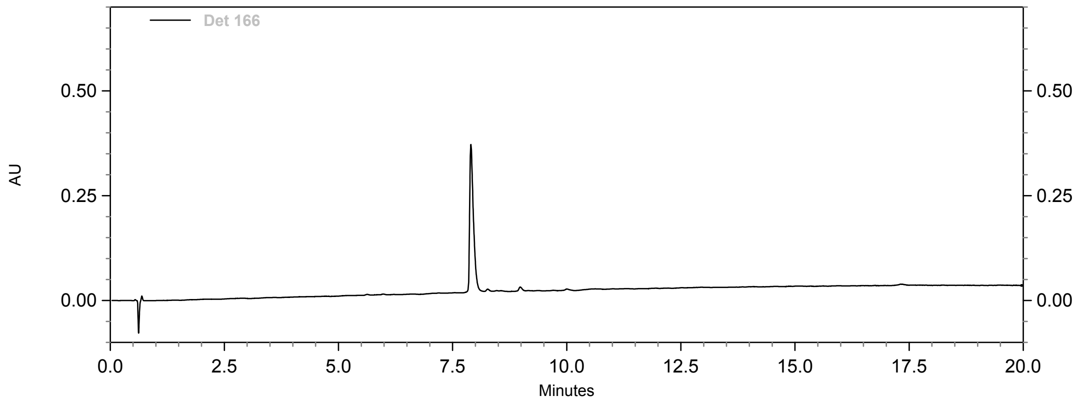
F2 - Processing parameters
SI                 65536
SF           500.2200044 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 74.46 cm
F1P               10.000 ppm
F1               5002.20 Hz
F2P               -0.500 ppm
F2               -250.11 Hz
PPMCM            0.46053 ppm/cm
HZCM           230.36449 Hz/cm
```

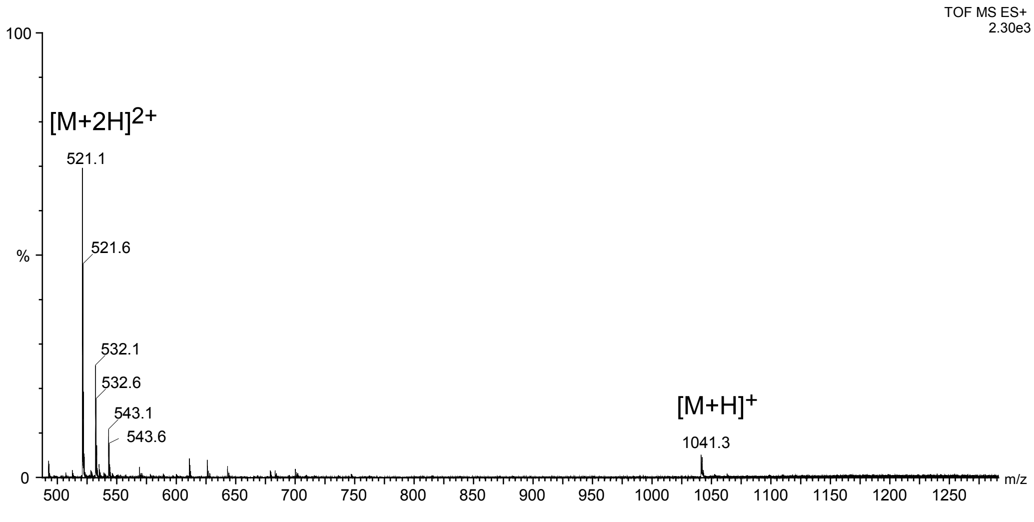
H-(Abc^{2K})$_3$-NH$_2$ TFA salt **9c**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



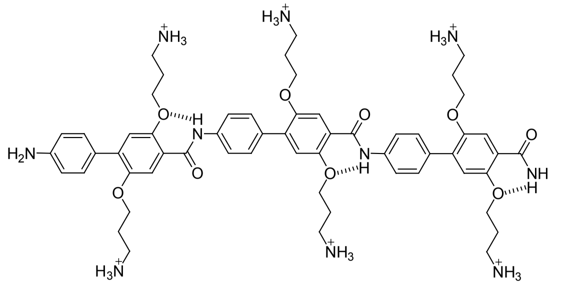
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



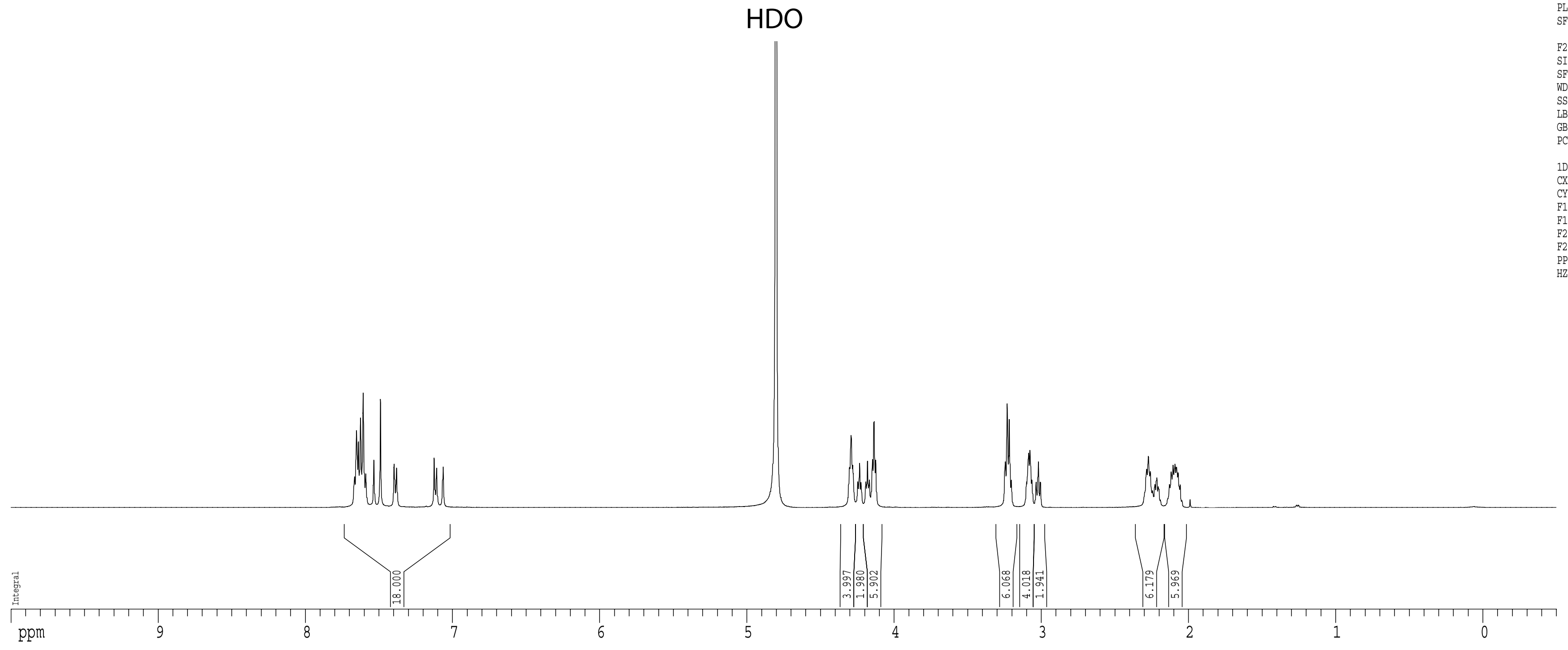
(b) ESI Mass spectrum. (Calcd exact mass for $C_{57}H_{72}N_{10}O_9$ [M] = 1040.55)



^{1}H NMR of Abc^{2K} Trimer H-(Abc^{2K})$_3$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_3$-NH$_2$ (**9c**)



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Current Data Parameters
USER              cgotha
NAME             cg-6-40
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050521
Time               20.12
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                    16
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                 203.2
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1         500.2135015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2100062 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                 75.00 cm
F1P               10.000 ppm
F1               5002.10 Hz
F2P               -0.500 ppm
F2               -250.10 Hz
PPMCM            0.46053 ppm/cm
HZCM           230.35988 Hz/cm
```
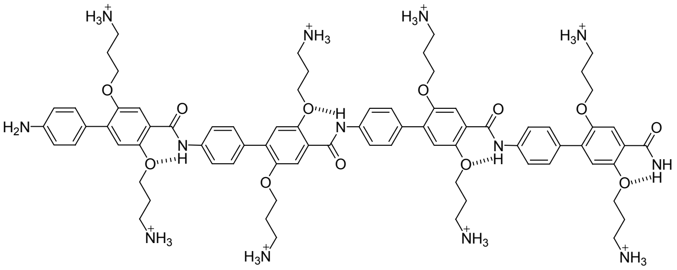
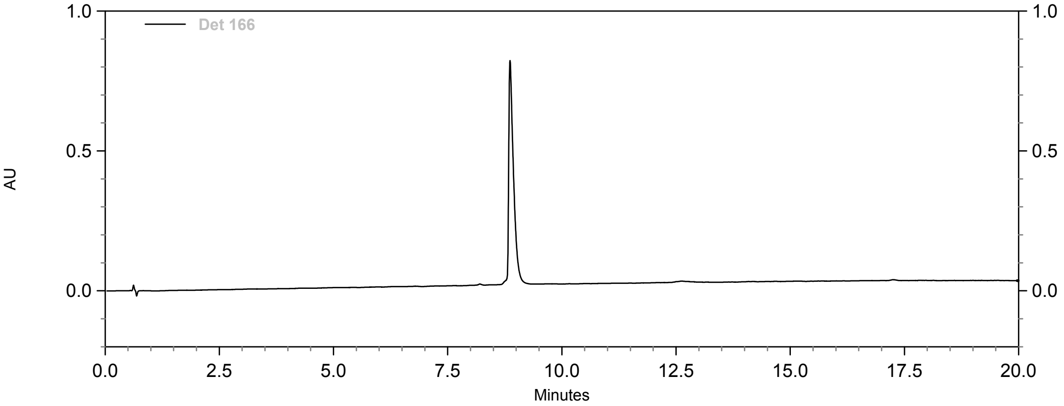
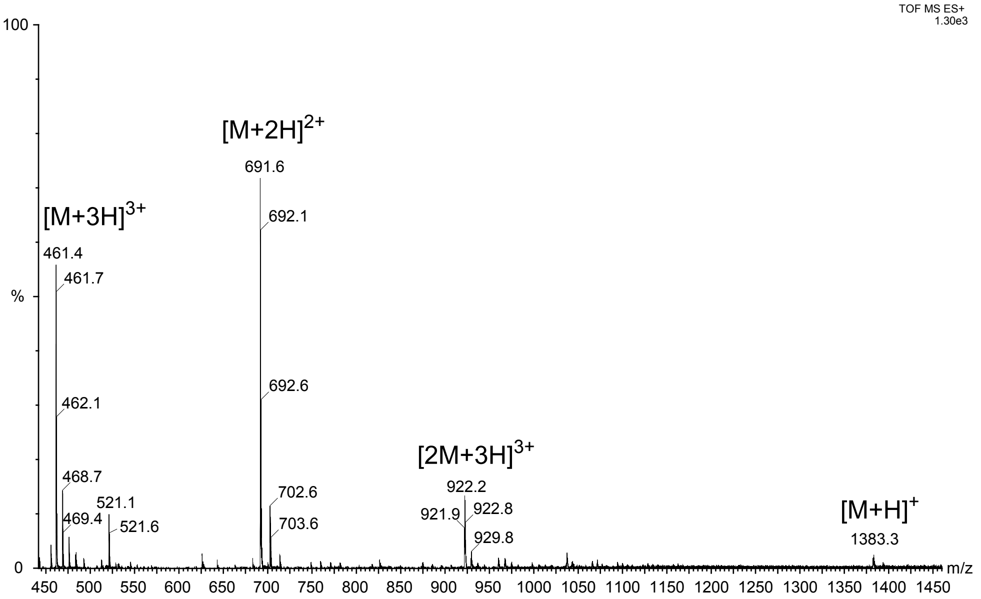

$H\text{-}(Abc^{2K})_4\text{-}NH_2$ TFA salt **9d**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



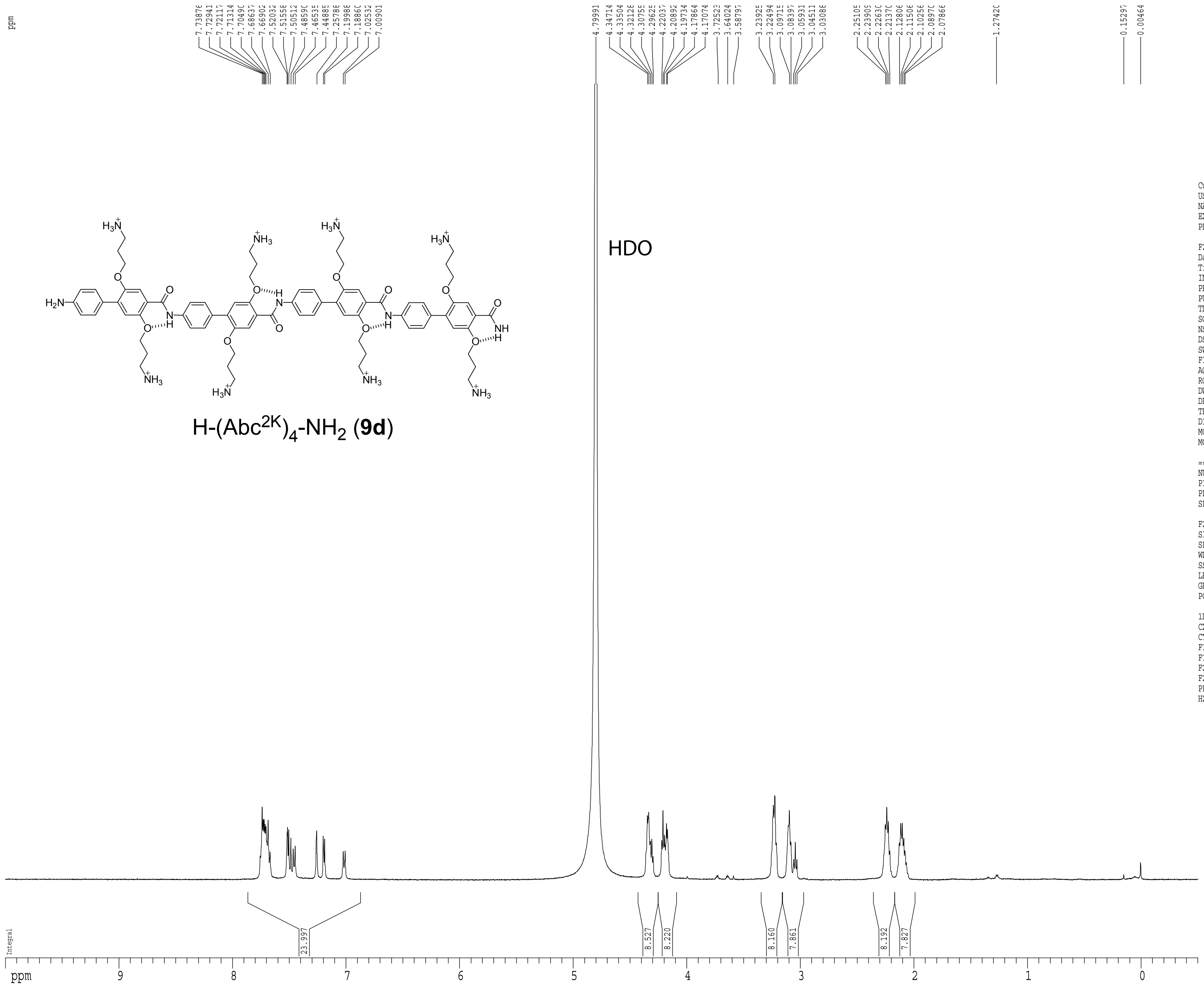
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



(b) ESI Mass spectrum. (Calcd exact mass for $C_{76}H_{95}N_{13}O_{12}$ [M] = 1381.72)



^{1}H NMR of Abc^{2K} Tetramer H-(Abc^{2K})$_4$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_4$-NH$_2$ (**9d**)

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Current Data Parameters
USER              cgotha
NAME            cg-6-86-I
EXPNO                  1
PROCNO                 1

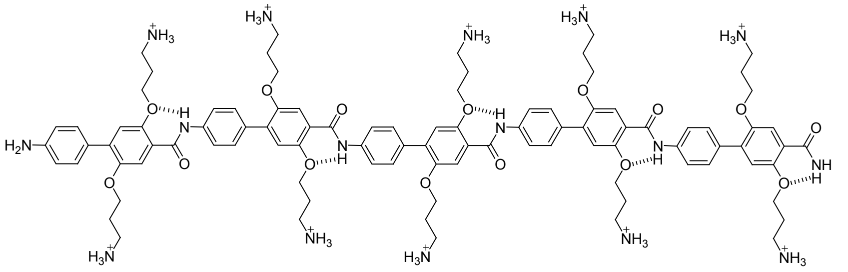
F2 - Acquisition Parameters
Date_           20050601
Time               19.48
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                   150
DS                     2
SWH            8012.820 Hz
FIDRES         0.098043 Hz
AQ            5.0998774 sec
RG                   256
DW               62.400 usec
DE                 6.00 usec
TE                298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1        500.2135015 MHz

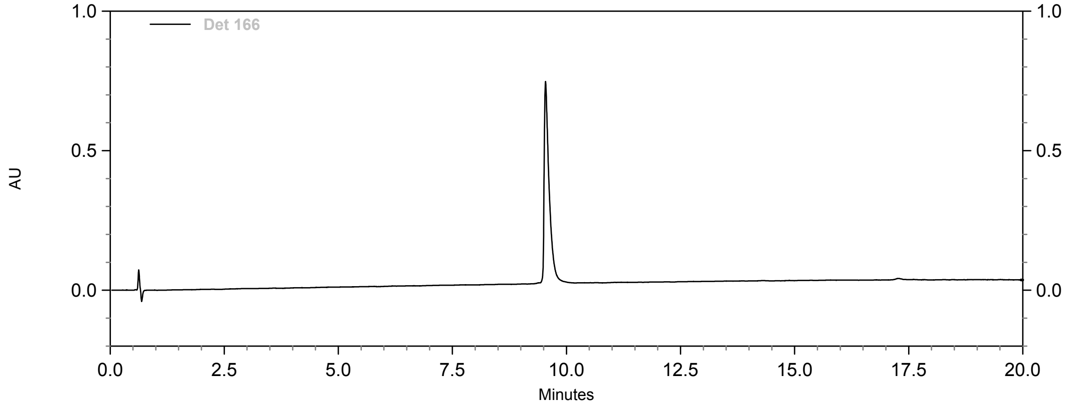
F2 - Processing parameters
SI                 65536
SF          500.2100063 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                483.86 cm
F1P               10.000 ppm
F1               5002.10 Hz
F2P               -0.500 ppm
F2               -250.10 Hz
PPMCM            0.46053 ppm/cm
HZCM           230.35988 Hz/cm
```

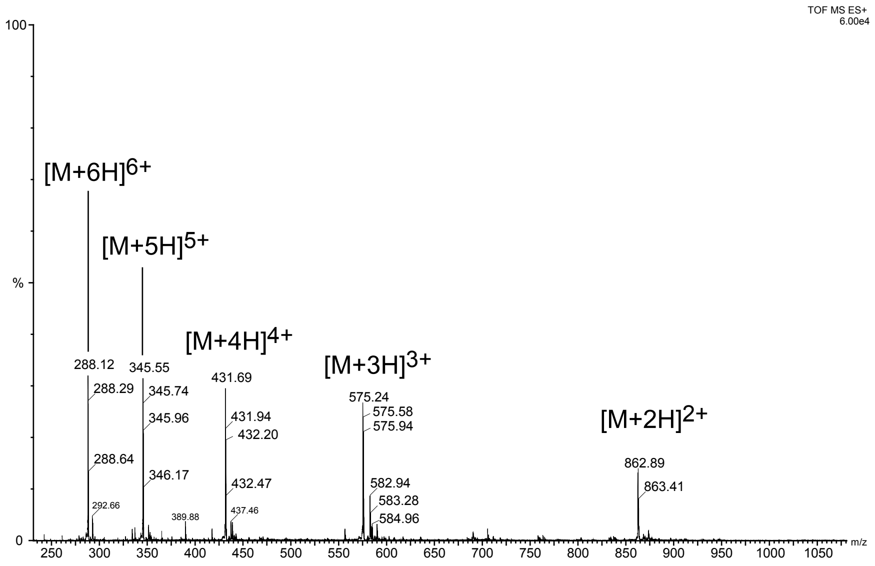
H-(Abc^{2K})$_5$-NH$_2$ TFA salt **9e**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



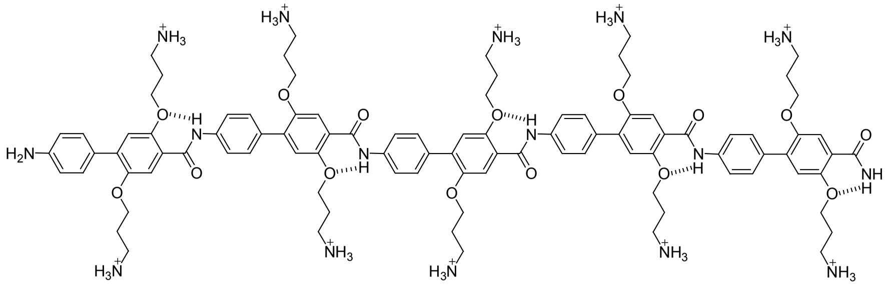
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



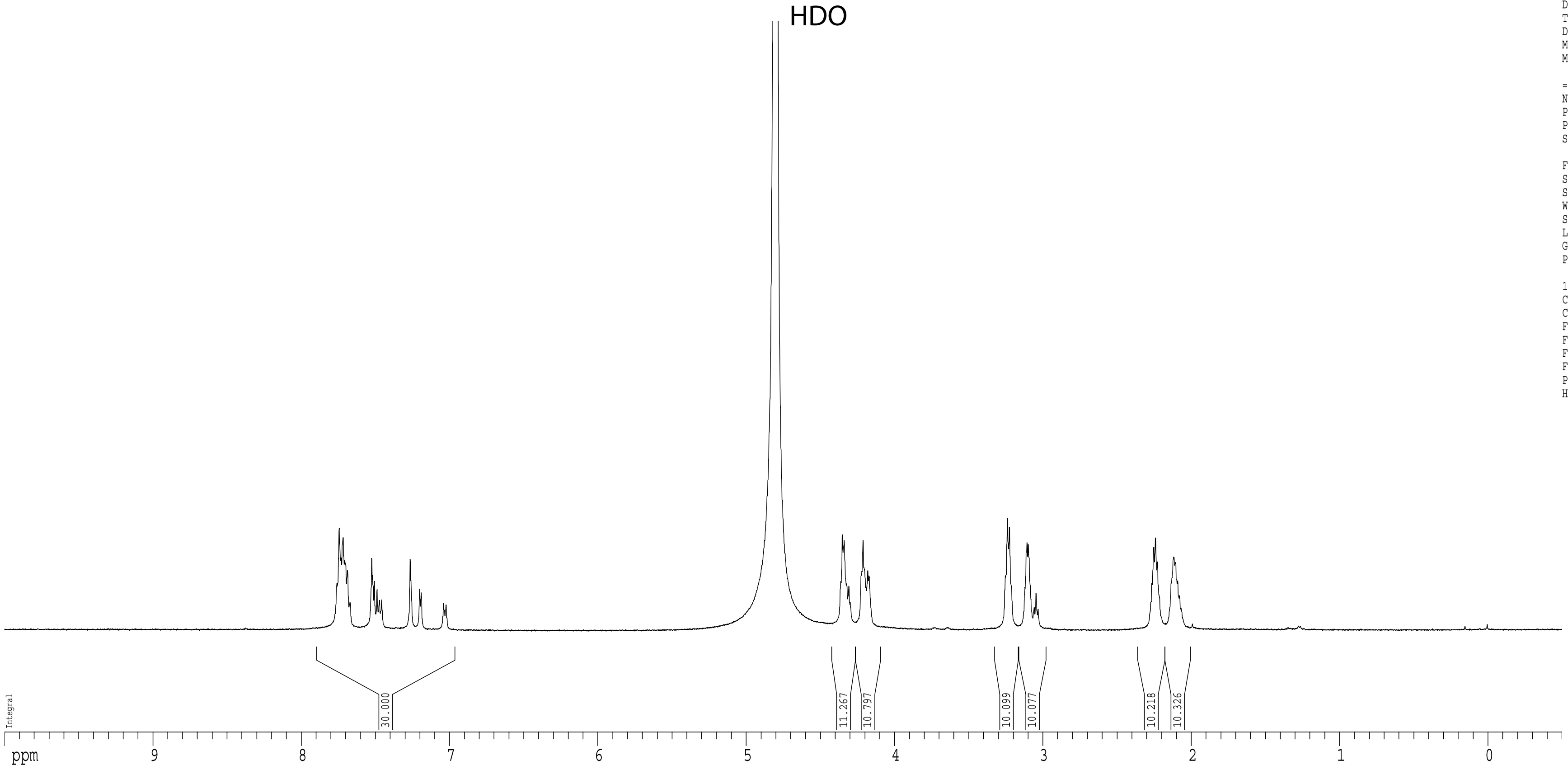
(b) ESI Mass spectrum. (Calcd exact mass for $C_{95}H_{118}N_{16}O_{15}$ [M] = 1722.90)



^{1}H NMR of Abc^{2K} Pentamer H-(Abc^{2K})$_5$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_5$-NH$_2$ (**9e**)



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Current Data Parameters
USER              cgotha
NAME             cg-6-93
EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050603
Time               21.30
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                   128
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                   362
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1         500.2135015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2100061 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                352.52 cm
F1P               10.000 ppm
F1               5002.10 Hz
F2P               -0.500 ppm
F2               -250.10 Hz
PPMCM            0.46053 ppm/cm
HZCM           230.35988 Hz/cm
```
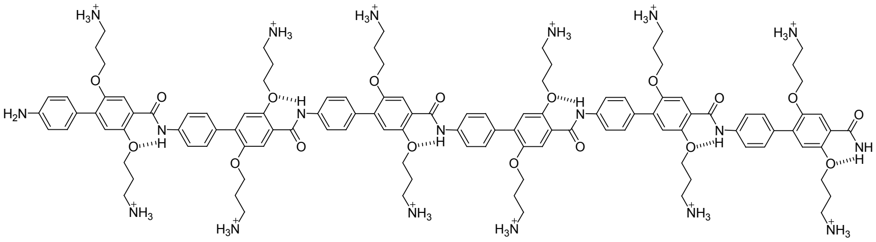
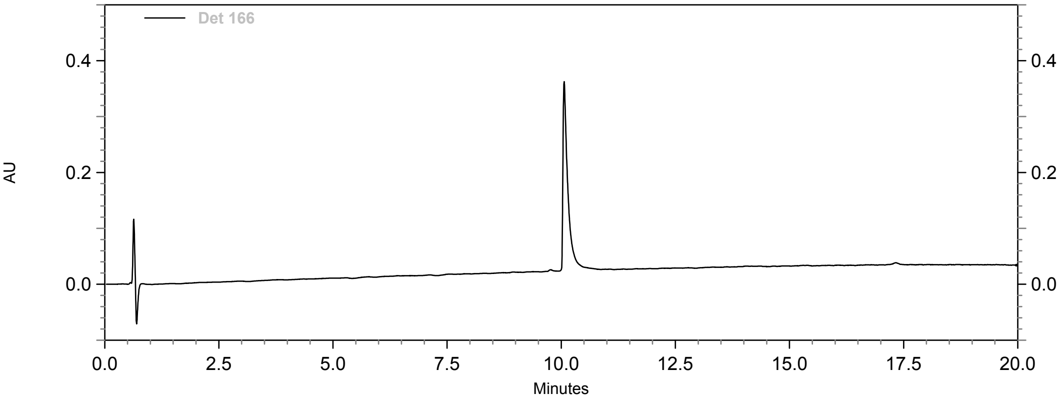
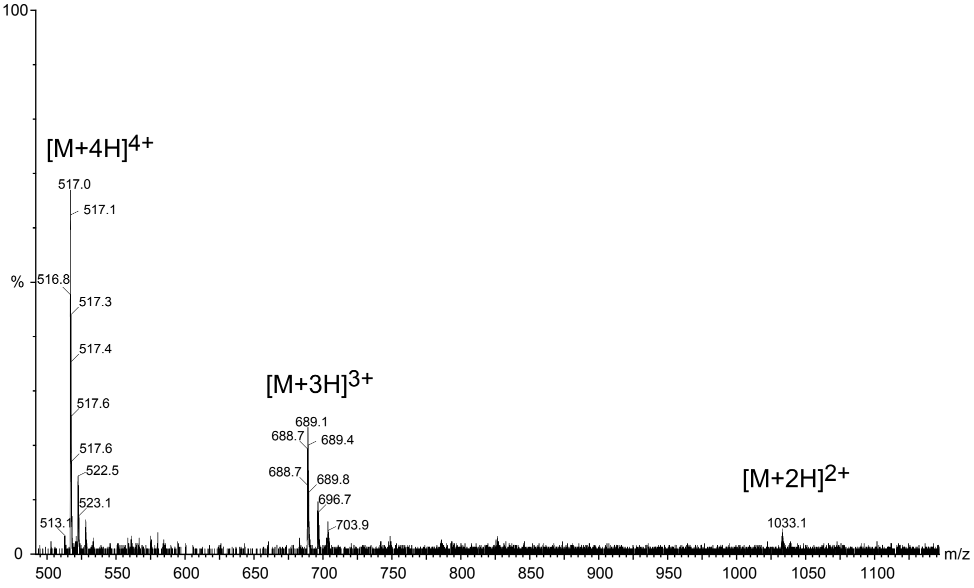

H-(Abc^{2K})$_6$-NH$_2$ TFA salt **9f**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



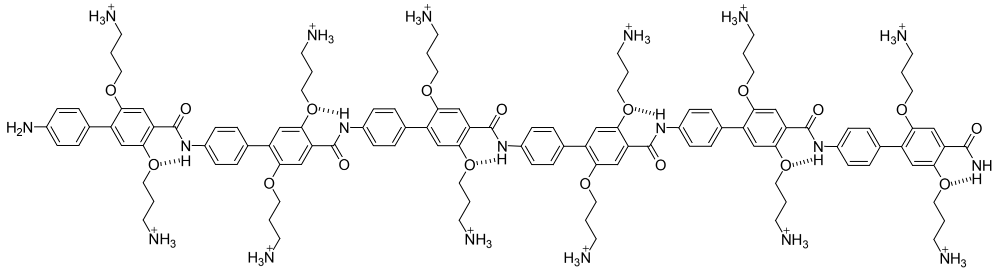
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



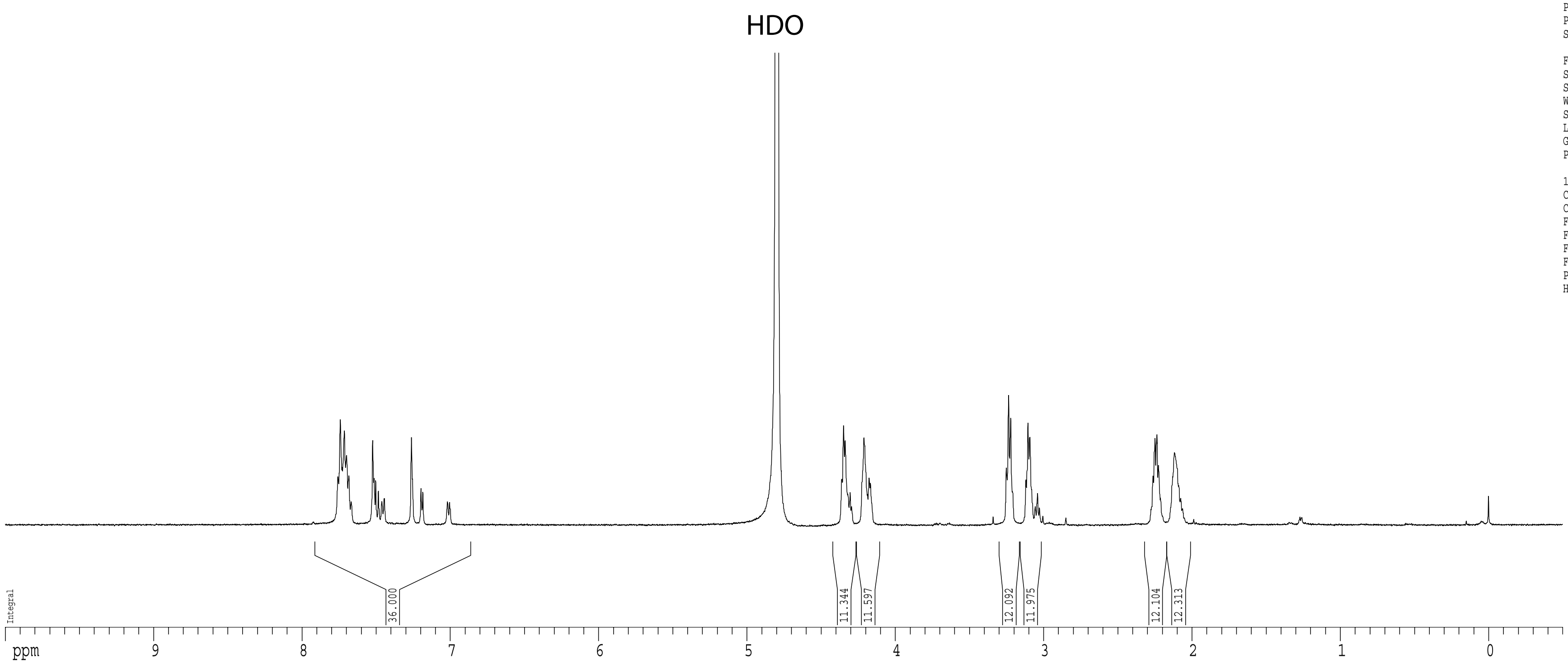
(b) ESI Mass spectrum. (Calcd exact mass for $C_{114}H_{141}N_{19}O_{18}$ [M] = 2064.07)



^{1}H NMR of Abc^{2K} Hexamer H-(Abc^{2K})$_6$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_6$-NH$_2$ (**9f**)



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Current Data Parameters
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NAME            cg-6-94
EXPNO                 4
PROCNO                1

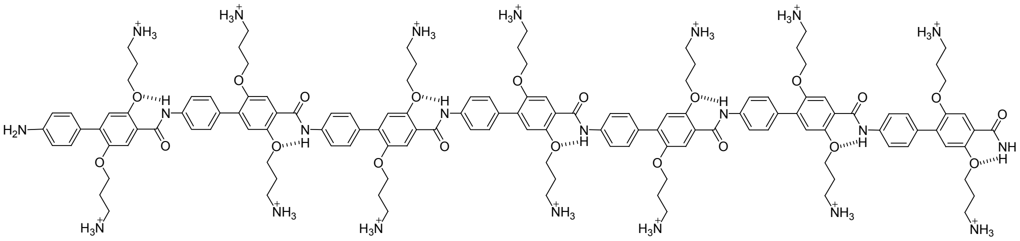
F2 - Acquisition Parameters
Date_          20050603
Time              20.35
INSTRUM         cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG            zg30
TD                81728
SOLVENT             D2O
NS                   32
DS                    2
SWH          8012.820 Hz
FIDRES       0.098043 Hz
AQ          5.0998774 sec
RG                228.1
DW             62.400 usec
DE               6.00 usec
TE              298.0 K
D1         0.10000000 sec
MCREST     0.00000000 sec
MCWRK      0.01500000 sec

======== CHANNEL f1 ========
NUC1                 1H
P1               8.00 usec
PL1              1.60 dB
SFO1     500.2135015 MHz

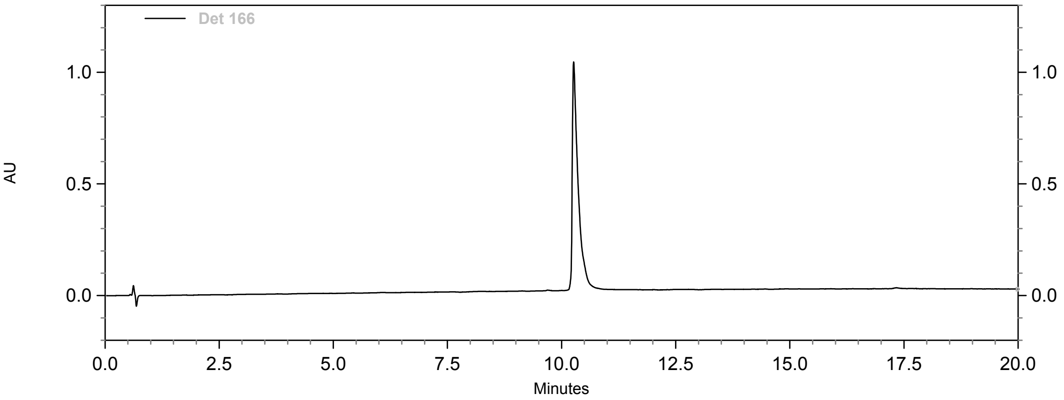
F2 - Processing parameters
SI                65536
SF       500.2100081 MHz
WDW                  EM
SSB                   0
LB               0.30 Hz
GB                    0
PC                 4.00

1D NMR plot parameters
CX              22.80 cm
CY             354.39 cm
F1P            10.000 ppm
F1            5002.10 Hz
F2P            -0.500 ppm
F2            -250.11 Hz
PPMCM        0.46053 ppm/cm
HZCM       230.35989 Hz/cm
```

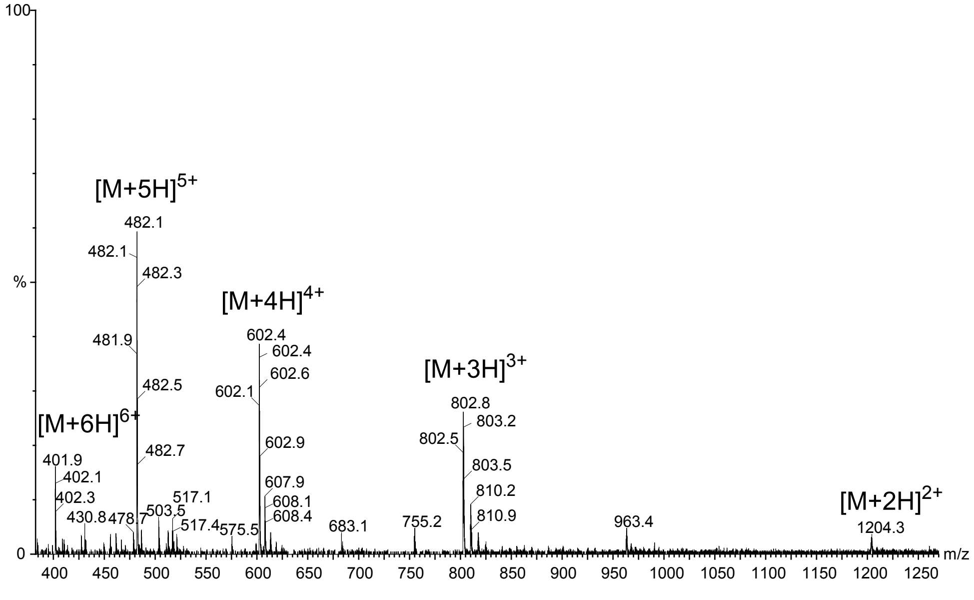
H-(Abc^{2K})$_7$-NH$_2$ TFA salt **9g**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



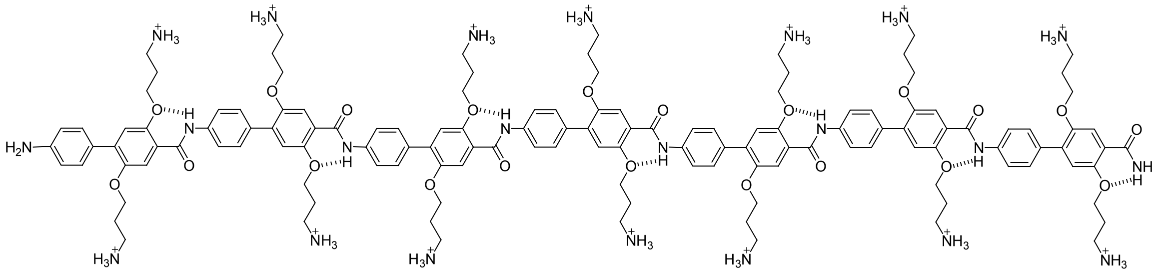
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



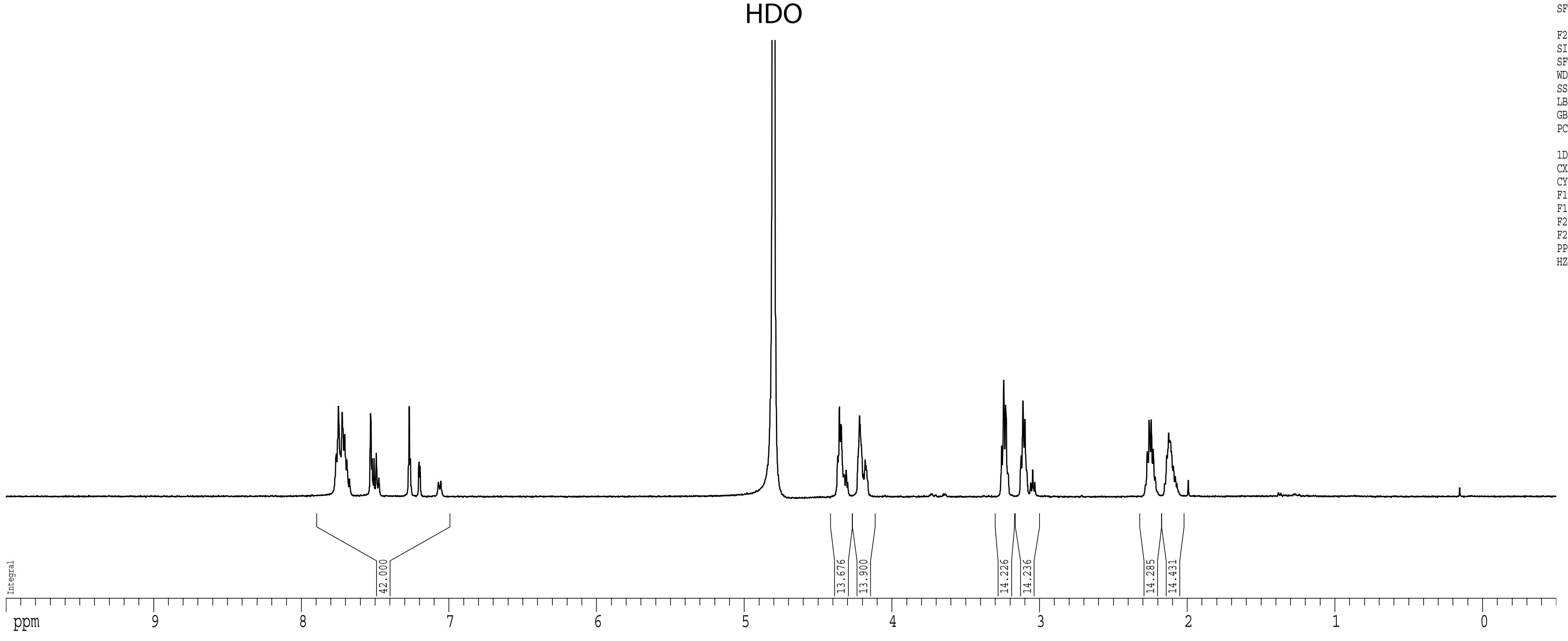
(b) ESI Mass spectrum. (Calcd exact mass for $C_{133}H_{164}N_{22}O_{21}$ [M] = 2405.24)



^{1}H NMR of Abc^{2K} Heptamer H-(Abc^{2K})$_7$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_7$-NH$_2$ (**9g**)



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Current Data Parameters
USER              cgotha
NAME             cg-6-90
EXPNO                  1
PROCNO                 1

F2 - Acquisition Parameters
Date_           20050601
Time               23.18
INSTRUM          cryo500
PROBHD   5 mm CPTCI 1H-
PULPROG             zg30
TD                 81728
SOLVENT              D2O
NS                   150
DS                     2
SWH             8012.820 Hz
FIDRES          0.098043 Hz
AQ             5.0998774 sec
RG                   362
DW                62.400 usec
DE                  6.00 usec
TE                 298.0 K
D1            0.10000000 sec
MCREST        0.00000000 sec
MCWRK         0.01500000 sec

======== CHANNEL f1 ========
NUC1                  1H
P1                  8.00 usec
PL1                 1.60 dB
SFO1        500.2135015 MHz

F2 - Processing parameters
SI                 65536
SF           500.2100062 MHz
WDW                   EM
SSB                    0
LB                  0.30 Hz
GB                     0
PC                  4.00

1D NMR plot parameters
CX                 22.80 cm
CY                575.93 cm
F1P               10.000 ppm
F1               5002.10 Hz
F2P               -0.500 ppm
F2               -250.10 Hz
PPMCM            0.46053 ppm/cm
HZCM           230.35988 Hz/cm
```
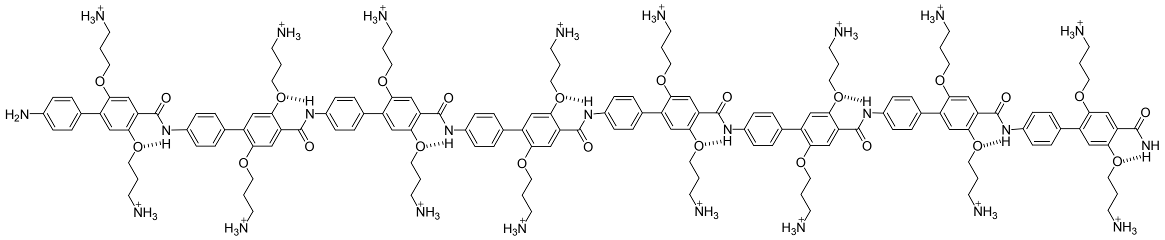
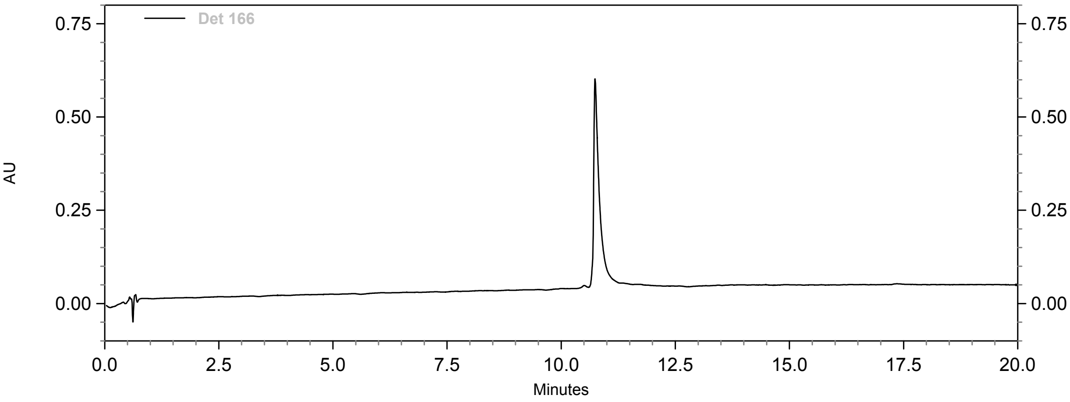
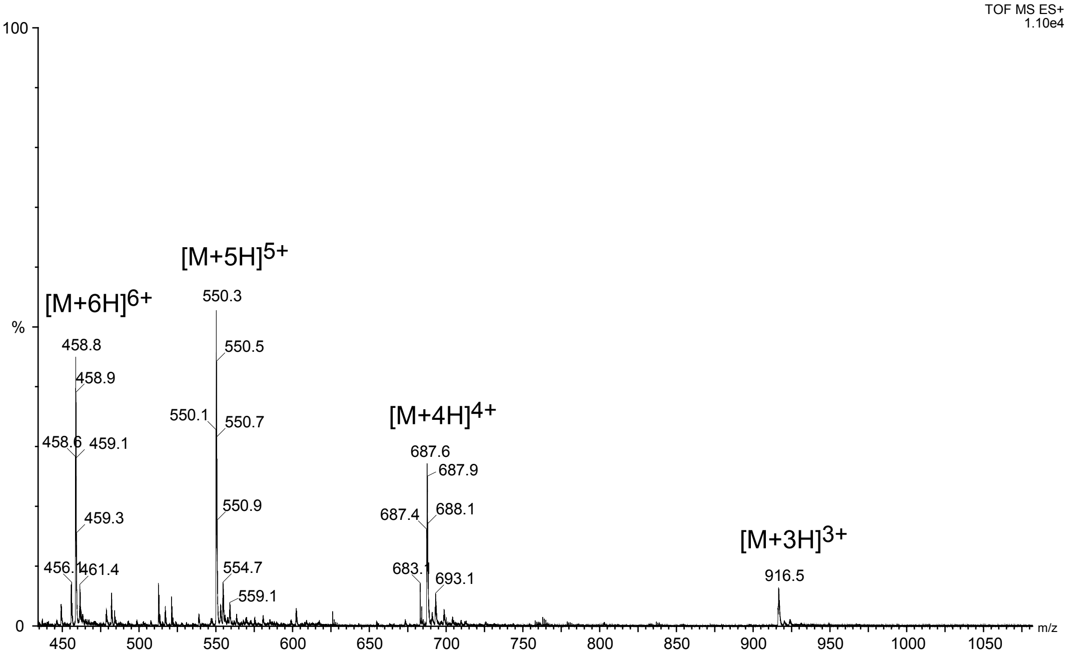

H-(Abc^{2K})$_8$-NH$_2$ TFA salt **9h**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



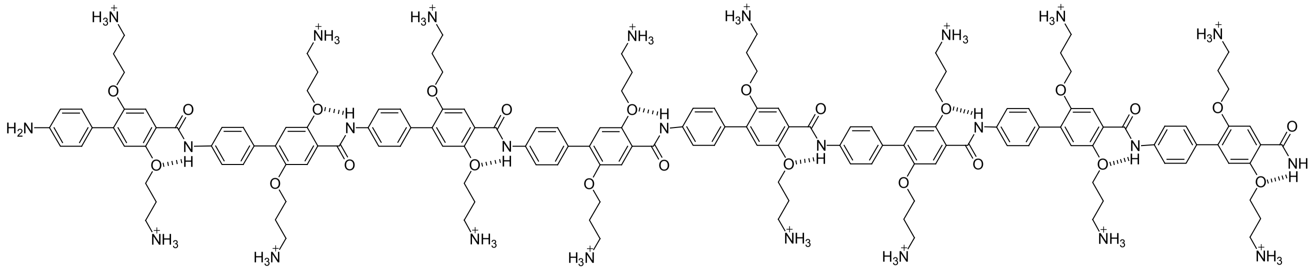
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



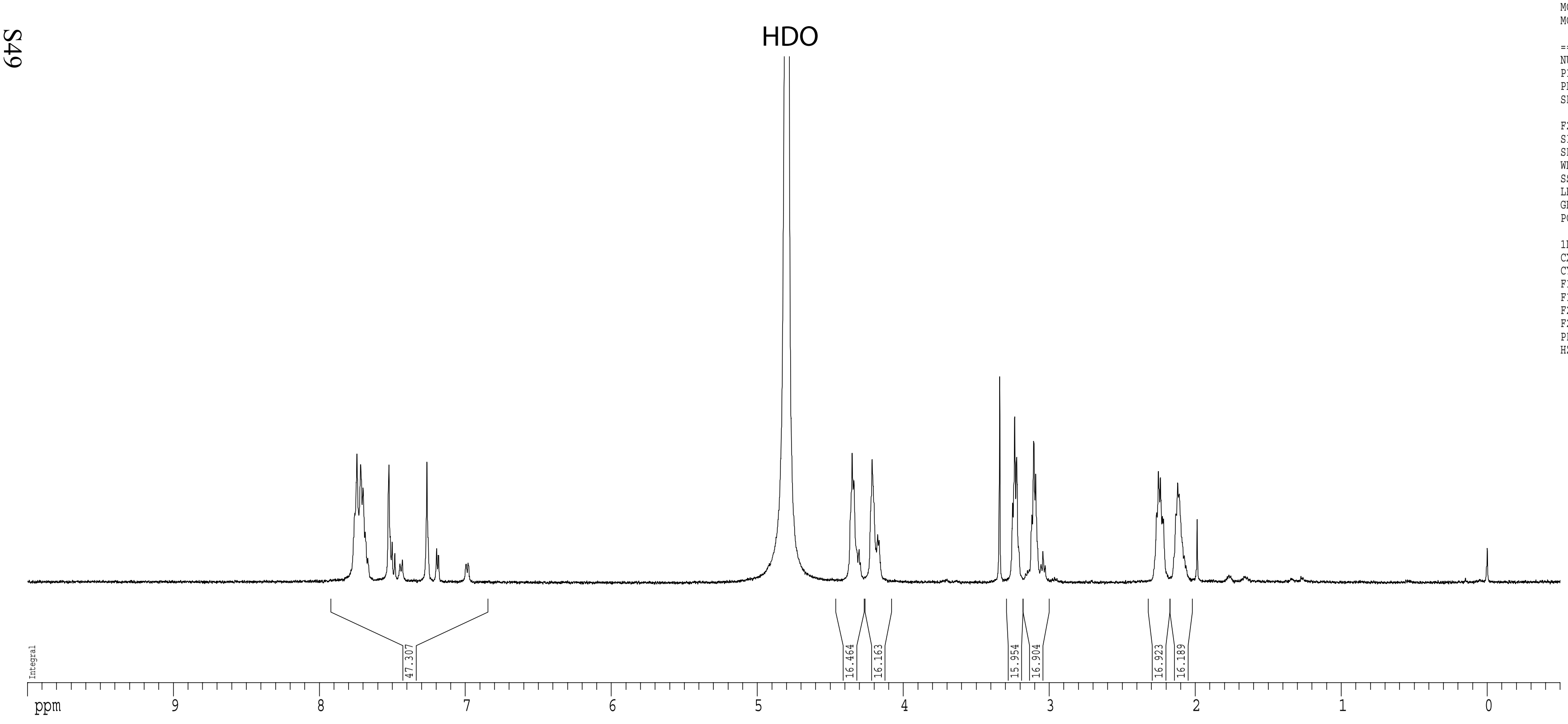
(b) ESI Mass spectrum. (Calcd mass for $C_{152}H_{187}N_{25}O_{24}$ [M] = 2746.42)



^{1}H NMR of Abc^{2K} Octamer H-(Abc^{2K})$_8$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_8$-NH$_2$ (**9h**)



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CY               528.20 cm
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F1              5002.10 Hz
F2P              -0.500 ppm
F2              -250.11 Hz
PPMCM          0.46053 ppm/cm
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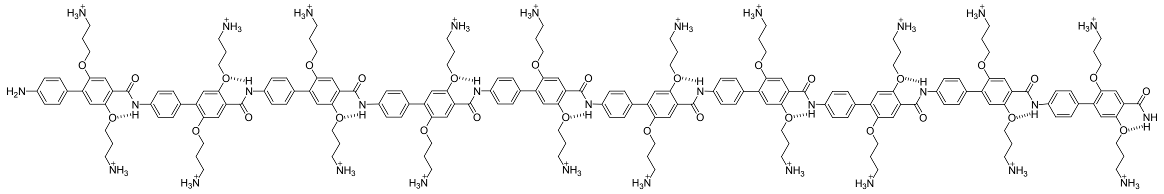
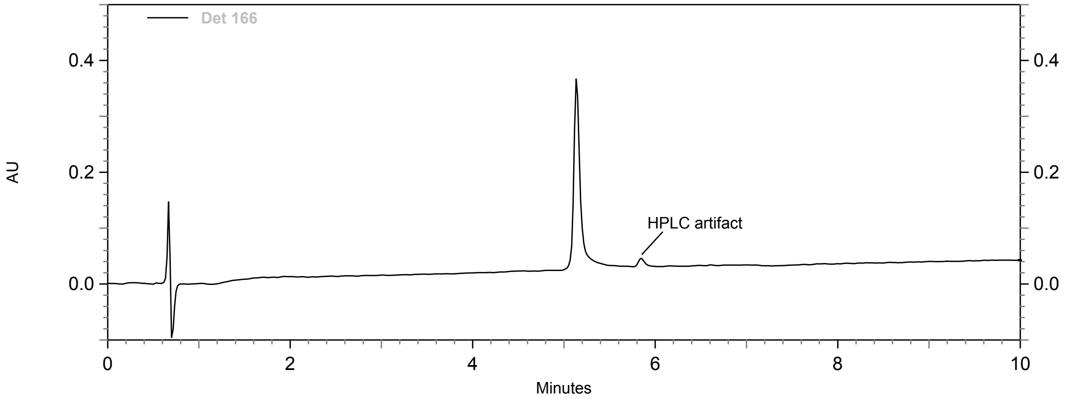
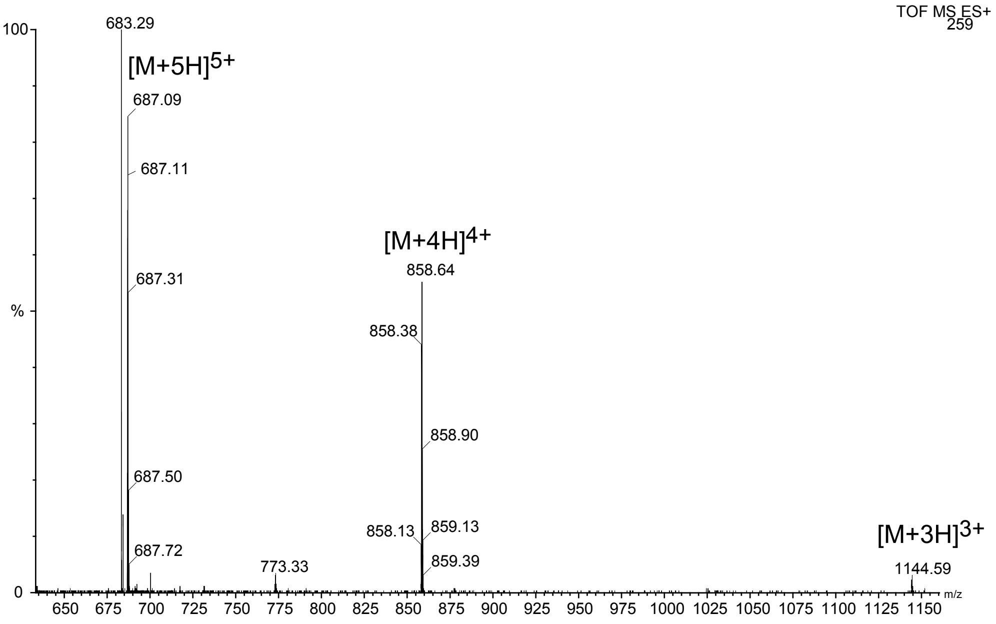
H-(Abc^{2K})$_{10}$-NH$_2$ TFA salt **9i**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



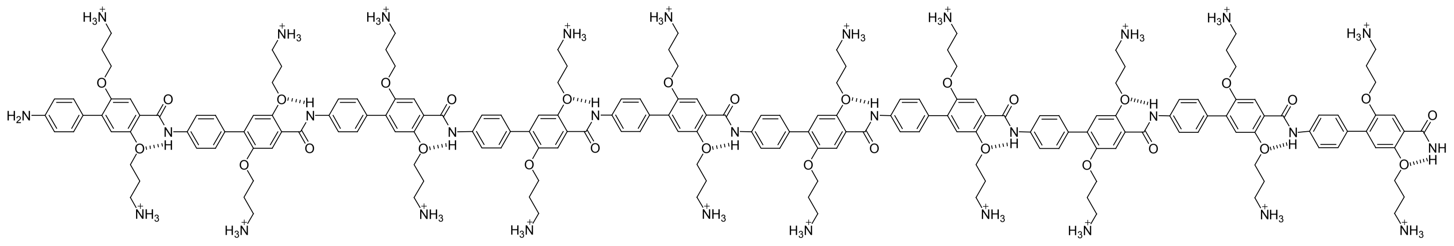
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 10 min, λ = 214)



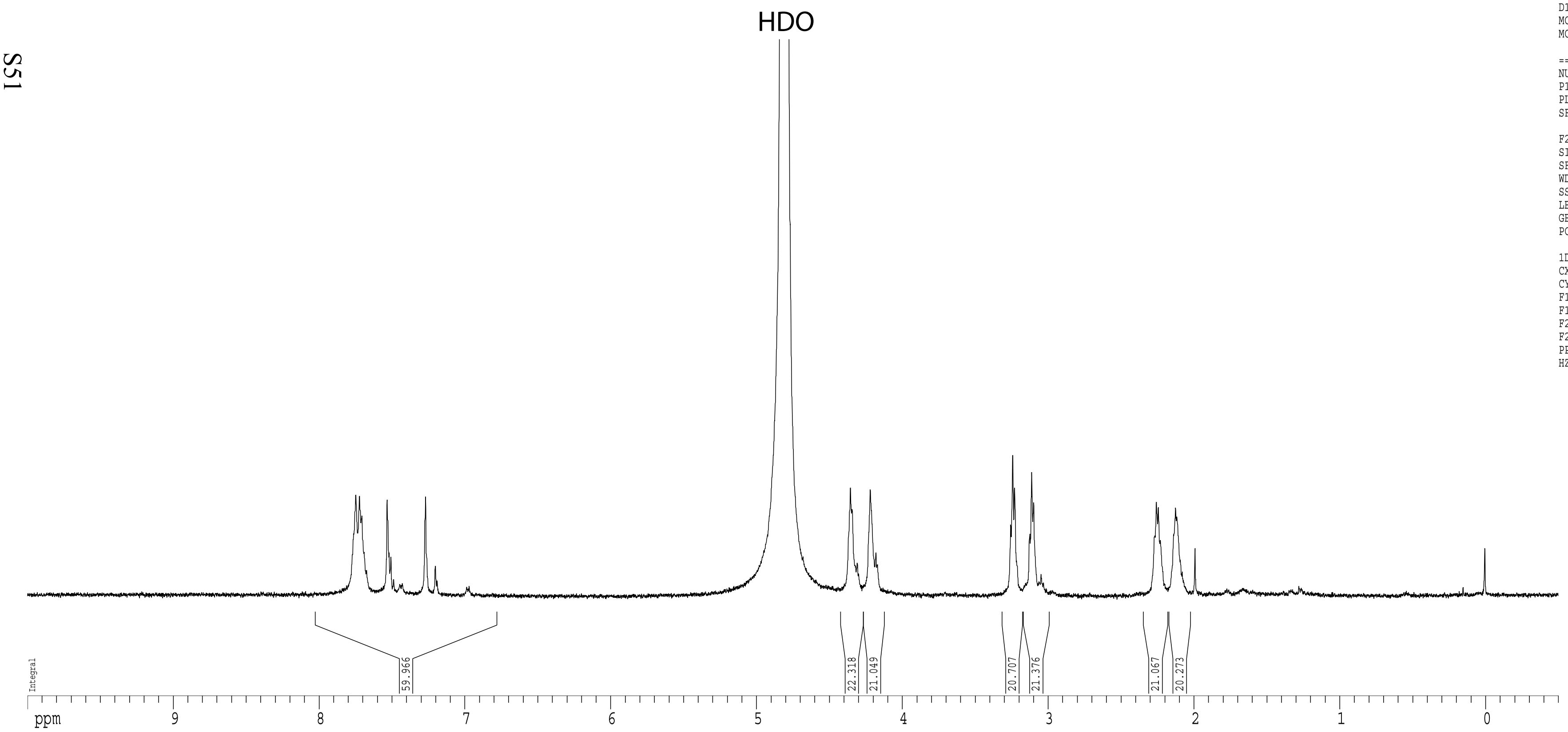
(b) ESI Mass spectrum. (Calcd exact mass for $C_{190}H_{233}N_{31}O_{30}$ [M] = 3428.77)



^{1}H NMR of Abc^{2K} Decamer H-(Abc^{2K})$_{10}$-NH$_2$ (500 MHz, 298 K, D$_2$O)



H-(Abc^{2K})$_{10}$-NH$_2$ (**9i**)



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SWH            8012.820 Hz
FIDRES         0.098043 Hz
AQ            5.0998774 sec
RG                   228.1
DW              62.400 usec
DE                6.00 usec
TE                 298.0 K
D1          0.10000000 sec
MCREST      0.00000000 sec
MCWRK       0.01500000 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                8.00 usec
PL1                1.60 dB
SFO1         500.2135015 MHz

F2 - Processing parameters
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SF           500.2100062 MHz
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SSB                      0
LB                 0.30 Hz
GB                       0
PC                    4.00

1D NMR plot parameters
CX                22.80 cm
CY              1248.66 cm
F1P              10.000 ppm
F1               5002.10 Hz
F2P              -0.500 ppm
F2               -250.10 Hz
PPMCM           0.46053 ppm/cm
HZCM          230.35988 Hz/cm
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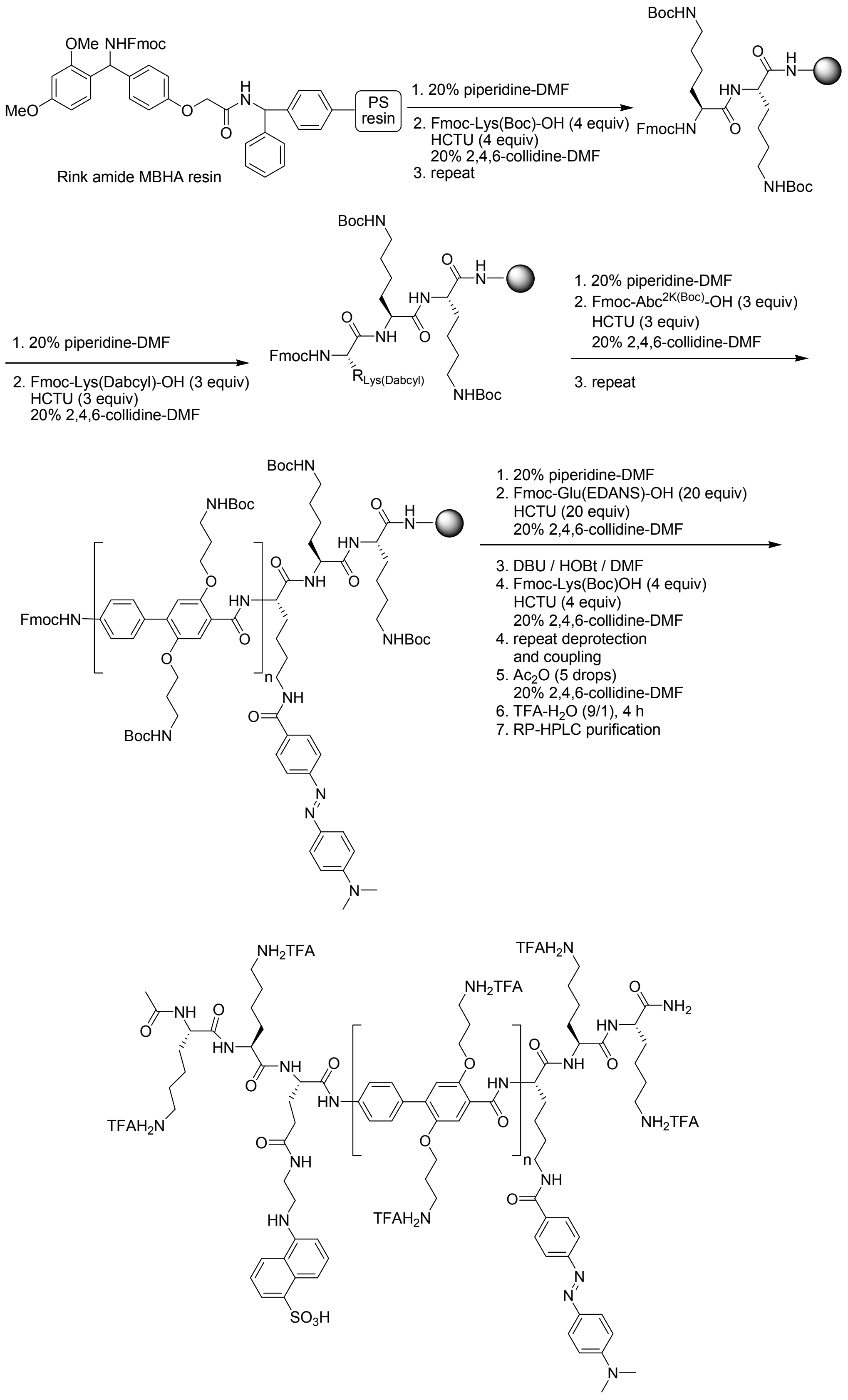

10a n=1; **10b** n=2; **10c** n=3; **10d** n=4; **10e** n=5; **10f** n=6; **10g** n=7; **10h** n=8; **10i** n=9; **10j** n=10

Synthesis of Abc^{2K} Oligomers 10a-10j: Ac-(Lys)$_2$-Glu(EDANS)-(Abc^{2K})$_n$-Lys(Dabcyl)-(Lys)$_2$-NH$_2$ (n=1-10). Rink amide MBHA resin (74 mg, 0.34 mmol/g, Novabiochem) contained in Bio-Rad Poly-Prep chromatography column was soaked in CH_2Cl_2 for 15 min and then washed with DMF (3 × ca. 5 mL, 1 min each). Fmoc deprotection was carried out using a solution of 20% piperidine–DMF (1 × ca. 5 mL for 1 min, 1 × ca. 5 mL for 20 min). Solutions were mixed with the resin by capping the column on both ends, and slowly agitating the column. Solutions were drained from the column using nitrogen pressure. After Fmoc deprotections, the resin was washed with DMF (6 × ca. 5 mL, 1 min each) and then CH_2Cl_2 6 × ca. 5 mL, 1 min each). Lysine residues were coupled to the resin by pre-activating Fmoc-Lys(Boc)-OH (47 mg, 0.10 mmol) with HCTU (41 mg, 0.10 mmol) in ca. 0.5 mL of 20% 2,4,6-collidine for 1 min and then adding the resultant solution to the resin and gently agitating the resin for ca. 2 h. Lysine couplings were determined to be complete by use of the ninhydrin test. Lys(Dabcyl) residues were coupled to the resin by dissolving Fmoc-Lys(Dabcyl)-OH (31 mg, 0.050 mmol) and HCTU (21 mg, 0.05 mmol) in ca. 0.5 mL of 20% 2,4,6-collidine–DMF, adding the resultant solution to the resin, and then gently agitating the resin for 6-12 h. Abc^{2K} residues were coupled to the resin by pre-activating Fmoc-Abc$^{2K(Boc)}$-OH (59 mg, 0.075 mmol) with HCTU (31 mg, 0.075 mmol) in ca. 0.5 mL of 20% 2,4,6-collidine–DMF. The coupling solution was then added to the resin and gently agitated for ca. 12 h. To determine if Abc^{2K} couplings were complete, a small amount of resin was treated in a new Bio-Rad column with a solution of CF_3COOH/water (9/1, *v*/*v*) and the column was rigorously agitated for ca. 2 h. The solution was then drained, concentrated by rotary evaporation, and the residue was dissolved in a mixture of water and CH_3CN

and then injected into an analytical RP-HPLC instrument to determine if any remaining aniline was present. (If the uncoupled Abc^{2K} aniline was observed on the chromatograph, an additional coupling was carried out.) The Glu(EDANS) residue was coupled to the resin by pre-activating Fmoc-Glu(EDANS)-OH (220 mg, 0.35 mmol) with HCTU (145 mg, 0.35 mmol) in ca. 1 mL of 20% 2,4,6-collidine–DMF. The coupling solution was added to the resin and the resin was gently agitated for ca. 48 h. To avoid degradation of the EDANS group, Fmoc deprotections that followed the couplings of Fmoc-Glu(EDANS)-OH were accomplished by soaking the resin with a solution of DBU (1.2 mL) and HOBT (0.99 g) in DMF (88 mL) (4 × ca. 2 mL for 1 min each).[6] The resin was then washed with DMF (6 × ca. 5 mL, 1 min each) and then CH_2Cl_2 6 × ca. 5 mL, 1 min each). After the coupling of the final two lysine residues and removal of last Fmoc group using the above DBU procedure, the aniline was acetylated by the addition of acetic anhydride (7-10 drops) in ca. 2 mL of 20% 2,4,6-collidine–DMF and the resin was gently agitated for 10 min. After the resin was soaked with DMF (4 × ca. 5mL, for 1 min) and CH_2CH_2 (6 × ca. 5mL, for 1 min), the resin was then transferred to a small round bottomed flask equipped with a magnetic stirring bar, and mixed with 10-20 mL of CF_3COOH/water (9/1, *v*/*v*) for 4 h while being protected from light sources. The resin was then filtered off using a fritted funnel, washed with additional cleavage cocktail, concentrated by rotary evaporation, and the resultant oil was dissolved in a mixture of water and CH_3CN. The oligomer was purified by preparative RP-HPLC (water–CH_3CN buffers with 0.1 % TFA). (The oligomers typically eluted between 20 and 30% CH_3CN). Pure fractions of the product were concentrated by rotary evaporation to remove most of

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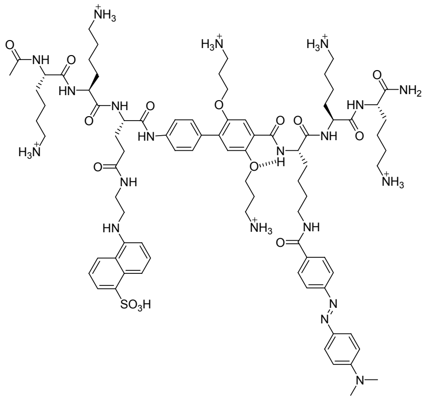
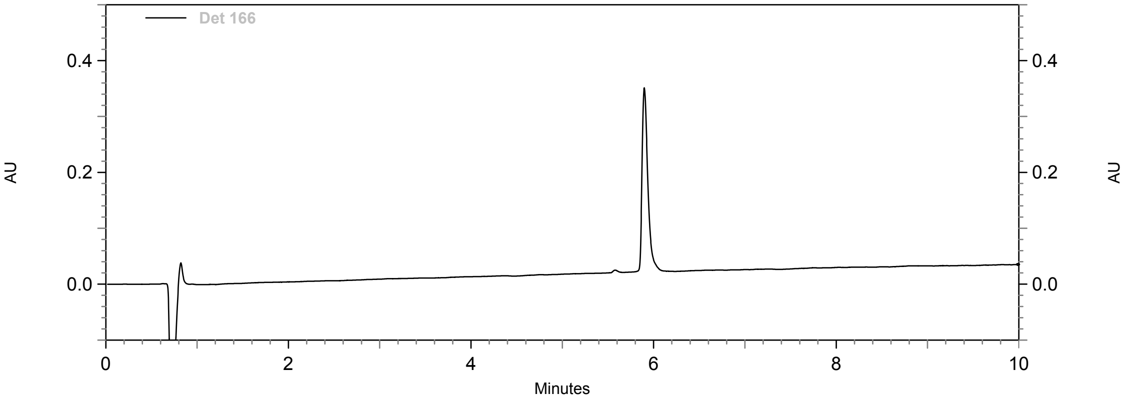
[6] Tickler, A. K.; Barrow, C. J.; Wade, J. D. *J. Pept. Sci.* **2001**, *7*, 488.

the CH_3CN, frozen, and then lyophilized to afford a red powder (5–10 mg). The remaining less pure HPLC fractions were also lyophilized into a red powder (5–10 mg) and stored for future use.

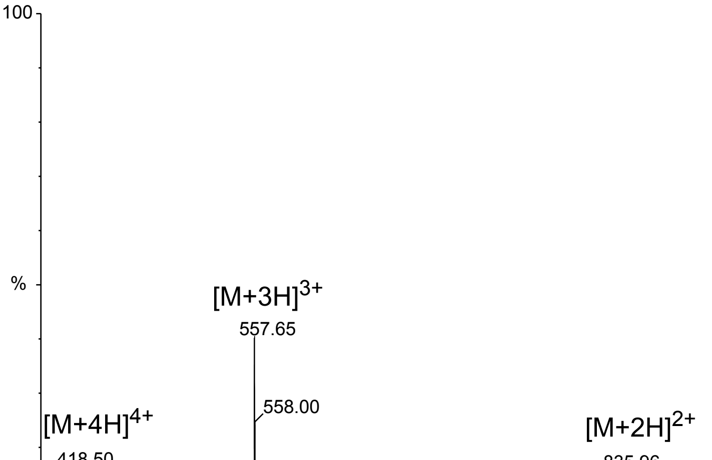
Ac-Lys-Lys-Glu(EDANS)-$(\text{Abc}^{2K})_1$-Lys(Dabcyl)-Lys-Lys-NH_2 TFA salt **10a**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



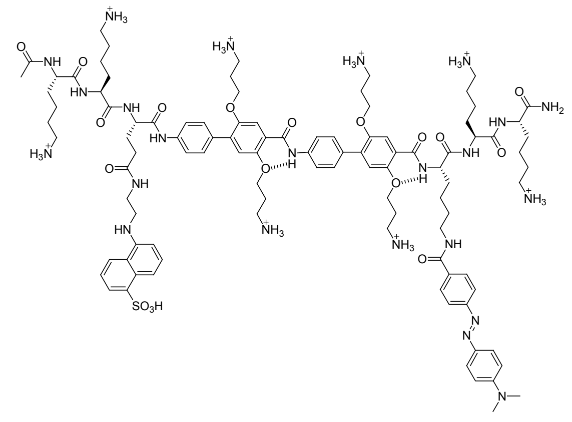
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 10 min, λ = 214)



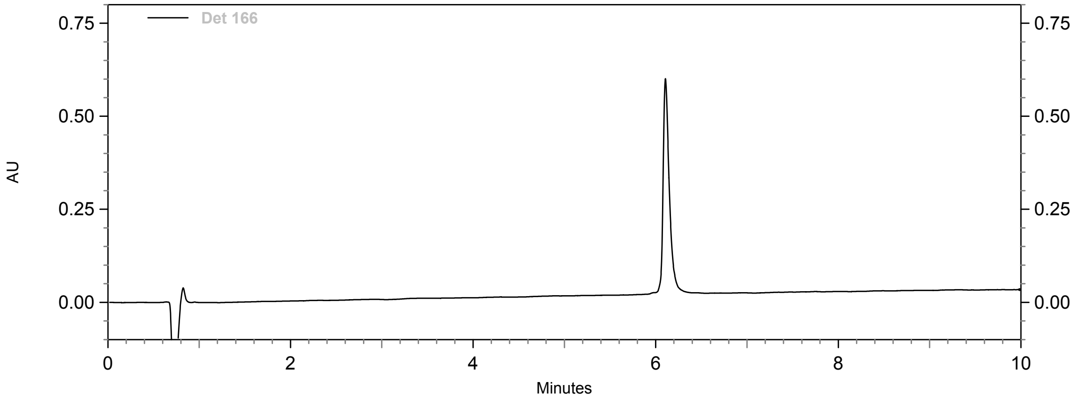
(b) ESI Mass spectrum. (Calcd exact mass for $C_{83}H_{120}N_{20}O_{15}S$ [M] = 1668.90)



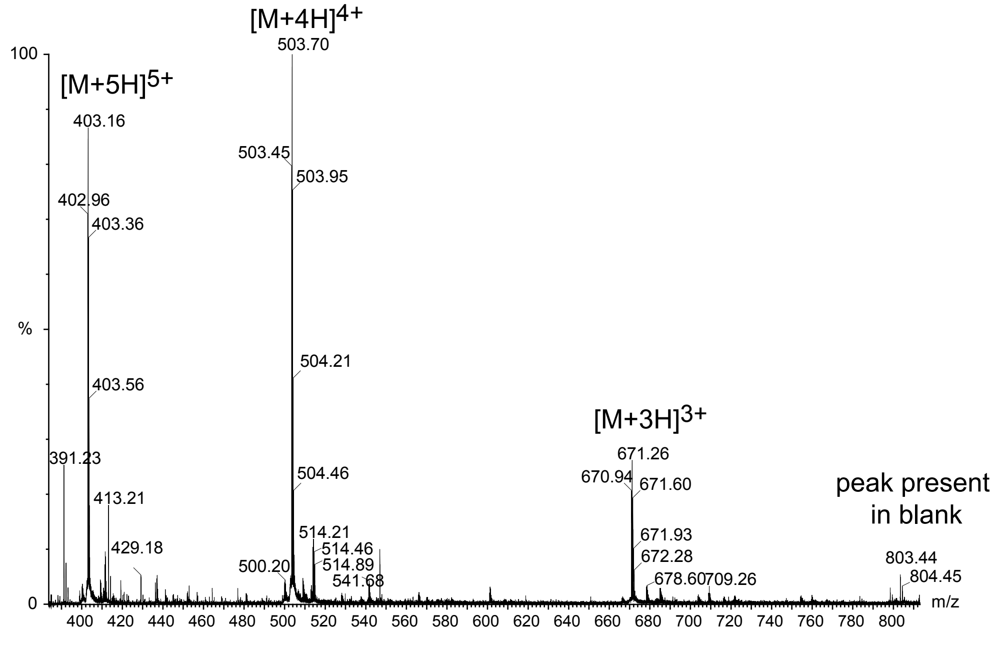
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_2$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10b**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



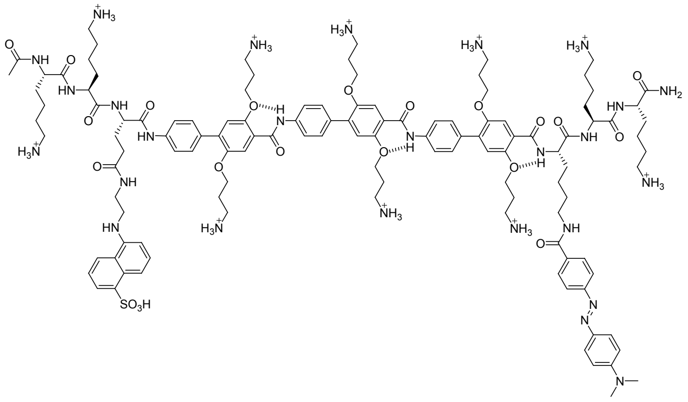
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 10 min, λ = 214)



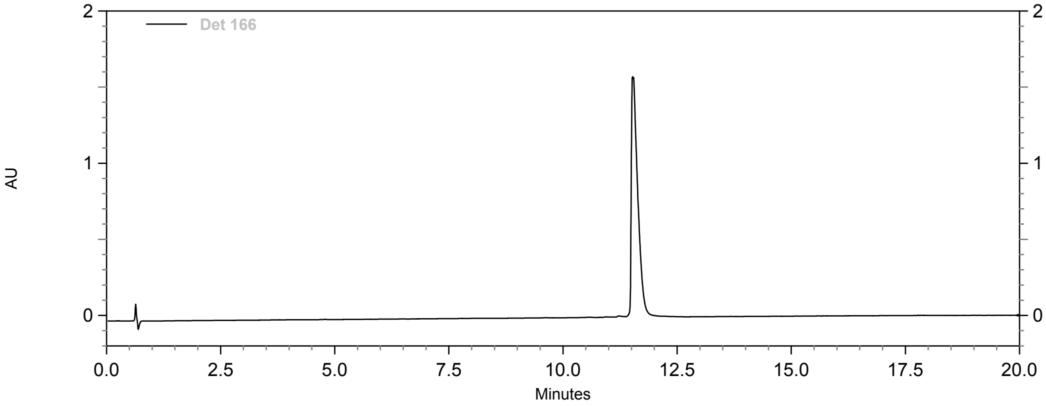
(b) ESI Mass spectrum. (Calcd exact mass for $C_{102}H_{143}N_{23}O_{18}S$ [M] = 2011.44)



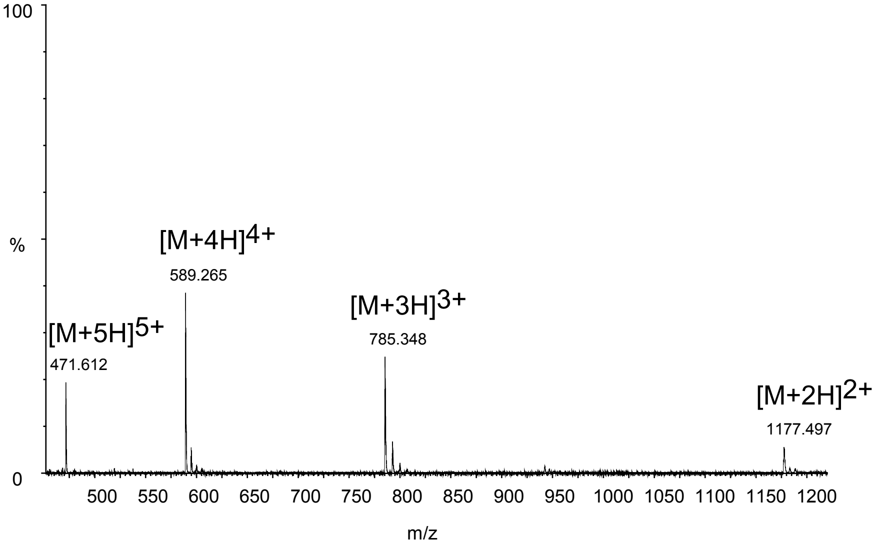
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_3$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10c**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



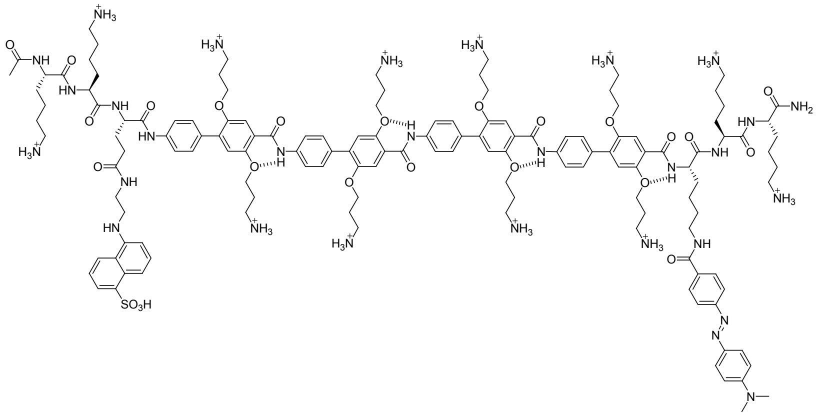
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



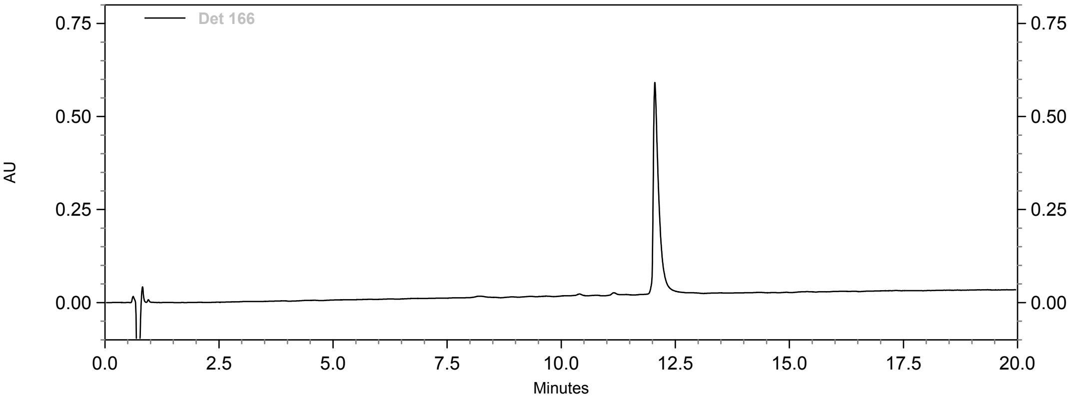
(b) ESI Mass spectrum. (Calcd mass exact for $C_{121}H_{166}N_{26}O_{21}S$ [M] = 2351.24)



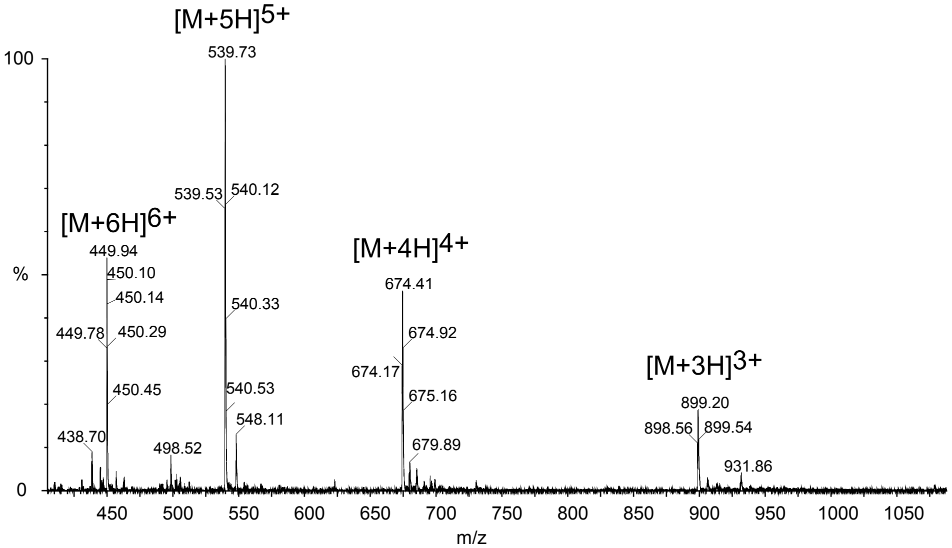
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_4$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10d**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



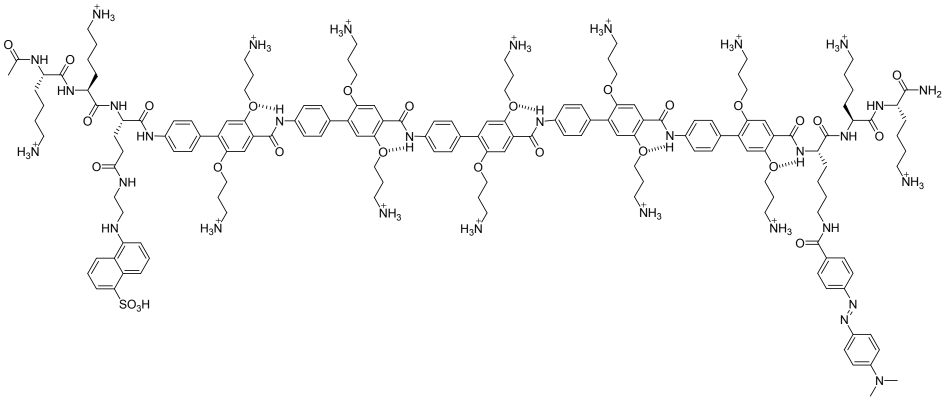
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



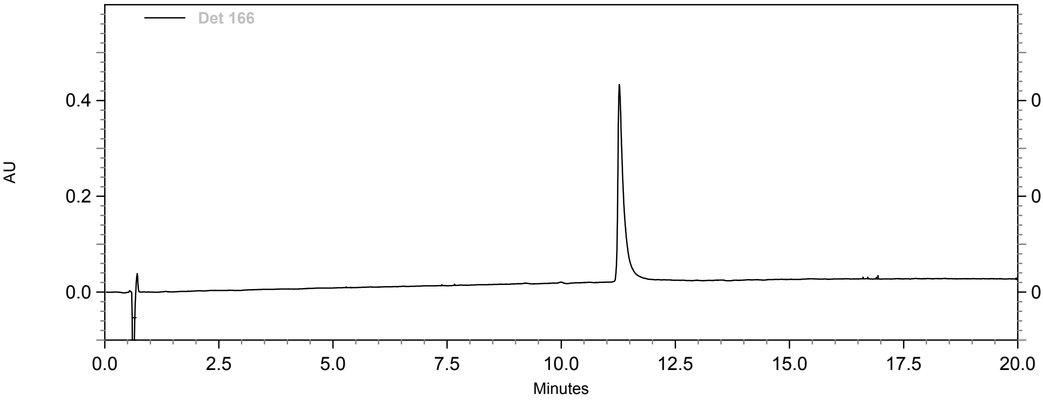
(b) ESI Mass spectrum. (Calcd exact mass for $C_{140}H_{189}N_{29}O_{24}S$ [M] = 2692.42)



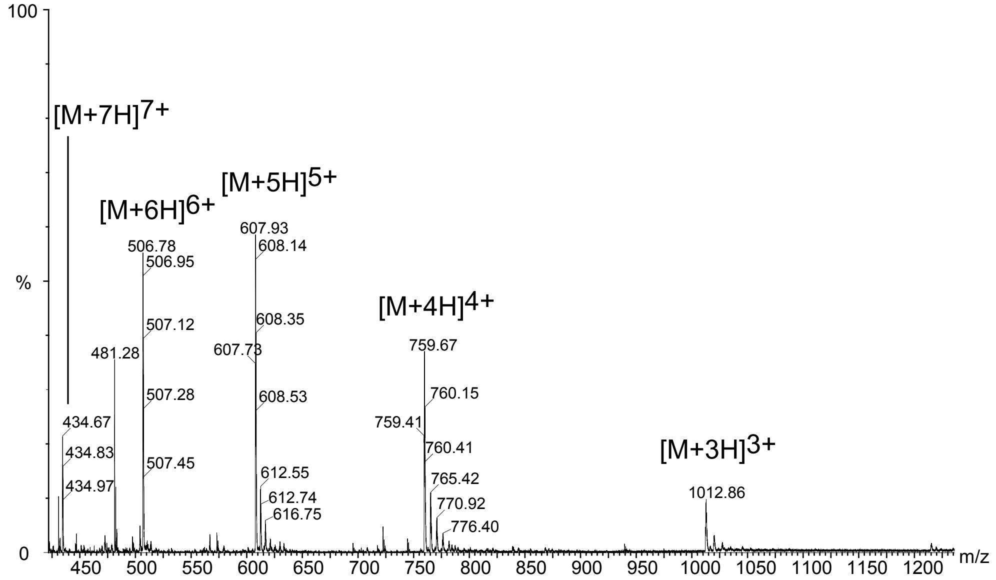
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_5$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10e**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



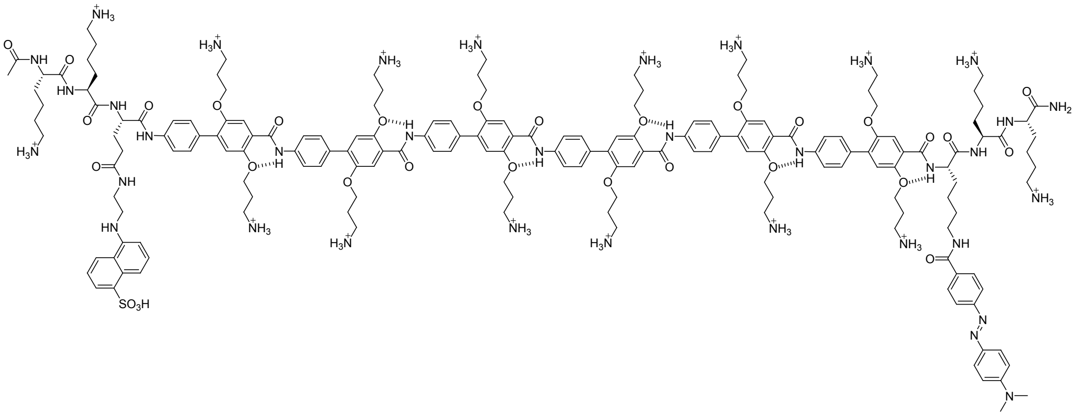
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



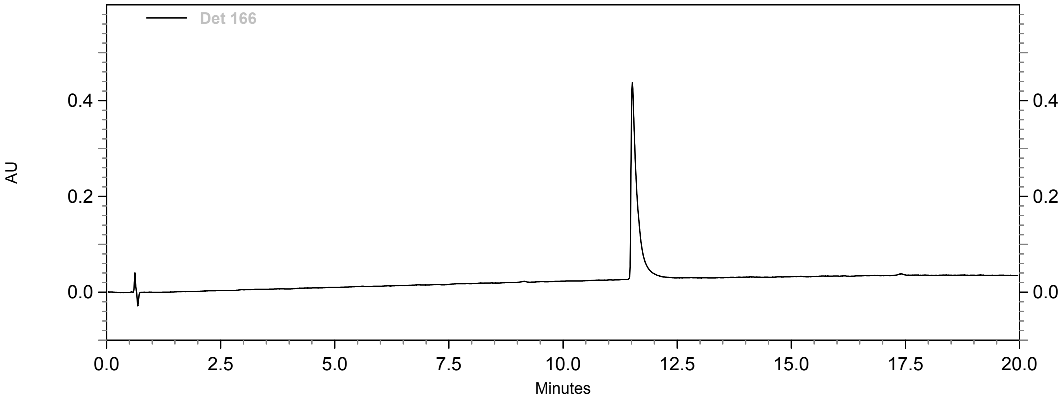
(b) ESI Mass spectrum. (Calcd exact mass for $C_{159}H_{212}N_{32}O_{27}S$ [M] = 3033.59)



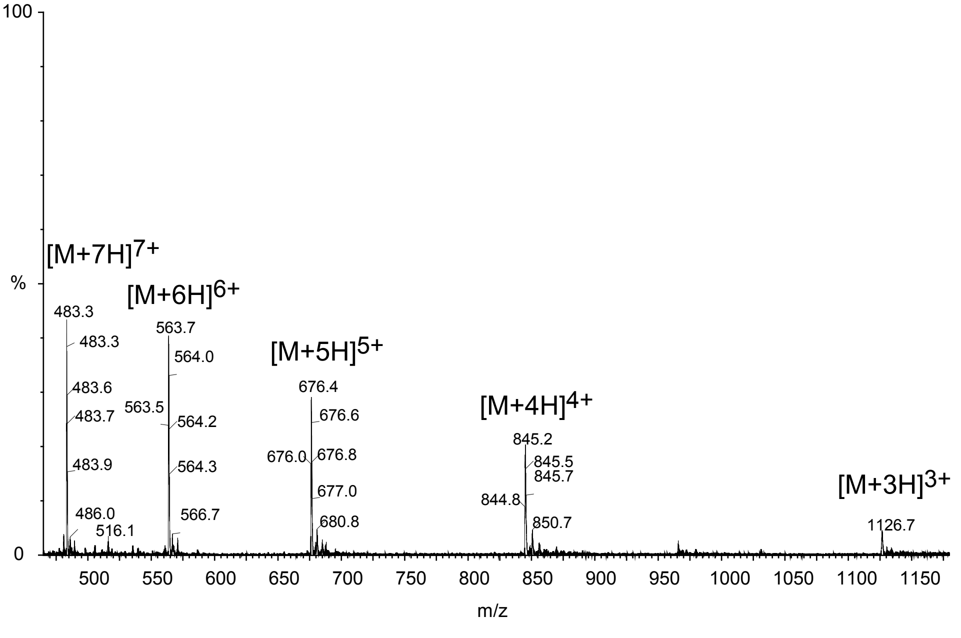
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_6$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10f**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



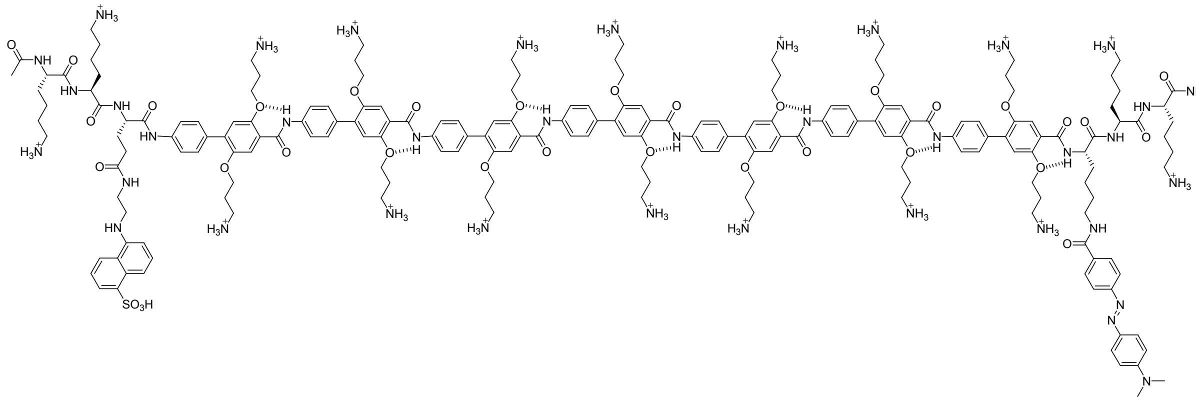
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



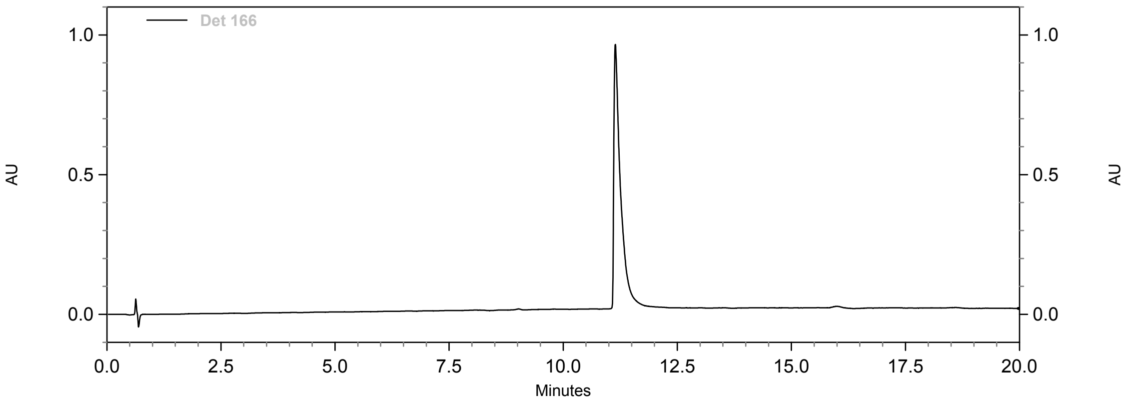
(b) ESI Mass spectrum. (Calcd exact mass for $C_{178}H_{235}N_{35}O_{30}S$ [M] = 3374.77)



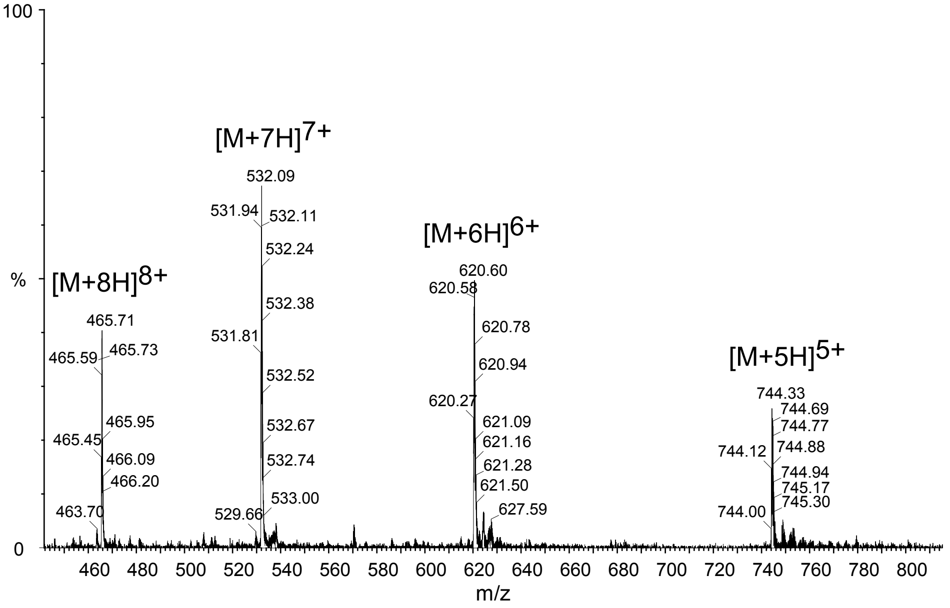
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_7$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt (**10g**)
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



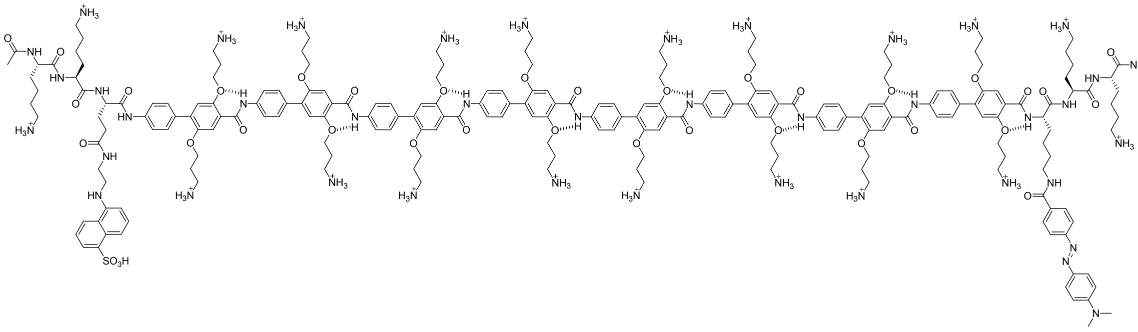
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



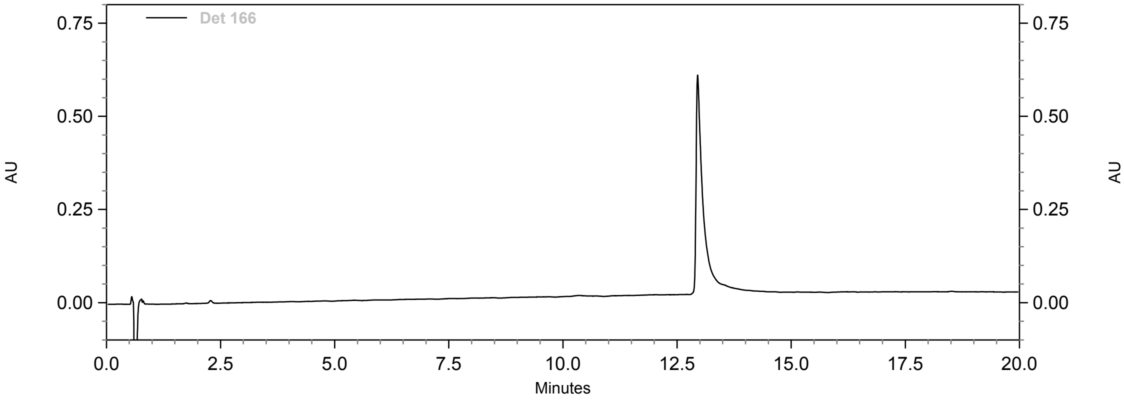
(b) ESI Mass spectrum. (Calcd exact mass for $C_{197}H_{258}N_{38}O_{33}S$ [M] = 3715.94)



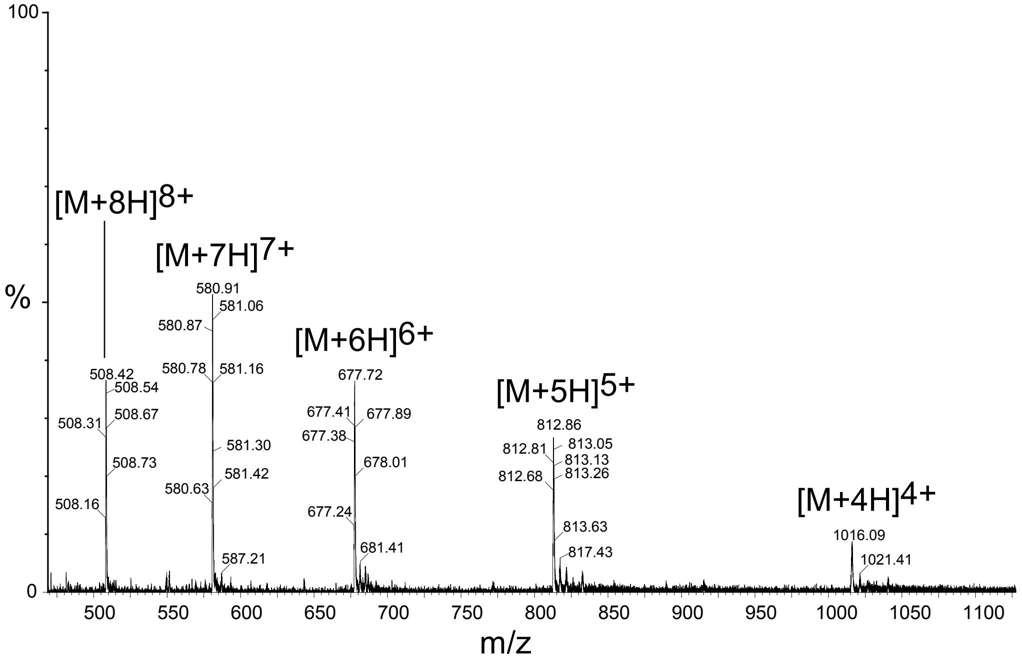
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_8$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10h**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



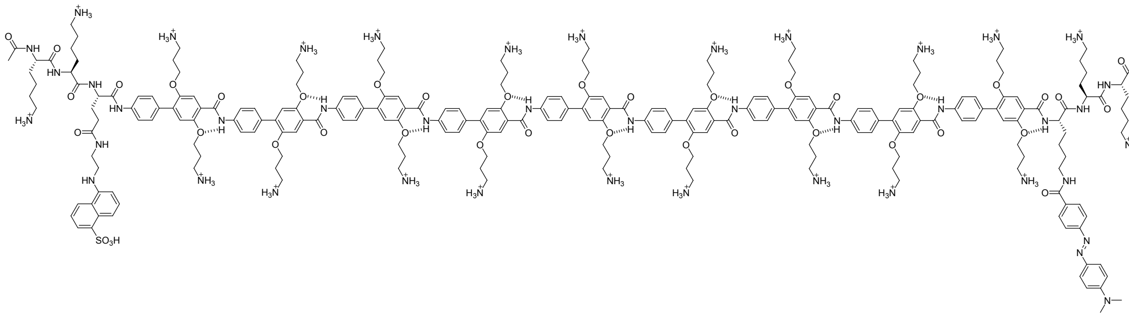
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



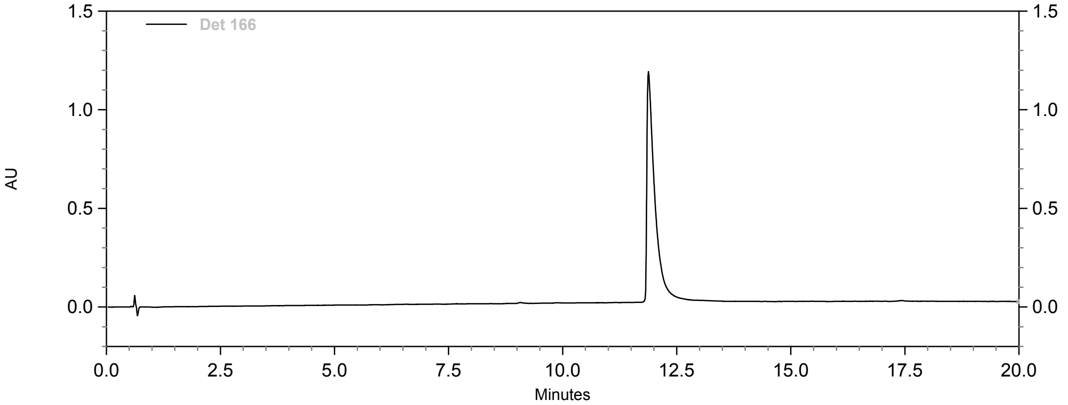
(b) ESI Mass spectrum. (Calcd exact mass for $C_{216}H_{281}N_{41}O_{36}S$ [M] = 4057.11)



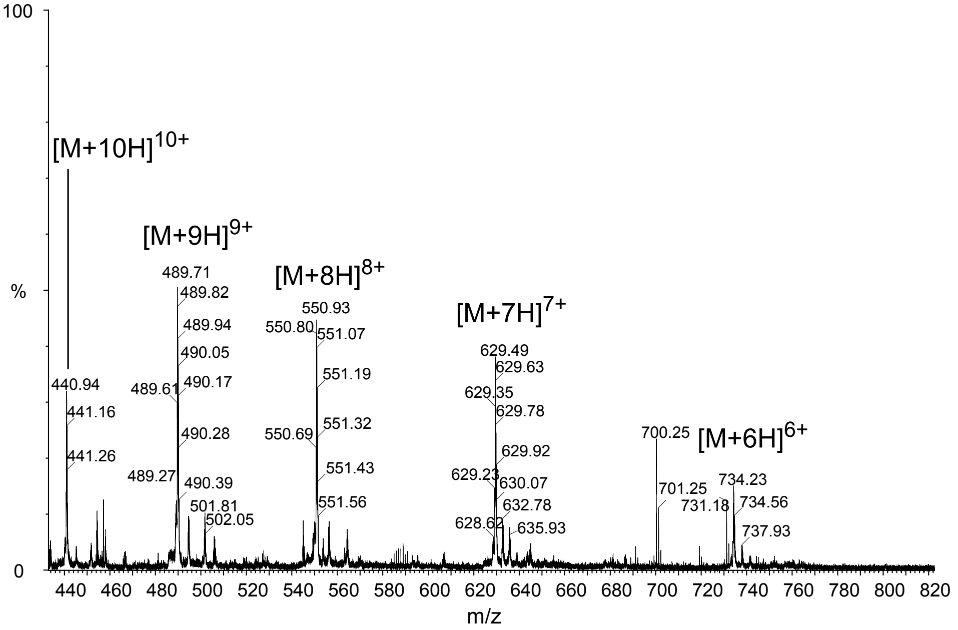
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_9$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10i**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



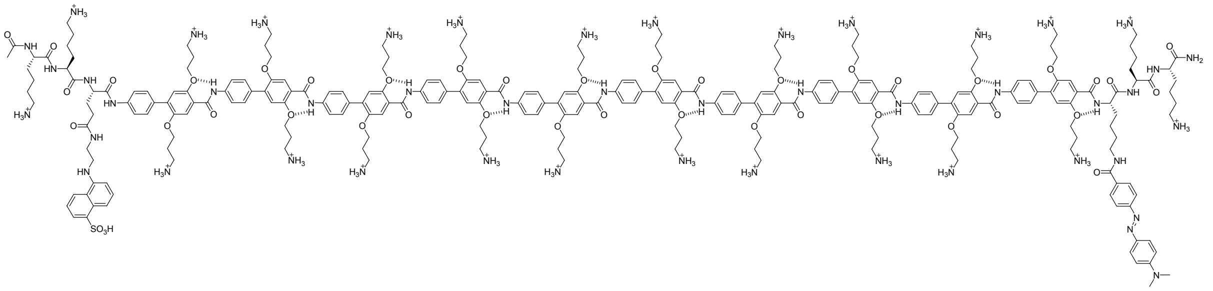
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)



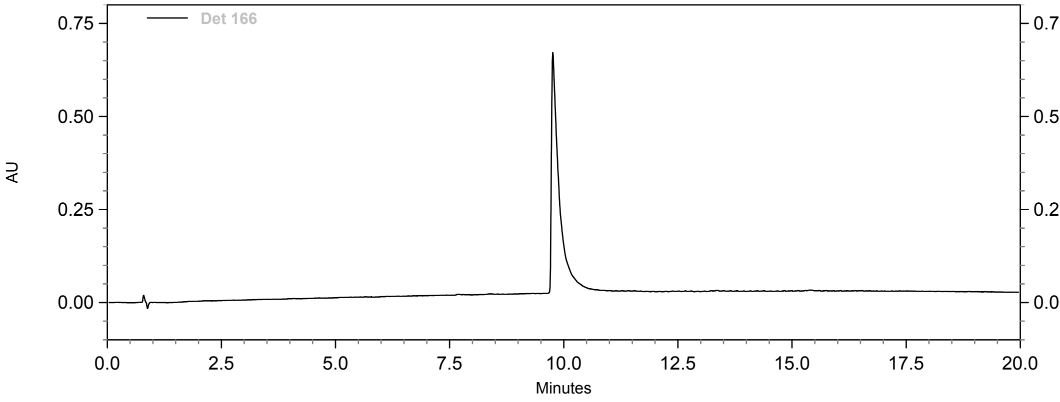
(b) ESI Mass spectrum. (Calcd exact mass for $C_{235}H_{304}N_{44}O_{39}S$ [M] = 4398.29)



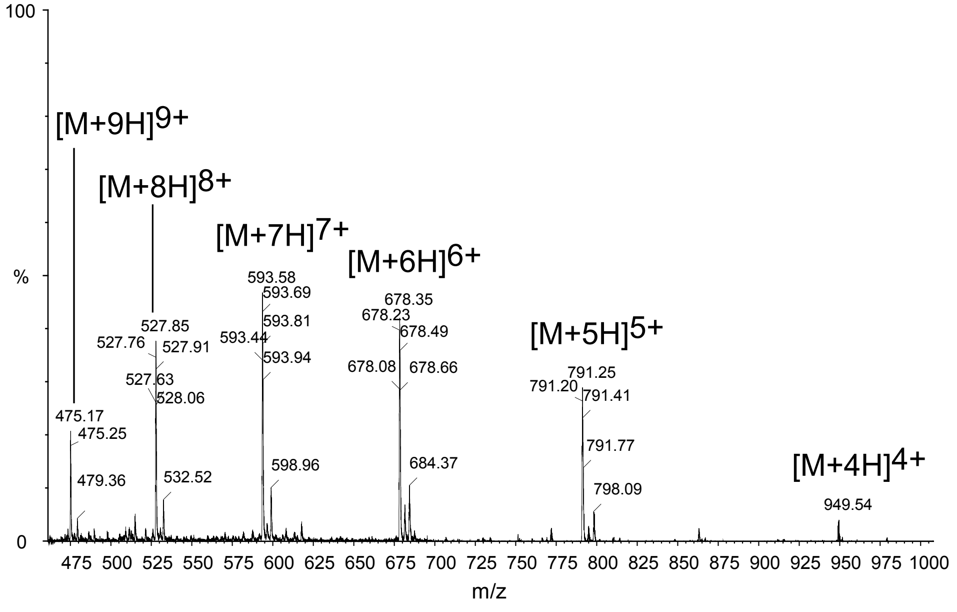
Ac-Lys-Lys-Glu(EDANS)-(Abc^{2K})$_{10}$-Lys(Dabcyl)-Lys-Lys-NH$_2$ TFA salt **10j**
Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)

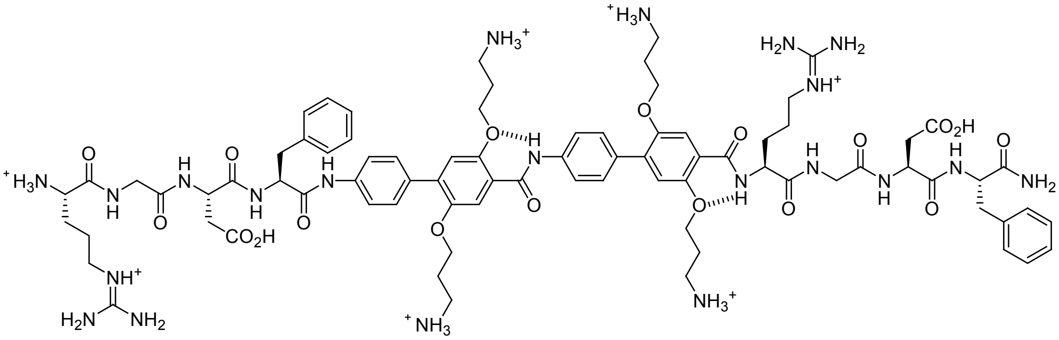


(b) ESI Mass spectrum. (Calcd exact mass for $C_{254}H_{327}N_{47}O_{42}S$ [M] = 4739.46)

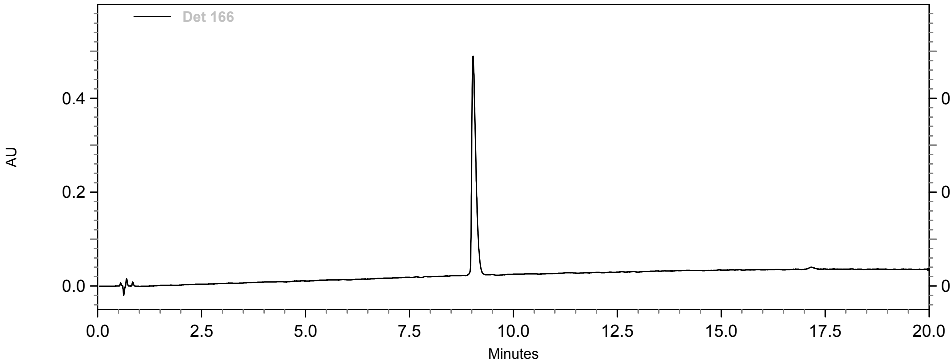


Synthesis of H-Arg-Gly-Asp-Phe-(Abc^{2K})$_2$-Arg-Gly-Asp-Phe-NH_2 (11). Rink amide MBHA resin (59 mg, 0.34 mmol/g, Novabiochem) contained in Bio-Rad Poly-Prep chromatography column was soaked with DMF (3 × ca. 5 mL, 1 min each) and drained under nitrogen pressure. Fmoc deprotection was carried out by soaking the resin with a solution of 20% piperidine–DMF (1 × ca. 5 mL for 1 min, 1 × ca. 5 mL for 20 min) and gently agitating the resin. After deprotection of the Fmoc group, the resin was soaked with DMF (5 × ca. 3 mL for 1 min) and CH_2Cl_2 (5 × ca. 3 mL for 1 min). Standard amino acids were coupled to the resin using 4 equiv with HCTU (4 equiv) in a ca. 1-mL solution of 20% 2,4,6-collidine–DMF, and the resin was gently agitated for 2–4 h (or in some cases was allowed to couple overnight). Fmoc-$Abc^{2K(Boc)}$-OH (**1**) was coupled to the resin using 2 equiv with HCTU (2 equiv) in a ca. 1-mL solution of 20% 2,4,6-collidine–DMF. The solution was added to the resin and the resin was gently agitating for 4–12 h. Couplings to the α-amino groups of standard amino acids were monitored by the ninhydrin test to determine coupling completeness. Couplings to the aniline amino groups of Abc^{2K} were not monitored and assumed to be complete. The peptide was cleaved from resin using 10–20 mL of CF_3COOH/water/triisopropylsilane (8/1/1, *v*/*v*/*v*) and mixed for ca. 6 h. Purification was accomplished using preparative RP-HPLC (water–CH_3CN buffers with 0.1 % TFA) and resulted in a yield of 12 mg (29%) of peptide **11**. (The 12 mg of peptide **11** had a purity of >99% and the 29% yield does not include the HPLC fractions that showed a purity level of 95%.)

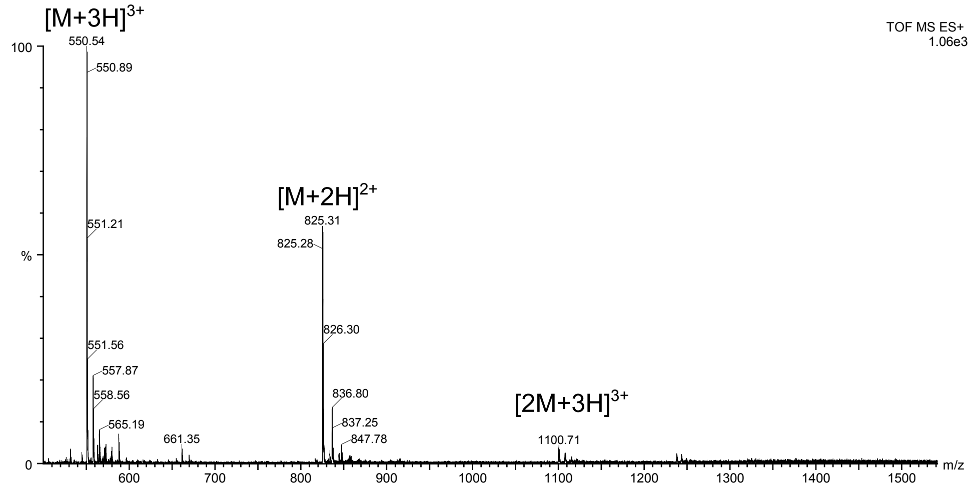
H-Arg-Gly-Asp-Phe-(Abc^{2K})$_2$-Arg-Gly-Asp-Phe-NH$_2$ TFA salt (**11**) Analytical RP-HPLC chromatograph and mass spectrum (ESI-MS)



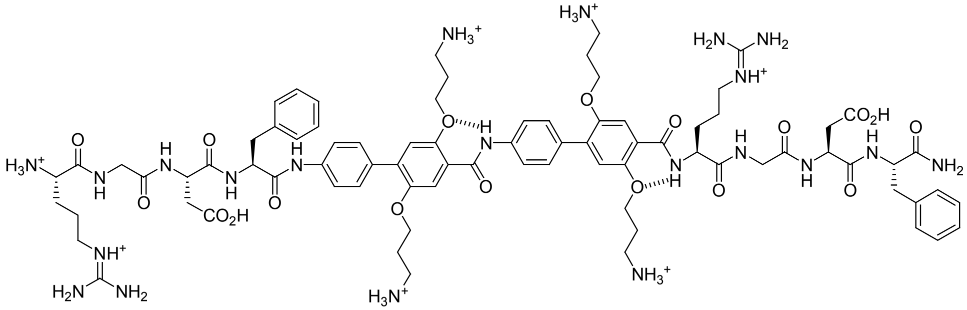
(a) Analytical RP-HPLC (5-50% acetonitrile with 0.1% TFA over 20 min, λ = 214)

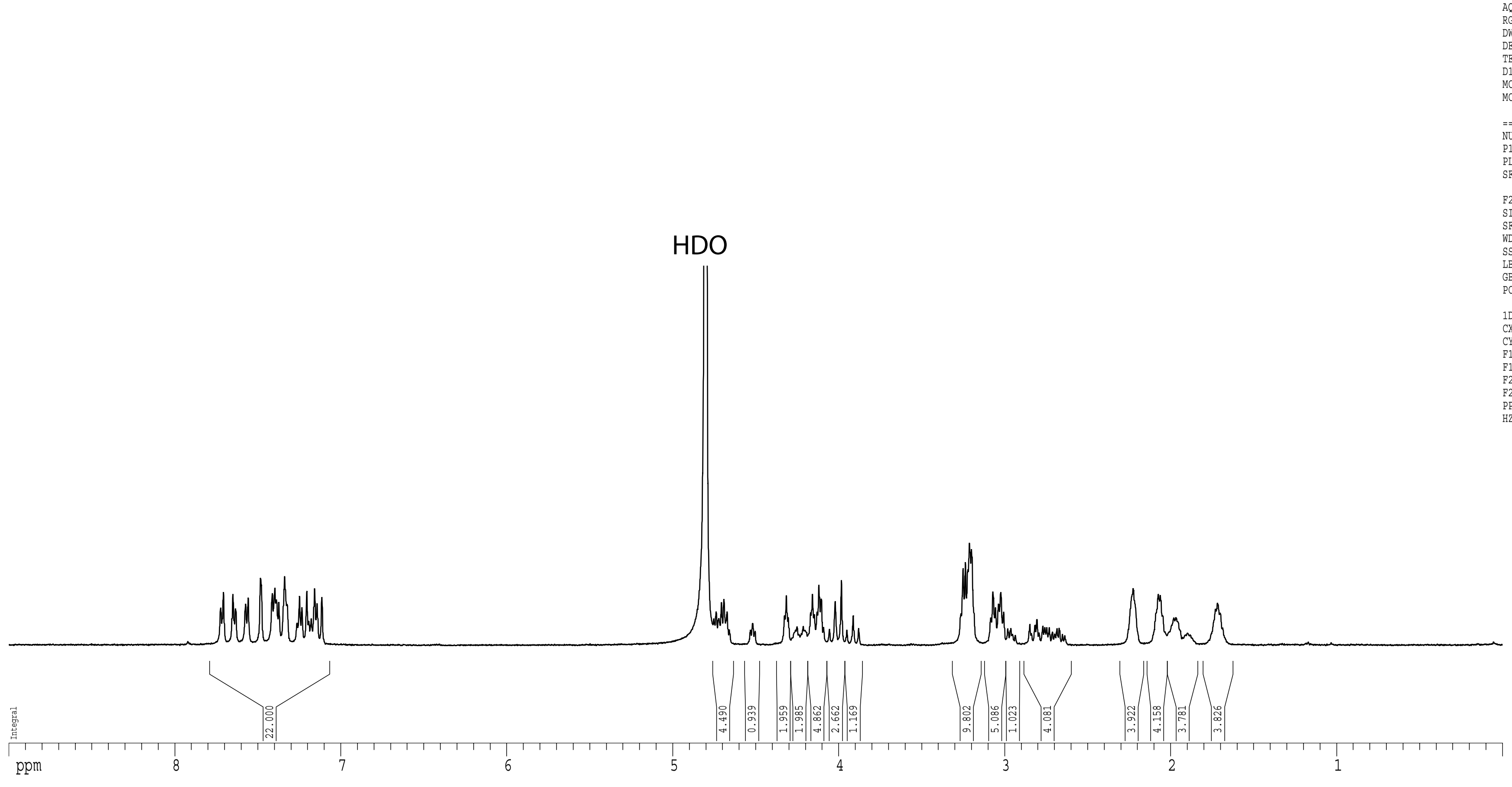


(b) ESI Mass spectrum. (Calcd exact mass for $C_{80}H_{107}N_{21}O_{18}$ [M] = 1649.81)



H-Arg-Gly-Asp-Phe-(Abc^{2K})$_2$-Arg-Gly-Asp-Phe-NH$_2$ TFA salt **11**





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NAME          cg-10-290
EXPNO                 2
PROCNO                1

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Time              15.42
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PULPROG            zg30
TD                81728
SOLVENT             D2O
NS                  128
DS                    2
SWH           8012.820 Hz
FIDRES        0.098043 Hz
AQ           5.0998774 sec
RG                  6.3
DW               62.400 usec
DE                 6.00 usec
TE                298.0 K
D1           0.10000000 sec
MCREST       0.00000000 sec
MCWRK        0.01500000 sec

======== CHANNEL f1 ========
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P1                 8.00 usec
PL1                1.60 dB
SFO1        500.2235015 MHz

F2 - Processing parameters
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SF          500.2200014 MHz
WDW                  EM
SSB                   0
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GB                    0
PC                 4.00

1D NMR plot parameters
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CY                97.22 cm
F1P               9.000 ppm
F1              4501.98 Hz
F2P               0.000 ppm
F2                 0.00 Hz
PPMCM           0.39474 ppm/cm
HZCM          197.45528 Hz/cm
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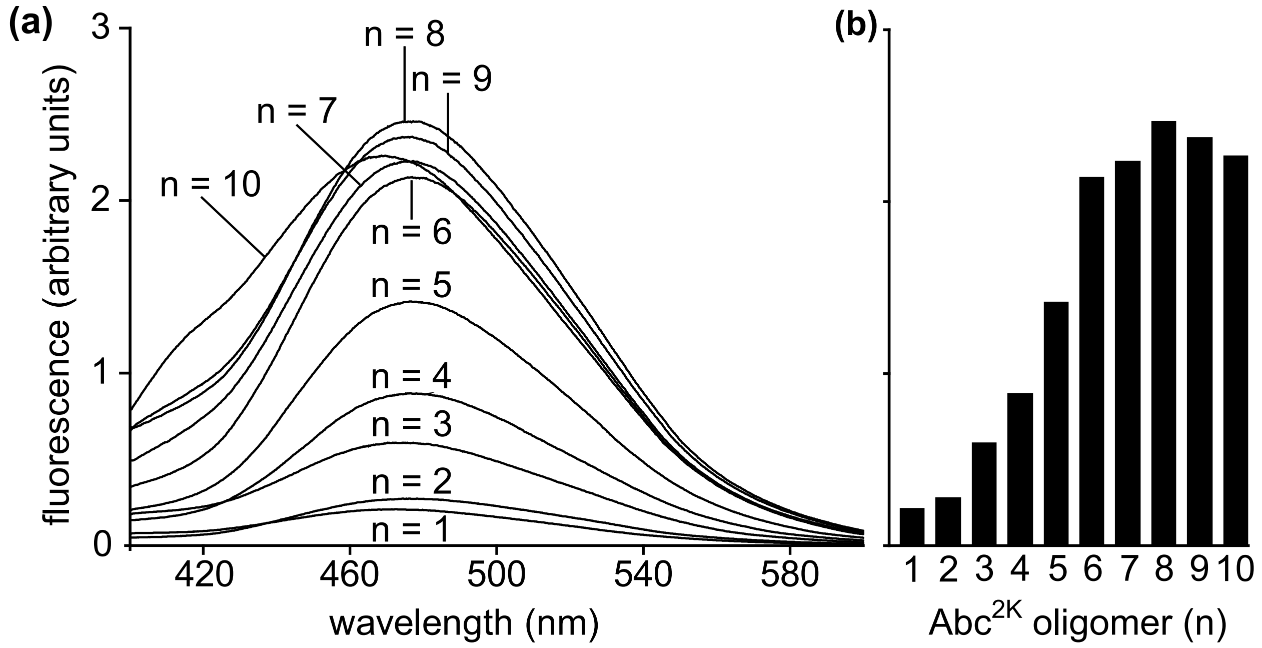
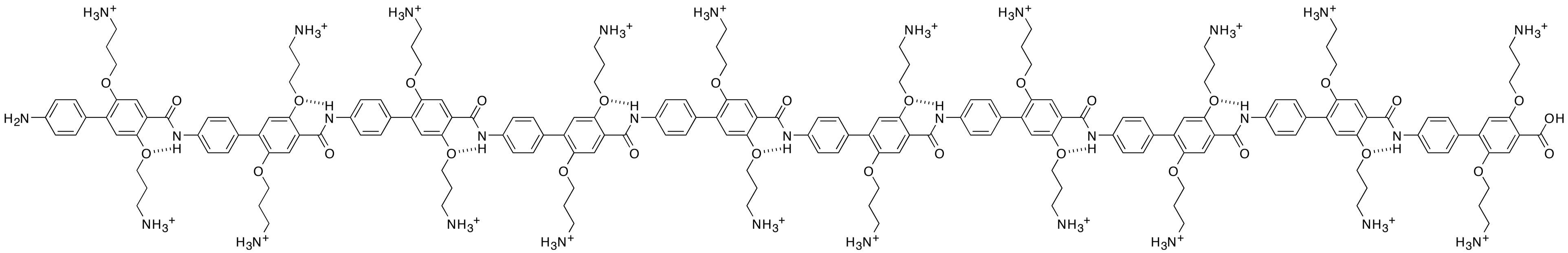
FRET Experiments. Fluorescence resonance energy transfer studies on labeled Abc^{2K} oligomers, Ac-(Lys)$_2$-Glu(EDANS)-(Abc^{2K})$_n$-Lys(Dabcyl)-(Lys)$_2$-NH$_2$ (n=1–10), were carried out using a Hitachi F-4500 Fluorescence Spectrophotometer. Concentrations for initial stock solutions were determined spectrophotometrically based on the extinction coefficient of Dabcyl (ε = 32,000). Serial dilutions were carried out on the stock solutions to make 1.75 μM (water/DMSO 1/1) solutions. Samples were excited at 335 nm and their fluorescence was observed from 400 to 600 nm. Additional instrument parameters were set as follows: excitation slit (nm) = 10, emission slit (nm) = 10, PMT voltage (V) = 700, response (sec.) = auto, shutter control = on, scan speed = 60.

FRET Experiments of Compounds 10a-10j.

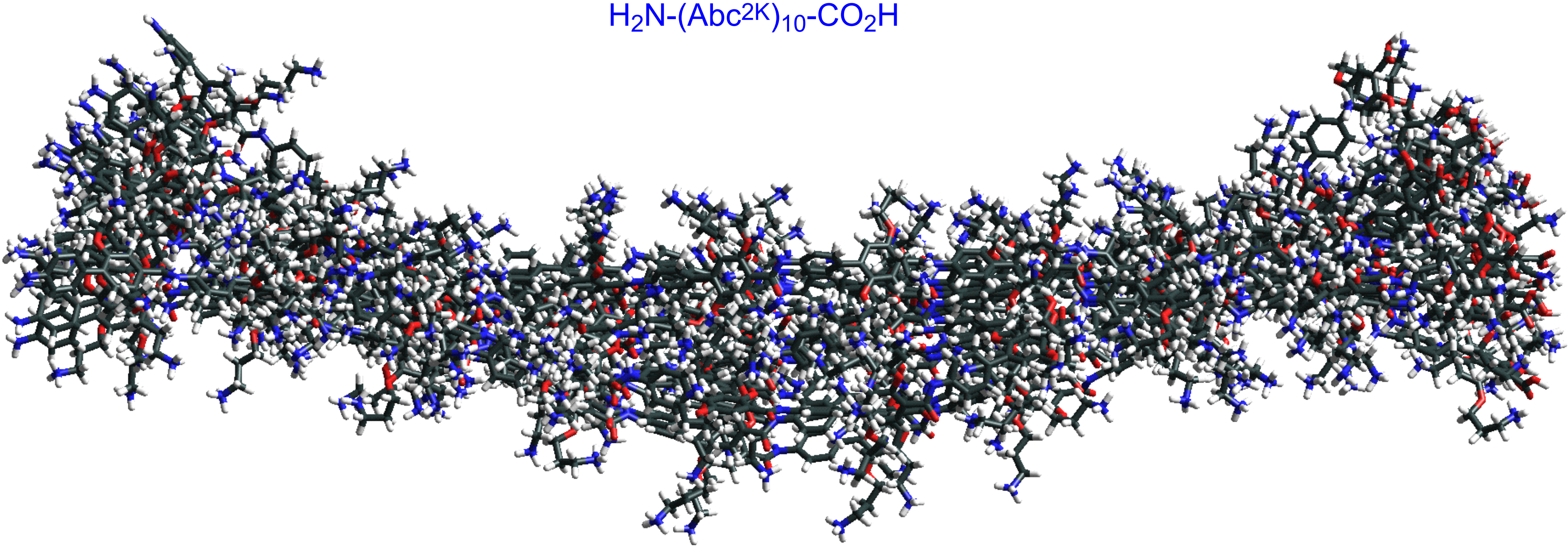


Conformational Flexibility and Dynamics of Abc^{2K} Oligomers

Molecular mechanics and dynamics studies of an Abc^{2K} oligomers show only minor effects from torsional and bending motions. Monte Carlo-stochastic dynamics (MC/SD) simulations support a model in which Abc^{2K} oligomers are relatively straight and rigid.



$H_2N\text{-}(\mathrm{Abc}^{2K})_{10}\text{-}CO_2H$



average length = 10.1 nm
standard deviation = 0.5 nm

Superposition of 20 structures generated during a 1000 picosecond Monte Carlo-stochastic dynamics simulation of Abc^{2K} decamer in GB/SA water at 300 K as calculated with MacroModel/Maestro and the AMBER* force field.