8 EXPERIMENTAL PART

8.1 General

All commercially available substances were purchased from Aldrich, Merck, or Acros, and used without further purification. Solvents were purified and dried – if necessary – according to standard methods. The catalyst $Pd(PPh_3)_4$ was synthesized according to literature and used freshly. For reactions with this catalyst, the solvents, solutions or suspensions were degassed by three repeated cycles of freeze-pump-thaw and flushing with nitrogen. The nitrogen was purchased from Messer-Griesheim as Nitrogen 4.0 or 5.0.

Analyses

NMR spectrometry:

The spectra were recorded on a Bruker AB 250 MHz, WH 270 MHz or AC 500 MHz instrument with the solvent itself as inner standard. If not stated otherwise, measurements were done at room temperature. All shifts are given in ppm. The deuterated solvents were purchased from Merck or Deutero GmbH.

EI and FAB(+) mass spectrometry:

Spectra were recorded with a Varian MAT 771 or MAT 112 S spectrometer.

MALDI-TOF mass spectrometry:

Spectra were recorded with a Kratos MALDI 3 from Shimadzu. Please note that values given for signals in MALDI TOF MS generally refer to the lowest mass isotope of a specific ion (not for the isotope with highest intensity!).

Elemental analysis:

It was used a Perkin-Elmer EA 240.

Chromatographic Methods

Analytical TLC:

Reactions were checked by TLC with TLC-ready charts by Merck (no. 5554, aluminium sheets with silica gel Si 60 with fluorescence indicator F254), or TLC-ready charts by Macherey-Nagel (Polygram Alox N/UV254, ready foils with 0.2 mm aluminium oxide with fluorescent indicator F254). Detection was in UV light with wavelength λ = 254 or λ = 366 nm. If not stated otherwise, silica gel TLC charts were used.

Preparative column chromatography:

The chromatography was run with Merck flash silica gel (230-400 mesh ASTM, grain size 40-60 pm), Machery-Nagel silica gel 60 M (230-400 mesh ASTM, grain size 40-63 pm), or Fluka aluminium oxide neutral (Typ 507 C, 0.05-0.15 mm)

Analytical HPLC:

Reversed-Layer: Knaur Eurosphere® 7μm C18, 4·120 mm, UV-detection at 335 nm or 254 nm.

Silica gel: Analytical: Knaur Eurosphere® 7μm C18, 4·120 mm, UV-detection at 335 nm or 254 nm.

Preparative HPLC:

Preparative: Machery-Nagel, Nucleosil® 5μm C18, 32·250 mm, UV-detection at 335 nm or 254 nm.

Preparative: Knaur Eurosphere® 5μm C18, 32·250 mm, UV-detection at 335 nm or 254 nm.

Analytical GPC:

Measurements were performed with a Waters Assoc. 150-c Alc/GPC chromatograph by using the column set Waters Styragel HR columns. As mobile phase, THF was used. Detection was by a Waters 410 RI detector or a 484 UV/VIS detector against polystyrene as calibration standard.

Preparative GPC:

Separation was by using a Waters machine with UV detection; the mobile phase was THF. Separation columns were Waters Styragel HR columns. THF was filtrated through neutral aluminumoxide, and freshly distilled prior to use to avoid contamination with THF oligomers.

In vitro chemosesitivity assay

In vitro chemosensitivity assay: The in vitro testing of the dendrimers on the cytotoxic activity was carried out on exponentially dividing MCF-7 cells according to a previously published microtiter assay. Briefly, in 96-well microtiter assay plates (Nunc), 100 μL of a cell suspension at 7000 cells/ mL culture medium were plated into each well and incubated at 37 °C for 2-three daysays in a humidified atmosphere (5% CO_2). By addition of an adequate volume of a stock solution of the respective compound (solvent: DMF) to the medium the desired test concentration was obtained. For each test concentration and for the control, which contained the corresponding amount of DMF, 16 wells were used. After the proper incubation time the medium was removed, the cells were fixed with a glutaraldehyde solution and stored at 48C. Cell biomass was determined by a crystal violet staining technique. The influence of the dendrimers on cell growth, was obtained by corrected T/C values according to Equations (1) and (2).

Cytostatic effect :

$$\frac{T}{C_{corr}}[\%] = \left[\frac{T - C_0}{C - C_0}\right] \times 100 \qquad (1)$$

Cytocidal effect :

$$T[\%] = \left[\frac{T - C_0}{C_0}\right] \times 100 \qquad (2)$$

In Equations (1) and (2), T (test) and C (control) are the optical densities at 578 nm of the crystal violet extract of the cell lawn in the wells (i.e. the chromatin-bound crystal violet extracted with ethanol 70%), and C_0 is the density of the cell extract immediately before treatment. Equation (2) allows the automatic estimation of the optical density of the crystal violet extract in the wells of a Flashscan S19 microplatereader (Analytikjena, Jena, Germany).

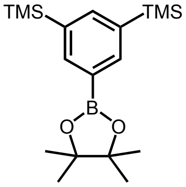
8.2 Syntheses

Compounds 2a,[189] 3a/b,[157, 168] 4,[175, 176] 6a/b, 7a/b,[174] 11a, 12,[162] 13, 16,[164, 190] 17a,[163] 19, 21a,[164, 190] 29, 30, 31, 32,[166] 38,[191, 192] 44[165], 47,[39] 53,[193] 61,[157, 168, 194] 125, 126,[188] 127[188, 195] were prepared according to literature procedures.

Compound was kindly provided by Dr. T. Lehmann and prepared by students in the Grundpraktikum at FU Berlin.

8.3 Compounds of Chapter 4.3.1

2-[3,5-bis(trimethylsilyl)phenyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5**



To a solution of 5.56 g **4** (18.5 mmol) in 100 ml diethylether at -78 °C, 33 ml (52.3 mmol) of a 1.6 M solution of n-butyl lithium in hexane was added dropwise under N_2. The mixture was allowed to warm to room temperature and cooled to -78 °C again. 13.7 g (72.8 mmol] triisopropyl borate was added and the mixture was allowed to warm to room temperature over night. The layers were separated and the aqueous phase extracted with diethylether (3 × 50 ml). The combined organic phases were dried over $MgSO_4$ and the solvent was removed in vacuo. Chromatographic separation through silica gel with hexane/ ethylacetate gave **5**.

Yield: 1.69 g (65%) of a colorless solid.

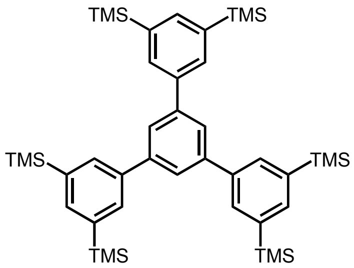
R_f = 0.31 (Silica gel; hexane/ethyl acetate 30:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 0.29 (s, 18H, -Si(C*H*$_3$)$_3$) 1.37 (s, 12H, -C*H*$_3$), 7.78 (s, 1H, Ar-*H*), 7.97 (s, 2H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = -1.06, 24.79, 83.60, 138.29, 140.29, 141.05, 154.15.

MS (EI, 80eV, 170°C): m/z (%) = 347.0 (4) $[M]^+$; 333.0 (100) $[M-CH_3]^+$.

1,3,5 Tris[3,5-bis(trimethylsilanyl)phenyl]benzene ***7c***



0.144 g (0.46 mmol) **1** and 0.572 g (1.64 mmol) **5** were dissolved in 12 ml toluene and 12 ml (12 mmol) 1M Na_2CO_3 were added. The mixture was degassed by three *freeze-pump-thaw* cycles and flushed with nitrogen. 0.023 g (0.02 mmol) $Pd[PPh_3]_4$ were added and the degassing procedure was repeated. The mixture was refluxed for one day. The layers were separated and the aqueous phase extracted with toluene (3 × 30 ml). The combined organic phases were washed with brine, dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation through silica gel with hexane gave **7c**.

Yield: 0.303 g (89%) of a colorless solid.

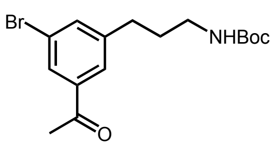
R_f = 0.26 (Silica gel; hexane).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 0.38 (s, 54H, -Si(C*H*$_3$)$_3$) 7.80 (s, 6H, TMS-Ar-*H*), 7.87 (s, 6H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = -1.08, 125.89, 133.21, 137.36, 140.06, 140.29, 143.24.

MS (EI, 80eV, 220°C): m/z (%) = 738.0 (74.4) $[M]^+$; 724.0 (22.0) $[M-CH_3]^+$; 666.0 (2.0) $[M-TMS]^+$; 73.0 (30.0) $[TMS]^+$.

tert-Butyl 3-(3-acetyl-5-bromophenyl)propylcarbamate ***10a***



1.18 g (9.70 mmol) 9-BBN were dissolved in 18 ml toluene and 1.39 g (8.84 mmol) *tert*-Butyl-allylcarbamate were added at room temperature. The mixture was stirred for one day. 13.0 ml 1 M aqueous KOH, 6 ml toluene, and 0.940 g (3.38 mmol) **2a** were added. The mixture was degassed by three *freeze-pump-thaw* cycles and flushed with nitrogen. 0.151 g (0.130 mmol) $Pd[PPh_3]_4$ were added and the degassing procedure was repeated. The mixture was refluxed for three days. The layers were separated and the aqueous phase extracted with toluene (3 × 30 ml). The combined organic phases were washed with brine, dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation through silica gel with hexane/ ethylacetate) gave **10a**.

Yield: 0.315 g (26%) of a yellowish oil.

R_f = 0.26 (Silica gel; hexane/ ethylacetate 3:1).

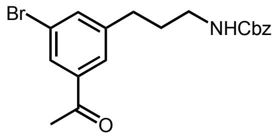
^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.33 (s, 9H, -C(C*H*$_3$)$_3$), 1.71 (m, 2H, β-C*H*$_2$), 2.48 (s, 3H, -C*H*$_3$), 2.58 (t, 2H, $^3J_{H\text{-}H}$ = 7.0 Hz, α-C*H*$_2$), 3.05 (br s, 2H, γ-C*H*$_2$), 4.86 (br s, 1H, -N*H*), 7.41(s, 1H, Ar-*H*), 7.59 (s, 1H, Ar-*H*), 7.77 (s, 1H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 26.5, 28.2, 31.2, 32.4, 37.7, 78.8, 122.5, 126.7, 128.8, 135.6, 138.5, 144.2, 155.8, 196.5.

MS (EI, 80eV, 170°C): m/z (%) = 355.0 (1.0) $[M]^+$; 257 (8.0) $[M\text{-}C_5H_9O_2]^+$; 57.0 (100) $[C_4H_9]^+$.

EA	$C_{16}H_{22}BrNO_3$	calc.	C	53.94	H	6.22	N	3.93,
	(356.25)	found		53.91		6.27		3.82.

Benzyl 3-(3-acetyl-5-bromophenyl)propylcarbamate ***10b***



1.13 g (9.26 mmol) 9-BBN were dissolved in 18 ml toluene and 1.61 g (8.42 mmol) **2b** were added at room temperature. The mixture was stirred for one day. 12.2 ml 1 M aqueous KOH, 6 ml toluene, and 0.896 g (3.22 mmol) **6a** were added. The mixture was degassed by three *freeze-pump-thaw* cycles and flushed with nitrogen. 0.143 g (0.124 mmol) $Pd[PPh_3]_4$ were added and the degassing procedure was repeated. The mixture was refluxed for three days. The layers were separated and the aqueous phase extracted with toluene (3 × 30 ml). The combined organic phases were washed with brine, dried over $MgSO_4$, and the solvent was removed in vacuo. Chromatographic separation through silica gel with hexane/ ethylacetate gave **10b**.

Yield: 0.650 g (52%) of a yellowish oil.

R_f = 0.16 (Silica gel; hexane/ ethylacetate 3:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.80 (m, 2H, β-C*H*$_2$), 2.53 (s, 3H, -C*H*$_3$), 2.64 (t, 2H, $^3J_{H\text{-}H}$ = 7.0 Hz, α-C*H*$_2$), 3.20 (br s, 2H, γ-C*H*$_2$), 4.90 (br s, 1H, -N*H*), 5.07 (s, 2H, -C*H*$_2$Ar), 7.32 (s, 5H, -OCH$_2$Ar-*H*), 7.48 (s, 1H, Ar-*H*), 7.65 (s, 1H, Ar-*H*), 7.85 (s, 1H, Ar-*H*).

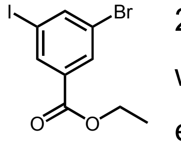
^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 26.5, 31.3, 32.5, 40.4, 66.6, 122.76, 126.75, 128.0, 128.4, 125.7, 129.1, 133.4, 136.5, 138.8, 144.2, 156.4, 196.7.

MS (EI, 80eV, 170°C): m/z (%) = 389.0 (2.0) $[M]^+$; 91.0 (100) $[C_7H_7]^+$.

EA	$C_{19}H_{22}BrNO_3$	calc.	C	58.47	H	5.17	N	3.59,
	(390.27)	found		58.55		5.07		3.45.

8.4 Compounds of Chapter 4.3.2

Ethyl-(3-bromo-5-iodo)-benzoate ***11b***



2.00 g (37.8 mmol) 3-bromo-5-iodo-benzoic acid and 0.10 g p-TsOH were dissolved in 10 ml ethanol and refluxed for 15 hours.The solvent evaporated. Chromatographic separation through silica gel with hexane/ ethylacetate gave **11b**.

Yield: 1.70 g (80%) of a colorless solid.

R_f = 0.40 (Silica gel; hexane/ ethylacetate 3:1).

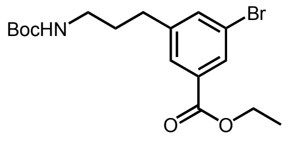
^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.36 (t, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, $-CH_2CH_3$), 4.35 (q, 2H, $^3J_{H\text{-}H}$ = 7.3 Hz, $-CH_2CH_3$), 7.96 (s, 1H, Ar-*H*), 8.06 (s, 1H, Ar-*H*), 8.23 (s, 1H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.21, 61.75, 93.93, 122.91, 131.86, 133.61, 137.05, 143.57, 152.22, 163.73.

MS (EI, 80eV, 60°C): m/z (%) = 357.0 (9.7), 356.0 (97.4), 355.0 (12.4), 354.0 (100.0) $[M]^{+\bullet}$.

EA	$C_9H_8BrIO_2$	calc.	C	30.45	H	2.27,
	(353.88)	Found		30.21		2.14.

Ethyl-3-(3-tert-butoxycarbonylamino-propyl)-5-bromo-benzoate ***17a***



0.503 g (3.20 mmol) **2a** and 0.430 g (3.50 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 1.00 g (3.20 mmol) **11a**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days. The phases are separated, the organic layer was subsequently washed three times with brine, and dried. The solvent was removed under reduced pressure. Chromatographic separation through silica gel with hexane/ ethylacetate gave **17a**.

Yield: 0.803 g (65%) of a colorless oil.

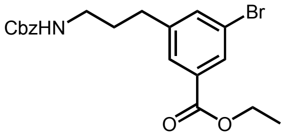
R_f = 0.21 (silica gel; hexane/ethyl acetate 3:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.36 (t, 3H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 1.41 (s, 9H, $-C(CH_3)_3$), 1.78 (m, 2H, β-CH_2), 2.63 (t, 2H, $^3J_{H\text{-}H}$ = 8.1 Hz, α-CH_2), 3.11 (m, 2H, γ-CH_2), 4.33 (q, 2H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 4.58 (br s, 1H, -N*H*), 7.47 (s, 1H, Ar-*H*), 7.74 (s, 1H, Ar-*H*), 7.95 (s, 1H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.23, 28.36, 31.46, 32.57, 40.08, 61.30, 79.25, 122.32, 128.10, 130.12, 131.25, 135.59, 144.06, 155.89, 165.27.

MS (pos. FAB): m/z (%) = 388.1 (3.6), 386.1 (3.9) $[M]^{+\bullet}$, 287.9 (86.9), 286.9 (9.3), 285.8 (100), 284.8 (8.7) $[M-C_4H_9O+H]^+$.

Ethyl-3-(3-benzyloxycarbonylamino-propyl)-5-bromo-benzoate ***17b***



Method A: 0.455 g (2.37 mmol) **2b** and 0.318 g (2.61 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 0.841 g (2.37 mmol) **11b**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days.

Method B: 1.224 g (6.40 mmol) **2b** and 0.860 g (7.00 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 1.00 g (3.20 mmol) **11a**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days.

The phases are separated, the organic layer was subsequently washed three times with brine, and dried. The solvent was removed under reduced pressure.

Chromatographic separation through silica gel with hexane/ ethylacetate and then with methylene chloride gave **17a**. The compound can be crystallized from methanol.

Yield: method A 0.946 g (95%) of a colorless spate.

method D 0.981 g (73%) of a colorless spate.

R_f = 0.19 (Silica gel; hexane/ethyl acetate 3:1).

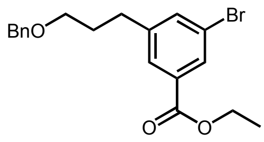
^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.31 (t, 3H, $^3J_{H-H}$ = 7.0 Hz, -CH_2CH_3), 1.75 (m, 2H, β-CH_2), 2.57 (t, 2H, $^3J_{H-H}$ = 7.7 Hz, α-CH_2), 3.14 (m, 2H, γ -CH_2), 4.29 (q, 2H, $^3J_{H-H}$ = 7.0 Hz, -CH_2CH_3), 4.91 (br s, 1H, -NH), 5.03 (s, 2H, -OCH_2Ar), 7.27 (m, 5H, -OCH_2Ar-H), 7.42 (s, 1H, Ar-H), 7.70 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.20, 31.27, 32.44, 61.29, 66.62, 122.30, 128.04, 128.43, 130.12, 132.34, 135.54, 136.49, 143.86, 156.36, 165.23.

MS (EI, 80eV, 140°C): m/z (%) = 421.0 (1.3), 419.0 (1.3) $[M]^{+\bullet}$, 91.0 (100) $[C_7H_7]^{+\bullet}$.

EA	$C_{20}H_{22}BrNO_4$	calc.	C	57.15	H	5.28	N	3.33,
	(419.07)	found		57.10		5.04		3.29.

*Ethyl-3-(3-benzyloxy-propyl)-5-bromo-benzoate **17c***



Method A:

0.455 g (2.37 mmol) **2c** and 0.318 g (2.61 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 0.841 g (2.37 mmol) **11b**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days.

Method B:

1.224 g (6.40 mmol) **2c** and 0.860 g (7.00 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 1.00 g (3.20 mmol) **11a**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol)

$Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days.

The phases were separated, the organic layer was subsequently washed three times with brine, and dried. The solvent was removed under reduced pressure.

Chromatographic separation through silica gel with hexane/ ethylacetate and then with methylene chloride gave **17a**. The compound can be crystallized from methanol.

Yield: method A 0.822 g (92%) of a colorless oil.

method B 0.821 g (68%) of a colorless oil.

R_f = 0.28 (Silica gel; hexane/ethyl acetate 3:1).

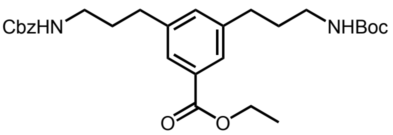
^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.37 (t, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, $-CH_2CH_3$), 1.92 (m, 2H, β-CH_2), 2.74 (t, 2H, $^3J_{H\text{-}H}$ = 7.7 Hz, α-CH_2), 3.46 (t, 2H, $^3J_{H\text{-}H}$ = 5.9 Hz, γ-CH_2), 4.36 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, $-CH_2CH_3$), 4.49 (s, 2H, $-OCH_2Ar$), 7.33 (m, 5H, $-OCH_2Ar$-H), 7.50 (m, 1H, Ar-H), 7.82 (m, 1H, Ar-H), 8.00 (m, 1H, Ar-H).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.08, 30.79, 31.70, 61.05, 68.73, 72.75, 122.05, 127.35, 127.40, 128.10, 128.14, 129.77, 132.10, 135.55, 138.21, 144.29, 165.07.

MS (EI, 80eV, 90°C): m/z (%) = 379.0 (9.84), 378.0 (43.02), 377.0 (10.50), 376.0 (42.58) $[M]^{+\bullet}$, 91.0 (100) $[C_7H_7]^{+\bullet}$.

EA	$C_{19}H_{21}BrO_3$	calc.	C	60.49	H	5.61,
	(377.27)	found		60.07		5.45.

*Ethyl-3-(3-benzyloxycarbonylamino-propyl)-5-(3-tert-butoxycarbonylamino-propyl)-benzoate **16***



0.503 g (3.20 mmol) **2a** and 0.430 g (3.50 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 1.26 g (3.00 mmol) **17b**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was refluxed for two days.

The phases are separated, the organic layer was subsequently washed three times with brine, and dried. The solvent was removed under reduced pressure.

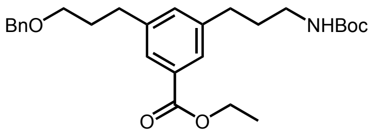
Chromatographic separation through silica gel with hexane/ ethylacetate and then with methylene chloride gave **16**.

Yield: 1.376 g (92%) of a colorless oil.

R_f = 0.17 (silica gel; hexane/ethyl acetate 3:1).

S. Koch synthesized this compound via another approach. The data obtained from spectroscopic and spectrometric methods fitted to those already published.

Ethyl-3-(3-benzyloxy-propyl)-5-(3-tert-butoxycarbonylamino-propyl)-benzoate ***18***



0.503 g (3.20 mmol) **2a** and 0.430 g (3.50 mmol) 9-BBN were dissolved in 10 ml dry toluene in a N_2-atmosphere at 0°C. The reaction was stirred for 12 hours. 1.00 g (3.00 mmol) **17c**, 5 ml 1M aqueous KOH and 5 ml toluene were added. The reaction mixture was degassed by three freeze-pump-thaw-cycles. 0.11 g (0.1 mmol) $Pd(PPh_3)_4$ were added and another freeze-pump-thaw-cycle was applied. The reaction was vigorously stirred at 60°C for two days.

The phases are separated, the organic layer was subsequently washed three times with brine, and dried. The solvent was removed under reduced pressure.

Further purification by flash chromatography, using hexane/ethylacetate 10:1 → 3:1 as solvent, followed by flash chromatography using methylene chloride as solvent.

Chromatographic separation through silica gel with hexane/ ethylacetate and then with methylene chloride gave **16**.

Yield: 1.202 g (88%) of a yellow oil.

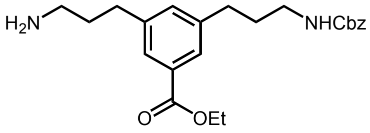
R_f = 0.22 (silica gel; hexane/ethyl acetate 3:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.38 (t, 3H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 1.45 (s, 9H, $-C(CH_3)_3$), 1.80 (m, 2H, β-CH_2), 1.94 (m, 2H, β-CH_2), 2.62 (t, 2H, $^3J_{H\text{-}H}$ = 7.7 Hz, α-CH_2), 2.74 (t, 2H, $^3J_{H\text{-}H}$ = 7.7 Hz, α-CH_2), 3.14 (m, 2H, γ -CH_2), 3.49 (t, 2H, $^3J_{H\text{-}H}$ = 5.9 Hz, γ-CH_2), 4.35 (q, 2H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 4.49 (s, 2H, $-OCH_2Ar$), 4.52 (br s, 1H, -N*H*), 7.15 (s, 1H, Ar-*H*), 7.33 (m, 5H, -OCH_2Ar-*H*), 7.67 (s, 1H, Ar-*H*), 7.72 (s, 1H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.33, 28.40, 31.26, 31.70, 32.16, 32.88, 40.25, 60.84, 69.36, 72.93, 79.27, 122.96, 127.27, 127.52, 127.62, 128.35, 130.69, 133.17, 141.83, 142.40, 152.95, 166.83.

MS (pos. FAB): m/z (%) = 456.3 (9.68) $[M]^{+\bullet}$, 356.4 (100) $[M-C_5H_9O_2+H]^+$.

*Ethyl-3-[3-(benzyloxycarbonylamino)propyl]-5-(trifluoro-acetato-3-amoniumpropyl)benzoate **19***



0.520 g (1.0 mmol) **16** were dissolved in 5 ml methylene chloride and 3 ml TFA was added. The mixture was stirred for 12 hours at room temperature. The reaction was monitored with TLC. After complete deprotection the solvent removed under reduced pressure.

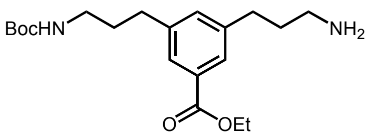
Chromatographic separation through silica gel with methylene chloride/ methanol gave **16**.

Yield: 0.475 g (95%) of a yellowish solid.

R_f = 0.11 (silica gel; methylene chloride/ methanol 10:1).

S. Koch synthesized this compound via another approach. The data obtained from spectroscopic and spectrometric methods fitted to those already published.

*Ethyl-3-[3-(tert-butoxycarbonylamino)propyl]-5-(3-aminopropyl)benzoate **20***



1.280 g (0.25 mmol) **16** were dissolved in 10 ml ethylacetate / ethanol (1:1). 0.012 g Pd/ C was added. The mixture was stirred for one hour in a hydrogen atmosphere. The reaction was monitored with TLC.

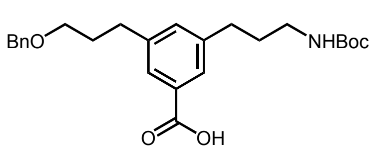
After complete deprotection the mixture was filtered and the solvent removed under reduced pressure. Further purification was not necessary.

Yield: 0.9 g (quant.) of a yellowish oil.

^{1}H NMR (CDCl$_3$, 500 MHz): δ [ppm] = 1.33 (t, 3H, $^{3}J_{H\text{-}H}$ = 7.2 Hz, -CH$_2$C*H*$_3$), 1.38 (s, 9H, -C(C*H*$_3$)$_3$), 1.76 (m, 4H, β/β'-C*H*$_2$), 2.61 (m, 6H, γ/γ'-C*H*$_2$ & NH$_2$), 2.70 (m, 2H, α-C*H*$_2$), 3.08 (m, 2H, α'-C*H*$_2$), 4.30 (q, 2H, $^{3}J_{H\text{-}H}$ = 7.1 Hz, -C*H*$_2$CH$_3$), 4.67 (br s, 1H, -N*H*), 7.14 (s, 1H, Ar-*H*), 7.62 (s, 1H, Ar-*H*), 7.63 (s, 1H, Ar-*H*).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 14.24, 28.32, 31.57, 32.76, 32.79, 34.35, 40.06, 41.23, 60.78, 79.00, 126.95, 127.05, 130.61, 133.01, 141.86, 142.16, 155.91, 166.71.

3-(3-benzyloxy-propyl)-5-(3-tert-butoxycarbonylamino-propyl)-benzoic acid ***21b***



1.89 g (4.15 mmol) **18** was dissolved in 50 ml ethanol and 10 ml 1M KOH$_{aq}$ added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl$_{aq}$ and the pH was adjusted to 5. After addition of methylene chloride, the phases were separated. The aequous phase was extracted with methylene chloride. The combined organic phases were dried and the solvent was removed under reduced pressure.

Yield: 1.720 g (96%) of a colorless oil.

R$_f$ = 0.19 (silica gel; methylene chloride/ methanol 15:1).

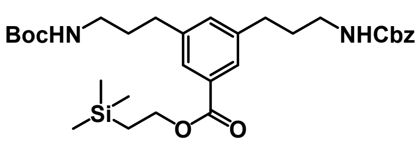
^{1}H NMR (CDCl$_3$, 250 MHz): δ [ppm] = 1.47 (s, 9H, -C(C*H*$_3$)$_3$), 1.85 (m, 4H, β-C*H*$_2$), 2.70 (m, 4H, α-C*H*$_2$), 3.17 (m, 2H, γ -C*H*$_2$), 3.39 (m, 2H, γ -C*H*$_2$), 4.49 (s, 2H, -OC*H*$_2$Ar), 7.18 (s, 1H, Ar-*H*), 7.29 (m, 5H, -OCH$_2$Ar-*H*), 7.59 (2s, 1H, Ar-*H*).

^{13}C NMR (CDCl$_3$, 63 MHz): δ [ppm] = 28.30, 31.20, 31.60, 32.45, 32.67, 40.40, 69.38, 72.99, 79.27, 123.11, 126.98, 127.46, 127.64, 128.15, 130.63, 134.01, 141.94, 143.00, 153.15, 167.23.

MS (pos. FAB): m/z (%) = 451.2 (3.70), 450.1 (12.16) [M+Na]$^{+}$, 428.2 (4.10) [M+H]$^{+}$, 91.0 (100) [C$_7$H$_7$]$^{+}$.

EA	$C_{25}H_{33}NO_5$	calc.	C	70.23	H	7.78	N	3.28,
	(427.53)	found		70.01		7.64		2.97.

Trimethylsilyl-ethanoyl-3-(3-benzyloxycarbonylamino-propyl)-5-(3-tert-butoxy carbonylamino-propyl)-benzoate ***25***



A solution of 0.557 g (2.70 mmol) DCC in 1.5 mL of methylene chloride was added to a solution of 1.00 g (2.12 mmol) **21a**, 0.330 g (2.7 mmol) trimethylsilylethanol, and 0.150 g (0.5 mmol) 4-dimethylaminopyridinium p-toluenesulfonate in 5 mL of methylene chloride. The mixture was stirred for 24 h, filtered, and the solvent evaporated.

Chromatographic separation through silica gel with hexane/ ethylacetate gave **25**.

Yield: 1.055 g (87%) of a yellow oil.

R_f = 0.27 (silica gel; hexane/ethyl acetate 3:1).

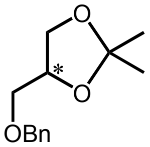
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 0.06 (s, 9H, -Si(C*H*$_3$)$_3$), 1.11 (m, 2H, -SiC*H*$_2$), 1.41 (s, 9H, -C(C*H*$_3$)$_3$), 1.77 (m, 2H, β-C*H*$_2$), 1.82 (m, 2H, β-C*H*$_2$), 2.62 (m, 4H, α-C*H*$_2$), 3.09 (m, 2H, γ -C*H*$_2$), 3.18 (m, 2H, γ -C*H*$_2$), 4.37 (m, 2H, -OC*H*$_2$), 4.64 (br s, 1H, -N*H*), 4.98 (br s, 1H, -N*H*), 5.07 (s, 2H, -OC*H*$_2$Ar), 7.15 (s, 1H, Ar-*H*), 7.31 (m, 5H, -OCH$_2$Ar-*H*), 7.65 (s, 2H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 1.50, 17.41, 28.35, 31.33, 31.50, 32.61, 32.66, 39.98, 40.40, 63.09, 66.55, 79.10, 127.03, 127.11, 127.99, 128.02, 128.42, 130.90, 133.04, 136.58, 141.67, 141.88, 155.93, 156.39, 166.81.

MS (EI, 130°C): m/z (%) = 470.0 (7.64) $[M-C_5H_9O_2]^{+\bullet}$, 356.4 (100) $[M-C_5H_9O_2+H]^+$, 91.0 (100) $[C_7H_7]^+$.

8.5 Compounds of Chapter 4.3.3

4-Benzyloxymethyl-2,2-dimethyl-[1,3]dioxolane ***35***



13.21 g (100 mmol) **34** in 100 ml dry THF were added dropwise to a suspension of 4.2 g (105 mmol) NaH (60% dispersion in mineral oil) in 100 ml THF at room temperature. The mixture was stirred for two hours. Afterwards 22.23 g (130 mmol) benzylbromide in 50 ml THF were added slowly at room temperature. The reaction was stirred for 12 hours and pourred into water. The water phase was separated and extracted three times with hexane. The combined organic phases were extracted with brine, dried and the solvent was removed under reduced pressure.

Purification by vacuum destillation (bp.: oilpump ~100°C).

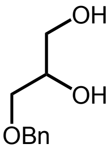
Yield: 17.77 g (80%) of a colorless oil.

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.35 (s, 3H, -C*H*$_3$), 1.41 (s, 3H, -C*H*$_3$), 3.50 (m, 2H, -C*H*$_3$), 3.72 (m, 1H, -C*H*$_2$), 4.04 (m, 1H, -C*H*$_2$), 4.29 (m, 1H, -C**H*), 4.56 (m, 2H, -C*H*$_2$Ar), 7.31 (m, 5H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 25.34, 26.72, 66.85, 70.55, 71.78, 73.47, 74.71, 109.34, 127.85, 128.43, 137.96.

MS (EI, 40°C): m/z (%) = 222.4 (1.53) $[M]^{+\bullet}$,208.4 (1.73), 207.4 (12.76) $[M-CH_3]^{+\bullet}$, 165.3 (3.12), 164.4 (26.73), 163.4 (8.14) $[M-C_3H_6O+H]^{+\bullet}$, 91.0 (100) $[C_7H_7]^+$.

3-Benzyloxy-propane-1,2-diol ***36***



A solution of 15 g (67.5 mmol) **35** in 40 ml THF, 20 ml H_2O and 5 ml 1M HCl_{aq} were refluxed. The reaction was monitored with TLC.

Phases were separeted, and the water phase was extracted twice with diethylether. The combined organic phases were extracted with brine, dried and the solvent was removed under reduced pressure.

The crude product was purified vacuum distillation (bp.: oilpump ~145°C).

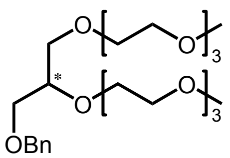
Yield: 11.55 g (94%) of a colorless oil.

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.43 (s, 2H, -O*H*), 3.47-3.74 (br m, 4H, -C*H*$_2$), 3.88 (m, 1H, -C**H*), 4.54 (s, 2H, -C*H*$_2$Ar), 7.32 (m, 5H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 63.59, 70.65, 71.21, 73.05, 127.46, 127.86, 128.10, 137.56.

MS (EI): m/z (%) = 182.1 (12.3) $[M]^{+\bullet}$; 107.9 (4.9), 106.9 (26.0), 104.8 (5.5) $[C_7H_7O]^\bullet$; 93.3 (2.8), 92.2 (36.8), 91.0 (100), 89.8 (3.7), 88.7 (3.5) $[C_7H_7]^+$.

1-(2,3-Bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propoxy)benzene ***37***



6.96 g (38.2 mmol) **36** in 150 ml dry THF were added dropwise to a suspension of 3.9 g (98 mmol) NaH (60% dispersion in mineral oil) in 250 ml dry THF at room temperature. The mixture was refluxed for two hours. Afterwards 36.4 g (114 mmol) **30** in 100 ml THF were added slowly at room temperature. The reaction was refluxed for 48 hours and pourred into water. The water phase was separated and extracted three times with diethylether. The combined organic phases were extracted with brine, dried and the solvent was removed under reduced pressure.

Chromatographic separation through silica gel with methylene chloride increasing to methylene chloride/ methanol 10:1 gave **37**.

Yield: 11.77 g (65%) of a colorless oil.

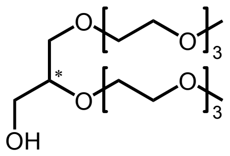
R_f = 0.22 (silica gel; methylene chloride/ methanol 20:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 3.29 (s, 3H, -C*H*$_3$), 3.30 (s, 3H, -C*H*$_3$), 3.42-3.64 (br m, 28H, -C*H*$_2$), 3.69 (m, 1H, -C**H*), 4.46 (s, 2H, -C*H*$_2$Ar), 7.20 (m, 5H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 58.78, 69.61, 70.05, 70.30, 70.38, 70.42, 70.60, 70.63, 71.08, 71.74, 73.12, 78.26, 127.29, 129.36, 128.08, 138.19.

MS (EI): m/z (%) = 474.9 (0.2), 474.0 (0.8) $[M]^{+\bullet}$; 353.9 (1.0), 353.0 (4.9) $[C_{16}H_{33}O_8]^{+\bullet}$.

2,3-Bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-1-ol ***32***



Method A: 11.54 g (24.3 mmol) **37** were dissolved in 200 ml ethanol. 1.15 g Pd/ C were added and the mixture was stirred for one day at 3.5 bar H_2-pressure. The solvent was removed after filtration. No further purification necessary.

Method B (improved protocol for the deprotection of Kutzner's **31**): 6.25 g (10 mmol) **31** were dissolved in 100 ml ethanol and 0.65 g Pd/ C were added. The mixture was stirred for one day at 50°C in a hydrogen atmosphere. The solvent was removed after filtration. Chromatographic separation through silica gel with methylene chloride/ methanol 10:1 gave **32**.

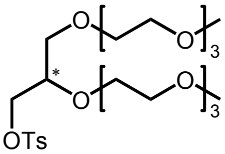
Yield: Method A: 8.87 g (95%) of a colorless oil.

Method B:

R_f = 0.49 (silica gel; methylene chloride/ methanol 10:1).

F. Kutzner synthesized this compound via another approach. The data obtained from spectroscopic and spectrometric methods fitted to those already published.

2,3-Bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propyl4-methylbenzene sulfonate **33**



8g (20.8 mmol) **32** were dissolved in 4 ml pyridine and added dropwise to an ice-cooled solution of 3.96g (20.8 mmol) 4-methylbenzene-1-sulfonyl chloride in 12 ml pyridine. After complete addition the external cooling was removed and the reaction stirred for 15 hours.

The mixture was acidified with conc. HCl (pH 1) and extracted with methylene chloride. The organic phase was washed once with brine, dried, and the solvent removed under reduced pressure. Chromatographic separation through silica gel with methylene chloride increasing to methylene chloride/ methanol 20:1 gave **33**.

Yield: 10.30 g (92%) of a yellowish oil.

R_f = 0.38 (silica gel; methylene chloride/ methanol 15:1.

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.41 (s, 3H, Ar- CH_3), 3.34 (s, 6H, -CH_3), 3.40-3.77 (br m, 27H, -CH_2 & -C**H*), 4.01 (dd, 1H, $^2J_{H\text{-}H}$ = 10.3 Hz, $^3J_{H\text{-}H}$ = 5.9 Hz, -C*H*HOCH_2), 4.13 (dd, 1H, $^2J_{H\text{-}H}$ = 10.3 Hz, $^3J_{H\text{-}H}$ = 4.1 Hz, -C*H*HOSO$_2$), 7.31 (d, 2H, $^3J_{H\text{-}H}$ = 8.8 Hz, Ar-*H*), 7.76 (d, 2H, $^3J_{H\text{-}H}$ = 8.8 Hz, Ar-*H*).

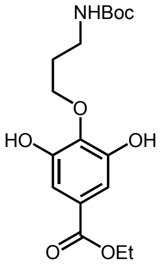
^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 21.84, 59.22, 69.86, 70.15, 70.27, 70.69, 70.75, 70.83, 70.91, 71.14, 72.17, 77.78, 128.22, 128.24, 130.02, 143.61.

MS (pos. FAB): m/z (%) = 577.3 (3.8) $[M+K]^+$; 563.2 (3.1), 562.2 (8.6), 561.1 (25.9) $[M+Na]^+$; 541.4 (3.7), 540.5 (32.9), 539.5 (2.7) $[M+H]^+$, 102.7 (100) $[C_5H_{11}O_2]^+$; 88.8 (83.6) $[C_4H_9O_2]^+$; 57.9 (67.7) $[C_3H_7O]^+$.

EA	$C_{24}H_{42}O_{11}S$	calc.	C	53.51	H	7.86,
	538.24	found		53.24		7.68.

8.6 Compounds of Chapter 4.3.4

Ethyl-4-(3-tert-butoxycarbonylamino-propoxy)-3,5-dihydroxy-benzoate ***54a***



7.49 g **52** (37.8 mmol), 9.00 g **53a** (37.8 mmol), 15.14 g dry $KHCO_3$ (151.2mmol) and 0.11 g KI (0.6 mmol) were suspended in 40 ml dry DMF. The mixture was degassed by three freeze-pump-thaw cycles, flushed with N_2, and stirred for 4 days at room temperature. After filtration the organic phase was quenched with 400 ml water, neutralized, and extracted seven times with 60 ml Diethylether. The combined organic phases were extracted three times with 100 ml 1M $NaHCO_3$, three times with 100 ml water, and once with 100 ml brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated. The crude product was purified by column chromatography (silica gel; hexane/ethyl acetate 3:1). The colorless oil was dissolved in dioxane, filtered and lyophilized.

Yield: 8.73 g (65%) of a colorless solid.

Alternatively, the same product was obtained by catalytic hydrogenation of **56**. 6.5 g (12.1 mmol) **56** were dissolved in 10 ml methanol . 0.65 g Pd/ C were added. The mixture was stirred for one hour in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtered and the solvent removed under reduced pressure. Further purification was not necessary.

Yield: 4.28 g (quant.) of a colorless solid.

R_f = 0.23 (Silica gel; hexane/ethyl acetate 3:1).

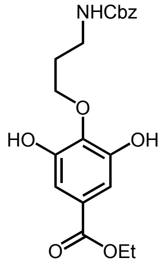
^{1}H NMR ($CDCl_3$ & d^4-methanol, 270 MHz): δ [ppm] = 1.29 (t, 3H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 1.39 (s, 9H, $-C(CH_3)_3$), 1.83 (m, 2H, β-CH_2), 3.36 (m, 2H, γ-CH_2), 4.02 (t, 2H, $^3J_{H\text{-}H}$ = 5.2 Hz, α-CH_2), 4.25 (q, 2H, $^3J_{H\text{-}H}$ = 7.0 Hz, $-CH_2CH_3$), 5.17 (br s, 1H, -NH), 7.09 (2H, Ar-H).

^{13}C NMR ($CDCl_3$ & d^4-methanol, 68 MHz): δ [ppm] = 13.85, 28.05, 30.29, 36.65, 60.79, 69.38, 79.50, 109.17, 125.45, 138.05, 149.77, 157.08, 166.80.

MS (EI, 80eV, 160°C): m/z (%) = 354.9 (5) $[M]^{+\bullet}$; 310.0 (3) $[M\text{-}OEt]^{+\bullet}$; 255.9 (4), 254.9 (27) $[M\text{-}C_5H_9O_2]^{+\bullet}$; 101.9 (100) $[C_5H_9O_2]^{+\bullet}$.

EA	$C_{17}H_{25}NO_7$	calc.	C	57.45	H	7.09	N	3.94,
	(355.16)	found		57.21		7.07		3.83.

Ethyl-4-(3-benzyloxycarbonylamino-propoxy)-3,5-dihydroxy-benzoate ***54b***



7.49 g **52** (37.8 mmol), 10.28 g **53b** (37.8 mmol), 15.14 g dry $KHCO_3$ (151.2mmol) and 0.11 g KI (0.6 mmol) were suspended in 40 ml dry DMF. The mixture was degassed by three freeze-pump-thaw cycles, flushed with N_2, and stirred for 4 days at room temperature. After filtration the organic phase was quenched with 400 ml water, neutralized, and extracted seven times with 60 ml Diethylether. The combined organic phases were extracted three times with 100 ml 1M $NaHCO_3$, three times with 100 ml water, and once with 100 ml brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated. The crude product was purified by column chromatography (silica gel; hexane/ethyl acetate 3:1). The colorless oil was dissolved in dioxane, filtered and lyophilized.

Yield: 8.54 g (58%) of a colorless solid.

R_f = 0.20 (Silica gel; hexane/ethyl acetate 3:1).

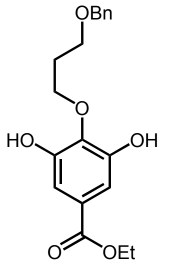
^{1}H NMR ($CDCl_3$ & d^4-methanol, 270 MHz): δ [ppm] = 1.29 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH_2CH_3), 1.86 (m, 2H, β-CH_2), 3.42 (t, 2H, $^3J_{H\text{-}H}$ = 5.8 Hz, γ-CH_2), 4.05 (t, 2H, $^3J_{H\text{-}H}$ = 5.5 Hz, α-CH_2), 4.25 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH_2CH_3), 5.06 (s, 2H, -OCH_2Ar), 5.66 (br s, 1H, -N*H*), 7.10 (2H, Ar-*H*: Gallate), 7.26 (m, 5H, -OCH_2Ar-*H*).

^{13}C NMR ($CDCl_3$ & d^4-methanol, 68MHz): δ [ppm] = 13.87, 16.81, 29.93, 37.39, 60.86, 66.59, 69.54, 109.20, 125.47, 127.68, 127.81, 128.20, 136.20, 138.08, 149.71, 157.40, 166.80.

MS (EI, 80eV, 170°C): m/z (%) = 390.1 (1), 389.0 (4) $[M]^{+\bullet}$; 344.0 (1) $[M\text{-}OEt]^{+\bullet}$; 281.0 (3) $[M\text{-}C_7H_8O]^{+\bullet}$; 92.0 (8), 91.1 (100) $[C_7H_7]^{+\bullet}$.

EA	$C_{20}H_{23}NO_7$	calc.	C	61.69	H	5.95	N	3.60,
	(389.15)	found		61.52		5.94		3.66.

Ethyl-4-[3-(benzyloxy)propoxy]-3,5-dihydroxy-benzoate



11.01 g **52** (55.5 mmol), 13.4 g **53c** (58.5 mmol), 22.25 g dry $KHCO_3$ (222.2mmol) and 0.25 g KI (1.4 mmol) were suspended in 60 ml dry DMF. The mixture was degassed by three freeze-pump-thaw cycles, flushed with N_2, and stirred for 4 days at room temperature. After filtration the organic phase was quenched with 400 ml water, neutralized, and extracted seven times with 60 ml Diethylether. The combined organic phases were extracted three times with 100 ml 1M $NaHCO_3$, three times with 100 ml water, and once with 100 ml brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated. The crude product was purified by column chromatography. The colorless oil was dissolved in dioxane, filtered and lyophilized.

Yield: 9.67 g (50%) of a colorless solid.

R_f = 0.30 (Silica gel; hexane/ethyl acetate 3:1).

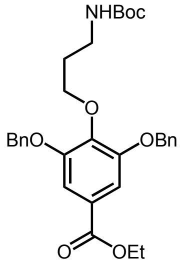
^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.34 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, -$CH_2C\mathit{H}_3$), 1.99 (m, 2H, β-$C\mathit{H}_2$), 3.76 (t, 3H, $^3J_{H\text{-}H}$ = 5.5 Hz, γ-$C\mathit{H}_2$), 4.15 (t, 2H, $^3J_{H\text{-}H}$ = 5.5 Hz, α-$C\mathit{H}_2$), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, -$C\mathit{H}_2CH_3$), 4.64 (s, 2H, -$OC\mathit{H}_2Ar$), 7.07 (br s, 2H, -$O\mathit{H}$), 7.20 (s, 2H, Ar-*H*: Gallate), 7.25-7.43 (m, 5H, -OCH_2Ar-*H*).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.20, 28.83, 60.99, 67.76, 71.64, 73.18, 109.47, 126.73, 128.05, 128.12, 128.49, 136.89, 137.61, 149.61, 166.43.

MS (EI, 80eV, 60°C): m/z (%) = 346.7 (8), 345.8 (41) $[M]^{+\bullet}$; 301.3 (11), 300.4 (8) $[M\text{-}OEt]^{+\bullet}$; 237.8 (8) $[M\text{-} C_7H_7O]^{+\bullet}$; 209.4 (4) $[M\text{-} C_9H_{11}O]^{+\bullet}$; 91.4 (100) $[C_7H_7]^{+\bullet}$.

EA	$C_{19}H_{22}O_6$	calc.	C	65.88	H	6.40,
	(346.14)	found		65.81		6.20.

Ethyl-4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(benzyloxy)-benzoate ***56***



5.0 g (<14 mmol) of a mixture of **54a** and **55a**, 7.74 g (56.0 mmol) dry K_2CO_3, and 5.78 g (33.7 mmol) benzylbromide were suspended in 30 ml dry DMF under N_2-atmosphere. The mixture was stirred for 1 day at 80°C. The reaction was quenched by the addition of 50 ml water. The mixture was extracted with ethyl acetate. The combined organic phases were washed with brine and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. The crude product was purified by column chromatography (Silica gel; hexane/ethyl acetate 10:1).

Yield: 6.5 g of a colorless solid.

R_f = 0.27 (Silica gel; hexane/ethyl acetate 10:1).

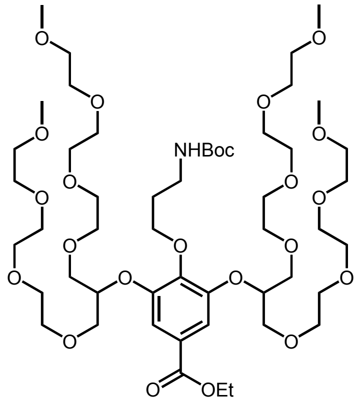
^{1}H NMR ($CDCl_3$, 270 MHz): δ [ppm] = 1.35 (t, 3H, $^3J_{H\text{-}H}$ = 6.9 Hz, $\text{-}CH_2CH_3$), 1.37 (s, 9H, $\text{-}C(CH_3)_3$), 1.85 (m, 2H, β-CH_2), 3.27 (m, 2H, γ-CH_2), 4.09 (t, 2H, $^3J_{H\text{-}H}$ = 5.8 Hz, α-CH_2), 4.32 (q, 2H, $^3J_{H\text{-}H}$ = 6.9 Hz, $\text{-}CH_2CH_3$), 5.15 (s, 4H, $\text{-}OCH_2Ar$), 5.24 (br s, 1H, -N*H*), 7.27-7.47 (12H, Ar-*H*).

^{13}C NMR ($CDCl_3$, 68 MHz): δ [ppm] = 14.28, 28.39, 29.92, 38.16, 61.02, 71.11, 71.77, 78.69, 108.85, 125.50, 127.50, 128.09, 128.58, 136.50, 142.20, 152.23, 156.00, 165.98.

MS (EI, 130°C): m/z (%) = 536.1 (0.07), 535.0 (0.18) $[M]^{+\bullet}$; 491.0 (0.10), 490.0 (0.21) $[M\text{-}OEt]^+$; 462.9 (0.24), 462.0 (1.18) $[M\text{-}C_3H_5O_2]^+$; 92.2 (14.78), 91.1 (100.00) $[C_7H_7]^+$.

EA	$C_{31}H_{37}NO_7$	calc.	C	69.51	H	6.96	N	2.62,
	(535.26)	found		68.90		6.84		2.52.

Ethyl-4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxy ethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***58a***



4.40 g (12.3 mmol) **54a**, 6.91 g (50.0 mmol) dry K_2CO_3 and 16.00 g (29.7 mmol) **45** were suspended in 30 ml dry DMF under N_2-atmosphere. The mixture was stirred for 3 days at 80°C. After filtration, the solvent was removed under reduced pressure. The crude product was purified by column chromatography. The slight yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 8.70 g (65%) of a yellowish oil.

R_f = 0.22 (Silica gel; methylene chloride/ methanol 30:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.35 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, $\text{-}CH_2CH_3$), 1.41 (s, 9H, $\text{-}C(CH_3)_3$), 1.85 (m, 2H, β-CH_2), 3.34 (hidden m, 2H, γ-CH_2), 3.34 (s, 12H,

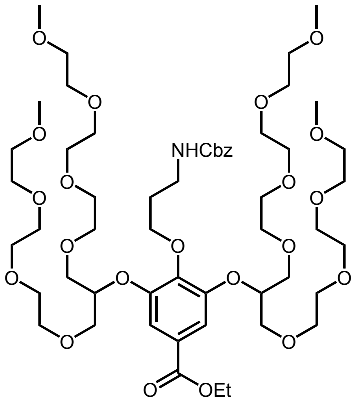
-OCH_3), 3.49-3.53 & 3.58-3.66 (2m, 48H, -OCH_2CH_2O), 3.71 (m, 8H, -OCH(CH_2)$_2$), 4.03 (t, 2H, $^3J_{H\text{-}H}$ = 5.5 Hz, α-CH_2), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, -CH_2CH$_3$), 4.57 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OCH(CH$_2$)$_2$), 5.60 (br s, 1H, -NH), 7.36 (s, 2H, Ar-H: Gallate).

^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 14.18, 28.33, 29.75, 37.79, 58.73, 60.74, 70.05, 70.28, 70.36, 70.73, 70.92, 71.69, 77.44, 78.42, 110.54, 125.19, 143.52, 151.66, 155.91, 161.75, 165.69.

MS (pos. FAB): m/z (%) = 1128.0 (4), 1127.0 $[M+K]^{+\bullet}$; 1113.0 (6), 1112.0 (14), 1111.0 (24) $[M+Na]^{+\bullet}$;1089.0 (4) $[M+H]^{+\bullet}$; 992.0 (10), 991.0 (12), 990.0 (53), 989.0 (100), 988.0 (15), 987.0 (30) $[M+H-C_5H_9O_2]^{+\bullet}$.

EA	$C_{51}H_{93}NO_{23}$	calc.	C	56.29	H	8.61	N	1.29,
	(1087.61)	found		56.62		8.18		0.71.

Ethyl-4-(3-benzyloxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxy ethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***58b***



2.00 g (5.6 mmol) **54b**, 3.10 g (13.5 mmol) dry K_2CO_3 and 7.27 g (13.5 mmol) **45** were suspended in 15 ml dry DMF under N_2-atmosphere. The mixture was stirred for 3 days at 80°C. After filtration, the solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1). The slight yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 3.64 g (58%) of a yellowish oil.

R_f = 0.21 (Silica gel; methylene chloride/ methanol 25:1).

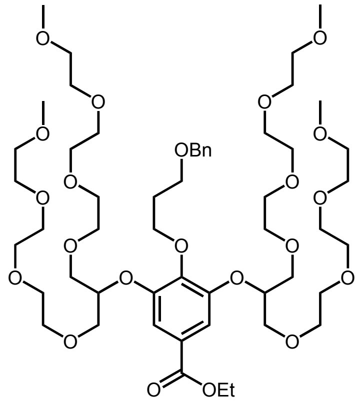
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.34 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH$_2$CH_3), 1.89 (m, 2H, β-CH_2), 3.29 (s, 12H, -OCH_3), 3.42 (m, 2H, γ-CH_2), 3.48-3.64 (2m, 48H, -OCH_2CH_2O), 3.66-3.76 (m, 8H, -OCH(CH_2)$_2$), 4.06 (t, 2H, $^3J_{H\text{-}H}$ = 5.7 Hz, α-CH_2), 4.30 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH_2CH$_3$), 4.60 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OCH(CH$_2$)$_2$), 5.04 (s, 2H, -CO$_2$CH_2Ar), 6.04 (t, 1H, $^3J_{H\text{-}H}$ = 6.0 Hz, -NH), 7.25-7.35 (m, 5H, -CH$_2$$Ar$), 7.38 (s, 2H, Ar-$H$: Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.1, 29.8, 38.4, 58.5, 60.9, 66.0, 70.2, 70.3, 70.4, 70.5, 70.6, 70.9, 71.9, 77.6, 107.8, 110.4, 125.6, 127.8, 128.0, 128.4, 137.3, 143.5, 151.9, 156.4, 165.7.

MS (pos. FAB): m/z (%) = 1145.0 (41) $[M+Na]^{+\bullet}$; 1124.5 (2), 1124.1 (8), 1123.3 (29), 1122.3 (49), 1121.4 (8) $[M+H]^{+\bullet}$; 1079.4 (76), 1078.0 (100), 1076.2 (27) $[M+H\text{-}OEt]^{+\bullet}$.

EA	$C_{54}H_{91}NO_{23}$	calc.	C	57.79	H	8.17	N	1.25,
	(1121.60)	found		57.32		7.87		1.26.

Ethyl-4-[3-(benzyloxy)propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy] ethoxy}propan-2-yloxy)-benzoate ***58c***



1.50 g (4.3 mmol) **54c**, 2.21 g (16.0 mmol) dry K_2CO_3 and 5.60 g (10.3 mmol) **45** were suspended in 15 ml dry DMF under N_2-atmosphere. The mixture was stirred for 3 days at 80°C. After filtration, the solvent was removed under reduced pressure. The crude product was purified by column chromatography. The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 2.83 g (61%) of a colorless oil.

R_f = 0.22 (Silica gel; methylene chloride/ methanol 30:1).

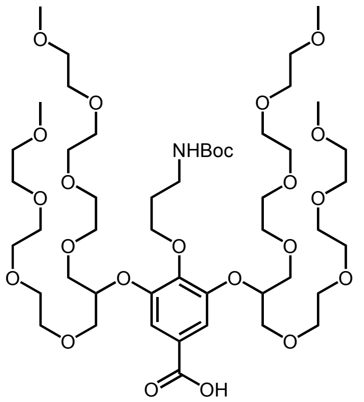
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.35 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, $\text{-}CH_2CH_3$), 2.02 (m, 2H, $\beta\text{-}CH_2$), 3.31 (s, 12H, $\text{-}OCH_3$), 3.44-3.65 (2m, 48H, $\text{-}OCH_2CH_2O$), 3.69 (hidden m, 2H, $\gamma\text{-}CH_2$), 3.70 (m, 8H, $\text{-}OCH(CH_2)_2$), 4.15 (t, 2H, $^3J_{H\text{-}H}$ = 6.3 Hz, $\alpha\text{-}CH_2$), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, $\text{-}CH_2CH_3$), 4.51 (s, 2H, $\text{-}CH_2OBn$), 4.58 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, $\text{-}OCH(CH_2)_2$), 7.32 (m, 1H, Ar-*H*: Bn), 7.31 (s, 2H, Ar-*H*: Bn), 7.33 (s, 2H, Ar-*H*: Bn), 7.39 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.19, 30.69, 58.58, 60.89, 67.51, 70.31, 70.37, 70.42, 70.49, 70.57, 70.67, 70.99, 71.90, 72.78, 77.89, 111.03, 125.29, 127.34, 127.48, 128.24, 138.99, 144.13, 151.88, 165.78.

MS (pos. FAB): m/z (%) = 1102.6 (36) $[M+Na]^{+\bullet}$; 1082.9 (5), 1081.2 (51), 1079.7 (52) $[M+H]^{+\bullet}$; 1036.0 (32), 1034.7 (43) $[M+H\text{-}OEt]^{+\bullet}$.

EA	$C_{53}H_{90}O_{22}$	calc.	C	58.98	H	8.41,
	(1078.59)	Found		58.64		8.05.

4-(3-tert-Butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxy ethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoic acid ***60a***



2.60 g (2.4 mmol) **58a** was dissolved in 80 ml ethanol and 10 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. Further purification by column chromatography (silica gel; methylene chloride/ methanol). The yellow oil was dissolved in benzene, filtered and lyophilized.

Yield: 2.493 g (98%) of a yellow oil.

R_f = 0.19 (Silica gel; methylene chloride/ methanol 10:1).

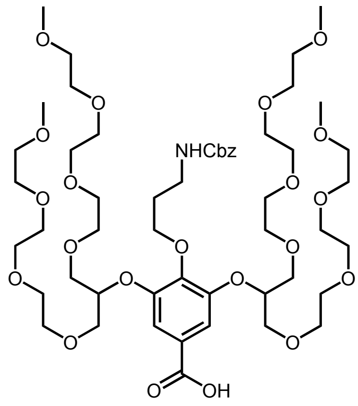
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.34 (s, 9H, -C(C*H*$_3$)$_3$), 1.79 (m, 2H, β-C*H*$_2$), 3.28 (hidden m, 2H, γ-C*H*$_2$), 3.28 (s, 12H, -OC*H*$_3$), 3.43-3.60 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.65 (m, 8H, -OCH(C*H*$_2$)$_2$), 3.98 (t, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, α-C*H*$_2$), 4.51 (quint, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OC*H*(CH$_2$)$_2$), 5.60 (t, 1H, $^3J_{H\text{-}H}$ = 5.4 Hz, -N*H*), 7.38 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 28.34, 29.69, 37.72, 58.68, 58.69, 70.18, 70.29, 70,38, 70.76, 70.78, 71.01, 71.02, 71.70, 77.56, 78.44, 111.08, 124.80, 143.69, 151.72, 155.98, 168.43.

MS (pos. FAB): m/z (%) = 1100.5 (1.0), 1099.5 (3.2), 1098.5 (6.1) $[M+K]^{+\bullet}$; 1084.0 (0.1), 1083.0 (0.2) $[M+Na]^{+\bullet}$1061.0 (0.1) $[M+H]^{+\bullet}$; 59.0 (100) $[C_3H_7O]^{+\bullet}$.

EA	$C_{49}H_{89}NO_{23}$	calc.	C	55.51	H	8.46	N	1.32,
	(1059.58)	found		55.71		8.47		1.02.

4-(3-Benzyloxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)-benzoic acid ***60b***



1.10 g (1.9 mmol) **58b** was dissolved in 40 ml ethanol and 5 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The yellow oil was dissolved in benzene, filtered and lyophilized.

Yield: 1.05 g (96%) of a yellow oil.

R_f = 0.18 (Silica gel; methylene chloride/ methanol 10:1).

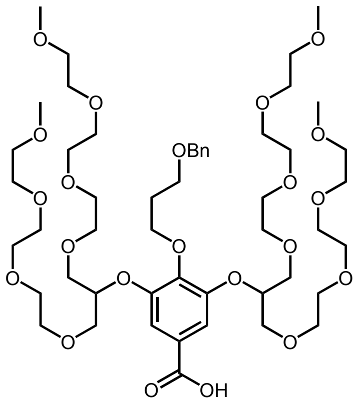
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.88 (m, 2H, β-C*H*$_2$), 3.35 (s, 12H, -OC*H*$_3$), 3.43 (m, 2H, γ-C*H*$_2$), 3.47-3.62 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.66 (d, 8H, $^3J_{H\text{-}H}$ = 4.8 Hz, -OCH(C*H*$_2$)$_2$), 4.05 (t, 2H, $^3J_{H\text{-}H}$ = 5.5 Hz, α-C*H*$_2$), 4.55 (quint, 2H, $^3J_{H\text{-}H}$ = 4.8 Hz, -OC*H*(CH$_2$)$_2$), 5.04 (s, 2H, C*H*$_2$OBn), 6.07 (t, 1H, $^3J_{H\text{-}H}$ = 5.8 Hz, -N*H*), 7.22-7.34 (m, 5H, Ar-*H*: Bn), 7.44 (s, 2H, Ar-*H*: Gallate)

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 29.28, 30.00, 58.42, 67.87, 69.81, 69.92, 70.02, 70.09, 70.48, 70.69, 71.42, 77.23, 110.66, 124.63, 127.50, 127.73, 127.96, 136.43, 143.32, 151.43, 156.23, 168.09

MS (pos. FAB): m/z (%) = 1118.6 (0.8), 1117.6 (2.4), 1116.6 (4.0) $[M+Na]^+$; 1051.4 (5.5), 1050.0 (8.8) $[M-CO_2+H]$; 1048.1 $[M-CO_2]$, 195.2 (1.1), 194.2 (1.0), 193.2 (6.4), 192.2 (46.9), 191.2 (1.2) $[C_{11}H_{14}NO_2]^+$; 148.9 (1.3), 147.9 (2.1), 146.9 (15.6) $[C_7H_{15}O_3]^+$;92.2 (6.5), 91.2 (77.5), 90.2 (2.4) $[C_7H_7]^+$; 59.3 (3.5), 59.1 (100.0) $[C_3H_7O]^{+\bullet}$

EA	$C_{52}H_{87}NO_{23}$	calc.	C	57.08	H	8.01	N	1.28,
	(1093.57)	found		56.78		7.98		1.25.

4-[3-(Benzyloxy)propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy} propan-2-yloxy)-benzoic acid ***60c***



2.00 g (1.85 mmol) **58c** was dissolved in 80 ml ethanol and 8 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 1.927 g (99%) of a colorless oil.

R_f = 0.25 (Silica gel; methylene chloride/ methanol 10:1).

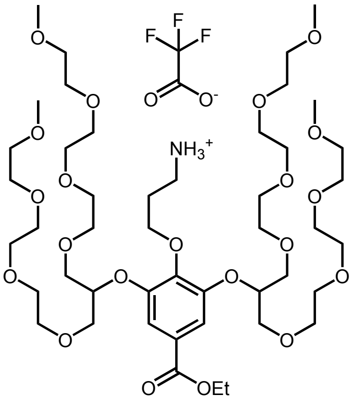
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.98 (m, 2H, β-C*H*$_2$), 3.34 (s, 12H, -OC*H*$_3$), 3.49-3.61 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.60 (m, 2H, γ-C*H*$_2$), 3.66 (m, 8H, -OCH(C*H*$_2$)$_2$), 4.11 (t, 2H, $^3J_{H-H}$ = 6.3 Hz, α-C*H*$_2$), 4.47 (s, 2H, -C*H*$_2$OBn), 4.51 (quint, 2H, $^3J_{H-H}$ = 5.0 Hz, -OC*H*(CH$_2$)$_2$), 7.22 (m, 1H, Ar-*H*: Bn), 7.27 (br s, 1H, Ar-*H*: Bn), 7.28 (br s,1H, Ar-*H*: Bn), 7.45 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 30.18, 58.37, 66.96, 69.88, 69.98, 70.05, 70.07, 70.49, 71.37, 72.38, 77.57, 111.46, 124.23, 126.93, 126.98, 127.79, 138.13, 144.05, 151.34, 168.29.

MS (pos. FAB): m/z (%) = 1129.2 (12), 1127.4 (34), 1126.4 (14) $[M\text{-}H+2K]^{+\bullet}$;1089.5 (50), 1088.5 (100), 1087.4 (7), 1086.3 (12), 1073.3 (18) $[M–H+2K]^{+\bullet}$; 1073.3 (18) $[M+Na]^{+\bullet}$.

EA	$C_{51}H_{86}O_{22}$	Calc.	C	58.27	H	8.25,
	(1050.56)	Found		58.00		8.28.

Ethyl-4-(trifluoro-acetato-3-amoniumpropoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxy ethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***59***



2.96 g (2.72 mmol) **58a** was dissolved in 30 ml methylene chloride and 4 ml trifluoro-acetic acid were added at room temperature. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 10:1). The slight yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 2.793 g (91%) of a yellowish oil.

R_f = 0.13 (Silica gel; methylene chloride/ methanol 10:1).

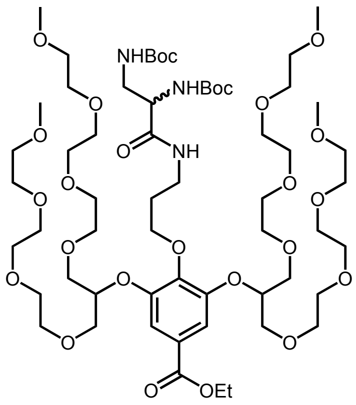
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.34 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, $-CH_2CH_3$), 2.04-2.11 (m, 2H, β-CH_2), 3.25 (m, 2H, γ-CH_2), 3.31 (s, 12H, $-OCH_3$), 3.45-3.68 (2m, 48H, $-OCH_2CH_2O$), 3.76 (m, 8H, $-OCH(CH_2)_2$), 4.22 (t, 2H, $^3J_{H\text{-}H}$ = 5.1 Hz, α-CH_2), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, $-CH_2CH_3$), 4.67 (quint, 2H, $^3J_{H\text{-}H}$ = 4.6 Hz, $-OCH(CH_2)_2$), 7.41 (s, 2H, Ar-*H*: Gallate), 7.52 (s, 3H, $-NH_3$).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.15, 26.91, 40.16, 61.20, 69.89, 70.20, 70.30, 70.34, 70.46, 70.88, 71.83, 73.39, 77.18, 109.69, 126.48, 141.92, 151.31, 165.52.

MS (pos. FAB): m/z (%) = 991.6 (3), 990.6 (17), 989.5 (53), 988.5 (100), 987.6 (4), 986.5 (7) $[M\text{-}TFA]^+$; 944.6 (4) $[M\text{-}TFA\text{-}OEt]^+$.

EA	$C_{48}H_{86}F_3NO_{23}$	calc.	C	52.31	H	7.86	N	1.27,
	(1101.55)	found		52.27		7.63		1.11.

Ethyl-4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***62***



0.797 g (2.62 mmol) **61** were dissolved in 5 ml dry DMF. 0.8 ml dry triethylamine were added and the mixture was cooled to -20°C. A solution of 0.925 g (2.88 mmol) TBTU in 6.5 ml dry DMF was added. The mixture was stirred for two hours at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 1.925 g (1.74 mmol) **59** and 0.8 ml dry triethylamine in 2 ml dry DMF was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 2.08 g (94%) of a yellowish oil.

R_f = 0.21 (Silica gel; methylene chloride/ methanol 20:1).

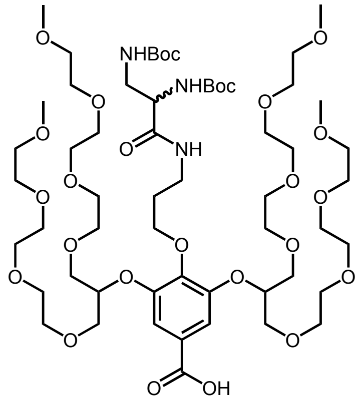
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.30 & 1.39 (2s, 18H, $-C(CH_3)_3$), 1.35 (t, 3H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 1.87 (m, 2H, β-CH_2), 3.31 (s, 12H, $-OCH_3$), 3.41 (m, 4H, α- & γ-CH_2), 3.45-3.49 & 3.53-3.67 (2m, 48H, $-OCH_2CH_2O$), 3.74 (m, 8H, $-OCH(CH_2)_2$), 4.03 (m, 1H, $-CH_2$NHBoc), 4.11 (m, 2H, $-CH_2$NHBoc & -CHNHBoc), 4.31 (q, 2H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 4.61 (quint, 2H, $^3J_{H-H}$ = 4.9 Hz, $-OCH(CH_2)_2$), 5.44 (br s, 1H, $-CH_2NH$Boc), 5.93 (br s, 1H, -CHNHBoc), 7.30 (br s, 1H, $-CH_2NH$COAr), 7.39 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 14.13, 27.94, 28.08, 29.20, 37.20, 42.55, 54.55, 58.68, 60.73, 69.88, 70.02, 70.19, 70.20, 70.27, 70.29, 70.58, 70.61, 71.62, 78.90, 79.17, 110.37, 125.24, 143.39, 151.63, 155.55, 156.16, 165.59, 170.09.

MS (pos. FAB): m/z (%) = 1297.4 (0.5) $[M+Na]^{+\bullet}$; 1276.4 (0.3), 1275.7 (0.4), 1275.2 (0.6) $[M+H]^{+\bullet}$; 1176.8 (0.2), 1174.9 (14.3), 1173.2 (0.5), 1172.3 (1.3) $[M-C_5H_9O_2]^{+\bullet}$; 1076.4 (0.2), 1076.1 (0.4), 1074.4 (7.8), 1073.0 (1.1), 1072.1 (2.45) $[M-2*C_5H_9O_2]^{+\bullet}$; 102.9 (38.2) $[C_5H_{11}O_2]^{+\bullet}$; 57.1 (100) $[C_4H_9]^{+\bullet}$.

EA	$C_{59}H_{107}N_3O_{26}$	calc.	C	55.60	H	8.46	N	3.30,
	(1273.71)	found		55.82		8.33		3.58.

4-[3-(2,3-Bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoic acid ***63***



0.790 g (0.62 mmol) **62** was dissolved in 20 ml ethanol and 2.5 ml 1M KOH$_{aq}$ added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl$_{aq}$ (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.749 g (97%) of a yellowish oil.

R_f = 0.17 (Silica gel; methylene chloride/ methanol 10:1).

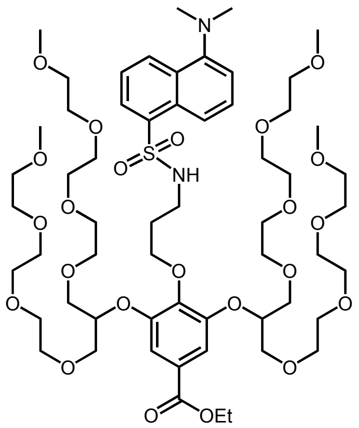
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.30 & 1.39 (2s, 18H, -C(C*H*$_3$)$_3$), 1.89 (m, 2H, β-C*H*$_2$), 3.33 (s, 12H, -OC*H*$_3$), 3.43 (m, 2H, α & γ-C*H*$_2$), 3.48-3.52 & 3.54-3.67 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.74 (m, 8H, -OCH(C*H*$_2$)$_2$), 4.05 (m, 2H, -C*H*$_2$NHBoc), 4.14 (m, 3H, -C*H*NHBoc & -C*H*$_2$NHBoc), 4.62 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 5.46 (br s, 1H, -CH$_2$N*H*Boc), 5.98 (br s, 1H, -CHN*H*Boc), 7.37 (br s, 1H, -CH$_2$N*H*), 7.46 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 27.79, 27.94, 29.03, 37.15, 42.33, 54.62, 58.47, 69.77, 69.91, 69.96, 70.03, 70.12, 70.45, 70.49, 71.46, 77.12, 78.76, 78.99, 110.61, 124.96, 143.30, 151.50, 155.34, 156.05, 168.00, 170.25.

MS (pos. FAB): m/z (%) = 1271.7 (5), 1270.7 (12), 1269.7 (20) [M+Na]$^{+\bullet}$; 1248.4 (7), 1247.3 (11) [M+H]$^{+\bullet}$; 1147.3 (2), 1146.4 (9), 1145.4 (28), 1144.4 (44), 1143.3 (4), 1142.4 (7) [M-$C_5H_9O_2$]$^{+\bullet}$; 1046.4 (4), 1045.3 (13), 1044.3 (24), 1043.3 (6), 1042.3 (11) [M-2*$C_5H_9O_2$]$^{+\bullet}$; 344.3 (100) [$C_{16}H_{30}$ N_3O_5]$^{+\bullet}$.

EA	$C_{57}H_{103}N_3O_{26}$	Calc.	C	54.93	H	8.33	N	3.37,
	(1245.68)	found		55.16		8.20		3.54.

Ethyl-4-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-3,5-bis(1,3-bis {2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***65***



0.850 g (0.77 mmol) **59** and 1.4 ml dry triethyl-amine were dissolved in 10 ml methylene chloride and added dropwise at room temperature to a stirred solution of 0.300 g (1.11 mmol) **64** in 25 ml dry methylene chloride. The mixture was stirred for two hours. The solvent was removed under reduced pressure. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 10:1). The green oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.934 g (99.3%) of a green oil.

R_f = 0.24 (Silica gel; methylene chloride/ methanol 20:1).

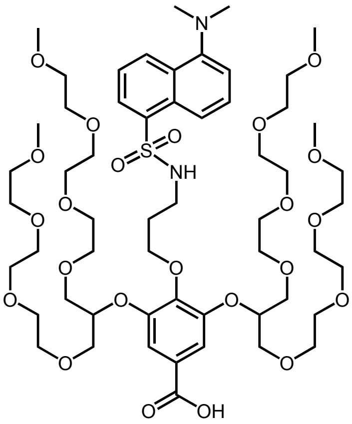
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.36 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH_2CH_3), 1.79 (tt, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, $^3J_{H\text{-}H}$ = 5.8 Hz, β-CH_2), 2.86 (s, 6H, -N(CH_3)$_2$), 3.22 (dt, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, $^3J_{H\text{-}H}$ = 5.8 Hz, γ-CH_2), 3.31 (s, 12H, -OCH_3), 3.45-3.59 (2m, 48H, -OCH_2CH_2O), 3.67 (d, 8H, $^3J_{H\text{-}C}$ = 5.0 Hz, -OCH(CH_2)$_2$), 3.99 (t, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, α-CH_2), 4.32 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH_2CH_3), 4.56 (quint, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH_2)$_2$), 6.23 (t, 1H, $^3J_{H\text{-}H}$ = 5.6 Hz, -N*H*), 7.15 (d, 1H, $^3J_{H\text{-}H}$ = 7.5 Hz, Ar-*H*: C6-Dansyl), 7.38 (s, 2H, Ar-*H*: Gallate), 7.49 (dd, 1H, $^3J_{H\text{-}H}$ = 7.5 Hz, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H*: C7-Dansyl), 7.54 (dd, 1H, $^3J_{H\text{-}H}$ = 7.3 Hz, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H*: C3-Dansyl), 8.22 (d, 1H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-*H*: C4-Dansyl), 8.32 (d, 1H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H*: C8-Dansyl), 8.52 (d, 1H, $^3J_{H\text{-}H}$ = 8.5 Hz Ar-*H*: C2-Dansyl).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.49, 30.49, 41.19, 45.50, 58.87, 61.26, 70.27, 70.38, 70.45, 70.50, 70.56, 70.92, 71.08, 71.93, 77.79, 110.61, 115.07, 119.30, 123.23, 125.60, 127.96, 129.01, 129.75, 129.95, 130.00, 136.04, 143.49, 151.83, 151.94, 165.78.

MS (pos. FAB): m/z (%) = 1224.0 (13), 1223.0 (46), 1221.7 (100), 1220.7 (53), 1219.8 (10) $[MH]^{+\bullet}$; 1175.4 (4) $[MH\text{-}OEt]^{+\bullet}$; 988.2 (1) $[MH\text{-}C_{12}H_{12}NO_2S]^{+\bullet}$; 294.3 (7), 293.3 (13), 292.3 (62), 291.3 (10), 290.4 (5) $[C_{15}H_{19}N_2O_2S+H]^{+\bullet}$.

EA	$C_{58}H_{96}N_2O_{23}S$	calc.	C	57.03	H	7.92	N	2.29,
	(1220.61)	found		56.78		7.63		2.26.

4-[3-(5-Dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoic acid ***66***



0.740 g (0.6 mmol) **65** was dissolved in 20 ml ethanol and 2.5 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The green oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.700 g (96.8%) of a green oil.

R_f = 0.21 (Silica gel; methylene chloride/ methanol 15:1).

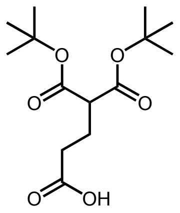
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.79 (m, 2H, β-CH_2), 2.86 (s, 6H, -N(CH_3)$_2$), 3.22 (m, 2H, γ-CH_2), 3.33 (s, 12H, -OCH_3), 3.49-3.59 (2m, 48H, -OCH_2CH_2O), 3.68 (d, 8H, $^3J_{H\text{-}C}$ = 5.0 Hz, -OCH(CH_2)$_2$), 4.01 (t, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, α-CH_2), 4.57 (quint, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH$_2$)$_2$), 6.28 (t, 1H, $^3J_{H\text{-}H}$ = 6.0 Hz, -NH), 7.16 (d, 1H, $^3J_{H\text{-}H}$ = 7.6 Hz, Ar-H: C6-Dansyl), 7.45 (s, 2H, Ar-H: Gallate), 7.49 (m, 1H, Ar-H: C7-Dansyl), 7.54 (m, 1H, Ar-H: C3-Dansyl), 8.22 (d, 1H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-H: C4-Dansyl), 8.31 (d, 1H, $^3J_{H\text{-}H}$ = 8.6 Hz, Ar-H: C8-Dansyl), 8.52 (d, 1H, $^3J_{H\text{-}H}$ = 8.5 Hz Ar-H: C2-Dansyl).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 30.20, 40.93, 45.24, 58.59, 70.28, 70.41, 70.42, 70.50, 70.55, 70.95, 71.92, 71.93, 77.94, 111.17, 115.08, 119.28, 123.23, 125.18, 127.96, 129.01, 129.74, 129.94, 130.01, 135.99, 143.57, 151.86, 151.92, 168.10.

MS (pos. FAB): m/z (%) = 1196.1 (7), 1194.7 (9), 1193.5 (10) $[M+H]^{+\bullet}$.

EA	$C_{56}H_{92}N_2O_{23}S$	calc.	C	56.36	H	7.77	N	2.35,
	(1192.58)	found		56.06		7.20		2.23.

*4,4-di(tert-Butoxycarbonyl)butanoic acid **70a***



4.00 g (18.5 mmol) di-*tert*-butyl malonate **67a**, 3.00 g (18.5 mmol) benzyl acrylate **68a**, 2.56 g (18.5 mmol) dry K_2CO_3, and 0.01 g Bu_4NI were suspended in 10 mL dry benzene under N_2. The mixture was refluxed for 1 day. After filtration the organic phase was washed with water and brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated. The crude product **69a** was filtered through silica gel with hexane/ethyl acetate 5:1 yielding a mixture of 6.60 g of mono- and bisalkylated malonate.

The mixture was dissolved in 20 mL methanol. 0.7 g Pd/ C were added. The mixture was stirred for 1h in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. Further purification by column chromatography (silica gel; methylene chloride/methanol 20:1) gave ***70a***.

Yield: 3.47 g (65%) of a colorless solid.

R_f = 0.24 (Silica gel; methylene chloride/methanol 20:1).

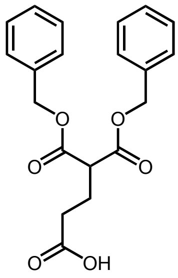
^{1}H NMR ($CDCl_3$, 270 MHz): δ [ppm] = 1.51 (s, 18H, -C(CH_3)$_3$, 2.07 (m, 2H, β-CH_2), 2.39 (t, 2H, $^3J_{H\text{-}H}$ = 7.3 Hz, α-CH_2), 3.30 (t, 1H, $^3J_{H\text{-}H}$ = 7.6 Hz, -CH).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ [ppm] = 24.94, 28.17, 32.09, 54.05, 82.82, 170.04, 176.22.

MS (pos. FAB): m/z (%) = 288.9 (13.16) $[M]^+$; 57.0 (69.67) $[C_4H_9]^+$.

EA	$C_{14}H_{24}O_6$	calc.	C	58.32	H	8.39,
	(288.16)	found		58.18		8.32.

4,4-di(Benzyloxycarbonyl)butanoic acid ***70b***



14.20 g (49.9 mmol) dibenzyl malonate **67b**, 6.39 g (49.9 mmol) *tert*-butyl acrylate **68b**, 6.91 g (49.9 mmol) dry K_2CO_3, and 0.03 g Bu_4NI were suspended in 30 mL dry benzene under N_2. The mixture was refluxed for 1 day. After filtration the organic phase was washed with water and brine. The organic phase was dried over $MgSO_4$, filtered and the solvent evaporated. The crude product was filtered through silica gel with hexane/ethyl acetate 5:1 yielding a mixture of 19.20 g of mono- and bisalkylated malonate.

The mixture was dissolved in 100 mL methylene chloride and 10 mL TFA were added. The mixture was stirred at RT and was monitored with TLC.

After complete deprotection the solvent removed under reduced pressure. Further purification by column chromatography (silica gel; methylene chloride/methanol 20:1) gave **70a**.

Yield: 11.91 g (67%) of a colorless solid.

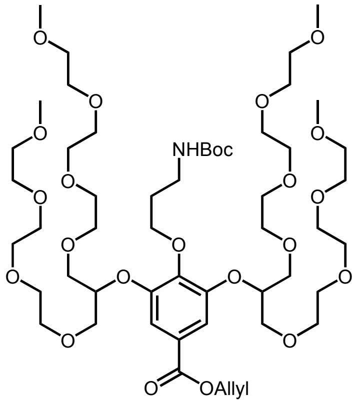
R_f = 0.21 (Silica gel; methylene chloride/methanol 20:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.24 (m, 2H, β-C*H*$_2$), 2.44 (t, 2H, $^3J_{H\text{-}H}$ = 7.4 Hz, α-C*H*$_2$), 3.58 (t, 1H, $^3J_{H\text{-}H}$ = 7.4 Hz, -C*H*), 5.14 (s, 4H, -C*H*$_2$Ar), 7.30 (m, 10H, Ar-*H*), 11.04 (br s, 1H, -COO*H*).

^{13}C NMR ($CDCl_3$, 62.9 MHz): δ [ppm] = 23.38, 30.98, 50.63, 67.28, 128.16, 128.37, 128.55, 135.18, 168.52, 178.24.

MS (EI): m/z (%) = 357.9 (0.03), 356.9 (0.13) $[M+H]^+$; 266.9(0.17), 265.9 (1.11), 264.9 (8.34) $[M-C_7H_7]^+$; 108.0 (15.90), 107.1 (100.00) $[C_7H_7O]^+$.

Allyl-4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxy ethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***71***



2.50 g (2.35 mmol) **60a**, 0.326 g (2.35 mmol) K_2CO_3 and 0.020 g tetrabutyl-potassium-iodide were suspended in 20 ml dry DMF and stirred for one hour at room temperature. 0.855 g (7 mmol) 3-bromo-propene was added. The mixture was stirred for 12 hours at room temperature. After filtration, the solvent was removed under reduced pressure. Further purification by column chromatography (silica gel; methylene chloride/ methanol 20:1). The yellow oil was dissolved in benzene, filtered and lyophilized.

Yield: 2.55 g (98.5%) of a yellow oil.

R_f = 0.24 (Silica gel; methylene chloride/ methanol 25:1).

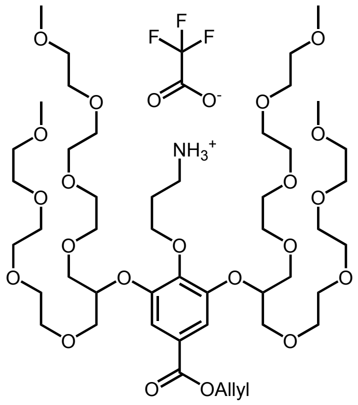
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.43 (s, 9H, -C(CH_3)$_3$), 1.88 (m, 2H, β-CH_2), 3.36 (s, 12H, -OCH_3), 3.36 (m, 2H, γ-CH_2), 3.51-3.69 (2m, 48H, -OCH_2CH_2O), 3.70-3.80 (m, 8H, -OCH(CH_2)$_2$), 4.07 (t, 2H, $^3J_{H-H}$ = 5.6 Hz, α-CH_2), 4.61 (quint, 2H, $^3J_{H-H}$ = 4.9 Hz, -OCH(CH$_2$)$_2$), 4.79 (ddd, 2H, $^3J_{H-H}$ = 5.7 Hz, $^4J_{H-H}$ = 1.5 Hz, $^4J_{H-H}$ = 1.5 Hz, -CO$_2$CH_2CHCH$_2$), 5.29 (ddt, 1H, $^2J_{H-H}$ = 1.5 Hz, Z-$^3J_{H-H}$ = 10.1 Hz, $^4J_{H-H}$ = 1.5 Hz, -CO$_2$CH$_2$CHC$H(Z)$H), 5.39 (ddt, 1H, $^2J_{H-H}$ = 1.5 Hz, E-$^3J_{H-H}$ = 16.9 Hz, $^4J_{H-H}$ = 1.5 Hz, -CO$_2$CH$_2$CHC$H(E)$H), 5.70 (t, 1H, $^3J_{H-H}$ = 5.8 Hz, -NH), 6.03 (ddt, 1H, Z-$^3J_{H-H}$ = 10.1 Hz, E-$^3J_{H-H}$ = 16.9 Hz, $^3J_{H-H}$ = 5.7 Hz, -CO$_2$CH$_2$CHC$H(E)$H), 7.42 (s, 2H, Ar-H: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 28.3, 29.6, 37.6, 58.7, 65.3, 70.0, 70.2, 70.2, 70.3, 70.3, 70.7, 70.9, 71.6, 77.4, 78.3, 110.5, 117.9, 124.7, 132.0, 143.6, 151.6, 155.8, 165.2.

MS (pos. FAB, 4kV): m/z (%) = 1123.3 (4), 1122.3 (5) $[M+Na]^{+\bullet}$; 1099.9 (3) $[M+H]^{+\bullet}$;1002.8 (5), 1001.8 (18), 1000.8 (53), 999.8 (100), 998.8 (18), 997.9 (31) $[M-C_5H_{10}O_2]^{+\bullet}$.

EA	$C_{52}H_{93}NO_{23}$	calc.	C	56.76	H	8.52	N	1.27,
	(1100.29)	found		56.68		8.31		1.16.

Allyl-4-(3-trifluoro-acetato-amonium-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)-benzoate ***72***



0.594 g (0.54 mmol) **71** was dissolved in 5 ml methylene chloride and 0.85 ml trifluoro-acetic acid were added at room temperature. The mixture was stirred for 12 hours. The solvent was removed under reduced pressure.

Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The slight yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.598 g (98%) of a yellowish oil.

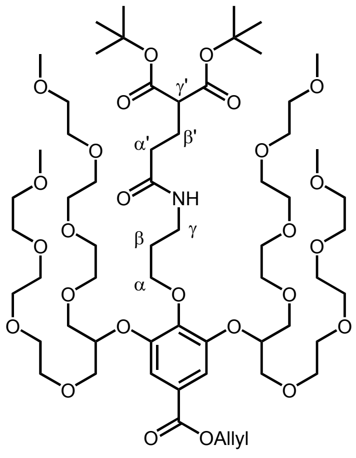
R_f = 0.15 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 2.06 (m, 2H, β-CH_2), 3.27 (hidden m, 2H, γ-CH_2), 3.30 (s, 12H, -OCH_3), 3.46-3.48 & 3.53-3.65 (2m, 48H, -OCH_2CH_2O), 3.75 (m, 8H, -OCH(CH_2)$_2$), 4.22 (t, 2H, $^{3}J_{H-H}$ = 5.3 Hz, α-CH_2), 4.65 (quint, 2H, $^{3}J_{H-H}$ = 4.6 Hz, -OCH(CH$_2$)$_2$), 4.76 (ddd, 2H, $^{3}J_{H-H}$ = 5.5 Hz, $^{4}J_{H-H}$ = 1.5 Hz, $^{4}J_{H-H}$ = 1.5 Hz, -CO$_2$CH_2CHCH$_2$), 5.25 (ddt, 1H, $^{2}J_{H-H}$ = 1.5 Hz, Z-$^{3}J_{H-H}$ = 10.4 Hz, $^{4}J_{H-H}$ = 1.5 Hz, -CO$_2$CH$_2$CHC*H(Z)*H), 5.36 (ddt, 1H, $^{2}J_{H-H}$ = 1.5 Hz, E-$^{3}J_{H-H}$ = 17.2 Hz, $^{4}J_{H-H}$ = 1.5 Hz, -CO$_2$CH$_2$CHC*H(E)*H), 6.01 (ddt, 1H, Z-$^{3}J_{H-H}$ = 10.4 Hz, E-$^{3}J_{H-H}$ = 17.2 Hz, $^{3}J_{H-H}$ = 5.5 Hz, -CO$_2$CH$_2$CHC*H(E)*H), 7.44 (s, 2H, Ar-*H*: Gallate), 7.53 (br s, 3H, -NH_3).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 26.92, 39.97, 58.46, 65.61, 69.98, 70.17, 70.27, 70.29, 70.42, 70.85, 71.79, 73.20, 77.34, 109.82, 117.86, 125.95, 132.40, 142.14, 151.39, 165.14.

MS (pos. FAB): m/z (%) = 1002.7 (23), 1001.5 (56), 1000.5 (100) [M-TFA^{-}]$^{+\bullet}$; 635.3 (2), 634.3 (7), 633.3 (8) [M-TFA^{-}C$_{17}$H$_{35}$O$_{8}$]$^{+\bullet}$.

Allyl-4-{3-[di-tert-butyl 2-(2-carbamoylethyl)malonyl]-propoxy}-3,5-bis(1,3-bis {2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***73***



0.551 g (1.73 mmol) **70a** were dissolved in 3 ml dry DMF. 0.6 ml dry triethylamine were added and the mixture was cooled to -20°C. A solution of 0.640 g (1.99 mmol) TBTU in 5 ml dry DMF was added. The mixture was stirred for two hours at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.968 g (0.87 mmol) **72** and 0.6 ml dry triethylamine in 2 ml dry DMF was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.938 g (85%) of a yellowish oil.

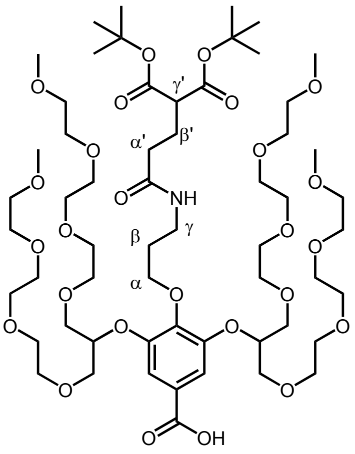
R_f = 0.27 (Silica gel; methylene chloride/ methanol 20:1).

^{1}H NMR (CDCl$_3$, 500 MHz): δ [ppm] = 1.26 (s, 18H, -OC(CH_3)$_3$), 1.74 (m, 2H, β-CH_2), 1.93 (m, 2H, β'-CH_2), 2.05 (m, 2H, α' -CH_2), 3.03 (t, 1H, $^3J_{H\text{-}H}$ = 7.4 Hz, γ'-CH), 3.19 (s, 12H, -OCH_3), 3.32 (m, 2H, γ-CH_2), 3.34-3.49 (2m, 48H, -OCH_2CH_2O), 3.57 (m, 8H, -OCH(CH_2)$_2$), 3.92 (t, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, α-CH_2), 4.43 (quint, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH$_2$)$_2$), 4.62 (br d, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, -CO$_2$CH_2CHCH$_2$), 5.11 (br d, 1H, Z-$^3J_{H\text{-}H}$ = 10.4 Hz, -CO$_2$CH$_2$CHC$H(Z)$H), 5.22 (br d, 1H, E-$^3J_{H\text{-}H}$ = 17.1 Hz, -CO$_2$CH$_2$CHC$H(E)$H), 5.85 (m, 1H, -CO$_2$CH$_2$CHC$H(E)$H), 6.65 (t, 1H, $^3J_{H\text{-}H}$ = 5.7 Hz, -NH), 7.26 (s, 2H, Ar-H: Gallate).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 24.05, 27.46, 29.16, 33.08, 36.72, 52.71, 58.52, 65.13, 69.86, 70.05, 70.09, 70.15, 70.16, 70.52, 71.22, 71.48, 77.37, 80.79, 110.61, 117.79, 124.63, 131.88, 143.53, 151.53, 165.06, 168.02, 171.37.

MS (pos. FAB; CsI Zusatz): m/z (%) = 1403.8 (0.1), 1402.8 (0.2), 1402.4 (0.3) 1401.9 (0.1) [M+Cs]$^+$; 1292.9 (0.5), 1292.7 (0.8), 1291.4 (0.1) [M+Cs]$^+$; 1271.5 (0.5), 1270.6 (0.7), 1270.2 (0.3) [M+H]$^+$; 57.0 (100) [C$_4$H$_9$]$^+$.

4-{3-[Di-tert-butyl-2-(2-carbamoylethyl)malonyl]-propoxy}-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoic acid ***74***



840 mg (0.66 mmol) **73** was dissolved in 10 ml methylene chloride and 40 mg (4 mol%) Pd(PPh_3)$_4$ was added. Then a solution of 130 mg (0.72 mmol) p-toluenesulfinic acid hydrate in 1 ml methanol was added. The reaction was monitored with TLC and stopped after 35 min. The solvent was removed under reduced pressure. Further purification by column chromatography (silica gel; methylene chloride/ methanol 10:1). The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.764 g (94%) of a colorless oil.

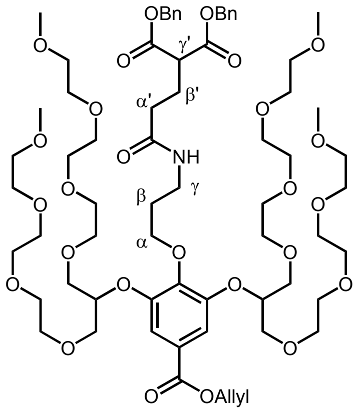
R_f = 0.24 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.40 (s, 18H, -OC(C*H*$_3$)$_3$), 1.87 (m, 2H, β-C*H*$_2$), 2.07 (m, 2H, β'-C*H*$_2$), 2.19 (m, 2H, α' -C*H*$_2$), 3.17 (t, 1H, $^3J_{H-H}$ = 7.4 Hz, γ'-C*H*), 3.36 (s, 12H, -OC*H*$_3$), 3.46 (m, 2H, γ-C*H*$_2$), 3.50-3.65 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.70 (m, 8H, -OCH(C*H*$_2$)$_2$), 4.05 (t, 2H, $^3J_{H-H}$ = 5.6 Hz, α-C*H*$_2$), 4.56 (quint, 2H, $^3J_{H-H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 6.74 (t, 1H, $^3J_{H-H}$ = 5.8 Hz, -N*H*), 7.48 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 24.42, 27.80, 29.50, 33.48, 37.10, 53.08, 58.81, 70.28, 70.38, 70.41, 70.49, 70.50, 70.90, 71.56, 71.82, 77.77, 81.22, 111.37, 137.08, 143.62, 151.83, 168.40 (2), 171.84.

MS (pos. FAB): m/z (%) = 1269.4 (20.5), 1268.9 (17.1), 1268.2 (44.9), 1267.6 (23.5) $[M+K]^+$; 1254.0 (17.6), 1253.5 (61.1), 1252.7 (84.5), 1251.9 (100) $[M+Na]^+$; 1231.8 (7.4), 1231.5 (13.6), 1231.2 (22.6), 1230.8 (62.0), 1229.9 (31.5) $[M+H]^+$.

Allyl-4-{3-[dibenzyl 2-(2-carbamoylethyl)malonyl]-propoxy}-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoate ***75***



0.619 g (1.73 mmol) **70b** were dissolved in 3 ml dry DMF. 0.6 ml dry triethylamine were added and the mixture was cooled to -20°C. A solution of 0.640 g (1.99 mmol) TBTU in 5 ml dry DMF was added. The mixture was stirred for two hours at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.968 g (0.87 mmol) **72** and 0.6 ml dry triethylamine in 2 ml dry DMF was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 1.00 g (86%) of a yellowish oil.

R_f= 0.23 (Silica gel; methylene chloride/ methanol 20:1).

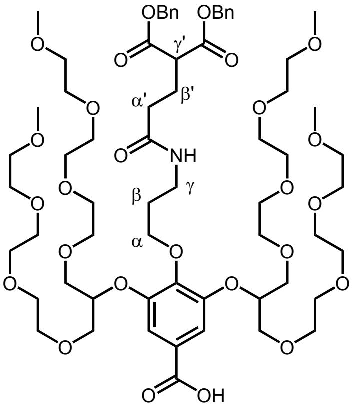
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.88 (m, 2H, β-CH_2), 2.21 (m, 4H, α' & β'-CH_2), 3.31 (s, 12H, -OCH_3), 3.45 (m, 2H, γ-CH_2), 3.45-3.66 (2m, 48H, -OCH_2CH_2O), 3.61 (m, 1H, γ'-C*H*), 3.74 (m, 8H, -OCH(CH_2)$_2$), 4.09 (t, 2H, $^3J_{H-H}$ = 5.6 Hz, α-CH_2), 4.61 (quint, 2H, $^3J_{H-H}$ = 4.9 Hz, -OC*H*(CH_2)$_2$), 4.78 (ddd, 2H, $^3J_{H-H}$ = 5.6 Hz, $^4J_{H-H}$ = 1.3 Hz, $^4J_{H-H}$ = 1.3 Hz, -CO_2CH_2CHCH_2), 5.11 (m, 4H, -OCH_2Ar), 5.27 (dpq, 1H, $^{2/4}J_{H-H}$ = 1.3 Hz, Z-$^3J_{H-H}$ = 10.5 Hz, -CO_2CH_2CHC*H(Z)*H), 5.39 (dpq, 1H, $^{2/4}J_{H-H}$ = 1.6 Hz, E-$^3J_{H-H}$ = 17.2 Hz, -CO_2CH_2CHC*H(E)*H), 6.04 (m, 1H, -CO_2CH_2CHC*H(E)*H), 6.67 (t, 1H, $^3J_{H-H}$ = 5.7 Hz, -N*H*), 7.25-7.35 (m, 10H, Ar-Bn), 7.44 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 24.50, 29.68, 33.01, 37.03, 51.06, 58.55, 65.48, 66.92, 70.24, 70.34, 70.40, 70.46, 70.53, 70.93, 71.67, 71.87, 77.72, 110.72, 117.74, 125.15, 127.98, 128.20, 128.47, 132.54, 135.63, 143.84, 151.98, 165.38, 168.80, 171.08.

MS (pos. FAB): m/z (%) = 1340.8 (4), 1339.8 (9), 1338.8 (12). 1337.8 (2), 1336.8 (2) $[M+H]^{+\bullet}$; 400.3 (1), 399.3(5), 398.3 (25), 397.3 (100), 396.3 (1), 395.3 (1) $[M-C_{20}H_{19}O_5+H]^{+\bullet}$.

EA	$C_{67}H_{103}NO_{26}$	calc.	C	60.12	H	7.76	N	1.05,
	(1337.68)	found		59.96		7.39		0.97.

*4-{3-[Dibenzyl 2-(2-carbamoylethyl)malonyl]-propoxy}-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoic acid **76***



434 mg (0.32 mmol) **75** was dissolved in 20 ml methylene chloride and 19 mg (5 mol%) $Pd(PPh_3)_4$ was added. Then a solution of 64 mg (0.35 mmol) p-toluenesulfinic acid hydrate in 0.5 ml methanol was added. The reaction was monitored with TLC and stopped after 30 min. The solvent was removed under reduced pressure. Further purification by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.404 g (96%) of a colorless oil.

Alternatively the allyl ester was cleaved as follows:

750 mg (0.56 mmol) **75** was dissolved in 20 ml methylene chloride and 11.3 mg (0.01 mmol) $(PPh_3)_2Pd^{II}Cl_2$ was added. Then, 360 mg (1.24 mmol) tributyltin was added dropwise.

The solvent was removed under reduced pressure. Remainings were again dissolved in THF, then extracted twice with saturated KF-solution (aq.) and 5-times with 1M KOH (aq.). The water phase was acidified to pH 5 and extracted with methylene chloride. Further purification by column chromatography [silica gel; methylene chloride/ methanol 10:1]. The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.454 g (68%) of a colorless oil.

R_f = 0.19 (Silica gel; methylene chloride/ methanol 10:1).

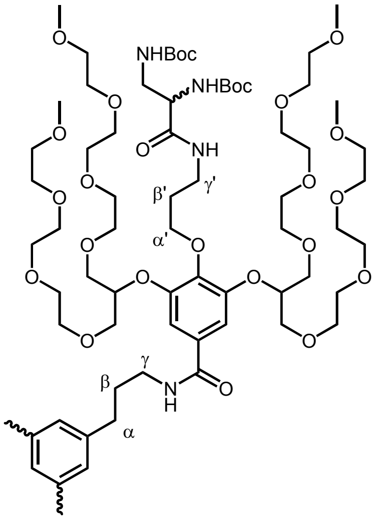
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.86 (m, 2H, β-CH_2), 2.21 (m, 4H, α' & β'-CH_2), 3.36 (s, 12H, -OCH_3), 3.45 (m, 2H, γ-CH_2), 3.47-3.64 (2m, 48H, -OCH_2CH_2O), 3.57 (m, 1H, γ'-C*H*), 3.69 (m, 8H, -OCH(CH_2)$_2$), 4.04 (t, 2H, $^3J_{H\text{-}H}$ = 5.7 Hz, α-CH_2), 4.56 (quint, 2H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OC*H*(CH$_2$)$_2$), 5.08 (m, 4H, -OCH_2Ar), 6.77 (t, 1H, $^3J_{H\text{-}H}$ = 5.8 Hz, -N*H*), 7.21-7.29 (m, 10H, Ar-Bn), 7.49 (s, 2H, Ar-*H*: Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 24.28, 29.29, 30.92, 36.79, 50.87, 58.55, 66.95, 70.03, 70.05, 70.14, 70.19, 70.22, 70.61, 71.36, 71.56, 77.38, 110.88, 127.83, 128.09, 128.29, 135.03, 143.20, 151.52, 168.70 (2), 171.94.

MS (pos. FAB): m/z (%) = 1323.8 (10), 1322.7 (30), 1321.7 (65), 1320.6 (100) $[M+Na]^{+\bullet}$; 1302,6 (1), 1301.6 (5), 1300.6 (17), 1299.6 (43), 1298.7 (64), 1297.8 (6), 1296.8 (8) $[M+H]^{+\bullet}$.

8.7 Compounds of Chapter 4.4.1

1,3,5-Tris-{[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-[3,5-bis (1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene **77**



0.254 g (0.200 mmol) **66** were dissolved in 5 ml dry methylene chloride. The solution was cooled to -20°C and 0.038 g (0.220 mmol) HOBt and 0.056 g (0.240 mmol) EDC were added. The mixture was stirred for 1 hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.021 g (0.058 mmol) **3b** and 0.5 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.182 g (80%) of a yellowish oil.

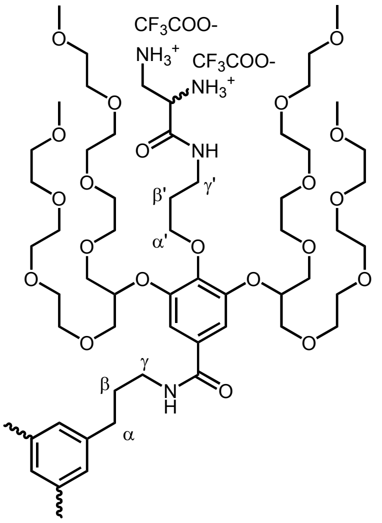
R_f = 0.15 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.22 & 1.29 (2s, 54H, -C(C*H*$_3$)$_3$), 1.79 (m, 12H, β/β' -C*H*$_2$), 2.51 (t, 6H, $^3J_{H\text{-}H}$ = 7.4 Hz, α-C*H*$_2$), 3.22 (s, 36H, -OC*H*$_3$), 3.32 (m, 18H, α'-, γ- & γ'-C*H*$_2$), 3.37-3.57 (2m, 144H, -OC*H*$_2$C*H*$_2$O), 3.62 (m, 24H, -OCH(C*H*$_2$)$_2$), 3.91 (m, 3H, -C*H*$_2$NHBoc), 3.98 (m, 3H, -C*H*$_2$NHBoc), 4.09 (m, 3H, -C*H*NHBoc), 4.48 (m, 6H, -OC*H*(CH$_2$)$_2$), 5.29 (m, 3H, -CH$_2$N*H*Boc), 5.78 (d, 3H, $^3J_{H\text{-}H}$ = 7.7 Hz, -CHN*H*Boc), 6.78 (s, 3H, Ar-*H*: Core), 7.04 (m, 3H, -CH$_2$N*H*COAr), 7.15 (s, 6H, Ar-*H*: Gallate), 7.27 (m, 3H, -CH$_2$N*H*').

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 27.88, 27.99, 29.17, 30.92, 32.96, 37.09, 39.57, 42.49, 54.45, 58.52, 69.95, 70.04, 70.05, 70.15, 70.35, 70.38, 71.41, 71.50, 77.39, 78.82, 79.08, 108.74, 125.73, 129.61, 141.42, 142.04, 151.55, 155.37, 156.10, 166.37, 169.99.

MS (MALDI-TOF, dithranol): m/z = 3955.12 $[M+Na]^+$ calc. monoisotopic peak ($^{12}C_{186}{}^{1}H_{330}{}^{14}N_{12}{}^{16}O_{75}{}^{23}Na$) 3955.23.

1,3,5-Tris-{[3-(2,3-diamino-propionylamido)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene hexakis-trifluoro-acetato ***78***



0.180 g (0.045 mmol) 77 were dissolved in 5 ml dry methylene chloride and 1 ml TFA was added at room temperature. The deprotection was monitored with ^{1}H-NMR.

The solvent was evaporated and dried in high vacuum. No further purification.

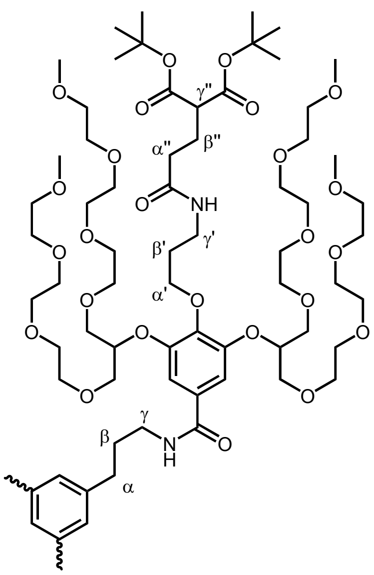
Yield: 0.176 g (79%) of a yellowish oil.

^{1}H NMR (CD_3OD, 500 MHz): δ [ppm] = 1.78 (m, 6H, β-C*H*$_2$), 1.84 (m, 6H, β'-C*H*$_2$), 2.50 (t, 6H, $^3J_{H-H}$ = 7.6 Hz, α-C*H*$_2$), 3.17 (s, 36H, -OC*H*$_3$), 3.24 (t, 6H, $^3J_{H-H}$ = 7.1 Hz, γ-C*H*$_2$), 3.31-3.54 (2m, 144H, -OC*H*$_2$C*H*$_2$O), 3.43 & 3.49 (2m, 12 H, α' & γ'), 3.63 (m, 24H, -OCH(C*H*$_2$)$_2$), 3.98 & 4.04 & 4.17 (3m, 9H, -C*H*NH$_3$ & -C*H*$_2$NH$_3$), 4.58 (quint, 6H, $^3J_{H-H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 6.78 (s, 3H, Ar-*H*: Core), 7.16 (s, 6H, Ar-*H*: Gallate).

^{13}C NMR ($CD_3OD/CDCl_3$, 125 MHz): δ [ppm] = 28.25, 30.14, 32.16, 37.29, 38.80, 38.94, 50.00, 52.62, 57.04, 69.01, 69.04, 69.11, 69.20, 69.55, 69.60, 71.31, 76.31, 107.56, 125.08, 128.94, 140.97, 150.89, 164.24, 166.64.

MS (MALDI-TOF, CCA): m/z = 3370.46 $[M+K]^+$ calc. monoisotopic peak ($^{12}C_{156}{}^{1}H_{282}{}^{14}N_{12}{}^{16}O_{63}{}^{39}K$) 3370.89; 3354.47 $[M+Na]^+$ calc. monoisotopic peak ($^{12}C_{156}{}^{1}H_{282}{}^{14}N_{12}{}^{16}O_{63}{}^{23}Na$) 3354.91; 3332.51 $[M+H]^+$ calc. monoisotopic peak ($^{12}C_{156}{}^{1}H_{283}{}^{14}N_{12}{}^{16}O_{63}$) 3332.93.

1,3,5-Tris-({3-[di-*tert*-butyl-2-(2-carbamoylethyl)malonyl]propoxy}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl])-benzene ***79***



0.200 g (0.162 mmol) **74** were dissolved in 8 ml dry methylene chloride. The solution was cooled to -20°C and 0.038 g (0.220 mmol) HOBt and 0.056 g (0.240 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and added to a cooled suspension of 0.015 g (0.041 mmol) **3b** and 0.5 ml dry triethylamine in 3.5 ml methylene chloride. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The reaction was quenched by the addition of 10 ml aequous 1M NaHCO$_3$. The phases were separated and the aeqeous phase was extracted with methylene chloride. The combined organic phases were dried. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.153 g (96%) of a yellowish oil.

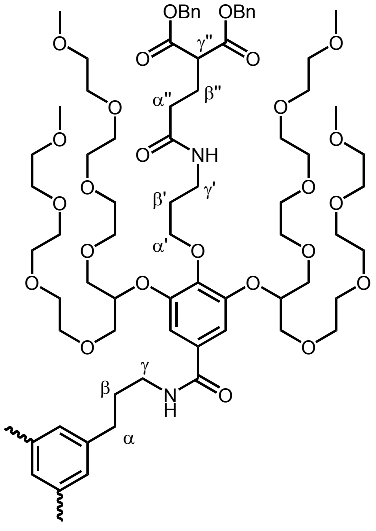
R$_f$ = 0.18 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (CDCl$_3$, 500 MHz): δ [ppm] = 1.33 (s, 54H, -C(C*H*$_3$)$_3$), 1.80 (m, 12H, β/β'-C*H*$_2$), 1.98 (m, 6H, β" -C*H*$_2$), 2.11 (m, 6H, α" -C*H*$_2$), 2.52 (t, 6H, $^3J_{H\text{-}H}$ = 7.6 Hz, α-C*H*$_2$), 3.10 (t, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, γ" -C*H*$_2$), 3.23 (s, 36H, -OC*H*$_3$), 3.32 (m, 6H, γ'-C*H*$_2$), 3.37 (m, 6H, γ -C*H*$_2$), 3.39-3.56 (2m, 144H, -OC*H*$_2$C*H*$_2$O), 3.62 (m, 24H, -OCH(C*H*$_2$)$_2$), 3.95 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, α' -C*H*$_2$), 4.49 (quint, 6H, $^3J_{H\text{-}H}$ = 4.5 Hz, -OC*H*(CH$_2$)$_2$), 6.69 (t, 6H, $^3J_{H\text{-}H}$ = 5.8 Hz, -N*H*'), 6.77 (s, 3H, Ar-*H*: Core), 7.06 (m, 3H, -N*H*), 7.16 (s, 6H, Ar-*H*: Gallate).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 24.22, 27.63, 29.38, 31.03, 33.09, 33.25, 36.84, 39.71, 52.91, 58.63, 70.12, 70.14, 70.16, 70.17, 70.26, 70.51, 71.28, 71.60, 77.55, 81.02, 108.90, 125.82, 129.69, 141.53, 142.14, 151.61, 166.50, 168.22, 171.60.

MS (MALDI-TOF, dithranol): m/z = 3923.04 [M+K]$^+$ calc. monoisotopic peak ($^{12}C_{189}{}^{1}H_{330}{}^{14}N_6{}^{16}O_{75}{}^{39}K$) 3923.18; 3907.07 [M+Na]$^+$ calc. monoisotopic peak ($^{12}C_{189}{}^{1}H_{330}{}^{14}N_6{}^{16}O_{75}{}^{23}Na$) 3907.21.

1,3,5-Tris-({3-[dibenzyl-2-(2-carbamoylethyl)malonyl]propoxy}-[3,5-bis(1,3-bis {2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl])-benzene ***80***



0.350 g (0.270 mmol) **76** were dissolved in 15 ml dry methylene chloride. The solution was cooled to -20°C and 0.050 g (0.290 mmol) HOBt and 0.067 g (0.287 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and added to a cooled suspension of 0.027 g (0.074 mmol) **3b** and 0.7 ml dry triethylamine and 0.5 ml dry triethylamine in 3.5 ml methylene chloride. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The reaction was quenched by the addition of 10 ml aequous 1M NaHCO$_3$. The phases were separated and the aeqeous phase was extracted with methylene chloride. The combined organic phases were dreid. After evaporation of the solvent, the crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.281 g (93%) of a yellowish oil.

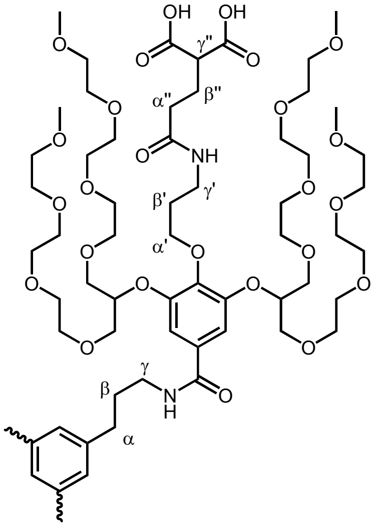
R$_f$ = 0.13 (Silica gel; methylene chloride/ methanol 10:1).

^{1}**H NMR** (CDCl$_3$, 500 MHz): δ [ppm] = 1.87 (m, 6H, β' -CH_2), 1.91 (m, 6H, β-CH_2), 1.98 (m, 6H, β'' -CH_2), 2.20 (m, 15H, α'', β'', γ'' -CH_2), 2.64 (t, 6H, $^3J_{H\text{-}H}$ = 7.8 Hz, α-CH_2), 3.30 (s, 36H, -OCH_3), 3.40 (m, 6H, γ -CH_2), 3.44 (m, 6H, γ'-CH_2), 3.45-3.65 (2m, 144H, -OCH_2CH_2O), 3.72 (m, 24H, -OCH(CH_2)$_2$), 4.04 (t, 6H, $^3J_{H\text{-}H}$ = 5.7 Hz, α'-CH_2), 4.61 (quint, 6H, $^3J_{H\text{-}H}$ = 4.7 Hz, -OCH(CH$_2$)$_2$), 5.12 (m, 12H, -OCH_2Ar), 6.68 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, -NH'), 6.91 (s, 3H, Ar-H: Core), 7.09 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, -NH), 7.24-7.39 (m, 36H, Ar-H: Gallate & Benzyl).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 24.55, 29.75, 31.39, 33.07, 33.32, 37.09, 39.87, 51.14, 58.59, 66.99, 70.36, 70.38, 70.42, 70.48, 70.86, 70.88, 71.62, 71.89, 77.78, 108.83, 126.14, 128.04, 128.25, 128.52, 130.23, 135.66, 141.98, 142.30, 151.97, 166.45, 168.87, 171.17.

MS (MALDI-TOF, dithranol): m/z = 4126.95 $[M+K]^+$ calc. monoisotopic peak $({}^{12}C_{207}{}^{1}H_{318}{}^{14}N_{06}{}^{16}O_{75}{}^{39}Na)$ 4127.09; 4111.01 $[M+Na]^+$ calc. monoisotopic peak $({}^{12}C_{207}{}^{1}H_{318}{}^{14}N_{06}{}^{16}O_{75}{}^{23}Na)$ 4111.11.

1,3,5-Tris-({3-[2-(2-carbamoylethyl)malonato]propoxy}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl])-benzene ***81***



Method A: 0.150 g (0.038 mmol) **79** were dissolved in 5 ml methylene chloride. 3 ml TFA were added. The reaction was monitored with ^{1}H-NMR. After complete deprotection, the solvent was removed under reduced pressure at room temperature. The remaining oil was coevaporated 5 times with 5 ml of methylene chloride to remove the remaining TFA. No further purification.

Yield: 0.132 g (96%) of a colorless oil.

Method B: 0.320 g (0.078 mmol) **80** were dissolved in 10 ml methanol and 0.030 g Pd/ C were added. The reaction was stirred for 1 day under a H_2-atmosphere at room temperature. The deprotection was monitored by ^{1}H-NMR. After filtration, the solvent was evaporated at room temperature. No further purification.

Yield: 0.253 g (91%) of a colorless oil.

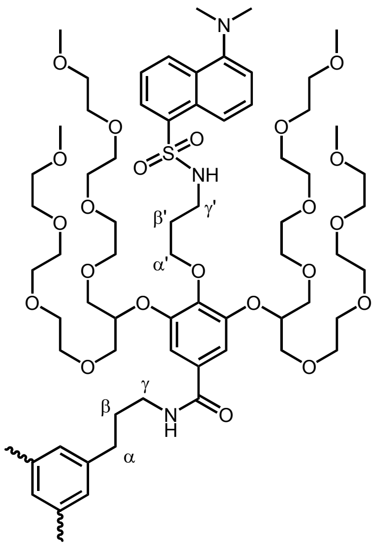
Both compounds showed equal spectroscopic and spectrometric parameters.

^{1}H NMR (CD_3OD, 500 MHz): δ [ppm] = 1.88 (m, 12H, β/β' -CH_2), 2.10 (t, 6H, $^3J_{H-H}$ = 7.2 Hz, β'' -CH_2), 2.26 (t, 6H, $^3J_{H-H}$ = 7.4 Hz, α'' -CH_2), 2.61 (t, 6H, $^3J_{H-H}$ = 7.1 Hz, α-CH_2), 3.28 (br s, 39H, -OCH_3 & γ''-C*H*), 3.35 (t, 6H, $^3J_{H-H}$ = 6.9 Hz, γ-CH_2), 3.41 (t, 6H, $^3J_{H-H}$ = 6.6 Hz, γ' -CH_2), 3.41-3.64 (2m, 144H, -OCH_2CH_2O), 3.72 (m, 24H, -OCH(CH_2)$_2$), 4.05 (t, 6H, $^3J_{H-H}$ = 5.7 Hz, α'-CH_2), 4.60 (quint, 6H, $^3J_{H-H}$ = 4.8 Hz -OC*H*(CH_2)$_2$), 6.89 (s, 3H, Ar-*H*: Core), 7.23 (s, 6H, Ar-*H*: Gallate).

^{13}C NMR (CD_3OD, 125 MHz): δ [ppm] = 25.77, 30.71, 32.19, 34.19, 34.35, 38.04, 40.79, 59.11, 71.16, 71.29, 71.35, 71.79, 72.39, 72.76, 78.86, 109.85, 127.13, 130.61, 143.00, 143.52, 153.10, 168.87, 172.17, 174.25.

MS (MALDI-TOF, dithranol): m/z = 3572.71 $[M+Na]^+$ calc. monoisotopic peak ($C_{165}H_{282}N_6O_{75}{}^{23}Na$) 3572.99.

*1,3,5-Tris-{[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene **82***



0.390 g (0.328 mmol) **63** were dissolved in 15 ml dry methylene chloride. The solution was cooled to -20°C and 0.064 g (0.418 mmol) HOBt and 0.090 g (0.470 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then the temperature was increased slowly to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.034 g (0.090 mmol) **3b** and 0.85 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then the temperature was increased very slowly to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The green oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.582 g (92%) of a green oil.

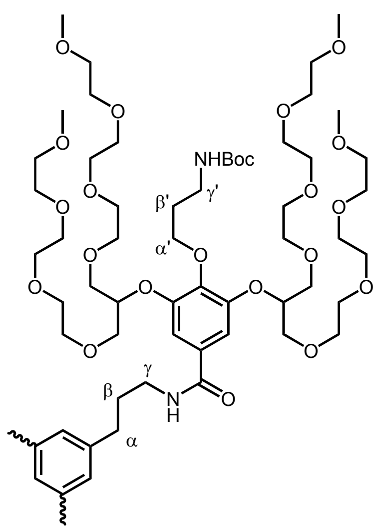
R_f = 0.31 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 1.63 (m, 6H, β'-CH_2), 1.76 (m, 6H, β-CH_2), 2.47 (t, 6H, $^3J_{H-H}$ = 6.8 Hz, α-CH_2), 2.68 (s, 18H, -N(CH_3)$_3$), 3.07 (m, 6H, γ'-CH_2), 3.15 (s, 36H, -OCH_3), 3.26 (m, 6H, γ-CH_2), 3.30-3.45 (2m, 144H, -OCH_2CH_2O), 3.50 (d, 32H, $^3J_{H-H}$ = 4.8 Hz, -OCH(CH_2)$_2$), 4.82 (t, 6H, $^3J_{H-H}$ = 5.3 Hz, α'-CH_2), 4.38 (quint, 6H, $^3J_{H-H}$ = 4.8 Hz, -OCH(CH$_2$)$_2$), 6.22 (t, 3H, $^3J_{H-H}$ = 6.0 Hz, -NH'), 6.72 (s, 3H, Ar-H: Core), 6.96 (d, 3H, $^3J_{H\text{-}H}$ = 7.6 Hz, Ar-*H*: C6-Dansyl), 7.10 (s, 6H, Ar-*H*: Gallate), 7.14 (t, 3H, $^3J_{H\text{-}H}$ = 5.3 Hz, -N*H*), 7.30 (dd, 3H, $^3J_{H\text{-}H}$ = 7.6 Hz, $^3J_{H\text{-}H}$ = 8.6 Hz, Ar-*H*: C7-Dansyl), 7.34 (dd, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, $^3J_{H\text{-}H}$ = 8.4 Hz, Ar-*H*: C3-Dansyl), 8.07 (d, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, Ar-*H*: C4-Dansyl), 8.19 (d, 3H, $^3J_{H\text{-}H}$ = 8.4 Hz, Ar-*H*: C8-Dansyl), 8.33 (d, 3H, $^3J_{H\text{-}H}$ = 8.4 Hz Ar-*H*: C2-Dansyl).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 29.54, 30.66, 32.73, 39.30, 40.30, 44.84, 58.30, 69.83, 69.85, 69.87, 69.95, 70.17, 70.35, 71.30, 77.19, 77.39, 108.54, 114.52, 118.92, 122.62, 125.57, 127.37, 128.37, 129.21, 129.32, 129.37, 129.39, 135.45, 141.24, 141.64, 151.16, 151.27, 166.19.

MS (MALDI-TOF, dithranol): m/z = 3811.70 $[M+K]^+$ ($^{12}C_{183}{}^{1}H_{297}{}^{14}N_{9}{}^{16}O_{66}{}^{32}S_{3}{}^{39}K$) calc. monoisotopic peak 3811.90; 3795.83 $[M+Na]^+$ calc. monoisotopic peak ($^{12}C_{183}{}^{1}H_{297}{}^{14}N_{9}{}^{16}O_{66}{}^{32}S_{3}{}^{23}Na$) 3795.92; 3773.78 $[M+H]^+$ ($^{12}C_{183}{}^{1}H_{298}{}^{14}N_{9}{}^{16}O_{66}{}^{32}S_{3}$) calc. monoisotopic peak 3773.94.

1,3,5-Tris-{[4-(3-tert-butoxycarbonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene ***83***



0.420 g (0.396 mmol) **60a** were dissolved in 10 ml dry methylene chloride. The solution was cooled to -20°C and 0.074 g (0.483 mmol) HOBt and 0.100 g (0.523 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.041 g (0.114 mmol) **3b** and 1 ml dry triethylamine in 2 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography. The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.365 g (95%) of a yellowish oil.

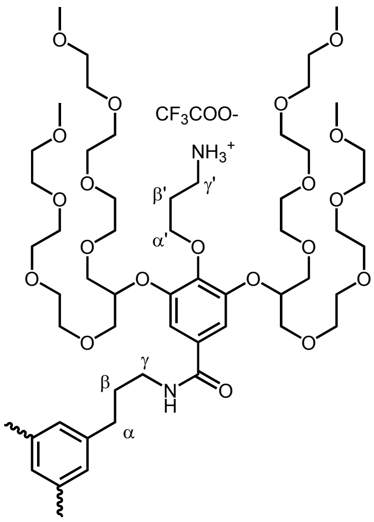
R_f = 0.24 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.40 (s, 27H, -C(CH_3)$_3$), 1.84 (m, 6H, β'-CH_2), 1.89 (m, 6H, β-CH_2), 2.62 (t, 6H, $^3J_{H\text{-}H}$ = 7.6 Hz, α-CH_2), 3.28 (s, 36H, -OCH_3), 3.30 (m, 6H, γ'-CH_2), 3.37 (m, 6H, γ-CH_2), 3.40-3.65 (2m, 144H, -OCH_2CH_2O), 3.71 (m, 32H, -OCH(CH_2)$_2$), 4.01 (t, 6H, $^3J_{H\text{-}H}$ = 5.7 Hz, α'-CH_2), 4.59 (quint, 6H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 5.60 (t, 3H, $^3J_{H\text{-}H}$ = 5.4 Hz, -N*H'*), 6.89 (s, 3H, Ar-*H*: Core), 6.95 (t, 3H, $^3J_{H\text{-}H}$ = 5.6 Hz, -N*H*), 7.21 (s, 6H, Ar-*H*: Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 28.26, 30.05, 31.23, 33.15, 37.88, 39.66, 58.53, 70.32, 70.33, 70.40, 70.83, 71.15, 71.85, 77.73, 78.21, 108.68, 126.11, 130.18, 141.87, 142.23, 151.93, 155.85, 166.42.

MS (MALDI-TOF, dithranol): m/z = 3412.59 $[M+K]^+$ ($^{12}C_{162}{}^1H_{288}{}^{14}N_6{}^{16}O_{66}{}^{39}K$) calc. monoisotopic peak 3412.90; 3396.65 $[M+Na]^+$ calc. monoisotopic peak ($^{12}C_{162}{}^1H_{288}{}^{14}N_6{}^{16}O_{66}{}^{23}Na$) 3396.93.

1,3,5-Tris-{[4-(3-amoniopropoxy)]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy] ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene tris-hydrotrifluoro acetate ***66***



0.360 g (0.1 mmol) D[(NHBoc)]³ were dissolved in 20 ml dry methylene chloride and 5 ml TFA were added at room temperature. The deprotection was monitored with ^{1}H-NMR.

After complete conversion, the solvents were evaporated and dried in high vacuum. No further purification.

Yield: 0.360 g (98%) of a yellowish oil.

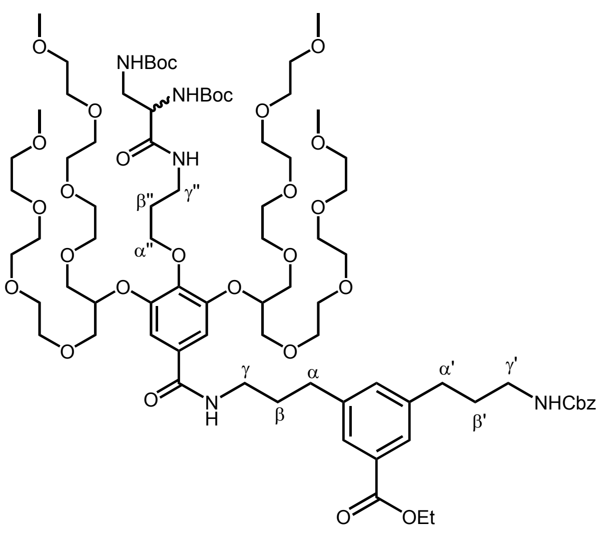
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.89 (m, 6H, β-CH_2), 1.93 (m, 6H, β'-CH_2), 2.48 (t, 6H, $^3J_{H\text{-}H}$ = 7.6 Hz, α-CH_2), 3.11 (m, 6H, γ'-CH_2), 3.22 (s, 36H, -OCH_3), 3.26 (m, 6H, γ-CH_2), 3.30-3.56 (2m, 144H, -OCH_2CH_2O), 3.63 (m, 32H, -OCH(CH_2)$_2$), 4.06 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, α'-CH_2), 4.58 (quint, 6H, $^3J_{H\text{-}H}$ = 4.6 Hz, -OC*H*(CH$_2$)$_2$), 6.74 (s, 3H, Ar-*H*: Core), 7.17 (s, 6H, Ar-*H*: Gallate), 7.30 (br m, -NH_3), 8.04 (t, 3H, $^3J_{H\text{-}H}$ = 5.5 Hz, -N*H*).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 26.09, 30.55, 32.77, 39.52, 39.64, 58.19, 69.37, 39.66, 69.76, 69.78, 69.80, 70.19, 71.23, 72.95, 76.32, 107.14, 125.55, 130.20, 139.78, 141.31, 150.68, 159.26, 156.56, 166.53.

MS (MALDI-TOF, dithranol): m/z = 3096.72 [M+Na]$^+$ (^{12}C$_{147}$^{1}H$_{264}$^{14}N$_6$^{16}O$_{60}$^{23}Na) 3396.77, 3074.73 [M+H]$^+$ (^{12}C$_{147}$^{1}H$_{265}$^{14}N$_6$^{16}O$_{60}$) 3074.79.

8.8 Compounds of Chapter 4.4.2

Ethyl-3-(3-benzyloxycarbonylamino-propyl)-5-(3-{4-[3-(2,3-bis-tert-butoxycarbonyl amino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy] ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoate ***87***



1.12 g (0.89 mmol) **63** were dissolved in 10 ml dry methylene chloride. The solution was cooled to -20°C and 0.154 g (1.00 mmol) HOBt and 0.167 g (1.07 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.552 g (1.07 mmol) **19** and 0.5 ml dry triethylamine in abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 1.181 g (80%) of a yellowish oil.

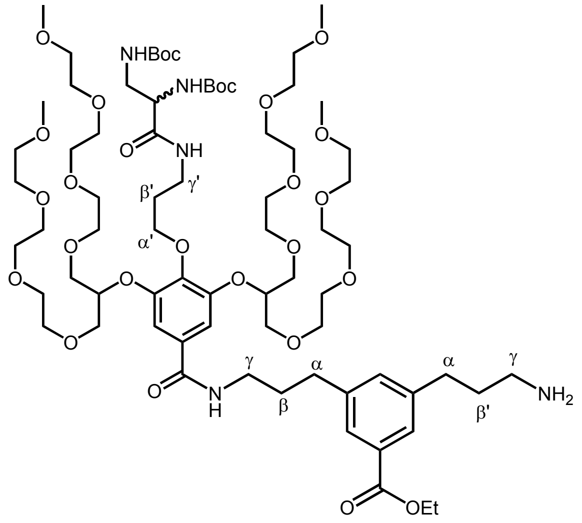
R_f = 0.40 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.32 & 1.40 (2s, 18H, $-C(CH_3)_3$), 1.36 (t, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, $-CH_2CH_3$), 1.83 (m, 4H, β'-CH_2 & β''-CH_2), 1.92 (m, 2H, β-CH_2), 2.66 (t, 2H, $^3J_{H\text{-}H}$ = 7.8 Hz, α'-CH_2), 2.71 (t, 2H, $^3J_{H\text{-}H}$ = 7.5 Hz, α-CH_2), 3.18 (m, 2H, γ'-CH_2), 3.30 (s, 12H, $-OCH_3$), 3.41 (m, 4H, γ-CH_2 & γ''-CH_2), 3.44-3.66 (2m, 48H, $-OCH_2CH_2O$), 3.73 (m, 8H, $-OCH(CH_2)_2$), 4.02 (m, 2H, $-CH_2$NHBoc), 4.12 (m, 3H, -CHNHBoc & α''-CH_2), 4.32 (q, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, $-CH_2CH_3$), 4.62 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, $-OCH(CH_2)_2$), 5.05 (s, 2H, benzyl CH_2), 5.30 (br s, 1H, -NH'), 5.57 (br s, 2H, -NH & -NH''), 7.02 (t, 1H, $^3J_{H\text{-}H}$ = 5.7 Hz, -NH), 7.25 (s, 2H, Ar-H Gallate), 7.26 (br s, 1H, Ar-H), 7.27-7.35 (br m, 5H, benzyl Ar-H), 7.68 (br s, 1H, Ar-H), 7.71 (br s, 1H, Ar-H).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.18, 28.04, 28.14, 29.15, 29.66, 31.25, 31.51, 32.71, 33.01, 37.49, 39.56, 40.52, 58.58, 60.84, 66.27, 70.35, 70.40, 70.44, 70.45, 70.46, 70.49, 70.78, 70.82, 71.89, 77.67, 79.07, 79.29, 108.70, 127.02, 127.05, 127.84, 127.91, 128.42, 130.24, 130.83, 133.21, 137.16, 142.12, 142.26, 142.32, 152.01, 156.38, 156.41, 166.55, 166.58, 170.25.

MS (MALDI-TOF, dithranol): m/z = 1664.82 $[M+K]^+$ ($^{12}C_{80}{}^{1}H_{131}{}^{14}N_5{}^{16}O_{29}{}^{39}K$) calc. monoisotopic peak 1664.86; 1648.84 $[M+Na]^+$ calc. monoisotopic peak ($^{12}C_{80}{}^{1}H_{131}{}^{14}N_5{}^{16}O_{29}{}^{23}Na$) 1648.88.

Ethyl-3-(3-amino-propyl)-5-(3-{4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy} propan-2-yloxy)-benzoylamino}-propyl)-benzoate ***88***



1.00 g (0.7 mmol) **87** were dissolved in 20 ml ethylacetate / ethanol (1:1). 0.125 g Pd/ C were added. The mixture was stirred for one hour in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. Further purification was not necessary.

Yield: 0.673 g (73%) of an yellowish oil (losses during work up).

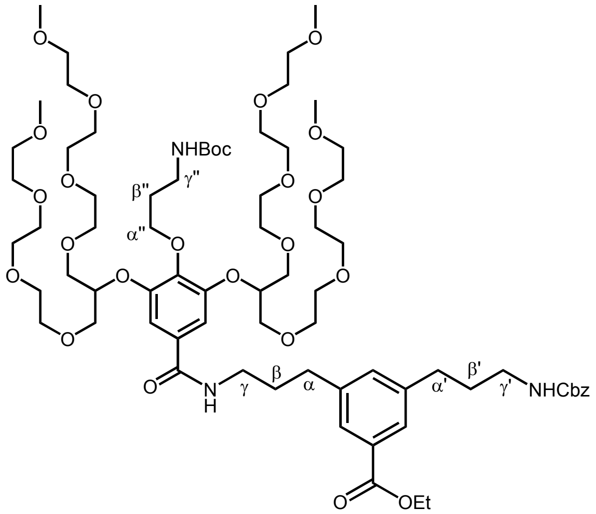
R_f = 0.11 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (d4-MeOH, 500 MHz): δ [ppm] = 1.38 & 1.45 (2s, 18H, $-C(CH_3)_3$), 1.39 (t, 3H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 1.94 (2m, 2H, β'-CH_2), 2.01 (m, 4H, β-CH_2), 2.75 (t, 2H, $^3J_{H-H}$ = 7.4 Hz, α-CH_2), 3.00 (m, 2H, γ-CH_2), 3.34 (s, 12H, $-OCH_3$), 3.43 (m, 4H, γ-CH_2 & γ' -CH_2), 3.50-3.72 (2m, 48H, $-OCH_2CH_2O$), 3.81 (m, 8H, $-OCH(CH_2)_2$), 4.11 (br s, 2H, α'-CH_2), 4.17 & 4.21 (2m, 3H, $-CH_2$NHBoc & -CHNHBoc), 4.36 (q, 2H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 4.78 (m, 2H, $-OCH(CH_2)_2$), 6.51 (br s, 1H, -NH), 6.55 (s, 1H, -NH), 7.37 (s, 1H, Ar-*H*), 7.39 (s, 2H, Ar-*H* Gallate), 7.72 (s, 1H, Ar-*H*), 7.75 (s, 1H, Ar-*H*), 7.99 (s, 1H, -N*H*), 8.49 (s, 1H, -N*H*).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.70, 28.64, 29.79, 30.60, 31.82, 32.98, 33.77, 38.18, 40.23, 40.43, 42.99, 56.42, 59.01, 61.82, 71.00, 71.09, 71.19, 71.60, 71.66, 72.62, 78.40, 79.96, 80.22, 109.34, 127.78, 128.22, 130.50, 131.72, 134.19, 142.17, 143.09, 143.72, 152.99, 157.06, 157.97, 167.56, 166.36, 172.21.

MS (MALDI-TOF, dithranol): m/z = 1530.86 $[M+K]^+$ ($^{12}C_{72}{}^{1}H_{125}{}^{14}N_5{}^{16}O_{27}{}^{39}K$) calc. monoisotopic peak 1530.82; 1514.85 $[M+Na]^{+\bullet}$ calc. monoisotopic peak ($^{12}C_{80}{}^{1}H_{131}{}^{14}N_5{}^{16}O_{29}{}^{23}Na$) 1514.85; 1492.88 $[M+H]^{+\bullet}$ calc. monoisotopic peak ($^{12}C_{80}{}^{1}H_{132}{}^{14}N_5{}^{16}O_{29}$) 1492.86.

Ethyl-3-(3-benzyloxycarbonylamino-propyl)-5-(3-{4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoate ***89***



0.800 g (0.75 mmol) **60a** were dissolved in 7 ml dry methylene chloride. 0.1 ml dry triethylamine were added and the mixture was cooled to -20°C. A solution of 0.266 g (0.83 mmol) TBTU in dry DMF was added. The mixture was stirred for two hours at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.250 g (0.57 mmol) **19** and 0.2 ml dry triethylamine in abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.702 g (64%) of a yellowish oil.

R_f = 0.27 (Silica gel; methylene chloride/ methanol 20:1).

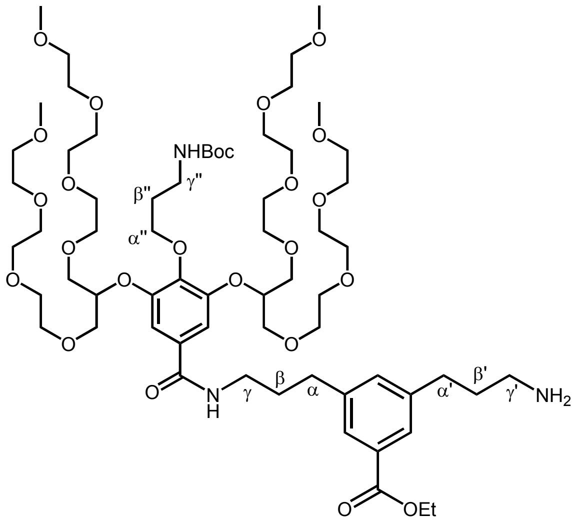
^{1}H NMR (CD$_2$Cl$_2$, 500 MHz): δ [ppm] = 1.35 (t, 3H, $^3J_{H\text{-}H}$ = 7.1 Hz, -CH$_2$C*H*$_3$), 1.40 (s, 9H, -C(C*H*$_3$)$_3$), 1.82 (m, 2H, β'-C*H*$_2$), 1.84 (m, 2H, β''-C*H*$_2$), 1.91 (m, 2H, β-C*H*$_2$), 2.65 (t, 2H, $^3J_{H\text{-}H}$ = 7.7 Hz, α'-C*H*$_2$), 2.70 (t, 2H, $^3J_{H\text{-}H}$ = 7.7 Hz, α-C*H*$_2$), 3.17 (m, 2H, γ''-C*H*$_2$), 3.28 (s, 12H, -OC*H*$_3$), 3.28 (hidden m, 2H, γ-C*H*$_2$), 3.38 (m, 2H, γ''-C*H*$_2$), 3.44-3.65 (2m, 48H, -OC*H*$_2$C*H*$_2$O), 3.72 (m, 8H, -OCH(C*H*$_2$)$_2$), 4.02 (t, 2H, $^3J_{H\text{-}H}$ = 5.7 Hz, α''-C*H*$_2$), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.1 Hz, -C*H*$_2$CH$_3$), 4.60 (quint, 2H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 5.03 (s, 2H, benzyl CH$_2$), 5.17 (br s, 1H, -N*H*'), 5.57 (br s, 1H, -N*H*''), 6.96 (br s, 1H, -N*H*), 7.22 (s, 2H, Ar-*H* Gallate), 7.25 (br s, 1H, Ar-*H*), 7.30-7.35 (br m, 5H, benzyl Ar-*H*), 7.67 (br s, 1H, Ar-*H*), 7.70 (br s, 1H, Ar-*H*).

^{13}C NMR (CD$_2$Cl$_2$, 125 MHz): δ [ppm] = 14.21, 28.34, 30.13, 31.27, 31.55, 32.75, 33.05, 38.01, 39.58, 40.57, 58.63, 60.88, 66.33, 70.40, 70.41, 70.47, 70.51, 70.53, 70.93, 71.31, 71.94, 77.88, 78.39, 108.77, 127.05, 127.10, 127.88, 127.94, 128.46, 130.21, 130.88, 133.24, 137.20, 142.14, 142.31, 142.38, 152.06, 156.00, 156.39, 166.60, 166.63.

MS (pos. FAB): m/z (%) = 1480.1 (3) $[M+H+K]^{+\bullet}$; 1479.2 (2) $[M+K]^{+\bullet}$; 1464.0 (20), 1463.1 (22) $[M+Na]^{+\bullet}$; 1440.9 (4) $[M+H]^{+\bullet}$; 1352.2 (2), 1351.1 (4), 1349.8 (4) $[M-C_7H_7+H]^{+\bullet}$; 1336.9 (40), 1335.8 (69), 1334.8 (100), $[M-C_7H_7O+H]^{+\bullet}$; 1333.9 (14), 1333.5 (11), 1332.7 (31) $[M-C_7H_7O+H]^{+\bullet}$.

EA	$C_{72}H_{117}N_3O_{26}$	Calc.	C	60.02	H	8.19	N	2.92,
	(1439.79)	found		59.95		7.79		2.78.

Ethyl-3-(3-amino-propyl)-5-(3-{4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoate ***90***



0.500 g (0.35 mmol) **89** were dissolved in 10 ml methanol. 0.050 g Pd/ C were added. The mixture was stirred for one hour in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. Further purification was not necessary.

Yield: 0.404 g (89%) of a yellowish oil (losses during work up).

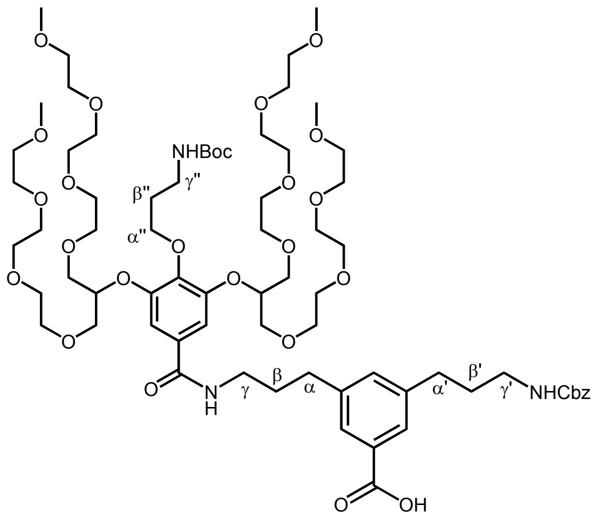
R_f = 0.14 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.35 (t, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, -CH_2CH_3), 1.41 (s, 9H, -$C(CH_3)_3$), 1.85 (m, 2H, β''-CH_2), 1.90 (m, 2H, β'-CH_2), 1.95 (m, 2H, β-CH_2), 2.61 (t, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, α'-CH_2), 2.70 (t, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, α-CH_2), 2.87 (m, 2H, γ'-CH_2), 3.28 (s, 12H, -OCH_3), 3.32 (m, 2H, γ''-CH_2), 3.36 (m, 2H, γ-CH_2), 3.43-3.67 (2m, 48H, -OCH_2CH_2O), 3.74 (m, 8H, -$OCH(CH_2)_2$), 4.05 (t, 2H, $^3J_{H\text{-}H}$ = 5.4 Hz, α''-CH_2), 4.31 (q, 2H, $^3J_{H\text{-}H}$ = 7.2 Hz, -CH_2CH_3), 4.68 (quint, 2H, $^3J_{H\text{-}H}$ = 4.4 Hz, -$OCH(CH_2)_2$), 5.57 (m, 1H, -N*H*Boc), 7.04 (br s, 2H, -NH_2), 7.20 (br s, 1H, Ar-*H*), 7.24 (s, 2H, Ar-*H* Gallate), 7.36 (m, 1H, -N*H*), 7.60 (br s, 1H, Ar-*H*), 7.70 (br s, 1H, Ar-*H*).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.15, 28.28, 28.34, 30.22, 30.31, 31.90, 32.70, 37.89, 39.30, 39.81, 58.53, 60.87, 70.18, 70.23, 70.30, 70.33, 70.39, 70.80, 71.36, 71.75, 77.45, 78.47, 108.23, 126.94, 127.56, 129.81, 130.87, 133.03, 140.43, 141.78, 142.66, 151.82, 156.08, 166.43, 166.55.

MS (pos. FAB): m/z (%) = 1440.7 (5), 1439.8 (15), 1438.7 (23) $[M+CsI]^{+\bullet}$; 1330.6 (4), 1329.7 (8), 1328.7 (10) $[M+Na]^{+\bullet}$; 1309.3 (4), 1308.6 (9), 1308.1 (32), 1307.4 (74), 1306.7 (100), 1305.0 (11) $[M+H]^{+\bullet}$.

*3-(3-Benzyloxycarbonylamino-propyl)-5-(3-{4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoic acid **91***



0.243 g (0.17 mmol) **89** was dissolved in 10 ml ethanol and 1 ml 1M KOH$_{aq}$ added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl$_{aq}$ (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. No further purification. The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.234 g (98%) of a colorless oil.

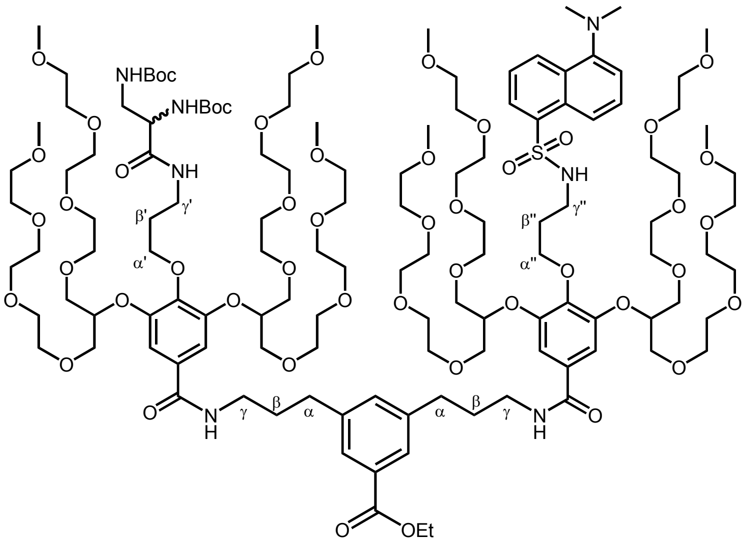
R$_f$ = 0.23 (Silica gel; methylene chloride/ methanol 15:1).

^{1}H NMR (CD$_2$Cl$_2$, 500 MHz): δ [ppm] = 1.40 (s, 9H, -C(CH_3)$_3$), 1.83 (m, 4H, β- & β''-CH_2), 1.93 (m, 2H, β'-CH_2), 2.56 (m, 2H, α-CH_2), 2.67 (m, 2H, α'-CH_2), 3.11 (m, 2H, γ-CH_2), 3.32 (s, 12H, -OCH_3), 3.35 (m, 2H, γ''-CH_2), 3.40 (m, 2H, γ'-CH_2), 3.42-3.64 (2m, 48H, -OCH_2CH_2O), 3.70 (m, 8H, -OCH(CH_2)$_2$), 4.00 (t, 2H, $^3J_{H\text{-}H}$ = 5.3 Hz, α''-CH_2), 4.57 (br s, 2H, -OCH(CH$_2$)$_2$), 4.98 (br s, 1H, -NH), 5.04 (s, 2H, benzyl CH$_2$), 5.21 (br s, 1H, -NH), 5.62 (br s, 1H, -NH), 7.22 (s, 2H, Ar-H Gallate), 7.25 (br s, 1H, Ar-H), 7.30-7.35 (br m, 5H, benzyl Ar-H), 7.67 (br s, 1H, Ar-H), 7.70 (br s, 1H, Ar-H).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 28.71, 30.21, 31.31, 31.62, 32.75, 33.17, 33.43, 38.09, 40.10, 40.68, 59.02, 66.77, 70.24, 70.41, 70.51, 70.56, 70.93, 71.31, 71.94, 77.86, 78.11, 109.08, 127.88, 128.11, 128.29, 128.76, 130.05, 132.66, 137.13, 142.06, 142.61, 142.38, 152.23, 157.04, 157.55, 167.85.

MS (MALDI-TOF, dithranol): m/z = 1434.94 [M+Na]$^+$ ($^{12}C_{70}{}^{1}H_{113}{}^{14}N_3{}^{16}O_{26}{}^{23}Na$) calc. monoisotopic peak 1434.75; 1450.89 [M+K]$^+$ ($^{12}C_{70}{}^{1}H_{113}{}^{14}N_3{}^{16}O_{26}{}^{39}K$) calc. monoisotopic peak 1450.72; 1456.90 [M-H+2Na]$^+$ ($^{12}C_{70}{}^{1}H_{112}{}^{14}N_3{}^{16}O_{26}{}^{23}Na_2$) calc. monoisotopic peak 1456.73.

Ethyl-3-(3-{4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis (1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)]-benzoate ***92***



0.439 g (0.37 mmol) **63** were dissolved in 5 ml dry methylene chloride. The solution was cooled to -20°C and 0.063 g (0.41 mmol) HOBt and 0.086 g (0.45 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.350 g (0.23 mmol) **88** and 0.2 ml dry triethylamine in 3 ml abs. methanol was added. The reaction was stirred for one hour at -40°C, allowed to rise to room temperature, and monitored with TLC. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.535 g (90%) of a yellowish oil.

R_f = 0.23 (Silica gel; methylene chloride/ methanol 15:1).

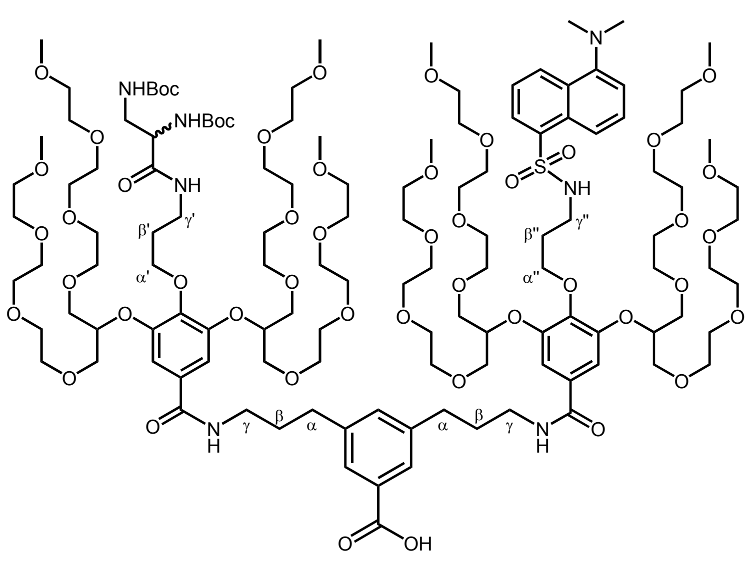
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.32 & 1.40 (2s, 18H, $-C(CH_3)_3$), 1.36 (t, 3H, $^3J_{H-H}$ = 7.2 Hz, $-CH_2CH_3$), 1.78 (m, 4H, β''-CH_2), 1.88 (m, 2H, β'-CH_2), 1.93 (m, 4H, β-CH_2), 2.72 (t, 4H, $^3J_{H-H}$ = 7.6 Hz, α-CH_2), 2.88 (s, 6H, $-N(CH_3)_2$), 3.22 (m, 2H, γ''-CH_2), 3.29 & 3.30 (2s, 24H, $-OCH_3$), 3.41 (m, 6H, γ-CH_2 & γ'-CH_2), 3.44-3.62 (2m, 96H, $-OCH_2CH_2O$), 3.63 (m, 2H, α'-CH_2), 3.67 (d, 8H, $^3J_{H-H}$ = 5.0 Hz, $-OCH(CH_2)_2$), 3.72 (d, 4H, $^3J_{H-H}$ = 4.9 Hz, $-OCH(CH_2)_2$), 3.75 (d, 4H, $^3J_{H-H}$ = 4.9 Hz,$-OCH(CH_2)_2$), 3.97 (t, 2H, $^3J_{H-H}$ = 5.6 Hz, α''-CH_2), 4.02 & 4.09 & 4.12 (m, 3H, $-CH_2$NHBoc & $-CH$NHBoc), 4.32 (q, 2H, $^3J_{H-H}$ = 7.2 Hz, $-CH_2CH_3$), 4.57 (quint, 2H, $^3J_{H-H}$ = 5.0 Hz,

-OC*H*(CH$_2$)$_2$), 4.63 (quint, 2H, $^{3}J_{H\text{-}H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 5.45 (br s, 1H, -CH$_2$N*H*Boc), 5.93 (br s, 1H, -CHN*H*Boc), 6.26 (t, 2H, $^{3}J_{H\text{-}H}$ = 6.1 Hz, -N*H*''), 7.12 (m, 2H, -N*H*Ar), 7.18 (d, 1H, $^{3}J_{H\text{-}H}$ = 7.6 Hz, Ar-*H* Dansyl), 7.23 & 7.25 (2 s, 4H, Ar-*H* Gallate), 7.29 (t, 1H, $^{4}J_{H\text{-}H}$ = 1.5 Hz, Ar-*H* Dendron), 7.32 (br s, 1H, -N*H*'), 7.50 (dd, 1H, $^{3}J_{H\text{-}H}$ = 8.7 Hz, $^{3}J_{H\text{-}H}$ = 7.6 Hz, Ar-*H* Dansyl), 7.54 (dd, 1H, $^{3}J_{H\text{-}H}$ = 8.5 Hz, $^{3}J_{H\text{-}H}$ = 7.3 Hz, Ar-*H* Dansyl), 7.71 (d, 2H, $^{4}J_{H\text{-}H}$ = 1.5 Hz, Ar-*H* Dendron), 8.22 (dd, 1H, $^{3}J_{H\text{-}H}$ = 7.3 Hz, $^{4}J_{H\text{-}H}$ = 1.2 Hz, Ar-*H* Dansyl), 8.33 (d, 1H, $^{3}J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.52 (d, 1H, $^{3}J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD$_2$Cl$_2$, 125 MHz): δ [ppm] = 14.19, 28.02, 28.13, 29.62, 30.16, 31.31, 33.12, 37.47, 39.71, 40.95, 42.73, 45.22, 45.25, 55.08, 58.57, 60.82, 70.33, 70.37, 70.38, 70.40, 70.42, 70.44, 70.45, 70.78, 70.81, 71.02, 71.87, 77.61, 77.87, 79.06, 79.31, 108.62, 108.75, 115.15, 119.49, 123.30, 126.95, 127.91, 129.00, 129.72, 129.84, 129.89, 130.10, 130.15, 130.78, 133.25, 136.03, 142.02, 142.19, 142.37, 151.59, 151.86, 151.97, 155.70, 156.44, 166.50, 166.52, 166.58, 170.28.

MS (MALDI-TOF, dithranol): m/z = 2689.42 [M+Na]$^+$ (^{12}C$_{128}$^{1}H$_{215}$^{14}N$_7$^{16}O$_{49}$^{23}Na) calc. monoisotopic peak 2689.42.

3-(3-{4-[3-(2,3-bis-tert-Butoxycarbonylamino-propionylamido)-propoxy]-*3,5-bis (1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis {2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)]-benzoic acid* ***93***



0.520 g (0.195 mmol) **92** were dissolved in 10 ml ethanol and 1 ml 1M KOH$_{aq}$ added at room temperature. The mixture was stirred for 12 hours in the dark. The reaction was quenched by the addition of 1M HCl$_{aq}$ (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. No further purification. The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.480 g (93%) of a yellowish oil.

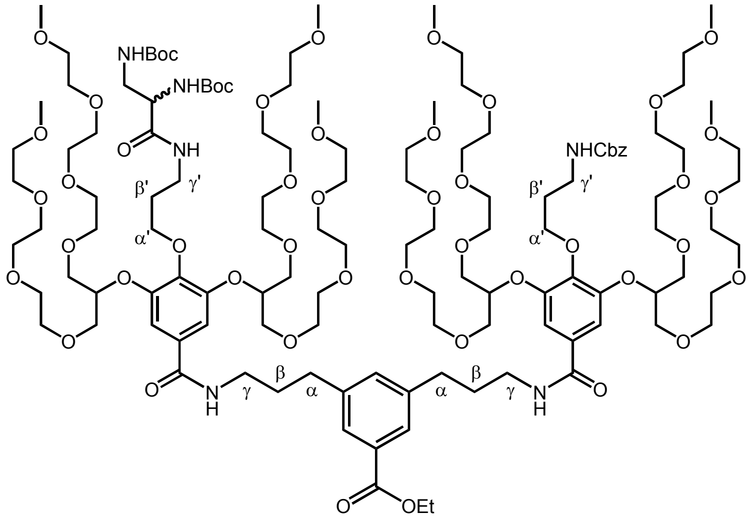
R_f = 0.14 (Silica gel; methylene chloride/ methanol 15:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.28 & 1.37 (2s, 18H, -C(C*H*$_3$)$_3$), 1.76 (m, 4H, β''-C*H*$_2$), 1.87 (m, 2H, β'-C*H*$_2$), 1.92 (m, 4H, β-C*H*$_2$), 2.67 (m, 4H, α-C*H*$_2$), 2.82 (s, 6H, -N(C*H*$_3$)$_2$), 3.21 (m, 2H, γ''-C*H*$_2$), 3.28 & 3.29 (2s, 24H, -OC*H*$_3$), 3.40 (m, 6H, γ-C*H*$_2$ & γ'-C*H*$_2$), 3.44-3.62 (2m, 96H, -OC*H*$_2$C*H*$_2$O), 3.61 (m, 2H, α'-C*H*$_2$), 3.64 (m, 8H, -OCH(C*H*$_2$)$_2$), 3.68 (m, 4H, -OCH(C*H*$_2$)$_2$), 3.72 (m, 4H, -OCH(C*H*$_2$)$_2$), 3.95 (t, 2H, $^3J_{H\text{-}H}$ = 5.2 Hz, α''-C*H*$_2$), 4.00 & 4.08 & 4.20 (m, 3H, -C*H*$_2$NHBoc & -C*H*NHBoc), 4.53 (m, 2H, -OC*H*(CH$_2$)$_2$), 4.59 (m, 2H, -OC*H*(CH$_2$)$_2$), 5.56 (br s, 1H, -CH$_2$N*H*Boc), 6.00 (br s, 1H, -CHN*H*Boc), 6.41 (t, 2H, $^3J_{H\text{-}H}$ = 6.2 Hz, -N*H*''), 7.10 (d, 1H, $^3J_{H\text{-}H}$ = 7.4 Hz, Ar-*H* Dansyl), 7.23 (s, 1H, Ar-*H* Dendron), 7.25 & 7.26 (2s, 4H, Ar-*H* Gallate), 7.43 (m, 1H, Ar-*H* Dansyl), 7.48 (m, 1H, Ar-*H* Dansyl), 7.69 (s, 2H, Ar-*H* Dendron), 8.20 (d, 1H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-*H* Dansyl), 8.32 (d, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.57 (d, 1H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 27.55, 27.69, 28.82, 29.43, 30.29, 32.42, 36.82, 38.98, 39.05, 40.15, 42.05, 44.70, 54.34, 58.14, 69.65, 69.69, 69.71, 69.79, 70.02, 70.05, 70.20, 71.14, 76.87, 77.13, 78.41, 78.66, 108.14, 108.30, 114.40, 118.78, 122.51, 126.72, 127.25, 128.23, 129.05, 129.12, 129.16, 129.23, 130.09, 132.51, 135.31, 141.41, 141.45, 141.55, 151.02, 151.09, 151.20, 155.06, 155.82, 166.09, 166.15, 167.76, 169.88.

MS (MALDI-TOF, dithranol): m/z = 2683.38 [M-H+2Na]$^+$ ($^{12}C_{126}{}^{1}H_{210}{}^{14}N_7{}^{16}O_{49}{}^{23}Na_2$) calc. monoisotopic peak 2683.37; 2677.38 [M+K]$^+$ ($^{12}C_{126}{}^{1}H_{211}{}^{14}N_7{}^{16}O_{49}{}^{39}K$) calc. monoisotopic peak 2677.36; 2661.42 [M+Na]$^+$ ($^{12}C_{126}{}^{1}H_{211}{}^{14}N_7{}^{16}O_{49}{}^{23}Na$) calc. monoisotopic peak 2661.38.

Ethyl-3-(3-{4-(3-benzyloxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-(3-{4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoate ***94***



0.400 g (0.36 mmol) **60b** were dissolved in 7 ml dry methylene chloride. The solution was cooled to -20°C and 0.062 g (0.40 mmol) HOBt and 0.085 g (0.44 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.350 g (0.23 mmol) **88** and 0.2 ml dry triethylamine in abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 15:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.488 g (77%) of a yellowish oil.

R_f = 0.21 (Silica gel; methylene chloride/ methanol 20:1).

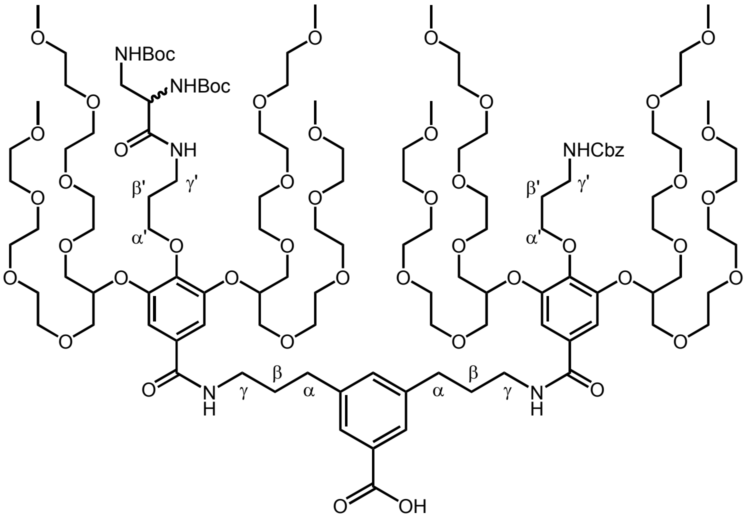
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.31 & 1.39 (2s, 18H, $-C(CH_3)_3$), 1.36 (t, 3H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 1.89 (m, 4H, β'-CH_2), 1.92 (m, 4H, β-CH_2), 2.71 (t, 4H, $^3J_{H-H}$ = 7.9 Hz, α-CH_2), 3.28 & 3.29 (2s, 24H, $-OCH_3$), 3.42 (m, 8H, γ-CH_2 & γ'-CH_2), 3.43-3.65 (2m, 96H, $-OCH_2CH_2O$), 3.72 (m, 16H, $-OCH(CH_2)_2$), 4.05 (t, 4H, $^3J_{H-H}$ = 5.6 Hz, α'-CH_2), 4.02 & 4.09 & 4.12 (m, 3H, $-CH_2$NHBoc & -CHNHBoc), 4.32 (q, 2H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 4.61 (m, 4H, $-OCH(CH_2)_2$), 5.05 (s, 2H, benzyl CH_2), 5.47 (m, 1H, -NH), 5.93 (m, 1H, -NH), 6.04 (t, 2H, $^3J_{H-H}$ = 5.4 Hz, -NH), 7.03 (t, 2H, $^3J_{H-H}$ =

5.6 Hz, -N*H*), 7.05 (t, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, -N*H*), 7.22 (s, 2H, Ar-*H*), 7.24 (s, 2H, Ar-*H* Gallate), 7.26-7.36 (m, 5H, benzyl Ar-*H*), 7.71 (s, 1H, Ar-*H*).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.18, 28.00, 28.12, 29.62, 29.87, 31.27, 33.07, 37.47, 38.49, 39.66, 42.73, 55.06, 58.55, 60.78, 66.07, 70.32, 70.33, 70.37, 70.39, 70.41, 70.42, 70.43, 70.44, 70.75, 70.80, 70.82, 71.86, 77.65, 77.79, 79.01, 79.26, 108.66, 126.94, 127.83, 127.99, 128.37, 130.13, 130.16, 130.78, 133.21, 137.31, 142.17, 142.31, 142.32, 151.96, 151.97, 156.42, 166.52, 166.55, 170.23.

MS (MALDI-TOF, dithranol): m/z = 2606.33 $[M+K]^+$ ($^{12}C_{124}{}^{1}H_{210}{}^{14}N_6{}^{16}O_{49}{}^{39}K$) calc. monoisotopic peak 2606.38; 2590.36 $[M+Na]^{+\bullet}$ calc. monoisotopic peak ($^{12}C_{124}{}^{1}H_{210}{}^{14}N_6{}^{16}O_{49}{}^{23}Na$) 2590.40.

3-(3-{4-(3-Benzyloxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-(3-{4-[3-(2,3-bis-tert-butoxy carbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-benzoic acid ***95***



0.465 g (0.18 mmol) **94** was dissolved in 10 ml ethanol and 1 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. No further purification. The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.457 g (99%) of a yellowish oil.

R_f = 0.17 (Silica gel; methylene chloride/ methanol 20:1).

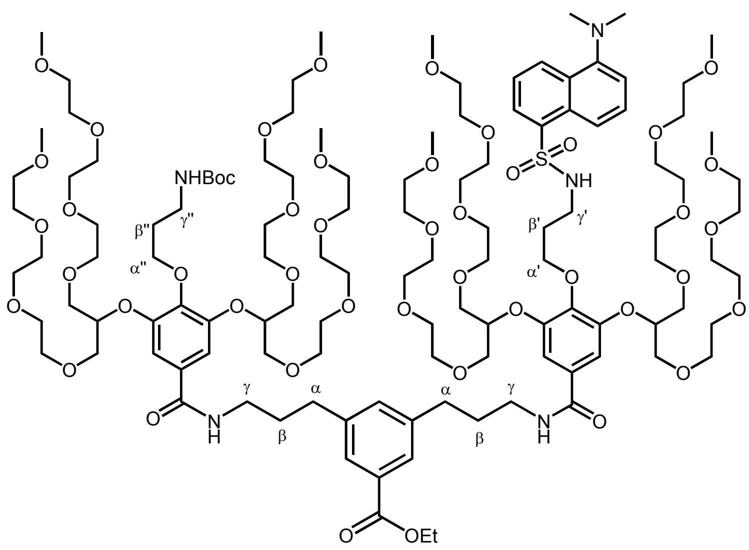
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.20 & 1.28 (2s, 18H, -C(C*H*$_3$)$_3$), 1.78 (m, 4H, β'-C*H*$_2$), 1.84 (m, 4H, β-C*H*$_2$), 2.59 (t, 4H, $^3J_{H\text{-}H}$ = 7.4 Hz, α-C*H*$_2$), 3.21 & 3.22 (2s, 24H, -OC*H*$_3$), 3.32 (m, 8H, γ-C*H*$_2$ & γ'-C*H*$_2$), 3.37-3.55 (2m, 96H, -OC*H*$_2$C*H*$_2$O), 3.60

(m, 16H, -OCH(CH_2)$_2$), 3.93 (t, 4H, $^3J_{H\text{-}H}$ = 5.8 Hz, α'-CH_2), 3.91 & 3.98 & 4.10 (m, 3H, -CH_2NHBoc & -C*H*NHBoc), 4.49 (m, 4H, -OC*H*(CH$_2$)$_2$), 4.96 (s, 2H, benzyl CH_2), 5.33 (m, 1H, -N*H*), 5.82 (t, 1H, $^3J_{H\text{-}H}$ = 7.4 Hz, -CHN*H*Boc), 6.05 (t, 2H, $^3J_{H\text{-}H}$ = 5.6 Hz, -N*H*), 7.13 (s, 2H, Ar-*H*), 7.14 (s, 2H, Ar-*H* Gallate), 7.16 (m, 2H, NH), 7.17-7.24 (m, 5H, benzyl Ar-*H*), 7.59 (s, 1H, Ar-*H*).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 27.81, 27.93, 29.08, 29.31, 30.51, 32.66, 37.06, 38.03, 39.27, 42.38, 54.48, 58.43, 58.44, 65.87, 69.96, 69.96, 69.98, 70.07, 70.27, 70.30, 70.32, 70.66, 71.42, 71.45, 77.19, 78.78, 79.02, 108.36, 127.01, 127.51, 127.72, 127.98, 129.46, 130.09, 132.83, 136.48, 141.67, 141.74, 141.82, 151.44, 155.34, 156.08, 156.23, 166.35, 166.42, 167.95, 170.08.

MS (MALDI-TOF, dithranol): m/z = 2578.42 [M+K]$^+$ ($^{12}C_{122}{}^1H_{206}{}^{14}N_6{}^{16}O_{49}{}^{39}K$) calc. monoisotopic peak 2578.34; 2562.44 [M+Na]$^+$ calc. monoisotopic peak ($^{12}C_{122}{}^1H_{206}{}^{14}N_6{}^{16}O_{49}{}^{23}Na$) 2562.37.

Ethyl-3-(3-{4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-{5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)}-benzoate ***96***



0.240 g (0.20 mmol) **63** were dissolved in 5 ml dry methylene chloride. The solution was cooled to -20°C and 0.034 g (0.22 mmol) HOBt and 0.046 g (0.24 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.190 g (0.14 mmol) **90** and 0.3 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C, allowed to rise to room temperature, and monitored with TLC. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 20:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.340 g (95%) of a yellowish oil.

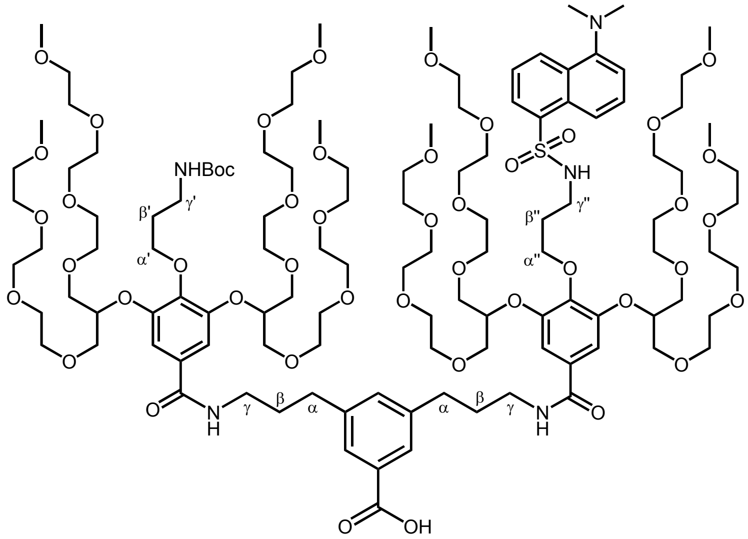
R_f = 0.28 (Silica gel; methylene chloride/ methanol 15:1).

^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.36 (t, 3H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 1.41 (s, 9H, $-C(CH_3)_3$), 1.78 (m, 2H, β'-CH_2), 1.86 (m, 2H, β''-CH_2), 1.93 (m, 4H, β-CH_2), 2.71 (t, 4H, $^3J_{H-H}$ = 7.6 Hz, α-CH_2), 2.86 (s, 6H, $-N(CH_3)_2$), 3.22 (m, 2H, γ'-CH_2), 3.29 (2s, 24H, $-OCH_3$), 3.33 (m, 2H, γ''-CH_2), 3.40 (m, 4H, γ-CH_2), 3.43-3.60 (2m, 96H, $-OCH_2CH_2O$), 3.60-3.76 (3m, 16H, $-OCH(CH_2)_2$), 3.97 (t, 2H, $^3J_{H-H}$ = 5.4 Hz, α'-CH_2), 4.04 (t, 2H, $^3J_{H-H}$ = 5.4 Hz, α''-CH_2), 4.32 (q, 2H, $^3J_{H-H}$ = 7.1 Hz, $-CH_2CH_3$), 4.48 & 4.56 & 4.62 (3m, 4H, $-OCH(CH_2)_2$), 5.62 (br s, 1H, -NH''), 6.25 (t, 1H, $^3J_{H-H}$ = 6.1 Hz, -NH'), 7.03 (br s, 2H, -NH), 7.16 (m, 1H, Ar-*H* Dansyl), 7.22 & 7.24 (2 s, 4H, Ar-*H* Gallate), 7.29 (s, 1H, Ar-*H* Dendron), 7.48 (m, 1H, Ar-*H* Dansyl), 7.53 (m, 1H, Ar-*H* Dansyl), 7.71 (m, 1H, Ar-*H* Dendron), 8.22 (d, 1H, $^3J_{H-H}$ = 7.3 Hz, Ar-*H* Dansyl), 8.31 (d, 1H, $^3J_{H-H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.51 (d, 1H, $^3J_{H-H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 14.17, 28.28, 29.62, 30.15, 31.26, 33.08, 37.91, 39.63, 40.90, 45.18, 58.53, 58.54, 60.77, 70.28, 70.30, 70.33, 70.35, 70.38, 70.39, 70.41, 70.43, 70.44, 70.47, 70.74, 70.84, 71.83, 71.84, 71.86, 77.71, 77.81, 78.26, 108.63, 108.70, 115.02, 119.27, 123.18, 126.94, 127.89, 128.93, 129.70, 129.89, 129.92, 130.07, 130.09, 130.73, 133.23, 136.01, 142.35, 151.82, 151.87, 151.95, 155.91, 166.48, 166.54.

MS (MALDI-TOF, dithranol): m/z = 2519.24 $[M+K]^+$ ($^{12}C_{120}{}^1H_{201}{}^{14}N_5{}^{16}O_{46}{}^{39}K$) calc. monoisotopic peak 2519.29; 2503.45 $[M+Na]^+$ ($^{12}C_{120}{}^1H_{201}{}^{14}N_5{}^{16}O_{46}{}^{23}Na$) calc. monoisotopic peak 2503.32.

3-(3-{4-(3-tert-Butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-{5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)}-benzoic acid ***97***



0.330 g (0.132 mmol) **96** was dissolved in 5 ml ethanol and 1 ml 1M KOH_{aq} added at room temperature. The mixture was stirred for 12 hours in the dark. The reaction was quenched by the addition of 1M HCl_{aq} (pH = 5). The solvent was removed under reduced pressure. The crude product was diluted with methylene chloride and filtered. No further purification. The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.235 g (73%) of a yellowish oil.

R_f = 0.24 (Silica gel; methylene chloride/ methanol 10:1).

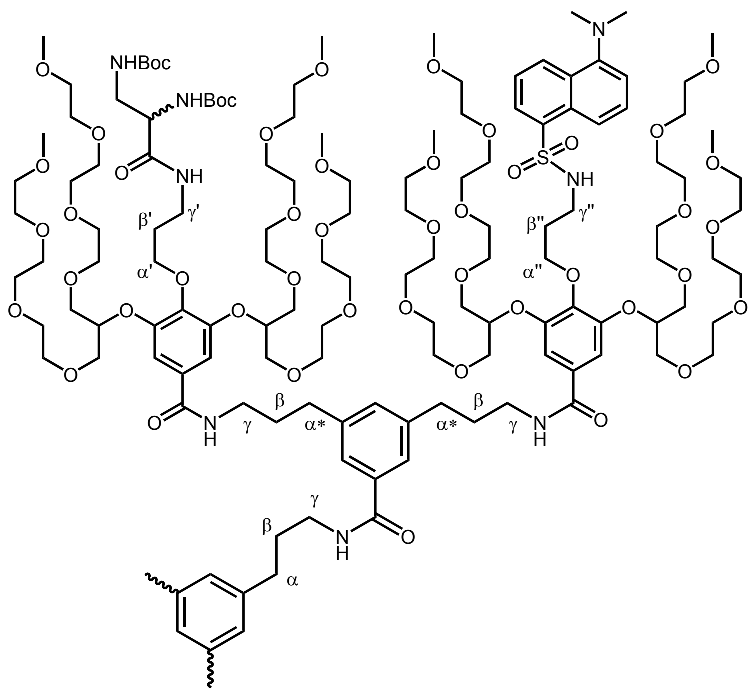
^{1}H NMR (CD_2Cl_2, 500 MHz): δ [ppm] = 1.41 (s, 9H, -C(CH_3)$_3$), 1.78 (m, 2H, β''-CH_2), 1.85 (m, 2H, β'-CH_2), 1.94 (m, 4H, β-CH_2), 2.70 (t, 4H, $^3J_{H\text{-}H}$ = 6.9 Hz, α-CH_2), 2.85 (s, 6H, -N(CH_3)$_2$), 3.22 (m, 2H, γ''-CH_2), 3.29 (m, 24H, -OCH_3), 3.33 (m, 2H, γ'-CH_2), 3.40 (m, 4H, γ-CH_2), 3.43-3.60 (2m, 96H, -OCH_2CH_2O), 3.60-3.77 (3m, 16H, -OCH(CH_2)$_2$), 3.97 (t, 2H, $^3J_{H\text{-}H}$= 6.1 Hz, α''-CH_2), 4.04 (t, 2H, $^3J_{H\text{-}H}$= 5.6 Hz, α''-CH_2), 4.48 & 4.57 & 4.63 (3m, 4H, -OC*H*(CH$_2$)$_2$), 5.65 (br s, 1H, -N*H*'), 6.32 (m, 1H, -N*H*''), 7.16 (m, 1H, Ar-*H* Dansyl), 7.20 (br s, 2H, -N*H*), 7.22 & 7.24 (2s, 4H, Ar-*H* Gallate), 7.26 (s, 1H, Ar-*H* Dendron), 7.48 (m, 1H, Ar-*H* Dansyl), 7.53 (m, 1H, Ar-*H* Dansyl), 7.70 (m, 1H, Ar-*H* Dendron), 8.21 (d, 1H, $^3J_{H\text{-}H}$ = 7.2 Hz, Ar-*H* Dansyl), 8.32 (d, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.51 (d, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 28.26, 30.03, 30.14, 30.89, 32.99, 37.91, 39.58, 40.87, 45.18, 58.51, 70.24, 70.26, 70.31, 70.35, 70.37, 70.38, 70.40, 70.41, 70.72, 70.81, 70.95, 71.19, 71.81, 71.82, 77.56, 77.66, 108.09, 108.55, 115.03, 119.30, 123.19, 127.31, 127.89, 128.91, 129.68, 129.86, 129.91, 130.02, 135.98, 142.24, 151.75, 151.88, 155.96, 166.59.

MS (MALDI-TOF, dithranol): m/z = 2475.28 $[M+Na]^+$ ($^{12}C_{118}{}^{1}H_{197}{}^{14}N_5{}^{16}O_{46}{}^{23}Na$) calc. monoisotopic peak 2475.28; 2491.24 $[M+K]^+$ ($^{12}C_{118}{}^{1}H_{197}{}^{14}N_5{}^{16}O_{46}{}^{39}K$) calc. monoisotopic peak 2491.26.

8.9 Compounds of Chapter 4.4.3

1,3,5-Tris-[3-(3-{4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)] benzamidopropyl]–benzene ***98***



0.437 g (0.165 mmol) **93** were dissolved in 10 ml dry methylene chloride. The solution was cooled to -20°C and 0.030 g (0.196 mmol) HOBt and 0.040 g (0.209 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature.

The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.017 g (0.049 mmol) **3b** and 0.5 ml dry triethylamine in 2 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvent was evaporated. The crude product was extracted twice with 1M aqueous $NaHCO_3$and once with brine, and purified by column chromatography. The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.334 g (84%) of a yellowish oil.

R_f = 0.10 (Silica gel; methylene chloride/ methanol 10:1).

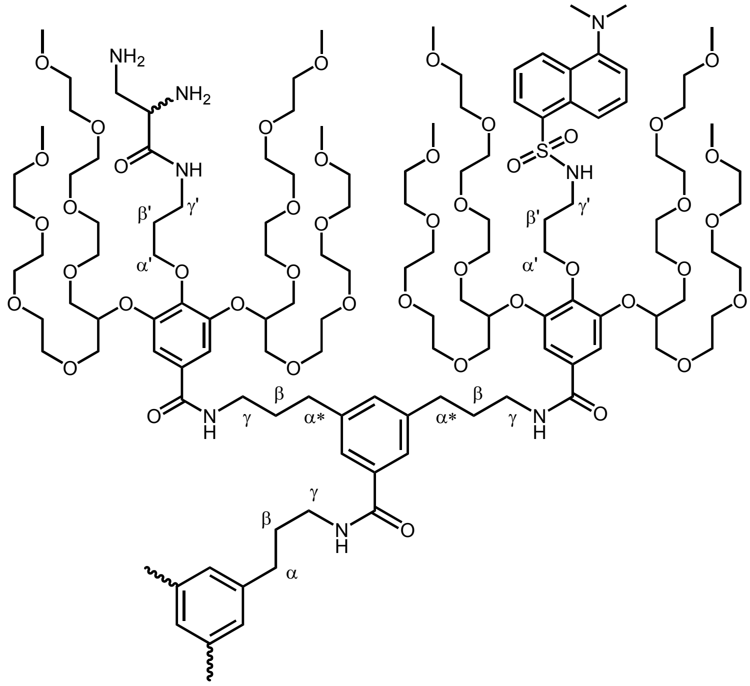
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.24 & 1.30 (2s, 18H, -C(C*H*$_3$)$_3$), 1.69 (m, 6H, β'-C*H*$_2$), 1.79 (m, 6H, β''-C*H*$_2$), 1.82 (m, 18H, β-C*H*$_2$), 2.53 (m, 6H, α-C*H*$_2$), 2.56 (m, 12H, α*-C*H*$_2$), 2.77 (s, 18H, -N(C*H*$_3$)$_2$), 3.13 (m, 6H, γ'-C*H*$_2$), 3.21 & 3.23 (2s, 72H, -OC*H*$_3$), 3.31 (m, 18H, γ-C*H*$_2$), 3.35 (m, 6H, γ-''C*H*$_2$), 3.37-3.55 (2m, 288H,

-OC*H*$_2$C*H*$_2$O), 3.57 & 3.60 & 3.66 (3m, 48H, -OCH(C*H*$_2$)$_2$), 3.89 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, α'-C*H*$_2$), 3.97 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, α''-C*H*$_2$), 3.93 & 3.99 & 4.10 (m, 9H, -C*H*$_2$NHBoc & -C*H*NHBoc), 4.44 & 4.49 (2m, 12H, -OC*H*(CH$_2$)$_2$), 5.30 (br s, 3H, -CH$_2$N*H*Boc), 5.77 (d, 3H, $^3J_{H\text{-}H}$ = 7.2 Hz, -CHN*H*Boc), 6.26 (t, 3H, $^3J_{H\text{-}H}$ = 5.9 Hz, -N*H*''), 6.78 (s, 3H, Ar-*H* Core), 7.04 (d, 1H, $^3J_{H\text{-}H}$ = 7.6 Hz, Ar-*H* Dansyl), 7.06 (s, 3H, Ar-*H* Dendron), 7.08 (m, 3H, -N*H*), 7.16 & 7.18 (2 s, 12H, Ar-*H* Gallate), 7.22 (m, 6H, -N*H*), 7.27 (m, 1H, -N*H*'), 7.36 (m, 3H, Ar-*H* Dansyl), 7.39 (s, 6H, Ar-*H* Dendron), 7.41 (m, 3H, Ar-*H* Dansyl), 8.13 (d, 1H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-*H* Dansyl), 8.25 (d, 1H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.41 (d, 1H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 27.96, 28.07, 29.27, 30.67, 30.71, 32.75, 32.92, 37.16, 39.29, 39.33, 39.49, 40.54, 42.59, 45.12, 58.59, 70.01, 70.10, 70.21, 70.41, 70.45, 70.54, 70.64, 71.56, 77.20, 77.42, 77.66, 78.93, 79.18, 108.77, 108.84, 114.80, 119.22, 122.90, 124.50, 124.59, 125.93, 127.62, 128.65, 129.47, 129.56, 129.60, 131.15, 131.21, 131.23, 134.71, 135.65, 141.44, 141.65, 141.70, 141.97, 142.11, 151.35, 151.53, 151.62, 155.43, 156.16, 166.48, 166.53, 167.54, 170.06.

MS (MALDI-TOF, dithranol): m/z = 8137.30 [M+Na]$^+$ ($C_{393}H_{654}N_{24}O_{144}S_3Na$) calc. molecular weight peak 8138.61.

1,3,5-Tris-[3-(3-{4-[3-(2,3-diamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)]benzamido propyl]–benzene hexakis-trifluoro-acetato ***99***



0.300 g (0.165 mmol) **98** were dissolved in 10 ml methylene chloride and 5 ml TFA was added at room temperature.

The deprotection was monitored with ^{1}H-NMR. The solvent was evaporated and remaining TFA was removed by co-evaporation with methylene chloride. The sample was dried in high vacuum. No further purification.

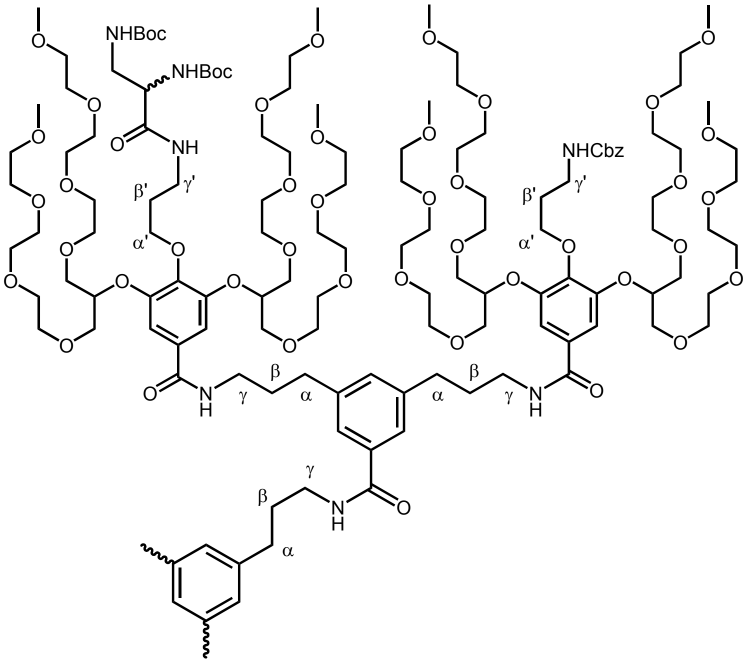
Yield: 0.297 g (98%) of a yellowish oil.

^{1}H NMR (CD$_3$OD, 500 MHz): δ [ppm] = 1.72 (m, 12H, β'-CH_2), 1.86 (m, 12H, β-CH_2), 1.91 (m, 6H, β-CH_2), 2.55 (t, 6H, $^3J_{H\text{-}H}$ = 7.1 Hz, α-CH_2), 2.63 (m, 12H, $^3J_{H\text{-}H}$ = 7.1 Hz, α*-CH_2), 2.97 (s, 18H, -N(CH_3)$_2$), 3.10 (t, 12H, $^3J_{H\text{-}H}$ = 6.9 Hz, γ'-CH_2), 3.21 & 3.24 (2s, 72H, -OCH_3), 3.31 (m, 18H, γ-CH_2), 3.37-3.50 (2m, 288H, -OCH_2CH_2O), 3.51 & 3.56 (2m, 48H, -OCH(CH_2)$_2$), 3.91 (t, 12H, $^3J_{H\text{-}H}$ = 5.7 Hz, α'-CH_2), 4.05 & 4.13 & 4.21 (m, 9H, -CH_2NHBoc & -CHNHBoc), 4.48 & 4.65 (2m, 12H, -OCH(CH$_2$)$_2$), 6.84 (s, 3H, Ar-*H* Core), 7.17 (s, 6H, Ar-*H* Gallate), 7.19 (s, 3H, Ar-*H* Dendron), 7.23 (s, 6H, Ar-*H* Gallate), 7.40 (d, 1H, $^3J_{H\text{-}H}$ = 7.8 Hz, Ar-*H* Dansyl), 7.43 (m, 6H, Ar-*H* Dendron), 7.55 (m, 3H, Ar-*H* Dansyl), 7.60 (m, 3H, Ar-*H* Dansyl), 8.19 (d, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-*H* Dansyl), 8.45 (m, 6H, Ar-*H* Dansyl).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 30.41, 30.67, 31.58, 32.13, 32.17, 34.09, 34.32, 39.56, 40.68, 40.78, 41.04, 41.82, 46.04, 52.14, 59.05, 59.10, 71.18, 71.26, 71.37, 71.45, 71.71, 71.76, 71.88, 71.97, 72.80, 72.88, 73.62, 78.47, 79.03, 109.61, 109.83, 116.78, 121.29, 124.81, 126.02, 126.11, 127.34, 129.11, 130.22, 130.66, 130.96, 131.10, 132.85, 136.03, 137.44, 153.16, 153.25, 166.38, 168.87, 168.99, 169.99.

MS (MALDI-TOF, CCA): m/z = 7926.26 $[M+3*CCA-6*H_2O]^+$ ($C_{393}H_{615}N_{27}O_{132}S_3$) calc. molecular weight peak 7926.48.

1,3,5-Tris-[3-(3-{4-(3-Benzyloxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-5-(3-{4-[3-(2,3-bis-tert-butoxycarbonylamino-propionylamido)-propoxy]-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)]benzamido propyl]–benzene ***100***



0.265 g (0.104 mmol) **95** were dissolved in 4 ml dry methylene chloride. The solution was cooled to -20°C and 0.022 g (0.144 mmol) HOBt and 0.027 g (0.144 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.010 g (0.028 mmol) **3b** and 0.3 ml dry triethylamine in 0.5 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solution was extracted twice with 1M aqueous $NaHCO_3$and once with brine, and purified by column chromatography. The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.201 g (91%) of a colorless oil.

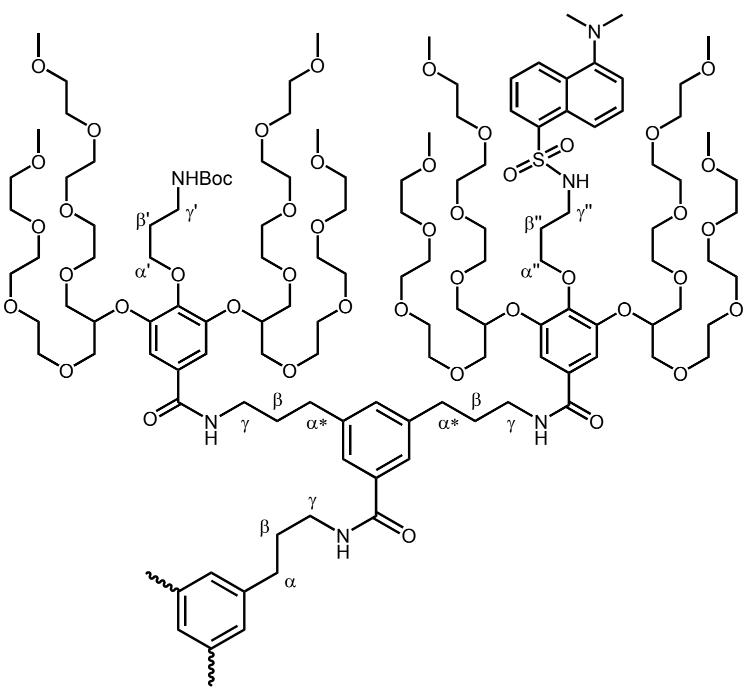
R_f = 0.12 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.26 & 1.32 (2s, 54H, $-C(CH_3)_3$), 1.82 (m, 30H, β-CH_2), 2.55 (m, 6H, α-CH_2), 2.58 (m, 12H, α^*-CH_2), 3.13 (m, 6H, γ'-CH_2), 3.24 & 3.25 (2s, 72H, -OCH_3), 3.34 (m, 18H, γ-CH_2), 3.38 (m, 12H, γ'-CH_2), 3.39-3.59 (2m, 288H, -OCH_2CH_2O), 3.62 & 3.66 (2m, 48H, -OCH(CH_2)$_2$), 3.96 (t, 12H, $^3J_{H\text{-}H}$ = 5.6 Hz, α'-CH_2), 3.94 & 4.01 & 4.12 (m, 9H, -CH_2NHBoc & -C*H*NHBoc), 4.50 (m, 12H, -OC*H*(CH$_2$)$_2$), 4.99 (s, 6H, benzyl CH_2), 5.30 (br s, 3H, -CH$_2$N*H*Boc), 5.80 (d, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, -CHN*H*Boc), 6.05 (t, 3H, $^3J_{H\text{-}H}$ = 5.8 Hz, -N*H'*), 6.80 (s, 3H, Ar-*H* Core), 7.05 (m, 3H, NH), 7.08 (s, 3H, Ar-*H* Dendron), 7.13–7.33 (br m, 33H, Ar-*H* Gallate, benzyl Ar-*H*, -N*H*), 7.40 (s, 6H, Ar-*H* Dendron).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 28.06, 28.16, 29.38, 29.58, 30.82, 30.92, 32.83, 33.03, 37.26, 38.23, 39.42, 39.45, 39.60, 42.71, 54.57, 58.70, 58.71, 66.10, 70.16, 70.22, 70.23, 70.32, 70.33, 70.52, 70.55, 70.57, 71.67, 77.20, 77.58, 77.63, 79.06, 79.32, 108.82, 108.94, 124.60, 124.66, 126.02, 127.74, 127.96, 128.22, 129.70, 131.25, 134.84, 136.74, 141.52, 141.77, 141.79, 142.18, 142.27, 151.74, 155.52, 156.26, 156.43, 166.60, 166.67, 167.63, 170.16.

MS (MALDI-TOF, dithranol): m/z = 7841.79 $[M+Na]^+$ ($C_{381}H_{639}N_{21}O_{144}Na$) calc. molecular weight peak 7841.19.

1,3,5-Tris-[3-(3-{4-(3-tert-butoxycarbonylamino-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamino}-propyl)-{5-[3-(5-dimethylamino-naphthalene-1-sulfonylamino)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzoylamino]-propyl)}benzamido propyl]–benzene ***101***



0.225 g (0.095 mmol) **97** were dissolved in 6 ml dry methylene chloride. The solution was cooled to -20°C and 0.016 g (0.104 mmol) HOBt and 0.022 g (0.151 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.010 g (0.029 mmol) **3b** and 0.5 ml dry triethylamine in 2 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvent was evaporated. The crude product was redissolved in methylene chloride, extracted twice with 1M aqueous $NaHCO_3$and once with brine, and purified by column chromatography. The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.180 g (82%) of a yellowish oil.

Alternatively, the same compound was synthesized as follows:

0.200 g (0.188 mmol) **60a** were dissolved in 10 ml dry methylene chloride. The solution was cooled to -20°C and 0.032 g (0.208 mmol) HOBt and 0.044 g (0.302 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.250 g (0.050 mmol) **110** and 0.5 ml dry triethylamine in 2 ml abs. methanol was added.

The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The crude product was extracted twice with 1M aqueous $NaHCO_3$, once with brine, and purified by column chromatography. The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.350 g (89%) of a yellowish oil.

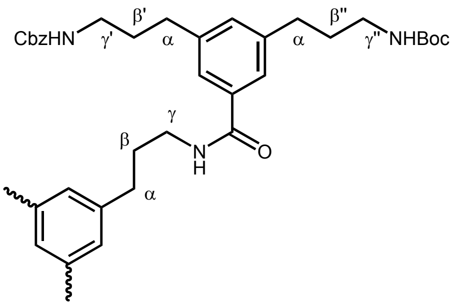
R_f = 0.19 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.36 (s, 27H, -C(C*H*$_3$)$_3$), 1.72 (m, 6H, β'-C*H*$_2$), 1.80 (m, 6H, β''-C*H*$_2$), 1.86 (m, 18H, β-C*H*$_2$), 2.56 (m, 6H, α-C*H*$_2$), 2.60 (m, 12H, α*-C*H*$_2$), 2.81 (s, 18H, -N(C*H*$_3$)$_2$), 3.18 (m, 6H, γ'-C*H*$_2$), 3.25 & 3.26 (2s, 72H, -OC*H*$_3$), 3.30 (m, 6H, γ''-C*H*$_2$), 3.35 (m, 18H, γ-C*H*$_2$), 3.40-3.58 (2m, 288H, -OC*H*$_2$C*H*$_2$O), 3.61 & 3.66 (2m, 48H, -OCH(C*H*$_2$)$_2$), 3.92 (t, 6H, $^3J_{H-H}$ = 5.4 Hz, α'-C*H*$_2$), 3.97 (t, 6H, $^3J_{H-H}$ = 5.6 Hz, α''-C*H*$_2$), 4.39 & 4.47 & 4.52 (3m, 12H, -OC*H*(CH$_2$)$_2$), 5.60 (br s, 3H, -N*H*'), 6.26 (m, 3H, -N*H*''), 6.81 (s, 3H, Ar-*H* Core), 7.10 (m, 3H, Ar-*H* Dansyl), 7.15 (m, 6H, -N*H*), 7.18 & 7.19 (2s, 12H, Ar-*H* Gallate), 7.20 (s, 3H, Ar-*H* Dendron), 7.42 (m, 9H, Ar-*H* Dansyl), 8.16 (d, 1H, $^3J_{H-H}$ = 7.2 Hz, Ar-*H* Dansyl), 8.29 (d, 1H, $^3J_{H-H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.45 (d, 1H, $^3J_{H-H}$ = 7.8 Hz, Ar-*H* Dansyl).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 28.40, 29.48, 29.79, 29.90, 30.84, 30.86, 30.95, 32.88, 33.07, 37.73, 39.47, 39.66, 40.67, 40.72, 45.28, 58.75, 70.05, 70.23, 70.24, 70.25, 70.27, 70.29, 70.33, 70.35, 70.38, 70.54, 70.63, 70.68, 70.76, 70.97, 71.70, 71.71, 71.72, 77.20, 77.68, 77.81, 78.45, 108.93, 108.99, 114.96, 119.43, 123.07, 124.68, 126.04, 127.73, 128.79, 129.60, 129.61, 129.67, 129.70, 131.28, 132.08, 134.86, 135.80, 140.28, 141.55, 141.81, 141.83, 141.85, 142.12, 142.32, 142.35, 151.67, 151.80, 151.90, 155.99, 166.66, 166.70, 167.66, 170.66.

MS (MALDI-TOF, dithranol): m/z = 7580.60 $[M+Na]^+$ ($C_{396}H_{612}N_{18}O_{135}S_3Na$) calc. molecular weight peak 7580.03.

1,3,5-Tris-[3-(3-benzyloxycarbonylamino-propyl)-5-(3-tert-butoxycarbonylamido-propyl)-benzoylamido-propyl]–benzene ***102***



2.00 g (4.25 mmol) **21a** were dissolved in 20 ml dry methylene chloride. The solution was cooled to -20°C and 0.715 g (4.67 mmol) HOBt and 0.983 g (5.14 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.425 g (1.18 mmol) **3b** and 1 ml dry triethylamine in 5 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The organic phase was extracted twice with 1M $NaHCO_3$, once with brine, and dried. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1).

Yield: 1.694 g (89%) of a colorless solid.

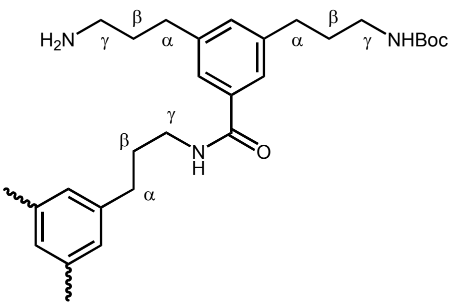
R_f = 0.30 (Silica gel; methylene chloride/ methanol 30:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.39 (s, 27H, -C(C*H*$_3$)$_3$), 1.69 (m, 6H, β''-C*H*$_2$), 1.73 (m, 6H, β'-C*H*$_2$), 1.87 (m, 6H, β-C*H*$_2$), 2.52 (m, 6H, α''-C*H*$_2$), 2.53 (m, 6H, α'-C*H*$_2$), 2.56 (m, 6H, α-C*H*$_2$), 3.01 (m, 6H, γ''-C*H*$_2$), 3.10 (m, 6H, γ'-C*H*$_2$), 3.37 (m, 6H, γ-C*H*$_2$), 4.77 (br s, 3H, -N*H*''), 5.03 (s, 6H, -C*H*$_2$Ar), 5.20 (br s, 3H, -N*H*'), 6.81 (s, 3H, Ar-*H* Core), 7.02 (s, 3H, Ar-*H* Dendron), 7.04 (br s, 3H, -N*H*), 7.22-7.30 (m, 15H, benzyl Ar-*H*), 7.36 (s, 3H, Ar-*H* Dendron), 7.38 (s, 3H, Ar-*H* Dendron).

^{13}C NMR (CD_3OD, 125 MHz): δ [ppm] = 28.18, 30.64, 30.85, 31.03, 32.22, 32.89, 39.43, 39.93, 66.17, 78.75, 124.62, 124.68, 125.89, 127.65, 127.71, 128.16, 131.25, 134.60, 136.42, 141.44, 141.48, 141.56, 155.94, 156.42, 167.63.

MS (MALDI-TOF, dithranol): m/z = 1645.99 [M+Na]$^+$ ($^{12}C_{93}{}^{1}H_{123}{}^{14}N_9{}^{16}O_{15}{}^{23}Na$) calc. monoisotopic peak 1629.99.

1,3,5-Tris-[3-(3-amino-propyl)-5-(3-tert-butoxycarbonylamido-propyl)-benzoylamido-propyl]–benzene ***103b***



1.017 g (0.632 mmol) **102** were dissolved in 10 ml ethylacetate/ ethanol (1:1). 0.101 g Pd/ C were added. The mixture was stirred for five hours in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. No further purification.

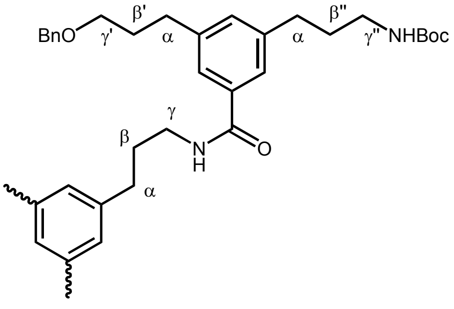
Yield: 0.754 g (99%) of a colorless solid.

^{1}H NMR (CD_3OD, 500 MHz): δ [ppm] = 1.35 (s, 27H, -C(C*H*$_3$)$_3$), 1.72 (m, 6H, β-C*H*$_2$), 1.86 (m, 6H, β-C*H*$_2$), 1.94 (m, 6H, β-C*H*$_2$), 2.57 (m, 12H, α-C*H*$_2$), 2.68 (t, 6H, $^3J_{H\text{-}H}$ = 7.7 Hz, α-C*H*$_2$), 2.88 (m, 6H, γ-C*H*$_2$), 2.97 (m, 6H, γ-C*H*$_2$), 3.32 (m, 6H, γ-C*H*$_2$), 6.85 (s, 3H, Ar-*H* Core), 7.19 (s, 3H, Ar-*H* Dendron), 7.42 (s, 3H, Ar-*H* Dendron), 7.45 (s, 3H, Ar-*H* Dendron).

^{13}C NMR (CD_3OD, 125 MHz): δ [ppm] = 28.84, 29.97, 32.07, 32.48, 33.24, 33.74, 34.28, 40.27, 40.78, 40.91, 79.79, 125.93, 126.32, 127.20, 132.78, 136.08, 142.28, 143.10, 143.87, 158.40, 170.08.

MS (MALDI-TOF, CCA): m/z = 1204.46 $[M+H]^+$ ($^{12}C_{69}{}^{1}H_{106}{}^{14}N_9{}^{16}O_9$) calc. monoisotopic peak 1204.81; 904.58 $[M+H\text{-}2^*Boc]^+$ ($^{12}C_{54}{}^{1}H_{82}{}^{14}N_9{}^{16}O_3$) calc. monoisotopic peak 904.65.

1,3,5-Tris-[3-(3-benzyloxy-propyl)-5-(3-tert-butoxycarbonylamido-propyl)-benzoylamido-propyl]–benzene ***104***



1.06 g (2.48 mmol) **21b** were dissolved in 20 ml dry methylene chloride. The solution was cooled to -20°C and 0.456 g (2.97 mmol) HOBt and 0.626 g (3.27 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.270 g (0.75 mmol) **3b** and 1 ml dry triethylamine in 5 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The organic phase was extracted twice with 1M $NaHCO_3$, once with brine, and dried. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1).

Yield: 1.031 g (93%) of a colorless solid.

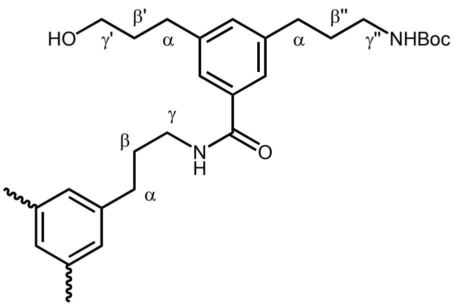
R_f = 0.28 (Silica gel; methylene chloride/ methanol 40:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.40 (s, 27H, -C(CH_3)$_3$), 1.69 (m, 6H, β”-CH_2), 1.84 (m, 6H, β’-CH_2), 1.86 (m, 6H, β-CH_2), 2.53 (m, 6H, α”-CH_2), 2.56 (m, 6H, α-CH_2), 2.63 (m, 6H, α’-CH_2), 3.04 (m, 6H, γ”-CH_2), 3.37 (m, 6H, γ-CH_2), 3.41 (t, 2H, $^3J_{H\text{-}H}$ = 6.2 Hz, γ’-CH_2), 4.45 (s, 6H, -CH_2Ar), 4.75 (br s, 3H, -N*H*”), 6.80 (s, 3H, Ar-*H* Core), 6.95 (br s, 3H, -N*H*), 7.04 (s, 3H, Ar-*H* Dendron), 7.21-7.32 (m, 15H, benzyl Ar-*H*), 7.37 (s, 3H, Ar-*H* Dendron), 7.42 (s, 3H, Ar-*H* Dendron).

^{13}C NMR (CD_3OD, 125 MHz): δ [ppm] = 28.19, 30.76, 30.98, 31.16, 31.98, 32.28, 32.88, 39.39, 69.16, 72.59, 78.74, 124.37, 124.80, 125.90, 127.26, 127.35, 128.09, 131.33, 134.56, 138.28, 141.40, 141.45, 142.21, 155.90, 167.60.

MS (MALDI-TOF, dithranol): m/z = 1499.71 $[M+Na]^+$ ($^{12}C_{90}{}^1H_{120}{}^{14}N_6{}^{16}O_{12}{}^{23}Na$) calc. monoisotopic peak 1499.89; 1515.67 $[M+K]^+$ ($^{12}C_{90}{}^1H_{120}{}^{14}N_6{}^{16}O_{12}{}^{39}K$) calc. monoisotopic peak 1515.86.

*1,3,5-Tris-[3-(3-amino-propyl)-5-(3-tert-butoxycarbonylamido-propyl)-benzoylamido-propyl]–benzene **105***



0.500 g (0.338 mmol) **104** were dissolved in 10 ml ethylacetate/ ethanol (1:1). 0.101 g Pd/ C were added. The mixture was stirred for three hours in a hydrogen atmosphere. The reaction was monitored with TLC.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. No further purification.

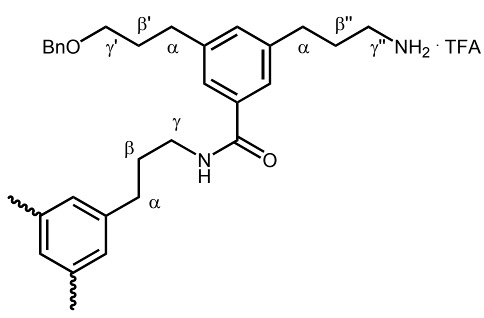
Yield: 0.451 g (96%) of a colorless solid.

^{1}H NMR (CDCl$_3$, 500 MHz): δ [ppm] = 1.33 (s, 27H, -C(C*H*$_3$)$_3$), 1.66 (m, 6H, β”-C*H*$_2$), 1.72 (m, 6H, β’-C*H*$_2$), 1.83 (m, 6H, β-C*H*$_2$), 2.50 (m, 6H, α”-C*H*$_2$), 2.54 (m, 6H, α-C*H*$_2$), 2.56 (m, 6H, α-C*H*$_2$), 2.96 (t, 6H, $^3J_{H\text{-}H}$ = 6.9 Hz, γ”-C*H*$_2$), 3.31 (t, 6H, $^3J_{H\text{-}H}$ = 6.8 Hz, γ-C*H*$_2$), 3.36 (m, 3H, -O*H*), 3.45 (t, 6H, $^3J_{H\text{-}H}$ = 6.3 Hz, γ-C*H*$_2$), 6.80 (s, 3H, Ar-*H* Core), 7.01 (s, 3H, Ar-*H* Dendron), 7.27 (s, 3H, Ar-*H* Dendron), 7.28 (s, 3H, Ar-*H* Dendron).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 28.34, 30.76, 31.22, 31.68, 32.45, 33.09, 33.83, 39.64, 53.34, 61.21, 79.00, 124.66, 124.85, 126.03, 131.59, 134.52, 141.62, 142.34, 155.21, 168.08.

MS (MALDI-TOF, dithranol): m/z = 1229.75 [M+Na]$^+$ ($^{12}C_{69}{}^{1}H_{102}{}^{14}N_6{}^{16}O_{12}{}^{23}Na$) calc. monoisotopic peak 1229.74; 1245.74 [M+K]$^+$ ($^{12}C_{69}{}^{1}H_{102}{}^{14}N_6{}^{16}O_{12}{}^{39}K$) calc. monoisotopic peak 1245.72.

*1,3,5-Tris-[3-(3-benzyloxy-propyl)-5-(trifluoro-acetato-3-amoniumpropyl)-benzoylamido-propyl]–benzene **106***



0.500 g (0.338 mmol) **104** were dissolved in 10 ml methylene chloride and 5 ml TFA were added at room temperature.

The deprotection was monitored with ^{1}H-NMR. The solvent was evaporated and remaining TFA was removed by co-evaporation with methylene chloride. The sample was dried in high vacuum. No further purification.

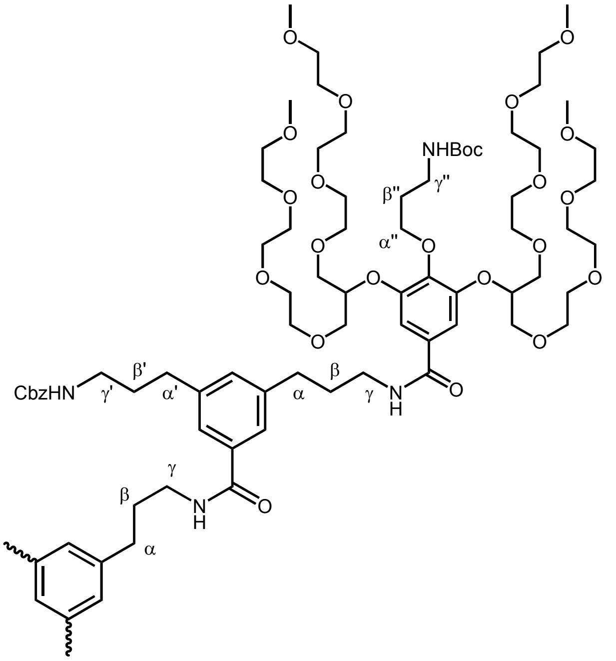
Yield: 0.503 g (98%) of a colorless solid.

^{1}H NMR (CDCl$_3$, 500 MHz): δ [ppm] = 1.81 (m, 12H, β’-C*H*$_2$), 1.87 (m, 6H, β-C*H*$_2$), 2.52 (m, 12H, α- & α’-C*H*$_2$), 2.59 (t, 6H, $^3J_{H\text{-}H}$ = 7.7 Hz, α’-C*H*$_2$), 2.77 (m, 6H, γ-C*H*$_2$), 3.29 (m, 6H, γ’-C*H*$_2$), 3.40 (m, 6H, γ’-C*H*$_2$), 6.77 (s, 3H, Ar-*H* Core), 7.00 (s, 3H, Ar-*H* Dendron), 7.17-7.30 (m, 15H, benzyl Ar-*H*), 7.27 (s, 3H, Ar-*H* Dendron), 7.35 (s, 3H, Ar-*H* Dendron).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 30.43, 30.83, 31.83, 31.85, 32.87, 38.70, 39.45, 69.23, 72.66, 124.08, 125.02, 125.89, 127.43, 127.49, 128.11, 131.42, 134.56, 137.90, 140.33, 141.53, 142.55, 168.40.

MS (MALDI-TOF, dithranol): m/z = 1177.85 [M+H]$^+$ ($^{12}C_{75}{}^{1}H_{97}{}^{14}N_6{}^{16}O_6$) calc. monoisotopic peak 1177.75; 1199.83 [M+Na]$^+$ ($^{12}C_{75}{}^{1}H_{96}{}^{14}N_6{}^{16}O_6{}^{23}Na$) calc. monoisotopic peak 1199.73.

1,3,5-Tris-[3-(3-benzyloxycarbonylamino-propyl)-5-(3-{4-(3-tert-butoxy carbonylamido-propoxy)-3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy} propan-2-yloxy)-benzoylamido}-propyl)-benzoylamido-propyl]–benzene ***107***



0.300 g (0.280 mmol) **60a** were dissolved in 10 ml dry methylene chloride. The solution was cooled to -20°C and 0.048 g (0.313 mmol) HOBt and 0.066 g (0.345 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.133 g (0.080 mmol) **103** and 0.5 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1), but purification with column chromatography turned out to be very difficult.

Alternatively, the compound was synthesized as follows:

0.204 g (0.144 mmol) **91** were dissolved in 7 ml dry methylene chloride. The solution was cooled to -20°C and 0.025 g (0.163 mmol) HOBt and 0.034 g (0.180 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.015 g (0.042 mmol) **3b** and 0.5 ml dry triethylamine in 1.5 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The organic phase was extracted twice with 1M $NaHCO_3$, once with brine, and dried. The solvents were evaporated under reduced pressure. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The colorless oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.178 g (96%) of a yellowish oil.

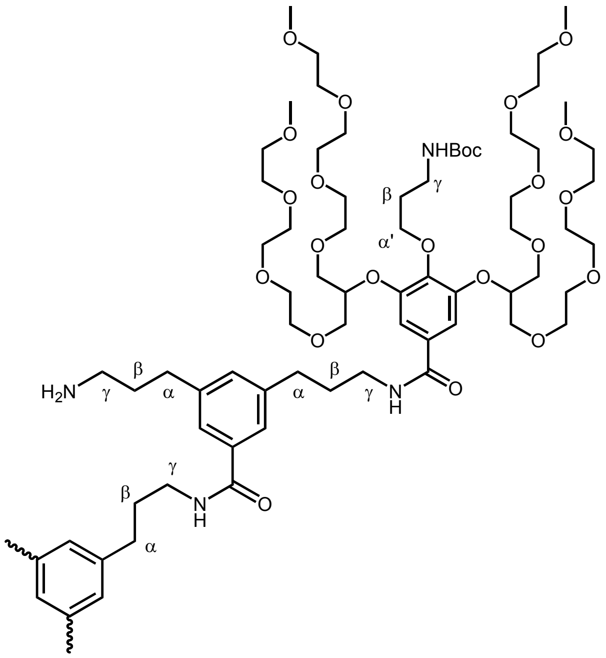
R_f = 0.23 (Silica gel; methylene chloride/ methanol 30:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.38 (s, 27H, -C(C*H*$_3$)$_3$), 1.71 (m, 6H, β'-C*H*$_2$), 1.85 (m, 18H, β-C*H*$_2$ & β''-C*H*$_2$), 2.51 (t, 6H, $^3J_{H\text{-}H}$ = 7.4 Hz, α'-C*H*$_2$), 2.58 (m, 12H, α-C*H*$_2$), 3.07 (m, 6H, γ'-C*H*$_2$), 3.28 (s, 36H, -OC*H*$_3$), 3.34 (m, 18H, γ-C*H*$_2$ & γ''-C*H*$_2$), 3.43-3.59 (2m, 144H, -OC*H*$_2$C*H*$_2$O), 3.66 (m, 24H, -OCH(C*H*$_2$)$_2$), 3.98 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, α''-C*H*$_2$), 4.53 (quint, 6H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OC*H*(CH$_2$)$_2$), 4.99 (s, 6H, -C*H*$_2$Ar), 5.31 (s, 3H, -N*H*'), 5.60 (s, 3H, -N*H*''), 6.83 (s, 3H, Ar-*H* Core), 7.00 (s, 3H, -N*H*), 7.04 (s, 3H, Ar-*H* Dendron), 7.12 (s, 3H, -N*H*), 7.20 (s, 6H, Ar-*H* Gallate), 7.24 (m, 15H, benzyl Ar-*H*), 7.32 (s, 3H, Ar-*H* Dendron), 7.39 (s, 3H, Ar-*H* Dendron).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 28.08, 29.50, 30.33, 30.37, 30.64, 32.02, 32.43, 32.71, 37.43, 39.00, 39.16, 39.72, 58.39, 65.86, 69.89, 69.90, 69.93, 69.96, 70.04, 70.31, 70.65, 71.38, 77.20, 77.29, 78.07, 108.52, 124.34, 124.46, 125.78, 127.37, 127.46, 127.94, 129.37, 130.93, 134.45, 136.30, 141.20, 141.34, 141.43, 141.93, 151.47, 155.67, 156.21, 166.40, 167.33.

MS (MALDI-TOF, dithranol): m/z = 4456.51 $[M+Na]^+$ ($C_{225}H_{360}N_{12}O_{75}Na$) calc. molecular weight peak 4456.29.

1,3,5-Tris-[3-(3-amino-propyl)-5-(3-{4-(3-tert-butoxycarbonylamido-propoxy)-3,5-bis (1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)-benzoylamido}-propyl)-benzoylamido-propyl]–benzene ***108***



0.170 g (0.038 mmol) **107** were dissolved in 5 ml ethylacetate/ ethanol (1:1). 0.020 g Pd/ C were added. The mixture was stirred for three hours in a hydrogen atmosphere. The reaction was monitored with ^{1}H-NMR.

After complete deprotection the mixture was filtrated and the solvent removed under reduced pressure. No further purification.

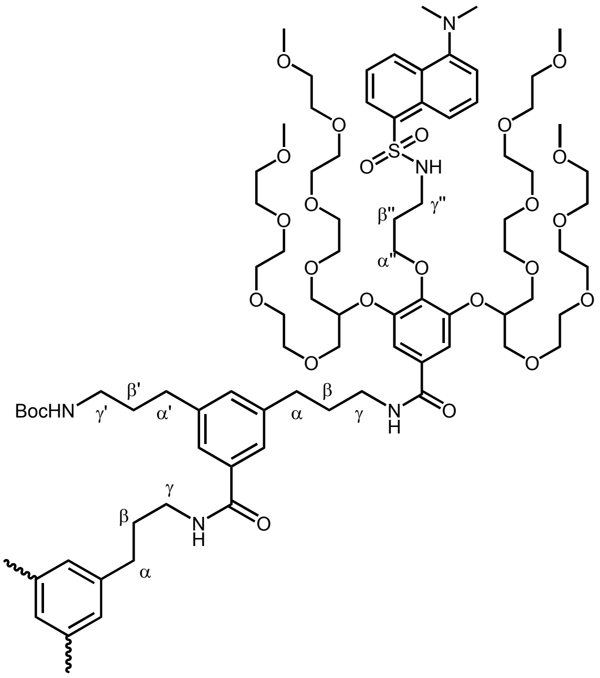
Yield: 0.152 g (98%) of a yellowish oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.32 (s, 27H, $-\mathrm{C}(\mathrm{C}H_3)_3$), 1.75 (br s, 12H, β-$\mathrm{C}H_2$), 1.83 (br s, 12H, β-$\mathrm{C}H_2$), 2.34 (br s, 6H, α-$\mathrm{C}H_2$), 2.48 (br s, 12H, α-$\mathrm{C}H_2$), 2.64 (m, 6H, γ-$\mathrm{C}H_2$), 3.21 (s, 36H, $-\mathrm{OC}H_3$), 3.25 (m, 18H, γ-$\mathrm{C}H_2$), 3.32-3.57 (m, 144H, $-\mathrm{O}\mathrm{C}H_2\mathrm{C}H_2\mathrm{O}$), 3.64 (m, 24H, $-\mathrm{OCH}(\mathrm{C}H_2)_2$), 3.93 (m, 6H, α'-$\mathrm{C}H_2$), 4.69 (m, 6H, $-\mathrm{OC}H(\mathrm{CH}_2)_2$), 5.57 (s, 3H, -N*H*), 6.79 (s, 3H, Ar-*H* Core), 6.88 (s, 3H, -N*H*), 7.28 (s, 3H, Ar-*H* Dendron), 7.31 (s, 3H, -N*H*), 7.35 (s, 6H, Ar-*H* Gallate), 7.83 (s, 6H, Ar-*H* Dendron).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 27.92, 28.25, 29.75, 30.49, 31.78, 32.72, 33.17, 37.60, 39.07, 39.33, 39.59, 58.59, 67.79, 70.03, 70.07, 70.09, 70.14, 70.50, 70.79, 71.45, 78.31, 108.38, 124.06, 125.36, 125.94, 129.36, 131.00, 134.53, 139.87, 141.68, 141.77, 142.02, 151.44, 155.86, 166.32, 167.37.

MS (MALDI-TOF, dithranol): m/z = 4031.32 $[M+H]^+$ ($C_{201}H_{343}N_{12}O_{69}$) calc. molecular weight peak 4031.91.

1,3,5-Tris-[3-(3-tert-butoxycarbonylamino-propyl)-5-({4-[3-(5-dimethylamino-naphthalene-1-sulfonylamido)-propoxy]}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy) ethoxy]ethoxy}propan-2-yloxy)]benzoylamido-propyl)-benzoylamido-propyl]–benzene ***109***



0.965 g (0.808 mmol) **63** were dissolved in 30 ml dry methylene chloride. The solution was cooled to -20°C and 0.144 g (0.940 mmol) HOBt and 0.194 g (1.014 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.250 g (0.207 mmol) **103b** and 0.3 ml dry triethylamine in 3 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 25:1). The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.950 g (97%) of a yellowish oil.

R_f = 0.29 (Silica gel; methylene chloride/ methanol 25:1).

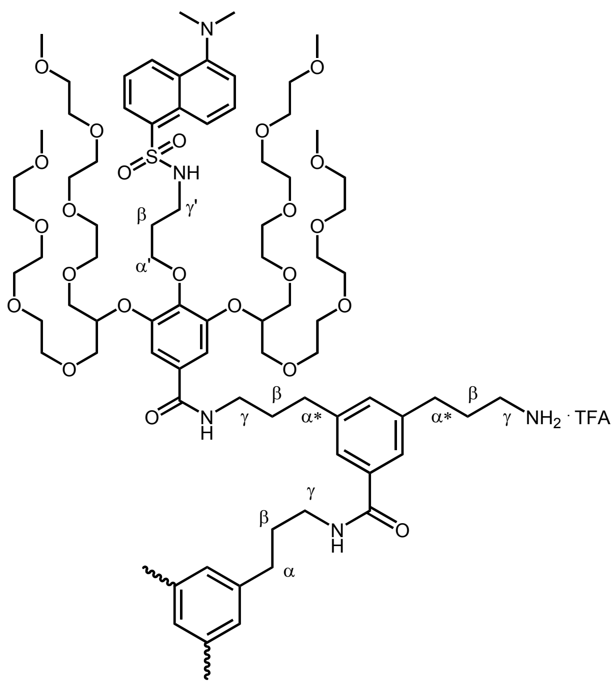
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.32 (s, 27H, -C(CH_3)$_3$), 1.64 (m, 6H, β'-CH_2), 1.70 (m, 6H, β''-CH_2), 1.83 (m, 12H, β-CH_2), 2.47 (t, 6H, $^3J_{H\text{-}H}$ = 7.4 Hz, α'-CH_2), 2.54 (m, 12H, α-CH_2), 2.77 (s, 18H, -N(CH_3)$_2$), 2.96 (m, 6H, γ'-CH_2), 3.15 (m, 6H, γ''-CH_2), 3.23 (s, 36H, -OCH_3), 3.32 (m, 12H, γ-CH_2), 3.37-3.52 (2m, 144H, -OCH_2CH_2O), 3.58 (d, 24H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH_2)$_2$), 3.89 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, α''-CH_2), 4.46 (quint, 6H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH$_2$)$_2$), 4.91 (t, 3H, $^3J_{H\text{-}H}$ = 5.6 Hz, -NH'), 6.28 (t, 3H, $^3J_{H\text{-}H}$ = 6.3 Hz, -NH''), 6.79 (s, 3H, Ar-H Core), 7.01 (s, 3H, Ar-H Dendron), 7.04 (d, 3H, $^3J_{H\text{-}H}$ = 7.6 Hz Ar-H Dansyl), 7.09 (t, 3H, $^3J_{H\text{-}H}$ = 5.5 Hz, -NH), 7.17 (s, 6H, Ar-H Gallate), 7.23 (t, 3H, $^3J_{H\text{-}H}$ = 5.6 Hz, -NH), 7.32 (s, 3H, Ar-H Dendron), 7.36 (m, 3H, Ar-H

Dansyl), 7.36 (s, 3H, Ar-*H* Dendron), 7.41 (dd, 3H, $^3J_{H\text{-}H}$ = 8.5 Hz, $^3J_{H\text{-}H}$ = 7.4 Hz, Ar-*H* Dansyl), 8.14 (dd, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, $^4J_{H\text{-}H}$ = 1.1 Hz, Ar-*H* Dansyl), 8.25 (d, 3H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.41 (d, 3H, $^3J_{H\text{-}H}$ = 8.4 Hz, Ar-*H* Dansyl).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 27.81, 29.50, 30.25, 30.70, 31.92, 32.30, 32.56, 38.92, 39.02, 39.09, 40.20, 44.71, 58.15, 69.66, 69.70, 69.72, 69.75, 69.82, 70.04, 70.22, 71.17, 77.19, 78.03, 108.43, 114.42, 118.80, 122.52, 124.24, 125.55, 127.26, 128.24, 129.08, 129.19, 129.26, 130.72, 134.22, 135.35, 141.15, 141.23, 141.58, 151.06, 151.16, 155.55, 166.17, 167.11.

MS (MALDI-TOF, dithranol): m/z = 4754.01 $[M+Na]^+$ ($C_{237}H_{375}N_{15}O_{75}S_3Na$) calc. molecular weight peak 4754.01; 4428.57 $[M+H]^+$ ($^{12}C_{222}{}^1H_{352}{}^{14}N_{15}{}^{16}O_{69}{}^{32}S_3$) calc. monoisotopic peak 4428.37.

1,3,5-Tris-[3-(3-amino-propyl)-5-({4-[3-(5-dimethylamino-naphthalene-1-sulfonylamido)-propoxy]}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy} propan-2-yloxy)]benzoylamido-propyl)-benzoylamido-propyl]–benzene tris-hydrotrifluoro acetate ***110***



0.655 g (0.138 mmol) **109** were dissolved in 10 ml dry methylene chloride and 5 ml TFA were added at room temperature. The deprotection was monitored with ^{1}H-NMR.

After complete conversion, the solvents were evaporated and dried in high vacuum. No further purification.

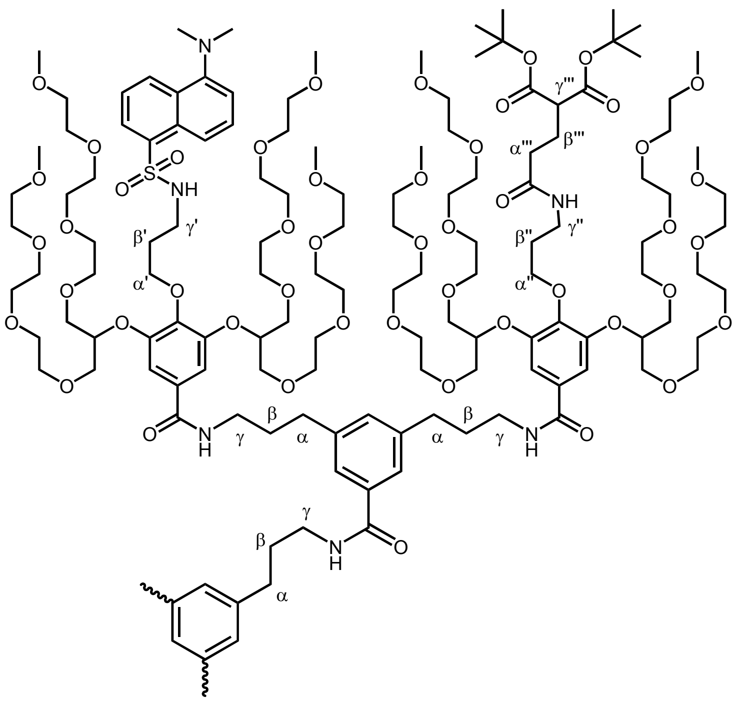
Yield: 0.658 g (99%) of a yellowish oil.

^{1}H NMR (CD_3OD, 500 MHz): δ [ppm] = 1.75 (m, 6H, β”-C*H*$_2$), 1.87 (m, 18H, β-C*H*$_2$), 2.57 (m, 6H, α-C*H*$_2$), 2.61 (m, 6H, α’-C*H*$_2$), 2.65 (t, 6H, $^3J_{H\text{-}H}$ = 7.6 Hz, α-C*H*$_2$), 2.85 (m, 6H, γ-C*H*$_2$), 2.88 (s, 18H, -N(C*H*$_3$)$_2$), 3.12 (t, 6H, $^3J_{H\text{-}H}$ = 7.1 Hz, γ”-C*H*), 3.24 (s, 36H, -OC*H*$_3$), 3.26 (sept, 3H, $^4J_{H\text{-}H}$ = 1.7 Hz, -N$^+$*H*(C*H*$_3$)$_2$), 3.33 (t, 12H, $^3J_{H\text{-}H}$ = 6.4 Hz , γ-C*H*$_2$), 3.39-3.52 (2m, 144H, -OC*H*$_2$C*H*$_2$O), 3.59 (m, 24H, -OCH(C*H*$_2$)$_2$), 3.96 (t, 6H, $^3J_{H\text{-}H}$ = 5.7 Hz, α''-C*H*$_2$), 4.52 (quint, 6H, $^3J_{H\text{-}H}$ = 4.8 Hz, -OC*H*(CH$_2$)$_2$), 6.86 (s, 3H, Ar-*H* Core), 7.16 (s, 3H, Ar-*H* Dendron), 7.17 (s, 6H, Ar-*H* Gallate), 7.28 (d, 3H, $^3J_{H\text{-}H}$ = 7.6 Hz Ar-*H* Dansyl), 7.43 (m, 6H, Ar-*H* Dendron), 7.53 (dd, 3H, $^3J_{H\text{-}H}$ = 8.7 Hz, $^3J_{H\text{-}H}$ = 7.7 Hz Ar-*H* Dansyl), 7.57 (dd, 3H, $^3J_{H\text{-}H}$ = 8.5 Hz, $^3J_{H\text{-}H}$ = 7.4 Hz Ar-*H* Dansyl), 8.18 (dd, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, $^4J_{H\text{-}H}$ = 1.1 Hz, Ar-*H* Dansyl), 8.36 (d, 3H, $^3J_{H\text{-}H}$ = 8.7 Hz, Ar-*H* Dansyl), 8.50 (d, 3H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 29.92, 31.57, 31.89, 31.92, 32.12, 33.20, 33.99, 34.28, 40.29, 40.58, 40.79, 41.79, 46.17, 59.07, 71.19, 71.38, 71.84, 71.99, 72.82, 78.97, 109.68, 117.12, 121.91, 125.05, 126.06, 126.26, 126.28, 127.28, 129.06, 130.22, 130.37, 130.50, 130.65, 130.91, 132.71, 136.18, 137.55, 142.30, 143.18, 143.34, 143.76, 151.08, 153.21, 168.92, 169.88.

MS (MALDI-TOF, CCA): m/z = 4450.63 [M+Na]$^+$ ($^{12}C_{222}{}^{1}H_{351}{}^{14}N_{15}{}^{16}O_{69}{}^{32}S_{3}{}^{23}Na$) calc. monoisotopic peak 4450.35; 4428.57 [M+H]$^+$ ($^{12}C_{222}{}^{1}H_{352}{}^{14}N_{15}{}^{16}O_{69}{}^{32}S_{3}$) calc. monoisotopic peak 4428.37.

1,3,5-Tris-[3-({4-[3-(5-dimethylamino-naphthalene-1-sulfonylamido)-propoxy]}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]amido-propyl)-5-{[4-{3-[di-tert-butyl-2-(2-carbamoylethyl)malonyl]-propoxy}]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]benzoyl amido-propyl}-benzoylamido-propyl]–benzene ***111***



0.143 g (0.110 mmol) **74** were dissolved in 7 ml dry methylene chloride. The solution was cooled to -20°C and 0.019 g (0.124 mmol) HOBt and 0.026 g (0.136 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.150 g (0.031 mmol) **110** and 1 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.235 g (94%) of a greenish oil.

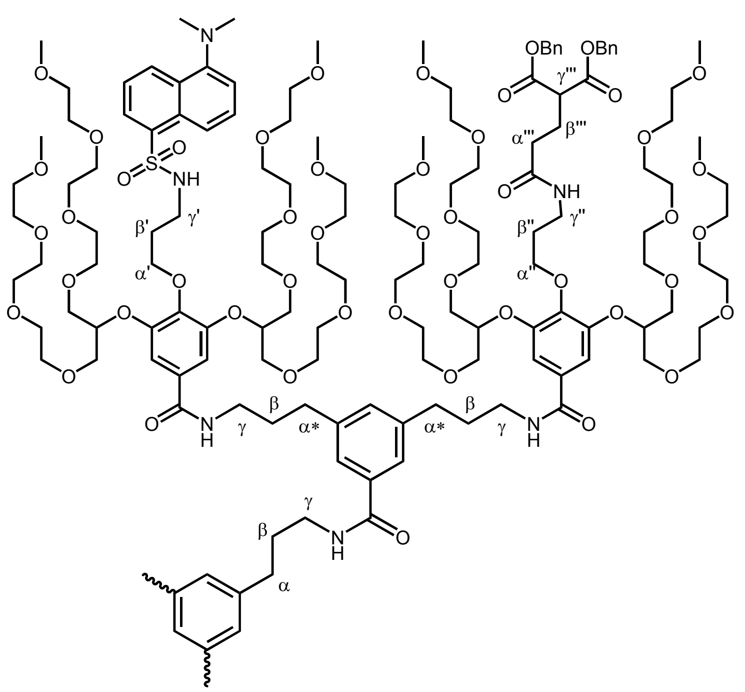
R_f = 0.27 (Silica gel; methylene chloride/ methanol 15:1).

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.31 (s, 54H, -C(CH_3)$_3$), 1.67 (m, 6H, β''-CH_2), 1.77 (m, 6H, β'-CH_2), 1.80 (m, 18H, β-CH_2), 1.97 (m, 6H, β'''-CH_2), 2.09 (m, 6H, α'''-CH_2), 2.52 (m, 18H, α-CH_2), 2.74 (s, 18H, -N(CH_3)$_2$), 3.08 (t, 3H, $^3J_{H\text{-}H}$ = 4.9 Hz, γ'''-CH), 3.11 (m, 6H, γ''-CH_2), 3.19 & 3.20 (2s, 72H, -OCH_3), 3.28 (m, 18H, γ-CH_2), 3.33-3.52 (2m, 288H, -OCH_2CH_2O), 3.36 (m, 6H, γ'-CH_2), 3.54 & 3.59 (2m, 48H, -OCH(CH_2)$_2$), 3.87 (t, 6H, $^3J_{H\text{-}H}$ = 5.4 Hz, α''-CH_2), 3.93 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, α'-CH_2), 4.41 (quint, 6H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OC*H*(CH_2)$_2$), 4.45 (quint, 6H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OC*H*(CH_2)$_2$), 6.22 (t, 3H, $^3J_{H\text{-}H}$ = 6.1 Hz, -N*H*''), 6.67 (t, 3H, $^3J_{H\text{-}H}$ = 5.7 Hz, -N*H*'), 6.76 (s, 3H, Ar-*H* Core), 7.01 (s, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, Ar-*H* Dansyl), 7.04 (s, 3H, Ar-*H* Dendron), 7.08 (m, 3H, -N*H*), 7.12 (m, 6H, -N*H*), 7.14 & 7.15 (2s, 12H, Ar-*H* Gallate), 7.33 (m, 3H, Ar-*H* Dansyl), 7.35 (m, 6H, Ar-*H* Dendron), 7.39 (m, 3H, Ar-*H* Dansyl), 8.11 (d, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, Ar-*H* Dansyl), 8.23 (d, 3H, $^3J_{H\text{-}H}$ = 8.8 Hz, Ar-*H* Dansyl), 8.38 (d, 3H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 24.10, 27.51, 29.27, 29.69, 30.57, 32.59, 32.78, 33.10, 36.74, 39.18, 39.32, 40.44, 45.01, 52.77, 70.00, 70.02, 70.12, 70.32, 70.38, 70.53, 71.15, 71.46, 77.43, 77.54, 80.87, 108.73, 108.80, 114.69, 119.09, 122.79, 124.42, 124.50, 125.86, 127.52, 128.53, 129.36, 129.46, 129.52, 131.05, 134.60, 135.57, 141.35, 141.54, 141.86, 142.08, 151.30, 151.43, 151.51, 166.42, 167.43, 168.09, 171.44.

MS (MALDI-TOF, CCA): m/z = 8088.55 $[M+K]^+$ ($^{12}C_{395}{}^{1}H_{654}{}^{14}N_{18}{}^{16}O_{144}{}^{32}S_{3}{}^{39}K$) calc. monoisotopic peak 8089.32.

1,3,5-Tris-[3-({4-[3-(5-dimethylamino-naphthalene-1-sulfonylamido)-propoxy]}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]benzoylamido-propyl)-5-{[4-{3-[dibenzyl-2-(2-carbamoylethyl)malonyl]-propoxy}]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]benzoylamido-propyl}-benzoylamido-propyl]–benzene ***112***



0.143 g (0.110 mmol) **112** were dissolved in 7 ml dry methylene chloride. The solution was cooled to -20°C and 0.019 g (0.124 mmol) HOBt and 0.026 g (0.136 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.150 g (0.031 mmol) **110** and 1 ml dry triethylamine in 1 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 15:1). The greenish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.190 g (74%) of a greenish oil.

R_f = 0.24 (Silica gel; methylene chloride/ methanol 15:1).

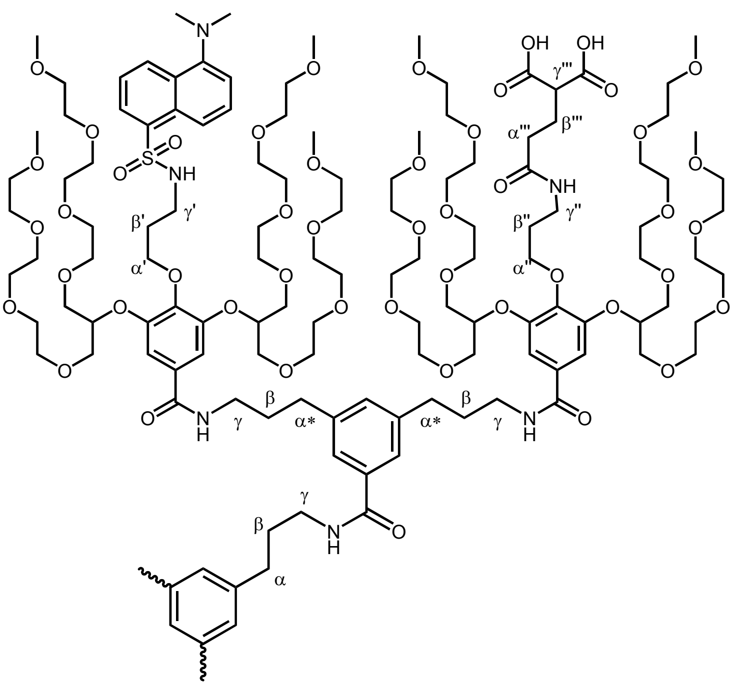
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.77 (m, 6H, β''-CH_2), 1.85 (m, 6H, β'-CH_2), 1.91 (m, 12H, β-CH_2), 2.24 (m, 12H, α'''-CH_2 & β'''-CH_2), 2.61 (m, 6H, α-CH_2), 2.65 (m, 6H, α*-CH_2), 3.22 (m, 6H, γ''-CH_2), 3.30 (s, 90H, -OCH_3 & -N(CH_3)$_2$), 3.42 (m, 18H, γ-CH_2), 3.45-3.61 (2m, 288H, -OCH_2CH_2O), 3.62 (m, 3H, γ'''-CH_2), 3.66 & 3.69 (2m, 48H, -OCH(CH_2)$_2$), 3.96 (t, 6H, $^3J_{H-H}$ = 5.4 Hz, α''-CH_2), 4.01 (t, 6H, $^3J_{H-H}$ = 5.6 Hz, α'-CH_2), 4.54 (q, 6H, $^3J_{H-H}$ = 4.9 Hz, -OCH(CH$_2$)$_2$),4.57 (q, 6H, $^3J_{H-H}$ = 5.0 Hz,

-OC*H*(CH$_2$)$_2$), 5.09 (m, 12H, -OC*H*$_2$Ar), 6.42 (br s, 3H, -N*H*''), 6.82 (t, 3H, $^3J_{H\text{-}H}$ = 5.6 Hz, -N*H*'), 6.86 (s, 3H, Ar-*H* Core), 7.13 (m, 3H, -N*H*), 7.15 (s, 3H, Ar-*H* Dendron), 7.25 (s, 12H, Ar-*H* Gallate), 7.22-7.28 (m, 39H, Ar-*H* Dansyl, benzyl Ar-*H*, -N*H*), 7.47 (m, 6H, Ar-*H* Dendron), 7.49 (m, 6H, Ar-*H* Dansyl), 8.22 (d, 3H, $^3J_{H\text{-}H}$ = 7.4 Hz, Ar-*H* Dansyl), 8.38 (m, 3H, Ar-*H* Dansyl), 8.56 (m, 3H, Ar-*H* Dansyl).

^{13}C NMR (CDCl$_3$, 125 MHz): δ [ppm] = 24.18, 29.29, 29.78, 30.66, 30.70, 30.75, 32.69, 32.81, 32.89, 36.86, 39.27, 39.32, 39.46, 40.54, 45.12, 50.76, 58.58, 66.66, 70.09, 70.10, 70.11, 70.12, 70.22, 70.40, 70.45, 70.62, 71.28, 71.56, 77.20, 77.56, 77.69, 108.88, 108.96, 114.82, 119.23, 122.92, 124.49, 124.58, 125.92, 127.59, 127.70, 127.93, 128.19, 128.64, 129.46, 129.56, 129.58, 131.13, 134.73, 135.08, 135.66, 141.42, 141.61, 141.65, 142.02, 142.21, 151.54, 151.61, 166.51, 166.53, 167.48, 168.50, 171.14.

MS (MALDI-TOF, CCA): m/z = 8305.72 [M+K]$^+$ (^{12}C$_{414}$^{1}H$_{642}$^{14}N$_{18}$^{16}O$_{144}$^{32}S$_3$^{39}K) calc. monoisotopic peak 8305.23; 8289.92 [M+Na]$^+$ (^{12}C$_{414}$^{1}H$_{642}$^{14}N$_{18}$^{16}O$_{144}$^{32}S$_3$^{23}Na) calc. monoisotopic peak 8289.25.

1,3,5-Tris-[3-({4-[3-(5-dimethylamino-naphthalene-1-sulfonylamido)-propoxy]}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]benzoylamido-propyl)-5-{[4-{3-[2-(2-carbamoylethyl)malonato]-propoxy}]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)]benzoylamido-propyl}-benzoylamido-propyl]–benzene ***113***



0.200 g (0.025 mmol) **111** were dissolved in 7 ml methylene chloride and 4 ml TFA was added at room temperature.

The deprotection was monitored with ^{1}H-NMR. The solvent was evaporated. Remaining TFA was removed by coevaporation with methylene chloride. The sample was dried in high vacuum. No further purification.

Yield: 0.186 g (97%) of a colorless oil.

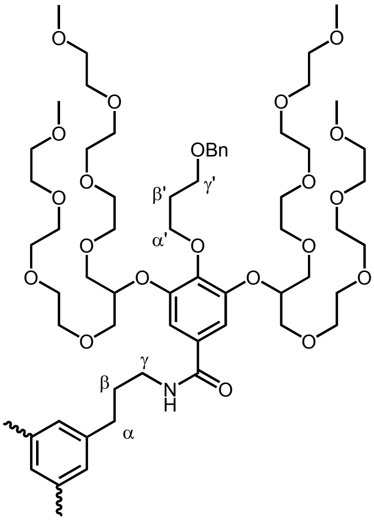
^{1}H NMR (CD$_3$OD, 500 MHz): δ [ppm] = 1.61 (m, 6H, β''-CH_2), 1.74 (m, 24H, β-CH_2 & β'-CH_2), 1.96 (m, 6H, β'''-CH_2), 2.13 (m, 6H, α'''-CH_2), 2.45 (t, 6H, $^3J_{H\text{-}H}$ = 7.2 Hz, α-CH_2), 2.52 (m, 12H, $^3J_{H\text{-}H}$ = 6.8 Hz, α*-CH_2), 3.03 (t, 6H, $^3J_{H\text{-}H}$ = 6.9 Hz, γ''-CH_2), 3.11 (s, 18H, -N(CH_3)$_2$), 3.12 (2s, 72H, -OCH_3), 3.21 (m, 21H, γ'''-CH & γ-CH_2), 3.26 (m, 6H, γ'-CH_2), 3.27-3.42 (2m, 288H, -OCH_2CH_2O), 3.45 & 3.56 (2m, 48H, -OCH(CH_2)$_2$), 3.80 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, α''-CH_2), 3.92 (t, 6H, $^3J_{H\text{-}H}$ = 5.6 Hz, α'-CH_2), 4.37 (q, 6H, $^3J_{H\text{-}H}$ = 5.0 Hz, -OCH(CH$_2$)$_2$), 4.45 (q, 6H, $^3J_{H\text{-}H}$ = 4.9 Hz, -OCH(CH$_2$)$_2$), 6.74 (s, 3H, Ar-*H* Core), 7.05 (s, 6H, Ar-*H* Gallate), 7.09 (s, 3H, Ar-*H* Dendron), 7.11 (s, 6H, Ar-*H* Gallate), 7.33 (m, 6H, Ar-*H* Dendron), 7.55 (m, 3H, Ar-*H* Dansyl), 7.63 (m, 6H, Ar-*H* Dansyl), 8.18 (d, 3H, $^3J_{H\text{-}H}$ = 7.3 Hz, Ar-*H* Dansyl), 8.32 (d, 6H, $^3J_{H\text{-}H}$ = 8.8 Hz, Ar-*H* Dansyl), 8.87 (d, 6H, $^3J_{H\text{-}H}$ = 8.5 Hz, Ar-*H* Dansyl).

^{13}C NMR (CD$_3$OD, 125 MHz): δ [ppm] = 25.93, 30.83, 31.43, 32.07, 34.04, 34.27, 34.38, 38.19, 40.70, 40.79, 41.86, 47.52, 59.04, 71.19, 71.31, 71.38, 71.41, 71.80, 71.85, 72.49, 72.80, 78.90, 78.94, 109.83, 119.84, 126.04, 127.29, 127.82, 128.75, 130.62, 130.66, 130.98, 132.86, 135.90, 138.68, 143.16, 143.38, 143.56, 143.58, 153.13, 153.28, 160.00, 160.01, 160.30, 169.02, 169.05, 170.01, 172.33, 174.51.

MS (MALDI-TOF, dithranol): m/z = 7753.58 $[M+Na]^+$ ($C_{372}H_{605}N_{18}O_{144}S_3Na$) calc. molecular weight peak 7753.00.

8.10 Compounds of Chapter 4.4.4

1,3,5-Tris-{4-[3-(benzyloxy)propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy] ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene ***114***



0.730 g (0.694 mmol) **60c** were dissolved in 15 ml dry methylene chloride. The solution was cooled to -20°C and 0.120 g (0.784 mmol) HOBt and 0.160 g (0.862 mmol) EDC were added. The mixture was stirred for one hour at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.068 g (0.189 mmol) **3b** and 1 ml dry triethylamine in 2 ml abs. methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1). The yellowish oil was dissolved in benzene, filtered and lyophilized.

Yield: 0.582 g (92%) of a yellowish oil.

R_f = 0.27 (Silica gel; methylene chloride/ methanol 10:1).

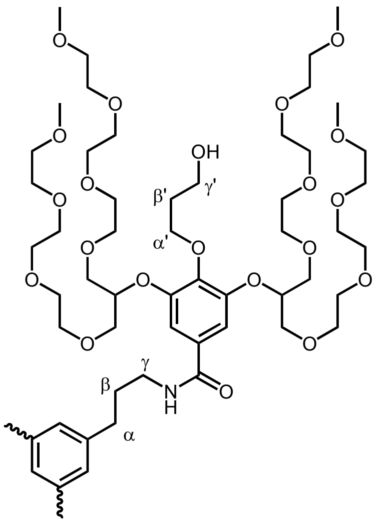
^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.81 (m, 6H, β-CH_2), 1.93 (m, 6H, β'-CH_2), 2.53 (t, 6H, $^3J_{H-H}$ = 7.9 Hz, α-CH_2), 3.23 (s, 36H, -OCH_3), 3.32 (m, 6H, γ-CH_2), 3.35-3.56 (2m, 144H, -OCH_2CH_2O), 3.59 (hidden m, 6H, γ'-CH_2), 3.60 (m, 32H, -OCH(CH_2)$_2$), 4.02 (t, 2H, $^3J_{H-H}$ = 6.2 Hz, α'-CH_2), 4.42 (s, 6H, -CH_2OBn) 4.44 (quint, 6H, $^3J_{H-H}$ = 4.9 Hz, -OC*H*(CH$_2$)$_2$), 6.78 (s, 3H, Ar-*H*: Core), 6.90 (t, 3H, $^3J_{H-H}$ = 5.8 Hz, -N*H*), 7.15 (m, 12H, Ar-*H*: Bn), 7.22 (br s, 9H, Ar-*H*: Bn & Gallate).

^{13}C NMR (CD_2Cl_2, 125 MHz): δ [ppm] = 30.29, 30.87, 32.91, 39.49 (2), 58.51, 67.16, 70.05, 70.07, 70.16, 70.43, 71.49, 72.51, 77.79, 109.44, 125.71, 127.04, 127.10, 127.09, 127.92, 129.29, 138.29, 141.40, 142.66, 151.51, 166.43.

MS (MALDI-TOF, dithranol): m/z = 3385.69 $[M+K]^+$ ($^{12}C_{168}{}^1H_{279}{}^{14}N_6{}^{16}O_{66}{}^{39}K$) calc. monoisotopic peak 3385.84; 3396.79 $[M+Na]^+$ calc. monoisotopic peak

($^{12}C_{168}{}^{1}H_{279}{}^{14}N_{6}{}^{16}O_{66}{}^{23}Na$) 3396.86; 3347.73 [M+K]$^+$ ($^{12}C_{168}{}^{1}H_{280}{}^{14}N_{6}{}^{16}O_{66}$) calc. monoisotopic peak 3347.88.

1,3,5-Tris-{4-(3-hydroxypropoxy)-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy] ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene ***115***



0.335 g (0.1 mmol) **114** were dissolved in 8 ml methanol and 40 mg Pd/ C were added. The reaction was stirred for 24h under a H_2-atmosphere at room temperature. The deprotection was monitored by ^{1}H-NMR. After filtration, the solvent was evaporated and dried under high vacuum. No further purification.

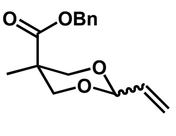
Yield: 0.300 g (97%) of a colorless oil.

^{1}H NMR ($CDCl_3$, 500 MHz): δ [ppm] = 1.82 (m, 12H, β/β‘-CH_2), 2.53 (t, 6H, ${}^3J_{H-H}$ = 7.5 Hz, α-CH_2), 3.20 (m, 3H, -O*H*), 3.25 (s, 36H, -OCH_3), 3.32 (m, 6H, γ-CH_2), 3.36-3.59 (2m, 144H, -OCH_2CH_2O), 3.63 (m, 32H, -OCH(CH_2)$_2$), 3.77 (m, 6H, γ'-CH_2), 4.04 (t, 2H, ${}^3J_{H-H}$ = 5.3 Hz, α'-CH_2), 4.49 (quint, 6H, ${}^3J_{H-H}$ = 4.7 Hz, -OC*H*(CH_2)$_2$), 6.78 (s, 3H, Ar-*H*: Core), 6.87 (t, 3H, ${}^3J_{H-H}$ = 5.2 Hz, -N*H*), 7.14 (s, 6H, Ar-*H*: Gallate).

^{13}C NMR ($CDCl_3$, 125 MHz): δ [ppm] = 30.77, 32.39, 38.82, 39.41, 58.51, 59.45, 69.91, 70.03, 70.13, 70.40, 70.67, 71.46, 77.20, 77.34, 108.63, 125.72, 129.50, 141.34, 142.07, 151.41, 166.39.

MS (MALDI-TOF, CCA): m/z = 3115.42 [M+K]$^+$ ($^{12}C_{147}{}^{1}H_{261}{}^{14}N_{3}{}^{16}O_{63}{}^{39}K$) calc. monoisotopic peak 3115.69; 3099.47 [M+Na]$^+$ calc. monoisotopic peak ($^{12}C_{147}{}^{1}H_{261}{}^{14}N_{3}{}^{16}O_{63}{}^{23}Na$) 3099.72; 3077.51 [M+H]$^+$ ($^{12}C_{147}{}^{1}H_{262}{}^{14}N_{3}{}^{16}O_{63}$) calc. monoisotopic peak 3077.74.

Benzyl 5-methyl-2-vinyl-1,3-dioxane-5-carboxylate ***116a/b***



19.0 g (339 mmol) acrylaldehyde, 50.0 g (222 mmol) **38** and 0.9 g p-TsOH were dissolved in 300 ml toluene and refluxed for 12h with a dean stark-condenser. After cooling the organic phase was washed twice with 100 ml aqueous $NaHCO_3$ and then twice with 100 ml brine. The solvent was dried and evaporated after filtration. The remaining acrylaldehyde was removed under reduced pressure. Further purification by column chromatography (Silica gel; hexane/ ethyl acetate).

Yield: 51.82 g (89%) od a colorless oil (both isomers).

^{1}H NMR (CDCl$_3$, 250 MHz):

116a:

δ [ppm] = 1.50 (s, 3H, -CH_3), 3.96 (s, 4H, -CH_2O), 4.86 (m, 1H, O-C*H*), 5.12 (s, 2H, -CH_2Ar), 5.35 (d, 1H, $^3J_{H\text{-}H}$ = 12.5 Hz, -CH=C*H*H), 4.97 (d, 1H, $^3J_{H\text{-}H}$ = 19.1 Hz, -CH=C*H*H), 5.86 (m, 1H, -C*H*=CH$_2$), 7.35 (m, 5H, Ar-*H*).

116b: 0.96 (s, 3H, -CH_3), 3.50 (d, 2H, $^2J_{H\text{-}H}$ = 15.0 Hz, -CH_2O), 4.54 (d, 2H, $^2J_{H\text{-}H}$ = 15.0 Hz, -CH_2O), 4.90 (d, 1H, $^3J_{H\text{-}H}$ = 7.5 Hz, O-C*H*), 5.21 (s, 2H, -CH_2Ar), 5.27 (d, 1H, $^3J_{H\text{-}H}$ = 11.0 Hz, -CH=C*H*H), 5.45 (d, 1H, $^3J_{H\text{-}H}$ = 16.5 Hz, -CH=C*H*H), 5.83 (m, 1H, -C*H*=CH$_2$), 7.35 (m, 5H, Ar-*H*).

^{13}C NMR (CDCl$_3$, 63 MHz):

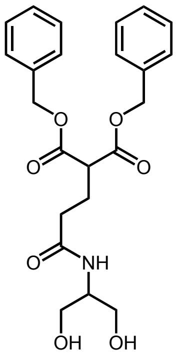
116a:

δ [ppm] = 19.08, 40.78, 66.26, 71.87, 100.64, 118,82, 127.80, 128.24, 128.52, 134.18, 135.53, 173.05.

116b:

δ [ppm] = 17.53, 42.20, 66.26, 72.81, 100.70, 118.56, 127.35, 127.72, 128.20, 134.13, 135.87, 173.53.

Dibenzyl 2-[2-(1,3-dihydroxypropan-2-ylcarbamoyl)ethyl]malonate ***121***



0.165 g (0.46 mmol) **70a** were dissolved in 3 ml dry methylene chloride. 0.1 ml dry triethylamine were added and the mixture was cooled to -20°C. A solution of 0.164 g (0.51 mmol) TBTU in 1 ml dry DMF was added. The mixture was stirred for two hours at -20°C and then allowed to rise to room temperature. The esterification was monitored with TLC.

After complete conversion, the mixture was cooled to -40°C, and a solution of 0.052 g (0.55 mmol) **120** and 0.5 ml dry triethylamine in 1 ml dry methanol was added. The reaction was stirred for one hour at -40°C and then allowed to rise to room temperature. The solvents were evaporated. The crude product was purified by column chromatography (silica gel; methylene chloride/ methanol 30:1 increasing to 10:1).

Yield: 0.174 g (88%) of a yellowish oil.

R_f = 0.19 (Silica gel; methylene chloride/ methanol 10:1).

^{1}H NMR ($CDCl_3$, 250 MHz): δ [ppm] = 2.15 (s, 4H, -C*H*$_2$OH), 3.52 (m, 2H, -NHCOC*H*$_2$), 3.65 (m, 3H, -C*H*$_2$C*H*), 3.80 (br s, 1H, -NHC*H*), 5.15 (s, 4H, -C*H*$_2$Ar), 6.60 (m, 1H, -N*H*), 2.25 (m, 5H, Ar-*H*).

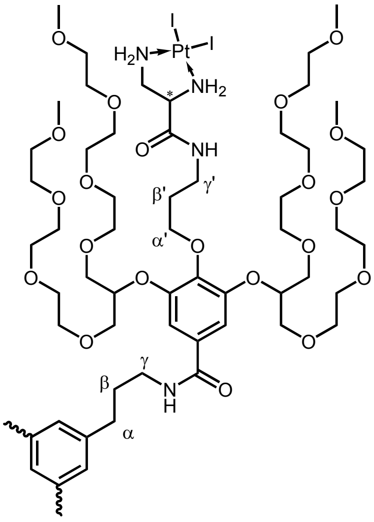
^{13}C NMR ($CDCl_3$, 63 MHz): δ [ppm] = 24.35, 33.24, 50.84, 52.55, 62.28, 67.22, 128.06, 128.30, 128.48, 135.12, 168.84, 172.54.

MS (pos. FAB): m/z (%) = 430.9 (2.49), 429.9 (9.62) $[M+H]^+$, 91.0 (34.47) $[C_7H_7]^+$.

EA	$C_{23}H_{27}NO_7$	calc.	C	64.32	H	6.34	N	3.26,
	(429.46)	found		63.97		6.15		3.07.

8.11 Compounds of Chapter 4.4.5

(1,3,5-Tris-{[3-(2,3-diamino-propionylamido)-propoxy]-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl]}-benzene) platinum(II)-iodide **129**



129 was synthesized by Anja Dullin, who is a member of the cooperating group of Prof. Gust, Institut für Pharmazie, Freie Universität Berlin, Berlin, Germany. The synthetic details can be obtained from her dissertation. The Compound was purified and characterized in the AG Schlüter. Therefore, this data is given here.

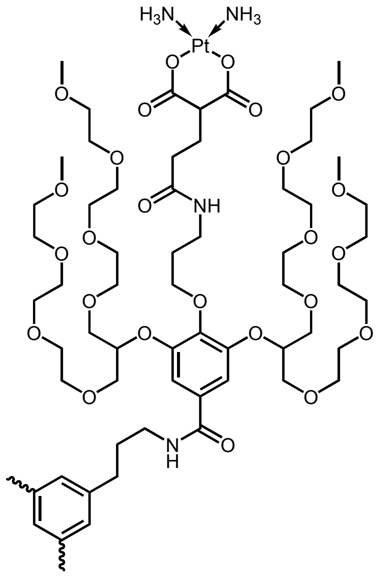
The main fraction was separated by RP-HPLC.

^{1}H NMR The resonances in the proton NMR were too broad for a reasonable assignment. The proton resonances for the methylene protons and the tertiary proton of the ligand shifted from δ = 4.20 ppm and δ = 4.27 ppm to lower field, δ = 4.33 and δ = 4.36 ppm.

^{13}C NMR (CD_3OD & CD_3CN, 125 MHz): δ [ppm] = 30.75, 32.18, 34.08, 38.15, 40.64, 45.60, 55.17, 59.21, 69.55, 70.48, 70.51, 70.98, 71.08, 71.25, 72.30, 78.09, 107.25, 127.22, 131.07, 140.73, 143.15, 153.35, 168.39.

UV-Absorbtion at 204 nm, 222nm.

Diamino-platinum(II)-[*(1,3,5-Tris-({3-[2-(2-carbamoylethyl)malonato]propoxy}-[3,5-bis(1,3-bis{2-[2-(2-methoxyethoxy)ethoxy]ethoxy}propan-2-yloxy)benzamidopropyl])-benzene]* ***130***



0.082 g (170 mmol) **126**, which was synthesized according to Dhara's method, was mixed with an aqueous solution of silver nitrate (1 ml D_2O, 0.058 mg $AgNO_3$) and stirred at 50°C for 15 minutes. The colorless precipitate (AgI) was removed by filtration through a GPC-filter. 0.100g (0.028 mmol) **81** were dissoveld in a solution of 0.008 g NaOH in 2 ml D_2O and the filtrate was added. The reaction was stirred for 24 hours at room temperature and the reaction was monitored by NMR.

A brown precipitate was removed by filtration. No further purification.

Yield: 0.052 g of a brownish oil.

^{1}H NMR The resonances in the proton NMR were too broad for a reasonable assignment. Neither measurements in different solvents (D_20, d^4-methanol, or CD_2Cl_2) nor the variation of other parameters (e.g. dilution conditions) improved the obtained spectra. The proton resonances for the methylene protons of the ligand shifted from δ = 2.05 ppm to lower field, δ = 2.18 and δ = 2.27 ppm.

^{13}C NMR (CD_3OD, 125 MHz): δ [ppm] = 26.97, 31.09, 32.33, 34.30, 37.86, 40.95, 59.14, 71.04, 71.23, 71.29, 71.44, 71.82, 72.51, 72.69, 78.82, 109.84, 127.20, 130.86, 143.23, 143.31, 153.07, 168.07, 175.31, 179.62.